MENOPAUSE AND MOOD DISORDERS

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OBJECTIVES

1. Identify the various mood disorders that increase in incidence during menopause

2. Describe the hormonal changes, life stressors, social conditions and preexisting tendencies toward mood disorders during menopause

3. Describe the treatment with antidepressants, hormonal replacement therapy, sleep medications, schizophrenia, panic disorder, OCD, bipolar disorder, and quality of life issues

DEFINITIONS

Menopause: permanent and last cycle of menstruation and loss of ovarian follicle development, when 12 cycles are missed

Perimenopause: onset of irregular cycles

- Menstrual irregularities, prolonged and heavy bleeding mixed with amenorrhea
- Decreased fertility
- Vasomotor symptoms
- Insomnia

Post-menopause

MOOD DISORDERS DURING MENOPAUSE

- Depression: 20%
- Sleep disorder: 40-50%
- Schizophrenia
- Panic disorder
- OCD
- Bipolar disorder

DEPRESSION

- Increased risk during perimenopause, decreased post menopause
- Strongest predictor was prior history of depression, along with fluctuating hormone levels
- Harvard study of women ages 36-44, twice the risk of depression in women not transitioning
- Hormones: testosterone loss shows increased risk of symptoms

ETIOLOGY

Hormonal changes

Life stressors

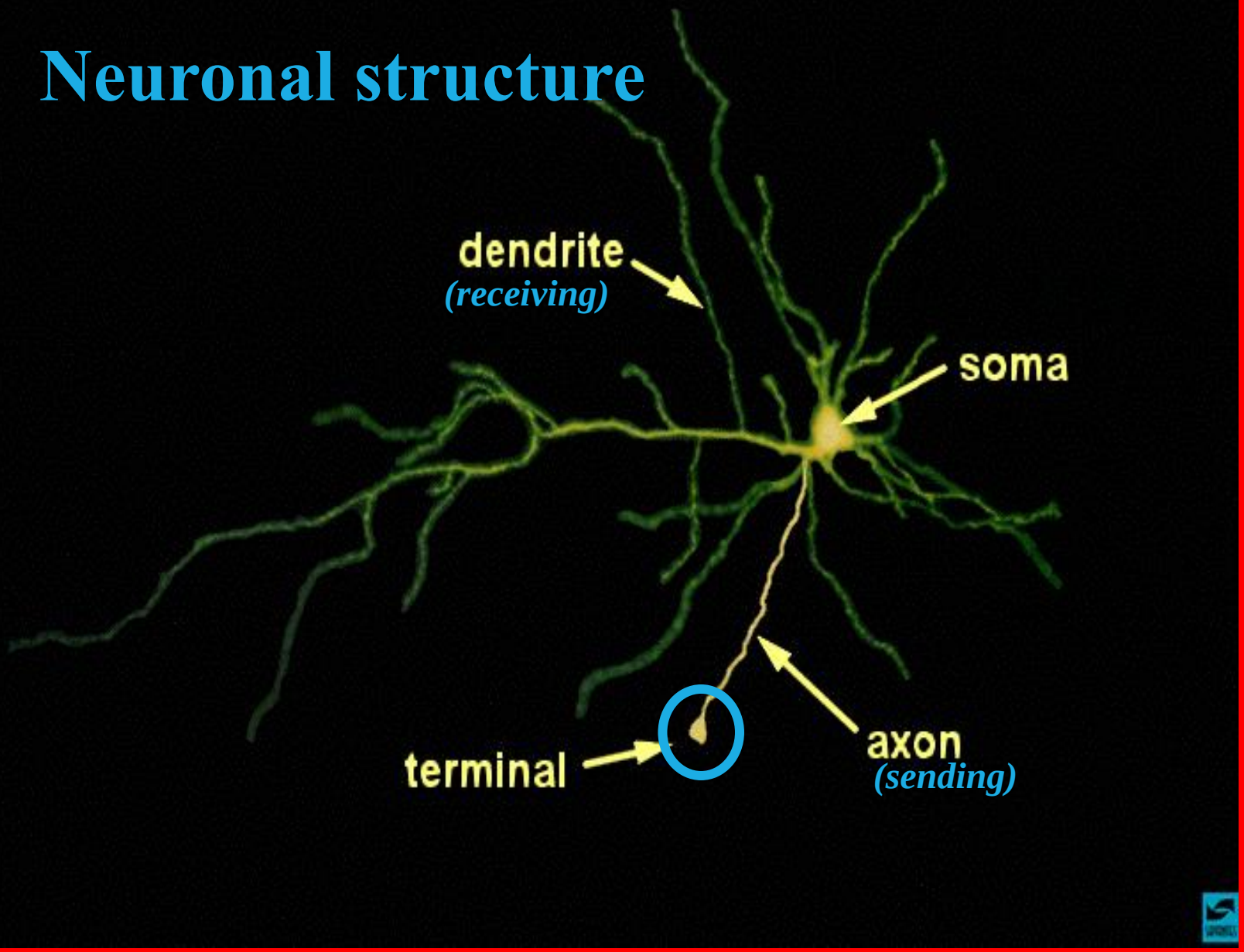
Psychological or social conditions

Pre-existing tendency toward depression

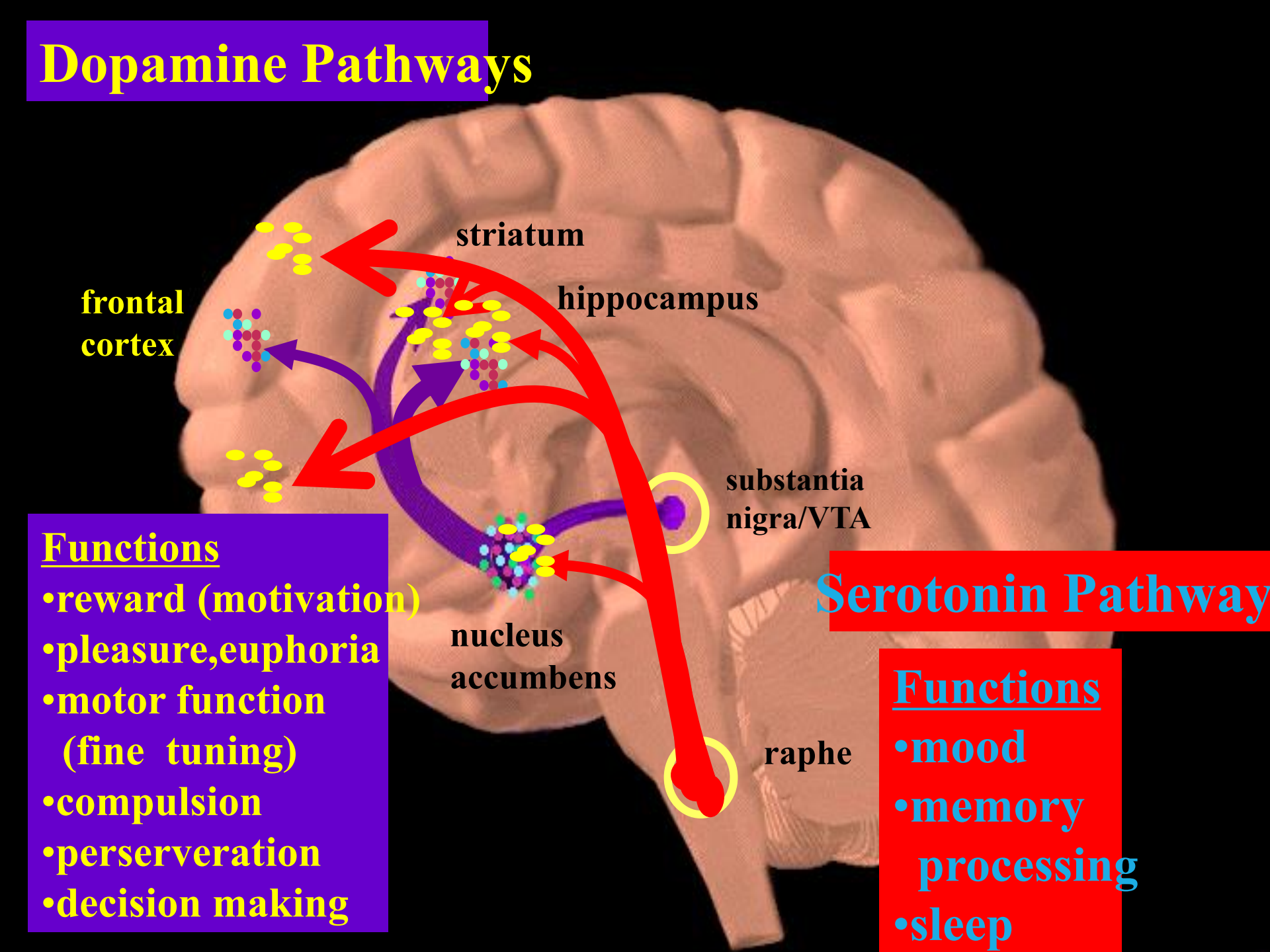
PATHOPHYSIOLOGY

- Depression due to fluctuating and declining estrogen levels
- Steroid hormones (estrogen) stimulate synthesis of neurotransmitters, work at receptor sites, influence membrane permeability
- Estrogen increases 5HT and NE receptor stimulation and decreases monoamine oxidase
- Increases serotonin synthesis, up regulates 5HT1 receptors and downregulates 5HT2 receptors
- Estrogen increases NE by decreasing reuptake and degredation

Neuronal structure



Dopamine Pathways



Functions

- reward (motivation)
- pleasure,euphoria
- motor function (fine tuning)
- compulsion
- perserveration
- decision making

Serotonin Pathway

Functions

- mood
- memory processing
- sleep

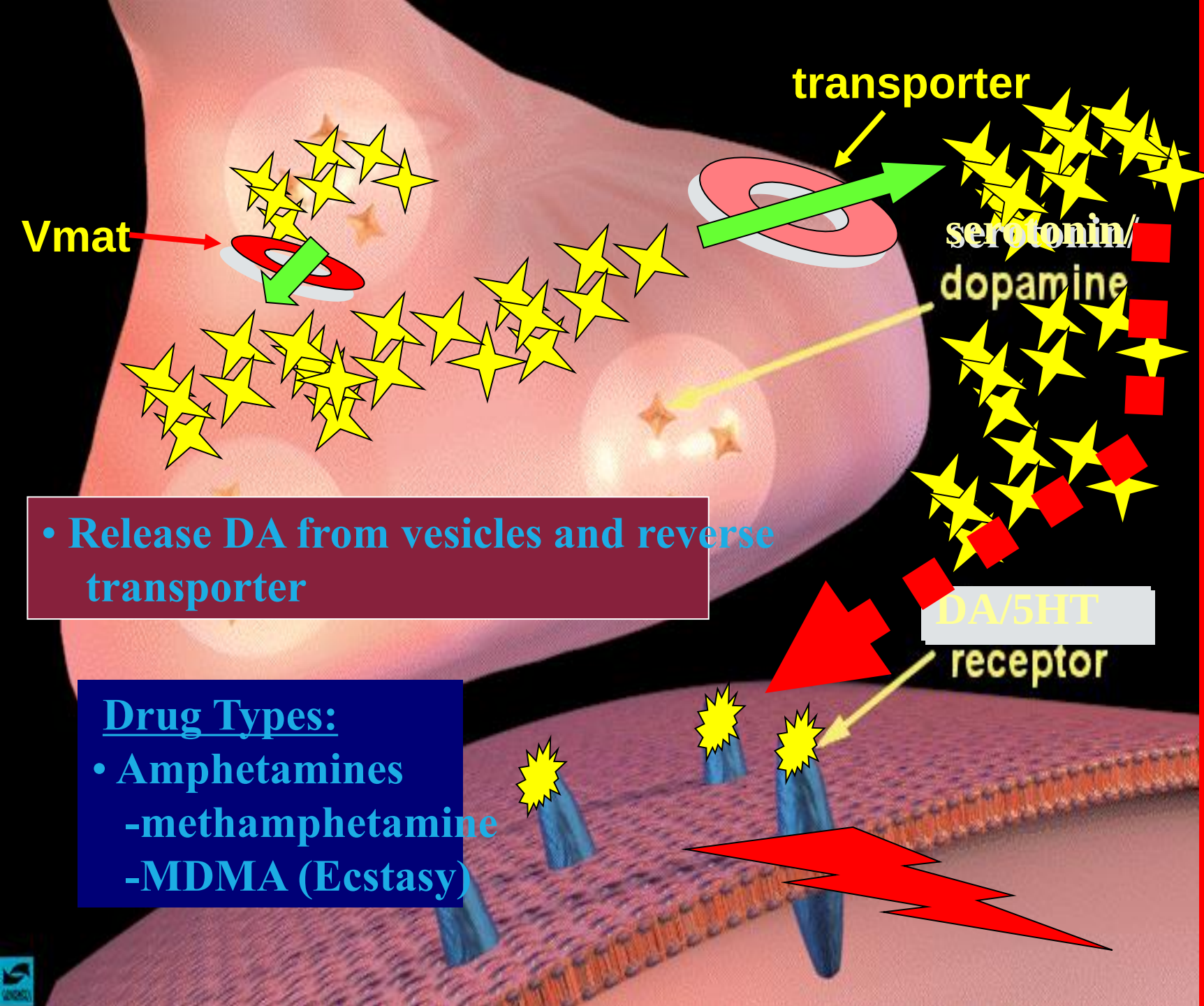
Serotonin: problems with serotonin are associated with depressed mood, anxiety, insomnia, OCD, SAD, and violence

5HT-1A and 5HT-2A

NEUROTRANSMITTERS

Norepinephrine: disorders in norepinephrine are associated with lack of energy, decreased alertness, and lethargy

NEUROTRANSMITTERS



- Release DA from vesicles and reverse transporter

Drug Types:

- Amphetamines
  - -methamphetamine
  - -MDMA (Ecstasy)

HORMONAL CHANGES

Depression significantly linked to changes in hormone levels in women

Estrogen affects both serotonin and norepinephrine

Risk of depression highest during perimenopause, when hormone levels are changing

LIFE STRESSORS

Highest rate of perimenopause depression with:

- Lack of social support including no partner
- Unemployment
- Surgical menopause
- Poor overall health
- Smoking
- Poor educational level
- Onset of illness
- Caring for parents

PSYCHOLOGICAL OR SOCIAL CONDITIONS

Theories on why women become depressed during menopause:

Change in childbearing role

Loss of fertility

Empty nest syndrome

Value of youth

PREEXISTING TENDENCY TOWARD DEPRESSION

Major risk factors exist, but depression occurs even when no history of depression:

- History of major depression
- Postpartum depression
- Premenstrual dysphoric disorder

EPIDEMIOLOGY

1.3 million women in US reach menopause yearly at mean age of 47.5 years

20% experience depression

Depression twice as common in women than men (21% vs 12.7%)

In women, episodes more impairing, more recurrent, longer, and worse prognosis

More dysthymia and minor depression also in women

If older women valued, that society has less symptoms during menopause

CLINICAL PRESENTATION

Symptoms of perimenopause:

- Hot flashes
- Cold sweats
- Irregular menstrual bleeding
- Urogenital atrophy with dryness and pain, itching and urinary urge incontinence
- Cognitive decline
- Affective disturbances

SYMPTOMS OF DEPRESSION AND PERIMENOPAUSE

Low energy

Impaired concentration

Sleep disturbances

Weight changes

Libido changes

Motor retardation

Slowed thought processes

Poverty of speech

DIFFERENTIAL DIAGNOSIS

Adjustment disorders

Anemia

Depression

Dysthymic disorder

Hypothyroidism

Dementia

Depression secondary to medical condition

Endocrine disorders

Substance abuse

Medications such as beta blockers

TREATMENT AND MANAGEMENT

- Treat depression
- Hormone replacement therapy
- Improve quality of life
- Treat hot flashes
- Treat sleep disorders
- Maintain cognitive function
- Other treatments

TREATMENT OF PERIMENOPAUSAL DEPRESSION

Standard treatment of depression

SSRIs most common inhibit reuptake transporters in the presynaptic neuron, making more serotonin available in the synaptic cleft. Onset 1-4 weeks

Generally safe and effective

- Serotonin syndrome
- Wean slowly
- Adverse events: nausea, diarrhea, anorexia, excessive sweating, decreased libido, headache, jitteriness, dizziness, sedation or activation, insomnia, akathisia
- Watch drug interactions with CYP 450

SSRIS

Citalopram (Celexa) 20-40mg.day

Escitalopram (Lexapro) 10-20mg/day

Fluoxetine (Prozac) 20-80mg/day

Paroxetine (Paxil) 20-50mg/day

Sertraline (Zoloft) 50-150mg/day

Vilazodone (Viibryd) 40mg/day

SNRIS

Desvenlafaxine (Pristiq) 50-100mg/day

Duloxetine (Cymbalta) 40-60mg/day

Levomilnacipran (Fetzima) 40-120mg/day

Milnacipran (Savella) 100-200mg/day fibrmyalgia

Venlafaxine (Effexor) 150-225mg/day

OTHERS

Buproprion SR (Wellbutrin SR) 300-400mg/day

Buproprioin XL (Wellbutrin XL) 300-450mg/day

Mirtazaprine (Remeron) 15-45mg/day

Trazadone (Desyrel) 100-400mg/day

HORMONE REPLACEMENT THERAPY

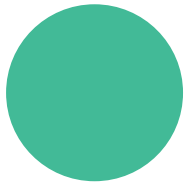
Estrogen may be used if antidepressants fail, patient refusal of psychotropic medications, or those with significant vasomotor symptoms. Women with surgically induced menopause have increased risk of depression and may especially benefit from HRT.

Data suggest HRT had antidepressant activity or enhanced activity, which may be more helpful in perimenopause rather than postmenopause

SLEEP PROBLEMS

MAY OR MAY NOT BE CONNECTED TO MOOD DISORDERS

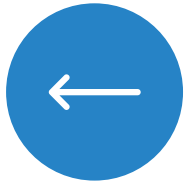
WOMEN WITH SLEEP PROBLEMS MANY TIMES HAVE ANXIETY, STRESS, TENSION, DEPRESSION



SLEEP DISTURBANCES ASSOCIATED WITH ESTROGEN DEFICIENCY, EXOGENOUS ESTROGEN IMPROVES SLEEP, DECREASES HOT FLASHES

ELEVATED LH LEVELS PRODUCE POOR SLEEP THROUGH A THERMOREGULATORY MECHANISM, RESULTING IN HIGH BODY CORE TEMPERATURE

SLEEP APNEA INCREASES 6.5% TO 16% (WEIGHT GAIN/DECREASED PROGESTERONE WHICH STIMULATES BREATHING)



DECREASED MELATONIN AND GROWTH HORMONE

TREATMENT OF SLEEP DISORDERS

Estrogen: relieves vasomotor symptoms and has direct effect on sleep

- Oral estrogens: Premarin
- Vaginal estrogens: Estrace vaginal, FemRing
- Transdermal estrogens: EstroGel, Estrasorb, Climara
- Injectable estrogens: Depo-Estrodiol
- Low dose estrogen/micronized progesterone improve sleep: Femhrt, Prefest

Isoflavone treatment

Other treatments: antidepressants, melatonin, and misc sleep agents

MISC AGENTS USED FOR SLEEP

Eszopiclone (Lunesta) 2-3mg at hs

Ramelteon (Rozerem) 8mg at hs

Zaleplon (Sonata) 5-10mg at hs

Zolpidem (Ambien) 5-10mg at hs

SCHIZOPHRENIA

Peak at early adulthood, then peak again of women only at 45-50 years

If already diagnosed, symptoms may worsen

Worsening of course of schizophrenia in women during menopause due to the role of estrogen and pathophysiology of schizophrenia

Treatment involves antipsychotic agents, mood stabilizers, possible antidepressants

ATYPICAL ANTIPSYCHOTICS

Serotonin-dopamine antagonists, therefore broader coverage of symptoms

Examples:

- Clozaril (clozapine)
- Risperdal (risperidol)
- Seroquel (quetiapine)
- Zyprexa (olanzapine)
- Geodon (ziprasidone)
- Abilify (aripiprazole)
- Invega (paliperidone)
- Saphris (asenapine)
- Fanapt (iloperidone)
- Latuda (lurasidone)

Brexpiprazole (Rexulti)

Cariprazole (Vraylar)

PANIC DISORDER

Common during perimenopause; includes new onset and worsening of pre-existing disease

Most common in women with physical signs of menopause

Most common in post menopausal women 59 and older causing functional impairment and medical comorbidity

Treatment includes antidepressants as drugs of choice, not anti-anxiety agents. Acutely, use of barbiturates

OBSESSIVE COMPULSIVE DISORDER

During menopause increased new onset, worsening of pre-existing symptoms, relapse of OCD

Hormone levels play a role in this disease

Treatment usually higher doses of antidepressants; longer response time

Effective in 60% of cases

Clomipramine (Luvox)

Antipsychotics as adjunctive treatment to antidepressants or clomipramine

BIPOLAR DISORDER

Menopause: exacerbation of mood symptoms

Higher rates of depressive symptoms

Frequency of depressed phase increases

Possible increase in rapid cycling

Treatment includes mood stabilizers, possible antipsychotics, possible antidepressants

Mood stabilizers with FDA approval: lithium, divalproex acid, carbamazepine, lamotrigine

ARIPIPRAZOLE (ABILIFY)

Indications: schizophrenia in adults as well as 13-17yr old, acute and maintenance bipolar disorder in adults as well as acute bipolar disorder in 10-17 yr old, adjunctive treatment for major depression in adults, acute agitation associated with schizophrenia in adults

Dosage forms: 2mg, 5mg, 10mg, 15mg, 20mg, and 30mg tab, liquid, fast dissolving tab and depot formulation NOT available

Dosage schedule: 1 time/day

Dosage range: 2.5-30mg, usual I/DD dosage 10-15mg

FANAPT (ILOPERIDONE)

Indication: schizophrenia and adjunctive bipolar depression

Dosage: twice daily dosing 1mg po bid x 1 day, then 2mg bid x 1 day, then increase by 4 mg/day qd, max 24mg/day with or without food (needs more titration to therapeutic dosage than most others)

Side effects: drowsiness, dry mouth, weight gain, orthostatic hypotension, QT prolongation (greater than others)

LATUDA (LURASIDONE)

Once daily dosage

Indication: for schizophrenia and adjunctive bipolar depression

Recommended dosage: 40mg 1-2 hours after dinner or a 350cal snack

Maximum dose: 80mg

No titration

Take with food (different than others)

Minimal metabolic issues (best of newer meds)

BREXPIPRAZOLE (REXULTI)

Approved for schizophrenia and adjunctive bipolar depression

MOA: agonist at serotonin 5-HT1A and dopamine and antagonist at serotonin 5-HT2A receptors

Dosage: MDD: 0.5mg/d-1mg/d with or w/o food. Titrate weekly based on response and tolerability to 2mg/d. Schizophrenia: max dose 4mg/d

CARIPRAZINE (VRAYLAR)

New antipsychotic to treat bipolar disorder and schizophrenia

High selectivity for D-3 receptors

Once daily dosing as a capsule

Typical side effects: akathisia, drowsiness, dyspepsia, EPS, restlessness, dizziness, anxiety, constipation and vomiting

QUALITY OF LIFE ISSUES

Women with mild mood disorders that do not meet criteria for MDD may also benefit from HRT, as studies have suggested an impact on mood.

TREATMENT OF HOT FLASHES

SSRIs and other antidepressants and misc drugs

- Paroxetine (Paxil)
- Venlafaxine (Effexor)
- Escitalopram (Lexapro)
- Clonidine (antihypertensive)
- Gabapentin (Neurontin)

MAINTENANCE OF COGNITION

Estrogen may prevent or delay onset of dementia, including Alzheimer's disease if started early in post-menopausal women

OTHER ISSUES

Unipolar depression is the leading cause of disease related disability

Second only to ischemic heart disease in morbidity and mortality

Diet and exercise important for symptoms as well as depression

Education of client, caregivers and family members important

QUESTIONS? COMMENTS?