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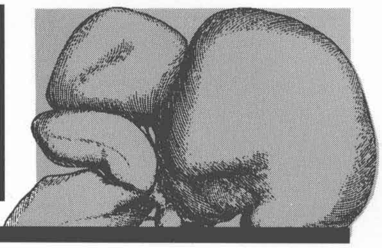

An Atlas of Developmental Stages

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ABBREVIATIONS

a.	Artery
Aff.tr.	Common afferent tract
A.-H.	Adenohypophysis
Amyg.	Amygdaloid region, nuclei, body
Ansa	Ansa cervicalis
Bas.a.	Basilar artery
C	Cervical
Cbl	Cerebellar plate, cerebellum
Ch.	Chiasmatic plate
Ch.tymp.	Chorda tympani
CN	Cranial nerve
CNS	Central nervous system
Comm.	Commissural plate
C-R	Crown-rump length
D1, D2	Diencephalic neuromeres
Di.	Diencephalon
Dors.f.	Dorsal longitudinal fasciculus
End.div.	Endolymphatic diverticulum
Ep.	Epiphysis
Ext.cbl	External cerebellar swelling
Ggl	Ganglion
GL	Greatest length
Hab.-interp.tr.	Habenulo-interpeduncular tract
Hem.	Cerebral hemisphere
Hipp.	Hippocampus
Hyp.-th.sulc.	Hypothalamic sulcus
Hyp.-th.-teg.-tr.	Hypothalamotegmental tract
Infund.	Infundibulum
Int.cbl	Internal cerebellar swelling
Interst.nu.	Interstitial nucleus
Isth.	Isthmus rhombencephali
Isth.rec.	Isthmic recess
I.-v.f.	Interventricular foramen
Lat.f.	Lateral longitudinal fasciculus
Lat.(vent.)em.	Lateral ventricular eminence
L.l.f.	Lateral longitudinal fasciculus
LMP	Last menstrual period
Long.fiss.	Longitudinal fissure
L.t.	Lamina terminalis
M or Mes.	Mesencephalon
M1, M2	Mesencephalic neuromeres
M.l.f.	Medial longitudinal fasciculus
Mam.	Mamillary region, nuclei, body
Mam.-teg.tr.	Mamillotegmental tract
Marg.ridge	Marginal ridge
Med.fore.b.	Medial forebrain (or prosencephalic) bundle
Med.tectobulb.tr.	Medial tectobulbar tract
Med.(vent.)em.	Medial ventricular eminence

Mes. tr. 5	Mesencephalic tract of trigeminal nerve
n.	Nerve
Nas.	Nasal plate, pit, sac, septum
N.-H.	Neurohypophysis
Not.	Notochord
Nu.mes.5	Mesencephalic trigeminal nucleus
Nu.post.X	Nucleus of posterior commissure
Olf.bulb	Olfactory bulb
Olf.n.	Olfactory nerve
Olf.tub.	Olfactory tubercle
Opt.	Optic sulcus, vesicle, cup
Opt.stalk	Optic stalk
Ot.	Otic plate, pit, vesicle
Post.-lat.fiss.	Posterolateral fissure
Post.X	Posterior commissure
Pros.	Prosencephalon
Red.nu.	Red nucleus
Rh. or Rhomb.	Rhombencephalon; rhombomere
Rh. A to D	Specifically identified rhombomeres
Rh. 1 to 4	Specifically numbered rhombomeres
Rh.lip	Rhombic lip
Sp.ggl	Spinal ganglion
Subarach.	Subarachnoid space
Subth.nu.	Subthalamic nucleus
Sulc.lim.	Sulcus limitans
Supramam.X	Supramamillary commissure
Supra-opt.X	Supra-optic commissure
Syn.	Synencephalon
Tel.	Telencephalon
Tel.med.	Telencephalon medium
Tent.	Tentorium cerebelli
Th.d. or Thal.d.	Dorsal thalamus
Th.v. or Thal.v.	Ventral thalamus
Tr.	Tract(us); transversum
V	Ventricle
V3, V4	Third ventricle, fourth ventricle
Velum tr.	Velum transversum
V.-n.	Vomeronasal nerve, ganglion
X3	Commissure of the oculomotor nerves
X4	Commissure of the trochlear nerves
X sup.coll.	Commissure of the superior colliculi
1–12	Cranial nerves
5i	Intermediate trigeminal fibers
5m	Motor trigeminal fibers
5s	Sensory trigeminal fibers
7i	Nervus intermedius
8c	Cochlear component of vestibulocochlear nerve
8v	Vestibular component of vestibulocochlear nerve

THE EMBRYONIC HUMAN BRAIN

In memory of
Ernest Gardner, M.D.,
neuroscientist, colleague, and friend

. . . ce feroit vn grand bon-heur pour le genre humain, fi cette partie, qui eft la plus délicate de toutes, & qui eft fujette à des maladies tres-frequentes, & tres-dangereufes, eftoit auffi bien connuë, que beaucoup de Philofophes & d'Anatomiftes fe l'imaginent.

Niels Stensen, *Discovrs svr l'Anatomie du cerveau,* 1669.

PREFACE

The main objective of this monograph is to provide drawings, photographs, and photomicrographs of the human embryonic brain, and to include summarizing statements of the morphological status of the brain at each stage. The staging used is the internationally accepted Carnegie system. The drawings include at least a lateral view and a median reconstruction of the brain at each stage, as well as a clear indication of the plane of section of further illustrations, either drawings or photomicrographs. The vast majority of the drawings are based on extremely precise graphic reconstructions. At the end of the description of the normal at most stages, a brief statement concerning relevant anomalous conditions is added. Some illustrations of the fetal brain are included, in order to indicate some of the main trends that occur shortly after the completion of the embryonic period proper.

The reasons for concentrating on the embryonic period proper (the first eight postovulatory weeks) are:

(1) The embryonic brain is extremely difficult to comprehend and to visualize;

(2) Serial sections of first-class quality that show the human embryonic brain are rarely accessible;

(3) The correct interpretation of the appropriate serial sections requires years of specialized work;

(4) The time-consuming preparation of accurate three-dimensional reconstructions is essential for correct interpretation;

(5) The embryonic period is of particular importance because most major congenital anomalies appear during that time;

(6) No accurate, detailed, well-illustrated account of the human embryonic brain is available in book form, or even in a chapter of a book.

A set of standardized abbreviations, mostly self-evident, is used throughout for the illustrations, and a list of them is placed immediately inside the front cover. Furthermore, definitions of certain technical terms (such as neuromere and neuropore) are provided in Chapter 6. A selection of references to the chief studies of the prenatal human brain is included, but is not intended to be complete. In the interest of brevity, as well as of immediate relevance, items from the profuse literature relating to other species have not been included. In an appendix are listed 167 features associated with the brain during the first seven postovulatory weeks; the features are arranged in order of appearance and are related to embryonic stage, age, and length.

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R.O'R.
F.M.

C O N T E N T S

CHAPTER 1

Historical Aspects

Although Malpighi in the 1670s observed the neural folds in the chick embryo, their significance escaped him, and he thought that the brain developed between them (Adelmann, 1966). Even von Baer was unaware that the neural folds are the primordium of the CNS, a role that was first appreciated by Rusconi and Reichert. Pander, however, understood that the neural folds form a tube. Nevertheless, the CNS was thought to be merely a fluid at first, and "the monotonous chronicle of vesicles and bubbles" (Adelmann) continued into the nineteenth century—if not, indeed, beyond it.

The *vesiculae cerebrales*, said to have been first noted by Coiter in 1573 (Tiedemann, 1816), were promoted by Meckel the younger, von Baer, and Bischoff, although the concept is largely a myth (Streeter, 1927). The current acceptance of three main divisions in the brain (prosencephalon, mesencephalon, and rhombencephalon) dates mainly from von Baer, who also identified the five subdivisions that appear a little later (telencephalon, diencephalon, mesencephalon, metencephalon, and myelencephalon). In addition, His included a sixth part, the isthmus rhombencephali, which becomes very evident during development.

Specific References to the Prenatal Human Brain

Some key studies are mentioned here for convenience, but the list is not intended to be complete.

One of the earliest specific accounts of the prenatal human brain is that by Friedrich Tiedemann (1816), which was translated into French (1823) and English within a decade. The monograph is arranged according to nine prenatal months, but early examples of the human embryonic brain were inevitably lacking.

In 1896, the detailed atlas of the gross morphology of the brain by Gustaf Retzius appeared. In addition to the adult organ, more than 35 plates included the fetal brain from "the third to the tenth month," the smallest being from two 35-mm fetuses. Retzius referred to the work of His on the embryonic brain, and he also cited Hochstetter.

In 1901, Florence Sabin prepared solid (Born) reconstructions of the brain stem of a newborn, and the published illustrations were accompanied by a detailed description of some 90 pages.

In 1904, Wilhelm His, the real founder of human embryology, wrote an account of the human brain for embryos from 3.1 to 160 mm C-R. His had been very interested in photography, and a striking feature of his book is the high quality of the photomicrographs. It is to be regretted that neither this work nor his *Anatomie menschlicher Embryonen* has been translated into English.

In 1919, Ferdinand Hochstetter published a well-known monograph on the human brain from 23 somitic pairs (stage 12) to 125 mm C-R. It includes attractive illustrations of solid (Born) reconstructions and a series of photomicrographs of high quality. In 1923, the same author wrote an account of the development of the epiphysis cerebri. In 1929, he produced a further work, on the mesencephalon and rhombencephalon, based on a study of embryos from 6 mm GL to 250 mm C-R. The illustrations include solid (Born) reconstructions and many photomicrographs of first-class sections. Hochstetter wrote also on the choroid plexuses (1913) and on the development of the meninges (1939).

In 1938, a detailed investigation of the development of the human CNS was written by Barbé. This work, extending to 340 pages, covers the range from 14 mm C-H to 470 mm C-H (320 mm C-R). Many photographs and photomicrographs are included. Unfortunately neither His nor Hochstetter is mentioned.

In 1944, a richly illustrated work on the external features of the later fetal brain (from "4 months") was published by Fontes. A few years later (n.d.), some excellent external photographs (from "3 months") were included in a comparative study by Friant. The work of Fontes was unknown to Friant, as it still is to most authors.

In 1948, a very valuable series of reconstructions of the cranial arteries (in relation to the cranial nerves) was published by Padget, who subsequently (1957) produced a comparable work on the cranial venous system. The stages of the Carnegie embryos she studied are known.

In 1962, the very important study by Bartelmez and Dekaban appeared and was based on the Carnegie Collection. This was the first detailed investigation of the internal structure of the human brain in staged embryos, from stage 10 to stage 22, with the omission of stages 9, 18, 21, and 23. The account is more complete than that of Streeter (revised by O'Rahilly and Müller, 1987a) and was not surpassed until the study of many embryos at each stage by Müller and O'Rahilly began to be published in 1981-1983.

In 1965, an excellent and well illustrated study of the globus pallidus and the corpus striatum was published by Richter. This important work was based on 13 embryos and 35 fetuses from 18.5 to 370 mm C-R.

In 1969, a very valuable and well illustrated investigation of the development of the human cerebral hemispheres was published by Kahle. The work is arranged from the "second month" to the "eighth month" and includes examples from 3 mm GL to more than 275 mm C-R.

In 1970, Windle published a noteworthy study of the "development of neural elements in human embryos of four to seven (postovulatory) weeks." The examples range from about 3 to 16.5 mm GL. Although Streeter's "horizons" were stated to be "helpful," the embryos studied were unfortunately not staged. On the positive side, however, the use of Ranson's pyridine-silver method enabled early neurons and neurofibrillary differentiation to be investigated thoroughly.

In 1975, much useful information concerning the normal and abnormal development of the human nervous system was consolidated by Lemire, Loeser, Leech, and Alvord. Streeter's "horizons" and postovulatory ages were used.

Important studies that have appeared since 1980 will be cited in appropriate places in the various chapters of this text.

The present work is the first book devoted to the staged, embryonic human brain and serves as the necessary prolegomenon for accounts of the fetal period. It should be stressed, however, that very much further work on the fetal brain needs to be undertaken before a level of detail comparable with that now available for the embryonic brain can be attained.

CHAPTER 2

Techniques

A number of matters related to human embryology in general, which also have particular relevance to human neuroembryology, will be summarized in the first few chapters.

The present work is based largely on personal investigations of the embryonic brain, stage by stage, carried out over some two decades and published in more than 30 research articles. The source material was mostly the Carnegie Embryological Collection and involved a careful study of 340 serially sectioned embryos (including 51 instances of silver impregnation), the preparation of graphic reconstructions from 89 brains, and the examination of 55 solid, three-dimensional reconstructions (modified method of Born).* No similarly detailed and adequately illustrated documentation of the developing human brain had been previously attempted, and a comparable study of the fetal brain has to await the future. Moreover, because most studies of the developing brain of other mammalian species are based on timing, but not on staging, comparative tabulation in neuroembryology is still in its infancy, and a standard for the human is an advisable preliminary.

When the first morphological indication of the nervous system is distinguishable, the greatest length of the embryo is only 1 mm. Hence histological study is essential. Throughout the embryonic period, serial sections of excellent quality are indispensable. The examination of isolated or haphazard sections, or of those of poor histological quality, is almost useless and is frequently misleading.

* Specimen numbers are given in the legends (e.g., No 836) and are generally those of the Carnegie Collection.