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V. Problems of Identification and Nomenclature

One major impediment to understanding nervous system development is the general lack of reliable ways to identify specific neuronal phenotypes before recognizable adult features have differentiated. For example, while it is relatively easy to identify the presumptive cerebral cortex quite early in development, the precise location of specific areas (such as the primary auditory area) is problematic, as is the unequivocal identification of specific types of neuron in the cortical plate. The problem until recently has revolved around the fact that classical morphological features have been of little help, except in very special cases such as the dorsal root ganglion and cerebellar granule cells. Young neurons tend to be relatively simple, and may undergo striking morphological changes while differentiating into adult phenotypes. One new approach offers special promise: the histochemical localization of signature gene products that are expressed before adult morphology can be recognized. One particularly good example is the expression of dopamine-related molecules in young neurons of the early neural tube ventral midbrain region generating the presumptive adult substantia nigra and ventral tegmental area (see Kawano et al. 1995). Another example involves characterizing by the expression of homeobox genes the presumptive region of the interbrain neural tube that generates the hypothalamic paraventricular nucleus (Alvarez-Bolado et al. 1995), where neuropeptides such as corticotropin releasing hormone and vasopressin may be used as markers.

Another problem in morphology, discrepancies in nomenclature, has been dealt with in a general way for the adult nervous system in Swanson (1992a). However, modern nomenclature for the adult central nervous system is relatively uniform compared to that in the embryo. There are at least three principal reasons for this. First, much less work has been done on the embryonic brain, and because this field is so difficult, there is much less agreement on basic principles once discussion gets past fundamental subdivisions (vesicles and rhombomeres). Second, there are no modern textbook accounts of central nervous system morphological changes during embryogenesis—synthetic reviews that might lead to greater standardization of terminology. Much of the terminology is scattered in difficult to obtain work that is at least 50 years old. And third, without a clear understanding of how the various parts of the brain differentiate, it is not possible to provide a logical, systematic nomenclature. Nevertheless, authors should attempt to follow reasonable, well-established guides to the use of particular terms. They should be simple, descriptive, unambiguous, and applicable across species, and when a number of synonyms are in common use, that with historical precedence should be favored.

In so far as possible, we have tried to use a nomenclature consistent with that employed in the adult brain (Swanson 1992a).

VI. Comparing Mouse and Rat Brain Development

Mice have recently become very important in developmental neuroscience because of the numerous mutants that have been characterized and catalogued, and because they are so widely used for mammalian genetic manipulation (gene ‘knockouts’ and so on; see Rosenfeld et al. 1988). Mice are preferred to rats for this type of work mostly because of their relatively small size (and thus cheaper purchase, feeding, and housing costs). In contrast, the size advantage here is a major disadvantage for experimental neuroanatomical work. At the present time, the mouse brain is too small for the stereotaxic placement of axonal tracer injections into all but the largest specific cell groups, whereas the rat brain is near the limit of practicality for most cell groups. Thus, the vast majority of neuroanatomical work in mammals carried out over the last 25 years has been in the rat. This naturally raises the question of how similar the brain of rats and mice is during development and in the adult.

Two general statements can be made without fear of contradiction. First, at the level of cytoarchitecture and macroconnections between cell groups, no clear differences have been described between the brain of the adult rat and mouse, although we are aware of no detailed comparisons of rat and mouse neuroanatomy in the literature. There undoubtedly are quantitative differences between the species in terms of the number and precise distribution of neurons for a particular region, and in terms of axon and synapse numbers for particular projections—just as there are subtle differences in their behavioral repertoire. However, adult brain organization in rats and mice is qualitatively very similar. And second, considering how similar early stages of central nervous system differentiation are among mammals in general, it should not be surprising that no significant differences between rats and mice have been described. Again, this is not to

say that differences in gene expression patterns should not be expected to be found between the species. For example, there is accumulating evidence that homologous pathways in different species may use somewhat different complements of neurotransmitters and/or transmitter receptors. Having said this, it appears safe to conclude that, leaving aside differences in scale and time, it is not yet possible to distinguish histologically between the neural plate and tube of the rat and mouse.

Having said this, it is useful to compare the temporal sequence of rat and mouse development, so that advantage can be taken of work carried out in one species or the other. For this, reference should be made to tables published by Schneider and Norton (1979) and Kaufman (1990), where ages for events from attachment of the blastocyst to birth are compared; and to Hoving et al. (1990), where equivalent ages for appearance of somites 8-30 are compared. As a starting point, it is interesting to note that whereas the adult brain weighs about twice as much in the rat as in the mouse (see Sidman et al. 1971), the average gestation time for the rat is only about one day longer (21 vs. 20 days). In practical terms, then, the major difference between rats and mice is in the timing of specific developmental events, and in determining what stage of mouse development corresponds to one of the rat developmental stages illustrated by the atlases in section VIII. Based on information in the references just cited, a useful starting point for comparisons would appear to be that during the first week of gestation rat development is about one to one and a half days behind that in mouse; during the second week it is about two days behind (for example, compare our atlases with those of Theiler 1972); and by birth it is about three to four days behind.

All of this should be tempered by knowledge of several variables. First, of course, different strains of rats and mice may have different average gestation times. For example, this is

18 days for the house mouse (Theiler 1972) and 20 days for Swiss mice; and it is 21 days for Sprague-Dawley rats (used here) versus 22 days for Wistar rats (Iffa-Credo 1987). And second, even within the same litter, differences of up to 20 hours in stage of development can be observed between embryos (see Schneider and Norton 1979), which is probably a reflection of differences in the time of mating and the fertilization of each egg.

In the text thus far, information from the rat has been reviewed when available, and information from the mouse (and other species) has been used when it is not. Important work on the early mouse head region, not referred to above, includes that of Meier and Tam (1982), Tam et al. (1982), Jacobson and Tam (1982), and Trainor et al. (1994).