Withdrawal/Redaction Sheet
(George Bush Library)

Doc. No. / Type	Subject/Title	Date	Restriction	Classification
01. Form	Grant Application [redaction] (9 pp.)	n.d.	C	

Collection:

Record Group: Donated Historical Materials
Office:
Series:
Subseries:
WHORM Cat.:
File Location: Disability Pain Management Center (Grant App) [n.d.]

Pinksheet Number: MB10690
OA/ID Number: 52087-007
Date Closed: 8/16/2016
FOIA/Sys Case #: 2016-2624-S
Re-review Case #:
P-2/P-5 Review Case #:

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(George Bush Library)

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Collection:

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Date Closed: 8/16/2016	**OA/ID Number:** 52087-007
FOIA/SYS Case #: 2016-2624-S	**Appeal Case #:**
Re-review Case #:	**Appeal Disposition:**
P-2/P-5 Review Case #:	**Disposition Date:**
AR Case #:	**MR Case #:**
AR Disposition:	**MR Disposition:**
AR Disposition Date:	**MR Disposition Date:**

RESTRICTION CODES

Presidential Records Act - [44 U.S.C. 2204(a)]

P-1 National Security Classified Information [(a)(1) of the PRA]
P-2 Relating to the appointment to Federal office [(a)(2) of the PRA]
P-3 Release would violate a Federal statute [(a)(3) of the PRA]
P-4 Release would disclose trade secrets or confidential commercial or financial information [(a)(4) of the PRA]
P-5 Release would disclose confidential advice between the President and his advisors, or between such advisors [a)(5) of the PRA]
P-6 Release would constitute a clearly unwarranted invasion of personal privacy [(a)(6) of the PRA]

C. Closed in accordance with restrictions contained in donor's deed of gift.

PRM. Removed as a personal record misfile.

Freedom of Information Act - [5 U.S.C. 552(b)]

(b)(1) National security classified information [(b)(1) of the FOIA]
(b)(2) Release would disclose internal personnel rules and practices of an agency [(b)(2) of the FOIA]
(b)(3) Release would violate a Federal statute [(b)(3) of the FOIA]
(b)(4) Release would disclose trade secrets or confidential or financial information [(b)(4) of the FOIA]
(b)(6) Release would constitute a clearly unwarranted invasion of personal privacy [(b)(6) of the FOIA]
(b)(7) Release would disclose information compiled for law enforcement purposes [(b)(7) of the FOIA]
(b)(8) Release would disclose information concerning the regulation of financial institutions [(b)(8) of the FOIA]
(b)(9) Release would disclose geological or geophysical information

AA

Form Approved Through 6/30/94
OMB No. 0925-0001

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE

GRANT APPLICATION

Follow instructions carefully. Type in the unshaded areas only. Type density must be 10 c.p.i.

LEAVE BLANK FOR PHS USE ONLY			
Type	Activity	Number	
Review Group		Formerly	
Council/Board (Month, Year)		Date Received	

1. TITLE OF PROJECT (Do not exceed 56 typewriter spaces)
Disability and Pain Management Center (DPMC)

2a. RESPONSE TO SPECIFIC REQUEST FOR APPLICATIONS OR PROGRAM ANNOUNCEMENT ☒ NO ☐ YES (If "YES," state number and title)
Number: Title:

2b. TYPE OF GRANT PROGRAM: P01

3. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR

3a. NAME (Last, first, middle)
Grabois, Martin

3b. DEGREE(S)
BS MD

3c. SOCIAL SECURITY NO.
(C)

3d. POSITION TITLE
Professor and Chairman

3e. MAILING ADDRESS (Street, city, state, zip code)
Department of Physical Medicine
& Rehabilitation
Baylor College of Medicine
One Baylor Plaza
Houston, Texas 77030

3f. DEPARTMENT, SERVICE, LABORATORY, OR EQUIVALENT
Physical Medicine & Rehabilita

3g. MAJOR SUBDIVISION

3h. TELEPHONE AND FAX (Area code, number and extension)
TEL: (713) 799-5086
FAX: (713) 799-5058

BITNET/INTERNET ADDRESS

4. HUMAN SUBJECTS — 4a. NO [X] YES [ ] — If Yes, exemption no. or IRB approval date: Pending — 4b. Assurance of compliance no.:

5. VERTEBRATE ANIMALS — 5a. NO [ ] YES [X] — If Yes, IACUC approval date: 05/15/95 — 5b. Animal welfare assurance no.: AN-1200

6. DATES OF ENTIRE PROPOSED PROJECT PERIOD		7. COSTS REQUESTED FOR INITIAL BUDGET PERIOD		8. COSTS REQUESTED FOR ENTIRE PROPOSED PROJECT PERIOD	
From (MMDDYY)	Through (MMDDYY)	7a. Direct Costs ($)	7b. Total Costs ($)	8a. Direct Costs ($)	8b. Total Costs ($)
4/1/96	3/31/01	$504,456	$659,580	$2,507,624	

9. PERFORMANCE SITES (Organizations and addresses)
Baylor College of Medicine
One Baylor Plaza, Houston, TX

TIRR
1333 Moursund Ave, Houston, TX

Houston VA Medical Center
2002 Holcombe Blvd, Houston

10. INVENTIONS AND PATENTS (Competing continuation application only)
[X] NO [ ] YES — If "YES," [ ] Previously reported [ ] Not previously reported

11. NAME OF APPLICANT ORGANIZATION
Baylor College of Medicine
ADDRESS: One Baylor Plaza
Houston, Texas 77030

12. TYPE OF ORGANIZATION
☐ Public: Specify ☐ Federal ☐ State ☐ Local
XX Private Nonprofit
☐ Forprofit (General) ☐ Forprofit (Small Business)

13. ENTITY IDENTIFICATION NUMBER: 74-1613878
Congressional District: 25

14. BIOMEDICAL RESEARCH SUPPORT GRANT CREDIT
Code: Cl Identification: School of Medicine

15. NAME OF ADMINISTRATIVE OFFICIAL TO BE NOTIFIED IF AWARD IS MADE
Thomas Wilson
TELEPHONE: (713) 798-6970
FAX: (713) 798-6990
TITLE: Director of Sponsored Programs
ADDRESS: Baylor College of Medicine
One Baylor Plaza
Houston, Texas 77030
BITNET/INTERNET ADDRESS:

16. NAME OF OFFICIAL SIGNING FOR APPLICANT ORGANIZATION
Thomas Wilson
TELEPHONE: (713) 798-6970
FAX: (713) 798-6990
TITLE: Director of Sponsored Programs
ADDRESS: Baylor College of Medicine
One Baylor Plaza
Houston, Texas 77030
BITNET/INTERNET ADDRESS:

17. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR ASSURANCE: I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application. Willful provision of false information is a criminal offense (U.S. Code, Title 18, Section 1001). I am aware that any false, fictitious, or fraudulent statement may, in addition to other remedies available to the Government, subject me to civil penalties under the Program Fraud Civil Remedies Act of 1986 (45 CFR 79).

SIGNATURE OF PERSON NAMED IN 3a. (In ink. "Per" signature not acceptable.) Martin Grabois MD — DATE

18. CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true and complete to the best of my knowledge, and accept the obligation to comply with Public Health Service terms and conditions if a grant is awarded as the result of this application. A willfully false certification is a criminal offense (U.S. Code, Title 18, Section 1001). I am aware that any false, fictitious, or fraudulent statement may, in addition to other remedies available to the Government, subject me to civil penalties under the Program Fraud Civil Remedies Act of 1986 (45 CFR 79).

SIGNATURE OF PERSON NAMED IN 16. (In ink. "Per" signature not acceptable.)
Bush Library Photocopy — DATE

DESCRIPTION: State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project. Describe concisely the research design and methods for achieving these goals. Avoid summaries of past accomplishments and the use of the first person. This abstract is meant to serve as a succinct and accurate description of the proposed work when separated from the application. **DO NOT EXCEED THE SPACE PROVIDED.**

Disability and Pain Management Center. The proposed Disability and Pain Management Center (DPMC) was developed to establish an organizational infrastructure to support long-term multidisciplinary approaches to the management of chronic pain in people with disabilities. The proposed program draws upon the resources of one of the largest academic Physical Medicine and Rehabilitation Deparments in the country, located at Baylor College of Medicine in Houston, Texas, to explore current and emerging aprroaches for treating pain in persons with permanent physical disabilities. The specific aims of the DPMC are to: (1) create an administrative structure that provides for effective oversight for a multidisciplinary, interinstitutional research program on chronic pain and disability; (2) implement research projects targeting promising approaches for alleviating pain in persons with different types of disability; (3) establish a research subject pool and database on chronic pain in a mixed disability population that can serve as a resource for future research on current and experimental approaches to chronic pain management in persons with different types of disabilities; (4) develop outcome measures that allow for comparisons of important therapeutic outcome indicators across disability populations; (5) provide mentoring and support required to foster development of research expertise in junior faculty who can contribute to research on chronic pain and disability; and (6) disseminate the results of research efforts and other important activities of the DPMC to various target audiences, including other clinical and basic science professionals, people with disabilities and family members, and policy makers and others who influence programmatic development related to disability services. The DPMC will be comprised initially of three research projects--(1) A Placebo-controlled Trial of Tetrahydrocannabinol in Treatment of Neurogenic Pain Due to Spinal cord Injury; (2) The Effect of Magnetic Fields on Chronic Pain Due to Overuse in People with Disabilities; and (3) Peripheral Nerve Stimulation in Amputees with Neuropathic Pain. A fourth research project, Testing the Efficacy of a Pain Clinic for Management of Disability-Related Pain, will be initiated in the third year of funding, following two years of preliminary studies to establish baseline data on a demographically mixed group of individuals with physical disabilities who have chronic pain. Also, two cores--an administrative core (Core A) and an outcome measures core (Core B) will be implemented to support all research and related activities.

PERSONNEL ENGAGED ON PROJECT, INCLUDING CONSULTANTS/COLLABORATORS. *Use continuation pages as needed* to provide the required information in the format shown below on *all* individuals participating in the project.

Name Grabois, Martin Degrees(s) M.D. Social Security No. (C)
Position Title Professor and Chairman Date of Birth (MM/DD/YY) (C) Role on Project Principal Investigator
Organization Baylor College of Medicine Department Physical Medicine & Rehab.

Name Strayer, Jonathan Degrees(s) M.D. Social Security No. (C)
Position Title Assistant Professor Date of Birth (MM/DD/YY) (C) Role on Project Project Director
Organization Baylor College of Medicine Department Physical Medicine & Rehab.

Name Hazlewood, Carlton Degrees(s) Ph.D. Social Security No. (C)
Position Title Associate Professor Date of Birth (MM/DD/YY) (C) Role on Project Project Director
Organization Baylor College of Medicine Department Physical Medicine & Rehab.

Name Simpson, Richard K., Jr. Degrees(s) M.D., Ph.D. Social Security No. (C)
Position Title Chief, Neurological Service Date of Birth (MM/DD/YY) (C) Role on Project Project Director
Organization VAMC Houston, Baylor College of Medicine Department Neurosurgery

Name Nosek, Margaret Degrees(s) Ph.D. Social Security No. (C)
Position Title Associate Professor Date of Birth (MM/DD/YY) (C) Role on Project Core Director
Organization Baylor College of Medicine Department Physical Medicine & Rehab.

COMPOSITE DPMC FIRST-YEAR BUDGET
DETAILED BUDGET FOR INITIAL BUDGET PERIOD
DIRECT COSTS ONLY

FROM 04/01/96 THROUGH 03/31/97

PERSONNEL (Applicant organization only) NAME	ROLE ON PROJECT	TYPE APPT. (months)	% EFFORT ON PROJ.	INST. BASE SALARY	DOLLAR AMOUNT REQUESTED (Omit cents) SALARY REQUESTED	FRINGE BENEFITS	TOTALS
Project 1, J. Strayer Personnel Request	Principal Investigator				49,000	10,589	59,589
Project 2, C. Hazlewood Personnel Request	Principal Investigator				71,785	19,830	91,615
Project 3, R. Simpson Personnel Request	Principal Investigator				42,620	11,934	54,554
Project 4, M. Grabois Personnel Request	Principal Investigator				0	0	0
Core A, M. Grabois Personnel Request	Core Director				26,900	5,714	32,614
Core B, M. Nosek Personnel Request	Core Director				51,806	14,618	66,424
SUBTOTALS----------					242,111	62,685	304,796

CONSULTANT COSTS	Project 1 = $0; Project 2 = $4,460; Project 3 = $0; Project 4 = $0 Core A = $6,550; Core B = $0	11,010
EQUIPMENT (Itemize)	Project 1 = $0; Project 2 = $24,035; Project 3 = $43,595; Project 4 = $0 Core A = $0; Core B = $3,200	70,830
SUPPLIES (Itemize by category)	Project 1 = $30,815; Project 2 = $10,030; Project 3 = $32,160; Project 4 = $0; Core A = $1,200; Core B = $2,400	76,605
TRAVEL	Project 1 = $2,400; Project 2 = $5250; Project 3 = $1,200; Project 4 = $0 Core A = $1,200; Core B = $4,140	14,190
PATIENT CARE COSTS	INPATIENT	0
	OUTPATIENT Project 1 = $5,875	5,875
ALTERATIONS AND RENOVATIONS (Itemize by category)		0
OTHER EXPENSE (Itemize by category)	Project 1 = $7,500; Project 2 = $2,500; Project 3 = $1,000; Project 4 = $0; Core A = $1,000; Core B = $9,150	21,150
SUBTOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD		504,456
CONSORTIUM/CONTRACTUAL COSTS DIRECT COSTS / INDIRECT COSTS	TOTAL------	0
TOTAL DIRECT COSTS FOR FIFTH BUDGET PERIOD	(Item 7a, Face Page)--------	$ 504,456

COMPOSITE BUDGET FOR ENTIRE PROPOSED BUDGET PERIOD DIRECT COSTS ONLY

BUDGET CATEGORY TOTALS		INITIAL BUDGET PERIOD (from page 4)	ADDITIONAL YEARS OF SUPPORT REQUESTED 2nd	3rd	4th	5th
PERSONNEL (Salary and fringe benefits) (Applicant organization only)		304,796	313,528	372,497	386,676	400,487
CONSULTANT COSTS		11,010	15,550	15,550	14,550	11,550
EQUIPMENT		70,830	23,570	18,000	0	0
SUPPLIES		76,605	79,775	52,400	51,700	52,200
TRAVEL		14,190	15,440	14,240	13,740	12,740
PATIENT CARE COSTS	INPATIENT	0	0	0	0	0
	OUTPATIENT	5,875	5,875	20,000	22,000	24,000
ALTERATIONS AND RENOVATIONS		0	0	0	0	0
OTHER EXPENSES		21,150	21,650	15,150	15,150	15,150
SUBTOTAL DIRECT COSTS		504,456	475,388	507,837	503,816	516,127
CONSORTIUM/ CONTRACTUAL COSTS		0	0	0	0	0
TOTAL DIRECT COSTS		504,456	475,388	507,837	503,816	516,127

TOTAL DIRECT COSTS FOR ENTIRE PROPOSED PROJECT PERIOD (Item 8a)--------> $2,507,624

JUSTIFICATION (Use continuation pages if necessary):

See individual research project and core budgets for justifications of expenses.

DD Principal Investigator/Program Director (Last, first,middle): Grabois, Martin, M.D.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD
DIRECT COSTS ONLY

FROM 04/01/96 THROUGH 03/31/97

PERSONNEL (Applicant organization only) NAME	ROLE ON PROJECT	TYPE APPT. (months)	% EFFORT ON PROJ.	INST. BASE SALARY	DOLLAR AMOUNT REQUESTED (Omit cents) SALARY REQUESTED	FRINGE BENEFITS	TOTALS
Jonathan Strayer, M.D.	Principal Investigator	12	20.00%	110,000	22,000	4,682	26,682
Michael Priebe, M.D.	Co-Principal Investigator	12	10.00%	115,000	0	0	0
Jay Rosenfeld, M.D.	Co-Investigator	12	10.00%	110,000	11,000	2,341	13,341
To Be Named	Research Associate	12	40.00%	30,000	16,000	3,566	19,566
SUBTOTALS----------					49,000	10,589	59,589

CONSULTANT COSTS		0
EQUIPMENT (Itemize)		0
SUPPLIES (Itemize by category) Phase I THC medication at $546 per patient (25 patients) = $13,650 Phase II THC medication at $2,778 per patient (5 patients) = $13,890 Placebo @ $81 per patient (25 patients) = $2,025 Pharmacist placebo prep Time @ $50 per patient (25 patients) = $1,250		30,815
TRAVEL One trip by PI and Co-PI to present research findings @ $1,200 each		2,400
PATIENT CARE COSTS	INPATIENT	0
	OUTPATIENT Screening of potential participants = $3,750	0
	Phase i Pain and functional evaluations ($625 & $250)	
	Phase II Pain and functional evaluations ($750 & $500)	5,875
ALTERATIONS AND RENOVATIONS (Itemize by category)		0
OTHER EXPENSE (Itemize by category) Publication Costs = $1,000 Recruitment Activities = $1,000; Subject transportation = $2,500 Tranportation for individuals to be screened for participation = $3000		7,500
SUBTOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD		106,179
CONSORTIUM/CONTRACTUAL COSTS DIRECT COSTS INDIRECT COSTS	TOTAL-------	0
TOTAL DIRECT COSTS FOR FIFTH BUDGET PERIOD (Item 7a, Face Page)--------	$	106,179

BUDGET FOR ENTIRE PROPOSED BUDGET PERIOD
DIRECT COSTS ONLY

BUDGET CATEGORY TOTALS	INITIAL BUDGET PERIOD (from page 4)	ADDITIONAL YEARS OF SUPPORT REQUESTED 2nd	3rd	4th	5th
PERSONNEL (Salary and fringe benefits) (Applicant organization only)	59,589	61,973	0	0	0
CONSULTANT COSTS	0	0	0	0	0
EQUIPMENT	0	0	0	0	0
SUPPLIES	30,815	30,815	0	0	0
TRAVEL	2,400	2,400	0	0	0
PATIENT CARE COSTS INPATIENT	0	0	0	0	0
PATIENT CARE COSTS OUTPATIENT	5,875	5,875	0	0	0
ALTERATIONS AND RENOVATIONS	0	0	0	0	0
OTHER EXPENSES	7,500	7,500	0	0	0
SUBTOTAL DIRECT COSTS	106,179	108,563	0	0	0
CONSORTIUM/ CONTRACTUAL COSTS	0	0	0	0	0
TOTAL DIRECT COSTS	106,179	108,563	0	0	0

TOTAL DIRECT COSTS FOR ENTIRE PROPOSED PROJECT PERIOD (Item 8a)--------> $214,742

JUSTIFICATION (Use continuation pages if necessary):

Personnel

Jonathan Strayer, M.D., will serve as principal investigator on the project with overalll responsibility for project planning and implementation, including subject recruitment and evaluation of potential participants, provision of clinical services, data collection and analyses, and interpretation of the results. Plans call for evaluation of 150 to 200 individuals in order to identofy 25 intervention and 25 control subjects for the study each year. Dr. Strayer will devote 20% time and effort to this project.

Michael Priebe, M.D., will serve as co-principal investigator and will assist with all phases of project activity, including provision of clinical services, collection of data, and follow-up of patients. He will devote 10% time and effort to the project. As a full-time VA physician, he will draw no salary support from grant sources.

Jay Rosenfeld, M.D., will serve as co-investigator. He will assist Drs. Strayer and Priebe with participant evaluation, data collection, and interpretation of the findings. He will devote 10% time and effort to the project.

A research associate will be responsible for scheduling of patients, follow-up with study subjects, collection and entry of clinical data, drafting of reports and other documents, and other support for the project. This individual will devote 40% time and effort to the project.

Supplies

Supplies requested are for drug (THC) and placebo needed in the first year for 25 intervention and 25 control subjects. Amounts requested reflect current costs for the drug and placebo, including preparation time for assuring similarity in appearance.

Travel

Funds are requested for travel by the PI and Co-PI to a professional meeting to present on the research. These costs are estimated at $850 discounted roundtrip airfare, $50 for ground transportation and parking/mileage, $110 per night for two nights lodging, and $40 per day for two days meals.

Patient Care Costs

Patient care costs reflect the estimated amounts required for evaluation of potential subjects and people selected for the study. Since the evaluation is being done for research purposes, these costs will not be borne by the VA or by other third-party payers. Initial screening evaluations of up to 100 people per year are expected to cost $25 per person. Thereafter, costs for study subjects are estimated at $35 per person for phase I and $50 per person for phase II of the study.

Other Expenses

Other expenses include the cost of publications (e.g., graphics, photography), recruitment costs (e.g., newspaper advertisements, radio announcements), and transportation for potential subjects estimatedat $20 per person for up to 100 individuals and $100 per person for the 25 selected for follow-up.

Year-Two Costs

Year two costs refelect a projected 4% increase in salaries. Otherwise, year two costs are expected to be similar to those incurred in year one. In year two an additional 25 intervention and 25 control subjects will be selected and evaluated. This study will be completed in year two.

DD | Principal Investigator/Program Director (Last, first,middle): | Grabois, Martin, M.D.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD
DIRECT COSTS ONLY

FROM 04/01/96 THROUGH 03/31/97

PERSONNEL (Applicant organization only) NAME	ROLE ON PROJECT	TYPE APPT. (months)	% EFFORT ON PROJ.	INST. BASE SALARY	DOLLAR AMOUNT REQUESTED (Omit cents) SALARY REQUESTED	FRINGE BENEFITS	TOTALS
Carlton Hazlewood, Ph.D.	Principal Investigator	12	10.00%	82,360	8,236	2,028	10,264
Carlos Vallbona, M.D.	Co-Principal Investigator	12	5.00%	190,000	0	0	0
Hallie Hartmann, Ph.D.	Co-Investigator	12	50.00%	40,098	20,049	5,386	25,435
Vladimir Slesarev, Ph.D.	Post-Doctoral Associate	12	50.00%	30,000	15,000	4,457	19,457
Gabor Jurida, M.D.	Post-Doctoral Associate	12	50.00%	30,000	15,000	4,457	19,457
To Be Named	Phys. Asst./ Nurse Pract.	12	30.00%	45,000	13,500	3,502	17,002
SUBTOTALS----------					71,785	19,830	91,615

CONSULTANT COSTS — Jan Post, Ph.D., UT Medical Branch, Galveston = $1,000; Wendall Winters, Ph.D., UT Health Science Center, San Antonio = $3,460 — 4,460

EQUIPMENT (Itemize) — Magnetic Field Sensor = $3,030; Amplifier = $3,350; Interface = $2,195; Manipulators (R&L) = $2,460; Microscope = $13,000 — 24,035

SUPPLIES (Itemize by category)
Animals (delivery and care) = $1,870
Molecular Biology Supplies = $1,870
Chemicals = $1,000
NMR = $1,690
Electrophysiological Supplies $1,700
Plasticware, glassware, disposables = $1,400
Magnets = $500
10,030

TRAVEL Two trips per month to analyze samples at $30 per trip (25 trips) = $750
Two investigators to present at national meetings at $1,200 each = $2,400
Six trips to San Antonio to conduct experiments @ $350 per trip = $2,100 — 5,250

PATIENT CARE COSTS — INPATIENT 0; OUTPATIENT 0

ALTERATIONS AND RENOVATIONS (Itemize by category) — 0

OTHER EXPENSE (Itemize by category) Publication Costs = $1,000
Equipment maintenance & pro-rated repair agreements = $1,500 — 2,500

SUBTOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD — 137,890

CONSORTIUM/CONTRACTUAL COSTS
DIRECT COSTS
INDIRECT COSTS
TOTAL------- 0

TOTAL DIRECT COSTS FOR FIFTH BUDGET PERIOD (Item 7a, Face Page)-------- $ 137,890

BUDGET FOR ENTIRE PROPOSED BUDGET PERIOD
DIRECT COSTS ONLY

BUDGET CATEGORY TOTALS	INITIAL BUDGET PERIOD (from page 4)	ADDITIONAL YEARS OF SUPPORT REQUESTED 2nd	3rd	4th	5th
PERSONNEL (Salary and fringe benefits) (Applicant organization only)	91,615	95,280	99,091	103,054	107,177
CONSULTANT COSTS	4,460	9,000	9,000	8,000	5,000
EQUIPMENT	24,035	23,570	18,000	0	0
SUPPLIES	10,030	12,000	12,500	13,000	13,500
TRAVEL	5,250	6,500	6,500	6,000	5,000
PATIENT CARE COSTS INPATIENT	0	0	0	0	0
PATIENT CARE COSTS OUTPATIENT	0	0	0	0	0
ALTERATIONS AND RENOVATIONS	0	0	0	0	0
OTHER EXPENSES	2,500	3,000	3,000	3,000	3,000
SUBTOTAL DIRECT COSTS	137,890	149,350	148,091	133,054	133,677
CONSORTIUM/ CONTRACTUAL COSTS	0	0	0	0	0
TOTAL DIRECT COSTS	137,890	149,350	148,091	133,054	133,677
TOTAL DIRECT COSTS FOR ENTIRE PROPOSED PROJECT PERIOD (Item 8a)------->					$702,061

JUSTIFICATION (Use continuation pages if necessary):

A. PERSONNEL:

1. Principle Investigator, Dr. Carlton F. Hazlewood, Ph.D., will oversee the conduction of the study with Dr. Carlos Vallbona. Biweekly meetings with Drs. Vallbona and Hartmann will be held to discuss the progress of the project and to identify any problems that may arise. Dr. Hazlewood will be actively involved in all the magneto therapy studies as well as participating in the electrophysiological studies addressing the Basic Science experiments.

2. Co-Principle Investigator, Carlos Vallbona, M.D., will oversee the conduction of the study with Dr. Hazlewood. In particular, Dr. Vallbona will advise and direct the Clinical studies. All problems arising in the Clinical studies will be addressed by Dr. Vallbona.

3. Co-Investigator, Dr. Hali A. Hartmann, Ph.D., will devote 50% of her time to this project. Her remaining salary support will come from institutional sources. Dr. Hartmann's effort in these studies will be focused on performing the molecular biology and electrophysiological experiments. The routine molecular biology experiments are quite minimal and consist of preparing DNA stocks and the *in vitro* synthesis of the cRNA of the ion channels. Dr. Hartmann will supervise the tissue culture experiments of the mammalian cell line, HEK-293 cells. Dr. Hartmann's main efforts on this project will involve the whole cell and single channel electrophysiological experiments of the voltage-gated ion channels. These experiments will be performed at Baylor College of Medicine in the Department of Molecular Physiology and Biophysics and at the University of Texas Health Sciences Center at San Antonio, in Dr. Wendall Winters laboratory.

4. Dr. Vladimir Slesarev, M.D., Ph.D., a Post-Doctoral Fellow, will perform the Magnetic Resonance Imaging experiments at the laboratory of Dr. Jan M.F. Post at University of Texas Medical Branch at Galveston, Texas. Dr. Slesarev has over eight years experience in NM and MR imaging of human tissue. It is anticipated that Dr. Slesarev will make two trips every month to UTMB to perform experiments with magnetite, iron oxides, and Dextran PM 40000 in the *Xenopus* oocytes. Oocytes will be easily transported to the MRI laboratory as the eggs remain stable at room temperature for greater than 24 hours.

5. Dr. Gabor Jurida, M.D., also a Post-Doctoral Fellow, will be assisting Drs. Hazlewood and Vallbona in the Post-Polio Pain Clinic. Dr. Jurida's responsibility will entail the organization of the various field-strength magnets and the placebo magnets. He will manage the patients during clinic visits for the placement and removal of the magnets.

6. Physician Assistant or Nurse Assistant: To be named. The responsibilities of this position include recording keeping of Drs. Hazlewood and Vallbona patients in the Post-Polio Pain Clinic.

7. Jan F.M. Post, Ph.D., will serve as a consultant to the Magnetic Resonance Imaging phase of the basic sciences section. Dr. Post will supervise Dr. Slesarev in the oocyte imaging experiments with magnetite and the ion channels. His facilities at UTMB are available on a basis of need and availability with a consulting/service fee of $1,000.00 per year.

8. Wendall D. Winters, Ph.D., will serve as a consultant to the electrophysiological experiments performed in one of the few available magnetically-shielded rooms in the United States. Dr. Winters has agreed to offer his expertise in magnetic field effects. His estimated costs which are being negotiated are $5,000 per 6 months for the usage of his magnetic field exposure facility at UT Health Sciences in San Antonio. His consultant fees have been estimated at $1,800.00 per day.

B. MAJOR EQUIPMENT:

In the first year of the outlined research, equipment is needed for both clinical and basic sciences. The magnetometer **(item #1)** is requested for the clinical studies and a whole-cell electrophysiological setup **(items #3,4,6, and 7)** for the basic science experiments. The effects of magnetic fields on whole-cell currents will be studied during the first year. In year 02, single-channel experiments will be phased in the basic science experiments **(items #2 and 5)**. Also during year 02, a static magnetic field generator is requested for the clinic **(item #8)**. In year 03, the pulsed magnetic field generator **(item #9)** will be necessary, and the funds are requested in the third-year budget for the purchase of this equipment.

1. **Magnetic Field Sensor: Bartington Fluxgate magnetometer, Model MAG-03** **$3,030.00**
   It is essential that magnetic field output of all magnet and electromagnetic devices be monitored. This sensor will be used also to monitor the magnetic fields (in space and time) in patient rooms and laboratories where the experiments are conducted.

2. **Patch-clamp amplifier: Axopatch-1D** **7,500.00**
   An Axopatch -1D patch-clamp amplifier is requested for the single channel recording experiments. Its circuitry has been optimized for a low signal\noise ratio: RMS pf 0.2 pA.

3. Two-electrode oocyte clamp amplifier:Warner OC-725B **3,350.00**
A whole-cell amplifier is requested for this project. The Warner amplifier is a standard oocyte clamp amplifier that has been used for most of Co-investigator, Dr.Hartmann's, projects with oocytes.

4. Axon Digital Interface w/ Labmaster DMA board: **2,195.00**
This is a basic model for A\D and D\A interfacing. It allows one to store data on the hard disk for off-line analysis.

5. Narashige Manipulator for patch-clamp setup- MX-2 XYZ with tilt stand: **6,070.00**
This manipulator is suited for the single-channel experiments. These funds are for the accompanying separate parts and include: MZ-9 ball mounted single axis manipulator, a NS-Y mounting plate, a M-35 course positioner, and a MN-35 fine movement micromanipulator.

6. Narashige manipulators MMM-333 (XYZ right and left): **2,460.00**
These manipulators are necessary for proper placement of the current and voltage recording microelectrodes.

7. Inverted Nikon Microscope, Diaphot 300: **13,000.00**
The Diaphot 300 is a basic model with good optics. This package includes the ocular, condenser, lamp house, and lenses. This model can be easily upgraded later for imaging and patch-clamp studies.

8. Static Electromagnetic Field Generator, Joules Electric: **10,000.00**
Static electromagnetic fields have been shown to be effective in relieving generalized pain. This pain reduction results from applying the static field to the forearm. Simply, the arm is placed in a shielded coil and the magnetic field exposure is approximately 800 gauss. The original device was constructed and tested on cells and tissues. Subsequent models were scaled up for human studies and evaluated in Mexico on protocols approved by their health ministry. We will have a similar model machine constructed.

9. Pulsed Electromagnetic Generator, Model Sof-Pulse 912: **18,000.00**
Pulsed electromagnetic fields will be produced by a generator from Electro-pharmacology, Inc. We are negotiating a 3 year payback arrangement. This instrument is essential for the pulsed electromagnetic studies outlined in our proposal.

C. TRAVEL:

Funds requested for travel in this proposal are from three phases. 1) Travel funds for each of three investigators are requested for presentations at yearly meetings. 2) Funds are requested for the NMR micro-imaging aims in the basic science section. Dr. Slerasev will travel to Galveston approximately twice each month for experiments in Dr. Post's laboratory. 3) Also outlined in the basic science section are the electrophysiological experiments to be performed in Dr. Winter's magnetically-shielded room at University of Texas Health Sciences Center in San Antonio. Funds are requested for Dr. Hartmann and either Dr.

Hazlewood or Dr. Slesarev for travel and room expenses for two days in San Antonio. The electrophysiology experiments will increase throughout the five year project, thus, progressively increasing funds are requested in both Travel and Consultant categories.

1. UTMB at Galveston NMR Facilities: The current milage basis is 0.30 per mile. A round trip to Galveston (100 miles) is $30.00. Two trips per month are estimated to be necessary to proceed with the magnetic resonance imaging project.

2. UT Health Sciences Center at San Antonio: A round trip to San Antonio (250 miles) is $150.00. Lodging for two persons for two nights is estimated at $200.00. During the first year, it is estimated at least six trips will be needed with increasing use of the facilities through year four.

DD | Principal Investigator/Program Director (Last, first,middle): Grabois, Martin, M.D.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD
DIRECT COSTS ONLY

FROM 04/01/96 THROUGH 03/31/97

PERSONNEL (Applicant organization only) NAME	ROLE ON PROJECT	TYPE APPT. (months)	% EFFORT ON PROJ.	INST. BASE SALARY	DOLLAR AMOUNT REQUESTED (Omit cents) SALARY REQUESTED	FRINGE BENEFITS	TOTALS
Richard K. Simpson, Jr., M.D	Principal Investigator	12	25.00%	0	0	0	0
To Be Named	Research Nurse	12	100.00%	42,620	42,620	11,934	54,554
SUBTOTALS----------					42,620	11,934	54,554

CONSULTANT COSTS		0
EQUIPMENT (Itemize)	Nicolet Viking IV	43,595
SUPPLIES (Itemize by category)	Trial Electrodes (#24 each at $1,340)	32,160
TRAVEL One trip by PI to present on research results		1,200
PATIENT CARE COSTS	INPATIENT	0
	OUTPATIENT	0
ALTERATIONS AND RENOVATIONS (Itemize by category)		0
OTHER EXPENSE (Itemize by category)	Publication Costs	1,000
SUBTOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD		132,509
CONSORTIUM/CONTRACTUAL COSTS DIRECT COSTS	TOTAL------	0
INDIRECT COSTS		
TOTAL DIRECT COSTS FOR FIFTH BUDGET PERIOD (Item 7a, Face Page)--------	$	132,509

BUDGET FOR ENTIRE PROPOSED BUDGET PERIOD
DIRECT COSTS ONLY

BUDGET CATEGORY TOTALS	INITIAL BUDGET PERIOD (from page 4)	ADDITIONAL YEARS OF SUPPORT REQUESTED 2nd	3rd	4th	5th
PERSONNEL (Salary and fringe benefits) (Applicant organization only)	54,554	56,736	59,006	61,366	63,820
CONSULTANT COSTS	0	0	0	0	0
EQUIPMENT	43,595	0	0	0	0
SUPPLIES	32,160	32,160	32,160	32,160	32,160
TRAVEL	1,200	1,200	1,200	1,200	1,200
PATIENT CARE COSTS INPATIENT	0	0	0	0	0
PATIENT CARE COSTS OUTPATIENT	0	0	0	0	0
ALTERATIONS AND RENOVATIONS	0	0	0	0	0
OTHER EXPENSES	1,000	1,000	1,000	1,000	1,000
SUBTOTAL DIRECT COSTS	132,509	91,096	93,366	95,726	98,180
CONSORTIUM/ CONTRACTUAL COSTS	0	0	0	0	0
TOTAL DIRECT COSTS	132,509	91,096	93,366	95,726	98,180

TOTAL DIRECT COSTS FOR ENTIRE PROPOSED PROJECT PERIOD (Item 8a)-------> $510,877

JUSTIFICATION (Use continuation pages if necessary):

Personnel. Dr. Simpson will direct all aspects of the research. He will devote 25% time and effort to the project. However, as a full-time VA physician, no salary support is requested from grant sources.

The research nurse will perform day-to-day research activities, including patient services, data collection and analyses, and follow-up on the project. This person will devote 100% time and effort to the research.

Equipment. The Nicolet Viking IV is essential for simulataneous nerve stimulation and evoked potential monitoring using multiple channels. This equipment is not currently available at the VA, and moving the study out of the VA would drive costs up substantially beyond the incremental cost of this equipment.

Supplies. The Medtronic On-point electrode is the only FDA approved direct peripheral nerve stimulating electrode for such trials. The cost request is based on actual charges for these electrodes.

Travel and Other. The PI will make one trip to present on the research, and publication charges are based on previous costs for preparation of similar materials for publication.

DD Principal Investigator/Program Director (Last, first,middle): Grabois, Martin, M.D.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD
DIRECT COSTS ONLY

FROM 04/01/96 THROUGH 03/31/97

PERSONNEL (Applicant organization only) NAME	ROLE ON PROJECT	TYPE APPT. (months)	% EFFORT ON PROJ.	INST. BASE SALARY	DOLLAR AMOUNT REQUESTED (Omit cents) SALARY REQUESTED	FRINGE BENEFITS	TOTALS
Martin Grabois, M.D.	Principal Investigator	12	10.00%	190,000	0	0	0
John Strayer, M.D.	Co-Investigator	12	10.00%	110,000	0	0	0
K. Meroney*	Research Assistant	12	10.00%	21,000	0	0	0

*Salary support for the Research Assistant is included in the budget for the Outcome Measures Core (Core B) A Portion of her time will be used in collecting baseline data on Pain Clinic patients.

SUBTOTALS----------	0	0	0
CONSULTANT COSTS			0
EQUIPMENT (Itemize)			0
SUPPLIE (Itemize by category)			0
TRAVEL			0
PATIENT CARE COSTS INPATIENT			0
PATIENT CARE COSTS OUTPATIENT			0
ALTERATIONS AND RENOVATIONS (Itemize by category)			0
OTHER EXPENSE (Itemize by category)			0
SUBTOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD			0
CONSORTIUM/CONTRACTUAL COSTS DIRECT COSTS		TOTAL-------	0
CONSORTIUM/CONTRACTUAL COSTS INDIRECT COSTS			

TOTAL DIRECT COSTS FOR FIFTH BUDGET PERIOD (Item 7a, Face Page)-------- $ 0

BUDGET FOR ENTIRE PROPOSED BUDGET PERIOD
DIRECT COSTS ONLY

BUDGET CATEGORY TOTALS	INITIAL BUDGET PERIOD (from page 4)	ADDITIONAL YEARS OF SUPPORT REQUESTED 2nd	3rd	4th	5th
PERSONNEL (Salary and fringe benefits) (Applicant organization only)	0	0	107,281	110,852	113,629
CONSULTANT COSTS	0	0	5,000	5,000	5,000
EQUIPMENT	0	0	0	0	0
SUPPLIES	0	0	1,200	1,200	1,200
TRAVEL	0	0	1,200	1,200	1,200
PATIENT CARE COSTS INPATIENT	0	0	0	0	0
PATIENT CARE COSTS OUTPATIENT	0	0	20,000	22,000	24,000
ALTERATIONS AND RENOVATIONS	0	0	0	0	0
OTHER EXPENSES	0	0	1,000	1,000	1,000
SUBTOTAL DIRECT COSTS	0	0	135,681	141,252	146,029
CONSORTIUM/ CONTRACTUAL COSTS	0	0	0	0	0
TOTAL DIRECT COSTS	0	0	135,681	141,252	146,029

TOTAL DIRECT COSTS FOR ENTIRE PROPOSED PROJECT PERIOD (Item 8a)-------> $422,962

JUSTIFICATION (Use continuation pages if necessary):

Personnel. For the first two years of prelimnary studies, the estimated time commitment for Drs. Gabois and Strayer (10% each) will be contributed to the project. The time required for data collection during these two years has been budgeted in the Outcome Measures Core Unit budget and is reflected in the time request for the research assistant and data analyses staff.

Beginning in year three, when investigative studies begin, support is requested for 10% of Dr. Grabois' time and 20% of Dr. Strayer's time that will be devoted to research on testing the efficacy of the clinic and on application on innovative treatment approaches in relief of disability-related pain. Also, a full-time rehabilitation nurse clinician or physician assistant will be brought on board to assist with subject recruitment, conduct of clinical research, patient follow-up, and preparation of results for publication in professional journals. The salary level project for this individual at the time of hiring is $46,000, with fringe benefits estimated at 28%.

Consultant Costs. A request for up to five days of consultation on innovative therapies has been included in the budget. The consultation rate for these services is estimated at $500 per day.

Equipment. At present, no equipment needs have been identified for this project. Preliminary studies may indicate the need for clinical or data collection equipment prior to initiating experimental studies.

Supplies. Consumable supplies for data collection, storage, and retrieval and for other research related activities are estimated at $100 per month.

Travel. Funds are requested for the PI or Co-PI to attend one professional meeting to present on the research and results. These costs are estimated at $850 discounted roundtrip airfare, $50 for ground transportation and parking/mileage, $110 per night for two nights lodging, and $40 per day for two days meals.

Patient Care Costs. It is expected that some experimental therapies will involve patient care costs that are not covered by insurance. Such costs may include purchase of electrodes or other equipment, experimental drug purchases, or other costs. The third year budget request includes $20,000 for such costs, with a $2,000 increase in year's two and three based on projected increases in patients recruited into experimental treatments.

Alterations/Renovations. No funds are requested for these purposes.

Other Expenses. Funds are requested for publication charges.

DD | Principal Investigator/Program Director (Last, first,middle): Grabois, Martin, M.D.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD
DIRECT COSTS ONLY

FROM 04/01/96 THROUGH 03/31/97

PERSONNEL (Applicant organization only) NAME	ROLE ON PROJECT	TYPE APPT. (months)	% EFFORT ON PROJ.	INST. BASE SALARY	DOLLAR AMOUNT REQUESTED (Omit cents) SALARY REQUESTED	FRINGE BENEFITS	TOTALS
Martin Grabois, M.D.	Principal Investigator	12	10.00%	190,000	12,500	2,389	14,889
To Be Named Research Director	Research Specialist	12	5.00%	110,000	5,500	1,254	6,754
Lex Frieden	Policy Specialist	12	5.00%	103,000	5,250	1,204	6,454
Karen Hart, Ph.D.	Dissemination Specialist	12	5.00%	73,000	3,650	867	4,517
Support Staff	Administrative Support	12	25.00%	28,000	0	0	0
SUBTOTALS----------					26,900	5,714	32,614

CONSULTANT COSTS	Honoraria for 7 advisory committee members @ $250 each = $1.750. Travel for 4 out-of-town committee members at $1,200 each = $4,800.	6,550
EQUIPMENT (Itemize)		0
SUPPLIES (Itemize by category)	Consumable office supplies @ $100 per month	1,200
TRAVEL	One trip by PI to present on DPMC activities	1,200
PATIENT CARE COSTS	INPATIENT	0
	OUTPATIENT	0
ALTERATIONS AND RENOVATIONS (Itemize by category)		0
OTHER EXPENSE (Itemize by category)	Publication Costs	1,000
SUBTOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD		42,564
CONSORTIUM/CONTRACTUAL COSTS DIRECT COSTS / INDIRECT COSTS	TOTAL-------	0
TOTAL DIRECT COSTS FOR FIFTH BUDGET PERIOD	(Item 7a, Face Page)--------	$ 42,564

BUDGET FOR ENTIRE PROPOSED BUDGET PERIOD
DIRECT COSTS ONLY

BUDGET CATEGORY TOTALS	INITIAL BUDGET PERIOD (from page 4)	ADDITIONAL YEARS OF SUPPORT REQUESTED 2nd	3rd	4th	5th
PERSONNEL (Salary and fringe benefits) (Applicant organization only)	32,614	33,919	35,275	36,686	38,154
CONSULTANT COSTS	6,550	6,550	6,550	6,550	6,550
EQUIPMENT	0	0	0	0	0
SUPPLIES	1,200	1,200	1,200	1,200	1,200
TRAVEL	1,200	1,200	1,200	1,200	1,200
PATIENT CARE COSTS INPATIENT	0	0	0	0	0
PATIENT CARE COSTS OUTPATIENT	0	0	0	0	0
ALTERATIONS AND RENOVATIONS	0	0	0	0	0
OTHER EXPENSES	1,000	1,000	1,000	1,000	1,000
SUBTOTAL DIRECT COSTS	42,564	43,869	45,225	46,636	48,104
CONSORTIUM/ CONTRACTUAL COSTS	0	0	0	0	0
TOTAL DIRECT COSTS	42,564	43,869	45,225	46,636	48,104

TOTAL DIRECT COSTS FOR ENTIRE PROPOSED PROJECT PERIOD (Item 8a)-------> $226,398

JUSTIFICATION (Use continuation pages if necessary):

Personnel. Dr. Grabois will devote 10% time and effort to the DPMC administration. He will direct overall center activities and will have responsibility for oversight of fiscal management of the DPMC.

The to-be-announced research director will assist with research project design and implementation, as well as with data analyses and interpretation of findings. He will devote 5% time and effort to DPMC activities.

Mr. Frieden will assist research personnel with national and institutional policy issues, as well as on issues of consumer involvement in research. He will devote 5% time and effort to DPMC activities.

Dr.Hart will coordinate educational activities related to the project and will assist research personnel with dissemination activities. She will devote 5% time and effort to the DMPC.

Management support staff will be provided through institutional resources. The time and effort of support staff on DPMC activities is conservatively estimated at 25%.

Consultant Costs. All seven members of the DPMC advisory committee, including professionals and consumers, will be provided an honoraria of $250 per year to cover a portion of their time. Additionally, the four members of the advisory committee who are nationally recognized experts in pain mamagement and/or disability will have their travel costs covered. Travel costs are estimated at $1,200 per person for out-of-town committee members. Local travel costs and associated expenses, including any accommodation costs, for consumer members of the committee will be covered from institutional resources.

Equipment. No equipment needs are anticipated at this time.

Supplies. Consumable supply costs are estimated at $100 per month to cover costs of diskettes, reference materials, and other resources provided through the Administrative Core Unit.

Travel. Funds are requested for the DPMC director to attend one national meeting to present on the center and its activities. These costs are estimated at $850 discounted roundtrip airfare, $50 for ground transportation and parking/mileage, $110 per night for two nights lodging, and $40 per day for two days meals.

Patient Care Costs. It is expected that some experimental therapies will involve patient care costs that are not covered by insurance. Such costs may include purchase of electrodes or other equipment, experimental drug purchases, or other costs. The third year budget request includes $20,000 for such costs, with a $2,000 increase in year's two and three based on projected increases in patients recruited into experimental treatments.

Alterations/Renovations. No funds are requested for these purposes.

Other Expenses. Funds are requested for publication charges.

Subsequent Year Budgets

Budgets for years two through five reflect expected increases in personnel costs of 4% per year. Other costs are projected at level funding over the project period.

DD Principal Investigator/Program Director (Last, first,middle): Grabois, Martin, M.D.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD
DIRECT COSTS ONLY

FROM 04/01/96 THROUGH 03/31/97

PERSONNEL (Applicant organization only) NAME	ROLE ON PROJECT	TYPE APPT. (months)	% EFFORT ON PROJ.	INST. BASE SALARY	DOLLAR AMOUNT REQUESTED (Omit cents) SALARY REQUESTED	FRINGE BENEFITS	TOTALS
Margaret Nosek, Ph.D.	Principal Investigator	12	20.00%	65,520	13,104	3,365	16,469
Diana Rintala, Ph.D.	Co-Investigator	12	15.00%	57,036	8,555	2,143	10,698
Carol Howland (M.P.H.)	Project Manager	12	25.00%	39,586	9,897	2,669	12,566
Gail Champong, M.S.	Database Manager	12	30.00%	32,500	9,750	2,812	12,562
Kathy Meroney, B.A.	Research Assistant	12	50.00%	21,000	10,500	3,629	14,129
SUBTOTALS----------					51,806	14,618	66,424

CONSULTANT COSTS		0
EQUIPMENT (Itemize) One IBM-compatible 90 mHz Pentium computer with one gigabyte hard drive, 14,400 fax modem, CD Rom, and tape backup		3,200
SUPPLIES (Itemize by category) Consumable office supplies @ $200 per month		2,400
TRAVEL One trip by PI to present on outcome data (accompanied by 2 attendants) = $2,940 One trip by Co-PI to present at professional meeting = $1,200		4,140
PATIENT CARE COSTS	INPATIENT	0
	OUTPATIENT	0
ALTERATIONS AND RENOVATIONS (Itemize by category)		0
OTHER EXPENSE (Itemize by category) Space Rental = $5,250*; Telephone = $1,200*; Postage = $500*; Routine Duplicating = $1,200*; Publication Costs $1,000 *Not covered through off-campus indirect cost rate.		9,150
SUBTOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD		85,314
CONSORTIUM/CONTRACTUAL COSTS DIRECT COSTS INDIRECT COSTS	TOTAL------	0
TOTAL DIRECT COSTS FOR FIFTH BUDGET PERIOD (Item 7a, Face Page)--------	$	85,314

BUDGET FOR ENTIRE PROPOSED BUDGET PERIOD
DIRECT COSTS ONLY

BUDGET CATEGORY TOTALS	INITIAL BUDGET PERIOD (from page 4)	ADDITIONAL YEARS OF SUPPORT REQUESTED 2nd	3rd	4th	5th
PERSONNEL (Salary and fringe benefits) (Applicant organization only)	66,424	69,081	71,844	74,718	77,707
CONSULTANT COSTS	0	0	5,000	5,000	5,000
EQUIPMENT	3,200	0	0	0	0
SUPPLIES	2,400	2,400	2,400	2,400	2,400
TRAVEL	4,140	4,140	4,140	4,140	4,140
PATIENT CARE COSTS INPATIENT	0	0	0	0	0
PATIENT CARE COSTS OUTPATIENT	0	0	0	0	0
ALTERATIONS AND RENOVATIONS	0	0	0	0	0
OTHER EXPENSES	9,150	9,150	9,150	9,150	9,150
SUBTOTAL DIRECT COSTS	85,314	84,771	92,534	95,408	98,397
CONSORTIUM/ CONTRACTUAL COSTS	0	0	0	0	0
TOTAL DIRECT COSTS	85,314	84,771	92,534	95,408	98,397

TOTAL DIRECT COSTS FOR ENTIRE PROPOSED PROJECT PERIOD (Item 8a)-------> $456,424

JUSTIFICATION (Use continuation pages if necessary):

Personnel

Margaret A. Nosek, Ph.D., will serve as principal investigator for the core project. She has extensive experience in conducting psychological and social outcome assessments in studies of independent living and community integration of persons with physical disabilities, as well as health outcomes for women with physical disabilities. She has served as principal investigator for an R01 from the NIH National Center for Medical Rehabilitation Research, conducting a three-year, large scale, national study of psychosocial behaviors of women with physical disabilities and constructing an extensive database of survey results on 970 women. On the core project, she will be responsible for guiding conceptual activities, overseeing developmental activities, assigning project tasks to project staff, supervising staff activities, monitoring fiscal management, and assuring adherence with commitments described in the proposal. She will devote 20% time and effort to the project.

Diana Rintala, Ph.D., will serve a co-principal investigator for the core project. Her expertise in social psychology, outcome assessment for persons with severe disabilities, quantitative survey development and implementation, and data analysis will be a valuable asset for the project. She has served as co-principal investigator with Dr. Nosek on the NIH women's study. She will be responsible for assisting with overseeing and guiding tasks related to instrument development, sample selection, data analysis and interpretation, and documenting and presenting findings. She will devote 15% time and effort to the project.

Carol Howland, M.P.H. (in progress) will serve as project manager for the core project. Her outstanding skills in organizing multi-phased, complex projects will ensure efficient implementation of the core project. She served as one of the coordinators on Dr. Nosek's NIH women's study. She will be responsible for reviewing and summarizing literature related to the topic, collation and refinement of assessment instruments to be included in the survey interview, coordination of all project activities related to pilot testing and implementing data collection efforts, coordination of activities related to data coding and entering, preparation of reports, and coordination of documentation and presentation of findings. She will devote 25% time and effort throughout the project.

Gail Chanpong, M.S., will serve as database manager for the core project. In the NIH women's study, she has held primary responsibility for coding and entering data, implementing quality control strategies, and conducting basic analyses of the data. She created the current relational database consisting of 970 responses to a comprehensive survey questionnaire, with each questionnaire containing over 1,000 bits of information. For the core project, she will assist in instrument design and response coding, oversee data entry, implement quality control techniques for the data set, and conduct statistical analyses at the direction of the senior investigators. She will devote 30% time and effort to the project.

Kathy Meroney, B.A., will serve as research assistant for the core project. She has performed with excellence as research assistant on numerous studies under the principal investigator. Under the supervision of Carol Howland, project manager, she will be responsible for collecting and maintaining information on all study participants, supervising data collection activities of the research assistants in three of the clinical studies, taking primary responsibility for data collection from participants in the Pain Clinic Study, preparing correspondence (including securing informed consent) for distribution to participants, preparing and delivering survey instruments to participants or research assistants in three of the clinical studies, entering data into computer storage, and assisting with preparation of draft reports and other information generated through project efforts. She will devote 40% time and effort to the project.

Fringe Benefits

Costs for fringe benefits for project staff are requested at the current Baylor College of Medicine rate of 28% of salaries and wages.

Equipment

Funds are requested for purchase on one IBM compatible pentium computer with 90 MHz, 16 megabytes of RAM, a 1 gigabyte hard disc, CD Rom, HD 3 1/4 inch floppy disk drive, and 14.4 fax/modem. This equipment will be used by the project manager and database manager in preparing project materials, data entry and storage, and data analysis. The $3,200 cost request is based on a current price quote with the Baylor discount.

Supplies

Office supplies requested for this project are directly related to research activities, including computer diskettes, printer toner, and other supplies. These supply costs are estimated at $200 per month throughout

the project. In addition $1,200 is requested in the first year for the cost of duplicating materials for participants and distribution of project findings at the request of interested parties. Postage and shipping expenses of $500 are requested for the distribution of survey instruments to participants in all four clinical projects.

Travel

Travel support is requested for the principal investigator to attend one national meeting to present findings from the project. Travel cost estimates are based on $750 round trip airfare, $125 per night for 2 nights lodging, $40 per day for 3 days meals, and $80 for ground transportation and miscellaneous expenses ($1,200). Because of the severity of Dr. Nosek's physical disability (advanced spinal muscular atrophy), she must travel with two personal care attendants to ensure safe transfers and manage her respiratory equipment. Travel costs for 2 attendants on each trip are requested in the amount of $750 airfare and $40 per day for three days meals ($870 x 2 = $1,740). Thus, expenses for one 3-day trip for Dr. Nosek total $2,940. Funds are also requested for one co-principal investigator to present on project findings at a national conference, based on $750 round trip airfare, $125 per night for 2 nights lodging, $40 per day for 3 days meals, and $80 for ground transportation and miscellaneous expenses ($1,200). This amount is requested for each project year.

Telephone

$100 per month is requested for coverage of rental of telephone equipment, line service fees, and long distance charges.

Office Space Rental

Office rent is requested because we are located off campus and office rental is a direct cost. It is calculated as a product of the total full time equivalent staff (FTEs), square feet of space, and price per square foot. The FTEs for the first year total 1.3. Office rental costs are calculated at the rate of $15 per square foot per year for an estimated 250 square feet of space per FTE. The 250 square feet includes common areas and is based on a somewhat larger estimate than is often used. This somewhat larger amount of space is required to accommodate faculty and staff who use wheelchairs and who need additional office space and common areas in order to negotiate the work environment.

Indirect Costs

Indirect costs are charged at Baylor's negotiated off-campus rate of 29.5% percent of modified total direct costs.

OTHER SUPPORT

(Use continuation pages if necessary)

FOLLOW INSTRUCTIONS CAREFULLY. Incomplete, inaccurate, or ambiguous information about OTHER SUPPORT could lead to significant delays in the review and/or possible funding of the application.If there are changes in the information after submission, notify the scientific review administrator of the initial review group before the review; if changes occur after the review, notify the appropriate institute.

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Name Martin Grabois, M.D. Active _____ Pending _____ None X

a. Source and identifying no. _____ P.I. _____

Title _____

b. Your role on project _____ % Effort _____

c. Dates and costs of entire project _____

d. Dates and costs of current year _____

e. Specific aims of project _____

f. Describe scientific and budgetary overlap _____

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.)_____

OTHER SUPPORT

(Use continuation pages if necessary)

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Name Jonathan Strayer, M.D. Active _____ Pending _____ None X

a. Source and identifying no. _____ P.I. _____

Title _____

b. Your role on project _____ % Effort _____

c. Dates and costs of entire project _____

d. Dates and costs of current year _____

e. Specific aims of project _____

f. Describe scientific and budgetary overlap _____

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.)_____

OTHER SUPPORT

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Name Carlton F. Hazlewood, Ph.D. Active _____ Pending XX None _____

a. Source and identifying no. NASA P.I. Hali A. Hartmann, Ph.D.

Title Human Voltage-Dependent Ion Channels: Electromagnetic Interactions

b. Your role on project Co-Investigator % Effort 10%

c. Dates and costs of entire project 05/01/95 - 06/30/96; $140,000.

d. Dates and costs of current year N/A

e. Specific aims of project 1) Identify and quantify the effects of AC, DC, and transient magnetic field strengths on electrophysiological properties of ion channels, 2) Test hypothesis that magnetite may be a cellular coupler of transducer which causes the channels to respond to the fields, and 3) Explore distribution of magnetite and ion channels in oocytes with NMR micro-imaging.

f. Describe scientific and budgetary overlap This proposal's scientific aims coincide with the present application. Budgetary overlap includes only those items itemized under supplies. Equipment requests were not allowed on the NASA proposal.

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.)

Supplies will not be purchased. Replacement funds for facilities at Dr. Winters magnetically-shielded laboratory will be requested.

OTHER SUPPORT

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Name Carlton F. Hazlewood, Ph.D. Active _____ Pending XX None _____

a. Source and identifying no. NSCORT NRA 94-OLMSA-04 P.I. M. Zouhair Atassi, Ph.D.

Title Effect of Microgravity on the Muscular System and the Neuromuscular Junction

b. Your role on project Co-Investigator % Effort 15%

c. Dates and costs of entire project 11/01/95 - 10/31/00; $4,514,343.

d. Dates and costs of current year 11/01/95 - 10/31/96; $815,363.

e. Specific aims of project 1) Synthesis of peptides corresponding to exposed regions of β, γ, and δ-chains of mACHR and preparation of antibodies against these peptides, 2) Optimization of the culture conditions of the mouse cell line in order to obtain maximum proliferation, growth, and muscle fiber formation, 3) Determination of the AChR density by binding studies, 4) Determine subunit levels in culture conditions, 5) Determine growth profile - will require space -flight experiments, and 6) Determine electrophysiological properties of cell line and muscles from mice in spaceflight.

f. Describe scientific and budgetary overlap There is no overlap.

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.)

No adjustments will be necessary.

OTHER SUPPORT

(Use continuation pages if necessary)

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Name Carlton F. Hazlewood, Ph.D. Active _____ Pending XX None _____

a. Source and identifying no. NIH P.I. Carlton F. Hazlewood, Ph.D.

Title Testing A Dehydration Theory of Intoxication

b. Your role on project Principal Investigator % Effort 15%

c. Dates and costs of entire project 12/01/94 - 11/30/99; $133,022.

d. Dates and costs of current year 12/01/94 - 11/30/95; $31,325.

e. Specific aims of project 1) Study relaxation times of H_2O in the brain before and after alcohol intoxication.

f. Describe scientific and budgetary overlap There is no scientific or budgetary overlap.

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.)

No adjustments will be needed.

OTHER SUPPORT

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Name Richard K. Simpson Jr., M.D., Ph.D. Active X Pending _____ None _____

Department of Health and Human Services

a. Source and identifying no. (1741613878A1) P.I. Robert G. Grossman, M.D.

Title Treatment of Physiological Disturbances After Head Injury

b. Your role on project Co-Principal Investigator % Effort 10%

c. Dates and costs of entire project 3/1/94-2/28/99 $5,459,481.00

d. Dates and costs of current year 3/1/94-2/28/95 $578,317.00

e. Specific aims of project To evaluate the physiological consequences of head injury and develop specific treatments.

f. Describe scientific and budgetary overlap None

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.)

I will withdraw from this project and be replaced by another neurosurgeon if the current project is funded.

OTHER SUPPORT

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Name Richard K. Simpson Jr., M.D., Ph.D. Active X Pending _____ None _____

a. Source and identifying no. Medtronic Neurological (FN8219.01, SN01) P.I. Richard K. Simpson Jr, MD.

Title The Modulation of Pain by Glycine and Related Compounds

b. Your role on project Principal Investigator % Effort 10%

c. Dates and costs of entire project 5/1/95-4/30/97 $60,000.00

d. Dates and costs of current year 5/1/95-4/30/96 $30,000.00

e. Specific aims of project An animal study (rat) to determine the efficacy of intrathecally administered glycine on neuropathic pain.

f. Describe scientific and budgetary overlap None

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.)

None

OTHER SUPPORT

(Use continuation pages if necessary)

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Name Richard K. Simpson Jr., M.D., Ph.D. Active X Pending _____ None _____

a. Source and identifying no. Janssen Pharmaceutica, Inc. (74 161 3878) P.I. Richard K. Simpson Jr, MD.

Title Transdermal Fentanyl Patches (Duragesic) as Treatment of Chronic Low Back Pain

b. Your role on project Principal Investigator % Effort 10%

c. Dates and costs of entire project 3/1/94-2/28/95 $135,009.00

d. Dates and costs of current year 6/1/94-5/31/95 $135,009.00

e. Specific aims of project To determine the efficacy of the fentanyl patch on chronic low back pain.

f. Describe scientific and budgetary overlap None

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.)

None, this project terminates on 5/31/95

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Name Richard K. Simpson Jr., M.D., Ph.D. Active X Pending _____ None _____
Faculty

a. Source and identifying no. American College of Surgeons Fellowship P.I. Richard K. Simpson Jr, MD.

Title The Role of Glycine in Spinal Cord Injury

b. Your role on project Principal Investigator % Effort 10%

c. Dates and costs of entire project 7/1/94-6/30/96 $60,000.00

d. Dates and costs of current year 7/1/94-6/30/95 $30,000.00

e. Specific aims of project An immunohistology study of changes in the quantity and distribution of glycine containing interneurons and glycine receptors in the spinal cord of spastic rabbits, and rats with neuropathic pain.

f. Describe scientific and budgetary overlap None

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.)

None

OTHER SUPPORT

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Name Richard K. Simpson Jr., M.D., Ph.D. Active X Pending _____ None _____

a. Source and identifying no. VARAGS/Program 821 Center 103 P.I. Richard K. Simpson Jr, MD.

Title The Role of Glycine in Spinal Cord Injury-Induced Spasticity

b. Your role on project Principal Investigator % Effort 10%

c. Dates and costs of entire project 10/1/93-9/30/95 $103,100.00

d. Dates and costs of current year 10/1/94-9/30/95 $42,900.00

e. Specific aims of project An animal study (rabbit) to determine the efficacy of intrathecally administered glycine on spasticity.

f. Describe scientific and budgetary overlap None

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.)

None, this project terminates on 9/30/95

OTHER SUPPORT

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Name Margaret A. Nosek, Ph.D. Active X Pending _____ None _____

a. Source and identifying no. NIDRR/H133G30073 P.I. Nosek, Margaret A.

Title Relationships among age at onset, adequacy of personal assistance, negative health incidents, and health care utilization for persons with physical disabilities.

b. Your role on project Principal Investigator % Effort 20

c. Dates and costs of entire project October, 1993 - September, 1996, $410,615

d. Dates and costs of current year October, 1994 - September, 1995, $135,081

e. Specific aims of project To determine the strength of relationships among age at onset of disability, use of personal assistance services for activities of daily living, health status, and use of health care services by persons with a variety of severe disabilities.

f. Describe scientific and budgetary overlap None.

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.) None.

Principal Investigator/Program Director (Last, first, middle): Grabois, Martin, M.D.

OTHER SUPPORT - Margaret A. Nosek, Ph.D.

Name Nosek, Margaret A. Active X Pending _____ None _____

a. Source and identifying no. BCM, Dept. of Phys. Med. & Rehab. P.I. N/A

Title N/A

b. Your role on project Associate Professor % Effort 14

c. Dates and costs of entire project N/A

d. Dates and costs of current year N/A

e. Specific aims of project N/A

f. Describe scientific and budgetary overlap None.

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.) None.

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Name Charles F. Contant, Jr. Active X Pending _____ None _____

a. Source and identifying no. Office of Maternal and Child Health P.I. Edward Gomperts

Title Collaborative Study of Effects of HIV on Development of Hemophilic Children

b. Your role on project Co-Investigator/Biostatistician % Effort 20%

c. Dates and costs of entire project 88/06/01 to 95/05/31; $5,300,000

d. Dates and costs of current year 93/06/01 to 94/05/31; $865,000

e. Specific aims of project The specific aims of the project are to:

1. Examine the effects of HIV on neurological, psychological and physical development
2. Determine the time course of HIV changes
3. Examine the effects of Hemophilia on these changes

f. Describe scientific and budgetary overlap No scientific or budgetary overlap

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.)

No adjustments will be necessary

NOTE: This page is a close reproduction of the printed "other support" page. For those with multiple sources of other support, the following page is a condensed version which I believe NIH would like you to use - don't use one page per person per source if you can condense information. Save a Tree!

Name Charles F. Contant, Jr., Ph.D. Active _____ Pending X None _____

a. Source and identifying no. NINDS, NIH PO1-NS27617 P.I. Robert G. Grossman, MD

Title Treatment of Physiological Disturbances in Head Injury

b. Your role on project Co-Investigator/Biostatistician % Effort 70%

c. Dates and costs of entire project 94/06/01 to 99/05/31 ; $ 3,750,000

d. Dates and costs of current year 94/06/01 to 95/05/31 ; $ 750,000

e. Specific aims of project Program Project to examine the causes and effects of secondary injury in patients with head injury.

f. Describe scientific and budgetary overlap No scientific or budgetary overlap

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.)

No adjustments will be necessary

Name _____ Active _____ Pending _____ None _____

a. Source and identifying no. _____ P.I. _____

Title _____

b. Your role on project _____ % Effort _____

c. Dates and costs of entire project _____

d. Dates and costs of current year _____

e. Specific aims of project _____

f. Describe scientific and budgetary overlap _____

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.)

OTHER SUPPORT

(Use continuation pages if necessary)

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Name Lex Frieden Active X Pending _____ None _____

a. Source and identifying no. NIDRR H133D10131 P.I. Lex Frieden

Title Southwest Disability and Business Technical Assistance Center

b. Your role on project Project Director % Effort 25%

c. Dates and costs of entire project 10/01/91-09/30/96 $2,200,000

d. Dates and costs of current year $510,800 10/01/94-09/30/94

e. Specific aims of project To foster effective implementation of the Americans with Disabilities Act throughout the five-state area comprising federal Region VI.

f. Describe scientific and budgetary overlap There is no scientific or budgetary overlap.

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.)No adjustments will be necessary.

OTHER SUPPORT - Continued

Name Lex Frieden, M.A. Active X Pending _____ None _____

a. Source and identifying no. NIDRR H133B00008 P.I. Lex Frieden

Title Research and Training Center on Improving Management Effectiveness in Independent Living Centers

b. Your role on project Center Director % Effort 25%

c. Dates and costs of entire project 10/01/90-09/30/95 $2,474,633

d. Dates and costs of current year 10/01/94-09/30/95 $520,000

e. Specific aims of project To carry out research, training, and technical assistance activities designed to strengthen the capacities of consumer-controlled, community-based service agencies to address the support service needs of people with disabilities.

f. Describe scientific and budgetary overlap No overap in budgetary or scientific areas.

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.) No adjustment is necessary.

Name Lex Frieden, M.A. Active X Pending _____ None _____

a. Source and identifying no. The Robert Wood Johnson Foundation P.I. Lex Frieden

Title Improving Service Systems for People with Disabilities

b. Your role on project National Program Director % Effort 25%

c. Dates and costs of entire project 06/01/89-05/30/96 $2,800,000

d. Dates and costs of current year 06/01/94-05/30/95 $450,000

e. Specific aims of project To provide support and assistance to 11 independent living centers nationally selected as demonstration sites for testing innovative approaches for delivering services to people with disabilities in community settings and for diversifying funding bases available to support community-based services.

f. Describe scientific and budgetary overlap No overlap in budgetary or scientific areas.

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.) No adjustment necessary.

Name _____ Active _____ Pending _____ None _____

a. Source and identifying no. _____ P.I. _____

Title _____

b. Your role on project _____ % Effort _____

OTHER SUPPORT

(Use continuation pages if necessary)

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Name Jurida Gabor, Ph.D. Active _____ Pending _____ None X

a. Source and identifying no. _____ P.I. _____

Title _____

b. Your role on project _____ % Effort _____

c. Dates and costs of entire project _____

d. Dates and costs of current year _____

e. Specific aims of project _____

f. Describe scientific and budgetary overlap _____

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.)_____

OTHER SUPPORT

(Use continuation pages if necessary)

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Name Hali A. Hartmann, Ph.D. Active _____ Pending XX None _____

a. Source and identifying no. NSF IBN-9511011 P.I. Hali A. Hartmann, Ph.D.

Title Cardiac-Like Na^+ Channels in Brain: Location and Function

b. Your role on project Principal Investigator % Effort 50%

c. Dates and costs of entire project 07/01/95 - 06/30/98; $376,737.

d. Dates and costs of current year 07/01/95 - 12/31/95; $117,856.

e. Specific aims of project 1) Identify with *in situ* hybridization the location of cardiac Na^+ channel mRNA in rat brain, 2) Electrophysiological characterization of currents, and 3) Clone the cDNA if a new channel is indicated.

f. Describe scientific and budgetary overlap There is no scientific overlap. Budgetary overlap entails requests for electrophysiological amplifier, interface, manipulators, and microscope.

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.)

Electrophysiological equipment will still be needed for this project as the projects do not overlap.

OTHER SUPPORT

(Use continuation pages if necessary)

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Name Hali A. Hartmann, Ph.D. Active _____ Pending XX None _____

a. Source and identifying no. NASA P.I. Lucie Parent, Ph.D.

Title Effect of Altered Gravity on Regulation and Expression of Ca^{2+} and Na^{+} Channels in Cardiac Cells

b. Your role on project Co-Principal Investigator % Effort 50%

c. Dates and costs of entire project 05/01/95 - 06/30/96; $140,000.

d. Dates and costs of current year N/A

e. Specific aims of project 1) Investigate the effect of microgravity on gene expression of cardiac Na^{+} and Ca^{2+} channels with *in situ* hybridization, 2) Quantify changes in ion channel density after exposure to altered gravity by measuring specific antagonist binding sites, and 3) Assess modifications in ion channel function induced by a vector-free gravity environment.

f. Describe scientific and budgetary overlap There is no scientific or budgetary overlap.

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.)

No adjustments will be made.

OTHER SUPPORT

(Use continuation pages if necessary)

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Name Hali A. Hartmann, Ph.D. Active _____ Pending XX None _____

a. Source and identifying no. NASA P.I. Hali A. Hartmann, Ph.D.

Title Human Voltage-Dependent Ion Channels: Electromagnetic Interactions

b. Your role on project Principal Investigator % Effort 50%

c. Dates and costs of entire project 05/01/95 - 06/30/96; $140,000.

d. Dates and costs of current year N/A

e. Specific aims of project 1) Identify and quantify the effects of AC, DC, and transient magnetic field strengths on electrophysiological properties of ion channels, 2) Test hypothesis that magnetite may be a cellular coupler of transducer which causes the channels to respond to the fields, and 3) Explore distribution of magnetite and ion channels in oocytes with NMR micro-imaging.

f. Describe scientific and budgetary overlap This proposal's scientific aims coincide with the present application. Budgetary overlap includes only those items itemized under supplies. Equipment requests were not allowed on the NASA proposal.

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.)

Supplies will not be purchased. Replacement funds for facilities at Dr. Winters magnetically-shielded laboratory will be requested.

OTHER SUPPORT

(Use continuation pages if necessary)

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Name Carol A. Howland Active X Pending _____ None _____

a. Source and identifying no. NIDRR/H133G30073 P.I. Nosek, Margaret A.

Title Relationships among age at onset, adequacy of personal assistance, negative health incidents, and health care utilization for persons with physical disabilities.

b. Your role on project Project Director % Effort 35

c. Dates and costs of entire project October, 1993 - September, 1996, $410,615

d. Dates and costs of current year October, 1994 - September, 1995, $135,081

e. Specific aims of project To determine the strength of relationships among age at onset of disability, use of personal assistance services for activities of daily living, health status, and use of health care services by persons with a variety of severe disabilities.

f. Describe scientific and budgetary overlap None.

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.) None.

OTHER SUPPORT

(Use continuation pages if necessary)

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Name Trilok N. Monga, M.D. **Active** A855-RC **Pending** Oct. 1995 **None** _____

a. Source and identifying no. Rehabilitation Research & Development (117A) **P.I.** Trilok N. Monga, M.D.

Title Upper Limb Amputee Services: The VA Approach as a Model Service System

b. Your role on project Prinicinal Investigator **% Effort** _____

c. Dates and costs of entire project (For renewals, include only the most recent competitive award. List direct and indirect costs separately.)

October, 1995 to September, 1998 Total operating cost over 3 years $234038

d. Dates and costs of current year Nil

e. Specific aims of project Aims are to assess the current strengths and weaknesses of the VA services for persons with upper limb loss; develop an assessment tool that can be used in continuous quality improvement of these services; to determine if the VA model can be used for servicing other populations that may have limited access to services at present; and to expand the current national data base on upper limb amputee.

f. Describe scientific and budgetary overlap None.

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.)

None.

OTHER SUPPORT

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Name Michael Priebe, M.D. Active _____ Pending _____ None X

a. Source and identifying no. _____ P.I. _____

Title _____

b. Your role on project _____ % Effort _____

c. Dates and costs of entire project _____

d. Dates and costs of current year _____

e. Specific aims of project _____

f. Describe scientific and budgetary overlap _____

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.)_____

Dr. Priebe's salary is covered 100% from VA sources. However, in conjunction with his role as a faculty member of the Baylor College of Medicine Department of Physical Medicine and Rehabilitation, he is actively engaged in research projects with the Baylor's Research and Training Center in Community Integration for Individuals with Spinal Cord Injury and with a project funded through the VA on Objective Assessment of Spasticity in Spinal Cord Injury.

OTHER SUPPORT

(Use continuation pages if necessary)

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Name Diana H. Rintala, Ph.D. Active X Pending _____ None _____

a. Source and identifying no. NIDRR/H133B40011 P.I. Rintala, Diana H.

Title Rehabilitation Research and Training Center in Community Integration for Individuals with Spinal Cord Injury

b. Your role on project Research Director % Effort 15

c. Dates and costs of entire project January, 1994 - January, 1999, $3,250,000

d. Dates and costs of current year January, 1994 - January, 1995, $650,000

e. Specific aims of project To develop and disseminate new knowledge and techniques to improve personal and psychological adjustment after SCI by improving and maintaining health status, enhancing family life through involvement of family members in rehabilitation, identifying options for marriage, sexuality, reproduction, and parenthood, enhancing participation in community life, improving community health and other support systems, and identifying gender and culture difference relevant to community integration.

f. Describe scientific and budgetary overlap None.

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.) None.

OTHER SUPPORT - Continued

Name Diana H. Rintala, Ph.D. Active X Pending _____ None _____

a. Source and identifying no. NIDRR/H133840011 (R04) P.I. Alfred, Wayne G.

Title A vocational Intervention for Persons with Spinal Cord Injury (A Menu Option)

b. Your role on project Co-Investigator % Effort 5

c. Dates and costs of entire project January, 1994 - January, 1999, $98,105

d. Dates and costs of current year January, 1995 - January, 1996

e. Specific aims of project To provide group counseling to enhance control over one's life, pschosocial adjustment, and vacational decision-making. The effectiveness of the program will be evaluated using a delayed-entry control group design.

f. Describe scientific and budgetary overlap None.

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.) None.

Name Diana H. Rintala, Ph.D. Active X Pending _____ None _____

a. Source and identifying no. NIDRR/H133840011 (R01) P.I. Rintala, Diana H.

Title Community Integration of Persons with Spinal Cord Injury: A Two-Panel Study

b. Your role on project Co-Principal Investigator % Effort 25

c. Dates and costs of entire project January, 1994 - January, 1999, $741,155

d. Dates and costs of current year January, 1994 - January, 1995, $148,231

e. Specific aims of project To expand the knowledge base about a) the extent to which a random sample of individuals with SCI already living in the community have become integrated within it and b) the factors with which community integration is correlated. Each participant will be assisted in making a step-by-step plan (A Menu of Options) to assist them in making a Plan of Action to improve the quality of their lives in ways they choose.

f. Describe scientific and budgetary overlap None.

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.) None.

Principal Investigator/Program Director *(Last, first, middle):* Grabois, Martin, M.D.

Name Diana H. Rintala, Ph.D. Active X Pending _____ None _____

a. Source and identifying no. NIDRR/H133840011 (R02) P.I. Rintala, Diana H.

Title Reintegration into the Community by Persons with Recent Spinal Cord Injury: A Longitudinal Study

b. Your role on project Co-Principal Investigator % Effort 5

c. Dates and costs of entire project January, 1994 - January, 1999, $234,830

d. Dates and costs of current year January, 1994 - January, 1995, $46,966

e. Specific aims of project To expand the knowledge base about the process of reintegration into the community of persons with SCI during the first two years following initial hospitalization, via qualitative interviews with the participants and their families about their experieinces relevant to becoming reintegrated into the community after SCI.

f. Describe scientific and budgetary overlap None.

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.) None.

Name Diana H. Rintala, Ph.D. Active X Pending _____ None _____

a. Source and identifying no. NIDRR/H133840011 (R05) P.I. Rintala, Diana H.

Title Abilities Exchange: A Time Dollars Volunteer Program to Enhance Community Integration

b. Your role on project Principal Investigator % Effort 10

c. Dates and costs of entire project January, 1994 - January, 1999, $166,460

d. Dates and costs of current year January, 1995 - January, 1996, $33,292

e. Specific aims of project This volunteer project will emphasize abilities rather than disabilities, promote psychological well-being and active participation in the community, and to fill unmet needs of our constituency. Participants will receive service credits for services provided and will be able to spend these credits to obtain services from others.

f. Describe scientific and budgetary overlap None.

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.) None.

Principal Investigator/Program Director *(Last, first, middle):* Grabois, Martin, M.D.

Name Diana H. Rintala, Ph.D. Active X Pending _____ None _____

a. Source and identifying no. NIDRR/H133840011 (R06) P.I. Rintala, Diana H.

Title Service Dogs: Effect on the Community Integration of Persons with Spinal Cord Injury (A Menu Option)

b. Your role on project Principal Investigator % Effort 5

c. Dates and costs of entire project January, 1994 - January, 1999, $53,940

d. Dates and costs of current year January, 1995 - January, 1996, $10,788

e. Specific aims of project To promote functional independence and enhance social integration and community participation through use of service dogs to assist persons with mobility impairments by performing various services for the participants. Community integration, functional independence, economic status, psychological well-being, and empowerment will be assessed before and following placement of a service dog with each participant.

f. Describe scientific and budgetary overlap None.

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.) None.

OTHER SUPPORT

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Name Jay Rosenfeld, M.D. Active X Pending _____ None X

a. Source and identifying no. Kent Waldrep Ntl. Paralysis Fdt. P.I. Milan R. Dimitrijevic, M.D.

Title Training Grant

b. Your role on project Co-Investigator % Effort 10%

c. Dates and costs of entire project 07/01/94-06/30/95: $40,000

d. Dates and costs of current year 07/01/94-06/30/95: $40,000

e. Specific aims of project This is a one-year project for training on the full battery of motor and sensory assessment procedures used in evaluating patients with spinal cord injury. Dr. Rosenfeld supervises the fellow being provided training.

f. Describe scientific and budgetary overlap There is no overlap scientifically or budgetarily.

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.)No adjustments are necessary.

Dr. Priebe's salary is covered 100% from VA sources. However, in conjunction with his role as a faculty member of the Baylor College of Medicine Department of Physical Medicine and Rehabilitation, he is actively engaged in research projects with the Baylor's Research and Training Center in Community Integration for Individuals with Spinal Cord Injury and with a project funded through the VA on Objective Assessment of Spasticity in Spinal Cord Injury.

OTHER SUPPORT

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Name Vladimir I. Slesarev, M.D., Ph.D. Active _____ Pending X None _____

a. Source and identifying no. NASA P.I. Hali A. Hartman, Ph.D.

Title Human Voltage-Dependent Ion Channels: Electromagnetic Interactions

b. Your role on project Postdoctoral Associate, NMR study % Effort 50%

c. Dates and costs of entire project 05/01/95-06/30/96 $140,000

d. Dates and costs of current year Not Applicable

e. Specific aims of project (1) Identify and quantify the effects of the AC, DC, and transient magnetic field strengths on electrophysiological properties of ion channels; (2) Test hypotheses that magnetite may be a cellular coupler or transducer which causes the channels to respond to the field; and (3) Explore distribution of magnetite and ion channels in oocytes with NMR micro-imaging.

f. Describe scientific and budgetary overlap This project's scientific aims coincide with the present application. There may be some modest overlap in funding for supplies. No equipment was allowed in the NASA proposal.

g. Describe adjustments you will make if the present application is funded (budget, % effort, aims, etc.) The supply request will be reduced somewhat due to overlap between the two projects.

BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME	POSITION TITLE
MARTIN GRABOIS, M.D.	CHAIRMAN, DEPARTMENT OF PHYSICAL MEDICINE AND REHABILITATION

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Baylor College of Medicine, Department of Physical Medicine and Rehabilitation 1333 Moursund Avenue, Suite A-221 Houston, Texas 77030	M.D.	1966	Physical Medicine and Rehabilitation

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

1990-Present: Chairman, Department of Physical Medicine and Rehabilitation; Professor of Clinical Physical Medicine and Rehabilitation, Clinical Restorative Neurology and Human Neurobiology and Clinical Anesthesiology, Baylor College of Medicine, Houston, TX.
1977-90: Chairman, Department of Physical Medicine, Baylor College of Medicine, Houston, TX.
1977-78: Acting Chairman, Department of Physical Medicine, Baylor College of Medicine, Houston, TX.
1973-77: Staff Physiatrist and Assistant Professor, Departments of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, TX.
1977-87: Associate Professor, Departments of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, TX.

Physician's Recognition Award for Participation in Continuing Medical Education of the American Medical Association, 1977, 1982, 1987, 1991, 1994.
Visiting Professor, University of Tokyo, Tokyo, Japan, 1988.
Gold Key Award, American Congress of Rehabilitation Medicine, 1993

Grant Advisory Board: Chairman Internal Advisory Board Program Project Grant, Enhancement of Residual Functional Below Spinal Cord Lesion, Baylor College of Medicine Division of Restorative Neurology and Human Neurology.

Principal Investigator: Transcutaneous Electrical Nerve Stimulation (TENS): Efficacy in Managing Post Operative Pain. Funded by: Stimtech Incorporated; 1979-1981; $27,000.

Member Editorial Board, "Pain" 1988-present
Member Editorial Advisory Board, "Journal of Disability" 1992-1993
Member Editorial Board, "Disability Rights and Resources 1992-present
Manuscript Reviewer - "Pain" 1988-1995; "The Clinical Journal of Pain 1991; "Archives of Physical Medicine and Rehabilitation" 1977, 1982, 1991

Selected Book Contributions:

Grabois M and Smith K: Chronic Pain. in: State of the Art Review Sexuality and Disability. (ed) Monga T; Hanley & Belfus, Inc. Philadelphia, 1995.

Grabois M, Straja A, Schramm D and McCann M: Prevention and Management of Chronic Pain. in: Textbook on Physical Medicine and Rehabilitation. (ed) Braddom R; Williams and Wilkins, Philadelphia, 1995.

Grabois M and VanDeventer J: Chronic Pain. in: Handbook of Physical Medicine and Rehabilitation Basics. (ed) Garrison SJ; JB Lippincott, Philadelphia, 1995.

Grabois M: Breast Cancer: Postmastectomy Lymphedema. in: Physical Medicine and Rehabilitation State of the Art Reviews Cancer Rehabilitation. (ed) Garden F; Hanley & Belfus, Inc., Philadelphia 1994.

Grabois M: Chronic Pain: Evaluation and Treatment. in: Rehabilitation Medicine. (ed) Goodgold J; CV Mosby Co., St. Louis, 1988.

Grabois M: Treatment of Pain Syndromes Through Exercise. in: Therapeutics Through Exercise. (eds) Lowenthal DT, Bharadwaja K and Oaks WW; Grune & Stratton Incorporated, New York, 1979.

Selected Scientific Publication Published in Proceedings:

Grabois M and Blacker HM: Chronic Pain: Measurement and Assessment. Proceedings of the Second European conference on Research in Rehabilitation, Dusseldorf, 1985.

Selected Manuscripts:

Chiou-Tan FY, Lenz ML, Robertson CS and Grabois M: Pharmacologic Treatment of Autonomic Dysreflexia in the Rat. Am J Phys Med Rehab 1994; 73(4):251-255.

Sandin KJ and Grabois M: Effect of Course Offerings in Physical Medicine and Rehabilitation on Medical Students' Understanding and Perception of Physiatrics. European J Phys Med Rehab 1992; 2(6):195-200.

Blocker WP and Grabois M: Gait as a Diagnostic Aid. European J Phys Med Rehab 1992; 2(1):15-20.

Grabois M: Academic Physiatry: Balancing Clinical Practice and Academic Activities. Am J Phys Med Rehab 1992; 71(2):77-80.

Grabois M and Blacker HM: Chronic Pain: Measurement and Assessment. International J Rehab Res Supplement 5 1987; 10(4):266-270.

Grabois M: Pain Clinics - Role in Rehabilitation of Patients with Chronic Pain. Annals Acad Med Singapore 1983; 12(3):428-433.

Grabois M: Chronic Pain Clinics. Houston Society of Internal Medicine News Notes 1982; 70(3):3-4.

Grabois M: Comprehensive Evaluation and Management of Patients with Chronic Pain. Cardiovascular Research Center Bulletin 1981; 19:113-117.

BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants listed on page 2.
Begin with the Principle Investigator/Program Director. Photocopy this page for each person.

NAME	POSITION TITLE
Jonathan R. Strayer, M.S., M.D.	Attending Physician, Spinal Cord Injury Program

EDUCATION (Begin with baccalaureate or other initial professional education, such as nursing and include postdoctoral training)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
DePauw University, Greencastle, IN	BA	1982	Zoology
Wright State University, Dayton, OH	MS	1984	Physiology
University of Cincinnati, Cincinnati, OH	MD	1988	Medicine
The Christ Hospital, Cincinnati, OH	Internship	1988-89	Internal Medicine
Baylor College of Medicine, Houston, TX	Residency	1989-92	Phys Med & Rehab

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principle investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

Professional Experience

1983 - 1984 — Graduate Research Assistant, Laboratory of Applied Physiology, Department of Physiology, Wright State University, Dayton, OH Thesis Topic: Metabolic responses to various combinations of voluntary arm and electrically stimulated leg exercises in spinal cord injured individuals. Advisor: Roger M. Glaser, Ph.D.

1985 — Research Liaison, Department of PM&R, Rhode Island Hospital, Providence, RI

1985-1986 — Academic Tutor, Learning Resources Office, University of Cincinnati, College of Medicine (Physiology and Microanatomy)

1992 - present — Basic Science Research at Johnson Space Center, National Aeronautics and Space Administration, Houston, TX; Effects of space flight on gait.

1992 - present — Associate Director, Musculoskeletal Program, Staff Physiatrist and Spinal Cord Injury Program, The Institute for Rehabilitation and Research (TIRR), Houston, TX

1992 - present — Assistant Professor, Department of Physical Medicine and Rehabilitation, Division of Restorative Neurology and Human Neurobiology, Baylor College of Medicine, Houston, TX.

Publications:

1. Strayer, J.R., Tuel, S.P., Dimitrijevic, M., Sherwood, A. The discomplete syndrome: clinical implications of residual suprasegmental influence across a clinically complete spinal cord injury, Arch Phys Med & Rehab, 1992;73(10):969.

2. Strayer, J.R., Tuel, S.P., Spinal decompression sickness in divers: neurophysiologic assessment of paraplegia, Arch Phys Med & Rehab, 1992;73(1):1003 (abstract).

3. Glaser, R.M., Strayer, J.R., May, K.P., Combined FES leg and volunary arm exercises of SCI patients. Proceedings of the IEEE Electronics in Medicine and Biology Conferences, pp. 308-313, 1985.

4. Glaser, R.M., Strayer, J.R., Glaser, M., A closed loop stimulator for exercising paralyzed muscles. Proceedings of the 8th Annual Conference on Rehabilitation Technology. pp. 388-390, 1985.

5. Strayer, J.R., Glaser, R.M., May, K.P. Metabolic responses to voluntary arm and electrically stimulated leg exercises in spinal cord injured individuals (abstract). Fed Proc., 44:1367, 1985.

6. May, K.P., Glaser, R.M., Strayer, J.R. Central hemodynamic responses for voluntary arm and electrically stimulated leg exercises in spinal cord injured individuals (abstracts). Clinical Research 33:932A, 1985.

Strayer, Jonathan R., M.S., M.D.

Presentations:

"Clinical Implications of Discomplete Spinal Cord Injury". Lewis A. Leavitt Memorial Lecturship. Baylor College of Medicine. Houston, Texas. June 17, 1994

"Spinal Cord Injury - Medical Complications and Spasticity". 27th & 28th Comprehensive Review Course in Physical Medicine and Rehabilitation. Baylor College of Medicine. Houston, Texas. March 17, 1993 and March 24, 1994. (Moderator/Lecturer)

"Clinical Implications of Discomplete Spinal Cord Injury - Part II". Weekly Research Conference. Baylor College of Medicine. Houston, Texas. February 11, 1994.

"Difficult Care Decisions". Human Values in Medicine Physical Medicine and Rehabilitation Elective Course. Baylor College of Medicine at The Institute For Rehabilitation and Research. Houston, Texas. January 26, 1993

"Historical Perspectives on Humanism in Medicine". Human Values in Medicine Physical Medicine and Rehabilitation Elective Course. Baylor College of Medicine at The Institute for Rehabilitation and Research. Houston, Texas. October 13, 1992.

"The Discomplete Syndrome: Clinical Implications of Residual Suprasegmental Influence Across a Clinically Complete Spinal Cord Injury". Research Conference at The Institute For Rehabilitation and Research (TIRR). Houston, Texas. September 29, 1992.

"Sports and the Disabled Athlete". The Department of Physical Medicine and Rehabilitation Grand Rounds. Baylor College of Medicine. Houston, Texas. January 15, 1992.

COMMUNITY SERVICE:

1993-Present	Volunteer Medical Director, The Institute for Rehabilitation and Research Sports Association (TIRR Sports)
1989–1991	Volunteer Screening Medical Examiner, Houston Challengers, Disabled Athletics Association
1990	Medical Coverage, The International Les Autres Association, International Meet
1990–1991	Camp Physician, Houston Multiple Sclerosis Society's Camp Can-Do

BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME	POSITION TITLE
Carlton Frank Hazlewood	Professor

EDUCATION (*Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.*)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Texas A&M University, College Station, TX	B.S.	1957	Science
University of Tennessee, Medical Units Memphis, TN	Ph.D.	1962	Medical Physiology

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

RESEARCH AND PROFESSIONAL EXPERIENCE:

1962 - 1964 Postdoctoral Fellowship, Johns Hopkins University, Baltimore, Maryland.
1963 - 1964 Lecturer, Westinghouse School of Applied Engineering.
1964 - 1967 Instructor: Department of Pediatrics and Physiology, Baylor College of Medicine.
1967 - 1972 Assistant Professor, Departments of Pediatrics and Physiology, Baylor College of Medicine.
1972 - 1976 Associate Professor, Departments of Pediatrics and Physiology, Baylor College of Medicine.
1976 - Pres Professor, Departments of Pediatrics and Physiology, Baylor College of Medicine.
1977 - Pres Adjunct Professor, Rice University, Physics Department, Houston, Texas.

PROFESSIONAL MEMBERSHIPS:

1965 - Pres American Association for the Advancement of Science
Biophysical Society
Sigma Xi
American Physiology Society
New York Academy of Science
UNESCO: European and North American Scientific Cooperation; Biophysics, Co-chairman of Program on Water and Ions in Biological Systems.

RESEARCH INTEREST

Physical State of Ions and Water in Living Tissues and Model Systems.
Mechanisms of Tumorigenesis.
Mechanisms of NMR Relaxation Times.
Diffusive Motion of Water in Cells
Molecular Motion in Aqueous Phases

PUBLICATIONS (Past 3 years and representative earlier publications)

Hazlewood, C.F.; Editor, vol. 204 of the *Annals of the New York Academy of Sciences*, Titled, "The Physicochemical State of Ions and Water in Living Tissues and Model Systems", 1973.

Hazlewood, C.F.; A View of the Significance and Current Understanding of the Physical Properties of Cell-Associated Water. In: *Cell Associated Water.* Edited by Walter Drost-Hansen and J.S. Clegg. Academic Press, 1979.

Hazlewood, C.F.; Chang, D.C.; Medina, D.; Cleveland, G.; Nichols, B.L. Distinction Between the Preneoplastic State of Murine Mammary Glands. *Proc. Natl. Acad. Sci.* **69**:1478-1480, 1972.

Hazlewood, C.F.; Cleveland, G.; Medina, D. Relationship Between Hydration and Proton Nuclear Magnetic Resonance Relaxation Times in Tissue of Tumor Bearing and Non-Tumor Bearing Mice. *J. Natl. Cancer Inst.* **52**:1849-1852, 1974.

Hazlewood, C.F.; Chang, D.C.; Nichols, B.L.; Woessner, D.E. NMR Transverse Relaxation Times of Water Protons in Skeletal Muscle. *Biophysical J.* **14**:583-606, 1974.

Cleveland, G.G.; Chang, D.C.; Hazlewood, C.F.; Rorschach, H.E. Nuclear Magnetic Resonance Measurement of Skeletal Muscle: Anisotropy of the Diffusion Coefficient of the Intracellular Water. *Biophys. J.* **16**:1043-53, 1976.

Seitz, P.T.; Hazlewood, C.F.; Clegg, J. Proton Magnetic Resonance Studies on the Physical State of Water in *Artemia* Cysts. In: G. Persoone, P. Sorgeloos, O. Roels and E. Jaspers, eds. *The Brine Shrimp Artemia.* Vol. 2, Universal Press, Belgium, 1980;545-555.

Beall, P.T.; Asch, B.B.; Chang, D.C.; Medina, D.; Hazlewood, C.F. Distinction of Normal, Preneoplastic and Neoplastic Mouse Mammary Primary Cell Cultures by Water Nuclear Magnetic Resonance Relaxation Times. *J. Natl. Cancer Inst.* **64(2)**:335-338, 1980.

Seitz, P.T.; Chang, D.C.; Hazlewood, C.F.; Rorschach, H.E.; Clegg, J.S. The Self-Diffusion of Water in *Artemia* Cysts. *Arch. Biochem. Biophys.* **210(2)**:517-525, 1981.

Cameron, I.L.; LaBadie, D.R.L.; Hunter, K.E.; Hazlewood, C.F. Changes in Water Proton Relaxation Times and in Nucleur to Cytoplasmic Element Gradients During Meiotic Maturation of *Xenopus* Oocytes. *J. Cellular Physiology* **116**:87-92, 1983.

Kasturi, S.R.; Hazlewood, C.F.; Yamanashi, W.S.; Dennis, L.W. Evidence for Chemically Shifted Water in the Brine Shrimp *Artemia*: Possible Interpretations. *Physiol. Chem. Physics Med. NMR* **15**:5-11, 1983.

Trantham, E.C.; Rorschach, H.E.; Clegg, J.S.; Hazlewood, C.F.; Nicklow, R.M.; Wakabayashi, N. The Diffusive Properties of Water in *Artemia* Cysts as Determined from Quasi-Elastic Neutron Scattering Spectra. *Biophys. J.* **45**:927-938, 1984.

Kasturi, S.R.; Hazlewood, C.F.; Yamanashi, W.S.; Dennis, L.W. The Nature and Origin of Chemical Shift for Intracellular Water Nuclei in *Artemia* Cysts. *Biophys. J.* **52**:249-256, 1987.

Kasturi, S.R.; Seitz, P.K.; Chang, D.C.; Hazlewood, C.F. Intracellular Water in *Artemia* Cysts (Brine Shrimp) Investigations by Deuterium and Oxygen-17 Nuclear Magnetic Resonance. *Biophys. J.* **58**:483-491, 1990.

Rorschach H.E.; Lin, C.; Hazlewood, C.F. Diffusion of Water in Biological Tissues. *Scanning Microscopy Supplement* **5**:S1-S10, 1991.

Hazlewood, C.F.; Rorschach, H.E.; Lin, C. Diffusion of Water in Tissues and MRI. *Mag. Res. in Med.* **19**:214-216, 1991.

Zheng, N.J.; Rau, G.; Hazlewood, C.F.; Rau, C. High-Resolution, Real Space Imaging of Conformational Structures of Poly-L-Proline Helixes. *Scanning Microscopy* **5**:631-636, 1991.

Hazlewood, C.F.; Van Zandt, R.L. An Hypothesis Defining an Objective End Point for the Relief of Chronic Pain. *Med Hypothesis* **44(1)**:63-65, 1995.

BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME	POSITION TITLE	
Richard K. Simpson, Jr.	Associate Professor	9/10/53

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Coker College, Hartsville, SC	B.A.	1975	Biology/Chemistry
Medical University of South Carolina, Charleston, SC	Ph.D.	1980	Physiology - Neurophysiology
Medical University of South Carolina, Charleston, SC	M.D.	1982	Medicine

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. If the list of publications in the last three years exceeds two pages, select the most pertinent publications. DO NOT EXCEED TWO PAGES.

PROFESSIONAL EXPERIENCE:

Laboratory Assistant, Coker College, Department of Biology, 1973-1975
Teaching Assistant, Medical University of South Carolina, Department of Physiology, 1976-1980
Research Associate, Medical University of South Carolina, Department of Physiology, 1980-1981
Internship, Medical University of South Carolina, Department of Neurology, 1/83-6/83
Internship, Baylor College of Medicine, Department of Surgery, 7/83-6/84
Residency, Baylor College of Medicine, Department of Neurosurgery, 7/84-7/89
Assistant Professor, Baylor College of Medicine, Department of Neurosurgery, 7/89-6/94
Assistant Professor, Baylor College of Medicine, Department of Anesthesiology, 4/92-6/94
Chief, Neurosurgery Section, Houston VA Medical Center, Baylor College of Medicine, 9/91-present
Associate Professor, Baylor College of Medicine, Department of Neurosurgery and Anesthesiology, 7/94-

HONORS:

Watson Scholar, 1974; Sigma Xi, 1978; Alpha Omega Alpha, 1982; MUSC Neurology Clinical Research Award, 1983; American College of Surgeons Scholar, 1986; Minora Suzuki Neuroscience Award, 1989; AANS/CNS Mayfield Award, 1989; Young Alumni Award, 1990; ACS Franklin H. Martin Faculty Fellowship Award, 1994; AANS William H. Sweet Young Investigator Award, 1994; Who's Who in America, 1995

PUBLICATIONS: (selected from 95)

1. Fischer DK, Simpson RKJr, Narayan RK, Mattox KL: Shielding of the spinal cord by cervical and facial structures in penetrating trauma. Neurochirurgia, 34:37-41, 1991.
2. Robertson CS, Simpson RKJr: Neurophysiologic monitoring of patients with head injuries. In: Management of head injury, (eds) Eisenberg HM, Aldrich F, WB Saunders Company, Philadelphia, v. 2, n. 2, pp 285-299, 1991.
3. Simpson RKJr, Robertson CS, Goodman JC: Segmental release of amino acid neurotransmitters from transcranial stimulation. Neurochem Res 16:89-94, 1991.
4. Simpson RKJr, Robertson CS, Goodman JC, Halter JA: Recovery of amino acid neurotransmitters from the spinal cord during posterior epidural stimulation: A preliminary report. J Am Paraplegia Soc, 14:4-9, 1991.
5. Simpson RKJr, Contant CF, Fischer DK, Cech DA, Robertson CS, Narayan RK: Subarachnoid Hemorrhage in an Urban Population: The Influence of Ethnic Background, Gender, and Hypertension on Outcome. Headache Quarterly, 2:201-205, 1991.
6. Simpson RKJr, Contant CF, Fischer DK, Cech DA, Robertson CS, Narayan RK: Epidemiological characteristics of subarachnoid hemorrhage in an urban population. J Clin Epidemiol, 44:641-648, 1991.
7. Simpson RK, Hsu CY, Dimitrijevic MR: The experimental basis for early pharmacological intervention in spinal cord injury. Paraplegia, 29:364-372, 1991.
8. Robertson DP, Simpson RKJr, Narayan RK: Lumbar disc herniation from a gunshot wound to the spine: A report of two cases. Spine, 16:994-995, 1991.
9. Simpson RKJr, Azordegan PA, Sirbasku DM, Weathers WS, Lidsky MD, Baskin DS: Rapid onset of quadriplegia from a panspinal epidural abscess. Spine, 16:1002-1005, 1991.

10. Simpson RKJr, Robertson CS, Goodman JC: Release of segmental amino acid neurotransmitters in response to peripheral afferent and motor cortex stimulation: A pilot study. Life Sci, 49:113-118, 1991.
11. Simpson RKJr, Baskin DS, Dudley AW: The influence of long-term nifedipine or indomethacin therapy on neurologic recovery from experimental spinal cord injury. J Spinal Disord, 4:420-427, 1991.
12. Simpson RKJr, Contant CF, Fischer DK, Cech DA, Robertson CS, Narayan RK: The influence of diabetes mellitus on outcome from subarachnoid hemorrhage. Diabetes Res, 16:165-169, 1991.
13. Robertson DP, Simpson RKJr: Penetrating injuries restricted to the cauda equina: A retrospective analysis. Neurosurgery, 31:265-270, 1992.
14. Fischer DK, Simpson RKJr, Baskin DS: Spinal spondylosis and disk disease. In: Prognosis of neurological disease, (eds) Evans RW, Baskin DS, Yatsu FM, Oxford Univ Press, Oxford, chap 24, pp 335-351,1992.
15. Simpson RKJr, Halter JA, Auzzene DG: Tissue adhesive to secure epidural spinal cord stimulating electrodes: Technical note. Surg Neurol, 38:391-393, 1992.
16. Simpson RKJr, Robertson CS, Goodman JC: Segmental amino acid neurotransmitter recovery during posterior epidural stimulation after spinal cord injury. J Am Paraplegia Soc, 16:34-41, 1992.
17. Simpson RKJr, Goodman JC, George RE, Laurent JP, Cheek WR: Solitary scalp hamartoma in identical twins. Pediatr Neurosurg, 19:89-92, 1993.
18. Simpson RKJr, Robertson CS, Goodman JC: Glycine: An important potential component of spinal shock. Neurochem Res, 18:887-892, 1993.
19. Baskin DS, Simpson RK, Browning JL, Dudley AW, Rothenberg F, Bouge L: The effect of long term high dose naloxone infusion in experimental blunt spinal cord injury. J Spinal Disord, 6:38-43, 1993.
20. Rambo WM, Simpson RKJr: Carotid-cavernous fistula from facial shotgun wounds. Neurochirurgia, 36:96-100, 1993.
21. Simpson RKJr, Robertson CS, Goodman JC: Spinal epidural corticomotor evoked potentials as a predictor of outcome from ischemic myelopathy. Neurol Res, 15:104-108,1993.
22. Simpson RKJr, Robertson CS, Goodman JC: Glycine: A potential mediator of electrically induced pain modification. Biomed Lett, 48:193-207, 1993.
23. Robertson DP, Simpson RKJr, Rose JE, Garza J: Video assisted endoscopic thoracic ganglionectomy. Technical Note. J Neurosurg, 79:238-240,1993.
24. Simpson RKJr, Contant CF, Robertson CS, Goodman JC: Compressed spectral analysis of corticomotor evoked potentials in spinal cord injury, Part I: Acute studies. Neurol Res, 15:367-372, 1993.
25. Simpson RKJr, Contant CF, Robertson CS, Goodman JC: Compressed spectral analysis of corticomotor evoked potentials in spinal cord injury, Part II: Chronic studies. Neurol Res, 15:373-378, 1993.
26. Edmondson EA, Simpson RK, Beric A, Stubler DK: Systemic lidocaine therapy for "thalamic pain". South Med J, 1093-1096,1993.
27. Simpson RKJr, Goodman JC: Response to a letter from Dr. Martinez-Lage: Solitary scalp hamartoma in identical twins. Pediatr Neurosurg, 20:9, 1994.
28. Simpson RKJr, Robertson CS, Goodman JC: Pain and spasticity reduced by intrathecal administration of glycine and related compounds. Pain Newsletter, 2:4-5, 1995.
29. Robertson DP, Simpson RKJr: CSF diversion in adults. In: The Practice of Neurosurgery, (eds) Tindall GT, Cooper PR, Barrow DL, Williams & Wilkins, In Press, 1995.
30. Simpson RKJr, Robertson DP, Narayan RK: Penetrating spinal cord injuries. In: Neurotrauma, (eds) Narayan RK, Wilberger JE, Povlishock JT, McGraw-Hill, Inc., In Press, 1995.
31. Goodman JG, Simpson RKJr: Biochemical monitoring in head injury. In: Neurotrauma, (eds) Narayan RK, Wilberger JE, Povlishock JT, McGraw-Hill, Inc., In Press, 1995.
32. Simpson RKJr, Bick D: Current Opinion in General Surgery: A review of the journal. JAMA, In Press, 1995.
33. Simpson RKJr, Leis AA: Neurosurgical management of spasticity, Part I. In Press, Contemp Neurosurgery, 1995.
34. Simpson RKJr, Leis AA: Neurosurgical management of spasticity, Part II. In Press, Contemp Neurosurgery, 1995.
35. Rambo WM, Simpson RKJr, Narayan RK: Vascular sequelae of penetrating head injury. In: Penetrating Head Injury, (ed) Dagi TF, Little Brown Co, Boston, In Press, 1995.
36. Simpson RKJr, Venger BH, Narayan RK: Penetrating injuries of the spine. In: Penetrating Head Injury, (ed) Dagi TF, Little Brown Co, Boston, In Press, 1995.
37. Zimmermann K, Simpson RKJr: "Slinky" coils for neuromagnetic stimulation. In Press, Electroencephalogr Clin Neurophysiol, 1995.
38. Simpson RKJr, Robertson CS, Goodman JC: Reduction of mechanonociceptive and thermonociceptive responses by intrathecal administration of glycine and related compounds. In Press, Surgical Forum, 1995.

BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME	POSITION TITLE
Nosek, Margaret A.	Associate Professor

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Baldwin-Wallace College, Berea, Ohio	BM	1974	Music(magna cum laude)
Case Western Reserve Univ., Cleveland, Ohio	MA	1976	Music
The University of Texas, Austin, Texas	MA	1982	Rehab. Counseling
The University of Texas, Austin, Texas	Ph.D.	1974	Rehab. Research

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

EMPLOYMENT

1982-1983 **Assistant** to Justin W. Dart, Chair, Governor's Long Range Planning Group for Texans with Disabilities, Austin, Texas.

1984-1993 **Assistant Professor**, Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, Texas.

1993-Present **Associate Professor**, Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, Texas.

1984-Present **Director of Research**, Independent Living Research Utilization Program of The Institute for Rehabilitation and Research, Houston, Texas.

1993-Present **Adjunct Associate Professor**, College of Occupational Therapy, Texas Women's University, Houston, Texas.

1993-Present **Director**, Center for Research on Women with Disabilities, Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, Texas.

CURRENT RESEARCH ACTIVITIES

1992-1995 **Principal Investigator**, Psychosocial Behaviors Among Women with Physical Disabilities (NIH/NCMRR).

1993-1996 **Principal Investigator**, Relationships among age at onset, adequacy of personal assistance, negative health incidences and health care utilization for persons with physical disabilities (NIDRR).

1990-1995 **Director of Research**, Research and Training Center on Improving Management Effectiveness in Independent Living Center, National Institute on Disability and Rehabilitation Research.

HONORS

Listed in 10 Who's Who directories.

1989 Fellowship recipient, World Rehab. Fund, International Exchange of Experts and Information in Rehab.

1990 Outstanding graduate (one of five), The University of Texas, Austin, Dept. of Special Education.

1991 Disability patriot recognition, President's Comm. on Employment of People with Disabilities.

1991 Recipient, The Americans with Disabilities Act Award, U.S. House Task Force on the Rights and Empowerment of Americans with Disabilities, Congressman Major R. Owens, Chairman.

1991 Honorable Mention, American Rehabilitation Counseling Association Research Award.

1992 Certificate of Appreciation, Governmental Relations Committee, American Association for Counseling and Development.

1993 Baylor College of Medicine, Physical Medicine and Rehab. Research Award, Houston, Texas.

1993 Outstanding Young Texas Ex Award, The University of Texas, Austin, Texas. (one of four)

1993 Women on the Move Award, (one of ten), Houston Post, Texas Executive Women.

1994 American Psychological Association, James Garrett Early Career Achievement Award.

1994 Co-chair National Institutes of Health Conference on "The Health of Women with Physical Disabilities," May 1994.

PUBLICATIONS - Nosek, Margaret A.

Nosek, M.A., (1994) Sexual abuse of women with physical disabilities: Findings from a qualitative study. (in press). In Monga, T.N., (Ed.), Sexuality and Disability, Hanley and Belfus Publishers, Philadelphia.

Nosek, M.A., Howland, C.A., Young, M.E., Georgiou, D., Rintala, D.H., Foley, C.C., Bennett, J.L., and Smith, Q.W., (1993) (accepted). Wellness models and sexuality among women with physical disabilities. Journal of Applied Rehabilitation Counseling.

Matson, C.C., Holleman, W.L., Nosek, M.A., and Wilkinson, W., (1993). The effect of the Americans with Disabilities Act on the delivery of medical services. NARPPS Journal, 8(3), 115-120

Nosek, M.A., Fuhrer, M.J., Rintala, D.H., and Hart, K.A., (1993). The use of personal assistance services by persons with spinal cord injury. Journal of Disability Policy Studies, 4(1), 89-103.

Nosek, M.A., (1993). A response to Kenneth R. Thomas' commentary: some observations on the use of the word "consumer." Journal of Rehabilitation, Apr.-Jun. issue, 9-10.

Howland, C.A., Walden, E., and Nosek, M.A., (1993). Independent living centers and private sector rehabilitationists: A dynamic partnership for implementing the ADA. Journal of the National Association of Rehabilitation Professionals in the Private Sector, April issue.

Nosek, M.A., (1993). Personal assistance services for persons with mental illness and mental retardation. [Chiteki Shogaishya ya seishin shogaishyaeno personal assistance services]. Current Study of Rehabilitation, 22(4), 27-32.

Nosek, M.A., (1993). The effect of personal assistance on the long term health of a rehabilitation population. Archives of Physical Medicine and Rehabilitation, 74, 119-126.

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Nosek, M.A., (1990). Personal assistance: Key to employability of persons with physical disabilities. Journal of Applied Rehabilitation Counseling, 21(4), 3-8.

Nosek, M.A., Roth, P., and Zhu, Y., (1990). Independent living programs: The impact of program age, consumer control, and budget on program operation. Journal of Rehabilitation, 56(4), 28-35.

Fuhrer, M.J., Rossi, D., Gerken, L., Nosek, M.A., and Richards, L., (1990). Relationships between independent living centers and medical rehabilitation programs. Archives of Physical Medicine and Rehabilitation, 71, 519-522.

BIOGRAPHICAL SKETCH

Give the following information for all new key personnel, consultants, and collaborators.
Copy this page for each person.

NAME	POSITION TITLE
Gail Chanpong	Manager of Data and Information

EDUCATION (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
San Diego State University, San Diego, CA	BS	1975	Microbiology
San Diego State University, San Diego, CA	MS	1984	Health Care Management

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individual who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

EMPLOYMENT

1975 - 1982	Senior Research Technologist, Caribbean Epidemiology Centre, Trinidad, West Indies, Medical Research Council, St. George's, Grenada and Bridgetown, Barbados.
1983 - 1984	Research Associate, Center for Business and Economic Research, California State University, Bakersfield, California.
1985 - 1987	Research Analyst, Kern Council of Governments, Bakersfield, California.
1988 - 1993	Educator, Meridian School, American International School, Republique Gabonaise, Africa.
1993 - 1994	Senior Research Associate, Center for Transportation Training and Research, Texas Southern University, Houston, Texas.
1994 - Present	Manager of Data and Information, Center for Research on Women with Disabilities, Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, Texas.

PROFESSIONAL LICENSES

1976	ASCP, certified Medical Technologist (ASCP #108147)
1981	Microbiologist, California state licensed (#00432)
1982	Clinical Laboratory Technologist, California state licensed (#29731, file 31403)

CONTINUING EDUCATION/SEMINAR PARTICIPATION

1986	Census Bureau Methodology Seminar, Phoenix, Arizona, for population estimates and projections based on component, administrative record, ratio correlation and composite methods for computation of estimates based on historic trends and cohort survival.
1987	American Statistical Association Seminar on Sub-national Population Estimates, California State Department of Finance Population Research Workshop, Western Regional State Data Center, San Francisco, California
1994	Doctoral student, University of Houston/University of Texas cooperative Health Science program completing seminars database management, research methodology, biomedical statistics requiring familiarity with SPSS, Minitab, and SAS, Houston, Texas

BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME	POSITION TITLE
Charles F. Contant, Jr.	Assistant Professor

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Univ. of Texas School of Public Health, Houston, TX	Ph.D.	1988	Biometry
Univ. of Texas School of Public Health, Houston, TX	M.P.H.	1979	Disease Control
Case Western Reserve University, Cleveland, Ohio	B.A.	1972	Natural Science

RESEARCH AND/OR PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

Professional Experience:

1988-present Assistant Professor, Department of Neurosurgery, Baylor College of Medicine

1981 - 1988 Faculty Associate in Biometry
Epidemiology Research Unit
University of Texas School of Public Health,
Houston, Texas.

Contant, C.F., Robertson, C.S., Crouch, J., Gopinath, S.P., Narayan, R.K., Grossman, R.G. Intracranial pressure waveform indices in transient and refractory intracranial hypertension. *Journal of Neuroscience Methods*. 1994. (In Press)

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Simpson, R.K., Jr., Contant, C.F., Robertson, C.S., Goodman, J.C. Spectral analysis of corticomotor evoked potentials in spinal cord injury. Part 2. Chronic studies. *Neurology Research,* vol 15 pgs 373-378, 1993.

Troisi, C.L., Hollinger, F.B., Hoots, W.K., Contant, C., Gill, J., Ragni, M., Parmley, R., Sexauer, C., Gomperts, E., Buchanan, G., et al. A multicenter study of viral hepatitis in a United States hemophilic population. *Blood,* vol 81 pgs 412-418, 1993.

Biographical Sketch
Charles F. Contant, Jr.
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Yamashita, Y., Goddard-Finegold, J., Contant, C.F., Martin, C.G., Michael, L.H. Phenobarbital and cerebral blood flow during hypotension in newborn pigs. *Pediatric Research,* vol 33 pgs 598-602, 1993.

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Robertson, C.S., Contant, C.F., Gokaslan, Z.L., Narayan, R.K., Grossman, R.G. Cerebral blood flow, arteriovenous oxygen difference, and outcome in head injured patients. *Journal of Neurology, Neurosurgery, and Psychiatry,* vol 55 pgs 594-603, 1992.

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Sheinberg, M., Kanter, M.J., Robertson, C.S., Contant, C.F., Narayan, R.K., Grossman, R.G. Continuous monitoring of jugular venous oxygen saturation in head-injured patients. *Journal of Neurosurgery,* vol 76 pgs 212-217, 1992.

Taber, K.H., Ford, J.J., Jensen, R.S., Chin, H.Y., Udden, M.M., Plishker, G.A., Contant, C.F., Hayman, L.A. Change in red blood cell relaxation in hydration: application to MR imaging of hemorrhage. *Journal of Magnetic Resonace Imaging*, vol 2, pgs 203-208, 1992.

Feldman, Z., Contant, C.F., Robertson, C.S., Narayan, R.K., Grossman, R.G. Evaluation of the Leeds prognostic score for severe head injury. *The Lancet,* vol 337, pgs 1451-1453, 1991.

Robertson, C.S., Goodman, J.C., Narayan, R.K., Contant, C.F., Grossman, R.G. The effect of glucose administration on carbohydrate metabolism after head injury. *Journal of Neurosurgery,* vol 74 pgs 43-50, 1991.

Robertson, C.S., Narayan, R.K., Goodman, J.C., Contant, C.F., Grossman, R.K. The effect of glucose administration on carbohydrate metabolism after head injury. *Journal of Neurosurgery.* vol 74, pgs 43-50, 1991.

Simpson, R.K., Contant, C.F., Fischer, D.K., Cech, D.A., Robertson, C.S., Narayan, R.K. Subarachnoid hemorrhage in an urban population: The influence of ethnic background, gender, and hypertension on outcome. *Headache Quarterly,* vol 2, pgs 201-205, 1991.

Simpson, R.K., Jr., Contant, C.F., Fischer, D.K., Cech, D.A., Robertson, C.S., Narayan, R.K. Epidemiological characteristics of subarachnoid hemorrhage in an urban population. *Journal of Clinical Epidemiolology,* vol 44 pgs 641-648, 1991.

BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME	POSITION TITLE
Lex Frieden	TIRR Senior Vice President/ Baylor College of Medicine Associate Professor of Physical Medicine & Rehab.

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
University of Tulsa	B.S.	1971	Psychology
University of Houston	M.A.	1979	Psychology

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

Research Instructor, Department of Rehabilitation, Baylor College of Medicine, Houston, Texas, 1978-1980

Director, Independent Living Research Utilization Program, The Institute for Rehabilitation and Research, Houston, Texas, 1979-1984 and 1989-present

Assistant Professor, Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, Texas, 1980-1993

Visiting Scholar, Human Service Administration Program, Cornell University, Cornell, New York, Summer, 1981

Executive Director, National Council on the Handicapped (an independent federal agency), Washington, DC, 1984-1988

Executive Director, TIRR Foundation, Houston, Texas, 1988-1991

Senior Vice President, The Institute for Rehabilitation and Research (TIRR), Houston, Texas, 1991-present

Clinical Associate Professor, Departments of Physical Medicine and Rehabilitation and Community Medicine, Baylor College of Medicine, Houston, Texas, 1993-present

SELECTED HONORS, AWARDS, AND CITATIONS:

Honored as one of America's Ten Outstanding Young Men by the U.S. Jaycees, 1983

Awarded Presidential Citations from Ronald Reagan for Meritorious Service as Executive Director of the National Council on the Handicapped, and for Distinguished Service to the President's Committee on employment of the Handicapped, 1988

Awarded Presidential Citation from George Bush for Distinguished Service to America in Promoting the Dignity, Equality, Independence and Employment of People with Disabilities, 1991

Awarded the Gold Key by the American Congress of Rehabilitation Medicine, 1994

SELECTED NATIONAL/INTERNATIONAL SCIENTIFIC COMMITTEE MEMBERSHIPS:

Chairman, National Advisory Board, National Center on Medical Rehabilitation Research, National Institute on Child Health and Human Development, National Institutes of Health, 1991-1993; Member, 1991-1995
Member, Panel on Social Security Disability Program Reform, National Academy of Social Insurance, 1993-present

JOURNAL AND EDITORIAL BOARDS:

Consulting Editor, Rural Special Education Quarterly, 1986-1994
Member, Editorial Advisory Board, Rehabilitation Education, 1987-present
Member, Editorial Board, Journal of Disability Policy Studies, 1989-present
Contributing Analyst, Health Line, 1992-present

RECENT PUBLICATIONS:

Frieden, L and Nosek, M: The Issue is--The Americans with Disabilities Act--Will It Work? American Journal of Occupational Therapy, May, 1992, Vol. 46, No. 5, pp 466-469.

Smith, Q, Wilkinson, W, Frieden, L, and Holcomb, J: The Americans with Disabilities Act ADA): New Challenges for the Health Professions. Journal of Allied Health, Summer, 1992, Vol. 21, No. 3, pp 149-159.

Fasser, C. E., Smith, Q. W., Frieden, L., Smith, L., and Holcomb, J. D: Addressing the Healthcare Needs of People with Disabilities. Journal of the American Academy of Physician Assistants, January, 1994, Vol. 7, No. 1, pp 26-32.

Wilkinson, W., Frieden, L., and Smith, Q: Implications of the Americans with Disabilities Act for the Training of Independent Living Center Personnel. Rehabilitation Education, Winter, 1994, Vol. 8, No. 1, pp 47-58.

Smith QW, Richards LK, Redd LG, and Frieden L. Improving Management Effectiveness in Independent Living Centers through Research and Training. OSERS, Winter-Spring, 1994, Vol. VI, No., 2, pp 30-36.

Smith LW, Smith QW, Richards L, Frieden L, and King K. Independent Living Centers: Moving into the 21st Century. American Rehabilitation, Spring, 1994, Vol. 20, No. 1, pp 14-22.

Smith QW, Frieden L, and Richards L. Independent Living. Encyclopedia of Disability and Rehabilitation. New York: MacMillan Reference, in press, 1995.

Smith QW, Frieden L, Nelson MR, Tilbor AG. Transition to Adulthood for Young People with Spinal Cord Injury. The Child with a Spinal Cord Injury. Chicago: American Academy of Orthopedic Surgeons, in press, 1995.

Nelson MR, Tilbor AG, Frieden L, Smith QW. Introduction to Rehabilitation: Adult Vs. Pediatric Centers. The Child with a Spinal Cord Injury. Chicago: American Academy of Orthopedic Surgeons, in press, 1995.

BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME	POSITION TITLE	BIRTHDATE (Mo., Day, Yr.)
Karen A. Hart	Assistant Professor	XXXXXXXXXXXXXX XXXXXXXXXXXXXX

EDUCATION (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Northeast Missouri State Univ., Missouri	B.S.Ed.	1971	Health & Physical Education
Univ. of Missouri - Columbia, Missouri	M.Ed.	1973	Rehabilitation Counseling
Univ. of Missouri - Columbia, Missouri	Ed.S.	1975	Adult Education Admin.
Univ. of Missouri - Columbia, Missouri	Ph.D.	1979	Higher & Adult Ed. Admin.

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

PROFESSIONAL EXPERIENCE:

Director, Pre-Vocational Evaluation, and Rehabilitation Counselor/Instructor, Department of Physical Medicine and Rehabilitation, University of Missouri Medical School, Columbia, Missouri 12/73-07/76

Director, Rehabilitation Counseling, and Rehabilitation Counselor/Instructor, Department of Physical Medicine and Rehabilitation, University of Missouri Medical School, Columbia, Missouri 07/76-09/78

Project Coordinator, "Show-Me" Regional Model Spinal Cord Injury System, and Director, Rehabilitation Counseling, Department of Physical Medicine and Rehabilitation, University of Missouri, Columbia, Missouri 09/78-10/79

Program Coordinator, Central Nervous System Trauma Center, Division of Neurosurgery, The University of Texas Medical School at Houston, Houston, Texas 11/79-11/82

Coordinator of Research, Division of Neurosurgery, The University of Texas Medical School at Houston, Houston, Texas 11/82-08/85

Assistant Professor and Director of Education, Department of Physical Medicine and Rehabilitation; Director of Training, Rehabilitation Research and Training Centers for Community Integration of Individuals with Spinal Cord Injury and Rehabilitation of Individuals with Traumatic Brain Injury, Baylor College of Medicine; Vice President for Education, The Institute for Rehabilitation and Research, Houston, Texas 09/85-present

PUBLICATIONS:

Miner, M.E., and **K.A. Wagner** (eds), Neurotrauma: Treatment, monitoring and rehabilitation and related issues, Nos. 1, 2, and 3, Stoneham, MA: Butterworth Publishers, 1985, 1987, 1989.

Fuhrer, M.J., Alfred, W.G., Cardus, D., Clearman, R.R., Lehmkuhl, L.D., Rintala, D.H., **Hart, K.A.**: Aging in relation to spinal cord injury. International Journal of Rehabilitation Research 12(1):107, 1989.

White, M.J., Rintala, D.H., **Hart, K.A.**, Young, M.E., Fuhrer, M.J.: Sexual activities, concerns and interests of men with spinal cord injury living in the community. American Journal of Physical Medicine and Rehabilitation 71(4):225-231, 1992.

Fuhrer, M.J., Rintala, D.H., **Hart, K.A.**, Clearman, R.R., Young, M.E.: Relationship of life satisfaction to impairment, disability, and handicap among persons with spinal cord injury living in the community. Archives of Physical Medicine and Rehabilitation 73(6):552-557, 1992.

Rintala, D.H., Young M.E., **Hart, K.A.**, Clearman, R.R., Fuhrer, M.J.: Social support and the well-being of persons with spinal cord injury living in the community. Rehabilitation Psychology 37(3):155-163, 1992.

Fuhrer, M.J., Rintala, D.H., **Hart, K.A.**, Clearman, R.R., Young, M.E.: Depressive symptomatology in persons with spinal cord injury who reside in the community. Archives of Physical Medicine and Rehabilitation 74(3):255-260, 1993.

Nosek, M.A., Fuhrer, M.J., Rintala, D.H., **Hart, K.A.**: Use of personal assistance services by persons with spinal cord injury: Policy issues surrounding reliance on family and paid providers. Journal of Disability Policy Studies. 4(1):89-103, 1993.

Fuhrer, M.J., Garber, S.L., Rintala, D.H., Clearman, R.R., **Hart, K.A.**: Pressure ulcers in community-resident persons with spinal cord injury: Prevalence and risk factors. Archives of Physical Medicine and Rehabilitation. 74(11): 1172-1177, 1993.

White, M.J., Rintala, D.H., **Hart, K.A.**, Fuhrer, M.J.: Sexual activities, concerns, and interests of women with spinal cord injury living in the community. American Journal of Physical Medicine and Rehabilitation. 72(6): 372-378, 1993.

Rintala, D.H., Young, M.E., **Hart, K.A.**, Fuhrer, M.J.: The relationship between the extent of reciprocity with social supporters and measures of impairment, disability and handicap in persons with spinal cord injury. Rehabilitation Psychology. 39(1): 15-27, 1994.

Young, M.E., Alfred, W.G., Rintala, D.H., **Hart, K.A.**, Fuhrer, M.J.: Vocational status of persons with spinal cord injury living in the community. Rehabilitation Counseling Bulletin. 37(3): 229-243, 1994.

White, M.J., Rintala, D.H., **Hart, K.A.**, Fuhrer, M.J.: Sexual behaviors and concerns: Comparisons of responses from men and women with spinal cord injury. Rehabilitation Nursing. 20: 1995 (in press).

Hart, K.A., Rintala, D.H.: Long-Term Outcome Following Spinal Cord Injury. NeuroRehabilitation. (in press)

BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME	POSITION TITLE
Hali A. Hartmann	Research Assistant Professor

EDUCATION (*Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.*)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
University of Louisville, Louisville, Kentucky	B.A.	1979	Biology
University of Hawaii, Honolulu, Hawaii	Ph.D.	1986	Pharmacology

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

RESEARCH AND PROFESSIONAL EXPERIENCE:

1993 - Present — Research Assistant Professor, Department of Molecular Physiology and Biophysics, Baylor College of Medicine, One Baylor Plaza, Houston, Texas 77030.

1991 - 1993 — Research Instructor, Department of Molecular Physiology and Biophysics, Baylor College of Medicine, One Baylor Plaza, Houston, Texas 77030.

1990 - 1991 — Postdoctoral Fellowship, Department of Molecular Physiology and Biophysics, Baylor College of Medicine, One Baylor Plaza, Houston, Texas 77030, Supervisor: Dr. A.M. Brown.

1987 - 1990 — Research Associate, Department of Pharmacology, Georgetown University Medical Center, Washington, D.C. 20007, Sponsors: Dr. Robert E. Sheridan, Dr. Kenneth J. Kellar.

1986 - 1987 — Postdoctoral Fellowship (NIH), Department of Physiology, Temple Univ. School of Med., Phila., PA 19140, Supervisor: Dr. Steven R. Houser.

1979 - 1988 — Graduate Student Teaching Assistant, Department of Chemistry, University of Hawaii, Honolulu, Hawaii.

HONORS AND AWARDS:

1988 — Finalist, Georgetown Interdepartmental Research Group and Sigma XI Student Research Day, Postdoctoral Division

1982 — Achievement Rewards for College Scientists Scholarship

BIBLIOGRAPHY:

A. ARTICLES IN JOURNALS:

1. Hartmann, H.A., Mazzocca, N.J., Kleiman, R.B. and Houser, S.R. Effects of phenylephrine on calcium current and contractility of feline ventricular myocytes. *Am. J. Physiol. (Heart Circ. Physiol.)* **24:** H1173-H1180, 1988.

2. Hartmann, H.A., Drewe, J.A., Kirsch, G.E., Taglialatela, M., Joho, R.H. and Brown, A.M. Exchange of conduction pathways between two related potassium channels. *Science* **251:** 942-944, 1991.

3. Kirsch, G.E., Drewe, J.A., Taglialatela, M., Hartmann, H.A. and Brown, A.M. A single non-polar residue in the deep pore of related K^+ channels acts as a K^+:Rb^+ conductance switch. *Biophys. J.* **62:**136-144, 1992.

4. Kirsch, G.E., Drewe, J.A., Hartmann, H.A., Taglialatela, M., DeBiasi, M., Brown, A.M. and Joho, R.H. Differences between the deep pores of K^+ channels determined by an interacting pair of non-polar amino acids. *Neuron* **8:**499-505, 1992.

5. Taglialatela, M., Kirsch, G.E., VanDongen, A.M.J., Drewe, J.A., Hartmann, H.A., Joho, R.H., Stefani, E. and Brown, A.M. Gating currents from a delayed rectifier K^+ channel with altered pore structure and function. *Biophys. J.* **62:**34-36, 1992.

6. DeBiasi, M., Hartmann, H.A., Drewe, J.A., Taglialatela, M., Brown, A.M. and Kirsch, G.E. Inactivation determined by a single site in K^+ pores. *Pflügers Arch.* **422**:354-363, 1993.
7. Taglialatela, M., Drewe, J., Kirsch, G.E., DeBiasi, M., Hartmann, H. and Brown, A.M. Regulation of K^+/Rb^+ selectivity and internal TEA blockade by mutations at a single site in K^+ pores. *Pflügers Arch.* **423**:104-112, 1993.
8. Kirsch, G.E., Drewe, J.A., DeBiasi, M., Hartmann, H. and Brown, A.M. Functional interactions between K^+ pore residues located in different subunits. *J. Biol. Chem.* **268**:13799-13804, 1993.
9. Hartmann, H.A., Tiedeman, A.A., Chen, S-F., Brown, A.M. and Kirsch, G.E. The effects of III-IV linker mutations on human heart Na^+ channel inactivation gating. *Circ. Res.* **75:** 114-122, 1994.
10. Kirsch, G.E., Alam, M., and Hartmann, H.A. Differential effects of sulfhydryl reagents on saxitoxin and tetrodotoxin block of voltage-dependent Na^+ channels. *Biophys. J.* **67**: 2305-2315, 1994.
11. Dumaine, R., Hartmann, H.A. and Brown, A.M. A comparison of the effects of dolasetron (MDL 73,147EF), the metabolite MDL 74,156, a racemic mixture, and the positive enantiomer of this metabolite MDL 73,405 with flecainide on human heart α-subunit of the sodium channel expressed in *Xenopus* oocytes. *Molec. Pharmacol.* Submitted, 1995.
12. Dumaine, R., Hartmann, H.A. and Kirsch, G.E. Inactivation-deficient mutant reveals two conformational states involved in the use-dependent TTX blockade of human cardiac Na^+ channel. *Am. J. Physiol.* Submitted, 1995.

B. ARTICLES IN BOOKS:

1. Hartmann, H.A. and Brown, A.M. Identification of the amino acids forming the conduction pathway in potassium channels. In: *Molecular and Cellular Biology.* M. Wolfe, ed. (Belmont, CA.: Wadsworth Publishing Co.), pp. 198-200, 1993.
2. Drewe, J.A., Hartmann, H.A. and Kirsch, G.E. K^+ channels in mammalian brain: A molecular approach, in Narahashi, T.(ed): *Methods in Neuroscience*, Vol. 19., pp. 243-260, San Diego, Academic Press; 1994.

C. ABSTRACTS:

1. Hartmann, H.A. and Bailey, L.E. The effect of ethanol and stress on the extracellular matrix of cardiac muscle cells of hamsters. *The Pharmacologist* **24:** 228, 1982.
2. Hartmann, H.A. and Bailey, L.E. The effect of exercise on sarcolemmal glycosylation. *Fed. Proc.* **43:** 1984.
3. Hartmann, H.A. and Houser, S.R. The effect of phenylephrine on calcium current in isolated feline myocytes. *Biophys. J.* **51:** 199a, 1987.
4. Bahinski, A., Hartmann, H.A. and Houser, S.R. Two TTX-insensitive inward currents in feline ventricular myocytes. *Biophys. J.* **51:** 188, 1987.
5. Kleiman, R.B., Hartmann, H.A. and Houser, S.R. Calcium currents in hypertrophied feline myocytes. *Fed. Proc.* **46:** 336, 1987.
6. Houser, S.R., Bahinski, A., duBell, W.H., Duthinh, V., Hartmann, H.A., Kleiman, R.B. and Philips, C. Electrical properties of isolated feline myocytes. *Biology of Isolated Adult Cardiac Myocytes Symposium*, Pacific Grove, California, September 22-25, 1987.
7. Hartmann, H.A. and Sheridan, R.E. Divalent cation modulation of nicotinic receptors channels. *Biophys. J.* **53:** 359a, 1988.
8. Hartmann, H.A., Taglialatela, M., Drewe, J.A. and Brown, A.M. Amino acid determinants of internal TEA blockade in KV2.1. *Biophys. J.* **61:**870, 1992.
9. DeBiasi, M., Taglialatela, M., Hartmann, H.A., Drewe, J.A., Brown, A.M. and Kirsch, G.E. Pore mutations control voltage-independent gating transitions in a chimeric K^+ channel. *Biophys. J.* **61:**869, 1992.
10. Taglialatela, M., Drewe, J.A., Hartmann, H., Kirsch, G.E. and Brown, A.M. Influence of side chain charge and size on an amino acid determinant of K^+/Rb^+ conductance in a voltage-sensitive K^+ channel. *Biophys. J.* **61:**865, 1992.
11. Taglialatela, M., Payne, J.A., Hartmann, H. and Brown, A.M. Rescue of lethal subunits into functional heteromultimeric voltage-dependent K^+ channels. *Biophys.J.* **64**:A225, 1993.
12. DeBiasi, M., Kirsch, G.E., Drewe, J.A., Hartmann, H.A. and Brown, A.M. Cesium selectivity conferred by histidine substitution in the pore of the potassium channel Kv2.1. *Biophys. J.* **64**:A341, 1993.
13. Hartmann, H.A., Joho, R.H., and Aryee, D. Primary structure and expression of a variant of human brain Type II sodium channel cDNA. *Society for Neuroscience* **20**:63, 1994.

BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME	POSITION TITLE
Howland, Carol A.	Assistant Professor

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Indiana Univ. of PA, Indiana, PA	BA	1975	English and Psychology
Syracuse Univ., Syracuse, NY	MA(course work)	1977-1978	Literacy Communications
Amer. Med. Writers Assoc., Bethesda, MD	PostGrad.	1984	Biomed. Communications
Univ. of TX/Sch. of Publ. Hlth., Houston, TX	(MPH)	In progress	Hlth. Svcs. Organization

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

EMPLOYMENT

1979-1982 **Scientific Editor**, Department of Psychiatry, Baylor College of Medicine, Houston, Texas.

1982-1987 **Research Instructor**, Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, Texas.

1984-1987 **Consultant**, Program and Publications, First and Second Research Symposia on the Late Effect of Poliomyelitis.

1988-1990 **Research Manager and Medical Writer**, Cardiovascular Surgery of Texas, Houston, Texas.

1990 **Research Associate**, Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, Texas.

1992-1994 **Research Instructor**, Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, Texas.

1994-Present **Assistant Professor**, Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, Texas.

1994-Present **Associate Director**, Center for Research on Women with Disabilities, Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, Texas.

HONORS

1982-1987 Editorial Board, Current Concepts in Rehabilitation Medicine

1986-1987 Editorial Board, American Medical Writers Assoication Journal

1985-1986 Board of Directors, Southwest Chapter, American Medical Writers Association

1986-1987 Board of Directors, National, American Medical Writers Association

1986-1987 President, Southwest Chapter, American Medical Writers Association

1987-1988 Award of Excellence, STC International Technical Publications Competition

PUBLICATIONS - Howland, Carol A.

Howland, C.A., Nosek, M.A., Rossi, C.D., and Walden, E., (1993). Profiles of independent living centers that provide services to rural areas: Preliminary report. Houston: I.L.R.U., pp. 1-9.

Nosek, M.A., and Howland, C.A., (1993). Personal assistance services: The hub of the policy wheel for community integration of people with severe physical disabilities. Policy Studies Journal, 21, 789-800.

Howland, C.A., Walden, E., and Nosek, M.A., (1993). Independent living and private sector rehabilitationists: A dynamic partnership for implementing the ADA. NARPPS Journal.

Howland, C.A., and Nosek, M.A., (1993). A qualitative approach to studying sexuality among women with physical disabilities. Women's Health Forum, 3, 3.

Nosek, M.A., Howland, C.A., Young, M.E., et al (1993) (accepted). Wellness models and sexuality among women with physical disabilities. Journal of Applied Rehabilitation Counseling.

Nosek, M.A., Fuhrer, M.J., and Howland, C.A., (1992). The role of independent living centers in delivering rehabilitation services to rural communities. American Rehabilitation, 18, 2-6.

Nosek, M.A., Fuhrer, M.J., and Howland, C.A., (1992). Independence among people with disabilities. II. Personal independence profile. Rehabilitation Counseling Bulletin, 36, 21-36.

Nosek, M.A., Zhu, Y., and Howland, C.A., (1992). The evolution of independent living programs. Rehabilitation Counseling Bulletin, 35, 190-199.

Nosek, M.A., Davidson, K., Zhu, Y., and Howland, C.A., (1992). Relationships between compliance with federal standards for independent living centers and diversity and amount of funding. Rehabilitation Counseling Bulletin, 35, 174-189.

BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME	POSITION TITLE
Gabor Jurida	Postdoctoral Fellow

EDUCATION (*Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.*)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
SZEGED Medical School, Hungary	M.D.	1986	Medicine

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

RESEARCH AND PROFESSIONAL EXPERIENCE:

1984 - 1986	Clinical Research, SZEGED Medical School, Department of Surgery, Hungary
1985 - 1986	Rotating Internship, Forchheim Krankenhaus, Germany, Ja'nos Hospital, Budapest, Hungary
1991 - 1993	Pediatric Management, Children's Clinic, Dublin, Virginia
1994 - Present	Postdoctoral Fellowship, Baylor College of Medicine, Department of Molecular Physiology and Biophysics, Houston, TX

HONORS AND AWARDS:

1986	Cum Laude, Medical Degree; SZEGED Medical School

PROFESSIONAL MEMBERSHIPS:

Hungarian Association of Physicians

Thesis: Symptomatology of the Surgical Abdomen, 1986

BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME	POSITION TITLE
Trilok Nath Monga, M.D.	Chief, Physical Medicine and Rehabilitation Professor, Physical Medicine & Rehabilitation

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Agra University, India	B.Sc.	1955	Biology
Lucknow University, India	M.B.B.S	1960	Medicine
Royal College of Physician & Surgeons, Ireland	M.R.C.P.	1971	PM&R
Royal College of Physician & Surgeons, Canada	F.R.C.P.	1975	PM&R

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. If the list of publications in the last three years exceeds two pages, select the most pertinent publications. DO NOT EXCEED TWO PAGES.

Academic Appointments:

1976-1981	Assistant Professor, Dept. PM&R, Queen's University, Canada
1981-1985	Associate Professor, Dept. PM&R, Queen's University, Canada
1985-1987	Professor, Dept. PM&R, Queen's University, Canada
1987-1991	Professor & Asst. Chairman, Dept. PM&R, Northwestern University Medical School, Chicago, Illinois
1992-present	Professor, Dept. PM&R, Baylor College of Medicine, Houston, Texas

Relevant Publications:

Monga TN, Jacksic T: Acupuncture in phantom limb pain. Arch Phys Med Rehabil 62:229-231, 1981

Beidermann HJ, Monga TN: Relaxation oriented EMG biofeedback with back pain patients: evaluation of paraspinal muscles activity. Clinical Biofeedback and Health 8(2):119-123, 1985.

Biedermann HJ, Monga TN, Shanks GL, McGhie A: The classification of back pain patients: functional versus organic. J Psychosomatic Res 30(3):273-276, 1986.

Lapeer GL, Monga TN: Myofacial trigger point acupuncture in relieving chronic pain after endarterectomy. Canadian Family Physician 32:1955-1958, 1986.

Walmsley RP, Monga TN, Prouix M: Effect of transcutaneous nerve stimulation on sensory nerve conduction velocity: A pilot project. Physiotherapy Practice 2:117-120, 1986.

Beidermann HJ, McGhie A, Monga TN, Shanks GL: Perceived and actual control in EMG treatment of back pain. Behav Res Ther 25:137-147, 1987

Lapeer GL, Monga TN: Pain secondary to acupuncture therapy. Cranio 6:188-190, 1988

Anderson SS, Press JM, Jantra P, Monga TN: Saphenous nerve-ten year history of leg pain: a case study and review. Arch Phys Med Rehabil 9:70, 1989.

Biedermann HJ, Inglis J, Monga TM, Shanks GL: Differential treatment responses on somatic pain indicators after EMG biofeedback training in back pain patients. Int J Psychosom 36:53-57, 1989.

Philip PA, Philip M, Monga TN: Reflex sympathetic dystrophy in central cord syndrome. Paraplegia 28:48-54, 1990.

Chen D, Philip M, Philip PA, Monga TN: Cardiac pacemaker inhibition by transcutaneous electrical nerve stimulation. Arch Phys Med Rehabil 71:27-30, 1990

Jantra P, Monga TN, Press JM, Gravais B: Management of apraxic gait in stroke patient. Arch Phys Med Rehabil 73:95-97, 1992.

Press JM, Monga TN, Philip N, Katz R: Intra-operative monitoring of an unusual brachial plexus tumor. Arch Phys Med Rehabil 73:297-299, 1992.

Marciniak C, Monga TN: Changes in medical stability upon admission to a rehabilitation facility. Arch Phys Med Rehabil 74:1157-1160, 1993.

Monga TN, Tan G, Ostermann HJ, Grabois M: Sexuality in patients with chronic pain. Proceedings, IRMA VII, A43, 1994.

Monga TN, Zimmermann K, Darouiche R, Lawrence S: Proceedings, IRMA, VII, A77, 1994.

Zimmermann KP, Monga TN, Darouiche RO, Lawrence SA: Post-Stroke autonomic nervous system function: Palmar sympathetic skin responses thirty or more days after cerebrovascular accident. Arch Phys Med Rehabil 76:250-256, 1995.

Zaweed MM, Grana EA, Glennon TP, Monga TN, Mirabi B: Neuromuscular adaptations during 30 days of cast-immobilization and head- down bed rest. J Gravit Physiol 2:1995 (in press)

Biedermann HJ, McGie A, Monga TN, Shanks GL: Electromyographic biofeedback treatment of patients with back pain: the contribution of perceived and actual control of muscle tension. Behav Ther Res (in press).

Tan G, Snow-Turek L, Monga TN, Thornby J: Is the Multidimensional pain inventory sufficient in the assessment of chronic pain patients. Pain (in press).

CONSULTANT

BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME	POSITION TITLE
Jan F.M. Post	Assistant Professor

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
State University of Groningen, Netherlands	Kandidaats	1971	Chemistry
State University of Groningen, Netherlands	Doctoral	1975	Physical Chemistry & Economics
State University of Groningen, Netherlands	Ph.D.	1981	Biophysical Chemistry

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

1975 - 1977 Predoctoral fellowship, Laboratory of Physical Chemistry, University of Leeds, UK

1977 - 1981 Scientific Assistant, Laboratory of Physical Chemistry, University of Groningen, The Netherlands

1981 - 1984 Post-doctoral Research Associate, Dept. of Biology, Carnegie-Mellon University, Pittsburgh, PA

1984 - 1987 Research Assistant Professor, Dept. of Medicinal Chemistry, University of Pittsburgh, PA

1987 Consulting Scientist, Dept. of Chemistry, State University of New York, Stony Brook, NY

1987 Visiting Scientist, Dept. of Chemical and Petroleum Engineering, University of Pittsburgh, PA

1987 - Date Assistant Professor, Dept. of Human Biological Chemistry & Genetics, University of Texas Medical Branch, Galveston, TX

1993 - Date Adjunct Assistant Professor, Institute of Biosciences and Bioengineering, Rice University, Houston, TX

SELECTED PUBLICATIONS:

1. Post, J.F.M., Cottam, P.F., Simplaceanu, V. and Ho, C. A Fluorine-19 Nuclear Magentic Resonance Study of Histidine Binding Protein-J of *Salmonella Typhimurium*. J. of Molecular Biology 179:729-743, 1984.

2. Post, J.F.M., Cook, B.W., Dowd, S.R., Lowe, I.J. and Ho, C. A Fluorine-19 Multiple Pulse Nuclear Magnetic Resonance Investigation of Fluorine-19 Labeled Phospholipids. Biochemistry 23:6138-6141, 1984.

3. Pettegrew, J.W., Post, J.F.M., Withers, G., Panchalingam, K. and Woessner, D.E. A ^{7}Li-NMR Study of Normal Human Erythrocytes. J. Magnetic Resonance 71:504-519, 1987.

RESEARCH AND PROFESSIONAL EXPERIENCE CONTINUED

4. Post, J.F.M., Panchalingam, K., Withers, G., Woessner, D.E. and Pettegrew, J.W. A ^{7}Li-NMR Study of Human Erythrocytes. Ann. N.Y. Acad. Sci., 508:480-482, 1987.

5. Pettegrew, J.W., Withers, G., Panchalingam, K. and Post, J.F.M. Considerations for Brain pH Assessment By ^{31}P NMR. Magnetic Resonance Imaging 6:135-142, 1988.

6. Post, J.F.M. and Simplaceanu, V. NMR Determination of the CF_2 Order Parameter Tensor in a Lyotropic Liquid Crystal. J. Chemical Physics 89:7038-7039, 1988.

7. Marcelin, G., Stockhausen, N.J., Post, J.F.M. and Schutz, A. Dynamics and Ordering of Intercalated Water in Layered Metal Hydroxides. J. Physical Chemistry 93:4646-4650, 1989.

8. Post, J.F.M. Cation NMR. ^{7}Li-and ^{23}Na-NMR Results Obtained With Human Erythrocytes. Scanning Microscopy 3:877-886, 1989.

9. Post, J.F.M. and Baum, E. ^{31}P Nuclear Magnetic Resonance Studies of Growth Inhibition and Dexamethasone Resistance in Human Leukemic Cells. Cancer Letters 51:157-162, 1990.

10. Post, J.F.M. and Wilkinson, D.A. ^{7}Li-NMR and DSC Investigations of Lithium-Phospholipid Interactions. J. Colloid and Interface Science 143:174-179, 1991.

11. Post, J.F.M., Baum, E. and Ezell, E., ^{13}C-NMR Studies of Glucose Metabolism in Human Leukemic CEM-C7 and CEM-C1 Cells. Magnetic Resonance in Medicine, 23:356-366, 1992.

12. Jackson, G.R., Werrbach-Perez, K., Ezell, E.L., Post, J.F.M., and Perez-Polo, J.R. Nerve Growth Factor Effects on Pyridine Nucleotides After Oxidant Injury of Rat Pheochromocytoma Cells. Brain Research, 592:239-248, 1992.

13. Post, J.F.M. and Varma, R.S. Growth Inhibitory Effects of Bioflavonoids and Related Compounds on Human Leukemic CEM-C1 and CEM-C7 Cells Cancer Letters, 67:207-213, 1992.

14. Adebodun, F. and Post, J.F.M. ^{19}F-NMR Determination of Cell Volume and Membrane Potential During Programmed Cell Death in Human Leukemic Cells. Journal of Cellular Physiology 154:199-206, 1993.

15. Adebodun, F. and Post, J.F.M. Bulk Magnetic Susceptibility Induced Broadening in the ^{19}F-NMR of Suspended Leukemic Cells. NMR in BioMedicine 6:125-129, 1993.

16. Kao, T.L., Meyer, W.J., and Post, J.F.M. Inhibitory Effects of Ascorbic Acid on Growth of Leukemic and Lymphoma Cell Lines. Cancer Letters 70:101-106, 1993.

17. Adebodun, F. and Post, J.F.M. ^{31}P NMR Characterization of Cellular Metabolism During Dexamethasone Induced Apoptosis in Human Leukemic Cell Lines. Journal of Cellular Physiology 158:180-186, 1994.

18. Adebodun, F. and Post, J.F.M. The Role of Intracellular Free Ca(II) and Zn(II) in Dexamethasone Induced Apoptosis and Dexamethasone Resistance in Human Leukemic Cell lines. J. of Cellular Physiology 163:80-86, 1995.

19. Post, J.F.M. Local order in Protein Solutions. Journal of Biological Physics (In Press).

BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME	POSITION TITLE
Michael M. Priebe, M.D.	Assistant Professor Assistant Chief, SCI Service, VAMC

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Washington University, St. Louis, MO	A.B.	1983	
University of Utah, Salt Lake City, UT	M.D.	1987	Medicine
St. Joseph Mercy Hospital, Ann Arbor, MI	Internship	1988	Medicine
University of Michigan Hospitals, Ann Arbor, MI	Residency	1991	Physical Medicine and Rehabilitation

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

PROFESSIONAL EXPERIENCE

1991-present Assistant Professor, Baylor College of Medicine, Department of Physical Medicine and Rehabilitation, Houston, TX

1991-present Assistant Chief, Spinal Cord Injury Service, Veterans Affairs Medical Center, Houston, TX

RESEARCH SUPPORT

The Assessment of Functional Status in Persons with Spinal Cord Injury Living in the Community; Research Enrichment Program for Physiatrists/National Institute on Disability and Rehabilitation Research; Principal Investigator, 1991-1992, $1000 grant.

Objective Assessment of Spasticity in Spinal Cord Injury, Department of Veterans Affairs, Co-investigator, 1993-1995, $308,000 grant.

Rehabilitation Research and Training Center in Community Integration for Individuals with Spinal Cord Injury at Baylor College of Medicine and The Institute for Rehabilitation and Research, Houston, TX, National Institute on Disability and Rehabilitation Research, 1994-1999, $3,250,000 grant.

Co-Investigator, Project R-1 Community Integration of Persons with Spinal Cord Injury: A Two Panel Study

Co-Investigator, Project R-2 Reintegration into the Community of Persons with Recent Spinal Cord Injury: A Longitudinal Study

Co-Principal Investigator, Project R-3 Nutritional Status of Persons with Spinal Cord Injury: Relationship to Community Integration.

Faculty, Training Project T-6 Rehabilitation Clinical Research Training Course

Faculty, Training Project T-7 Sexuality after SCI: Understanding the effects of attitudes on information and dissemination

RESEARCH SUPPORT (CONT.)

Faculty, Training Project T-15 Community Integration for Persons with Spinal Cord Injury: A National Conference

Therapeutic Benefits from Marijuana Use in Persons with Spinal Cord Injury; Department of Physical Medicine and Rehabilitation Preliminary Research Grant, Principal Investigator, 1994-1995, $900 grant.

HONORS

1991-1992 Participant in the "Research Enrichment Program for Physiatrists" offered by the Missouri Arthritis Rehabilitation Research Center, funded by NIDRR

May, 1993 Second Place Ribbon for Poster Presentations, American Spinal Injury Association Annual Meeting, San Diego, CA. Priebe MM, Fuhrer MJ, Rintala DH: Community evaluation of functional independence in persons with spinal cord injury using an occasion-specific approach.

1993 Outstanding Teacher of the Year Award, Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, TX

1993, 1994 Teaching Award for Medical Aspects of Disability Course, Department of Occupational Therapy, Texas Womans University

PUBLICATIONS

Udall KS, Priebe MM: The impact of family practice literature of record on other medical literature. J Fam Pract 1985; 21:397-399

Priebe MM, Davidoff G, Lampman RM: Exercise testing and training in the patient with peripheral vascular disease and lower extremity amputation. In: Rehabilitation Medicine--Adding Life to Years [Special Issue]. West J Med 1991;154:598-601.

Priebe MM, Waring WP: The interobserver reliability of the revised American Spinal Injury Association standards for neurological classification of spinal injury patients. Am J. Phys Med Rehabil 1991;70:268-270.

Priebe MM, Werner RA, Davidoff GN: The diagnosis and treatment of reflex sympathetic dystrophy syndrome of the upper extremity. J Back Musculoskel Rehabil 1992;2(2):35-45.

Werner RA, Priebe MM, Davidoff GN: Reflex sympathetic dystrophy associated with hemiplegia. NeuroRehabil 1992;2(2):16-22.

Werner RA, Priebe MM: Stroke during pregnancy. Topics in Stroke Rehabilitation 1994 1(2):41-47.

Priebe MM, Rintala DH: Functional Assessment in a Community Setting. Topics in Stroke Rehabilitation 1994;1(3):16-29.

BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME	POSITION TITLE
Diana H. Rintala	Assistant Professor

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Ohio University, Athens, Ohio	B.S.Ed.	1961	Elementary Education
University of Houston, Houston, Texas	M.A.	1980	Social Psychology
University of Houston, Houston, Texas	Ph.D.	1982	Social Psychology

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

PROFESSIONAL EXPERIENCE:

3/83 - 7/84	Instructor in Psychology Baylor College of Medicine, Houston, TX
7/84 - present	Assistant Professor in Psychology Baylor College of Medicine, Houston, TX
3/85 - 8/89	Director of Behavioral Ecology Research Project The Institute for Rehabilitation and Research, Houston, TX
8/89 - present	Director of Rehabilitation Services Research The Institute for Rehabilitation and Research, Houston, TX
1/94 - present	Research Director of Rehabilitation Research and Training Center in Community Integration for Individuals With Spinal Cord Injury
1/95 - present	Co-Director of Rehabilitation Research and Training Center in Community Integration for Individuals With Spinal Cord Injury

RESEARCH DIRECTED OR CO-DIRECTED:

1/88 to 12/93	Principal investigator: The Influence of Caregiver Well-Being on Outcomes for Persons with Spinal Cord Injury. (NIDRR)
8/87 to 7/93	Co-director of principal mentorship: Rehabilitation Research Career Development Project. (NIDRR)
10/92 to present	Co-Principal Investigator: Psychosocial Behavior of Women with Physical Disabilities (NIH)
1/94 to present	Principal Investigator: Service Dogs: Effect on the Community Integration of Persons with Spinal Cord Injury. (NIDRR)
1/94 to present	Principal Investigator: Abilities Exchange: A Time Dollars Volunteer Program to Enhance Community Integration. (NIDRR)
1/94 to present	Co-Principal Investigator: Reintegration into the Community by Persons with Recent Spinal Cord Injury: A Longitudinal Study. (NIDRR)
1/94 to present	Co-Principal Investigator: Community Integration of Persons with Spinal Cord Injury: A Two Panel Study. (NIDRR)

PUBLICATIONS:

Fuhrer, M. J.; Rintala, D. H.; Hart, K. A.; Clearman, R. R.; & Young, M. E. (1992). Relationship of life satisfaction to impairment, disability, and handicap among persons with spinal cord injury living in the community. Archives of Physical Medicine and Rehabilitation, 73(6), 552-557.

Rintala, D. H.; Young, M. E.; Hart, K. A.; Clearman, R. R.; & Fuhrer, M. J. (1992). Social support and the well-being of persons with spinal cord injury living in the community. Rehabilitation Psychology, 37(3), 155-163.

White, M. J.; Rintala, D. H.; Hart, K. A.; Young, M. E.; & Fuhrer, M. J. (1992). Sexual activities, concerns, and interests of men with spinal cord injury. American Journal of Physical Medicine and Rehabilitation, 71(4), 225-231.

Bates, S.; Spencer, J. C.; Young, M. E.; & Rintala, D. H. (1993). Assistive technology and the newly disabled adult: Adaptation to wheelchair use. American Journal of Occupational Therapy, 47(11), 1014-1021.

Fuhrer, M. J.; Rintala, D. H.; Hart, K. A.; Clearman, R. & Young, M. E. (1993). Depressive symptomatology in persons with spinal cord injury who reside in the community. Archives of Physical Medicine and Rehabilitation, 74(3), 255-260.

Fuhrer, M. J.; Garber, S. L.; Rintala, D. H.; Clearman, R. R.; & Hart, K. A. (1993). Pressure ulcers in community-resident persons with spinal cord injury: Prevalence and risk factors. Archives of Physical Medicine and Rehabilitation, 74(11), 1172-1177.

Nosek, M.; Fuhrer, M. J.; Rintala, D. H.; & Hart, K. A. (1993). The use of personal assistance services among people with spinal cord injury: Policy issues surrounding reliance on family and paid providers. Journal of Disability Policy Studies, 4(1), 89-103.

White, M. J.; Rintala, D. H.; Hart, K. A.; & Fuhrer, M. J. (1993). Sexual activities, concerns, and interests of women with spinal cord injury living in the community. American Journal of Physical Medicine and Rehabilitation, 72(6), 372-378.

Priebe, M.; & Rintala, D. H. (1994). Functional assessment in a community setting. Topics in Stroke Rehabilitation, 1(3), 16-29.

Rintala, D. H.; Young, M. E.; Hart, K. A.; & Fuhrer, M. J. (1994). The relationship between the extent of reciprocity with social supporters and measures of impairment, disability, and handicap in persons with spinal cord injury. Rehabilitation Psychology, 39(1), 15-27.

White, M. J.; Rintala, D. H.; Hart, K. A.; & Fuhrer, M. J. (1994). A Comparison of the sexual concerns of men and women with spinal cord injuries. Rehabilitation Nursing Research, 3(2), 55-61.

Spencer, J.; Young, M. E.; Rintala, D., & Bates, S. (1995). Socialization to the culture of a rehabilitation hospital. American Journal of Occupational Therapy, 49(1), 53-62.

Young, M. E.; Rintala, D. H.; Rossi, C. D.; Hart, K. A.; Clearman, R. R.; & Fuhrer, M. J. (in press). Prevalence and correlates of alcohol and marijuana use in a community-based sample of persons with spinal cord injury. Archives of Physical Medicine and Rehabilitation.

Hart, K. A.; Rintala, D. H.; Rossi, C. D.; & Fuhrer, M. J. (in press). Educational interest of persons with spinal cord injury. Rehabilitation Nursing.

Hart, K. A.; & Rintala, D. H. (in press). Long term outcomes following spinal cord injury. NeuroRehabilitation.

Nosek, M. A.; Howland, C. A.; Young, M. E.; Georgiou, D.; Rintala, D. H.; Foley, C. C.; Bennett, J. L.; and Smith, Q. (in press). Wellness models and sexuality among women with physical disabilities. Journal of Applied Rehabilitation Counseling.

Priebe, M. M.; and Rintala, D. H. (in press). Spinal cord injury. In Arthur E. Dell-Orto and Robert P. Marinelli (Eds.) Encyclopedia of Disability and Rehabilitation. New York: MacMillan.

Rintala, D. H. (in press). Pressure ulcers: Quality of life considerations. Advances in Wound Care.

Rintala, D. H.; Young, M. E.; Spencer, J. C.; & Bates, P. S. (in press). Family relationships and adaptation to spinal cord injury: A qualitative study. Rehabilitation Nursing.

BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME	POSITION TITLE
Jay E. Rosenfeld	Assistant Professor, Physical Medicine & Rehabilitation Baylor College of Medicine

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Bowdoin College, Brunswick, Maine	A.B.	1979	Russian History
University of Pennsylvania, Philadelphia, PA			Post-Baccalaureate, Pre-health
Boston University School of Medicine	M.D.	1989	Medicine

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

Employment

1994-Present Assistant Professor, Division of Restorative Neurology and Human Neurobiology and Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, Texas

Post Graduate Training

1993-1994 Post-Doctoral Fellow, Division of Restorative Neurology and Human Neurobiology, Baylor College of Medicine, Houston, Texas; Mentor: Milan R. Dimitrijevic, M.D., D.Sc.

1993-1993 Chief Resident, Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, Texas

1990-1992 Resident, Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, Texas

1989-1990 Intern, Department of Internal Medicine, Faulkner Hospital, Boston, Massachusetts

Honors and Awards

1993 Oliver Smith, M.D., Resident Achievement Award, Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, Texas

1992 Resident Appreciation Award, The Institute for Rehabilitation and Research, Houston, Texas

1988 Alpha Omega Alpha Honor Society, Boston University School of Medicine

1978-1979 Bowdoin College Dean's List

Certification and Licensure

1990 Diplomate, National Board of Medical Examiners

1990 State of Vermont, Permanent Medical License

1994 Diplomate, American Board of Physical Medicine and Rehabilitation

1994 State of Texas, Permanent Medical License

1995 Diplomate, American Board of Electrodiagnostic Medicine

Professional Societies

American Academy of Physical Medicine and Rehabilitation
Association of Academic Physiatrists
American Association of Electrodiagnostic Medicine
Texas Medical Society
Southern Pain Society
American Pain Society

Abstracts/Presentations

Rosenfeld JE, Garden FH. Isolated axillary neuropathy in the wheelchair dependent population. Poster presentation at the American Academy of Physical Medicine and Rehabilitation National Convention, Washington, DC, October 1991.

Rosenfeld JF, Garden FH. Interdepartmental education and collaboration in the academic setting. Poster presentation at the Association of Academic Physiatrists National Meeting, Orlando, Florida, February 1992.

Rosenfeld JE, Tuel SM, Leis AA, Delapesse JS, Dimitrijevic MS. Control of spasmodic torticollis with subsensory threshold electrical stimulation. Poster presentation at the American Academy of Physical Medicine and Rehabilitation National Convention, San Francisco, California, November 1992.

Rosenfeld JE, Tuel SM, Shrwood AM, Dimitrijevic MR. Comprehensive neurophysiologic classification based on residual supraspinal control after spinal cord injury. Forum presentation at the American Congress of Physical Medicine and Rehabilitation, San Francisco, California, November 1992.

Rosenfeld JE. Neurophysiologic models of motor control. Grand Rounds, Baylor College of Medicine, Houston, Texas, May 1992.

Rosenfeld JE. Obstetrical brachial plexus injuries and intraoperative EMG monitoring. Panel co-moderator, Academy of Physical Medicine and Rehabilitation National Convention, San Francisco, California, November 1992.

Rosenfeld JE. Transcranial magnetic stimulation and motor evoked potentials. Grand Rounds, Baylor College of Medicine, February 1993.

Rosenfeld, JE. Evaluation and treatment of neurogenic bladder. Grand Rounds, M.D. Anderson Cancer Center, Department of Neuro-oncology, Houston, Texas June 1993.

Rosenfeld JE, Patcharawinol S-A, Dimitrijevic MR. The supraspinal contribution to the spasticity syndrome in spinal cord injury: Spasticity as disordered motor control. Poster presentation at IRMA Meeting, Washington, DC, April 1994.

Rosenfeld JE, Stokic DS, Dimitrijevic, MS. Mesh glove whole hand stimulation after stroke: Results of a pilot study. Poster presentation at IRMA Meeting, Washington, DC, April 1994.

Rosenfeld JE. The supraspinal contribution to the spasticity syndrome. Restorative Neurology Course. Baylor College of Medicine, Houston, Texas, October 1994.

Publications

Rosenfeld JE, Garden FH (1993). Interdepartmental education and collaboration in the academic setting. *American Journal of Physical Medicine and Rehabilitation*. 73:3.

Rosenfeld JE, Sherwood AM, Campos R, Dimitrijevic MR (1995). Motor control under ???? brain influence: Effects of intrathecal morphine in SCI. *American Journal of Physical Medicine and Rehabilitation*, submitted for publication.

BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME	POSITION TITLE
Vladimir I. Slesarev	Postdoctoral Fellow

EDUCATION (*Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.*)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Lugansk Medical Institute, Ukrainian SSR	M.D.	1980	Medicine
Institute of Chemical Physics, USSR Academy of Science, Moscow State University	Ph.D.	1986	Medical Physics

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

RESEARCH AND PROFESSIONAL EXPERIENCE:

Institute of Medical Radiology Academy of Medical Sciences, Obninsk
December 1986 - November 1989

Indiana University Medical School
Riley Hospital for Children
Department of Radiology -- 1990

Baylor College of Medicine
Department of Molecular Physiology & Biophysics
Postdoctoral Fellowship -- 1991-1994

HONORS AND AWARDS:

Honor diploma of physician, 1980
Soros Foundation, New York, 1989
International Union against Cancer, Geneva, 1989
Welch Foundation, Houston, Texas, 1991
Credit Swiss, Spectrospin, Switzerland, 1991
UNESCO, Mexico City, 1991

PROFESSIONAL MEMBERSHIPS:

Scientific Council of Diagnostic Imaging, Academy of Medical Sciences: - 1989
American Institute of Ultrasound in Medicine: - 1992

BIBLIOGRAPHY:

1. V. Slesarev, A.F. Tsyb, C.F. Hazlewood. On file (1995). Assigned to Baylor College of Medicine.
2. Slesarev, V.I., Spujut, H., Herrick, R., Hazlewood, C.F. NMR study of aging process in the intervertebral disk. *European Spine Journal*, In press 1995.
3. Hazlewood, C.F., Herrick, R., Slesarev, V.I., Spujut, H. NMR spectroscopic and imaging study of human intervertabral disk. *Proc. Soc. Magn. Res. Meeting*, 1994.
4. Slesarev, V.I., Komarevtzev, V.N., Fediev, E.B. Transvaginal high-resolution ultrasonography in the diagnosis of malignant urinary bladder and rectum tumors. *Japan J. Med. Ultrasonics* **6**, 31-34, 1992.
5. Berdov, B.A., V.I. Slesarev, E.B. Fediev. Ultrasound diagnosis of rectum tumors. *Voprosy Oncologii* **36(3)**, 346-351, 1990.
6. Slesarev, V.I. Protective magnetic resonance reactivity of lymphatic system in cancer patients. In Proc. Int. Symp. "Tissue Characterization in MR Imaging", Wiesbaden, West Germany, p. 67, April 17-22, 1989.
7. Tsyb, A.F., V.I. Slesarev. High resolution endosonography in diagnosis of tumors of small pelvis. In Proc. 17th Int. Congr. Radiol, Paris, p. 321, July 1-8, 1989.
8. Tsyb, A.F., V.I. Slesarev. NMR-investigation of lymph nodes and lymph in the diagnosis of malignant tumors. In Proc. 2nd European Congr. NMR Biol. Med., West Berlin, p. 203, June 23-26, 1988.
9. Tsyb, A.F., V.I. Slesarev, V.N. Komarevtzev. Transvaginal longitudinal ultrasonography in diagnosis of carcinoma of urinary bladder. *J. Ultrasound Med.* **7**, 4, 1988 (USA).
10. Tsyb, A.F., V.I. Slesarev. Magnetic resonance imaging in otorynolaryngology. *Vestnik Otorynolaringologii* **2**, 85-88, 1988.
11. V.I. Slesarev, V.N. Komarevtzev. Transvaginal longitudinal echography of urinary bladder. *Voprosy Oncologii* **9**, 1111-1114, 1988.
12. Tsyb, A.F., V.I. Slesarev, G.N. Grishin, O.N. Kariakin, V.N. Dunchik. Stellenwert der transrektalen und transvaginalen Ultraschalltomographie mit einem electronischen Linearscanner bei der Stadieneinteilung von Harnblasentumoren. *Radiologe* **27**, 314-319, 1987 (FRG).
13. Jushmanov, V.E., A.L., Pluish, A.F. Tsyb, V.I. Slesarev, V.I. Janzen, L.A. Sibeldina. NMR imaging of human lymph nodes. *Lymphology* **20**, 99-104, 1987 (USA).

BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME	POSITION TITLE
Carlos Vallbona, M.D.	Distinguished Service Professor Chairman, Department of Community Medicine

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
U of Barcelona, Spain	B.A., B.S.	1944	Humanities & Science
U of Barcelona School of Medicine, Spain	M.D.	1950	Medicine
School of Child Health, Barcelona, Spain	M.P.H. (Equiv.)	1952	Child Health Physician

RESEARCH AND PROFESSIONAL TRAINING: Concluding with present position, list, in chronological order, previous employment, experience and honor. Key personal include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personal typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

EXPERIENCE

1952-1956 Pediatric Residency Training, University of Paris (France), U of Louisville, KY, and Baylor College of Medicine, Houston, Texas
1956-1958 Instructor of Pediatrics and Physiology, Baylor College of Medicine (BCM), Houston, Texas
1957-1958 Instructor of Rehabilitation, BCM, Houston, Texas
1958 American Board of Pediatrics
1958-1962 Assistant Professor of Pediatrics, Physiology and Rehabilitation, BCM, Houston, Texas
1962-1963 Director of Education, Texas Institute for Rehabilitation and Research (TIRR), Houston 1962-63
1962-1967 Associate Professor of Rehabilitation, BCM, Houston, Texas
1962-1969 Associate Professor of Pediatrics and Physiology, BCM, Houston, Texas
1963-1968 Program Director, General Clinical Research Center for Chronic Illness, TIRR, 1963-68
1963-1968 Director of Research, TIRR, Houston, Texas
1967-present Professor of Rehabilitation, BCM, Houston, Texas
1969-present Professor and Chairman of Community Medicine, BCM
1981-present Professor of Family Medicine, BCM, Houston, Texas
1982-present Faculty Associate, Center for Health Promotion Research and Development, The University of Texas Health Science Center at Houston, Texas (UTHSC)
1984-present Adjunct Professor of Preventive Medicine, The University of Texas School of Public Health (UTSPH), Houston, Texas
1990-present Distinguished Service Professor, BCM, Houston, Texas
1992-present Adjunct Professor of Family Practice and Community Medicine, UTHSC at Houston, Houston, Texas
1992-present Adjunct Professor of Preventive Medicine, epidemiology, UTSPH, Houston, Texas
1993-present Adjunct Professor, Department of Social Psychology, University of Houston, Houston, Texas

HONORS

Society for Pediatric Research (elected 1962); Society of the Sigma Xi (elected 1962)
Scientific Exhibit Award, American Academy of Orthopedic Surgeons, 1963
Co-recipient of Gold Medal of the 6th International Congress of Physical Medicine, 1972
Baylor College of Medicine Outstanding Faculty, 1980, 1983, 1985, 1987, 1988
Alpha Omega Alpha Honorary Faculty, 1983
American College of Medical Informatics (elected founding member 1984)
National Academies of Practice (elected distinguished practitioner 1984)
American Public Health Association (APHA) (elected governing counselor 1985);
APHA Medical Care Section (chair 1990-91)
Honorary President, Catalonian Antihypertension League; Honorary member, Catalonian Society of Pediatrics, Spanish Society of Ambulatory Pediatrics, Argentinian Medical Association, Argentinian Society of Internal Medicine, Guayaquil
Society of Ambulatory Pediatrics, Argentinian Medical Association, Argentinian Society of Internal Medicine, Guayaquil (Ecuador) Geriatric Society, Costa Rica College of Physicians
Narcis Monturiol Medal of Merit in Science and Technology, Catalunya, 1991
Interamerican Institute for Border Health and Environment (The Institute), Associate 1993-present
Chairman, Scientific Committee, 2nd International Heart Health Congress to be held in Barcelona, Spain, May, 1995

CARLOS VALLBONA, M.D. (continued)

SCIENTIFIC COMMITTEES

V.A. Medical School Assistance Review Committee (1975-79); Pulmonary Disease Advisory Committee, NHLBI (1975-79); Health Care Technology Study Section, NCHSR (1969-73) (1978-82); Research Manpower Review Committee, NHLBI (1981-84); Biometry & Epidemiology Contract Review Committee, NCI (1988-90); Project Advisory Committee, Texas Diabetes Advisory Committee Project (1986-current)

MEMBERSHIPS

American Academy of Family Physicians (elected Fellow); American Association for the Advancement of Science, American Association of University Professors; American College of Chest Physicians (elected Fellow); American College of Preventive Medicine (elected Fellow); (former board member), American Congress of Rehabilitation Medicine; American Medical Association; American Public Health Association; Association of Teachers of Preventive Medicine (board member)

SELECTED PUBLICATIONS (from 263 publications and 60 abstracts)

Vallbona C, Canosa C: Present knowledge of the antipoliomyelitis Salk Vaccine (Conocimientos actuales sobre la vacuna antipoliomielítica de Salk). Archivos de Pediatria (Barcelona, Spain) 1955;5(30):599-610.

Spencer WA, Vallbona C: Estimation of inspiratory capacity in health and in subjects with respiratory muscle paralysis. J Appl Physiol 1959;14(3):279-283.

Vallbona C, Spencer WA: The total lung capacity and its subdivisions in respiratory poliomyelitis. J Chronic Dis 1959;9(6):617-635.

Vallbona C, Spencer WA, Jackson RR, Harrison GM: Chronic sequelae of poliomyelitis (Las secuelas crónicas de la poliomielitis). Revista del Colegio Médico de Guatemala. Abbott Laboratories: Guatemala, 1959;10(1):40-65.

Vallbona C: Problems in the rehabilitation of disabled children (Problemas que presenta la rehabilitación del niño lisiado). Boletin de la Sociedad Catalana Pediatria (Barcelona, Spain) 1960;21:188-198.

Vallbona C, Spencer WA: Systematic classification of the chronic sequelae of poliomyelitis. Arch Phys Med Rehab 1961;42:114-121.

Vallbona C, Spencer WA: Management of chronic sequelae of paralytic disease. The Pediatric Clinics of North America 1963;10:187-205.

Vallbona C, Cardus D, Spencer WA, Hoff HE: Patterns of sinus arrhythmia in patients with lesions of the central nervous system. Amer J Cardiol 1965;16(3):379-389.

Cardus D, Vallbona C, Spencer WA: Effects of three kinds of artificial respirators on the pulmonary ventilation and arterial blood of patients with chronic respiratory insufficiency. Chest 1966;50(3):297-306.

Vallbona C, Harrington PR, Freire RM, Harrison GM, Reese WO: Pitfalls in the interpretation of pulmonary function studies in scoliotic patients. Arch Phys Med Rehab 1969;50(2):68-74.

Vallbona C, Iddings D, Zeigler RK: Recovery of strength in acute polyneuritis and poliomyelitis. Arch Phys Med Rehabil 1969;50:512-521.

Recent papers have dealt with community aspects of diabetes, hypertension, and AIDS.

Baker S, Baker RL, Vallbona C, Hamill B, Higgins C: Effectiveness of diabetic eye disease detection by primary care physicians in a public health care setting. *In:* Chytil MK, Duru G, Eimeren Wv, Flagle Ch.D. (eds): Health Systems - the Challenge of Change. Proc Fifth Int. Conf. on System Science in Health Care. June 29-July 3, 1992: Prague, Czechslovakia: Omnipress. Pp. 152-158.

Merrill JM, Laux LF, Lorimor R, Thornby J, Vallbona C: Re-designing medical education for the 21st century. *In:* Chytil MK, Duru G, Eimeren Wv, Flagle Ch.D. (eds): Health Systems - the Challenge of Change. Proc Fifth Int. Conf. on System Science in Health Care. June 29-July 3, 1992: Prague, Czechoslovakia: Omnipress. Pp. 1419-1423.

Aruffo J, Coverdale J, Pavlik V, Vallbona C: AIDS knowledge in minorities: The significance of locus of control. Am J Prev Med 1993;9(1):15-20.

Vallbona C, Pavlik V: Advances in the community control of hypertension: from epidemiology to primary care practice. J Hypertension 1992;10(Suppl 7):S51-S57.

Vallbona C: Importance of immunization in child care and prevention. *In*: Proc. National Academies of Practice Fourth National Health Policy Forum Healthy Children 2000: Obstacles and Opportunities. April 24-25, 1992, Washington, D.C.

Vallbona C: Evolución del sistema MIR en Estados Unidos. *In:* Debate Sanitario: Medicina, Sociedad y Tecnología. Fundación BBV: Linea Documenta, Madrid, 1992. P. 56-66.

Vallbona C: El marco epidemiológico: incidencia económico-social. *In:* Debate Sanitario: Medicina, Sociedad y Tecnología. Fundacion BBV Linea Documenta, Madrid, 1992. P. 147-184.

Serra L, de Cambra S, Vallbona C, Tresseras R, Salto E, Taberner JL, Salleras L, Via Redons: JM Activitat física. *Salut Catalunya* 1993;7(2):94-101.

Baker SB, Vallbona C, Pavlik V, Fasser CE, Armbruster M, McCray R, Baker RL: A diabetes control program in a public health care setting. Public Health Reports 1993;108:595-605.

Vallbona C: Prevalence of sports activity and injury in Europe. *In:* Gordon SL, Gonzalez-Mestre X, Garrett, Jr. WE (Eds): Sports and Exercise in Midlife. American Academy of Orthopaedic Surgeons Seminar. Rosemont IL: American Academy of Orthopaedic Surgeons. 1993. P. 11-25.

Vallbona C., Pardell H: La Hipertensión Enfermedad Comunitaria (Hypertension, a Community Disease). *In:* Rodicio JL, Romero JC, Ruilope LM (eds): Tratado de Hipertensión, 2.ª edición (Textbook of Hypertension, 2nd edition), Barcelona, Spain: Salvat Editores, 1993.

Vallbona C, Pardell H, Portella E, Roca-Cusachs A, Martínez Amenós A: Observancia del tratamiento contra la hipertensión (Compliance to treatment for hypertensión). *In:* Rodicio JL, Romero JC, Ruilope LM (eds): Tratado de Hipertensión, 2.ª edición (Textbook of Hypertension, 2nd edition), Barcelona, Spain: Salvat Editores, 1993.

Vallbona C, Baker SB: Physical activity and aging. Quality and quantity of physical activity: their impact on aging. *In*: Llibre de Ponencies i Comunicacions del XVI Congrés de l'Association Internationale des Universitiés du Troisième Age. Barcelona, Spain. A.I.U.T.A., 1994.

Vallbona C, Hyman, DJ: Rebuttal: Improving Health Care for the Poor - Lessons from the 1980's (letter). JAMA 1994;272(5):352-3.

BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME	POSITION TITLE
Wendell D. Winters	Associate Professor

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
University of Illinois, Urbana	B.S.	1962	ZOOLOGY
University of Illinois	M.S.	1966	MICROBIOLOGY
College of Medicine	PH. D.	1968	MICROBIOLOGY

RESEARCH AND/OR PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

PROFESSIONAL EXPERIENCE:

1971-76 Assistant Professor, Department of Surgery and Department of Microbiology and Immunology, University of California at Los Angeles School of Medicine.

1977-Pres. Associate Professor, Department of Microbiology, The Univeristy of Texas Health Science Center at San Antonio, Texas.

POSTDOCTORAL TRAINING:

1968-1971 Postdoctoral Fellow (Medical Research Council, UK) and (Damon Runyon-Walter Winchell Cancer Fund), Division of Virology, National Institute for Medical Research, Mill Hill, London, England. (Dr. H. Pereira, Advisor), Studies on immune responses to respiratory viruses and virus assembly.

HONORS:

1968-70 Medical Research Council Award for Fellowship (UK).
1970-71 Damon Runyon Memorial Fund Cancer Research Fellow.
1974 National Academy of Sciences Fellowship.
1979-80 Burroughs-Wellcome Fund US-Britain Fellowship.
1983 Distinguished Teaching Professor, UTHSCSA
1989-95 Director, Aloe Research Foundation
1992-95 President, Aloe Research Foundation
1991 Fellow, American Academy of Microbiology
1991 Chairman, International Congress of Phytotherapy
1992; 95 Hijokinkoshi Award from Government of Japan
1992 Visiting Professor Award, University of Ljubljana, Slovenia
1994 YASUDA AWARD Bioelectrical Repair & Growth Society

PUBLICATIONS:

Cameron, I.L., Hardman, W.E., Winters, W.D., Zimmerman, S. and Zimmerman, A.M.: Environmental Magnetic Fields: Influences on early embryogenesis, J. Cell Biochem., 51:417-425. 1993.

Sakamoto, S., Hagino, N., and Winters, W.D.: *In Vivo* Studies of the Effect of Magnetic Field Exposure on Ontogeny of Choline Acetyltransferase in the Rat Brain. Bioelectromagnetics 14:373-381. 1993.

Hagino, N., Yuzurihara, M., and Winters, W.D. *In vivo* studies of the effect of magnetic fields on the ontogeny of nicotine acetylcholine receptors. (Abstr.) J. Neurochem. 61 (Suppl.), S22C. 1993.

Hagino, N., Foster, D.J. and Winters, W.D. In vivo studies of effect of magnetic field exposure on development of D2 dopamine receptor in the brain. First World Congress for Electricity and Magnetism in Biology and Medicine, 1:116 (P165). 1992.

Winters, W.D., Schirf, V., Hagino, N.: Influence of cyclic, rotating magnetic fields of extremely low frequency on NA+/K+ transport in rat embryo neuronal cells. First World Congress for Electricity and Magnetism in Biology and Medicine, 1:37 (K10), 1992.

Parker, J.E. and **Winters, W.D.**: Expression of gene specific mRNA in cultured cells exposed to cyclic 60 Hz magnetic fields. Biochem. Cell Biol., 70:237-241, 1992.

Winters, W.D., Hagino, N., Darnell, B., Yamaguchi, I., Matsumoto, Y.: New systems for *in vitro* culture of developing rat embryo neurons. In Electromagnetics in Biology and Medicine, (Eds.) CT Brighton and SR Pollack, San Francisco Press, Inc. San Francisco pp. 163-168, 1991.

Winters, W.D., Hagino, N.: Amino acid transport in rat embryo neural cells exposed to 60 Hz cyclic magnetic field *in vitro*. Trans. Bioelectrical Repair and Growth Society 11:29, 1991.

Zimmerman, S., Zimmerman, A.M., **Winters, W.D.**, and Cameron, I.L.: The influence of 60 Hz magnetic fields on sea urchin development. Bioelectromagnetics, 11:37-45, 1990.

Winters, W.D., and Rydzak, S.P.: Decreased swarming by *Proteus mirabilis* exposed to a cyclic 60 Hz magnetic field. Trans. Bioelectrical Repair and Growth Society (BRAGS) 9:6, 1989.

Winters, W.D., and Darnell, B.: Increased actin and fibronectin in normal humans cells induced by exposure to 60 Hz magnetic fields. Proc. Bioelectromagnetics Soc. (BEMS) 11:57, 1989 (P-1-10).

Parker, J.E., Kiel, J.L., and **Winters, W.D.**: Effect of radiofrequency radiation of mRNA expression in cultured rodent cells. Physiol. Chem. Physics and Med. NMR 20:129-134, 1988.

Winters, W.D., Darnell, B., Trump, B., Saenz, E., and Westerman, C.: Increased normal fibroblast cell contraction of collagen gels induced by exposure to 60 Hz magnetic fields. DOE/EPRI Contractors Review, Phoenix, AZ, Oct. 1988.

Winters, W.D., Darnell, B., Liboff, A.R., and McLeod, B.R.: Inhibition of normal fibroblast cell contraction by exposure to magnetic fields. Proc. Bioelectromag. Soc. 10:71, 1988.

Winters, W.D., Holt, B.R., Darnell, B.: Time dependent exposures to ac magnetic fields alter mitogen specific human lymphocyte blastogenic responses. Proc. Bioelectromagnetic Society 9:72, 1987.

Winters, W.D.: Biological functions of immunologically reactive human and canine cells influenced by in vitro exposure to 60 Hz electric and magnetic fields. New York State Power Lines Project, Final Report, pp 1-105, 1986.

Phillips, J.L., **Winters, W.D.** and Rutledge, L.: In vitro exposure to electromagnetic fields: Changes in tumor cell properties. Int. J. Rad. Biol. 49:463-469, 1986.

Phillips, J.L., Rutledge, L. and **Winters, W.D.**: Transferrin binding to two colon carcinoma cell lines: Characterization and effect of 60 Hz electromagnetic fields. Cancer Res. 46:239-244, 1986.

Winters, W.D., Darnell, B. and Parker, J.: Bioresponses of bone tumor (chondrosarcoma) cells exposed in vitro to 60 Hz ac magnetic fields. Bioelectrical Repair and Growth Society 6:80, 1986.

Winters, W.D., Crawley, R., Young, R.J. and Phillips, J.L.: Biological responses of canine leukocytes after exposure to 60 Hz electromagnetic fields *in vitro*. Proc. Bioelectromag. Soc., 7:56 (#J-27), 1985.

Winters, W.D., Guest, G.F., Winters, B.T. and Phillips, J.L.: Human leukocyte responses after exposure to 60 Hz electromagnetic fields *in vitro*. Proc. Bioelectromag. Soc., 7:55 (#J-26), 1985.

Cameron, I.L., Hunter, K.E. and **Winters, W.D.** Retardation of fish embryogenesis by extremely low frequency 60 Hz electromagnetic fields. Physiol. Chem. & Physics & Medical. NMR 17, p. 135-138, 1985.

Winters, W.D. and Phillips, J.L.: Monoclonal antibody detection of tumor antigens in human colon cancer cells following electromagnetic field exposures. Proc. Bioelectromag. Soc., 6:82 (P-46), 1984.

Winters, W.D. and Phillips, J.L.: Enhancement of human tumor cell growth by electromagnetic and magnetic fields. Proc. Bioelectromag. Soc., 6:9 (A2-6), 1984.

Stamm, M.D., **Winters, W.D.**, Morton, D.L. and Warren, S.L.: Microwave characteristics of human tumor cells. Oncology 29:294-301, 1974.

BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME	POSITION TITLE
Kuno Peter Zimmermann	Staff Physician, Physical Medicine and Rehabilitation Assistant Professor, Physical Medicine and Rehabilitation

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Federal Inst. Technol., Lausanne, Switzerl.	Dipl. Ing.	1966	Electrical Engineering
Lehigh University, Bethlehem PA	MS	1971	Electrical Engineering
Lehigh University, Bethlehem PA	PhD	1975	Electrical Engineering
Rochester Inst. Technol., Rochester NY	MS	1984	Appl. & Math. Statistics
Univ. of Health Sciences, Kansas City MO	DO	1987	Osteopathic Medicine

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. If the list of publications in the last three years exceeds two pages, select the most pertinent publications. DO NOT EXCEED TWO PAGES.

PROFESSIONAL EXPERIENCE

1966-1968: Field Engineer, Tektronix International, Zug Switzerland
1968-1973: Teaching and Research Assistant, Lehigh University, Bethlehem PA
1973-1975: Research Fellow, National Science Foundation of Switzerland
1975-1978: Assistant Professor, Electrical Engineering, Lafayette College, Easton PA
1978-1979: Member of Technical Staff, RCA Laboratories, Sarnoff Research Center, Princeton NJ
1979-1987: Associate Professor, Electrical Engineering, University of Missouri, Columbia MO
1987-1988: Intern, Still Regional Medical Center, Jefferson City MO
1988-1989: Family Practice Resident Physician, Still Regional Medical Center, Jefferson City MO
1989-1990: PM&R Resident Physician, Univ. of Medicine & Dentistry of New Jersey, Newark NJ
1990-1992: PM&R Resident Physician, Metrohealth Medical Center, Cleveland OH
1992-Current: Assistant Professor, PM&R, Baylor College of Medicine, Houston TX
1992-1994: Staff Physician, Spinal Cord Injury Service, VAMC, Houston TX
1994-Current: Staff Physician, Director-EMG Laboratory, Physical Medicine and Rehabilitation Service, VAMC, Houston TX

RELEVANT PUBLICATIONS

Zimmermann K, Kuo W. *Image Processing Techniques in the Wiener Analysis of Transient Wavelets.* Proceedings of the 3rd Annual IEEE-EMBS Conference, Houston, September 1981

Zimmermann K, Main P. *Low-Pass Digital Differentiators with Minimal Squared Error.* Proceedings of the 3rd Annual IEEE-EMBS Conference, Houston, September 1981

Zimmermann K, Smith JC. *Ultrasound Velocity in Fixed Human Liver.* Proceedings of the 4th Annual IEEE-EMBS Conference, Philadelphia, September 1982

Zimmermann K, Smith JC. *Ultrasound Velocity in Fixed Human Liver: Empirical ANOVA and Regression Modeling on Histologically Assessed Abnormalities.* Ultrasonic Imaging, Vol. 5, 280-94, 1983

Zimmermann K, Weilert DR, Robertson CR, Smith JC. *On Velocity Changes Caused by Tissue Fixation.* Ultrasound in Medicine and Biology, July 1984

Zimmermann K. *Linear Feedback Models for Polarization and Magnetization.* IEEE Transactions on Education, Vol. 3-28, #1, February 1985

Zimmermann K, Varady M. *Handwriter Identification from One-Bit Quantized Pressure Patterns.* Pattern Recognition, Vol. 18, #1, 1985

Zimmermann K. *On Frequency-Domain and Time-Domain Phase Unwrapping.* IEEE Proceedings, Vol. 75, #4, April 1987, 519-20

Kamins D, Lam CF, Zimmermann K. *Signature Recognition Through Spectral Analysis.* Proceedings of the IEEE International Conference on Acoustics, Speech and Signal Processing, Dallas, April 1987, Paper 41.18

Zimmermann K. *Mellin Transforms of Closed Curves and One-Dimensional Functions: Direct Computation and Scaling Properties.* IEEE Proceedings, Vol. 74, #6, June 1987, 859-60

Bills GA, Varady MJ, Zimmermann KP. *Spectral Analysis of Script and Signatures.* Proceedings of the 3rd International Conference on Handwriting and Computer Applications, Montreal, July 1987

Zimmermann KP, Simpson RK. *"Slinky" Coils for Neuromagnetic Stimulation.* Electroencephalography and clinical Neurophysiology, In Press.

Zimmermann KP, Monga TN, Darouiche RO, Lawrence SA. *Post-Stroke Autonomic Nervous System Function: Palmar Sympathetic Skin Responses Thirty or More Days after CVA.* Arch. Phys. Med. Rehab., 1995;76:250-6

DESCRIPTION: State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project. Describe concisely the research design and methods for achieving these goals. Avoid summaries of past accomplishments and the use of the first person. This abstract is meant to serve as a succinct and accurate description of the proposed work when separated from the application. **DO NOT EXCEED THE SPACE PROVIDED.**

Disability and Pain Management Center. The proposed Disability and Pain Management Center (DPMC) was developed to establish an organizational infrastructure to support long-term multidisciplinary approaches to the management of chronic pain in people with disabilities. The proposed program draws upon the resources of one of the largest academic Physical Medicine and Rehabilitation Deparments in the country, located at Baylor College of Medicine in Houston, Texas, to explore current and emerging aprroaches for treating pain in persons with permanent physical disabilities. The specific aims of the DPMC are to: (1) create an administrative structure that provides for effective oversight for a multidisciplinary, interinstitutional research program on chronic pain and disability; (2) implement research projects targeting promising approaches for alleviating pain in persons with different types of disability; (3) establish a research subject pool and database on chronic pain in a mixed disability population that can serve as a resource for future research on current and experimental approaches to chronic pain management in persons with different types of disabilities; (4) develop outcome measures that allow for comparisons of important therapeutic outcome indicators across disability populations; (5) provide mentoring and support required to foster development of research expertise in junior faculty who can contribute to research on chronic pain and disability; and (6) disseminate the results of research efforts and other important activities of the DPMC to various target audiences, including other clinical and basic science professionals, people with disabilities and family members, and policy makers and others who influence programmatic development related to disability services. The DPMC will be comprised initially of three research projects--(1) A Placebo-controlled Trial of Tretrahydrocannabinol in Treatment of Neurogenic Pain Due to Spinal cord Injury; (2) The Effect of Magnetic Fields on Chronic Pain Due to Overuse in People with Disabilities; and (3) Peripheral Nerve Stimulation in Amputees with Neuropathic Pain. A fourth research project, Testing the Efficacy of a Pain Clinic for Management of Disability-Related Pain, will be initiated in the third year of funding, following two years of preliminary studies to establish baseline data on a demographically mixed group of individuals with physical disabilities who have chronic pain. Also, two cores--an administrative core (Core A) and an outcome measures core (Core B) will be implemented to support all research and related activities.

PERSONNEL ENGAGED ON PROJECT, INCLUDING CONSULTANTS/COLLABORATORS. *Use continuation pages as needed* to provide the required information in the format shown below on *all* individuals participating in the project.

Name Grabois, Martin Degrees(s) M.D. Social Security No. (C)
Position Title Professor and Chairman Date of Birth (MM/DD/YY) (C) Role on Project Principal Investigator
Organization Baylor College of Medicine Department Physical Medicine & Rehab.

Name Strayer, Jonathan Degrees(s) M.D. Social Security No. (C)
Position Title Assistant Professor Date of Birth (MM/DD/YY) (C) Role on Project Project Director
Organization Baylor College of Medicine Department Physical Medicine & Rehab.

Name Hazlewood, Carlton Degrees(s) Ph.D. Social Security No.
Position Title Associate Professor Date of Birth (MM/DD/YY) Role on Project Project Director
Organization Baylor College of Medicine Department Physical Medicine & Rehab.

Name Simpson, Richard K., Jr. Degrees(s) M.D., Ph.D. Social Security No. (C)
Position Title Chief, Neurological Service Date of Birth (MM/DD/YY) (C) Role on Project Project Director
Organization VAMC Houston, Baylor College of Medicine Department Neurosurgery

Name Nosek, Margaret Degrees(s) Ph.D. Social Security No. (C)
Position Title Associate Professor Date of Birth (MM/DD/YY) (C) Role on Project Core Director
Organization Baylor College of Medicine Department Physical Medicine & Rehab.

Section II - Research Plan

1. Introductory Overview

A. History and Purpose of the Program. The chairman of Baylor College of Medicine's Department of Physical Medicine and Rehabilitation (PM&R), Dr. Martin Grabois, has, over the last several years, focused attention on the issue of pain management in people with disabilities. Under his leadership, a number of research initiatives, funded primarily through institutional sources, have been undertaken at Baylor and its clinical affiliates, most notably The Institute for Rehabilitation and Research (TIRR) and the Houston Department of Veterans Affairs (VA) Hospital, to examine the problem of pain in people with disabilities and effective strategies for bringing relief to people with disabilities who experience chronic pain. Today there are activie clinical programs in pain management directed by Department of PM&R faculty operating at The Methodist Hospital, and the VA Hospital. A pain management clinic targeted to the specific needs of people with disabilities is scheduled to begin operations at TIRR in July 1995. This clinic will be directed by Dr. Grabois and Dr. Jonathan Strayer, an assistant professor of PM&R and staff physician in TIRR's spinal cord injury program.

Concurrent with the development of disability-related pain initiatives among physicians at Baylor and its clinical affiliates, there has been increasing national attention to the issue of pain as an influencing factor in the outcomes of rehabilitative efforts designed to reduce the deleterious affects of disability resulting from injury and disease. Dr. Grabois was one of several clinicians and researchers who participated the DHHS-sponsored planning workshop on *Chronic Pain Management: Developing a Treatment System for People with Disabilities*. Many of the recommendations that emerged from that meeting were consistent with activities ongoing or under development through the Baylor PM&R Department and its clinical affiliates. The nexus of these developmental efforts--the local interests in pain and disability spurred by Dr. Grabois' focus on the issue and national attention to these issues that emerged through leadership provided by staff of the National Center for Medical Rehabilitation and Research (NCMRR)--offered an opportunity to strengthen research efforts currently underway on a limited basis at Baylor and its affiliates.

The overriding goal, then, of the proposed research program, organized as the Disability and Pain Management Center (DPMC), is to develop an organizational structure which will support ongoing multidisciplinary clinical and basic science research designed to find solutions to the problems of chronic pain and its deleterious affect on people with physical disabilities. Specific functional objectives of the DPMC are to:

- create an administrative structure that provides for effective oversight for a multidiscplinary, interinstitutional research program on chronic pain and disability;
- implement research projects targeting promising approaches for alleviating pain in persons with different types of disability;
- establish a research subject pool and database on chronic pain in a mixed disability

population that can serve as a resource for future research on current and experimental approaches to chronic pain management in persons with different types of disabilities;

- develop outcome measures that allow for comparisons of important therapeutic outcome indicators across disability populations;

- provide mentoring and support required to foster development of research expertise in junior faculty who can contribute to the research on chronic pain and disability; and

- disseminate the results of research efforts and other important activities of the DPMC to various target audiences, including other clinical and basic science professionals, people with disabilities and family members, and policy makers and others who influence programmatic development related to disability services.

The proposed programmatic activities will provide a means of accelerating research that has, heretofore, been supported almost exclusively through institutional resources. As the descriptions of individual research projects and core activities indicate, preliminary studies completed thus far have been supported almost entirely with funding from Baylor, TIRR, and the VA, with only modest support from certain vendors in the form of reduced costs for certain drugs and equipment. The funding requested will allow for coordination of disparate research efforts currently underway and will focus the research on the issue of greatest concern--Do efforts to ameliorate chronic pain in persons with disabilies result in a better quality of life for these individuals and their families?

B. Administration, Organization, and Operation. The collaborating institutions are fully committed to an aggessive program of research on chronic pain and people with disabilities. As suggested from the previous discussion, efforts were underway to establish and operate a pain clinic for people with disabilities well before the announcement of the availability of funds for this research. Dr. Grabois, chairman of Baylor's PM&R Department and principal investigator and director of the proposed center, initiated development of the pain clinic and is fully authrorized to commit the extensive resources of the PM&R Department to the proposed research program. Furthermore, TIRR's commitment to pain management is evidenced by its commitment of clinical space and support personnel to establish and operate a pain clinic. The pain clinic will be established whether or not funding for this program is obtained; however, the research component of the pain clinic will be extremely limited without the support requested. Space for the program, described in some detail in the write-up of the Administrative Core Unit, includes research space in Baylor facilities, as well as inTIRR and VA Hospital facilities. Clinical space is also available in TIRR and the VA Hospital, both of which are fully accesible to people with disabilities.

The commitment to excellence in the research program is demonstrated by plans to appoint an external DPMC advisory committee composed of four nationally recognized experts in pain management and disability and three individuals with disability who have experience with chronic pain. The advisory committee will be provided with complete planning documents for the DPMC, as well as with data on results of research and other activities conducted through the

center. An organizational chart indicating relationships between collaborating institutions, the DPMC, the advisory committee, individual research projects, and core units is provided on the last page of this introduction.

C. Selected Relevant Publications. Relevant recent publications by primary researchers in the proposed DPMC are listed below. Additional relevant publications for these researchers and for collaborating researchers are cited in the biosketches provided with this application.

M. Grabois

Grabois M and Smith K (1995). Chronic pain. In Monga T (ed.), *State of the Art Review: Sexuality and Disability*. Philadelphia, PA: Hanley and Belfus, Inc.

Grabois M, Straja A, Schramm D, and McCann M (1995). Prevention and management of chronic pain. In Braddom R (ed.), *Textbook on Physical Medicine and Rehabilitation*. Philadelphia, PA: Williams and Wilkins.

Grabois M and VanDeventer J (1995). Chronic pain. In Garrison SJ (ed.), *Handbook of Physical Medicine and Rehabilitation Basics*. Philadelphia, PA: Lippincott.

R. Simpson

Simpson RKJr, Robertson CS, and Goodman JC (1993). Glycine: A potential indicator of electrically induced pain modification. *Biomedical Letters*, 48:193-207.

Edmondson EA, Simpson RKJr, Beric A, Stubler DK (1993). Systemic lidocaine therapy for "thalamic pain." *Southern Medical Journal*, 1093-1096.

Simpson RKJr and Leis AA (1995). Neurosurgical management of spasticity, Part I. *Contemporary Neurosurgery,* (in press).

Simpson RKJr and Leis AA (1995). Neurosurgical management of spasticity, Part II. *Contemporary Neurosurgery,* (in press).

Zimmerman K and Simpson RKJr (1995). "Slinky"coils for neuromagnetic stimulation. *Electroencephalography and Clinical Neurophysiology,* (in press).

J. Strayer

Strayer JR, Tuel SP, Dimitrijevic M, Sherwood A (1992). The discomplete syndrome: Clinical implications of residual suprasegmental influence across a clinically complete spinal cord injury. *Archives of Physical Medicine and Rehabilitation*, 73(10):969.

Strayer JR and Tuel SP (1992). Spinal decompression sickness in divers: Neurophysiologic assessment of paraplegia. *Archives of Physical Medicine and Rehabilitation*, 73(1):1003.

C Hazlewood

Hazlewood CF and Van Zandt RL (1995). An hypothesis defining an objective end point for the relief of chronic pain. *Medical Hypothesis*, 44(1):63-65.

H. Hartmann

Hartmann HA and Brown AM (1993). Identification of the amino acids forming the conduction pathway in potassium channels. In Wolfe M (ed.), *Molecular and Cellular Biology*. Belmont, CA.: Wadsworth Publishing Co.

Kirsch GE, Drewe JA, DeBiasi M, , Hartmann H and Brown AM (1993). Functional interactions between K^+ pore residues located in different subunits. *J. Biol. Chem.* 268:13799-13804.

Hartmann HA, Tiedeman AA, Chen S-F, Brown AM and Kirsch GE (1994). The effects of III-IV linker mutations on human heart Na^+ channel inactivation gating. *Circ. Res.* 75: 114-122.

Kirsch GE, Alam M, and Hartmann HA (1994). Differential effects of sulfhydryl reagents on saxitoxin and tetrodotoxin block of voltage-dependent Na^+ channels. *Biophys. J.* 67: 2305-2315.

Drewe JA, Hartmann HA,. and Kirsch GE (1994). K^+ channels in mammalian brain: A molecular approach. In Narahashi T (ed.), *Methods in Neuroscience*. San Diego, CA: Academic Press.

M. Nosek

Nosek M and Fuhrer MJ (1992). Independence among people with disabilities I. A heuristic model. *Rehabilitation Counseling Bulletin*, 36(1):6-20.

Nosek M and Fuhrer MJ (1992). Independence among people with disabilities II. The personal independence profile. *Rehabilitation Counseling Bulletin*, 36(1):6-20.

D. Rintala

Rintala D, Young ME, Hart KA, and Fuhrer MJ (1994). The relationship between the extent of reciprocity with social supporters and measures of impairment, disability, and handicap in persons with spinal cord injury. *Rehabilitation Psychology.*

Loubser P, Rintala D, Fuhrer MJ, and Castro J (1995). Chronic pain associated with spinal cord injury (abstract). In *Proceedings of the American Spinal Injury Association.*

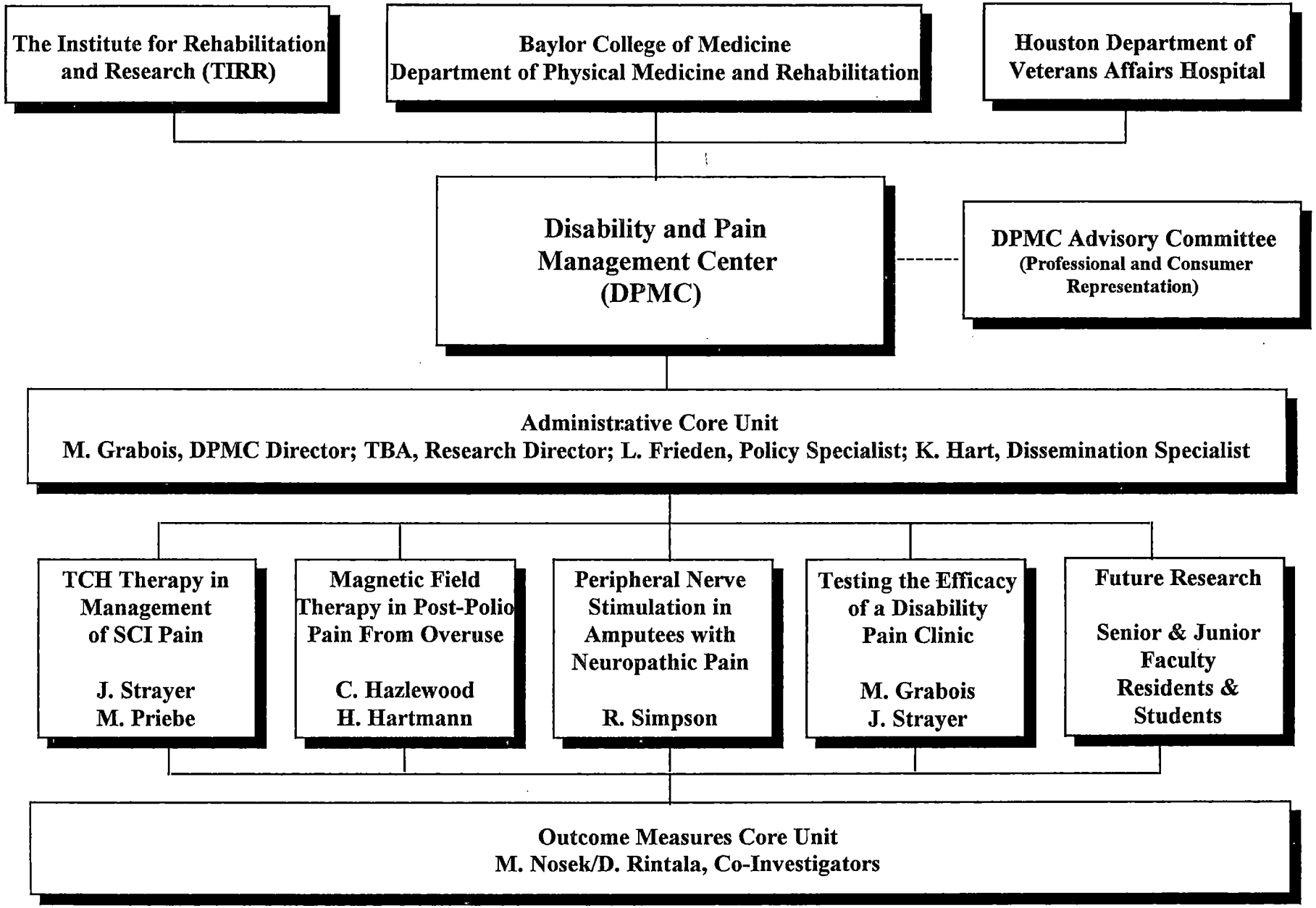
Hart K and Rintala DH (1995). Long term outcomes following spinal cord injury. *Neurorehabilitation* (in press).

Priebe MM and Rintala DH (1995). Spinal cord injury. In Dell-Orto AE and Marinelli RP (eds.), *Encyclopedia of Disability and Rehabilitation,* New York: MacMillan (in press).

Rintala DH (1995)). Pressure ulcers: Quality of life considerations. *Advances in Wound Care* (in press).

Rintala DH, Young ME, Spencer JC, and Bates PS (1995). Family relationships and adaptation to spinal cord injury: A qualitative study. *Rehabilitation Nursing* (in press).

D. Assurances and Collaborative Agreements. The proposed DPMC program involves a number of collaborative arrangements, including those between various Baylor College of Medicine clinical and basic science departments and those between Baylor and its primary clinical affiliates. Interdepartmental agreements are covered through a sign-off arrangement on sponsored research that must be executed prior to the submission of any funding application. This sign-off has been completed for the proposed program grant and approval records are maintained on file in Baylor's Research Office. As regards agreements with clinical affiliates, Baylor has affiliation agreements with TIRR and the Houston VA Hospital that cover jointly conducted research projects such as those proposed. However, as with interdepartmental research agreements, interinstitutional research projects require sign-off by authorized representatives of the clinical affiliate institutions prior to submission of funding applications. Signed forms indicating approval of the this program and of specific projects to be carried out in clinical affiliate institutions are on file in the Baylor Research Office.


The Institute for Rehabilitation and Research (TIRR)
Baylor College of Medicine Department of Physical Medicine and Rehabilitation
Houston Department of Veterans Affairs Hospital
Disability and Pain Management Center (DPMC)
DPMC Advisory Committee (Professional and Consumer Representation)
Administrative Core Unit
M. Grabois, DPMC Director; TBA, Research Director; L. Frieden, Policy Specialist; K. Hart, Dissemination Specialist
TCH Therapy in Management of SCI Pain
J. Strayer
M. Priebe
Magnetic Field Therapy in Post-Polio Pain From Overuse
C. Hazlewood
H. Hartmann
Peripheral Nerve Stimulation in Amputees with Neuropathic Pain
R. Simpson
Testing the Efficacy of a Disability Pain Clinic
M. Grabois
J. Strayer
Future Research
Senior & Junior Faculty Residents & Students
Outcome Measures Core Unit
M. Nosek/D. Rintala, Co-Investigators

DESCRIPTION: State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project. Describe concisely the research design and methods for achieving these goals. Avoid summaries of past accomplishments and the use of the first person. This abstract is meant to serve as a succinct and accurate description of the proposed work when separated from the application. DO NOT EXCEED THE SPACE PROVIDED.

Project 1: A Placebo-controlled Trial of Tetrahydrocannabinol (THC) in Treatment of Neuropathic Pain Due to Spinal Cord Injury. The proposed two-year project will examine the effectiveness of tetrahydrocannabinol (THC) in reducing chronic neuropathic pain experienced by persons with spinal cord injury (SCI). Preliminary data gathered by the investigators for the proposed project suggest that THC, provide prescribed for a limited number of patients to control spasticity, also brings relief from pain. The specific aims of this project are to: (1) identify at least 100 individuals with neuropathic pain related to SCI who are willing to participate in a study of THC as a treatment for their pain; (2) determine, through comparison of intervention and control groups, if therapy using controlled dosages of THC can be shown to alleviate neuropathic pain related to SCI; (3) identify measures of pain relief in persons with SCI that appear to be indicative of the efficacy of treatment; (4) document any side effects related to use of THC in treatment of neuropathic SCI pain; and (5) disseminate the results of the research using appropriate methods for addressing the information needs of health and research professionals, as well as of people with disabilities. Using a double-blind, placebo-controlled design, 50 individuals with chronic pain related to their SCI will be selected for participation in each of the two project years. Over a four-week period, participants randomly assigned to treatment and control groups to will be provided specified doses of either THC or a visually identical placebo. During the treatment period, standardized pain measures will be used with both groups, as will other measures of functional ability and quality of life. Following the four-week test, a limited number of patients will be continued into a second phase of the study designed to determine if a maintenance dosage of THC is effective in long-term (four-month) pain relief. Data collected through the study will be used to test four hypotheses: H_1: THC has significantly greater effect than placebo in the treatment of neuropathic pain due to SCI as determined using the Visual Analog Scale. H_2: THC has significantly greater effect than placebo in treatment of SCI as determined using the McGill Pain Questionnaire. H_3: Functional ability as measured by the Rand SF-36 will be greater during treatment of neuropathic pain due to SCI in patients treated with THC as compared to patients given placebo. H_4: THC will remain effective in control of neuropathic pain due to SCI over a four-month period of treatment. Data analyses will be done using appropriate statistical procedures (e.g., MANOVA for data from the McGill Pain Questionnaire, and results will be reported in through appropriate media and forums.

PERSONNEL ENGAGED ON PROJECT, INCLUDING CONSULTANTS/COLLABORATORS. *Use continuation pages as needed* to provide the required information in the format shown below on *all* individuals participating in the project.

Name Strayer, Jonathan Degrees(s) M.D. Social Security No. [redacted] (C)
Position Title Assistant Professor Date of Birth (MM/DD/YY) [redacted] (C) Role on Project Project Director
Organization Baylor College of Medicine Department Physical Medicine & Rehab.

Name Priebe, Michael M. Degrees(s) M.D. Social Security No. [redacted] (C)
Position Title Assistant Professor Date of Birth (MM/DD/YY) [redacted] (C) Role on Project Investigator
Organization Baylor College of Medicine Department Physical Medicine & Rehab.

Name Rosenfeld, Jay Degrees(s) M.D. Social Security No. [redacted] (C)
Position Title Assistant Professor Date of Birth (MM/DD/YY) [redacted] (C) Role on Project Investigator
Organization Baylor College of Medicine Department Physical Medicine & Rehab.

Name _____ Degrees(s) _____ Social Security No. _____
Position Title _____ Date of Birth (MM/DD/YY) _____ Role on Project _____
Organization _____ Department _____

Name _____ Degrees(s) _____ Social Security No. _____
Position Title _____ Date of Birth (MM/DD/YY) _____ Role on Project _____
Organization _____ Department _____

A Placebo-controlled Trial of Tetrahydrocannabinol (THC) in the Treatment of Neuropathic Pain due to Spinal Cord Injury

Investigators:
Jonathan R. Strayer, MD
Michael Priebe, MD
Jay Rosenfeld, MD

1. Specific Aims

The specific aims of this study are to: (1) identify at least 100 individuals with neuropathic pain related to spinal cord injury (SCI) who are willing to participate a study of tetrahydrocannabinol (THC) as a treatment for their pain; (2) determine, through comparison of intervention and control groups, if therapy using controlled dosages of THC can be shown to alleviate neuropathic pain related to SCI; (3) identify measures of pain relief in persons with SCI that appear to be indicative of the efficacy of treatment; (4) document any side effects related to use of THC in treatment of neuropathic SCI pain; and (5) disseminate the results of the research using appropriate methods for addressing the information needs of health and research professionals, as well of people with disabilities.

2. Background & Significance

Pain is a common and frequently severe complication of spinal cord injury (SCI). The incidence of chronic pain has been reported from 48% to 94% and severe pain from 18% to 63% in various studies. Rintala (1991) found that 53% of people with SCI reported frequent pain, and 31% reported severe pain that limits their daily activities. In a postal survey of persons with SCI, Rose (1988) found that pain, not paralysis, was the reason that 36% of those unemployed were not able to work. In addition, 83% of those working stated pain interfered with their work. Nepumuceno (1979) reported that 23% (higher injuries) to 37% (lower injuries) of persons with SCI indicated that they would chose resolution of pain over a restoration of bowel and bladder function plus a hypothetical cure for their paralysis. One particularly frustrating aspect to management of pain due to SCI is the heterogeneous nature of pain in SCI. To date there is no consensus in the categorization of the different types of pain in SCI, however it is fairly clear that pain of neurologic origin occupies one or several of these categories (Donovan, 1982). For purposes of this study, neuropathic pain is pain primarily due to nerve dysfunction or injury, wholly or in part, as differentiated by pain due to musculoskeletal (eg. rotator cuff tear) or primary organ pathology (eg. appendicitis). Clearly, neuropathic pain after SCI is responsible for considerable amounts of pain, and added disability, and poses a clinical problem incompletely managed with the current arsenal of pain treatment.

Treatment of neurologic pain due to SCI has encompassed a wide variety of modalities. Currently there is no one therapy recognized to optimally manage pain after SCI. Agents recognized to result in some degree of relief have included diverse pharmacologic agents, including Tricyclic Antidepressants (TCAs: amitriptyline, doxepin), neurileptics, anti-seizure medications (carbamazepine, valproate), typically in combination with a TCA, non-steroidal anti-inflammatory medications (naproxyn, ibuprofen), and even long-term narcotics (Balazy, 1992). The variety and controversy about therapeutics in this area is perhaps the most compelling evidence that no single agent manages all patients with neuropathic pain due to SCI.

Delta-9-tetrahydrocannabinol (THC), the major constituent of hashish and marijuana, has been reported to have many beneficial therapeutic uses including: antiemetic for chemotherapy, appetite stimulant in cachexia, anti-glaucoma agent, anticonvulsant, antispasmodic, and analgesic. Many persons with SCI report beneficial analgesic and antispasmodic effects with use of marijuana during confidential clinical interviews. Although marijuana is an illegal controlled substance and classified as a Schedule I drug, THC is available in an oral capsule (dronabinol, Marinol®, Roxane Pharmaceutical Co.) and is classified as a Schedule II agent, approved by the FDA for clinical use in cases of nausea associated with chemotherapy and appetite stimulation for cachexia associated with AIDS.

There are few controlled trials in the literature demonstrating a beneficial effect for THC in treating neuropathic pain due to SCI. There is relatively good evidence from a few controlled studies (described below) that marijuana and cannabinoids, including THC are effective in reducing spasticity in persons with SCI and MS. However, most of these studies directed toward both pain and other neurologic symptoms have been done with small sample sizes and have not convinced the medical community about the potential benefit of THC for spasticity relief.

Literature Review

Maurer et al. (1989) reported a double blind, placebo controlled, single subject trial in which THC (5 mg) was compared with codeine (50 mg) and placebo in a multiple cross over study. Their subject was a man with severe pain and spasticity due to SCI after removal of an ependymoma. They found that THC was superior to placebo in all variables including improved pain, spasticity, sleep, concentration, mood, and micturition. Codeine was superior to placebo in all categories except spasticity relief. Only THC had an anti-spasticity effect. Codeine and THC had equivalent results in pain relief. Lindstrom et al. (1987) reported a double blind, placebo controlled trial of oral cannabidiol (CBD), an analog of THC for pain relief in persons with neuropathic pain. He found no difference in pain scores using a daily visual analog scale between CBD and placebo. However, numbers involved in the study were reportedly limited and details unpublished. Priebe and Markowski (1994) reported the case of a man with severe dysesthetic pain due to post-traumatic syringomyelia associated with SCI who had dramatic relief of his pain with oral THC. After more than 6 months of therapy, the dose required for pain relief had increased and the patient reported that he occasionally supplemented the oral THC with smoked marijuana to relieve his pain. He reported no cognitive or psychotropic side-effects, and his sperm counts and quality have remained normal throughout the treatment period.

The effect of cannabinoids on other neurologic symptoms similarly shows mixed results in a series of small studies directed at effects on spasticity. Consroe and Snider (1986) reported an uncontrolled trial of THC in doses ranging from 5 mg to 15 mg in persons with Multiple Sclerosis (MS) and found a reduction in tremor and ataxia in two of 8 patients. They later reported a double-blind, placebo-controlled study with oral THC for persons with spasticity due to MS and found it reduced spasticity in all of the 9 persons studied. Ungerleider (1987) reported a double blind, placebo-controlled, cross over study comparing THC to placebo in persons with MS and spasticity. He reported subjective improvements in spasticity at a dose of 7.5 mg. However, objective measures did not reveal statistically significant differences between placebo and THC. Meinck, Scholnle and Conrad (1989) reported improvement in spasticity and ataxia in a 30 year old man with MS after smoking a marijuana cigarette. They demonstrated the improvements using both clinical ratings and electromyographic recordings.

The literature, although mixed, suggests that there is potential for a significant therapeutic benefit from oral administration of THC in the treatment of pain in persons with SCI.. However, the studies performed have had small subject numbers and have not carefully described the individuals who received benefit from THC in terms of neurologic features of their SCI or described the types of pain that responded. Additionally, none of the small group studies report efficacy of THC for periods above several weeks.

3. Progress Report/Preliminary Studies

Preliminary studies of THC therapy in managing neuropathic pain in persons with SCI have been done by the principal investigators on a very small sample of individuals. Thus far, only four subjects have been provided THC under very controlled conditions, and primarily for the purpose of treating SCI-related spasticity. Careful follow-up with these four individuals, all persons with SCI, has revealed that, while each reported varying degrees of relief from involuntary lower extremity spasms, all reported that chronic pain that they had been experiencing, and which they associated with their injuries, was relieved. Subjective data collected on all four individuals indicate that THC reduces significantly the intensity of pain that these individuals had been unable to alleviate otherwise for periods ranging from several months to several years. However, no controlled study of pain levels has been conducted in these individuals to date, and no standardized measures of pain and its impact on function and quality of life have been completed thus far, owing primarily to lack of resources to support such investigative activities. In addition, the investigators have received a small grant from the Baylor Department of Physical Medicine and Rehabilitation to send out a questionnaire to individuals with SCI on the TIRR and VA mailing lists. Questions will concern therapeutic uses of marijuana among the sample. The questionnaires will be mailed in the very near future and the results will be obtained prior to beginning the proposed study.

4. Research Design and Methods

The primary thrust of this proposal will be to investigate the following hypotheses:

H_1: Tetrahydrocannabinol has significantly greater effect than placebo in the treatment of neuropathic pain due to SCI as evaluated by the Visual Analog Scale.

H_2: Tetrahydrocannabinol has significantly greater effect than placebo in the treatment of neuropathic pain due to SCI as evaluated by the McGill Pain Questionnaire.

H_3: Functional ability as measured by the Rand SF-36 will be greater during treatment of neuropathic pain due to SCI with THC than with treatment with placebo.

H_4: THC will remain effective in control of neuropathic pain due to SCI over a 4 month (16 week) period of time.

This study will be integrated with the Outcome Measures Core portion of the study. In this portion, questions on the impact of THC on functional activities will be addressed. Additionally, should these treatments be at all efficacious, this study will be able to investigate the effective dosing range for THC in the treatment of neuropathic pain due to SCI. It is hoped that with these data, patients will be afforded a measure of pain relief, and increased function. Clinicians involved in managing persons with neuropathic

pain and SCI will gain an effective modality to add to their pain arsenal.

Subjects

Subjects will be recruited from the TIRR and VAMC outpatient SCI clinics. Participation will be voluntary. Subjects will be compensated travel expenses up to $50. All protocols have been reviewed and approved by the Baylor College of Medicine, VAMC, and TIRR human subjects review committees. It is anticipated that to reach a power of 0.80, a minimum of 28 subjects will be required (see data analysis section below). Accounting for dropout over the course of the study will add additional numbers for a total of 50 initial recruits per year. Inclusion and exclusion criteria for participation are detailed in Table 1. Overall recruitment policy will be directed to obtain a representatively broad sample of the SCI population, in terms of level and degree of injury, gender, age and ethnicity. In this regard, it is expected that as many as 150 potential subjects may need to be screened each year in order to obtain the 25 intervention subjects and 25 control subjects that will be studied in each of the two years. Funding has been requested to cover screening examinations, as well as for evaluation of individuals selected for the study.

Materials & Methods

This study is broadly divided into two phases: Phase I—a double-blind, placebo-controlled assessment of the short-term effectiveness of THC in management of neuropathic pain in SCI, and Phase II—evaluation of THC (open-label) as a long-term agent in management of neuropathic pain in SCI.

Phase I

Phase I, the double-blind, placebo-controlled assessment of THC in SCI pain, is designed as a single group repeated measures examination. This design will afford maximal power for the number of subjects and expense. In this 9-week study, all subjects will receive both treatments (THC and placebo). The treatment presentation order will be counterbalanced, and half of the subjects will randomly be assigned to each presentation order. There will be a 1-week washout period between treatment phases. This is illustrated in the Table 2.

Table 1. Subject inclusion and exclusion criteria

Inclusion criteria	**Exclusion criteria**
SCI of traumatic or medical origin of any level, ASIA grade A, B, C, or D	pain due to obvious non-neurologic origin (ie, musculoskeletal)
age > 21 years	frank drug-seeking-behavior
competent mental state	unmanaged medical problems
pain of neurologic origin onset since the SCI	inability to comprehend the informed consent
lacks medical complication: UTI, decubiti	allergy to THC or marijuana
no ongoing substance abuse	history of seizure disorder
	history of angina or mitral stenosis
	pregnancy

Table 2. Order of Administration of Treatments

Group 1	THC	Placebo
Group 2	Placebo	THC

Each trial will have a four week course. The overall duration of the study will be 9 weeks. Summary of protocol and examinations are given in Table 3. Following an initial medical examination and completion of informed consent, patients will undergo random assignment to one of the two presentation orders as per Table 2. All subjects will undergo an initial pain test battery detailed below. Subsequently they will receive instructions concerning their medication.

Initial medical examination battery will consist of the following: complete medical evaluation including medical history, general medical examination, and neurologic examination. Consistent with the recommendations of the Outcome Measures Core Unit, initial pain assessment will consist of the Visual Analog Scale (VAS), McGill Pain Questionnaire, Qualitative Pain Interview, and introduction to Pain Diary. Other assessment approaches may be added based on recommendations of Outcome Measures Core Unit.

Table 3: Schedule of examinations and interventions

Week*	Medical	Dose†	VAS (daily)	McGill	Qualitative Interview	Core Outcomes
1*	Full medical evaluation & orientation	A	x	x	x	x
2**	Check	A	x		x	
3		A	x			
4**	Check, review	A	x	x	x	x
5***		NONE	x			
6*	Check & orientation	B	x	x	x	x
7**	Check	B	x		x	
8		B	x			
9**	Check, review	B	x	x	x	x

*Weeks 1 & 6: Evaluations wll be made at the beginning of the week. Dose begins immediately thereafter.
** Weeks 2, 4, 7, & 9: Evaluations will be made at the end of the week.
***Week 5 is a wash-out period between placebo and control
†Dose refers to either placebo or THC dose plan as specified in Table 4

Detailed description of these pain and function measures are available elsewhere, and brief descriptions follow. The Visual Analog Scale is a relatively simple means of documenting both chronic and acute pain. It has particular power in evaluating changes in pain in the same person over time, and has been shown to have validity in the evaluation of chronic and acute pain (Price, 1983). The McGill Pain Questionnaire consists of several subsections designed to evaluate pain location, quality, and severity. It has been used to track chronic pain, and has provided robust quantitative measures that can be treated statistically (Melzack, 1975).The Qualitative Pain Interview will be in the form of a brief series of questions given orally to the patient at the time of their clinical check-in. Responses will be noted, examined and evaluated. In addition to gathering pain data, the questionnaire is anticipated to help maintain subject enrollment by increasing rapport with the investigators. The Pain Diary will be a recording form issued at each clinical contact containing measures of pain intensity (VAS), recording of required supplemental (non-study) pain medication, and an open-ended comments section.

Following their initial assessment, patients will receive a a two-week supply of Pain Diary sheets. These will be collected at the biweekly clinical check-in, and subjects will be issued their new medication dose, plus new Pain Diary forms. Medication will be issued in a new bottle for each week of the study. Each bottle will clearly state the week of the study, date, and instructions schedule for use. This visit will allow collection of the medication bottles for the previous two weeks and documentation of unused medication. Unused medication may serve as an index of medication use. During these visits opportunity will be given to address problems with the protocol, medication or other issues.

At the conclusion of each four-week drug trial, patients will again meet with the physician to discuss their medical response and review their general medical evaluation. They will again undergo the Full Pain

Assessment Battery (VAS , McGill, and Qualitative Pain Interview), as detailed above.

THC has been used in the past primarily as an antiemetic in conjunction with oncologic chemotherapy. Adverse reactions associated with THC are limited. Psychotropic effects are noted at therapeutic antiemetic doses in some individuals. This is typically evidenced by mood changes, perceptual distortions, and somnolence. Patients will be advised that they must exercise caution during the study period, particularly surrounding the period of dose changes. Caution is advised in patients with history of epilepsy and in patients with angina or mitral stenosis. Overall, the safety of oral THC has been well-established, and toxic effects are rare. Terminal elimination half-life for THC and its metabolites is 48 hours, thus the 1 week "wash-out" period between drug and placebo phases of the study should be sufficient. Drug will be dosed in accordance with recommended dosing practices as recommended by the American Hospital Formulary Service and less than that recommended for antiemetic use. Subjects will be placed on a program of increasing dose as per the protocol displayed in Table 4. Initial dose will start at 2.5 mg taken orally twice per day. Final dose will be 7.5 mg QID. If at any time adverse effects become excessive, subjects will reduce dosing to the highest comfortable level. Placebo will be standard dose of lactose powder. Both groups will utilize standard unlabeled capsules.

Table 4: THC and Placebo Dosing

Week	Dose of THC*	Dose of Placebo
1	2.5 mg BID	One Capsule BID
2	2.5 mg QID	One Capsule QID
3	5 mg QID	Two Capsules QID
4	7.5 mg QID†	Three Capsules QID

*—2.5 mg caps of THC will be used, therefore equal number of capsules used in each group
†—If adverse effects become excessive, subjects will reduce dose to the highest comfortable dose

Phase II

An open-label, long-term exploration of the effectiveness of THC in neuropathic SCI pain will commence following completion of Phase I of the study. Of those completing Phase I, those with a significant response will be considered candidates for Phase II. Significance of response will be determined by response on the Qualitative Pain Interview, question #6: "Based on your current experience with the study medication, do you think it would be useful to use in the long-term control of your pain?" The response following the period with actual THC (i.e., not placebo) will be used.

Subjects qualifying for this phase will enter a maintenance dosing with concurrent pain and functional monitoring for 4 months. They will be seen by the physician once per month. As with Phase I, the pain measures to be used will be the VAS, McGill Pain Questionnaire, and the Qualitative Pain Interview. The dose of THC required to maintain effective pain control will serve as an additional variable of interest in this trial. At the time of their monthly visits, subjects will be be assessed using the Core Measures in order to determine if the intervention has any impact on the functional abilities of study subjects over the short term and over an extended period. This follow-up will also be designed to determine how chronic pain affects the lives of people with disabilities and whether there is any perceived alteration in quality of life when individuals are obtaining treatment and after treatment. The types of follow-up to be done by staff of the

Outcome Measures Core Unit are described in detail in the section of this application about the Outcome Measures Core (Core B). This description includes information on the frequency and duration of follow-up to be done with subjects in this study, as well as with subjects in other studies to be performed under the auspices of the DPMC. The reviewer is referred to the description of the Outcome Measures Core (Core B) for details on follow-up activities related to functional and quality of life measures.

Data Analysis

Data from this investigation will be analyzed using a multivariate repeated measures design. Power calculations for single group repeated measures designs have been established by Green (1990, as cited in Stevens, 1992). These power estimates are based on the following measures: average correlation of the repeated measures, the number of repeated measures, the expected size of the effect and the level of Alpha for the analysis. Data from the McGill Pain Questionnaire will be analyzed in a repeated measures MANOVA design. The power estimate for this portion are based on four repeated measures with an expected average correlation of r=0.5 and moderate effect of 0.35 in magnitude and alpha of 0.05 suggests that the number of needed subjects is 28 to yield a power of 0.80. Allowing for attrition over the extended course of the study, and the variable dosing during the study which might lead to underestimation of effect initially, the number of subjects recruited will be 50. These power estimations are conservative, and true power of the study is expected to exceed the 0.80 target.

Qualitative data from pain interviews as well will be grouped and coded. These data will then be examined relative to other measured parameters and subject characteristics.

Table 5: Timeline for THC-Placebo Study

Month	Recruitment	Drug Trial	Data Analysis
1	√		
2	√	√	
12	√	√	√
18	√	√	√
20		√	√
22			√
24			√

Dissemination: The results of the study will be published in scientific journals such as Pain and the Archives of Physical Medicine and Rehabilitation and presented at national meetings such as the American Congress of Rehabilitation Medicine and the American Paraplegia Society.

5. Human Subjects

(1) Involvement of human subjects. A total of 100 individuals with spinal cord injury (SCI)who report chronic pain that is identified as neuropathic in origin will be involved in the investigative portion of this study. In selecting these individuals, it is expected that up to 300 persons with SCI may undergo screening

that may involve taking a health and social history and undergoing a complete or partial physical examination. Data on individuals not selected for participation in the study will be retained in their medical records in accordance with established standards for documentation. All medical and personal information will remain confidential and steps will be taken to safeguard confidentiality.

(2) Sources of research material. Research material obtained from human subjects will involve primarily information about the nature and intensity of the pain that the individual has been experiencing. However, in screening and selecting study subjects, other material may be taken to try to pinpoint the nature and cause of the pain reported by each individual. Blood and urine samples may be taken to rule out urogenic pain, x-rays may be taken to rule out musculoskeletal pain, and other diagnostic tests may be run based on the type of pain reported and the consent of the individual to undergo the procedure. Decisions regarding diagnostic and therapeutic interventions with study subjects will be made based on accepted standards of clinical practice. All subjects or potential subjects will be given complete information about all of the diagnostic and therapeutic options available to them, including the experimental options being tested here. They will also be informed about any known risks associated with any procedures that might be offered. All material gathered from research subjects will be maintained in a manner designed to protect confidentiality. This will include coding of information and reporting of results in aggregate form.

(3) Recruitment plans. People selected to participate in the study will be drawn from the Houston area community and are expected to be representative of the population of the area with respect to ethnicity. Efforts will be made to identify persons across the age range, but should be noted that SCI is a condition that often affects young men who engage in high risk behaviors. All study subjects will be 21 years of age or older, and it is expected, based on SCI prevalence data, that the group will be disproportionately representative of people under age 50. Also, the study group is likely to be composed primarily of men. While SCI is a low incidence condition in general, it is particularly low in women, who tend to engage in fewer high risk activities (e.g., drinking and driving, football) than do men. It is expected that the study group will be roughly 60% men and 40% women, although efforts will be made to achieve gender balance.

Recruitment efforts will target all segments of the community, from low income and minority neighborhoods to more affluent suburban areas. Information about the study will be prepared in both English and Spanish, and recruitment activities will involve use of media outlets (e.g., neighborhood newspapers, minority radio stations) that serve minority neighborhoods. A recruitment goal will be to attain a good mix of study subjects with respect to socioeconomic characteristics.

(4) Potential risks to study subjects. The potential risks associatedwith participation in this study are thought to be very low. There is a very slight risk that a study subject may have some sensitivity to a constituent of the THC or the placebos. However, normal precautions will be taken to identify any allergies or other drug or material sensitivities that might alert the clinician to potential problems.

A more likely risk is associated with functional and/or mental impairment related to the dosage of drug given to study subjects. In the very small number of patients (n = 4) with whom THC has been used on an experimental basis to date, the only potentially risky side effect that has been noted is some drowsiness in one patient. This resonse to the drug could pose a risk to an individual who might be engaged in behavior such as driving a car or operating equipment after taking the drug. The individual in whom this response was noted experienced less drowsiness when the dosage of drug was reduced. Careful observation of persons

taking medications, whether placebo or active drug, will be made under controlled conditions to assess the risk for impairment related to drowsiness or other unexpected responses to the medication. All individuals will be warned about the potential for drowsiness in taking the drug and will be cautioned against driving, operating equipment, or doing other tasks that require full alertness to avoid risk. With relatively little experience with THC, it is difficult to gauge the level of risk associated with its use. However, precautions will be taken to minimize risks through adequate warnings to participants and through careful observation of individual's response to the drug.

Another risk that bears mentioning has to do with positive results from drug tests that might be conducted by employers, law enforcement personnel, or others authorized to perform such testing. It is not the intent of this project to expose subjects to risk for loss of their jobs, arrest, or other actions that might be associated with illicit drug use. This risk can be alleviated by providing subjects with a letter indicating that they may test positively for certain illicit drugs and indicating which drug tests may be affected by use of THC. In cases where additional questions concerning the legality of THC use for medicinal purposes by employers or others are raised, one of the investigating physicians will become involved to determine if there is any likelihood that detection of drug use is related to participation in this study. Potential subjects will be advised of this risk prior to agreeing to be in the study.

(5) Procedures for protecting against or minimizing risk. Protection from or minimization of risk associated with participation in the study will be done in three ways. First, careful screening of potential participants to identify and exclude individuals who are likely to intentionally abuse prescrition, over-the-counter, or street drugs. Individuals reporting a history of non-medical drug use or who exhibit physical or behavioral signs of use of illicit drugs or abuse of alcohol will not be accepted into the study. Second, all individuals will be observed over a period of hours after being given the drug for the to determine if they experience any effects (e.g., drowsiness, decline of motor control) that suggests an impairing effect that may be related to the drug. If these effects do not respond to adjustments in drug dosage, then individual who exhibit them will be dropped from the study. Third, all individuals will be warned about any known or potential side effects that might occur after taking the medication. In the event that a study subject believes that he or she is experiencing any effect, other than spasticity and pain relief, that might be associated with the drug, he or she will be instructed to contact a staff physician on call at the VA Hospital who will, in turn, notify one of the physicians on the project who can speak with the study subject concerning his or her condition and determine if additional evaluation is required. If additional evaluation appears to be warranted, the physician will work with the study subject to arrange for travel to the VA Hospital for further assessment, or if the problem appears to be acute, to be seen by a physician at a facility nearer to the patient. Follow-up with the patient and the physician seeing him or her will be done to assess the likelihood that the reported effect was due to medication that the individual was given as part of this study. Data on all incidents that might be associated with participation in the study will be collected during assessment visits and through follow-up activities conducted by the Outcome Measures Core Unit.

(6) Reasonableness of risks in relation to benefits. Data from preliminary studies completed thus far suggest that there may be some risks associated with use of TCH in treatment of spasticity in people who are spinal cord injured. Risks identified thus far are limited to drowsiness that could impair functional ability. However, the limited data available also indicate a strong likelihood that THC relieves chronic pain in individuals with SCI. The benefit of this is significant. Chronic pain has a debilitating effect on the quality of life for people who experience it. It can result in diminished levels of activity and in decreased

involvement with family, work, and community. In this regard, chronic pain can result in disability that far surpasses that associated with loss of function from SCI. The limited data available suggest that THC can be a safe and effective means of ameliorating chronic pain that does not respond to other treatments. The risks associated with use of THC, at least to the extent that they are currently known, appear to be minimal when compared to the potential benefits that can accrue to people who are confronted with debilitating chronic pain.

6. Vertebrate Animals

Aside from the involvement of human subjects, there are no plans for use of animals in the proposed study.

7. Consultants/Collaborators

No collaboration with persons outside of project staff are proposed at this time.

8. Consortium/Contractual Arrangements

Collaboration between Baylor College of Medicine and the Houston Veterans Affairs Hospital is critical to the success of this project. There has been a formal cooperative arrangement between these two institutions for more than 25 years. This arrangement provides for staffing of VA facilities by Baylor physicians, as well as provision of learning experiences by Baylor health professions students assigned to the VA. The agreement also covers the conduct of mutually beneficial research, including assignment of indirect costs to the partner institutions when appropriate. The formal agreement of collaboration is renewed periodically and is maintained on file in the administrative offices of the two institutions.

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DESCRIPTION: State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project. Describe concisely the research design and methods for achieving these goals. Avoid summaries of past accomplishments and the use of the first person. This abstract is meant to serve as a succinct and accurate description of the proposed work when separated from the application. **DO NOT EXCEED THE SPACE PROVIDED.**

The long range plans of **Project 2** are to test **three hypotheses**: **(1)** A significant fraction of the chronic pain experience in people with disabilities is myofacial in nature. **a.** The pain referred from trigger points as defined by Travell and Simons (1992) is reduced by both permanent magnets and pulsed electromagnetic fields. **b.** Myofacial pain is alleviated best by application of magnetic fields to the trigger points; and, not necessarily, to the site of the pain experience. **(2)** Static electromagnetic fields induce a systemic response that causes a reduction in pain in patients suffering from disabilities including post polio syndrome. **(3)** Magnetic fields interact with Na^+ channels which cluster at trigger points.

The specific aims address both clinical and basic science studies. In polio survivors diagnosed as having post-polio syndrome and experiencing chronic pain, double-blind and placebo-controlled studies will be conducted on 250 randomly selected subjects to evaluate the effectiveness of permanent magnets of varying magnetic field strengths, pulsed electromagnetic fields, and static electromagnetic fields to reduce or eliminate chronic pain. The optimum application (to the site of pain, to trigger points, and or systemic application) of the magnetic fields will be evaluated.

In regard to mechanism, it is well known that appropriate ion channel transport is central to the integrity and proper functioning of nerve excitability and muscle contraction. Any disruption of their normal function would directly and markedly affect human neurosensory and neuromotor performance. Biophysical phenomena associated with ion transport are very low energy, in the millivolt and picoampere range. Therefore, electrophysiological changes in ion channel functions would be among the most sensitive indicators, if not the most sensitive indicator, to detect and quantify physiological effects of electromagnetic fields. In the *Xenopus* oocyte expression system, the cRNA of human voltage-dependent Na^+ channels is injected and their currents will be electrophysiologically characterized. **1)** The effects of AC, DC, and transient magnetic field strengths on the channel's current will be tested. **2)** The co-injection of magnetite and channel cRNA will test the well-developed hypothesis that magnetite may be a cellular coupler or transducer causing the channels to respond to the fields. **3)** The distribution and mobility of the magnetite and channel in the oocyte will be explored with magnetic resonance imaging (MRI) for comparison to that observed in mammalian cells. This plan of study will help elucidate the role of magnetic fields in the relief of pain and to begin to understand the underlying mechanisms of magnetotherapy.

PERSONNEL ENGAGED ON PROJECT, INCLUDING CONSULTANTS/COLLABORATORS. *Use continuation pages as needed* to provide the required information in the format shown below on ***all*** individuals participating in the project.

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EFFECT OF MAGNETIC FIELDS ON CHRONIC PAIN DUE TO OVERUSE IN PEOPLE WITH DISABILITIES

Investigators:
C. Hazlewood, Ph.D.
H. Hartmann, Ph.D.
C. Vallbona, M.D.

I. SPECIFIC AIMS

The long range plans of this project are to test three hypotheses: (1) A significant fraction of the chronic pain experience in people with disabilities is myofacial in nature. a. The pain referred from trigger points as defined by Travell and Simons (1992) is reduced by both permanent magnets and pulsed electromagnetic fields. b. Myofacial pain is alleviated best by application of magnetic fields to the trigger points; and, not necessarily, to the site of the pain experience. (2) Static electromagnetic fields induce a systemic response that causes a reduction in pain in patients suffering from disabilities including post polio syndrome. (3) Magnetic fields interact with sodium channels which cluster at trigger points.

The specific aims are divided into two parts: clinical studies and basic science studies.

A. Clinical Studies To Determine If Static And Pulsed Magnetic Fields Reduce Pain In Persons With Disabilities:

(1) In polio survivors diagnosed as having post-polio syndrome and experiencing chronic pain, conduct a double blind and placebo controlled study to evaluate the response to the application of permanent magnets of varying magnetic field strengths.

(2) To determine if pulsed electromagnetic fields relieve pain in the post-polio syndrome and other disabilities utilizing a double blind placebo-controlled protocol.

(3) By conducting a double blind placebo-controlled study, determine if a static electromagnetic field applied to the body attenuates pain.

B. Basic Science Studies To determine If Magnetic Fields Interact With Voltage-Dependent Sodium Channels:

It is well known that appropriate ion channel transport is central to the integrity and proper functioning of nerve excitability and muscle contraction. Any disruption of their normal function would directly and markedly affect human neurosensory and neuromotor performance. Biophysical phenomena associated with ion transport are very low energy, in the millivolt and picoampere range. Therefore, electrophysiological changes in ion channel functions would be among the most sensitive indicators, if not the most sensitive indicator, to detect and quantify physiological effects of electromagnetic fields.

(1) In *Xenopus* oocytes, identify and quantify the effects of AC, DC, and transient magnetic field strengths on electrophysiological properties of human voltage-dependent ion channels.

(2) Test the well-developed hypothesis that magnetite, Fe_3O_4, may be a cellular coupler or transducer which causes the ion channels to respond to the fields by co-injection of magnetite and ion channel cRNA into the oocytes.

(3) Explore the distribution and mobility of the magnetite and ion channels in the oocytes with magnetic resonance micro-imaging (MRI) for comparison to that observed in mammalian cells.

II. BACKGROUND AND SIGNIFICANCE

A. Clinical studies. Background Pain resulting from over use in people with disabilities is a problem that is being addressed by this RFA. The magnitude of the population involed with the malady is unknown; however, one well-known group within the broad group of disabilities is the survivors of polio. Within this group is found a sizable number people suffering from both chronic and acute pain: the Post-polio syndrome. This syndrome occurs in a high percentage (about 35%) of polio survivors, approximately 30-to-35 years after the onset of acute poliomyelitis. One of the typical manifestations of the syndrome is pain in the muscles initially affected by polio, as well as the muscles that seem to have been initially unaffected. The pain is considered to be due to myofascitis secondary to progressive denervation. Halstead *et al.* (1985) (see p.18) compiled responses to questionnaires sent in 1985 to polio survivors identified through informal networks. The responses describe the physiological impairments and their disability implications. Subsequent observations have revealed psychological and social effects. For our interests in this project, 75.5% of the patients had muscle pain and 75.4% had joint pain. We will address this point again later.

Historically, post-polio symptoms were reported by Carriere, Cornil and Lepine, and by Raymond and Charcot in 1875. C.S. Potts described "progressive muscular atrophy" in 1903 in *The University of Pennsylvania Medical Bulletin.* About 200 cases were described in reports between 1875-1975 and currently, those descriptions are considered clinically typical post-polio manifestations. Over 500 cases were specifically described since 1975. It has been recognized as a clinical entity since 1981.

Almost 2,000 cases have been diagnosed at The Institute of Rehabilitation and Research (TIRR) since 1983. Thus, in this population of disabled persons, we have a well-defined group that we assume represents the disabled in general.

The types of pain experienced in this group is multiple, including a lot of diffuse muscle and joint pain (Smith and Mabry, 1995). Recovery from the diffuse muscle pain can take many months and requires considerable compliance (Peach and Olejnik, 1991). The joint pain is thought to be due to degenerative arthritis caused by age and by a long-standing asymmetrical load on the joints which results from the typical asymmetrical skeletal load distribution brought about by the muscle paralysis. Subacute or chronic sacroiliitis occurs very often, but many times it is not recognized because it is masked by other forms of low back pain.

Static and time-variable electromagnetic fields have been applied with apparent success in the management of pain in a variety of orthopedic conditions, most commonly traumatic bone fractures or surgical osteotomies (Becker and Selden, 1985; Becker, 1990; Miner and Markoll, 1993). In the domain of osteoarthritis there are double blind Placebo controlled studies that demonstrate the efficacy of pulsed electromagnetic fields (Trock *et al.*, 1994; Bassett, 1994).

An excellent overview of the biological effects of electric and magnetic fields has been edited by Carpenter and Ayrapetyan (1994); it is clear that this is an emerging field in biology and medicine. Attempts are being made to scientifically document the impact of electric and magnetic fields on biological systems. In addition, the World Health Organization (1987, 1989) reports "the available evidence indicates the absence of any adverse effects on human health due to exposure to static magnetic fields up to 2T (2T = 20,000 Gauss).

In regard to the usefulness of permanent (static) magnetic fields in pain relief, poorly documented reports have been published (Davis and Rawls, 1974a; 1974b). Unfortunately, most of the studies on the application of static magnetic fields (i.e., permanent magnets) have been of the descriptive type and our search of the literature has not revealed any reports of what might be called serious scientific clinical trials. [In personal communication with the Scientific Attache, a Physicist, of the French Consulate here in Houston, we have learn of a lot of uses, in France, of permanent magnets of different configuration to relieve muscle and joint pain. Again, no studies of the double blind type. We, of course, are aware of the common use, in Japan, of permanent magnets to relieve pain. Also, here in the United States, various configurations of permanent magnets are being used. One such company, Magnaflex, Inc. has invited us to use their magnets in a scientific study and they are providing magnets and placebo controls.] To our knowledge, the use of static magnetic fields has not been tried on post-polio patients.

B. Basic Science Studies. Trigger points may be latent or active and Travell and Simons (1983) define them as "a focus of hyperirritability in a tissue that, when compressed, is locally tender and, if sufficiently hypersensitive, gives rise to referred pain and tenderness..." Thus, a trigger point is a functional, rather than an anatomical, entity. Because of this point we hypothesize that trigger points arise from the clustering of sodium channels. Indeed, the excitation processes of cells involves sodium channels. Therefore, it is thought that most, if not all, pain will be associated with sodium channels. Sodium channels are known to be concentrated in the depths of synaptic folds (Slater *et al.*, 1992). The speculation that sodium channels may cluster to form trigger points is not without possibility as is evident from recent studies (England *et al.*, 1994; Devor *et al.*, 1993; Dugandzija-Novakovic *et al.*, 1995; Worden *et al.*, 1994). Neuropathic pain has been responsive to agents that are use-dependent sodium channels blockers such as lidocaine, carbamazepine, and mexiletine (Abram and Yaksh, 1994; Tanelian and Brose, 1991).

1. ***Sodium channels are the basis of excitability in most excitable cells.*** The ability of neurons and most excitable cells to initiate an action potential is dependent upon voltage-gated sodium channel proteins (Hille, 1984). These proteins regulate the inward flux of Na^+ ions from the extracellular space into the cytoplasm at a rate of 10^6 ions/sec in response to the changing membrane voltage. As the wave of depolarizing current spreads around the cell, other voltage-driven ion channels specific for Ca^{2+}, K^+, and Cl^- ions are activated at their specific voltage ranges and the action potential propagates. The inactivation of the Na^+ channel occurs before the peak of the action potential and the Na^+ conductance falls. The axon hillock or first node of Ranvier is a localized region near the cell soma on the membrane of most vertebrate neurons rich in Na^+ channels (Dodge and Cooley, 1973). Its purpose is to transform incoming depolarizations from somatic and dendritic inputs into a firing pattern.

The cDNAs of voltage-dependent Na^+ channel proteins have been cloned and are now known to be a subset of a super-gene family that includes voltage-dependent Ca^{++} and K^+ channels and cyclic nucleotide (cNT)-gated channels. The family of voltage-gated sodium channels presently consists of seven distinct genes. In the mammalian brain and central nervous system, three cDNAs and two splice variants have been cloned and

localized to chromosome 2 (for review, see Mandel, 192). Recently, in central nervous system glial cells a sodium channel has been cloned and has also been detected in other peripheral tissues such as heart, skeletal muscle and lung (Gautron *et al.*, 1992). The heart and skeletal muscle each express a unique sodium channel gene from chromosome 3 and 17, respectively, (George *et al.*, 1991). The newest member, a peripheral nerve sodium channel, designated type I or PNI, has also been successfully cloned (D'Arcangelo *et al.*, 1993).

Dr. Hartmann has cloned both the human brain type II and human cardiac sodium channel cDNAs. Both cDNAs express functional voltage-gated sodium channel proteins in *Xenopus* oocytes and mammalian cell expression systems (Hartmann *et al.*, 1994a; Hartmann *et al.*,1994). In addition, she has available in her lab the rat skeletal muscle sodium channel cDNA (Trimmer *et al.*, 1989), the rat brain type III sodium channel cDNA (Joho *et al.*, 1990), rat brain type IIa sodium channel cDNA (Auld *et al.*, 1992), and several rat brain K^+ channel cDNAs (Frech *et al.*,1989; Drewe *et al.*, 1992). Although incomplete at this time, she has all the cDNA fragments of human brain type I to ligate together and complete that cDNA.

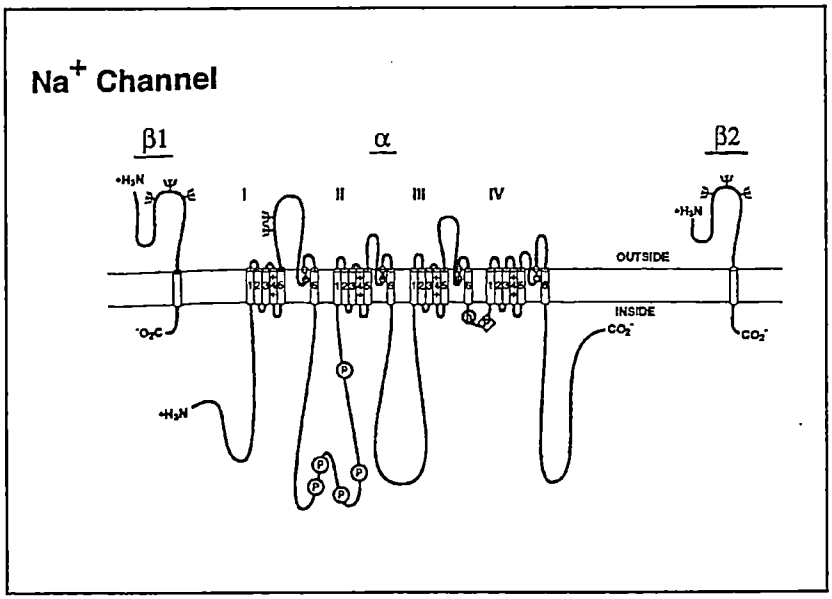

Figure 1

The general structural organization of the family of voltage-gated Na^+ channels is an integral membrane protein with homologous units repeated four times. Shown in figure 1, is an accepted topological map of the protein consisting of the α, β_1, and β_2 subunits. The α subunit is the ion conducting protein whereas the auxiliary subunit, β_1, speeds of activation and inactivation of the brain and skeletal isoforms. β_2 subunit is covalently attached to brain α subunits has a role in targeting the α subunit to the membrane. Each repeat in the α subunit is connected by a cytoplasmic domain, and each repeat contains 6 α-helical transmembrane segments. The degree of homology at the amino acid level is approximately 86% for the brain sodium channel proteins and lower between these and skeletal muscle (65%) and cardiac (70%) sodium channel proteins. However, the basic structural segments of the proteins are similar consisting of a pore or ion conducting region, an intracellular segment controlling the fast inactivation of the protein, and a highly-charged (positive) voltage sensor. These motifs although basic to all the sodium channel proteins, each subtype has different phenotypes of these perspective properties due to variations at the amino acid level. Therefore, any one member is suitable to the initial basic science experiments outlined in this proposal.

The voltage sensor has been delineated as the fourth transmembrane segment (S4) and is oriented such that the 5' to 3' end of the segment traverses the membrane from the outside to the cytoplasmic side of the membrane. The predicted structure is that of an α-helix and the S4 has the unique feature that positive side chains of the its amino acids are in register along its length. These features of S4 are conserved among voltage-gated Na^+, K^+, and Ca^{2+} channels. Site-directed mutagenesis studies demonstrated that these positive charges are necessary for the gating of the channel (Stuhmer *et al.*, 1989). It has been postulated that these positive charges are the positive

charge in the dipole that serve as the voltage sensor. External cations can influence the voltage dependence and ion permeation through the channel in a number of ways. The negative fixed charges surrounding the channel from the negative head groups of phospholipids or from acidic residues on the channel itself can be nonspecifically screened and therefore alter the intramembrane voltage sensor. It is estimated by Greene *et al.*, (1987) and Naranjo and Latorre (1993) that Na^+ channels have between 0.3 and $0.6e^-/nm^2$ of charge in the outer vestibule. Another source of negative charge to the proteins are the glycosylation sites on the extracellular segments of the proteins. Brain channels have a greater density of negatively-charged sialic acid residues that the cardiac isoform from studies with neuraminidase treatment (Hauser *et al.*, 1995).

2. ***The effects of magnetic fields on biological systems: The need to clearly define the exposure variables and other conditions.*** Electrical and magnetic field effects may be experienced by individuals in various environments; however, the determination of the variables of exposure and other environmental and physiological conditions which produce the biological consequences is ill-defined. For example, epidemiological reports of effects in humans have indicated the possibility that power-line-frequency magnetic fields can contribute to increased incidence of cancer in children (Wertheimer and Leeper, 1979; Feychting and Ahlbom, 1993). Other epidemiological studies have also reported that similar fields have adversely affected reproduction and development, particularly in the first trimester (Wertheimer and Leeper, 1986; Lindbohm *et al.*, 1992). Further research defining unequivocally the EMF parameters necessary for initiation of these insults is needed.

In vitro experiments correlating EMF effects on the immune system are well-documented (Walleczek, 1992). However it is clear from this review and that of Blanchard and Blackman, (1994) that simple linear relationships between parameters of field exposure and the EMF response is difficult to demonstrate. Signals can differ considerably from each other in field intensity, frequency and wave form. Mechanisms involving the Ca^{2+}-signaling pathway are inferred from these studies to have a role in the EMF-induced effects on cells of the immune system (Conti *et al.*, 1985a; Conti *et al.*, 1985b; Walleczek and Liburdy, 1990). The study by Weaver and Astrumian (1990) examined the minimum field intensity able to influence cells in the absence of a biological amplification system. Their calculations include a weak field intensity of 0.01-0.001mV/cm would significantly affect membrane-associated proteins, ie., receptors, enzymes, and channels. Calcium channel antagonists were used as magnetoprotective agents in a study of weak static field effects on human polymorphonuclear leukocytes demonstrating a physical interaction. (Papatheofanis, 1990).

3. ***Previous experiments with EMFs on ion channels did not control all experimental variables.*** Some previous studies have not demonstrated electrophysiological effects of low amplitude magnetic fields on several ion channel preparations. Galt *et al.*, (1993) and Wang and Hladky (1994a) utilized voltage-independent (and relatively uncharged) gramicidin channels in a synthetic lipid bilayer. Wang and Hladky (1994b) subjected excised patches of membrane from an insulin-secreting cell line (CRI-G1) containing K^+ ATP-sensitive channels to applied magnetic fields. The field strength tested on these channels was between 50-5000μT. These experiments did not incorporate elements that would have significant effects in an actual cellular system. The gramicidin ion channels are in a synthetic lipid bilayer; which does not incorporate ferromagnetite, as do membranes of human cells. Other membrane and intracellular structures with coupling effects were absent. Also, these experiments were not conducted at physiological temperatures. Blackman *et al.*, (1991) have shown a clear effect of temperature on calcium ion release from *in vitro* avian brain slices subjected to low strength magnetic field, 64nT. These studies were conducted at temperatures between 35° and 38° C; and demonstrated effects from applied fields only between 36° and 37° C.

Mathematical studies have presented theories that small numbers of magnetite crystals are sensitive to very weak magnetic (including geomagnetic) fields; and, in response to these fields, forces exerted by these crystals are capable of opening membrane ion channels (Kirschvink *et al.*, 1992). Magnetite is found in bacteria and algae and, in principle, can account for these organisms' magnetic alignment (Fankel and Blakemore, 1980). Magnetite may well be responsible for the magnetotactic response of honeybees (Kirschvink, 1981). Magnetite exists in human cells; its crystals have the same characteristics as those in the magnetotactic bacteria (Kirschvink *et al.*, 1992).

In the proposed experiments, the oocytes will be subjected to different applied magnetic fields and the currents through human brain, cardiac, and skeletal muscle Na^+ and K^+ channels embedded in the oocyte cell membrane will be measured at physiological temperatures. There is already a large bank of data and analyses in the principal investigator's laboratory on the electrophysiological function of these channels, to provide a baseline for precise analysis of EMF-induced effects.

III. PRELIMINARY DATA

A. Clinical Studies. 1. *Permanent Magnet Therapy.* Anecdotal reports of the benefits of these devices abound (even in post-polio patients who have reported pain relief to us), but the literature does not contain reports of well designed scientific evaluations of their effect. The investigators of this study have placed magnets on themselves on painful joint areas affected by arthritis and have observed significant benefits after a very brief application of magnetic discs (within minutes). Also, by applying the magnets to trigger points of referred pain (Travell and Simons, 1992), volunteer subjects have been relieved of their pain within twenty to forty (40) minutes. The amount of time that the magnets need to be applied, appears to be a function of the field strength of the magnet. This point, along with determining the optimum placement of the magnets (i.e., to the actual site of pain, or to the trigger point associated with the referred pain), are the major focal points of specific aim 1.

We are currently involved in an approved study of magnets for the relief of pain in the post-polio patients. The study is double blinded and placebo controlled. Static magnetic fields can be delivered to a localized area by placing magnets of different field strengths on the skin over the affected area. These magnets usually vary in strength from 300 to 500 Gauss (at the surface of the magnet), are disc-shaped, 40 mm in diameter and 1.5 mm thick. The disc magnets can be kept in place by means of adhesive tape. It is clear from initial studies that the application of the magnets to a trigger point does reduce or eliminate the pain referred from that trigger point. Application of the magnet to the site of the pain, did not always lead to pain reduction. This observation has prompted us to test, with stronger magnets, if pain relief can be achieved by treating the site of the pain.

An amendment to our original pilot study, approved for 50 subjects, has been approved for the inclusion of 250 subjects, magnets of different configuration, and larger magnetic field strengths. A variety of magnets are commercially available. They have different shapes, but all of them can be easily kept in place over any selected area of pain (or trigger point associated with referred pain) on the post polio patient. (The specific magnets that are used in our current study are the Bioflex Biomagnets with a pattern of concentrically arranged circles of alternating magnet polarity.) We have made arrangements to purchase additional magnets, varying in field strength from a few hundred to 5,000 Gauss. Placebos will also be provided.

We have consistently observed relief which has been evident by subjective evaluation and, in many cases, functional endpoints. Because we are in the midst of our 50 subject pilot study, we can not speak to the

magnitude of the placebo effect. We have, however, identified a potential problem having to do with adipose tissue. In subjects not approved for inclusion in our study and having heavy adipose tissue coverage over trigger points, we have learned that relief from myofacial pain can be achieved by the use of stronger magnets.

The mechanisms of the effect of magnetic fields on soft tissues have not been elucidated. We postulate that in addition to the known effect of magnetic fields on the nuclei of water molecules, there could be a change in the tensile properties of cartilage, ligaments, and other soft tissue structures which secondarily may relieve tension on arthritic joints or on chronically "inflamed" areas. Such ideas seem very possible in light of the work of Becker and Selden (1985) (see particularly pp. 126-135).

2. *Studies with Static Electromagnetic Fields.* Pilot studies, using a static electromagnetic device made by Joules Electric (DBA) and conducted in Mexico city, have provided rather convincing evidence that systemic effect can be evaluated. A dependent limb (usually the arm) is placed in coil and the limb is exposed to the magnetic field for 30-45 minutes (the approximate time to expose the entire blood volume to the magnetic field. In the few studies we have conducted on persons suffering from epileptic seizures, the patients were selected whose disease had been apparent for varying numbers of years, and who, despite having been treated with different treatment schemes, did not have the ability to control their (epileptic) crises. All of the patients that we have studied were characterized with electro-encephalography, computer axial tomography, and serum levels of anticonvulsants. In these preliminary studies the findings show that all patients improved. The improvements consisted of reduced number of episodes, their intensity, improvement in the degree of animation, and disappearance of post-episode depression. The cessation of seizures varied in duration from days to months. Anninos et al. (1991) have reported somewhat similar findings.

In other studies we have observed pain reduction in various arthritic conditions. We feel that the preliminary data are sufficiently encouraging to proceed with controlled clinical studies to evaluate its efficacy for the relief of chronic pain. Again, the subject simply places either forearm inside the covered coil of the static electromagnetic device for a period of 40-45 minutes (approximate time for exposure of the entire blood volume to the static electromagnetic field).

3. *Studies With Pulsed Electromagnetic Fields.* No studies have been completed in our laboratories because of lack of equipment; however, Dr. Hazlewood, as a consultant has reviewed the literature and several laboratories that use pulsed electromagnetic equipment for treatment of various disorders. In addition to the references given in the Background section, efficacy has been demonstrated, in a randomized, prospective, double blind study, reduction of swelling and pain from sprained ankles (Pennington, et al., 1993). Also, the healing of stage II and stage III pressure ulcers has been demonstrated following electromagnetic therapy (Itoh, et al., 1991).

B. Basic Science. 1. *Molecular cloning of human voltage-gated sodium channels.*
Dr. Hartmann has cloned the cDNAs for both the human cardiac and human brain Type II Na^+ channels. The 6.02 kb cardiac clone, designated hH1a (Hartmann *et al.*, 1994b), was cloned from a fetal cDNA library (75%) and adult ventricular myocytes (25%). The open-reading frame of the cDNA consists of 2015 amino acids and when translated by T_7 polymerase into cRNA and injected in *Xenopus* oocytes, expresses currents similar to those observed *in vivo* ventricular myocytes (Bustamante and McDonald, 1983) and to those produced by the cRNA of another human heart Na^+ channel, hH1, in oocytes (Gellens *et al.*, 1992). hH1a is also stably expressed in the human embryonic kidney cell line, HEK-293 cells.

The cRNA of the full-length human brain type II Na^+ channel cDNA, hB2, (Hartmann *et al.*, 1994a), expressed functional proteins in the *Xenopus* oocytes. The cRNA of the rat brain auxiliary subunit, $ß_1$ (Isom *et al.*, 1992), was co-injected with hB2 cRNA to normalize the kinetic properties to those observed in neurons *in vivo*. The partial cDNAs comprising the 6.4 kb cDNA of hB2 were found in a randomly-primed cDNA library made from human cortical tissue.

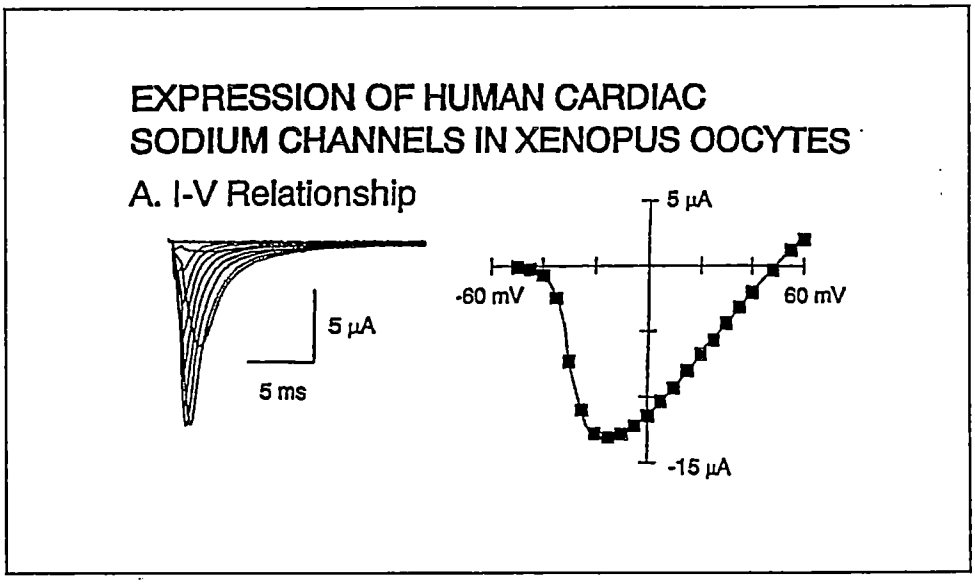

Figure 2

2. *Studies of channels in oocytes.* Structure-function studies with site-directed mutagenesis on the sodium channels have focused on inactivation properties (Hartmann *et al.*, 1994b) and properties attributed to the pore including Tetrodotoxin (TTX) and Saxitoxin (STX) blockade and elucidating a secondary structure model of the peptide segment comprising the pore (Kirsch *et al.*, 1994).
hH1a has a single channel conductance of 19.5 ± 3.2 pS with typical current-voltage relations for sodium channels, ie., reversal potential of $^+58.7 \pm 4.4$ mV, peak current at -10mV, and a midpoint potential of steady-state activation ($E_{0.5}$) of -45.3 ± 4.1 mV. Shown in figure 2 are macropatch tracings of a current-voltage family. Currents were evoked by test pulses ranging from -70 to +60mV.

Shown in figure 3 are typical whole-cell tracings of acurrent-voltage family of hB2 sodium channel currents.
Currents were evoked by test pulses from -50mV to +60mV.
The co-injection of rat brain $ß_1$ subunit cRNA with hB2
α subunit normalizes the inactivation kinetics.

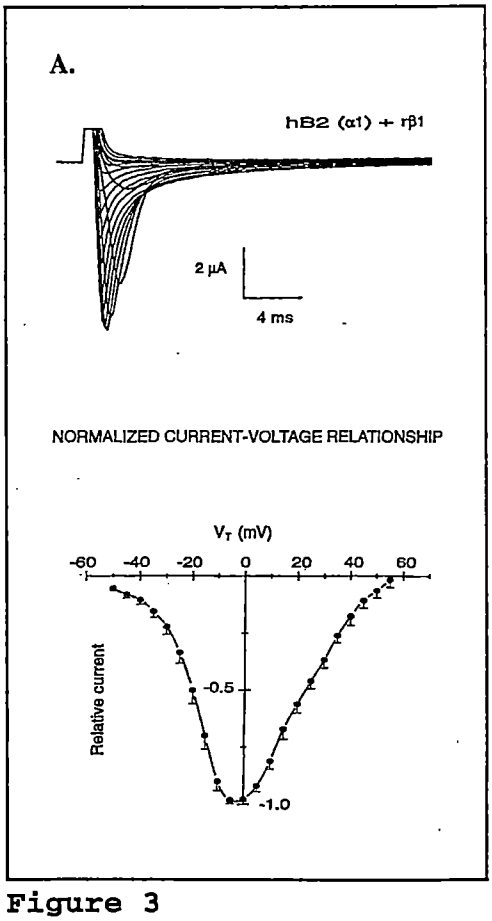

Figure 3

IV. RESEARCH DESIGN AND METHODS

A. Description of the Clinical Study. We intend to evaluate 250 patients seen in the TIRR Post Polio Clinic by one of the investigators (Carlos Vallbona, M.D.). Those who complain of pain in specific areas of the body will be invited to participate in the study by the attending physician or his designee (usually the Clinic's physical therapist or nurse). The purposes of this study will be thoroughly explained to the patients and those who agree to participate.

Those patients selected for the study will be randomized to receive permanent magnet therapy, static electromagnetic therapy, or pulsed electromagnetic therapy. In each of these categories, the subjects will be randomly selected to receive the magnetic field or placebo therapies.

In the case of the permanent magnets, all the devices (active and inactive) will be kept in labeled boxes from which they will be pulled out at random before applying them to the patient's skin on the site of pain or over the trigger points. All the devices will have identical size and shape and their magnetic activity will be known only by the manufacturer by a code number affixed on each device. The code number used in each instance will be duly recorded in a log kept by the investigators. Thus, neither the investigators, the clinic personnel, nor the patient will know which disc is magnetically active until the code is broken at the end of the study. An observer will be assigned to each room to ensure that neither patients nor investigators will check for magnetic activity of the discs.

Prior to the placement of the placebo or the active magnet, the patient will be asked to manifest the intensity of pain by the exact forms and procedures determined by the core. After the disc (magnetically active or inactive) has been in place for 40 minutes, the patient will be asked again to rate the pain according to the exact protocol designed by the core. The magnets will be removed and returned to the box for future use.

The static electromagnetic fields will be produced by a device which will be configured such that the field will be on or off. It will not be possible for the investigator or the subject to know if the field is actually on or off. The log book will be maintained by third party and will not be available until the end of the study. At which time the investigators will be informed as to which subjects actually received the therapy. All subjects will be ask to rate their pain before and after the application of the device.

In the case of the pulsed electromagnetic fields, the active, or inactive head will be placed over trigger points or the site of pain. It is at present, expected to apply the treatment for 30-45 minutes. Neither the subjects nor the investigators will know who actually receives the treatment until they are given the log book at the end of the study. All subjects will be ask to rate their pain before and after the application of the device.

B. Basic Science Experiments 1. ***Molecular Biology of human voltage-dependent ion channels.***
The cDNAs of human brain and cardiac Na^+ channels have been cloned by Dr. Hartmann and are routinely used in her laboratory for structure-function studies of kinetic and ion conduction properties of these proteins (Hartmann *et al.*, 1994a; 1994b; Kirsch *et al.*, 1994). The human brain Na^+ channel cDNA, hB2, is the counterpart of rat brain type II. From 24 hours after injection of 1-5ng of the channels' cRNA into *Xenopus* oocytes, nA-μA of Na^+ current can be recorded (Drewe *et al.*, 1994). Currents are routinely measured from injected oocytes maintained at 19° C for up two weeks after injection.

Presently, only hH1a is stably expressed in the mammalian cells, HEK-293. The brain channel, hB2, will be stably transfected into the HEK cells by lipofectin and selection for transfected cells is with geneticin or G418. The vector housing hB2 will be pcDNA (Invitrogen) which includes the DNA for geneticin resistance. Selection normally takes 4 weeks. HEK-293 cells are approximately 20 μM in diameter for round cells and 12 μM by 40 μM for cigar-shaped cells. Currents expressing hH1a range from 20nA to 5 pA depending on the clone.

2. ***Magnetite and/or iron oxide as an NMR Contrast Agent.*** The magnetite and/or iron oxide will be used

to form contrast to identify the distribution of the channels. Several approaches are designed for the incorporation of magnetite and/or iron oxides (Pouliquen *et al.*, 1991) into individual oocytes: 1) Arterial injection of a magnetite-dextran solution (Molday and Mackenzie, 1982); 2) Co-injection of oocytes with the magnetite-dextran particles with the ion channel cRNA; and 3) incubation of the oocytes with the material. Magnetite particles are 10nm mean size and 49nm mean size when complexed with Dextran PM 40000. In addition, we will use the iron oxide (Reimer *et al.*, 1994) which has been successfully used in imaging of receptors of rat pancreas and other tissues.

3. *Electrophysiology in applied magnetic fields.* Stage 5-6 *Xenopus* oocytes will be injected with approximately 5ng of cRNA. 0.5 to three days after injection oocytes will be screened for channel expression with the two-microelectrode voltage clamp. Whole-oocyte current will be measured in a flowing bath containing (in mM): 90 NaCl, 2.5 KCl, 1 $CaCl_2$, 1 $MgCl_2$, 10 Hepes, at pH 7.6. Electrodes will be manually broken to less than 0.5MΩ to improve the speed of the clamp. The clamp is a bath clamp with the oocyte held at virtual ground. To reduce resistance to the bath clamp we have found that wires placed directly in the bath are preferable to using agar bridges. The silver chloride bath clamp sensing and current-passing wires are placed downstream of the oocyte in a constantly flowing bath. A recording chamber with a Peltier temperature controlling device is used for recording at different temperatures. Due to variable levels of current expression from week to week, macropatch and single channel experiments will be performed on a parallel timetable. Oocytes expressing > 15 μA are useful for macropatch experiments and those expressing 2 to 15 μA of peak inward current will be used for single channel recordings. The biophysical properties of whole-cell currents to be assessed are the expression level, or the total amount of current and activation and inactivation kinetics of the channels. Single channel measurements will be done in two different modes: 1) cell-attached configuration and 2) excised patch configuration (Hartmann *et al.*, 1994a). Single channel conductance and the mean open-time and closed-time of a single channel will be measured. Single magnetic coils similar to the system utilized by Wang and Hladky (1994a and 1994b) are placed on each axis around the electrophysiological recording chamber. The applied fields with Helmholtz coils may be varied between 0.1 to 1000 gauss and will be positioned around the cell in the electrophysiological apparatus. The experiments will be conducted in the presence and absence of magnetite.

4. *Magnetically-shielded environment.* In collaboration with Dr. Wendell Winters, Ph.D., Director, Biomagnetics Studies Program and ELF Electromagnetics Program, Univ. Texas Health Science Center at San Antonio, we will have the opportunity to perform experiments of applied magnetic fields in one of the worlds few magnetically-shielded rooms. Most experiments will be done at 60Hz with applied fields between 0.1 and 1000 gauss. Function generators will be used to vary the frequency. Because of the importance of minimizing the ambient magnetic fields in space and time (Blanchard and Blackman, 1994, and references therein), we think that it is absolutely necessary to have this facility available to our studies.

5. *NMR Micro-Imaging.* In collaboration with Dr. Jan Post, Ph.D., at the Dept. of Human Biological Chemistry and Genetics, University of Texas Medical Branch at Galveston, we will use NMR micro-imaging to reconstruct a three-dimensional image of the oocyte. Magnetite and/or iron oxide will be used to form contrast to identify the distribution of Na^+ channels. 3-D images can be obtained on the Varian 400 MHZ wide bore instrument, equipped with a 25 mm imaging probe and three 60 amp Highland gradient drivers. On red blood cell ghost samples, an image can be obtained in a few minutes. T_1/T_2 weighted images are routinely obtained; diffusion weighted imaging can be programmed. Excellent preliminary results have been obtained with sections from intervertebral disks, positioned horizontally in standard 25mm sample tubes. Depending on accumulation time, gradient strength, and other experimental parameters, a resolution of less than 20μ is possible. The oocyte

is an ideal cell system for testing the membrane permeability of contrast agents as well as the interaction of a contrast agent with different types of intracellular water (Pauser *et al.*, 1993; 1995).

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DESCRIPTION: State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project. Describe concisely the research design and methods for achieving these goals. Avoid summaries of past accomplishments and the use of the first person. This abstract is meant to serve as a succinct and accurate description of the proposed work when separated from the application. **DO NOT EXCEED THE SPACE PROVIDED.**

Patients that have undergone an amputation suffer from the disability of the lost limb. In many cases chronic pain, arising from a variety of sources, adds to the burden of the disability. Neuropathic pain is frequently seen in patients with amputations and is often resistant to medical management or transcutaneous electrical nerve stimulation. Peripheral nerve stimulation (PNS) via surgical exposure, a relatively new technique, has been shown to be of some value in these cases although the reported successes are largely anecdotal. In addition, failure of electrical stimulation as treatment for pain is generally ascribed to accommodation or habituation of the nervous system to the periodic impulses. We hypothesize that surgically placed electrodes on the target peripheral nerve is an effective method of pain management in selected cases, that random intervals between impulses rather than standard periodic intervals is a superior method of delivering electrical stimulation for pain management, and that the differences in pain can be detected by somatosensory evoked potentials (SEPs). We propose a prospective study of the value of peripheral nerve stimulation in 120 patients with amputations and neuropathic pain that have failed to respond to standard treatments. Each patient will be randomized to either impulses delivered by random or periodic modalities. An electrode lead will be surgically placed onto the nerve serving the dermatomal area of neuropathic pain, the lead wires will be externalized, and an external power supply will be attached. Impulse intervals will be controlled by a standard output device either through or bypassing a random number generator. This will allow production of periodic (eg. 100 Hz) or random impulses (eg. average 100 Hz) to be delivered through the electrode. The degree of pain will be assessed before, during, and after application of the electrical stimulation using standard pain scales. All patients will be monitored for one week. In addition, SEPs recorded before and at the conclusion of the study will be recorded using the International 10-20 System. At the conclusion of the study the electrode will be removed by a simple procedure. Pain reduction by 50% will be defined as a successful treatment. Significant differences ($p<0.05$) will be determined by ANOVA for repeated measures and stratified to determine the influence of random versus periodic stimulation. Changes in amplitude and latencies of the SEPs from the two groups will be similarlly analyzed.

PERSONNEL ENGAGED ON PROJECT, INCLUDING CONSULTANTS/COLLABORATORS. *Use continuation pages as needed* to provide the required information in the format shown below on ***all*** individuals participating in the project.

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TITLE: Peripheral Nerve Stimulation in Amputees with Neuropathic Pain.

Investigator
Richard K. Simpson, Jr., M.D.

1. SPECIFIC AIMS

Patients that have undergone an amputation suffer from the disability of the lost limb and in many cases from chronic pain (30,38,40). This neuropathic pain adds to the burden of the disability and is often resistant to medical management, neural blockade, or transcutaneous electrical nerve stimulation (TENS) (22,104). Direct peripheral nerve stimulation (DPNS) and is felt to be superior to the more diffuse TENS unit application (10,14,19,20). Use of DPNS has recently shown promise as a minimally invasive technique for significant pain reduction in a number of these patients, however, failure rates remain high (52,55,69,81,89). Accommodation of the nervous system to the stimulus is a mechanism by which failure has been explained (33,34,49). Few electrophysiological techniques are available to directly study the phenomenon of accommodation (33,34,49). Clinically, cortically recorded somatosensory evoked potentials (SEPs) offer an estimate of the changes in neural function due to accommodating to a stimulus (51,100).

We hypothesize that DPNS will significantly reduce pain in the limb affected by amputation in patients suffering from neuropathic pain. We also hypothesize that non-periodic or random stimulus interval delivery by DPNS is significantly more effective in reducing pain than traditional periodic stimuli. Moreover, changes in the characteristic features of the SEP will reflect the phenomenon of accommodation. Our specific aim is to provide sufficient evidence that will support the use of DPNS as treatment for amputees with neuropathic pain. In addition, we aim to show that non-periodic stimulation by reducing the influence of neuronal accommodation is superior to periodic stimulation for pain reduction. Likewise, cortically recorded SEPs will provide electrophysiological support for the observing the changes in accommodation based on the stimulus type applied.

2. BACKGROUND AND SIGNIFICANCE:

Stimulation of the nervous system by a variety of electrical devices developed as a result of the creation of a theory proposed in 1965 by Melzack and Wall referred to as the "gate theory" of pain (56). This theory states that by stimulating large diameter nerve fibers the activity conducted in small diameter nerve fibers is blocked (56). Large diameter nerve fibers carry position sense, vibration, and some forms of touch, whereas small diameter nerve fibers carry pain, temperature sensation, and other forms of touch. By stimulating large diameter nerve fibers, the gate through which pain passes is, therefore, closed (9,56,113). Cells thought to be responsible for opening and closing the gate exist in the dorsal horn of spinal cord gray matter (18,39,66). Large diameter peripheral nerve activity stimulate these cells which in turn act as an inhibitory interneuron on activity delivered by small diameter peripheral nerve fibers (44,50).

Many mechanisms have been proposed to explain the desired effect of pain relief by electrical stimulation of the nervous system. These include both pre-synaptic and post-synaptic activity within the dorsal horn of the spinal cord gray matter (62). Primary afferent depolarization of nerve endings is likely to be involved. Axon terminals of small diameter fibers are depolarized by activity from large diameter fibers which reduces further conduction and transmission of pain impulses (41-43). Certainly the neurochemistry

of segmental spinal cord structures is involved in producing and inhibiting the pain response (1,2,6). Endogenous opiates, amino acids, polypeptides, and arachadonic acid derivatives are all likely to be involved in a complicated cascade of neurochemical events produced by nerve stimulation (1,2,124,129,130).

The complexity of the neurophysiological events responsible for pain perception is reflected in the limited methods of effective chronic pain treatment in patients. Pain management has been a highly elusive clinical problem for physicians to treat as well as a difficult matter to investigate in the laboratory. The degree and expression of pain from a patient has many complicating facets including cultural and psychological influences. The type of injury or physiological basis of pain is of highest importance, yet the support from family, secondary gain issues, external environmental circumstances such as the work place, basic personality traits, and coexisting illnesses and treatments all play a role in the expression of pain and the degree of pain perceived by the patient.

Quantifying pain, therefore, is an exceedingly difficult task. Although many types of pain response scales and physiological measurements have been designed, none are without their limitations. Reliance on simple visual analog scores has become the standard. This score or VAS has been employed for decades (25,26,86). Other commonly used methods of quantifying pain include the McGill Pain Questionnaire (MPQ), the Reading and Newton card sorting technique, Verbal Response Scales, and pain dairies, among others (82,83,118). None of the pain assessment measures are without fault. However, the VAS and the MPQ have been successfully used in many contemporary pain studies, are easy to use, and the results are easily interpreted and communicated (25,26,84). Physiological tools for pain assessment such as electromyography, sympathetic skin responses, motor evoked potentials, and sleep studies are of equivocal value (95,96).

Likewise few, if any, reliable animals have been developed to study the influence of a specific therapy on the pain response. Animal models of neuromas have been developed but demonstrate considerable inconsistency in their response to noxious stimulation (12). Deafferentation pain models have also been developed but frequently provide little quantitative information because of autotomy and other behavioral changes resulting from the creation of a painful extremity (21,88). Recently, a neuropathic pain model has been developed in the rat (5-8). A simple cut-down to the sciatic nerve in the upper hind limb is performed. Four chromic ligatures separated 1 mm apart are loosely secured around the entire nerve diameter. The ligatures are tightened around one sciatic nerve, to a point just reducing the diameter as visualized by an operative microscope. The result two weeks afterward is an animal with a limb that has features similar to those found in humans with reflex sympathetic dystrophy (93,125). Although this model is widely used, measuring the animal's response to pain remains a coarse approach and limits quantifying the more subtle alterations (60,87,97,107,108).

In general, however, pain in humans can be subdivided into nociceptive and neuropathic types. Nociceptive pain is pain that is produced by activation of pain receptors. A cutaneous laceration, visceral involvement with a neoplastic process, or joint tissue inflammation are examples. Nociceptive pain frequently responds to narcotics, anti-inflammatory medications, and local anesthetics. Neuropathic pain is the result of pathology within the neural tissue itself. This type of pain is classically described as burning and constant, with an associated electrical or crawling-like sensation. This pain generally does not respond well to opiates or opiate-like medications. Failure to respond to opiates drastically limits the utility of even the most modern pain management methods such as intrathecal drug delivery devices or the "morphine pump"

(36,37). Few medications are available for the treatment of neuropathic pain and include few anti-inflammatory medications, psychoactive substances, anticonvulsants, tricyclic antidepressants, and antiarrhythmics.

Amputation patients commonly have an associated neuropathic pain (30,38,40). Neuropathic pain in such patients has been described since 1864 by Mitchell in a review of many post amputation casualties from the American Civil War (57,58). In some contemporary clinical settings such as the Veteran's Affairs Medical Center, Houston, Texas, as many as 15%-20% of amputees have neuropathic pain. The types of pain suffered by these patients are frequently referred to as stump pain, painful neuroma, causalgia, reflex sympathetic dystrophy, deafferentation pain, and phantom limb pain. Patients with neuropathic pain remain some of the most formidable patients for any physician to successfully treat. If medications, physical therapy, psychological intervention, and nerve blockade or infusions fail to remedy the pain, few other options for treatment are available.

Prior to the development of electrical stimulating devices for the nervous system, only ablative neurosurgical methods offered hope for neuropathic pain patients that failed more conservative therapies (46,48,119,127,132). Ablative or destructive neurosurgical patients are still used for the most intractable neuropathic pain patients but are more commonly used in the terminal cancer pain patients. Sympathectomies are beneficial particularly in cases where a significant amount of the neuropathic pain contains a sympathetically mediated component (11,117). Neurectomies or rhizotomies done either with a caustic solution, thermocoagulation, or surgical transection are of limited value (32,54,68,79,85).

Other more invasive procedures including, dorsal root rhizotomies, ganglionectomies, and dorsal root entry zone lesions (DREZ) may be of some benefit but carry additional risk, often have associated side effects, and generally provide temporary pain relief (39,63,67,72). Cordotomies, myelotomies, commisurotomies, tractotomies - either spinal thalamic or mesencephalic, deep brain lesions such as thalamotomies, and cingulotomies or lobectomies carry the highest risk of complication and the most serious associated side effects with little or no chance of recovery (31,45,53,92,109,112,115,122,126,128).

Application of the gate theory to the medical management of pain began in 1968 when Sweet and Wepsic reported the successful treatment of several patients by stimulation of primary afferent neurons (114). Electrode designs advanced including the use of cuff-type electrodes for the entire trunk, and microelectrodes which were used to impale the nerve (64,114). Other methods of electrical stimulation were also developed including epidural spinal cord stimulation and deep brain stimulation, both thought to operate though the gate theory (4,70,71,119,132). Both epidural spinal cord and deep brain stimulation for pain relief carry significantly greater risk for neurological morbidity and are reserved for severe, intractable cases of neuropathic pain in patients with amputations or other similar causes, but not felt to be candidates for ablative neurosurgical procedures (70,71).

Early results of DPNS were mixed. Claims of 31%-87% of patients receiving significant pain relief were made, however, these results have been difficult to interpret because of the lack of randomization of the technique, and the wide variety of chronic pain patients that received this treatment (20,52,114). In addition, the equipment used in the late 1960's and 1970's was far less sophisticated (64,110,114,120). Moreover, the surgical technique for assessing the potential benefit of DPNS and subsequent implantation of the device, if applicable, provided the means for better patient selection (78,80). Contemporary reports of 90%

effectiveness are available using modern surgical technique and equipment (78,80,111,123). Yet, no carefully constructed and analyzed prospective investigation has validated the modest number of studies that are primarily based on clinical observation and experience.

Although modern technology has provided physicians with improved nerve stimulation equipment, and the development surgical techniques has minimized the degree of invasiveness, a considerable number of failures are reported with regard to DPNS and neuropathic pain reduction (10,20,52,114). These techniques use continuous repetitive stimuli which are applied at a given frequency generally using periodic intervals between each impulse. For example, a frequency of 100 Hz with periodic intervals between each requires that for as long as the stimulus is applied, the inter-impulse interval is a constant 0.01/sec. The nervous system when bombarded by constant repetitive impulses may accommodate to some degree to the stimulation as an adaptive phenomena (47,131). If such a mechanism were in force during DPNS delivered as continuous impulses with a uniform frequency and periodic interval, the resultant pain reduction may be lessened.

Non-periodic interval stimulation can be generated to provide a random delivery of impulses to the nerve within a defined range of frequencies. Intervals between pulses can be randomized and deliver and average frequency of 100 Hz yet vary at any particular point in time, as an example, from 50 - 500 Hz. Since the axonal membranes are not exposed to a constant periodic stimuli, mechanisms responsible for the adaptive response referred to as accommodation or habituation are less likely to be of influence. Nerve fibers, peripheral nerve fibers in the case of DPNS, would continue to propagate their action potentials at an average rate that reflects the impulse rate delivered by traditional periodic stimulus interval impulses. A more effective method of pain control, based on the gate theory, would be produced because the likely cause of failure from electrical stimulation treatments, accommodation, would be minimized.

Many mechanisms have been proposed to account for the phenomenon of accommodation or habituation of the nervous system to a stimulus (23,29,35,59). Activation of local recurrent inhibitory networks, a reduction in membrane conductance, axonal threshold alterations, prolongation of action potential refractory periods, and cortical influences have all been proposed to account for the phenomenon of accommodation or habituation of the nervous system to a constant stimulus (3,90,91,94,131). It likely represents an adaptive mechanism to insure that the nervous system can respond to other types of stimulation when presented simultaneously (47). However, if accommodation occurs as a result of an intended event such as that desired during DPNS therapy, this phenomenon will need to be circumvented to achieve the desired affect.

Electrophysiological monitoring of accomodation has relied on direct nerve action potential or evoked potetial records (105,106,116). Investigations into the phenomenon of neuronal accommodation or habituation have often focused on mechanisms involving synaptic activity or single unit electrical behavior (90,91,94). Evoked potentials, however, have become increasingly utilized to study the central processing involved in accommodation (49,51,100,121). Amplitude decrement in SEP waveforms is clearly seen in both animal and human studies undergoing continuous periodic stimulation. Latencies of these responses are also extended. Recently, a few animal studies and a single case report in a human revealed that random stimulation of a peripheral nerve can produce differences in waveform features of evoked potentials compared to periodic stimuli (49,61). Evoked potentials are, therefore, sufficiently sensitive to measure the subtle changes in the pain response as reflected in differences in the degree of existing neuronal accommodation (13,15-17,27,28).

3. PRELIMINARY STUDIES:

The authors' cumulative clinical experience includes over 200 cases of chronic pain patients treated with either DPNS or epidural spinal cord stimulation (ESCS). Approximately 50% of patients with neuropathic pain that undergo a trial of stimulation have a satisfactory response, or a 50% reduction in their pain. Of these patients, nearly 85% of patients continue to have satisfactory pain relief after one year. It is unfortunate, however, that 50% of carefully chosen patients in the authors' practices fail to perceive benefits during the trial of stimulation and, therefore, do not undergo implantation of the device. These patients continue to be treated by conservative measures, or occasionally, by ablative neurosurgical procedures. In experience of the authors, the latter two treatment modalities provide sub optimal pain relief in nearly all of patients within two years of the procedure. To provide the possibility of a successful trial of electrical stimulation for pain relief and using a minimally invasive technique such as DPNS would be an invaluable addition to our limited armamentarium of neuropathic pain management.

The authors have also demonstrated that DPNS and ESCS are effective means of pain management in the laboratory (103). Both methods of neural stimulation produce elevations in glycine within the gray matter of the spinal cord segments receiving the activated primary afferent fibers (1,2). Glycine, in turn, reduced pain when infused intrathecally. The change in glycine concentration was small and it is unclear whether or not differences in glycine concentration following either random or periodic interval stimulation could be measured (103). In addition, methods for assessing the degree of pain in animals are relatively crude and subtle changes in pain perception are not clearly demonstrated even in the best neuropathic pain model (7,8). Again, a distinction between the degree of pain relief from either, periodic or random interval stimulation would be of dubious value. The value of animal studies, therefore, to determine if periodic or random interval DPNS is most helpful, is of little merit. The importance of human studies to establish the potential benefits of DPNS applied in this fashion cannot be underestimated.

Objective neurophysiological methods to study the effect of DPNS on accommodation will employ the use of cortically recorded evoked potentials. The authors have extensive experience with study design, application, and data analysis with regard to evoked potentials and other neurophysiolical signals recorded from both animals and humans (98-102). In addition, the authors have utilized this experience to explore the phenomenon of accommodation using periodic or random stimulus techniques (98-102). Such studies have employed amphibian models, cats, higher order primates, and man (33,34,49,51,61,98-102). Changes in the features of evoked potential waveforms and compound action potentials have been measured and established that the type of applied stimulus will influence accommodation.

A randomized, prospective approach has not to date been undertaken to determine the value of DPNS. Since the perception of stimulation, or paresthesias, in the distribution of a patient's pain is the key element required to produce the greatest chance of benefit, based on many retrospective analyses, randomization to stimulation versus no stimulation after placement of an electrical device is not clinically practical. Effectiveness of DPNS as a legitimate method of pain management, therefore, will require careful clinical observation, particularly to the amount of pain medication administered, and attention to the responses obtained from patient generated pain scales. Randomization between periodic and non-periodic or random

interval impulse can be done. In addition, the SEP will provide objective neurophysioloigical measurements as to the degree of influence each stimulus technique has on accommodation.

4. RESEARCH DESIGN AND METHODS

We propose a prospective study of the value of peripheral nerve stimulation in 120 patients with amputations and neuropathic pain that have failed to respond to standard treatments including medications, nerve blocks, and TENS. The electrode will be placed over the parent nerve within the stump that corresponds to the perceived distribution of pain. For example, the electrode will be placed over the common peroneal nerve in the popliteal fossa for pain perceived in that nerve's distribution. Each patient will receive DPNS and will be randomized to either impulses delivered by random or periodic modalities. Approximately 24 patients per year over five years are expected to enter the study. A dedicated clinic within the Rehabilitation Medicine Service meets weekly and approximately 10-15 patients are seen. Patients will be admitted for pain control and will be offered the opportunity to participate in the study.

An operating room dedicated to the Neurosurgery Section of the Surgical Service at the Veteran's Affairs Medical Center, Houston, Texas will be used. After informed consent is obtained, each patient will undergo local or regional anesthesia with sedation and standard sterile surgical preparation will be undertaken. An incision will be made in the proximal portion of the amputated limb overlying the nerve subserving the dermatomal area of neuropathic pain. An electrode lead (Medtronic Inc. On-Point) will be surgically placed onto the nerve. The overlying tissues will be closed in a fashion to secure the electrode against the nerve. A subcutaneous tunnel several centimeters in length will be made proximal to the lead and the lead wires will be externalized through a small incision. Once secured to the skin, the patient will undergo general recovery procedures and the trial of stimulation will begin the following day. Each wound will be closed and dressed using standard surgical technique. Patients will be maintained on their usual pre-admission pain medication. Surgical discomfort from either the incision or electrode placement should be slight and brief and not require prolonged additional pain medication.

On the day following surgery, each patient will be randomized to either periodic or random stimulus intervals. The intensity and frequency necessary to produce parasthesias in the distribution of their pain will be determined prior to randomization to the stimulus modality. A standard clinical peripheral nerve stimulator device will be used to provide continuous stimuli for the duration of the study. Impulse intervals will be controlled by either the internal trigger of the stimulator producing periodic intervals or the stimulator will be triggered externally by random number generator producing random intervals between impulses. For example, this device would allow the production of periodic (e.g. 100 Hz) by the internal trigger or random impulses (e.g. average 100 Hz) by the external trigger to be delivered through the electrode to the nerve.

In addition, cortically recorded SEPs will be obtained by four silver disk electrodes placed in standard fashion using the International 10-20 System over the primary somatosensory receiving area for the limb undergoing stimulation, either midline, C3' or C4' and C7' or C8'. The reference electrode will be placed at FPZ. After standard skin preparation, all electrodes will be secured with colloidin to prevent movement during the trial of DPNS. Signals will be recorded, digitized, and averaged using a standard clinical evoked potential monitoring system beginning immediately prior to the onset of the study, and after the conclusion of the stimulation trail. Each averaged signal will reflect a 500 msec epoch consisting of 1000 individual responses and recorded through a bandpass of 3-3000 Hz. The nerves will be stimulated in standard bipolar

fashion (anode distal) for clinical evoked potential evaluation. A frequency of 2 impulses/sec for duration of 0.2 msec, and and intensity just below that necessary to produce muscle contraction will be used.

The random or non-periodic intervals between impulses will be generated by an external trigger based on the principle of stochastic point processes. A classic example of a stochastic point process is the homogeneous Poisson process and is characterized by the fact that interpoint spacings are not correlated. This implies that the probability of a point occurrence in an interval of time is constant, and is completely independent of the amount of time elapsed since the occurrence of the most recent prior point. Random stimulation from a trigger device based on the Poisson process should defeat habituation because the interval between successive stimuli is entirely random and successive intervals are uncorrelated. Such an external trigger device has been designed and patented by one of the investigators and will be used on the patients randomized to the non-periodic or random interval impulses for DPNS.

The degree of pain will be assessed immediately before the stimulation is to begin, during the stimulation on a daily basis, and at the conclusion of the stimulation using standard VAS and the MPQ. All patients will be monitored for one week. At the conclusion of the study the stimulation will cease and the electrode will be removed by a simple procedure. Using sterile technique and local anesthesia, the skin will be incised at the point where the electrode wires have been externalized. Gentle traction will be applied to remove the electrode through the subcutaneous tunnel. Pain reduction by 50% based on the VAS and MPQ will be defined as a successful treatment. The patients describing successful pain management will be stratified to determine the superiority of periodic or random interval stimulation. Sample size calculations reveal that 60 patients per group or a total of 120 patients are required to detect a 0.6 standard deviation unit difference with 90% power. Significant differences ($p<0.05$) will be determined by ANOVA for repeated measures and stratified to determine the influence of random versus periodic stimulation. Evoked potential latencies and amplitudes between the two stimulation delivery type subgroups measured before and at the conclusion of the study, will be analyzed using population t-test

5. Human Subjects

(1) Involvement of human subjects. The individuals selected for participation in this study will be chosen from the amputee population served by the Houston Veterans Affairs Hospitals. While this is, in some respects, a convenience sample, it allows for conduct of the study with significant support from the VA. Without this support, direct costs for the study would be prohibitive, and it would not be possible to test this therapy without significantly higher levels of funding than are requested here.

Also, because of the characteristics of the population served by the VA, it is very likely that a good mix of study subjects will be recruited into the research effort. The VA serves a high proportion of patients who are from minority backgrounds, and obtaining a sample that represents a good mix with regard to ethnicity should pose no problems. However, there is a good likelihood that women will be underrepresented in the study. The population of women served by the VA is comparatively small, and the population of women with upper limb amputation served by the VA is likely to be very small. At least at present, the limitation of underrepresentation of women in the study will be tolerated, and care will be taken not generalize the findings to the entire population. Funding may be secured from other sources that will allow for recruitment of a larger number of women into the study, however, this cannot be assured at this time.

In summary, the sample population to be studied through this research is expected to consist of 120 persons from a racial/ethnically and socioeconomically diverse group of people with upper extremity amputation. In terms of gender, the great majority (approximating 75%) are likely to be male.

(2) Sources of research material. Two types of research material will be collected through this study (1) subject-reported data on health, physical function, and quality of life; and (2) physiologic data generated via bioelectrical measurement techniques. In some cases, data of other types may be gathered to assess the overall health or physical status of potential or enrolled study subjects. These types of data may include laboratory tests using biological samples, such as urine or blood. However, such tests will only performed if clinically indicated, and procedures will be carried out in accordance with accepted standards for clinical practice. Laboratory testing of body fluids will not be a standardized component of the research process.

(3) Recruitment of study subjects. Study subjects will be recruited through the VA amputee program. This will provide access to an adequate number of subjects to carry out the proposed work. Consent will be sought from every patient who expresses interest in the proposed project. The request for consent will be handled by either the research nurse or the principal investigator. In seeking consent to participate in the project, the procedure will be fully explained to each individual being considered. This explanation will make it clear that the procedure is experimental in nature and that no assurance can be provided of any benefit from the treatment. It will also be made clear that data will be gathered for the purpose of research and that these data will be entered into a larger database for comparison with data gathered from other patients. Potential study subjects will be provided assurance of confidentiality with regard to any information or data provided for the study and will be assured that their refusal to participate will in no way influence the nature or scope of services that they can obtain through the VA Hospital or affiliated institution. Also, a name and telephone number of a person (the research nurse or PI) will be provided to every individual considered for the study so that they can obtain additional information or ask questions concerning the study or their role in it. Approval for this research project from Baylor's Affiliated Review has been sought, and documentation of approval will be sent to the funding agency within 90 days from the date of submission of this application.

(4) Potential risks. The potential risks associated with this project are minimal, and are of two types--inadvertant injury in conducting research procedures, and inadvertant revelation of subject information. The former of these, inadvertant risk of injury could arise from the very remote possibility that a person experiences discomfort from the electrodes used in the process. It is conceivable that someone could have an allergic reaction to the metal in the electrodes or to the adhesive used to attach the diagnostic electrodes. In such an instance, the adverse reaction would almost certainly occur while the procedure was underway and appropriate steps would be taken to deal with the problem immediately. Although the diagnostic and therapeutic equipment operats on electrical current, the risk of eletrical shock from this equipment, which has been thoroughly tested, is extremely remote. The equipment is fully and properly grounded and all staff will be trained in its proper use before they are allowed to use it with patients or study subjects.

Risks of inadvertant revelation of patient or subject information will be reduced through proper training of staff on confidentiality issues and through use of coded data entry that does not contain identifiers of individuals who participate in the research. Only authorized staff (i.e., the PI and the research nurse) will have information on the names that go with patient codes. These will be kept in a secured location to avoid any unintentional release of confidential information. Risks associated with this project are minimal.

(5) Protection from risks. Risks associated with participation in this study will be minimized through proper training of staff in operation of the equipment and through safeguards designed to protect confidentiality. As indicated above, the equipment to be used in the study has been fully tested and is very safe when used properly. Also, staff will be trained in procedures for maintaining confidentiality of patient information. Potential risks associated with this project are minimal, and minimizing their likelihood can be done very effectively.

(6) Reasonableness of risks in light of potential benefits. The potential benefits from this project are significant. For many people who experience amputation, neuropathic pain associated with the injury reduces their abilities to use prosthetic devices and to function effectively on a daily basis. Moreover, chronic pain has a debilitating effect on the individual, degrading his or her quality of life in a manner that can affect can affect other aspects of health and social functioning. If the proposed intervention is shown to be effective, it may lead to development of a portable treatment device that could be fitted into a prosthetic device or otherwise attached to provide relief during painful episodes. Such therapy might allow people with amputation to lead much more productive and better quality lives.

6. Vertebrate Animals

No use of animals is proposed through this study.

7. Consultants/Collaborators

No special consultative services are required for the proposed research.

8. Consortium/Contractual Arrangements

The activities described in this application require collaboration between Baylor College of Medicine and Houston Veterans Affairs Hospital. An affiliation agreement already exists between these two institutions that covers the proposed collaboration. Also, a representative of the VA Hospital provided sign-off approval for submission of this application. A copy of this approval is maintained in administrative offices of the two institutions.

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DESCRIPTION: State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project. Describe concisely the research design and methods for achieving these goals. Avoid summaries of past accomplishments and the use of the first person. This abstract is meant to serve as a succinct and accurate description of the proposed work when separated from the application. **DO NOT EXCEED THE SPACE PROVIDED.**

Research Project 4: Testing the Efficacy of a Pain Clinic for Managemnt of Disability-Related Pain. The proposed project will involve two years of preliminary studies for the purpose of developing a database on a demographically diverse population of individuals with different types of physical disabilities who will serve as a resource pool for investigational studies to begin beginning in year five of DPMC activities. The nine specific aims of the proposed project are to: (1) identify a population of individuals with a mix of disabilities who are seeking relief for chronic pain; (2) develop baseline data characterizing the nature and intensity of pain and its influence on the functional capacities of individuals with varying types of disabilities and from different population segments; (3) develop standardized evaluation techniques, including pain and functional measures, for patients for patients with disability-related pain; apply pain management approaches, including those generally used and newly developed techniques, according to standardized protocols with persons experiencing different types of pain; (5) collect data on the affects of different interventions in managing pain in the target populations using the same measures used in establishing baseline data on pain; (6) determine if there are unexpected risks or side affects associated with the use of different pain management approaches in different subsets of the population of people with disabilities; (7) assess the degree to which pain management interventions result in better or worse outcomes with different subsets of the target population as determined using quantifiable measures of pain and quantitative and qualitative measures of functional parameters and quality of life; (8) provide opportunities for exposure of medical students, residents, and students from other health professions to current approaches to pain management in people with disabilities and to basic clinical research procedures related to pain management; and (9) estimate the cost effectiveness of the pain clinic model in evaluation and treatment of patients who experience diability-related pain, with attention not only to the costs of clinical services, but also to outcomes of treatment with regard to enhanced functional capacities and overall quality of life. Multivariate analyses will be used in examining the wealth of data to be generated from these studies of a population estimated to include approximately 750 individuals.

PERSONNEL ENGAGED ON PROJECT, INCLUDING CONSULTANTS/COLLABORATORS. *Use continuation pages as needed* to provide the required information in the format shown below on *all* individuals participating in the project.

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Title: Testing the Efficacy of a Pain Clinic for Management of Disability-Related Pain

Investigators:
M. Grabois, M.D.
J. Strayer, M.D.

1. Specific Aims

The proposed project will be initiated with the establishment of the Baylor College of Medicine Department of Physical Medicine and Rehabilitation Disability and Pain Management Center (DPMC) with recruitment of a patient population for long-term follow-up; collection of baseline demographic, functional, and objective and subjective pain measures; and development of standardized protocols for follow-up. However, no funding for project support will be requested until the beginning of the third year of DPMC activities, when testing of experimental pain management approaches will begin and follow-up using standardized measures of pain and related parameters will be implemented. Data collected during the first two years of DPMC operations will constitute preliminary data to support the three years of research that will follow. The nine specific aims of this project will be to:

1. Identify a population of individuals with a mix of physical disabilities (e.g., SCI, amputation, congenital neuromuscular conditions) who are seeking relief for their pain.

2. Develop baseline data characterizing the nature and intensity of pain and its influence on the functional capacity of individuals with varying types of disabilities and from different segments of the population (e.g., individuals from a range of income levels, ethnic backgrounds, living situations).

3. Develop standardize evaluation technique(s) for patients with pain in primary disabilities to include measurement of pain and functional capacity.

4. Apply pain management approaches, including those generally used in managing different types of pain and newly developed techniques, according to standardized protocols with persons experiencing different types of pain.

5. Collect data on the affects of different interventions in managing pain in the target populations using the same measures used in establishing baseline data on pain.

6. Determine if there are unexpected risks or side affects associated with the use of different pain management approaches in different subsets of the population of people with disabilities.

7. Assess the degree to which different pain management interventions result in better or worse outcomes with different subsets of the target population as determined using quantifiable measures of pain and quantitative and qualitative measurers of functional parameters and quality of life.

8. Provide opportunities for exposure of medical students, residents, and students from other health professions to current approaches to pain management in people with disabilities and to basic clinical research procedures related to pain management.

9. Estimate the cost effectiveness of the pain clinic model in evaluation and treatment of patients who experience disability-related pain, with attention not only to the costs of clinical services, but also to outcomes of treatment with regard to enhanced functional capacities and overall quality of life.

2. Background and Significance

Disability-related chronic pain is a phenomenon that is poorly understood. In his discussion of chronic pain, Bonica (1990) estimated that one third of all Americans have a chronically painful condition. This estimate includes people with persistent headaches, back pain, and degenerative joint disease. It would appear logical that people who have disabling neurological and musculoskeletal conditions are likely to experience pain associated with their disability. While the National Institutes of Health (NIH, 1993) report *Chronic Pain Management: Developing a Treatment System for People with Disabilities* referred to "several surveys" suggesting that one of three people with physical disabilities experiences chronic pain, reliable data on the incidence and prevalence of pain in the population of people with physical disabilities in general or within specific disability diagnoses (e.g., spinal cord injury, amputation, post-polio syndrome) are lacking. It is therefore difficult to estimate with any accuracy the scope of the problem that pain represents in the population of people with physical disabilities.

Notwithstanding the lack of firm data on pain in the population of people with disability, it is clear that pain represents a significant problem that merits attention. Quoting from the planning group report on *Chronic Pain Management: Developing a Treatment System for People with Disabilities*, "Chronic pain can be a significant secondary problem resulting from a primary physical impairment or disability" (NIH, 1993, p. 1). The report went on to summarize the consensus of the expert panel that was convened to review issues of chronic pain in persons with disabilities. Because these consensus statements directly informed the planning process for this project, they are presented here:

- Chronic pain is a multidimensional problem with biomedical, psychological, behavioral, legal, and vocational components.

- The evaluation and treatment of people with chronic pain, particularly individuals with a primary physical impairment or disability, is best accomplished by an interdisciplinary approach that takes the multiple dimensions of the problem into consideration.

- A medical evaluation should be part of the initial assessment of a person with chronic pain, to define the pathophysiology of symptoms. Functional, vocational, environmental, and psychological evaluations should also be part of the initial assessment of a person with chronic pain, to evaluate the psychosocial, behavioral, and iatrogenic factors that contribute to suffering and added disability.

- Functional restoration and the relief of nociceptive symptoms and suffering should be the primary goals of care in the individual with chronic pain.

- Patients, family members, care givers, health care administrators, and clinicians should be educated about the multiple factors associated with chronic pain in people with physical disabilities to facilitate integration of these principles into practice.

- There is a significant lack of research specifically about chronic pain in persons with a primary physical impairment or disability. An extensive list of pertinent research questions has been developed in this Workshop and is offered for consideration by all clinicians and researchers involved in treating chronic pain in persons with physical disability (NIH, 1993, pp. 1-2).

The last of these consensus statements is particularly germane to the proposed project to evaluate the impact of a pain clinic in addressing the needs the people with different types of physical disabilities. The research priorities identified by the expert panel called for:

- Research on improving functional mobility, e.g., pain and muscle overuse.

- Studies of behavioral adaptation to functional loss, e.g., pain and suicide prevention, family, and recreation.

- Examination of the whole body system response to physical impairment and functional change, e.g., urinary tract infection post-SCI producing pain that inhibits excretion of body wastes.

- Facilitation of replacement of function through the development or modification of technical devices, e.g., pain inhibition through implanted electrical stimulation devices.

- Measurement, assessment. and epidemiology aspects of reduced function in people with disabilities, e.g., developing scales that reliably measure relationship between self-reported and physiological indices of pain.

- Treatment evaluation studies of new or currently used clinical therapies used to improve, restore, or replace function, e.g., testing pharmaceutical interventions, improved wheelchair cushions, and ergonomically designed work sites to reduce pain.

- Training research scientists in the field of rehabilitation, e.g., training scientists to consider multiple etiologies of pain in designing research programs (NIH, 1993, p.10).

These priorities grew out of the recognition of the paucity of research data--and also understanding--of the nature and scope of the problem that pain represents in people with disabilities. The need for this research may have been articulated most succinctly by one of the participants in the NIH workshop on *Chronic Pain Management: Developing a Treatment System for People with Disabilities*. Kanner (1993, p. 37) noted, "Participants in this workshop have considerable experience in treating patients with chronic pain, yet, few specialize in treating patients with disabilities who also experience chronic pain. There is little or no outcome data on chronic pain and persons with physical impairments or disabilities." Shindell (1993, p. 53) observed, "When a person with a disability reports pain, all too often that pain is viewed as a normal part of the original disease or injury process and, consequently, is not given appropriate attention from the health care provider."

In preparing this application for funding, a very thorough review of the literature related to pain was completed. As inferred from the previous discussion, while there is a considerable and growing body of

literature on rehabilitative approaches to chronic pain management in people without significant permanent disability--most notably with regard to headache and low back pain (Grabois and VanDeventer, 1995; Grabois et al., in press), cancer (Erdman, Oyama, and Pernak, 1984), and arthritis (Harkness, Higgs, and Dieppe, 1984; Grennan and Jayson, 1984)--there is relatively little in the literature on rehabilitative pain management in treatment of disability-related pain due to trauma, such as spinal cord and traumatic brain injury or amputation, or to severe musculoskeletal disorders resulting from polio or the various congenital dystrophic disorders. The comprehensive text on pain by Wall and Melzack (1984) included a chapter on central pain due to spinal cord and brain stem damage (Pagni, 1984) and a chapter on pain related to amputation (Jensen and Rasmussen, 1984). These chapters provided descriptions of pain mechanisms and management approaches that continue to be relevant ten years after they were written, indicative of the dearth of current research in this area. Other research on pain in people with physical disabilities has been reported in the literature reviewed for the Outcome Measures Core that has been proposed for this program project. In the interest of brevity this review is not repeated here, and reviewers are referred to the project description for the Outcome Measures Core for a more extensive literature review.

In summary, a review of the literature, while providing insights on pain management strategies that should be further tested, unequivocally supported the conclusion of the NIH (1993, p. 71) expert panel ". . . that there are many areas in need of scientific investigation in order to develop more effective treatments for chronic pain in persons with physical disabilities." The proposed project is designed to provide a venue for conducting needed investigations in a controlled setting with a demographically diverse population of individuals with different types of physical disabilities.

3. Progress Report/Preliminary Studies

During the first two years of operation of the DPMC, preliminary studies of pain in persons with disability will be underway for the purpose of establishing baseline data against which to assess the impact of pain management interventions that will be used in controlled studies that will be started beginning with the third year of operation of the DPMC. Preliminary studies that will be conducted during the first two years of DPMC operations will be designed to: (1) identify adequate numbers of individuals with disabilities of various types who report significant pain and who are willing to participate in testing clinical interventions that might result in pain relief and/or enhanced tolerance of pain with respect to day-to-day living; (2) develop a disability-related pain database that contains information on the demographic characteristics of individuals with different types of disabilities who seek pain relief through the DPMC clinic; (3) establish baseline pain measures that include both objective and subjective indicators of pain that were gathered using standardized instruments and methods; (4) prepare and refine protocols for pain management interventions and collection of pain-related data that can be applied with a population of persons with different kinds of disabilities beginning with the third year of DPMC operations; and (5) finalize data analysis procedures to assure appropriate analytic techniques and adequate power to draw defensible conclusions from results of studies to be conducted.

Beginning in July 1995, prior to receipt of funding from any outside sources, the DPMC Assessment and Intervention Clinic will be established in fully accessible space at The Institute for Rehabilitation and Research (TIRR), a Baylor College of Medicine primary clinical affiliate. Physician staffing for the clinic will be provided by Drs. Martin Grabois and Jonathan Strayer, with support to be provided by a physician assistant or advanced nurse practitioner and other appropriately credentialed support personnel. The clinic

will offer a full range of diagnostic and therapeutic services required to assess and manage the types of pain most often experienced by people with disabilities. In keeping with the recommendations developed by Grabois and VanDeventer (1995), the clinic will provide an array of diagnostic and therapeutic services. Diagnostic services will involve:

- taking a thorough clinical history emphasizing (a) the pain description in terms of location, radiation characteristics, time sequence, actions that make it worse or better, and the patient's activity level, (b) prior pain evaluations that involved physicians, hospital services, and various diagnostic tests; (c) psychosocial/vocational evaluations to assess behavioral responses to pain, adjustments to impairment and disability, and family and working history and dynamics; and (d) past medical, surgical, and rehabilitative treatment;

- performing a thorough physical examination, concentrating on the musculoskeletal and neuromuscular systems, as well as on body mechanics, with particular attention to body systems that may be implicated by location and type of pain;

- measuring pain and its effects using patient self reported indices and biomechanical, physiological, psychological/behavioral, functional, familial/social, and medical parameters (see Research Design and Methods section for additional details concerning assessment methods to be used);

- completing diagnostic tests that are suggested from the results of the physical examination and various pain measurement results; and

- and classifying patients for the purpose of comparative research using an appropriate classification system, such as the Emory Pain Estimate Model (Brena and Chapman, 1983).

Data from patient assessments will be entered into the DPMC database, and using a multidisciplinary clinical management approach, appropriate pain management services will be provided each patient. The goals of the treatment plan for each patient will be to modify and/or reduce medication, modulate the pain response, increase activity (except in cases where overuse may be implicated as a contributing factor in the patient's pain), restore physical functioning, and alleviate psychosocial and vocational dysfunction (Grabois and VanDeventer, 1995). In addition to pharmacologic management approaches, pain management techniques may involve spray and stretch techniques, electrical stimulation, acupuncture, hypnotherapy, mobilization and manipulation, prescription of adaptive equipment or other technology designed to reduce physical demands, biofeedback, psychosocial intervention, and surgical intervention. Decisions concerning the appropriate therapies for each patient will be made with input from the members of the multidisciplinary team that will provide staffing for the clinic, with ultimate decisions for therapeutic choice resting with the patient and physician. As indicated later in this section, over the course of therapy for each patient, all data on the type and intensity of therapy provided, as well as on indicators of pain, functional assessment, and quality of life that are selected or developed for use by the Outcome Measurement Core will be entered into the database.

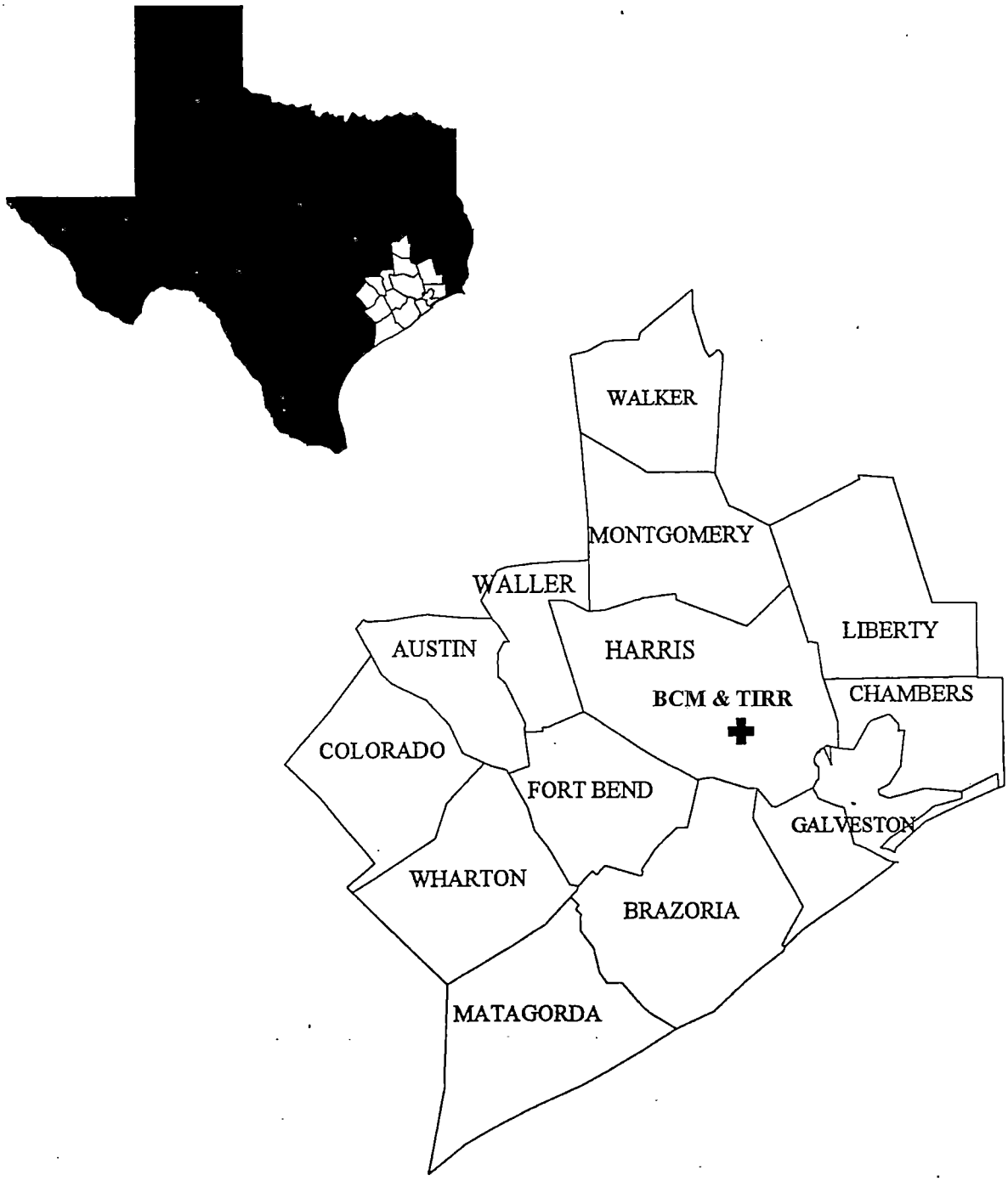
Once the clinic is operational, a comprehensive effort will be mounted to create awareness of the clinic and its services among people with physical disabilities in the geographic area that constitutes TIRR's primary service area. TIRR's primary service area was defined for the purposes of the Texas Model Spinal

Cord Injury System as the 13-county area that constitutes federally designated Health Services Area 11. Figure 1 (following page) illustrates these counties and their geographical location in Texas. This 11-county area will represent the primary target area for recruitment of patients to the clinic. People targeted through recruitment efforts will go beyond spinal cord injury to include people with traumatic brain injury (TBI), neuromuscular conditions, such as multiple sclerosis, post-polio syndrome, amputation, and other conditions that diminish one's ability to perform physical activities. Recruitment efforts over the two year period are intended to accomplish two things: (1) identify an adequate mix of individuals with different types of disabilities who may be enrolled in subsequent studies of pain manifestation and its treatment; and (2) develop a pool of individuals with disability-related pain who are from ethnic and socioeconomic backgrounds that reflect the diversity of the service area.

Developing the pool of individuals who can be recruited into later research on pain interventions will involve recruitment activities that draw upon Baylor and TIRR connections to various groups in the community. First, contact will be made with an array of disability groups around the area. These will include people who are served by Baylor and TIRR clinics offering services to people with SCI, TBI, amputation, post-polio syndrome, arthritis, stroke, and other disabling conditions. All persons currently receiving services through Baylor or TIRR disability-related clinics will be contacted regarding the clinic and the services to be provided through the clinic. In addition, Houston area organizations serving the needs of persons with different types of disabilities (e.g., the Houston Post Polio Association, the Multiple Sclerosis Society Southeast Texas Chapter, the Spina Bifida Association of Houston) will be notified of the clinic and will be provided information for inclusion in their newsletters and other products provided their members. Cross disability service and advocacy organizations, such as the Houston Center for Independent Living and the Coalition of Texans with Disabilities, will also be provided information about the clinic and how to access services. Furthermore, organizations in the Houston area, such as the League of United Latin American Citizens (LULAC) and the Urban League, serving minority individuals throughout the area will be provided information for distribution to their constituencies. In the case of LULAC, information will be provided in both English and Spanish versions so that it is accessible to persons with limited English proficiency.

Recruitment efforts will be sustained over the five-year period of proposed DPMC project activities. As individuals with disabilities who have pain are enrolled in the clinic, they will be asked about their willingness to participate in research on the effectiveness of different pain management approaches. Individuals who indicate unwillingness to participate in research will be provided services in accordance with accepted clinical practice standards. No data beyond that usually obtained from people seeking clinical treatment will be gathered on these individuals. However, for people expressing willingness to participate in testing of pain management interventions, a more thorough data set will be developed. The data set on these individuals will include detailed demographic information, including not only standard parameters (e.g., gender, age, ethnicity, marital status, educational level, employment status, income range), but also information on living arrangements, types of activities performed in home and work settings, and the nature of support currently available to assist the person in home and work. Also the data set will include information on the nature and time of onset of disability and the influence of disability on the individual's life. Information on overall health status and any intercurrent health problems will also be entered into the database.

Figure 1: Primary Area From Which Patients and Study Subjects will be Recruited



Also, a standardized data set on the nature and severity of pain experienced by these individuals will be developed. Data on the nature, severity, and impact of pain will be gathered using instruments and processes identified and/or developed by the DPMC's Outcome Measures Core. These will include subjective measures of pain that are generated using visual analog scales and other instruments that allow individuals to assess quantitatively the extent of their pain. Accepted and experimental objective pain measures, such as the McGill Pain Questionnaire (Melzack, 1975), the Visual Analogue Scale (Wewers and Loew, 1990), and the Emory Pain Estimate Model (Brena and Chapman, 1983), will also be used to characterize the types of pain experienced by individuals with different types of disabilities seen in the clinic. Also, standardized measures of the impact of pain on the functional abilities of individuals with disabilities, as well as on the quality of their lives, will be generated. These measures will initially involve data collected using the instruments and procedures described in detail in the section of this application dealing with the Outcome Measures Core Unit (Core B). Other functional and quality of life measures may be added as the work of the Outcome Measures Core progresses.

The end product of these data collection efforts will be a database that contains information on a population of people with different types of disabilities. The database will be entered into computer storage that allows for access according to (1) type of disability; (2) demographic factors (e.g., gender, ethnicity, age category), (3) nature of pain reported (e.g., CNS pain versus peripheral pain), (4) time since onset of pain; and (5) types of pain interventions previously tried. The goal of the preliminary studies conducted over this two-year period will be to establish a searchable database that provides information on individuals who can be recruited, using appropriate informed consent procedures, into studies designed to test the efficacy of various pain management interventions that are developed through the activities of the DPMC and through the efforts of clinical researchers in other settings.

These preliminary studies will provide one of the largest databases in the country on pain and disability. This database will ultimately be used in testing pain interventions with different groups of patients, using standardized assessment procedures to determine which interventions appear to be most effective in reducing pain and fostering an acceptable quality of life. The preliminary studies necessary to establish the database will be conducted without incremental research support from the funding agency. Based on estimates of the incidence of disabling conditions in the target area, and on demographic characteristics of the target population, the numbers of individuals who have been enrolled in preliminary studies, and on whom data will be included in the database are summarized in figure ? below, categorized according to disabling condition and ethnicity. Additional grouping of study subjects into age categories, more specific disability definitions (e.g., quadriplegia and paraplegia), and socioeconomic status (e.g., income groupings) may be possible if population sizes are adequate and if the analytical power that can be realized with such smaller groups is sufficient to permit additional categorizations.

Table 1: Expected Pain Clinic Enrollments Based on Ethnicity and Disabling Condition

Disabling Condition	White	African-American	Hispanic	Other	TOTAL
Spinal Cord Injury	50	25	25	25	125
Traumatic Brain Injury/Stroke	50	25	25	25	125

Limb Loss	30	15	15	10	70
Post Polio	50	10	20	5	85
Spina Bifida	20	10	10	5	45
Multiple Sclerosis	40	10	10	10	70
Other*	100	50	75	20	245
TOTAL	340	145	180	100	765

*May include a range of disabling conditions, such as arthritis, various dystrophic conditions, and low incidence congenital disorders, such as osteogenesis imperfecta.

These data suggest that by the end of two years of clinic operations, extensive descriptive data will have been collected approximately 750 individuals from diverse ethnic backgrounds and with different types and degrees of disability and different types and levels of chronic pain. These individuals will constitute the population from which samples will be drawn to test innovative approaches to pain management using experimental protocols that will be developed according to the process described below.

4. Research Design and Methods

The research design to be employed with this study will involve developing specific cohorts based on disability type, proposed treatment, and other relevant descriptive factors (e.g., age, gender, ethnicity) who can be followed over a three-year period to (1) assess their responsiveness to different pain management approaches, and (2) determine if operation of a pain clinic represents an efficacious approach to managing chronic pain in persons with disabilities. The types of data to be collected, selection of study subjects, clinic operations, and analyses of the data are discussed below.

Data parameters. Data that will be generated through operation of the clinic will be entered into the established DPMC database so that the efficacy of various treatment modalities in managing pain in different segments of the disability population can be assessed using appropriate quantitative and qualitative measures and analytic techniques. The primary parameters on which data will be collected have been identified by Grabois and VanDeventer (1995). These are summarized in Figure 2 below:

Figure 2. Parameters to be Assessed in Testing Pain Management Techniques

Subjective Pain	Whole body diagram Pain intensity rating scales Visual analogue scales General pain measurement (McGill Questionnaire)
Biomechanical Functioning	Flexibility (ROM measurements) Endurance (activity duration, such as walking or pushing wheelchair or ergonomic testing) Strength (number of repetitions of lifting a given weight; performance on Cybex; static and dynamic body mechanics)

Physiological	EMG muscle tension (biofeedback) Critical evoked potential (if indicated) Autonomic responses
Psychological/Behavioral	Personality factors (MMPI) Mood (Beck Depression Inventory) Frequency of "pain behaviors) Stress management and scoping skills "Meaning" of pain to patients and family
Functional	Basic ADL skills Job activities Housework Yard work "Up time" (activity diary of sitting, standing, pushing, reclining, lying) Hobbies Prevocational and/or vocational status
Familial/Social	Marital Distress Family Distress Social Withdrawal Prevocational and/or vocational status
Medical	Patterns of medication usage Use of healthcare system Effectiveness of therapies Sleep patterns Effects of other health problems

Selection of study subjects. Selection of individuals who will be enrolled in pain management studies will be done using established criteria. A primary source of individuals who will be recruited for pain management studies will be those individuals who have participated in preliminary studies during the first two years of DPMC operations. Conducting preliminary studies for two years prior to initiating tests of innovative therapeutic approaches will allow for identification of a known population of persons with disabilities who can then be recruited into studies of clinical management studies appropriate to the types and severity of pain that the individual is experiencing. Without the allowing for the preliminary studies scheduled in years one and two, initiation of pain management studies beginning in year three would be reliant on chance identification of sufficient numbers of individuals with specific types of disabilities and types and severity of pain to allow for adequate power in data analyses. By conducting the two years of preliminary studies, a core group of potential study subjects can be identified prior to attempting experimental interventions. This core group can be expanded over the three years of investigation to enhance the power of investigations undertaken.

Actual selection of study subjects will be made using a number of criteria that include:

- being at least 18 years of age;
- being someone with a type of disability under study at the clinic (e.g., spinal cord injury, amputation, post-polio syndrome);
- having had pain of more than six months duration;
- being sufficiently mobile to be able to travel to the clinic;
- having some source of financial sponsorship (e.g., Medicaid, Medicare, private insurance) for basic clinical services;
- having the capability to understand the concept of pain management and the purposes the study being initiated;
- expressing willingness to participate in all aspects of the study; and
- providing informed consent to participate in the study under terms and conditions described by clinic staff.

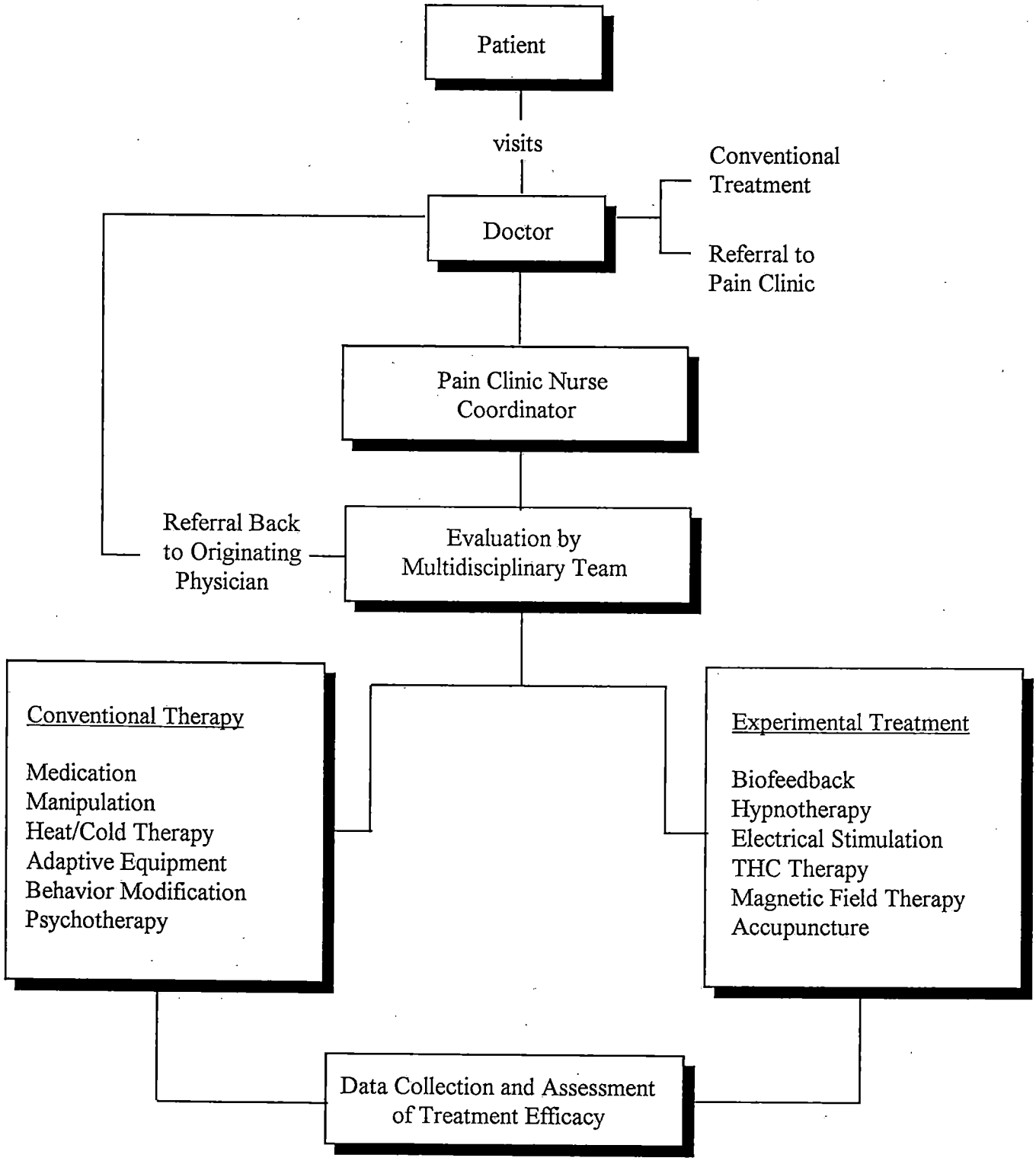
Also, efforts will be made to recruit study subjects that are representative of the population in the area in terms of age, ethnicity, income level, and other factors. However, given the relatively low incidence of some disabilities that is further reduced when the requirement of chronic pain is considered, some study cohorts may not reflect desired age, ethnic, and gender distributions. In cases where representation by certain population segments is less than desired, problems with representativeness of the study population will be fully discussed, as will efforts undertaken to try to enhance representation by individuals from underrepresented population segments. Projected numbers of individuals with primary disabilities of interest and from major ethnic groups represented in the target area who will be identified through preliminary study activities and on whom information will be included in the DPMC database are provided in Table 1 above.

Research activities and clinical services. Decisions concerning specific investigative protocols to be used with each study subject will be made by a multidisciplinary team headed by the physiatrist and having primary membership composed of a physical therapist, occupational therapist, social worker, rehabilitation nurse, and pharmacist. Consultative involvement of psychiatrists or psychologists, dieticians, vocational counselors, recreational therapists, and other physicians will be requested on an "as needed" basis to address specific issues identified by primary team members.

Although the exact nature of the investigative protocols that will be used with each patient will not be defined in detail until late in the second year of preliminary studies (corresponding to the second year of operation of the DPMC); the process that will be used with individuals recruited into various pain management protocols will generally follow the structure described by Grabois and VanDeventer (1995) for the Baylor College of Medicine Pain Management Program at The Methodist Hospital. That structure is represented by Figure 3 on the following page:

All patients referred to the clinic will undergo a thorough assessment of their general health and functional status, as well as being evaluated with regard to the etiology, type, duration, and nature of their pain. If it is determined that the pain is not chronic and is due to an acute health problem, or if clinical testing indicates that the pain is unrelated to an individuals disability, then the patient will be referred back to the physician originating the referral with a report of the diagnostic findings and clinical assessment results from the pain clinic. Patients who are diagnosed with chronic pain, but who may not have been treated using

Figure 3: Representation of Pain Clinic Structure



conventional therapies will be initially treated using accepted treatment approaches for pain of the type presenting in persons with similar disabilities (e.g., Elavil therapy for SCI related pain). Documentation of relief or lack of relief using conventional therapies will be done before patients who have not been treated using conventional therapy are placed in experimental treatment programs. The same outcome measures will be used in assessing patients who are treated using conventional therapy and patients who are treated using experimental methods. These measures are discussed briefly in the data analysis section of this project description, with additional information provided in the description of the outcome measures core included in this application.

Patients who have been treated using conventional therapies, and on whom appropriate data concerning the nature and results of such treatments are available, will be offered the option of treatment using one or more of the experimental methods developed through the DPMC by researchers elsewhere in the country. These individuals will be fully informed concerning the experimental nature of treatment options, any known or suspected risks associated with the treatments, and the results of any preliminary studies completed on various treatment options. As with conventional therapies, recommendations concerning the best options for treating a specific type of pain in a particular patient will be made with input from the multidisciplinary team. However, the final decision regarding selection of an experimental treatment regimen will be left to the patient, with concurrence by the attending physician that the treatment selected by the patient is medically indicated and appropriate given the patient's health and pain history and the risks involved with the treatment option selected. As with conventional treatment options, the patient will be fully informed about the treatment procedure and risks involved and will be required to sign a consent form before any treatment is initiated.

Data collection and analyses. Extensive data will be collected on all patients accepted for treatment in the pain clinic. Extensive demographic information (e.g., age, gender, ethnicity, income and educational levels, living arrangements) will be gathered on each patient. Also, data from thorough health, family, and social histories will be gathered and recorded using accepted methods and instruments. Measures of pain and its influence on the individual will be taken using both clinical observational techniques (i.e., localization of pain as described by the patient and assessed via clinical evaluation using palpation, manipulation, and quantitative measures of function such as range of motion and gripping strength) and instrument battery described in the section of this proposal dealing with outcome measures (Core B). Some of the information used in measuring pain will be gathered using a refined version of the Baylor College of Medicine Department of Physical Medicine Pain Questionnaire that has been in use by Baylor clinicians for several years. With input from the outcome measures core and based on experience with it gained over the two years of preliminary studies that will be conducted prior to initiating experimental treatments, the pain questionnaire will be refined to enhance its utility in gathering data that are most relevant in characterizing the nature of pain and its impact on the individual. In making these refinements, care will be taking to minimize redundancy in information collected by comparing data gathered on the Pain Questionnaire to information gathered using other instruments that are included as part of the outcome measures battery.

Data on the clinical outcomes of treatment will be tailored to the specific type of treatment used and will be informed by research information generated through DPMC efforts and through other research reported in the literature. These data will included subjective self-reported data on pain, as well as measures of functional improvement that are indicative of reduced pain. They may also include laboratory tests that measure physiologic responses to pain. Preliminary data suggest that some laboratory tests may, in fact,

provide empirical evidence of pain or its absence in individuals. As the efficacy of using such tests becomes better documented, they will be considered for use in assessing the efficacy of convention and experimental treatments used in the pain clinic.

In terms of analyses of data, a discussion of the analytical methods to be used with instruments included as part of the outcome measures core is included in the description of outcome core activities. Analyses of other types of data, beyond simple descriptive analyses, are difficult to forecast at this point in time. In order to generate a reasonable quantity of data for analyses, efforts will be made to assure that there are at least 20 individuals in each treatment group. While this will not pose problems for some conditions, such as spinal cord injury and traumatic brain injury--both conditions for which Baylor and its clinical affiliate, The Institute for Rehabilitation and Research, have large former patient pools and ongoing clinical service programs from which to draw--for other conditions, such as amputation and multiple sclerosis, drawing a sufficient and demographically mixed group of study subjects will require some effort. Conducting preliminary studies over the first two years of DPMC operations, during which outreach activities can be conducted with different disability groups and different segments of the community, is designed to minimize the risk that too few individuals will be recruited into studies to permit analyses resulting in significant findings.

Specification of analytic methods will not be made until closer to the time that experimental studies are to be initiated and some preliminary data have been gathered and analyzed. However, appropriate multivariate analyses will be completed in accordance with accepted standards with regard to group sizes and the types of data being analyzed. Likewise, calculations of analytical power cannot be projected without more firm estimates of group sizes. However, care will be taken to specify analytical power in reporting data generated through research efforts conducted in the clinic.

5. Human Subjects

(1) Involvement of human subjects. The subject population to be involved in this study will include people in the Houston area with a range of physical disabilities and from different socioeconomic backgrounds. Since the thrust of the research is on alleviation of pain in persons with physical disabilities, efforts will be made to secure as broad a range of people with disabilities as possible, including people with spinal cord injury, post polio, multiple sclerosis and other disabling conditions. An earnest effort will be made to involve people from minority backgrounds, as well as from low income households in the project. In this regard outreach efforts will be made via media targeted to minority neighborhoods and communities, as well as through contacts with churches, schools, and other organizations serving minority communities. The goal of these efforts will be to enroll people in research studies in proportions that roughly approximate their proportions in the community. Similarly efforts will be made to recruit both men and women into research studies, and to recruit people from different age ranges into appropriate studies. Senior citizen groups and other organizations serving older citizens will be informed of the clinic and its research program, and older individuals with chronic disability-related pain will be encouraged to seek services through the DPMC.

(2) Sources of research material obtained from individuals. Research materials obtained from individuals may include laboratory specimens used to rule out pain associated with infection or other acute problems, material generated using various imaging technologies, including x-rays and bioelectrical

measures (i.e., EEG, EMG), and material generated from clinical observation and examination. Also, material will be developed from administration of questionnaires, pain scales, and other instruments described under the write-up of the Outcome Measurements Core Unit. Some of these materials will be gathered for the purpose of general health assessment and some will be gathered for research purposes. Whenever possible, existing records and test results will be used to assess the etiology and nature of pain reported by patients, and efforts will be made to avoid duplication of information gathering activities that may be uncomfortable to the patient or that may result in unnecessary cost to the patient or third party payer. The goal of project efforts will be collect, in the most expeditious fashion possible, data necessary to characterize and treat the pain experienced by individuals using the most appropriate approach possible, whether that approach involves conventional therapy or an experimental treatment of the pain.

(3) Recruitment of subjects. Recruitment of subjects into the clinic will involve two strategies--one targeted to clinicians in the community who may encounter people with disabilities and chronic pain, and one targeted to individuals with disabilities living in the community. Strategies targeting clinicians will involve targeted mail-outs and postings in clinical facilities, particularly those serving high percentages of low income and minority individuals, such as the neighborhood health centers operated by the Harris County Hospital District. Strategies targeted to people with disabilities will involve sending notices to disability-related service and advocacy organizations (e.g., the Houston Center for Independent Living and the Multiple Sclerosis Society), and scheduling presentations to these and other groups addressing the needs of the disability community. Obviously the roster of former TIRR patients represents an obvious source or potential study subjects. Prior to initiating any experimental procedures related to pain management, approval will be obtained from Baylor's Affiliated Review Board (ARB). Prior to initiating innovative treatments, any baseline information gathered on pain will be obtained under the ARB approval to be obtained by the Outcome Measures Core Unit for the DPMC.

(4) Potential risks. It is difficult at this juncture to estimate potential risks to patients from experimental treatment procedures that have not yet been clearly identified. However, as with conventional therapies that are used to treat pain today, every effort will be made to use the safest treatment possible to achieve the best results in reducing disability-related pain. Any treatment that has been shown to have moderate to high risk associated with its use will only be used as a matter of last resort in treating pain. In every case, all risks, including those that might appear to be remote, will be fully explained to patients who will have the opportunity to decline any type of diagnostic or therapeutic procedure. It is expected that little risk will be associated with most procedures to be used in the clinic.

(5) Protecting against risk. Protection against risk will be done through proper training of clinic staff in all diagnostic and therapeutic procedures and through observance of strict confidentiality in management of patient information. Clinical and research competency afford the best protection against risk, and training of staff in conventional and experimental procedures will be a high priority. Also, adherence to established research protocols will protect against undue risk. For all research procedures carried out, clear protocols will be prepared describing the sequence and manner in which procedures are to be done. Staff will be given firm directions on how to use the protocols and on what to do if problems arise while research is being conducted. While there may be some risk associated with various procedures undertaken in the clinic, every effort will be made to minimize such risks through appropriate staff preparation and adherence to accepted clinical and research practices.

(6) Reasonableness of risks in light of potential benefits. There will undoubtedly be some risks associated with some of the diagnostic and therapeutic approaches to be tested through the DPMC. However, in every case involving risk careful consideration will be given to potential benefits that may accrue to the individual(s) exposed to risk. For some individuals who will be involved in research conducted through the psin clinic, months and years of episodic or unrelenting pain related to a disabling condition have degraded their life quality to the point where some risks are worth taking if the result of taking the risk is enhanced life quality through diminished pain. In every case, all known or suspected risks associated with a procedure will be fully described to potential study subjects, and decsions concerning involvement in conventional or experimental pain management procedures will be left to the patient, with concurrence by the attending physician that the choice is medically and ethically an appropriate choice and one with which the physcian can concur. For people with chronic pain, assuming a calculated risk that might result in relief may be a very attractive choice.

6. Vertebrate Animals

There are no plans to use animals in this project.

7. Consultants/Collaborators

Funding has been requested to pay for limited consultation time on this project. Consultants will be selected at an appropriate time based on their knowledge about and experience with disability and/or pain research.

8. Consortium/Contractual Arrangements

Collaboration between Baylor and TIRR is critical to the success of this project. In addition to being governed by the existing affiliation agreement between the two institutions, TIRR's board of trustees and senior administrative staff have approved establishment of the pain clinic as a regular TIRR program. This level of collaboration bodes well for success in the project.

9. Literature Cited

A limited literature review was conducted in planning for this study. A more thorough review of the literature on pain and disability was conducted in preparing the write-up of the Outcome Measures Core (Core B) included with this application. The reviewer is referred to the more extensive review provided under that description. Much of the same literature applies to both sets of activities. A review of the current liteature will be included in the continuation application prepared to request funding to initiate research through the clinic that extends beyond collection of baseline data.

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Harkness JAL, Higgs ER, and Dieppe PA (1984). Osteoarthritis. In Wall PD and Melzack R (eds), *Textbook of Pain*. New York: Churchill Livingtone.

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Kanner R (1993). Introduction to panel on treatment effectiveness. Presented at the Planning Workshop on *Chronic Pain Management: Developing a Treatment System for People with Disabilities*. Bethesda, MD, May 1-3, 1993.

Melzack (1975). The McGill pain questionnaire: Major properties and scoring methods. *Pain*, 1, 277-299.

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Wall PD and Melzack R (eds) (1984). *Textbook of Pain*. New York: Churchill Livingtone.

Wewers ME and Lowe NK (1990). A critical review of visual analogue scales in the measurement of clinical phenomena. *Research in Nursing and Health*, 13, 227-236.

DESCRIPTION: State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project. Describe concisely the research design and methods for achieving these goals. Avoid summaries of past accomplishments and the use of the first person. This abstract is meant to serve as a succinct and accurate description of the proposed work when separated from the application. **DO NOT EXCEED THE SPACE PROVIDED.**

Core A: Administrative Core Unit. The administrative core unit will provide coordination for the various research and related activities of the DPMC. The functional objectives of the Administrative Core Unit are to: (1) establish a structural framework in which to foster pursuit of a planned research agenda focusing on chronic pain in persons with disabilities; (2) provide support to research personnel in project design and development; (3) provide opportunities for exchange of research findings between members of the research team; (4) promote understanding of current research approaches, as well as of policy developments at various levels that influence research support and conduct; and (5) assist investigators in disseminating research results effectively through publications, professional presentations, and other relevant activities. Specific services that will be offered through the administrative core unit will include (a) coordination of research meetings (including DPMC advisory committee meetings); (b) preparation and distribution of DPMC progress reports; (c) oversight of fiscal operations of individual projects and for the DPMC as a whole; (d) assistance with research development and ongoing activities; (e) advisement and assistance with policy issues and issues related to consumer involvement in research; and (f) support for dissemination activities, including preparation of materials to be used in reports, manuscripts, presentations, and other activities designed to heighten awareness of issues related to chronic pain and disability and to research intended to reduce the deleterious effects of chronic pain on people with disabilities and their family members. The administrative core unit will draw heavily of departmental support, with the intent of minimizing administrative demands on research personnel who are engaged in investigative studies.

PERSONNEL ENGAGED ON PROJECT, INCLUDING CONSULTANTS/COLLABORATORS. *Use continuation pages as needed* to provide the required information in the format shown below on ***all*** individuals participating in the project.

Name Grabois, Martin | Degrees(s) M.D. | Social Security No. (C)
Position Title Professor and Chairman | Date of Birth (MM/DD/YY) (C) | Role on Project Director
Organization Baylor College of Medicine | Department Physical Medicine & Rehab.

Name Hart, Karen | Degrees(s) Ph.D. | Social Security No. (C)
Position Title Assistant Professor | Date of Birth (MM/DD/YY) (C) | Role on Project Dissemination Spec.
Organization Baylor College of Medicine | Department Physical Medicine & Rehab.

Name Frieden, Lex | Degrees(s) M.A. | Social Security No. (C)
Position Title Clinical Associate Professor | Date of Birth (MM/DD/YY) (C) | Role on Project Policy Spec.
Organization Baylor College of Medicine | Department Physical Medicine & Rehab.

Name To Be Named | Degrees(s) Ph.D. | Social Security No. Not Available
Position Title Research Director | Date of Birth (MM/DD/YY) Not Avail. | Role on Project Research Spec.
Organization Baylor College of Medicine | Department Physical Medicine & Rehab.

Administrative Core Unit

1. Objective

The the broad objectives of the administrative core unit are to provide adequate support for and coordination of the research and related activities of the Baylor College of Medicine Department of Physical Medicine and Rehabilitation Disability and Pain Management Center (DPMC). Specific functional objectives of the administrative core unit are to: (1) establish a structural framework in which to foster pursuit of a planned research agenda focusing on chronic pain in persons with disabilities; (2) provide support to research personnel in project design and development; (3) provide opportunities for exchange of research findings between members of the research team; (4) promote understanding of current research approaches, as well as policy developments at various levels that influence research support and conduct; and (5) assist investigators in disseminating research results effectively through publications, professional presentations, and other relevant activities.

2. Organizational Structure

The organizational structure to be employed for the administrative core is graphically depicted in the organizational chart (p. ??). The administrative core is organized in a manner to provide for external review and oversight by a project advisory committee composed of both professionals in pain management and disability and persons with disabilities who have experience with chronic pain. The seven-member advisory committee will be composed of four nationally recognized health care professionals who are knowledgeable about pain management and disability research, and three persons with disabilities from the Houston area who have experience with chronic pain The three individuals with disabilities serving on the committee will have different types of disabilities and will be selected with the goal of achieving a cross cultural perspective. The advisory committee will be convened in a face-to-face meeting once each year to review overall DPMC plans and plans for individual research projects, support cores, and related activities. Thereafter, committee members may be called on throughout the year to provide input on specific research issues related to chronic pain and disability. Members of the DPMC advisory committee will not be selected until after the review of applications has been completed. This approach avoids problems of excluding qualified individuals who might be forced to decline serving on an advisory committee because they are involved with a competing project or because they have been asked to serve on the study section which will review these applications. Input from NCMRR staff regarding appropriate and qualified individuals to serve on the advisory committee will be sought before selections are made.

Coordinating activities of the DPMC advisory committee will be the responsibility of Dr. Martin Grabois, DPMC principal investigator. Dr. Grabois will correspond with committee members and will provide them with copies of planning documents, reports, and other project materials on a regular basis. Dr. Grabois will also provide direction for the operation of the DPMC. In this role, he will be responsible for calling meetings of research and support staff, determining the allocation of DPMC core resources to various projects, and overseeing fiscal management of DPMC activities.

Assisting Dr. Grabois as DMPC co-director for research development will be the to-be-named Department of Physical Medicine and Rehabilitation Research Director. Final negotiations with a qualified candidate were being completed at the time of preparation of this proposal. However, at the request of the individual with whom negotiations are underway, a name could not be provided with this application. This individual filling this position will be responsible for assisting researchers with research design and implementation, data analyses, and interpretation of results.

Additional support of DPMC activities will be provided by Lex Frieden, associate professor of physical medicine and rehabilitation and senior vice president for grants management at TIRR, and Dr. Karen Hart, assistant professor and director of education for the physical medicine and rehabilitation department, and TIRR vice president for education. Mr. Frieden will provide assistance on institutional and national research policy issues and on consumer involvement in research, and Dr. Hart will coordinate activities designed to assure dissemination of research findings both within the DPMC and to outside audiences.

Non-professional support for DPMC activities will be provided by staff of the Department of Physical Medicine and Rehabilitation, chaired by Dr. Grabois, as well as staff of TIRR's Office of Grant's Management, headed by Mr. Frieden, and TIRR's Division of Education headed by Dr. Hart. In keeping with NIH policy regarding salary coverage for non-research support staff, no funding for administrative support staff is requested. Baylor College of Medicine and its affiliates in the proposed DPMC will assume responsibility for administrative support for DPMC operations.

3. Staffing Summary

The proposed administrative staffing for the DPMC is as follows:

Dr. Martin Grabois, Center Director and Principal Investigator	10%
To-be-named, Center Co-Director for Research Development	5%
Mr. Lex Frieden, Disability Policy Specialist	5%
Dr. Karen Hart, Dissemination Specialist	5%
Projected in-kind administrative support staff	50%

These time and effort commitments represent modest commitments to the proposed project. However, all of the individuals listed for these roles are currently engaged in work that complements the activities proposed, and all have support for their efforts from sources other than from grants funds being sought. The support requested for administrative activities represents that increment of effort required in dealing with DPMC activities that are consistent with other ongoing efforts of the Baylor Department of Physical Medicine and Rehabilitation and clinical affiliates.

4. Resources and Environment

The resources and environment to support administrative activities of the DPMC are more than adequate. The Department of Physical Medicine and Rehabilitation maintains office space in

the Baylor College of Medicine/Methodist Hospital Smith Tower, as well as in The Institute for Rehabilitation and Research. The Smith Tower office space consists of roughly 3,000 square feet of office space that includes offices for administrative faculty and departmental support staff. Office facilities are fully equipped with IBM-compatible computer systems, copying machines, and fax uints. The TIRR office space consists of roughy 1,000 square feet of space that includes an office for the chairman, two faculty members, the chairman's administrative assistant, and two secretary/receptionists. As with the Smith Tower space, the TIRR office space is equipped with desk-top IBM-compatible computer systems, fax capabilties, and duplicating equipment. Both office suites are served by e-mail through the Baylor-operated computer resource center.

In addition, TIRR provides administrative support through its Office of Grants Management located immediately adjacent to the physical medicine and rehabilitation offices. Office space for Lex Frieden and an administrative secretary are housed in this space and grant related reports and files are maintained in this area. Dr. Hart and Division of Education staff are also housed at TIRR in approximately 750 square feet of space that includes computer equipment, duplicating services, and training and educational equipment (e.g., projectors, microphones, etc.) used regularly. Also Dr. Hart and her staff manage the educational resources of TIRR, including a conference and meeting room suite that can accommodate groups ranging from six to 150 for focus groups, presentations, and other activities. Other meeting space for groups of up to 50 is also available in different locations throughout TIRR, with scheduling managed by Division of Education staff.

In summary, the administrative support required to operate the proposed DPMC is available, and the environment in which the DPMC will be located is one that fosters collaboration and information sharing. The proposed DPMC can be successfully administered with relatively modest support from grant sources.

5. Services Provided

The services to be provided by the Administrative Core Unit will include (1) coordination of research meetings (including DPMC advisory committee meetings); (2) preparation and distribution of DPMC progress reports; (3) oversight of fiscal operations for individual projects and for the DPMC as a whole; (4) assistance with research development and ongoing activities; (5) advisement and assistance with policy issues and issues of consumer involvement in research activities; and (6) support for dissemination activities, including preparation of materials to be used in reports, manuscripts, presentations, and other activities designed to heighten awareness of issues related to chronic pain and disability and to research designed to reduce the deleterious effects of chronic pain on people with disabilities and their family members.

DESCRIPTION: State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project. Describe concisely the research design and methods for achieving these goals. Avoid summaries of past accomplishments and the use of the first person. This abstract is meant to serve as a succinct and accurate description of the proposed work when separated from the application. DO NOT EXCEED THE SPACE PROVIDED.

This project will examine the correlates of pain in the lives of people with a variety of physical disabilities and evaluate several innovative interventions for the reduction or modification of chronic pain in this population. The aims include (a) assessing the relationship between pain and the physical, psychological, and social functioning of people with physical disabilities and to determine the significance of variables related to demographics, social support, spirituality and environmental accessibility as moderators of that relationship, and (b) evaluate the effectiveness of innovative interventions and moderators of such effectiveness. The Outcomes Core Unit will work with the investigators on the intervention projects, providing expertise in measuring outcomes relative to function, community integration, and quality of life. The core will provide data management for the diverse, large, data sets, collected over extended periods of time. Standardized measures such as the RAND SF-36, the FONE FIM, the Craig Handicap Assessment and Reporting Technique (CHART), and the Life Satisfaction Index A (LSIA) that have proven reliability and validity and have been used with persons with disabilities will be used to assess the relevant constructs. Data collection will be customized to the needs of each individual project's research design. Correlational and multivariate statistics will be used to assess the relationship of the variables with each other and the effectiveness of the interventions. One of the key results will be a wealth of information regarding pain in persons with primary disabilities that is currently nonexistent. The information gained from this study will allow clinicians to prescribe appropriate interventions. It will also suggest future research priorities relative to chronic pain in individuals with primary physical disabilities. Results will be disseminated through scientific journals and national meetings, as well as through consumer publications and other media.

PERSONNEL ENGAGED ON PROJECT, INCLUDING CONSULTANTS/COLLABORATORS. *Use continuation pages as needed* to provide the required information in the format shown below on *all* individuals participating in the project.

Name Margaret A. Nosek	Degrees(s) Ph.D.	Social Security No. (C)
Position Title Associate Professor	Date of Birth (MM/DD/YY) (C)	Role on Project P.I.
Organization Baylor College of Medicine		Department Phys. Med. & Rehab.
Name Diana H. Rintala	Degrees(s) Ph.D.	Social Security No. (C)
Position Title Assistant Professor	Date of Birth (MM/DD/YY) (C)	Role on Project Co-PI
Organization Baylor College of Medicine		Department Phys. Med. & Rehab.
Name Carol A. Howland	Degrees(s) M.P.H. (in progress)	Social Security No. (C)
Position Title Assistant Professor	Date of Birth (MM/DD/YY) (C)	Role on Project Project Manager
Organization Baylor College of Medicine		Department Phys. Med. & Rehab.
Name Gail F. Chanpong	Degrees(s) M.S.	Social Security No. (C)
Position Title Database Manager	Date of Birth (MM/DD/YY) (C)	Role on Project Database Manager
Organization Baylor College of Medicine		Department
Name	Degrees(s)	Social Security No.
Position Title	Date of Birth (MM/DD/YY)	Role on Project
Organization		Department
Name	Degrees(s)	Social Security No.
Position Title	Date of Birth (MM/DD/YY)	Role on Project
Organization		Department
Name	Degrees(s)	Social Security No.
Position Title	Date of Birth (MM/DD/YY)	Role on Project
Organization		Department

Core B: Outcome Measures Core Unit

SPECIFIC AIMS

Chronic pain can impact all areas of life. For a person who already has functional limitations resulting from physical disability, chronic pain may further reduce mobility and make basic activities of daily living difficult or impossible to perform. Chronic pain can prevent fulfillment of normal social roles, such as working for pay, homemaking, and parenting. It may affect relationships with other people and community integration. Standard pain treatments often are not effective in relieving the chronic pain of individuals with disabilities, and such treatments may have unintended effects such as drowsiness which further impair an individual's ability to function in an optimal manner. This study will examine the correlates of pain in the lives of people with a variety of physical disabilities and evaluate several innovative interventions for the reduction or modification of chronic pain in this population.

The specific aims of this core project will be to:

1. Assess the relationship between pain and the physical, psychological, and social functioning of people with physical disabilities. Determine the significance of variables related to demographics, social support, spirituality, and accessibility of the environment as moderators for the relationship between pain and physical, psychological, and social functioning.

2. Evaluate the effectiveness of innovative interventions for the reduction or modification of chronic pain among people with long-term physical disabilities.

2.1 Evaluate the impact of the four interventions presented in this proposal with regard to their short- and long-term impact on pain intensity and quality, and on physical, psychological, and social functioning.

2.2 Identify moderating variables that affect the degree of impact that the various interventions have on pain and physical, psychological, and social functioning. These may include socio-demographic and disability-related variables, social support, spirituality, and environmental supports (e.g., assistive technology, home and workplace modifications).

2.3 Determine predictive factors for positive outcomes of intervention modalities.

Data will be collected from participants in the four projects contained in this proposal to test the following hypotheses:

H_1: Variables related to demographics, social support, spirituality, and environmental accessibility significantly moderate **the relationship** between pain and level of physical, psychological, and social functioning among people with long-term physical disabilities.

H_2: Experimental pain reduction intervention is effective in reducing or modifying chronic pain among people with long-term physical disabilities.

H_3: Reduction or modification in chronic pain is significantly related to improvements in physical, psychological, and social functioning among people with long-term physical disabilities.

H_4: Variables related to demographics, social support, spirituality, and environmental accessibility significantly moderate the **effectiveness of interventions** on reducing or modifying pain and increasing level of physical, psychological, and social functioning among people with long-term physical disabilities.

BACKGROUND AND SIGNIFICANCE

Chronic pain was identified as a significant secondary problem resulting from a primary physical disability or impairment at a research planning workshop sponsored by the National Center for Medical Rehabilitation Research, Agency for Health Care Policy and Research, and National Institute on Disability and Rehabilitation Research (March 1993). Even persons with disabilities who were leading active, participatory lives reported that living with chronic pain seriously compromised their quality of life. Workshop attendees concurred that both functional restoration and relief of nociceptive symptoms and suffering should be primary goals of managing the individual with chronic pain. This proposed outcome study will address the following research priorities identified at the workshop on chronic pain management in people with disabilities:

- Test evaluation tools for chronic pain for sensitivity and validity with diagnosis-specific groups of patients with physical impairment;
- Validate the effectiveness of different treatment modalities in trials using evaluation tools that are appropriate for selected populations of patients with physical impairments or disabilities;
- Validate and assess reliability of usable physical and psychosocial tools for patients with diverse primary physical limitations, impairments, or disabilities;
- Determine appropriate medical, psychosocial and familial components of assessment as well as modifications needed to standardize assessment tools and practices for persons disabilities;
- Evaluate specific treatment modalities for different types of pain and for different subpopulations of patients with physical disabilities, including physical agents such as cold, heat, vibration, magnets, TENS, and pharmacologic agents such as Marinol (THC) and Elavil;
- Determine the most effective methods for treating the adverse cycle of chronic pain and

inadequate treatment, leading to psychological distress, leading to continued pain, leading to continued inadequate treatment, producing greater psychological distress;

- Determine predictive factors for positive treatment outcomes;
- Standardize criteria for treatment outcome evaluation;
- Determine coping strategies for individuals and families dealing with physical disability and chronic pain;
- Investigate factors that can reliably predict which patients are likely to be able to return to work.

Assessment of Pain

Chronic pain has been reported as a problem in from 30% to 100% of persons with spinal cord injury (Bors, 1959; Burke, 1973; Kennedy, 1946; Munro, 1950; Loubser, Rintala, Fuhrer, & Castro, 1995; Nepomuceno et al, 1979; Rintala, Hart, & Fuhrer, 1991; Waring, Karunas, & Douglas, 1995). A questionnaire was developed and tested specifically to assess pain after spinal cord injury (Nepomuceno et al, 1979). Of the 200 respondents, 80% reported abnormal sensation, 48% considered the discomfort painful, and nearly half indicated that it interfered with daily activities. Similarly, Rintala et al (1991) found that 31% of her cohort of 640 persons with spinal cord injury reported pain severe enough to interfere with daily activities. Pain that limited or prevented function was reported in 42.7% of Waring and colleague's spinal cord injured sample (1995), with the shoulder, neck and back the most disabling sites. Considering that the primary goal of many multi-disciplinary pain clinics is to increase function rather than reduce pain, it is interesting that 37% of patients with low level lesions were willing to exchange a chance of recovery or loss of reacquired physiologic functions for pain relief (Nepomuceno et al, 1979). Outcome assessment in the proposed studies will need to assess individual values, preferences, lifestyle priorities, and goals in balancing the costs and benefits of pain relief against changes in functional capacity.

Two approaches have been used to assess the effect of pain on performing daily activities: behavioral assessment and patient self-report. Behavioral assessment enables reliable observation and rating of pain behaviors (Keefe & Block, 1982), but is inconvenient in terms of cost and demand for staff time to perform ratings and doesn't allow comprehensive assessment which includes social and recreational activities in the community. In addition, paralysis, weakness, or involuntary movements may alter or reduce the number of pain behaviors in persons with primary disabilities who have chronic pain.

Self-reported pain may be assessed by detailed questionnaires dedicated to pain assessment alone or as part of a general measure of quality of life or health status. Subjective pain experienced will be measured in the proposed studies by the Visual Analogue Scale (Wewers & Lowe, 1990) and the McGill Pain Questionnaire (Melzack, 1975). Numerous studies support the reliability (Lowe and Holm, 1988; Revill et al, 1976; Seymour, 1982; Wewers &

Lowe, 1990) and validity (Ahles et al, 1984; Downie et al, 1978; Folstein & Luria, 1973; Lowe & Holm, 1988; Luria, 1979; Price et al, 1983; Seymour, 1982; Wewers et al, 1989) of using the VAS to measure pain. Seymour (1982) found that the VAS was more sensitive to fine changes in pain as compared to both numerical and 4-point rating scales. When a VAS including pain as one of its four dimensions was compared to a Likert scale in measuring improvement in function, no statistically significant differences were found in measuring improvement between the two types of scales (Guyatt et al, 1987).

The McGill has been found to be valid and reliable for use with a variety of chronic pain conditions, including spinal cord injury (Loubser, Rintala, Fuhrer, & Castro, 1995), osteoarthritis (Summers, Haley, Reveille, & Alarcon, 1988), phantom limb pain, low back pain, and rheumatoid arthritis (Lankveld et al, 1993, Melzack, 1975). Respondents choose sensory, affective, and evaluative words that best describe their pain experience as well as completing a present pain intensity scale. Data obtained with 297 patients experiencing several kinds of pain indicate that this instrument is sensitive enough to detect differences among various methods used to relieve pain.

Assessment of Physical and Social Functioning

Although the McGill Pain Questionnaire is an effective, multifaceted measure of pain, it does not assess the effects of pain on physical and social functioning as aspects of quality of life. There are, however, several general measures of health status and quality of life that include subscales for extent and impact of pain on function that have been used in the assessment of chronic pain patients: Sickness Impact Profile (SIP; Bergner et al, 1976), Medical Outcomes Study Short Form Health Survey (SF-36; McHorney et al, 1993; Ware & Sherbourne, 1992), Duke Health Profile (17-item DUKE; Parkerson et al, 1991; and 63-item Duke-UNC; Parkerson et al, 1981), the Patient-Generated Index (PGI) of quality of life (Ruta et al, 1994).

The Sickness Impact Profile (SIP) has been used only occasionally with patients who have chronic pain and disability such as rheumatoid arthritis (Deyo et al, 1982); severe lower extremity fractures (Greenwald, 1987); head and back-leg pain (Follick et al, 1985; Pilowsky et al, 1982; Watt-Watson & Graydon, 1989), spinal cord injury (Lundqvist et al, and modified for head injury (Temkin et al, 1988), and it has been recommended as a valid indicator of the extent to which an individual's usual activities have been disrupted as a result of chronic pain as well as the specific areas which have incurred the greatest disruptions (Watt-Watson & Graydon, 1989). The 12 categories of activities assessed include several that can be affected by pain: sleep-rest, emotional behavior, home management, social interaction, work, and recreation-pastimes. However, the SIP will not be used for the proposed study due to its lengthiness at 136 items.

The 36 item Short Form from the Medical Outcomes Study (SF-36) (Tarlov, Ware, Greenfield, Nelson, Perrin, & Zubkoff, 1989) will be administered in the proposed studies as a global measure of health-related quality of life. The SF-36 has been tested nationally on 9385 patients, 54% of them with chronic conditions, including conditions usually associated with pain such as arthritis, back pain, emphysema, colitis, and angina (Stewart et al, 1989). Patients with chronic conditions showed greater decrements in functioning and well-being than those with no

chronic condition, though the extent varied greatly within conditions. Functional measures included physical, role (work, housework, school), mental health, health perceptions, and bodily pain. Although relative precision of long-form scales is generally better than that of the short-form scales, the short pain scale performed nearly as well as the long scale (McHorney et al, 1992), and the short-form measure of social functioning actually achieved greater precision than its long-form counterpart. The SF-20, an even shorter form, was found to be a reliable and valid measure of quality of life for patients with different headache diagnoses (Solomon et al, 1993). Length of measures for the proposed studies will be chosen carefully since shorter measures achieve less statistical power, and the studies using fewer than 150 subjects will only be able to detect large group differences.

The Pain-Generated Index (PGI) of quality of life (Ruta et al, 1994), developed and tested for reliability and validity in Scotland, demonstrated a high correlation with SF-36 scales measuring pain, social functioning, and role limitations attributable to physical problems, as well as with scores on a clinical back pain questionnaire. It offers the advantage of being patient-generated rather than using externally imposed questions and values in that respondents list the important activities that are affected by their condition in an open-ended fashion. The PGI will not be used in the proposed studies. The failure of individuals to complete the PGI correctly who had low levels of physical functioning, high levels of role limitations attributable to physical problems, and lower levels of education suggests that it may not be as valid for use with persons with physical disabilities. It is also better suited to assessing an individual's perceived quality of life in a clinical setting than to comparing quality of life measures across samples. The PGI's applicability is also limited by being tested only in patients with low back pain.

The West Haven-Yale Multidimensional Pain Inventory (WHYMPI; Kerns et al, 1985), grounded in the cognitive-behavioral approach, has proven to be a reliable and valid measure of pain's interference with activity, social support, pain severity, self-control, negative mood, response of significant others to communications of pain, and extent to which patients engage in common daily activities at home and away from home. The WHYMPI is relatively brief, consisting of 52 items in 12 scales. It has not been tested on primary disability populations, and the test sample of 120 subjects only included 22 females. The WHYMPI will be tested as part of the outcome assessment package for the proposed studies.

Reliability and validity of the Pain Disability Index (PDI; Pollard, 1974; Tait et al, 1988; Tait et al, 1990) were tested on 444 patients seen consecutively at a multi-disciplinary pain clinic, nearly half of them females but none with a primary disability. The data generally support its reliability and validity, except for lower test-retest reliability than expected over a two-month period. Seven items measure degree of disability related to family/home responsibilities, recreation, social activity, occupation, sexual behavior, self-care, and life-support activity. Its use of only one item to operationalize each category of disability may not enable sufficient precision to determine the effects of pain in a population that already has significant disability for nonpain-related reasons. Therefore, it will not be used in the proposed studies.

Other measures of effects of pain on functional status related to quality of life will not be used in the proposed studies because they are geared to a specific disorder. These include the

Arthritis Impact Measurement Scale (AIMS; Meenan, Gertman, & Mason, 1980), the National Institutes of Health Activity Record (ACTRE; Gerber & Furst, 1992), developed to measure outcome of teaching patients with rheumatoid arthritis energy conservation behaviors and requiring cumbersome daily logs (Gerber et al, 1987; Furst et al, 1987), and the Oswestry Disability Questionnaire (Fairbank et al, 1980), which is specific to low back pain.

The addition of detailed measures of functional impairment and handicap will be necessary to adequately discriminate pain-related from nonpain-related interference with daily activities. The proposed study will use the telephone version of the Functional Independence Measure (Fone FIM; Smith, Hamilton, & Granger, 1990) to assess physical disability. The Mobility, Occupation, and Social Integration scales of the Craig Handicap Assessment and Reporting Technique (CHART; Whitehead, Charlifue, Gerhart, Overholser, & Richardson, 1992) will be used to assess handicap.

The Fone FIM assesses the type and amount of assistance required to perform activities of daily living (Smith et al, 1990), or degree of disability, defined by the WHO as "any restriction or lack (resulting from an impairment) of ability to perform an activity in the manner or within the range considered normal for a human being" (World Health Organization, 1980, p. 47). An abundance of other instruments exist to assess physical functioning, as reviewed elsewhere (Alexander & Fuhrer, 1984; Brown, Diller, Fordyce, Jacobs, & Gordon, 1980; Granger, Albrecht, & Hamilton, 1979; Granger & Gresham, 1984; Granger, Hamilton, Keith, Zielezny, & Sherwin, 1986; Keith, 1984; Salkind, Beckwith, Nelson, & McGregor, 1982), the most commonly used including the modified Barthel Index (Granger et al, 1979), The Functional Assessment Inventory (Granger et al, 1986), and PULSES Moskowitz & McCann, 1957). The Fone FIM was chosen for the present study, however, because it selectively measures independence in performing the most critical activities needed for self-care, sphincter control, mobility, and locomotion in people with a wide variety of impairments. This instrument is easy to administer and interpret by health care providers, non-clinicians, families, and consumers alike, and can be taken in a variety of settings, from the hospital to an individual's home (Hamilton et al, 1987). Most other functional assessment scales are designed for use in a hospital setting. To enable self-report by the participants, the telephone version of the FIM will be used in the present study (Smith et al, 1990).

The CHART (Whiteneck et al, 1992) was selected to measure handicap because it is the only instrument that fully and exclusively measures handicap in the community, defined by WHO as the inability to fulfill expected social roles (World Health Organization, 1980, p. 183), instead of disability or physical functioning. Other measures of handicap are generally limited to a few items added to instruments that predominantly assess disability (Wagner, 1987), such as the Level of Rehabilitation Scale (LORS) (Carey & Pasovac, 1978), the Functional Life Scale (Sarno, Sarno, & Levita, 1973), and the Self-Observation and Reporting Technique (SORT) (Rintala, Uttermohlen, Buck, Hanover, Alexander, Norris-Baker, Stephens, Willems, Halstead, 1984). Test-retest, proxies, and independent raters have established the validity and reliability of CHART, and its effectiveness in assessing the extent of handicap or social disadvantage was demonstrated in a group of 342 persons with spinal cord injury (Whiteneck et al, 1992). These

findings support the CHART's capacity to assess the ability of people with a wide range of disabilities to fulfill roles of parenting, working, interacting with others, and managing one's own affairs.

Assessment of Psychological Functioning

Several studies suggest that psychologic variables strongly influence both pain perception and the degree of functional impairment experienced by persons with chronic pain (Bukberg et al, 1984; Haley & Dolce, 1986; McIvor et al, 1984; Melzack & Wall, 1982; Summers et al, 1988). Pain and anxiety may decrease pain tolerance and perpetuate a chronic cycle of pain and inactivity (Fordyce, 1976). Consequently, psychometric instruments such as the Minnesota Multiphasic Personality Inventory (MMPI; Dahlstrom & Welsh, 1960), Beck Depression Inventory (BDI; Beck et al, 1961) and State-Trait Anxiety Inventory (Spielberger et al, 1972) are widely used for the evaluation of chronic pain patients. There has been much criticism recently in the literature of applying psychometric instruments standardized with psychiatric patients to assessment of psychological functioning of persons with medical diagnoses. These instruments contain many somatic items that are common to both depression and chronic illness (Frank et al, 1991; Peck et al, 1989; Turk et al, 1987). Scores tend to be artificially elevated for depression, anxiety, hysteria, and hypochondriasis because these scales contain a large number of items about physical problems which may stem from the individual's medical condition or the pain itself. Studies have demonstrated that such scores return to normal after persons with chronic pain have their pain reduced significantly or eradicated (Roberts & Reinhardt, 1980). There may be no reliable way to determine whether elevated scores on the MMPI reflect 1) preexisting personality traits, 2) current pain, disability, their sequelae, and drug side effects, or 3) some combination of both. Therefore, the meaning of elevations for persons with medical problems often is unclear (Merskey et al, 1985; Watson, 1982; Brennan et al, 1986-87). Persons with disabilities may be misclassified as depressed (Callahan et al, 1991; Pincus et al, 1986) and inappropriately treated for depression. In a study of depression in rheumatoid arthritis, energy, psychomotor impairment, appetite, and sleep were not efficient predictors of major depressive disorder, but cognitive and affective symptoms such as guilt, suicidal ideation, and dysphoric mood were (Frank et al, 1991). Brennan and colleagues (1986-87) concluded that the predictive value of psychological tests stems less from the reflection of a psychological state or attitude regarding pain and more from their tendency to reflect ongoing level of pain, disability, and other pain sequelae. They endorse the trend toward using psychological assessment instruments standardized specifically on pain patients.

Therefore, in the current study, instruments assessing depression and anxiety will be pilot tested on individuals with post-polio and spinal cord injury to make sure that items related to physical problems that may result from the underlying disease process or functional impairment are not artificially elevating dysfunction scores. Instruments with fewer somatic items and more dysphoric mood items, such as the Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977) which has two somatic items, or Geriatric Depression Scale (GDS), which has been validated for use among younger populations as well as the elderly (Alden et al, 1989; Rule et al, 1989; Sheikh & Yesavage, 1986), or Hospital Anxiety and Depression Scale (HAD; Zigmond & Snaith, 1983) will be selected over the Beck Depression Inventory, in which one-

third of the items are somatic, Zung Depression Inventory (ZDI; Zung, 1965), or MMPI. Both the CES-D (Fuhrer et al, 1992; Loubser et al, 1995; Rintala et al, 1992; Rintala et al, 1994) and GDS (Katz & Yelin, 1993) have been used to assess depressive symptoms in persons with disabling conditions such as spinal cord injury and rheumatoid arthritis. The State-Trait Anxiety Inventory (STAI; Spielberger, Gorusch, & Lushene, 1970; Spielberger, Vagg, Barker, Donham, & Westberry, 1980), a well-validated and widely used anxiety assessment instrument, will be used to differentiate situational anxiety from more generalized anxiety.

Mood will be assessed using the Positive and Negative Affect Schedule (PANAS; Watson, Clark, & Tellegen, 1988). These two 10-item mood scales were selected because they are brief, easy to administer, demonstrate good reliability and validity, and have been used with disability populations.

The Life Satisfaction Index A (LSIA; Adams, 1969) will be used to assess life satisfaction. This instrument has been used with persons with spinal cord injury (Decker & Schulz, 1985; Loubser, et al, 1995; Schulz & Decker, 1985; Rintala, Young, Hart, Clearman, & Fuhrer, 1992). The 18-item LSIA measures zest for life; fortitude; congruence between desired and achieved goals; physical, psychological, and social self-concept; and mood tone. This instrument has acceptable internal consistency (Schulz & Decker, 1985) and concurrent validity with other measures of life satisfaction (Lohman, 1977).

People with chronic pain commonly complain of difficulty with concentration and memory, but little is known about the extent to which they interfere with daily activities. Memory difficulties in pain patients may be related to problems in the registration of information rather than its retrieval (Solso, 1979). Persons with chronic pain may be distracted by the continuous sensory input of nociceptive pain, producing difficulty in storing new information. Jamison and coworkers (1988) found that problems in concentration and memory were related to emotional distress, poor family support, and interference with daily activities in their study of 363 persons with chronic pain. In the proposed study, concentration and memory will be assessed from two items from the SCL-90 (Derogatis, 1975; Jamison, Rock, & Parris, 1988):"How much are you bothered by trouble concentrating?" and "How much are you bothered by trouble remembering things?", as well as by oral administration of the Digit-Span subtest of the WAIS-R (Wechsler, 1981), a five-minute repetition of series of numbers forward and backwards.

Assessment of Social Support

Social support will be assessed due to its negative correlation with depressive symptoms (Decker & Schulz, 1985; Kleinke, 1984, 1988; Kleinke et al, 1982; Schulz & Decker, 1985; Rintala, Young, Hart, Clearman, & Fuhrer, 1992) and direct, positive impact on functional status factors of pain, psychological disability, and physical disability (Weinberger et al, 1986;1990). Attention and encouragement are believed to decrease suffering, improve adaptation, increase adherence to self-care recommendations, assist in rehabilitating those with chronic diseases (Meichenbaum & Turk, 1987; Wallston et al, 1983; Wortman & Conway, 1985), and lessen

depression in persons with chronic pain (Brown, Wallston, & Nicassio, 1989; Manne & Zautra, 1989). Not all forms of social support are positive, however; in some situations, support may foster dependency or be viewed as unhelpful. Proponents of operant models of chronic pain suggest that positive attention from significant others to individuals' overt expressions of pain may inadvertently increase expressions of pain and increase the likelihood of disability (Turk et al, 1992). Other findings indicate that not all social support is perceived as positive; negative responses to pain increase affective distress (Turk et al, 1992), and problematic support may be viewed as non-supportive (Revenson et al, 1991). Turk and colleagues (1992) conclude that negative aspects of social interactions may be more predictive of emotional distress than positive support. The effects of social support on chronic pain in persons with disabilities will be examined in the current study to determine which forms are helpful and harmful in this particular population. The Interpersonal Support Evaluation List (ISEL; Cohen et al, 1986) will be used to assess social support in the proposed studies. When the ISEL was compared with two other instruments, a rating of individual support persons on 11 types of support and a global rating of the same types of support, the ISEL was the most highly correlated in the expected direction with measures of depressive symptomatology, perceived stress, life satisfaction, and self-assessed health in 84 men with spinal cord injury living in the community (Rintala, Hart, Fuhrer, 1994). These results in a primary disability population indicate that social support is highly correlated with psychological and physical well-being.

A form of social support that is vital to persons with severe physical disabilities to enable maintenance of health, functioning, and life itself is personal assistance services (PAS) with activities of daily living. Satisfaction with personal assistance will be assessed by administering the Personal Assistance Satisfaction Index (PASI), a 16-item instrument developed by one of the principal investigators in the proposed study (Nosek & Fuhrer, 1992). This instrument is the only known comprehensive measure of satisfaction with the availability, cost, control, and quality of personal assistance. Twelve leaders of the independent living movement who use personal assistance services themselves, as well as a sample of 88 consumers who use these services, were involved in the validity testing of the PASI. It has proven to be a reliable (Cronbach alpha = .91) measure of satisfaction with personal assistance in people with a variety of physical disabilities.

Assessment of Meaning of Life and Spirituality

Meaning in life, or spirituality, is not adequately measured by quality of life scales (Warner & Williams, 1987). Therefore, the Meaning in Life (ML) Scale and Uniscale will be used to assess sense of purpose, beliefs, and faith in the proposed study. This instrument proved to be valid and reliable with patients having cancer, severe trauma, myocardial infarction, and end stage renal disease, and correlated with subjective well-being, social support, pain, activities of daily living, quality of life, and social desirability (Warner & Williams, 1987). It has not yet been tested with disability populations living independently in the community.

Gender Differences

Since many studies of chronic pain have involved primarily male patients or have ignored the possibility of gender effects, little is known about whether chronic pain outcomes are

different for women. In Flor's study (1989), spouse support was associated with reporting more severe pain only for married male patients. In Turk's (1992) sample with 57% females, no gender-related differences were found in the effects of social support on pain behavior. Most gender-related studies have been done with experimental acute pain only. Several studies have demonstrated that females report lower pain thresholds and lower pain tolerance to a variety of experimentally applied noxious stimuli compared to male subjects (Arendt-Nielsen & Bjerring, 1988; Buchanan & Midgley, 1987; Feine et al, 1991; Maixner & Humphrey, 1993; Otto & Dougher, 1985; Rollman & Harris, 1987), possibly due to the finding that in response to noxious stimuli, blood pressure in males increases, which decreases pain perception, but stays the same or decreases in females (Maixner & Humphrey, 1993). Others report no differences in pain threshold and tolerance (Harkins & Chapman, 1977; Neri & Agazzani, 1984; Lander et al, 1989; 1990), but that perceived self-efficacy and control exerts a greater pain modulatory influence on females than males (Fillingim et al, in press). However, the extent to which gender affects degree of functional impairment and disability associated with chronic pain is unknown. In a study of pain-related disability assessed using the PDI, women reported significantly less disability than men (Tait et al, 1990). Toomey and colleagues (1982) found that long-term outcomes following treatment of low-back pain were better for women than for men (Toomey et al, 1982). Tait and coworkers (1990) concluded that women may accommodate better to chronic pain than men do. The proposed study will elucidate the interactive effects of gender and psychological factors on pain and functional outcomes.

PRELIMINARY STUDIES

Nosek and Rintala, the principal investigators involved in assessing chronic pain outcomes, have extensive experience assessing pain and applying most of the outcome measures to be used in the proposed studies to persons with physical disabilities, such as spinal cord injury, living independently in the community. The investigators have assessed social support (Fuhrer, Rintala, Hart, Clearman, & Young, 1992; Nosek, 1993a; 1993b; Nosek, Fuhrer, & Potter, 1995; Rintala, Young, Hart, Clearman, Fuhrer, 1992; Rintala, Young, Hart, & Fuhrer, 1994), life satisfaction using the LSI-A (Fuhrer et al, 1992; Loubser, Rintala, Fuhrer, & Castro, 1995; Nosek, Fuhrer, & Potter, 1995; Rintala et al, 1992), depression using the CES-D (Fuhrer et al, 1992; Loubser et al, 1995; Rintala et al, 1992; Rintala et al, 1994), physical functioning using the Fone FIM (Fuhrer et al, 1992; Loubser et al, 1995; Nosek et al, 1995; Rintala et al, 1994), mobility, social, and occupational handicap using the CHART (Fuhrer et al, 1992; Loubser et al, 1995; Nosek et al, 1995; Rintala et al, 1994), and pain (Rintala, Hart, & Fuhrer, 1991) using the McGill Pain Questionnaire (Loubser et al, 1995).

Rintala and colleagues have conducted two studies assessing pain in persons with spinal cord injury (Loubser et al, 1995; Rintala et al, 1991). Prevalence of pain was assessed by telephone in a cohort of 640 persons with spinal cord injury. Results indicated that 53% reported experiencing frequent pain, and 31% reported pain severe enough to interfere with daily activities. Bivariate analyses revealed that frequent pain was reported by significantly more females (69%) than males (50%) and by more paraplegics (60%) than quadriplegics (47%). Those injured by violence reported pain more frequently (66%) than did those injured by falls (52%), motor vehicle accidents (51%), or sports (42%). Those reporting frequent pain were

older (40 years) on average than those without pain (36 years). Those with pain had a shorter duration of injury (9 years) than those without pain (11 years). Ethnicity was not related to the prevalence of reports of frequent pain. Stepwise logistic regression revealed that gender, age, duration of injury, and cause of injury each accounted for unique portions of variance in the reports of frequent pain. Neither level of injury nor ethnicity added significantly to the equation and there were no first-order interactions.

Loubser, Rintala, and coworkers did the first study to quantitate prevalence and characterize the sensory, affective, and evaluative qualities of chronic pain in a community-based group of 77 volunteers with spinal cord injury using a comprehensive pain assessment methodology. Pain symptoms were first characterized during an interview and physical examination. Pain was regarded as chronic if present for more than six months. Altered sensations were differentiated from pain symptoms and not included in the pain assessment. Evaluations of pain quality and intensity were performed using the McGill Pain Questionnaire (MPQ), Sternbach Pain Intensity Scale, and Zung Pain and Distress (PAD) Index. The MPQ was repeated for each pain site reported by each participant to compare the severity of various pain states. These data were then correlated (Pearson coefficient) with degree and completeness of paralytic impairment (Frankel grade, motor index) and multiple psychosocial and quality of life indicators including FIM, CHART, demographics, depression scale, life satisfaction scale, and self-assessed health. Subjects with pain were compared to subjects without pain using the unpaired Student's t test and ANOVA (significance $p<.05$). Of the 77 subjects, 58 reported chronic pain (75%), with 41 (53%) reporting one pain site and 17 (22%) more than one site. Periodic, intermittent pain (54%) was more common than continuous pain (29%). The Zung PAD index was significantly higher in subjects with pain compared to subjects without pain. The SPI rate for the day of the study was similar to that reported for the week before the study. Subjects reporting pain had a pain rating index of 14.3 sensory, 1.8 affective, 1.8 evaluative, and 4.3 supplementary; the number of pain descriptors chosen was 9.6. Correlation with psychosocial indicators revealed that subjects with chronic pain had worse self-assessed health ratings, higher perceived stress, less satisfaction with social support networks, and higher depression scores than subjects without pain. They concluded that chronic pain reduces quality of life among persons with spinal cord injury.

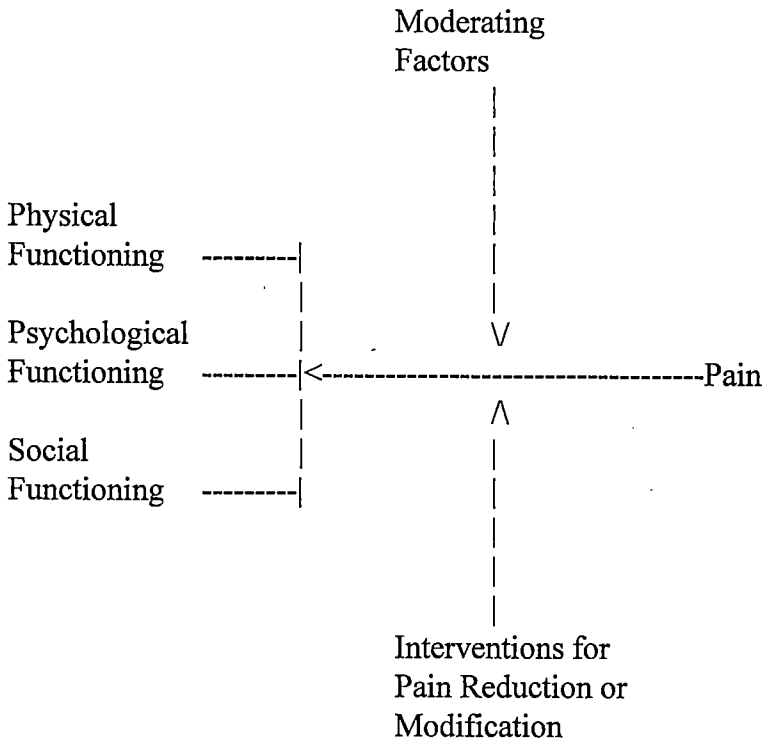
RESEARCH DESIGN AND METHODS

The investigation of chronic pain in the context of long-term physical disability requires considerably more than mere assessment of intensity and quality of pain in response to specific treatment modalities. First, very little is known about the nature of chronic pain in physical disability or the impact chronic pain has on the lives of persons with physical disabilities. Although a body of literature exists on chronic pain associated with disabilities resulting from trauma, very few studies have investigated chronic pain experienced by people with disabilities that result from diseases, birth defects, or degenerative conditions. Second, findings from studies conducted on populations without primary physical disabilities are not necessarily applicable to the population of people with disabilities. Physiologic responses to pain may be significantly altered by the pathogenesis of the impairment; the perception of pain may also be altered. Third, instruments used to assess the intensity and quality of pain or the effect of pain on physical,

psychological, and social functioning many be insensitive or invalid for persons with disabilities. Many standardized tests used in pain studies contain items that assess the ability to work or conduct self care tasks, aspects of functioning that this population would be unable to perform for disability reasons alone, whether or not they had chronic pain. Assessments of psychological functioning often contain somatic items that, for this population, reflect the disability and not necessarily an underlying psychological deficit. Fourth, based on past research conducted by the principal investigators, it is likely that there are a number of moderating factors that significantly influence the relationship between pain and functioning, and effectiveness of interventions for the reduction or modification of pain.

In light of these considerations, we propose an analytic paradigm that addresses the relationship between pain and physical, psychological, and social functioning as moderated by a variety of contextual factors and interventions for pain reduction or modification. The element of physical functioning represents the category of "disability" in the World Health Organization International Classification of Impairment, Disability, and Handicap (World Health Organization, 1980). The category of "handicap" is represented by psychological and social functioning. A graphic representation of our paradigm can be seen in Figure 1.

FIGURE 1



Instruments

Pain. Two dimensions of pain will be assessed--intensity and quality. The single-item Visual Analogue Scale (Wewers & Lowe, 1990), is a quick and easy means for assessing intensity of pain and can be completed by participants on a daily basis for interventions that are expected to have an effect of short duration. The McGill Pain Questionnaire (Melzack, 1975) contains 22 items related to the qualitative characteristics of pain, using adjective checklists, such as dull, stabbing, burning. These two measures can be completed in less than 10 minutes.

Physical Functioning. This domain primarily includes functioning at the level of activities of daily living, such as eating, toileting, bathing, dressing, transferring, and moving about. We will assess this type of functioning using 13 of the scales in the telephone version of the Functional Independence Measure (Fone FIM; Smith, Hamilton, & Granger, 1990); 10 of the 36 items in the Short Form from the Medical Outcomes Study (SF-36) (Tarlov, Ware, Greenfield, Nelson, Perrin, & Zubkoff, 1989) that assess the ability to walk, climb stairs, and lift objects; and the 7-item Mobility Scale from the Craig Handicap Assessment and Report Technique (CHART, Whiteneck et al, 1992). Completion of these 33 items will take

approximately 30 minutes.

Psychological Functioning. Constructs we consider important in the assessment of psychological functioning include: life satisfaction (The Life Satisfaction Index A, LSIA; Adams, 1969, 18 items); depression (Center for Epidemiologic Studies Depression Scale, CES-D, Radloff, 1977, 20 items); anxiety (State-Trait Anxiety Inventory, Spielberger et al, 1972); mood (Positive and Negative Affect Schedule, PANAS; Watson, Clark, & Tellegen, 1988, 20 items); and cognition, in terms of concentration and short term memory (2 items from the SCL-90 Derogatis, 1975; Jamison, Rock, & Parris, 1988; and the Digit-Span subtest of the WAIS-R, Wechsler, 1981). In addition, we will use five items from the West Haven-Yale Multidimensional Pain Inventory (WHYMPI; Kerns et al, 1985) that specifically assess the impact of pain on psychological functioning. These measures will take approximately 25 minutes to complete.

Social Functioning. Functioning in terms of instrumental activities of daily living, role fulfillment, social activities, and productivity will be assessed by 10 items from the SF-36, 44 items from the West Haven-Yale Multidimensional Pain Inventory, and the CHART Occupation Scale (7 items) and Social Integration Scale (6 items). This set will take approximately 10 minutes to complete.

Moderating Variables. Based on our previous research on psychological and social aspects of community living with long-term physical disability, we anticipate four contextual factors will moderate the relationship between pain and functioning: social support, in terms of family and friends (Interpersonal Support Evaluation List, ISEL; Cohen et al, 1986, 55 items) and individuals who provide paid and unpaid personal assistance (Personal Assistance Satisfaction Index, PASI, Nosek & Fuhrer, 1992); spirituality (Meaning in Life Scale and Uniscale, Warner & Williams, 1987); access to the environment (using 2 items developed for previous studies, assessing unmet needs for equipment and home modifications), and demographics, including age, gender, race, marital status, income, and education. These items will take approximately 30 minutes to complete.

Sample. Participants for this outcome study will include all of the participants in the four projects of this proposal. The outcomes core will ensure that standard sets of measures are used for all of the projects to the extent possible and create a data set incorporating the data on the aforementioned measures for all of the projects.

Implementation. The above listed measures will be administered to each participant in the four studies of this program project proposal according to a schedule specially designed for each study. Hereafter, these will be referred to as the Neurostimulation Study (led by Dr. Simpson), the Magnetic Study (led by Dr. Hazelwood), the THC Study (led by Dr. Strayer), and the Pain Clinic Study (led by Drs. Grabois and Strayer).

Following initial selection, each participant will be contacted via telephone or in the clinic, and the purpose of the study will be explained, as will the nature of the information to be requested from each participant and each participant's right to decline to participate in the study

without penalty. Assurances of confidentiality will also be provided, and each participant will be informed of the fee provided to those who agree to participate in the data collection activity. A time and place will be scheduled for administration of the survey instrument by a trained interviewer. The instrument may be completed either by paper and pencil, in person, or over the telephone with a trained interviewer. Those participants involved in studies that require daily completion of the Visual Analog Scale will be given diaries with copies of the Scale for each day, plus a pre-addressed stamped envelop for returning it. Participants will be encouraged to complete the survey instruments during their clinic visits to maximize effective use of their time. For those who prefer oral administration of the instrument, data collection interviews will be scheduled at times convenient to the study participants. They will be given a number of options for locations in which interviews may be conducted, including the participant's home, the clinical site for the study in which they are participating, the office of the Center for Research on Women with Disabilities, a community center, or other location in the community agreeable to the participant and the interviewer. Accommodations--such as administration of the instrument in Spanish, use of a sign language interpreter, or accessible transportation to the interview site--will also be identified at the time an interview is scheduled and appropriate arrangements will be made in advance. Also, at the time that the interview is scheduled, each participant will be encouraged to ask questions about the study, his or her role in it, and the use of information that will be generated through the study. During the initial phone call, the inclusion and exclusion will be verified. Those not meeting the inclusion criteria will be dropped from further consideration.

Instrument Development. The instrument to be used in this study will involve a comprehensive questionnaire to be administered to participants by trained interviewers during interview sessions that are expected to take up to two hours for completion. The scope of topics to be covered in these interviews was enumerated above. It is anticipated that approximately 300 items will be included in the instrument.

Although core staff are familiar with each of the measures to be included in the study instrument, the compilation of all the measures will require some refinement. A draft of the instrument will be pilot tested on 10 pain clinic participants. At the end of survey administration, each pilot participant will be asked to provide feedback concerning the clarity of survey items, the sequencing of survey questions, any items that might have been difficult to understand, and any recommendations as to how the survey might be altered to improve understanding and ease of completion. Based on the results of the field tests, a version of the instrument will be prepared for use during data collection activities to be conducted throughout the five years of the project.

Training of Data Collection Staff. Once the instrument has been finalized, at least four project staff will be trained in its use with individuals in the target populations, three within the staff of the clinical studies and one within the core project staff. The core project staff person will serve as the senior interviewer and supervisor of the other three. Initial training in the use of the instrument in conducting interviews will involve use of other project staff or other Baylor faculty or staff volunteers. However, before an interviewer is assigned to interview any selected study participants, he or she will have completed six to ten interviews with selected volunteers who are unfamiliar with the research topics, with at least four of those interviews having been

observed by the principal investigator or another senior project investigator. During these practice sessions each interviewer will be assessed with regard to adherence to the interview protocol, ability to interpret and record responses accurately, skills in managing unexpected questions or diversions from the protocol, and comfort with the content and sequencing of the interview format. Each interviewer will have been determined to be proficient in using the interview protocol prior to being assigned interviews with participants selected for the study. The skills and preparedness of the interviewers are critical to the success of this project, and adequate time has been set aside to assure that interviewers are prepared adequately for these roles.

Data Collection. The schedule for data collection will be specially designed for each clinical study. The nature of the intervention and the anticipated duration of its effect have been used to determine strategic time points for outcome assessment. Baseline data on all participants will be collected, pooled, and used to test hypotheses related to the relationship between chronic pain and physical, psychological, and social functioning in persons with long-term physical disability. Data collected after the introduction of a pain reduction intervention or placebo will be treated separately for each clinical study.

The Neurostimulation Study is designed to introduce a pain reduction agent for only a short period of time within the hospital setting; therefore, no long-term assessment of functional outcomes can be obtained. The Visual Analog Scale and McGill Pain Questionnaire will be the most valuable sources of information. The schedule of administration of outcome measures will be as follows:

Neurostimulation Study			
	Pre-test	Daily, for 5 days	5th Day
Pain measures	X	VAS only	X
Physical functioning measures	X		
Psychological functioning measures	X		PANAS only
Social functioning measures	X		
Moderating variables	X		

The Magnetic Study involves an intervention of short duration, but a possible effect lasting anywhere from a few hours to two weeks. Determining the most strategic timing for outcome assessment is problematic. We have designed the following data collection schedule to allow for the acquisition of minimal pain-related data on a continuous basis for one month, and

data on physical and psychological outcomes three days after the intervention. Full data on functioning will be collected only before intervention. The duration of impact from this intervention is not expected to be sufficiently long to produce change in social functioning.

Magnetic Study					
	Pre-test	Immediate Post-intervention Test	3rd Day	Daily, for 30 Days	31st Day
Pain measures	X	X	X	VAS only	X
Physical functioning measures	X		X		X
Psychological functioning measures	X		X		X
Social functioning measures	X				
Moderating variables	X				

The first phase of the THC Study will take place continuously over a period of nine weeks. As in the previous study, it is impossible to predict at this point the duration of the effect or when the effect of the drug will reach its maximum. To allow for some degree of continuous monitoring, we will ask each participant to complete the Visual Analog Scale on a daily basis. The full battery of measures will be administered before intervention, after four weeks, at the beginning of week six, and at the end of nine weeks. During the second phase of the THC study, some core measures will be obtained once a month for four months. Others will be obtained only at the end of the one and four months.

THC Study - Phase 1					
	Pre-test	Daily for 9 weeks	End of Week 4	Beginning of Week 6	End of Week 9
Pain measures	X	VAS only	X	X	X
Physical functioning measures	X		X	X	X
Psychological functioning measures	X		X	X	X
Social functioning measures	X		X		
Moderating variables	X		X		

THC Study - Phase 2				
	Month 1	Month 2	Month 3	Month 4
Pain Measures	X	X	X	X
Physical functioning measures	X	X	X	X
Psychological functioning measures	X	X	X	X
Social functioning measures	X			X
Moderating variables	X			X

The Pain Clinic Study does not propose a standard intervention for all participants; indeed, its strength is its individualized, multi-disciplinary approach that seeks to offer whatever intervention modalities offer the greatest possibility for benefit to the participant.
There will also be no standard for the length of time each participant will be involved in the clinic. Some may attend one clinic session, receive a prescription that effectively reduces their pain, return for one follow up visit, and never need to be seen again. Others may require many

clinic visits and multiple interventions before effectiveness is obtained. To accommodate this level of variation, outcome assessment will be conducted at the recommendation of the attending physician. At a minimum, the full battery of measures will be administered before treatment and after three months. Measures of pain, physical functioning, and psychological functioning will have one interim administration at the recommendation of the physician based on the anticipated point of maximum effectiveness for each intervention; for example, six weeks for Elavil, two weeks for TENS. For participants receiving multiple sequential interventions, this cycle of outcome assessment may be repeated for up to one year.

Pain Clinic Study			
	Pre-test	Post-intervention (at physician's recommendation)	90th Day
Pain measures	X	X	X
Physical functioning measures	X	X	X
Psychological functioning measures	X	X	X
Social functioning measures	X		X
Moderating variables	X		X

Data Management Including Quality Control Procedures. The collection and management of data will be closely supervised by the database manager. The instrument will be designed to be pre-coded to the extent possible. Prior to data entry the forms will each be checked for completeness accuracy, and consistency. Records will be kept by the interviewers of problems encountered so that retraining can be initiated as necessary.

The data entry program will be designed to be user friendly with screens that look like the survey instrument. The program will have built in error and consistency checks. The data entry system will be pilot tested prior to use and will be used to train the data entry personnel. There will be a detailed but clear data entry manual that will be used during the training of the data entry personnel and be available at all times for reference. The primary platform for the data base will be Paradox 5.0 for Windows.

There will be double entry of the data from each completed questionnaire to ensure accuracy of the data. Areas of disagreement will be checked against the raw data and corrected. A record will be kept of the accuracy of the data entry personnel so that retraining can be

initiated if necessary. There will be a logical system in place for tracking changes to the data. Computer hard drives are backed up weekly using a Colorado Tape Backup (Q1C-80) system. Daily back-up of newly entered data will be done on floppy disks. Copies of data tapes and disks are kept off site in the event of fire or flood.

Confidentiality of Data. Confidentiality will be maintained at all times by using subject numbers on all questionnaires and forms, by timely entry of data into computer files, and by storing data collection forms with identifying information in locked file cabinets. The data management system will contain a system of passwords and the personal computer on which the information is stored is accessible only to members of the research staff. The backup tapes and floppies will be kept in a locked cabinet when not in use.

Data Analysis. The proposed study uses a pretest / posttest control group design to evaluate the effectiveness of four pain reduction interventions. Subjects with disabilities and matched controls will participate in the four clinical trials for this program project. The study participants will be selected based on criteria established by each project and will be randomly assigned to the subject or control groups.

The effectiveness of pain reduction interventions will be assessed quantitatively using study participant pain self evaluation and completion of several assessment instruments. The impact of pain reduction will be assessed using a variety of measures of physical, psychological, and social functioning.

Data will be analyzed with statistical software including Minitab 10.0 and SAS 6.10 for Windows. The analytic plan for testing each of the hypotheses is as follows.

H_1: Variables related to demographics, social support, spirituality, and environmental accessibility significantly moderate **the relationship** between pain and level of physical, psychological, and social functioning among people with long-term physical disabilities.

The data to be use to test Hypothesis 1 will consist of baseline measures across all four clinical studies. The data will be analysed at the end of each year of the study. The first task will be to determine the bivariate relationship between each pain measure and the outcome measures of physical, psychological, and social functioning will be assessed. Next, a series of multiple regression analyses will be performed. Each outcome variable will be the dependent measure in separate analyses. The independent variables will be the two measures of pain (i.e., VAS and McGill). Demographic variables and measures of social support, spirituality, and environmental accessibilty, will be entered first as control (modertor) variables, followed by the measures of pain. If the hypothesis is supported, the partial correlation between the pain measure and the outcome (dependent) measure should be significantly different from the bivariate relationship.

H_2: Experimental pain reduction intervention is effective in reducing or modifying chronic pain among people with long-term physical disabilities.

To test Hypothesis 2, the data from each of the four clinical studies will be analyzed separately. For each of the studies with two randomly assigned groups (i.e., experimental vs. control for the THC and magnet studies; periodic or random stimulus for the neurostimulation study), a series of two-way repeated measures analyses of variance (ANOVA) will be conducted. The dependent variables in separate analyses will be the two measures of pain (i.e., VAS, McGill). The independent variables will be group assignment and the time of measurement (i.e., before intervention (Time 0) and each subsequent time of measurement (Time 1....Time X)). For the Pain Clinic study, in which there will be no control or comparison group, the data will be analyzed using a one-way repeated measures ANOVA. The dependent variables will be the two measures of pain and the independent variable will be time of measurement. Post-hoc pair-wise Bonferroni analyses will also be done to determine differences between pairs of measurements thereby assessing nonlinear patterns.

H_3: Reduction or modification in chronic pain is significantly related to improvements in physical, psychological, and social functioning among people with long-term physical disabilities.

To test Hypothesis 3, the data from each of the four clinical studies will be analyzed separately. The data will be analysed at the end of each year of the study. The relationship between the amount of change in each outcome variable (physical, psychological, and social functioning) and the amount of change in the two measures of pain between two time periods (e.g., four months in the long-term phase) will be assessed using multiple regression analyses. The dependent measure will be the outcome variable at "Time 2" and the independent variable will be one of the pain measures at "Time 2" but controlling for the levels of the outcome measure and the pain measure at "Time 1" by entering them into the equation first.. If the hypothesis is supported, the contribution of the "Time 2" pain measure to explained variance will be significant and in the expected direction.

H_4: Variables related to demographics, social support, spirituality, and environmental accessibility significantly moderate the **effectiveness of interventions** on reducing or modifying pain and increasing level of physical, psychological, and social functioning among people with long-term physical disabilities.

To test Hypothesis 4, the data from each of the four clinical studies will be analyzed separately. The data will be analysed at the end of each year of the study. A series of multiple regression analyses will be performed. The change in each outcome variable will be the dependent measure in separate analyses. The independent variables will be change in the two measures of pain (i.e., VAS and McGill). Demographic variables and measures of social support, spirituality, and environmental accessibilty, will be entered first as control (modertor) variables, followed by the measures of pain. If the hypothesis is supported, the partial correlation between the pain measure and the outcome (dependent) measure should be significantly different from the bivariate relationship assessed in Hypothesis 3.

Use of Results from Data Analyses.

It is important that innovative treatments for chronic pain in individuals with primary disabilities be evaluated because the current methods are insufficient to alleviate the pain for substantial numbers of persons with disabilities. However, simple relief from pain is insufficient as an solitary outcome measure. We need to know whether relief of the pain or moderating the pain in some way will have a positive impact on the quality of life of the individual. It is also important that we understand the other variables that may impact on the intensity and quality of pain so that other appropriate interventions can be implemented (e.g., improve social support). Finally it is important to know, for any given intervention, the factors that predict who is likely to benefit from the intervention and who is not. The information gained from the individual projects and from the combined data set across all projects will allow clinicians to prescribe appropriate interventions. It will also suggest future research priorities relative to chronic pain in individuals with primary physical disabilities.

Dissemination of the project outcomes will be handled using a variety of approaches. First, a series of manuscripts will be prepared for submission to appropriate professional journals, such as *Pain*, *Archives of Physical Medicine and Rehabilitation*, *Health Psychology*, and the *American Journal of Public Health*. As one would anticipate, these manuscripts will focus on research design and methods, as well as on statistical analyses and interpretation of results. It is expected that one manuscript will be prepared for submission early in the second project year. At least two manuscripts are expected to be produced during year three, and at least four manuscripts are expected to be generated from project results developed during the final project year. Similarly, submission of abstracts, posters, or manuscripts for presentations at appropriate professional meetings (e.g., American Public Health Association annual meeting, meeting of the American Congress of Rehabilitation Medicine) will occur routinely over the course of the project. It is expected that submissions for at least two presentations per year will be scheduled during years one through three, with at least three submissions in year four. As with journal articles, these presentations with focus on research design, methods, and outcomes and will be presented in formats appropriate to professional audiences.

In addition to dissemination to professional audiences using traditional methods, an earnest effort will be made to provide useful information to participants with and without disabilities who might benefit from the findings of this study. This will be addressed through activities that include preparing feature articles for consumer-oriented journals and newsletters, such as *Mainstream* and *The Disability Rag*. The intent of these efforts will be to provide important information in plain and understandable English for people who may have limited understanding of research and medical terminology.

In addition to published information targeted to consumer groups, efforts will be made to use other avenues for addressing the information needs of health care consumers. Along these lines, existing linkages with some 400 independent living centers, community-based service organizations operated by and for people with disabilities will be exploited. In order to heighten awareness of the pain reduction treatment options available to persons with disabilities, a series of brief fact sheets be prepared and distributed to centers for local duplicating and dissemination

to consumers of center services. These face sheets will provide practical hints for dealing with pain and will contain a contact number for additional information on pain treatment programs. Also, an abstract will be submitted each year for a presentation at the annual meeting of the National Council on Independent Living (NCIL). Recent attendance at NCIL conferences has exceeded 500 individuals per year, the overwhelming majority of whom are people with disabilities. This conference provides an ideal forum at which to present practical research findings to individuals who work in community-based settings serving people with a range of disabilities.

Lastly, efforts will be made to use current technology more effectively to address the information needs of people with disabilities. Individuals increasingly have access to computer technology and computer networks that can be accessed through Internet, as well as through specialized computer networks, such as DIMENET, national computer network serving people with disabilities that is accessible to people with physical, sensory, cognitive, and psychiatric disabilities. DIMENET and other electronic networking resources can be used to provide information to individuals in a variety of settings at relatively low cost. A major emphasis of the proposed project will be on more effective use of emerging technology in addressing the information needs of various audiences with diverse needs.

In summary, dissemination efforts are designed to assure that study results are provided not only to other researchers and clinicians, but also to other service providers, as well as to people with disabilities who may have limited access to research information through traditional channels. Project staffs' extensive contacts with both research/clinical organizations and consumer/advocacy organizations increases significantly the likelihood that such dissemination efforts will be successful.

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