ALLEN INSTITUTE for BRAIN SCIENCE
Fueling Discovery

ALLEN **Human Brain Atlas**

TECHNICAL WHITE PAPER:
ONTOLOGY AND NOMENCLATURE IN THE ALLEN HUMAN BRAIN ATLAS

OVERVIEW

Multiple atlases, ontologies, and nomenclatures have been used in the study and discussion of the human brain. To date, no single source or system has emerged as a "gold standard" for describing the entire brain. The Allen Human Brain Atlas, therefore, combines ontology and nomenclature information from an array of sources that, where possible, are regarded as providing leading ontologies and nomenclatures for the individual components of the brain. The Atlas provides the ability to view the ontology with an accompanying interactive anatomy guide for visualization of anatomic structure relationships within the ontology, as well as in the 2D maps of the human brain. Anatomic drawings were based on reference atlases in the BrainSpan Atlas of the Developing Human Brain (see the 'BrainSpan Reference Atlases' white paper in the Documentation tab) with modifications to bridge differences in ontologies and structural delineations between the two applications.

The backbone of the Allen Human Brain Atlas ontology and nomenclature is derived from *NeuroNames* (Bowden, 2002, http://braininfo.rprc.washington.edu/). Some names have been altered to be consistent with the use of English rather than Latin names. In some cases, where a structure is more commonly referred to by the Latin term, that name has been used (e.g., gyrus rectus; telencephalon). The nomenclature within this ontology incorporates the work of the most widely recognized experts in specific sub regions of the brain. For example, the ontologies and nomenclatures for the cerebellum and thalamus are derived from *MRI Atlas of the Human Cerebellum* (Schmahmann et al., 2000) and *The Thalamus* (Jones, 2007), respectively.

The primary goal behind the development of this ontology was to guide anatomically specific tissue sampling for gene expression analysis by microarray, thereby necessitating some structure groupings that differ from what is accepted as the biological norm. Where possible, acronyms and structure abbreviations were kept consistent with the source ontology. However, in some cases, deviations from the source were necessary and new acronyms/abbreviations were devised in order to provide unique identifiers across the integrated ontologies and nomenclatures.

ONTOLOGY AND NOMENCLATURE SOURCES BY BRAIN REGION

Cerebral Cortex

The ontology of the cerebral cortex is based primarily on two sources. First, the naming and delineation of the sulci are in alignment with *Atlas of the Cerebral Sulci* (Ono et al., 1990). Second, the naming of the gyri are in alignment primarily with Gray's *Anatomy of the Human Body* (Gray, 2000), the nomenclature of which is heavily relied upon by clinicians.

Consistent with Gray (2000), the cerebral cortex is divided into six lobes including the insula and the limbic lobe, which contains the cingulate gyrus as well as the hippocampal formation. Some adjustments have been made to accommodate our tissue sampling paradigm, which allows data acquisition, and, therefore, data presentation and analysis for users, at a finer level of anatomic resolution. These adjustments include the following:

- The lateral occipital gyri have been separated into superior and inferior portions, each portion providing multiple samples for microarray analysis.
- The parieto-occipital arcus, a term not commonly used, has been included within the superior parietal lobule.
- The orbital gyri are divided based on the sulcal delineations by Ono, rather than represented as a single entity.
- The sulci in the temporal cortex are referred to as the superior, middle, and inferior temporal sulci, rather than the superior, inferior, and temporo-occipital sulci. The latter term is reserved for the inferior temporal sulcus' extension into the occipital lobe.

Occasionally, structure delineations cannot be based on existing landmarks; in these instances, all attempts were made to keep the structure delineations consistent within individual brains and between cases. Guidelines for such delineations include the following:

- Temporal pole is defined as the cortex anterior to the junction (via white matter) of the temporal lobe to the remainder of the brain.
- Frontal pole is consistent with the delineation of the pole by FreeSurfer visualization of the MRI.
- Parahippocampal gyrus extends posterior to the point at which primary visual cortex appears; at that point it is referred to as the lingual gyrus.
- The division between fusiform gyrus and occipito-temporal gyrus is made at the same point as the division between the parahippocampal and lingual gyri.

Thalamus
The ontology and nomenclature of the thalamus is based on *The Thalamus* (Jones, 2007), the premier work on the thalamus, as well as on personal communication with Edward G. Jones, who kindly supplied his ontology and nomenclature. This ontology and nomenclature extends to the epithalamus, as well as to those structures included in the ventral thalamus division, such as the zona incerta and the reticular nucleus of the thalamus. For tissue sampling purposes, the thalamus is sampled at a gross level, combining nuclei in a manner consistent with Jones' subdivisions. Groupings for sampling from the dorsal thalamus, therefore, include anterior nuclei, medial nuclei, lateral nuclei (ventral and dorsal portions), posterior nuclei, caudal intralaminar nuclei, rostral intralaminar nuclei, the lateral geniculate nucleus, and the medial geniculate complex. From the ventral thalamus, the reticular nucleus and the zona incerta are sampled, the latter containing the Fields of Forel when present.

Hypothalamus
Hypothalamic nomenclature follows that of Saper (2004), which primarily follows the nomenclatures of Nauta and Haymaker (1969). Four divisions along the anterior-posterior axis include the preoptic, anterior, tuberal, and mammillary regions. These regions, in turn, are divided into a periventricular zone, medial zone and lateral zone. For sampling purposes, well known and well defined areas—such as the paraventricular nucleus, supraoptic nucleus, mammillary bodies, etc.—were sampled when possible. The less well defined medial and lateral zones from each of the four divisions were also sampled when possible.

Basal Forebrain and Basal Ganglia
The base ontology and nomenclature of the deep nuclei of the cerebrum are based on *NeuroNames* (Bowden, 2002; BrainInfo, 2007). Identification of these structures relied on multiple sources, including, but not limited to: Paxinos and Mai (2004); Schaltenbrand and Bailey (1959); and Mai et al. (2004). Additional sources specific to the nuclei were also used, including Martin et al. (1991), Mesulam (1983), and Andy and Stephan (1968).

Amygdaloid Complex
The ontology for the amygdaloid complex is mainly based on Johnston (1923) and de Olmos (2004) with reference to the nomenclature for non-human primates (Price et al., 1987). Specifically, the amygdaloid complex includes central, basolateral and corticomedial groups, as well as anterior amygdaloid area and intercalated nucleus of amygdala. Some of the amygdaloid transition areas and extended amygdaloid structures are separate from the amygdaloid complex.

Hippocampus
The ontology and nomenclature of the hippocampus is based on *The Human Hippocampus: An Atlas of Applied Anatomy* by Duvernoy (1988). The nomenclature of the human hippocampus differs somewhat from that of the rodent, most notably in that the hilus of the dentate gyrus in the rodent is considered the CA4 region of the human hippocampus. Additionally, delineation of the subicular regions is based on Duvernoy's work, but is sampled as a single entity comprised of all components. The uncus is not treated as a separate structure; rather it is separated into its functional components: subiculum and amygdalo-hippocampal transition areas. While the hippocampus contains multiple layers, only the pyramidal cell layer was assessed by microarray.

Cerebellum
The ontology and nomenclature of the cerebellum is based entirely on *MRI of the Human Cerebellum* (Schmahmann et al., 2000). As Schmahmann notes, there is "no true vermis in the anterior lobe," and it is present only in lobules VI-X. However, as he also points out, the use of the term vermis to reflect the midline of the hippocampus has become common. As such, we have included it in lobules I-V, as did Schmahmann.

Midbrain, Pons, and Medulla
The ontology of these structures—here separated into the metencephalon, mesencephalon, and myelencephalon—is based primarily on the work of Koutcherov et al. (2004). The cerebellum deviates from this ontology and nomenclature as stated above. Cytoarchitectonic identification of structures within the hindbrain is based on *Cytoarchitecture of the Human Brainstem* (Olszewski and Baxter, 1982). *Duvernoy's*

Atlas of the Human Brain Stem and Cerebellum: High-Field MRI, Surface Anatomy, Internal Structure, Vascularization and 3 D Sectional Anatomy (Naidich et al., 2008), *The Human Nervous System* (Paxinos and Mai, 2004), and *Introduction to Stereotaxis, with an Atlas of the Human Brain* (Schaltenbrand and Bailey, 1959) were also used as references for placing structures within MRI space or identification of midbrain structures. When appropriate or when further information was needed, additional sources were used to help identify structures. For example, identification of the ventral tegmental area was facilitated by Oades and Halliday (1987) and Halliday and Törk (1986). Chapters of *The Human Nervous System* by Buttner-Ennever and Horn (2004) and Hornung (2004) detailing the reticular formation and raphe nuclei, respectively, were also used for structure identification.

UPDATE TO THE ONTOLOGY (OCTOBER 2013)

In the October 2013 release of data in the Allen Human Brain Atlas, some changes were made to the ontology:

(1) The subcallosal gyrus (SCG) was moved from within the frontal lobe to within the cingulate lobe, where it was renamed “subcallosal cingulate gyrus” to more accurately reflect the regions that were sampled.
(2) The pallidohypothalamic nucleus of the hypothalamus was moved from within the “lateral hypothalamic area, anterior region” (LHA) to within the “lateral hypothalamic area, mammillary region” (LHM).
(3) Additional subdivisions were added to many subcortical regions and nuclei. These changes did not affect structural sampling of Atlas array data.
(4) Names and subdivisions of the amygdala were revised to better reflect the sampling paradigm that was used in the Allen Human Brain Atlas. These changes were to the naming conventions used, and do not affect the relationships of the samples to each other.

REFERENCES

Amaral DG, Price JL, Pitkänen A, Carmichael ST (1992) Anatomical organization of the primate amygdaloid complex. In: *The amygdala: Neurobiological aspects of emotion, memory, and mental dysfunction* (Aggleton JP, ed.) pp. 1-66. New York, NY: Wiley-Liss.

Andy OJ, Stephan H (1968) The septum in the human brain. *J. Comp. Neurol.* 133(3):383-410.

Bowden DM, Dubach MF (2003) NeuroNames 2002, *Neuroinformatics* 1:43-59.

BrainInfo (2007), Neuroscience Division, National Primate Research Center, University of Washington, http://www.braininfo.org**.**

Buttner-Ennever JA, Horn A (2004) Reticular formation: Eye movements, gaze and blinks. In: *The human nervous system* (Paxinos G, Mai JK, eds.) pp. 514-550. San Diego, CA: Elsevier Academic Press.

Duvernoy HM (1988) *The human hippocampus: An atlas of applied anatomy*. Munich, Germany: J.F. Bergmann-Verlag.

Gray H (2000) *Anatomy of the human body.* Philadelphia: Lea & Febiger, 1918; Bartleby.com, 2000. www.bartleby.com/107/. [2009].

Halliday GM, Törk I (1986) Comparative anatomy of the ventromedial mesencephalic tegmentum in the rat, cat, monkey and human. *J. Comp. Neurol.* 252(4):423-445.

Hornung J-P (2004) Raphe nuclei. In: *The human nervous system* (Paxinos G, Mai JK, eds.) pp. 514-550. San Diego, CA: Elsevier Academic Press.

Jones EG (2007) *The thalamus*. Cambridge, UK: Cambridge University Press.

Koutcherov Y, Huang X-F, Halliday G, Paxinos G (2004) Organization of human brain stem nuclei. In: *The human nervous system* (Paxinos G, Mai JK, eds.) pp. 273-321. San Diego, CA: Elsevier Academic Press.

Mai JK, Paxinos G, Assheuer JK (2004) *Atlas of the human brain.* San Diego, CA: Elsevier Academic Press.

Martin LJ, Powers RE, Dellovade TL, Price DL (1991) The bed nucleus-amygdala continuum in human and monkey. *J. Comp. Neurol.* 309(4):445-85.

Mesulam MM, Mufson EJ, Levey AI (1983) Cholinergic innervation of cortex by the basal forebrain: cytochemistry and cortical connections of the septal area, diagonal band nuclei, nucleus basalis (substantia innominate), and hypothalamus in the rhesus monkey. *J. Comp Neurol*. 214(2):170-197.

Naidich TP, Duvernoy HM, Delman BN, Sorensen AG, Kollias SS, Haacke EM (2008) *Duvernoy's atlas of the human brain stem and cerebellum: High-field MRI, surface anatomy, internal structure, vascularization and 3 D sectional anatomy.* Vienna: Springer-Verlag.

Nauta WJH, Haymaker W (1969) Hypothalamic nuclei and fiber connections. In: *The hypothalamus* (Haymaker W, Anderson E, Nauta WJH, eds.) pp. 136-209. Springfield, IL: Charles C Thomas, Publisher.

Oades RD, Halliday GM (1987) Ventral tegmental (A10) system: neurobiology. 1. Anatomy and connectivity. *Brain Research* 434(2):117-165.

Olszewski J, Baxter D (1982) *Cytoarchitecture of the human brainstem, 2nd Edition.* Basel: S. Karger.

Ono M, Kubik S, Abernathy CD (1990) *Atlas of the cerebral sulci*. New York, NY: Thieme Medical Publishers.

Paxinos G, Mai JK, eds. (2004) *The human nervous system*. San Diego, CA: Elsevier Academic Press.

Saper CB (2004) Hypothalamus. In: *The human nervous system* (Paxinos G, Mai JK, eds.) pp. 514-550. San Diego, CA: Elsevier Academic Press.

Schmahmann JD, Doyon J, Toga AW, Petrides M, Evans AC (2000) *MRI atlas of the human cerebellum*. San Diego, CA: Academic Press.

Schaltenbrand G, Bailey P (1959) *Introduction to stereotaxis, with an atlas of the human brain*. Stuttgart: Georg Thieme.

Schmahmann JD, Doyon J, Toga AW, Petrides M, Evans AC (2000) *MRI atlas of the human cerebellum*. San Diego, CA: Academic Press.