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Preface

The book's third edition has returned to the large format of the first, and its photo of each atlas level with accompanying drawing of gray and white matter distribution. The new feature is a second drawing that illustrates major features of gray matter regionalization in a color-coded way that is carried through the flatmaps of the rat CNS (Frontispiece, Fig. 11, and poster) and the hierarchical nomenclature tables of section VIII.

The nomenclature tables are considerably revised from the second edition, based on a deeper appreciation of the problem's history (Swanson 2000b) and abundant experimental evidence (Swanson 2000c, 2003a,b). Table A is now a taxonomy of major nervous system parts that applies to mammals in general, whereas Tables B-D consider specifically and in detail cell group regionalization, fiber systems, and the peripheral nervous system of the rat. Nomenclature and the taxonomy of nervous system parts are fundamentally important problems in nascent development of neuroscience databases and knowledge management systems, and a great deal of

work on basic principles remains to be done in this arena. For example, there is still no ontology of neuroanatomical terms—formal definitions of, and relationships between, names for structural features.

Computer graphics files of the atlas and flatmaps are provided on the CD-ROM. These *Interactive Brain Maps* can be used to learn more about the structure of the brain, to map experimental results on standard or reference templates, to form databases of spatial information about the rat brain, and to create 3-D models (Swanson 2001). The *Brain Maps, Computer Graphics Files 3.0 /COMPLETE* atlas (rendered in vector graphics) is very complete and features the color-coded regionalized atlas template, the gray and white matter atlas template, the Nissl-stained section used to derive the template drawings, stereotaxic and physical coordinate grids, an alignment box for databases and 3-D models, and a simple yellow mask for the templates (as in the second edition of the book). These brain maps can be adapted by the user in endless ways.

I would like to extend a special note of thanks to Dr. Johannes Menzel of Elsevier Science for his encouragement and help with the third edition. As usual, I dedicate this work to Neely and Reid.

April 5, 2003

Los Angeles

Contents

4. Database prototype

    a. Sample database (Atlas Level 19)

    b. Sample data layer (Atlas Level 19)

B. Abbreviation Lists (Microsoft® *Word*)

1. *Brain Maps III*
2. *Developmental Brain Maps* (Alvarez-Bolado & Swanson 1996)

C. Archival material (Adobe® *Illustrator* files)

1. *Brain Maps I*, shaded drawings (Swanson 1992, for book)
2. *Brain Maps, Computer Graphics Files 1.0* (Swanson 1993, from floppy discs)
3. *Brain Maps II, Computer Graphics Files 2.0/Map only* (Swanson 1998-1999, from CD-ROM)
4. D. User's Guide for CD-ROM (Adobe® *Acrobat*)

I. Overview

The core of this book is an atlas of the rat brain viewed from 73 representative transverse levels along its longitudinal axis. Each Atlas Level is based on a histological section through the brain stained to reveal the global distribution pattern of cell bodies—the organization of the brain as a tissue at that level. A map or drawing illustrating my interpretation of gray matter regionalization and readily identifiable white matter differentiations (fiber tracts) present in the section was then prepared and matched to a photomicrograph of the section. Finally, two color-coded versions of the maps were prepared. One version simply shows the overall distribution of gray and white matter masses, and is similar to the maps presented in the first edition (Swanson 1992a). The other version indicates where the major divisions of the brain lie within the map. It is color-coded to a flatmap of the central nervous system (CNS); it is indexed to a systematic nomenclature hierarchy; and it is new to this edition.

The atlas may of course be studied to appreciate more deeply the basic regional (topographic, gross) anatomy or architecture of the rat brain—the fundamental arrangement of the many neuronal cell groups (regions) and fiber tracts (pathways) that form the rostral CNS of this intensively studied mammal. However, the Atlas Level maps are even more useful as templates for the standardized representation of neuroanatomical data. In other words, they can be used as maps or templates to present in a schematic way, and then compare, results based on the application of various neuroanatomical methods—summaries whose files can be incorporated into computer graphics databases.

The intelligent use of these templates requires critical evaluation of their benefits and limitations. Therefore, the text begins with a brief overview of the rat brain itself (section II), followed by an account of how the atlas brain was prepared and the drawings created. This

section (III) also contains a discussion of brain coordinate systems and the related problems of using them for stereotaxic surgery and for the mathematical definition of structure location (position) within the brain.

Next, we consider the important problem of how to map experimental results onto the templates, and how these maps can be used in neuroanatomical databases, eventually at the level of 3-D computer graphics models or brain atlases. For this, it is important to discuss strengths and limitations of the various common neuroanatomical methods, as well as problems associated with transferring data to the templates. In section V, a more abstract level of data summary is considered: the use of a standardized flatmap to display circuit diagrams and overall gene expression patterns. It is shown here that all of the various functional systems of the CNS can be displayed on a single (*bilateral*) map where the major fiber systems and neuronal cell groups have been assigned standard locations. And finally, critical problems associated with neuroanatomical nomenclature, which has not yet been standardized (as has long been true for most other parts of the body such as the muscles, bones, and vascular system), are dealt with in section VI, and references in the primary literature for the nomenclature adopted here are given in section VIII (following the atlas drawings in section VII), which contains systematic nomenclature tables.

As will become apparent, there are many limitations associated with the use of standardized atlases, which must not be viewed as static, authoritative representations of the brain. Instead, they are convenient starting points—working models—based on current understanding, and will be modified for ever more accurate views. Fortunately, the use of the maps provided here as computer graphics files renders their modification trivially easy. Alternative interpretations of underlying structure can be displayed in overlying layers, or the templates themselves can be

modified however desired. Nevertheless, experience has shown that one major benefit of using an atlas such as that presented here for data summary is that it forces the beginner to consider systematically where labeling is present in relationship to the borders of all of the various brain structures dealt with critically in the primary literature to date. The process of mapping can thus be accelerated, more accurate, and related more easily to the previous neuroanatomical literature.

II. Summary of Adult Rat Brain Structure

Much more is known about the structure and chemistry of the brain in the rat than in any other animal. Many of the reasons for the popularity of the rat in neurobiological and behavioral work have been summarized in a delightful book written by S.A. Barnett (1963), but economy and small size are important factors, along with the fact that these animals have a relatively smooth cerebral cortical mantle, as opposed to the highly convoluted mantle found in many larger species.

Two major disadvantages associated with the use of rats come readily to mind. First, the organization of the rat brain obviously is not identical to that of the human brain. Therefore, the clinical relevance of neuroanatomical information obtained from the rat should, in principle, be confirmed in human material, which often may not be possible for ethical reasons. Furthermore, certain important problems like the neurobiology of language may be difficult if not impossible to study in the rat. And second, the types of genetic analyses that can be carried out in mice may not be practical anytime soon in rats. On the other hand, the mouse brain is often too small for critical analysis with available experimental neuroanatomical techniques (section IV).

Broadly speaking, the nervous system of all *vertebrates* has two major divisions, central and peripheral. The peripheral division (PNS) consists of sensory, autonomic, and enteric neurons, along with the various nerves that are attached to the central division. Topologically, the latter is a tube that is closed at both ends, and the wall of the tube is highly differentiated throughout its longitudinal axis. Based on embryological considerations (see Swanson 1992a; Alvarez-Bolado and Swanson 1996; Swanson 2003) the central division of the CNS has traditionally been divided into a massive rostral part within the skull, the brain; and a smaller caudal part within the vertebral column, the spinal cord. Furthermore, the peripheral division is derived from the

embryonic neural crest, whereas the central division is derived from the neural tube. Early in the embryo, the neural tube displays three rostrocaudal swellings, the forebrain, midbrain, and hindbrain vesicles; and somewhat later the forebrain vesicle is divided into paired endbrain vesicles and an interbrain vesicle, whereas the hindbrain vesicle is divided vaguely into a rostral pontine and a caudal medullary vesicle.

The general organization of the adult *rat* nervous system, as well as the parts of the body that it innervates, has been summarized thoroughly by Greene (1968) and by Hebel and Stromberg (1986), and the work of Donaldson (1924) contains a wealth of information about the changing size of various organs and major subdivisions of the CNS during the course of development.

Dorsal and ventral external views of rat brain gross anatomy are illustrated in Figure 1 (top). It is obvious that the brain is dominated by right and left *cerebral hemispheres* (the matured endbrain vesicles) and the *cerebellum* (which is continuous across the midline and derived from the dorsal or rhombic lip of the pontine vesicle). The cerebral and cerebellar hemispheres are attached to a much smaller core or *brainstem* that is derived from the interbrain, midbrain, and hindbrain vesicles and extends caudally as the *spinal cord*. Together, the brainstem and spinal cord form the *cerebrospinal trunk*.

The major parts of the adult rat brain are more easily appreciated in a midsagittal or bisected view (Fig. 1, bottom). While the nomenclature and groupings of these parts has changed over the centuries (sections VI and VIII), it is convenient from a functional systems perspective to regard the cerebral hemispheres (cerebrum, endbrain, or telencephalon) as consisting of *cerebral cortex* and *cerebral nuclei* (other traditionally names include corpus striatum, basal ganglia, and basal nuclei); the cerebellum (parencephalon) as consisting of *cerebellar cortex* and *cerebellar nuclei* (not shown in Fig. 1 because they do not reach the midline); and the brainstem as consisting

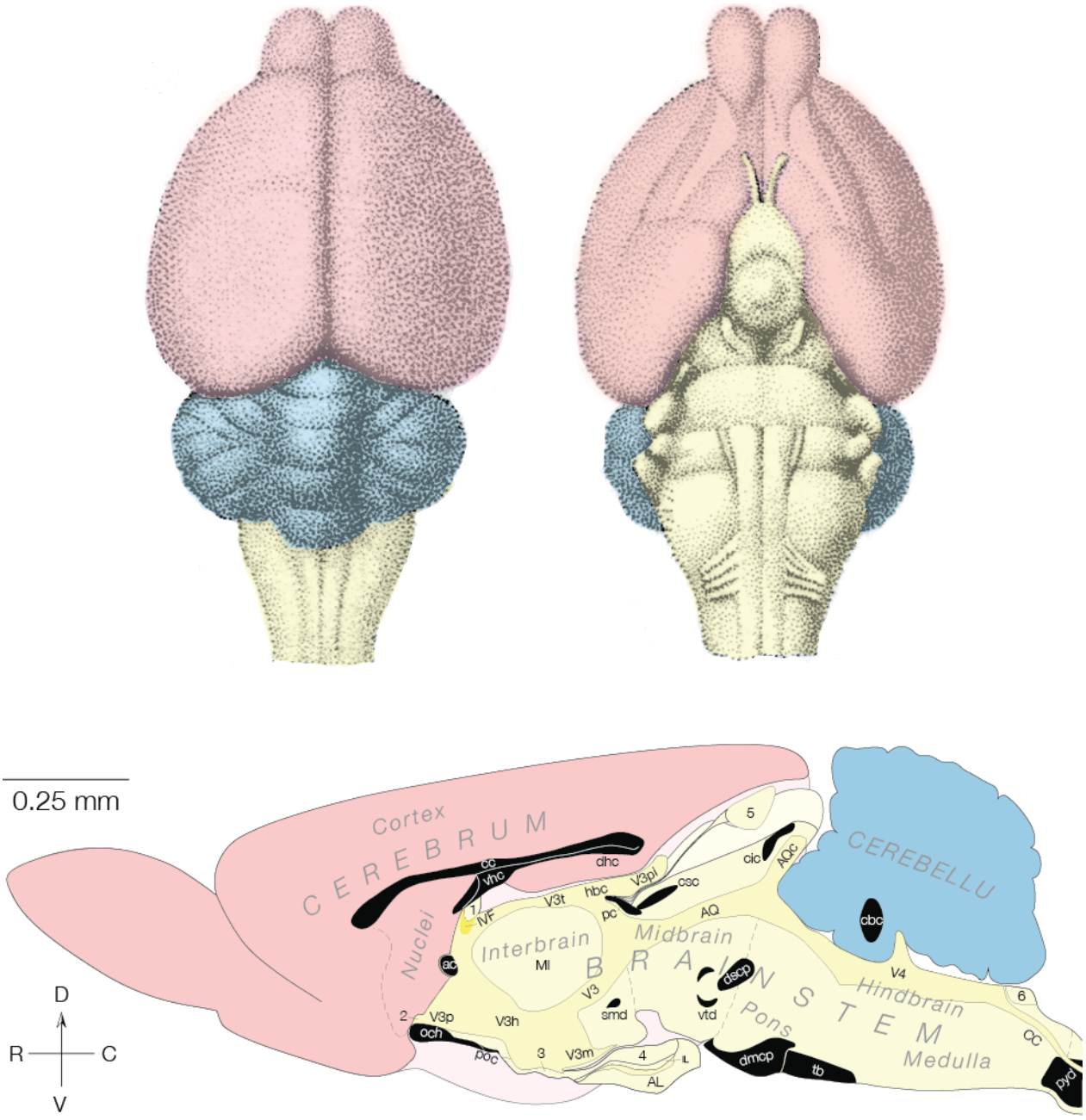

Fig. 1. *Top*. Dorsal (left) and ventral (right) views of the adult rat brain, with the cerebral hemispheres (cerebrum) in red, the cerebellum in blue and the brainstem in yellow (from Leuret and Gratiolet 1857). *Bottom*. A midsagittal view of the right half of the adult rat brain, reconstructed from the atlas series and color coded as in the top drawings. Major fiber systems crossing the midline are shown in black. Major circumventricular organs include: 1, subfornical organ; 2; vascular organ of the lamina terminalis; 3, median eminence; 4, posterior (neural lobe) pituitary; 5, pineal gland; and 6, area postrema. For abbreviations, see list at the end of the book.

successively of the *interbrain* (diencephalon), *midbrain* (mesencephalon), and *hindbrain*

(rhombencephalon), which in turn is somewhat arbitrarily divided into *pons* (metencephalon) and *medulla* (myelencephalon).

The brainstem and spinal cord contain virtually all motoneurons (except for a few neuroendocrine gonadotropin-releasing hormone motoneurons in the septal region of the basal or cerebral nuclei), with neuroendocrine motoneuron pools concentrated in the ventral interbrain (hypothalamus), and preganglionic autonomic and somatic motoneuron pools found along most of the length of the midbrain, hindbrain, and spinal cord. The brainstem is probably responsible for mediating all unconditioned reflexes as well as changes in behavioral state, such as the sleep-wake cycle. In contrast, it seems likely that the cerebral and cerebellar hemispheres together are essential for voluntary control of the motor systems and for long lasting associative learning.

A midline view of the brain also demonstrates two other sets of features that serve as useful landmarks. One set includes the so-called *circumventricular organs*, which lack a traditional blood-brain barrier to lipophobic substances, and certain *glands*. The subfornical organ is the most rostrodorsal circumventricular organ, and embryologically it lies at the dorsal junction between the cerebral hemispheres and interbrain; the tiny vascular organ of the lamina terminalis lies at the tip of the preoptic recess of the third ventricle; the median eminence lies along the floor of the third ventricle, just rostral to the infundibulum—which extends as the neural lobe of the pituitary gland and also lacks a blood-brain barrier; and the area postrema, which lies at the dorsal border between brainstem and spinal cord, just dorsal to the rostral end of the central canal. Figure 1 also shows the rest of the pituitary gland (the intermediate and anterior lobes, which are derived from Rathke's pouch in the embryonic roof of the mouth), and the pineal gland, an evagination of the caudal interbrain roof plate between the habenular and posterior commissures (see Swanson 1992a; Alvarez-Bolado and Swanson 1996).

The second set of midline features includes the *major fiber systems that cross to the other side of the brain*. In the cerebral hemispheres they include the corpus callosum (great cerebral commissure) and its embryologically caudal continuation, the dorsal and ventral hippocampal commissures. In the interbrain they include the anterior, postoptic (supraoptic) and habenular commissures; and the optic chiasm. The midbrain contains the posterior commissure, the commissures of the superior and inferior colliculi, the dorsal and ventral tegmental commissures, and the decussation of the superior cerebellar peduncle. The hindbrain contains the decussation of the middle cerebellar peduncle and caudally adjacent trapezoid body, and the decussation of the pyramid (corticospinal tract). And finally, the cerebellum contains the rather small cerebellar commissure.

While our primary concern in this book is with the disposition of the major cell groups (regions) and fiber systems (pathways) in the rat brain, certain other features should be mentioned for the sake of completeness. To begin with, the central nervous system of a 315 gram adult male rat (the size and sex of the rat used for our atlas) weighs on the order of 2.7 grams, with the brain contributing about 2.0 grams and the spinal cord about 0.7 grams (Donaldson 1924). Furthermore, the central nervous system is completely surrounded by connective tissue sheaths (*the meninges*), contains a fluid-filled central cavity (*the ventricular system*), and has a rich *blood supply*.

The general principles of *cerebrospinal fluid* (CSF) production by the *choroid plexuses*, and its flow through the ventricular system and *subarachnoid space*, as well as the flow of blood through the central nervous system, are similar in all mammals, and are reviewed in most textbooks of human neuroanatomy (for good accounts see Carpenter and Sutin 1983, and Williams 1995). The central nervous system does not, of course, have a true *lymphatic system*;

instead, the function of this system is generally thought to be subserved by the cerebrospinal fluid.

There are certain specializations or differences associated with these structures or systems in the rat itself. Nothing remarkable about *the meninges* in the rat has been reported; their general disposition is described by Zeman and Innes (1963), Greene (1968), and Hebel and Stromberg (1986). The shape of the *ventricular system* has been described in detail by McFarland et al. (1969), Westergaard (1969), and Jarvis and Andrew (1988). According to McFarland et al. (1969), it contains approximately 0.5 ml of cerebrospinal fluid in the adult, although the accuracy of this measurement is difficult to assess (Fig. 2). The *vascular system* of the rat CNS has not been the subject of detailed, systematic investigation. For general accounts of the major arteries and veins supplying the rat CNS, as well as the general distribution of capillaries, see Craigie (1920), Zeman and Innes (1963), Brown (1966), Greene (1968), Hebel and Stromberg (1986), and Scremin (1995). An introductory guide to more detailed accounts of particular regions would include the following: spinal cord (Tokioka 1973; Tveten 1976); brainstem and cerebellum (Craigie 1933; Moffat 1957); interbrain and pituitary (Ambach and Palkovits 1979; Szabó 1990, 1995); septal region (Ambach et al. 1975); amygdalar region (Merksz et al. 1978); and cerebral cortex (Craigie 1921, 1932; Eayrs 1954).

Finally, it is important to reemphasize that the maps presented here are from an adult male rat, and that the rat brain is sexually dimorphic. The best-established sexual dimorphisms are associated with the so-called sexually dimorphic circuit, which begins in the vomeronasal organ and extends through the accessory olfactory bulb to parts of the amygdalar region, bed nuclei of the stria terminalis, and hypothalamus (see Segovia and Guillamón 1993; Simerly 1995). Therefore, caution must be used when employing the maps presented here to display

neuroanatomical data from the female rat, and the maps need to be modified when known sexually dimorphic structures are involved.

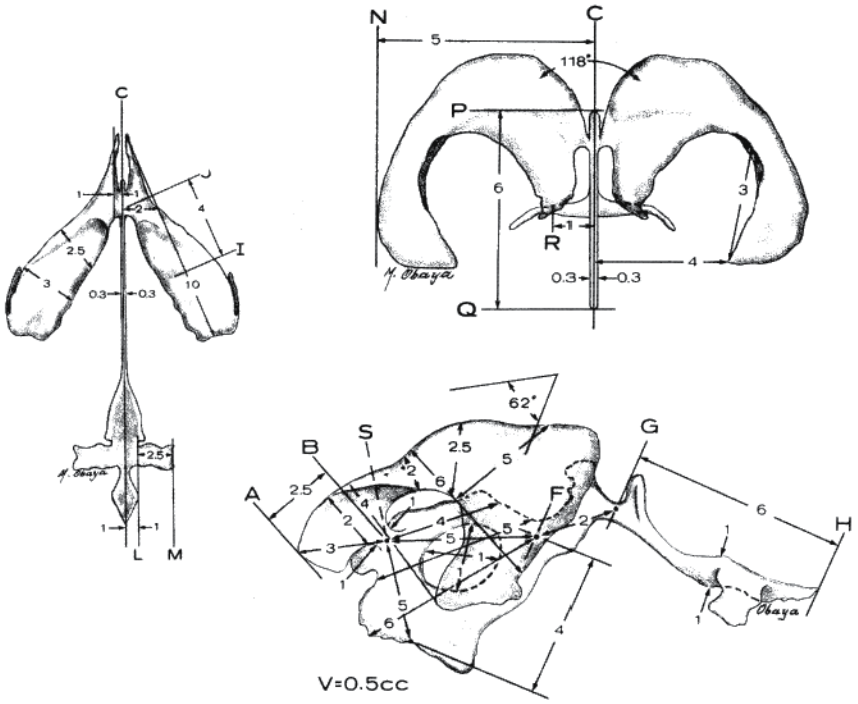

Fig. 2. The ventricular system of the adult rat brain as viewed from the top (left drawing), from the front (upper right drawing), and from the side (lower right drawing); measurements are in mm (from McFarland et al. 1969).