Stability of Large Cell-Medium Cell Clusters in the Mature Neostriatum*

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Summary. Large neurons of the mouse caudate nucleus contain profuse Nissl material, have a maximal pole-to-pole diameter of up to 25 μm, occur preferentially within a central or CORE zone of the neostriatum, and are almost always located within territories delimited by medium-sized clustered neurons. Examination of coronal sections taken through the head of the nucleus and stained with cresyl violet revealed the absence of age-related pathology as evaluated by three parameters: (1) there was no statistically significant difference in the frequency of large neurons in all areas of the head of the nucleus; (2) the large neuron continued to be confined preferentially to the CORE zone of the head of the nucleus throughout the time period studied; and (3) no statistically significant shifts were detected in the geometry of large cell-medium cell clusters.

Since postnatal age did not significantly affect the frequency, distribution or geometry of large cell-medium cell clusters, data from all animals was combined. This information was used to evaluate the possibility of an interaction between location within or outside the CORE zone and type of large cell-medium cell cluster, but these results were not statistically significant. Therefore, the data analyzed in this study support the view that the geometry of large cell-medium cell clusters is extremely stable in the mouse neostriatum and seems not to be influenced either by age of the animal or by location of the cell grouping.

Key words: Striatum – Cell clusters – Geometry – Aging – Stability

The neuropathology of the aged brain is a topic that has received much attention in recent years. Age-related pathology includes neuronal loss (Brody 1955; Ball 1977; Landfield et al. 1977; McGeer et al. 1977; Sturrock 1979; Wree et al. 1980), gliosis, especially as reflected in increased glia: neuron ratios (Brizzee 1968, 1973) and astroglial hypertrophy (Landfield et al. 1977; Geinisman et al. 1978). Evidence that neuronal cell loss need not be a concomitant of aging has been accumulated for the abducens nucleus (Vijayashankar and Brody 1977) and neocortex (Diamond et al. 1977). Yet, even in the absence of detectable neuronal cell loss, age-related alterations in synapses (Bondareff 1980; Uemura 1980; Geinisman 1981) and dendritic profiles, especially dendritic spines (Scheibel et al. 1975, 1977; Cupp and Uemura 1980) have been observed.

In the neostriatum, Sturrock (1980) reported no quantitatively detectable neuron cell loss in aged mice although several changes, including astrogliosis, occurred in the neuroglial cell population. In contrast, in human putamen, an age-related decrease in neuron cell number has been reported (Bugiani et al. 1978). Neurochemical data indicates that loss of dopamine and reduced turnover of this neurotransmitter (Finch 1973) and a decrease in dopaminergic receptor binding sites (Severson and Finch 1980; Thal et al. 1980) occurs in the aged neostriatum, whereas a decrease in cholinergic receptors (Freund 1980) or in synthesis of acetylcholine (Gibson et al. 1981) occurs in all brain regions in aged mice. However, the retention of other biochemical markers suggests that age-dependent decreases in the striatum may be independent of neuronal cell loss (Makman et al. 1980). Work directed at elucidating the basic organizational format of the mouse neostriatum has revealed the presence of and alignment of large cell-medium cell clusters in young animals (Mensah 1980). This paper will extend this previous work by...
presenting data on both large cell number and on the configurational patterning of large cell-medium cell clusters in the neostriatum of mature mouse.

Materials and Methods

Brains from four 4 month-old, five 10 month-old, and two 27 month-old male C57BL/6j mice without obvious neurological or motor abnormalities and representing adult, mature and senescent populations respectively were obtained from the laboratory of Dr. Caleb Finch. Mature mice (10 month old) are characterized by maximum skeletal size and stable body mass, whereas senescent mice are at the age of average longevity. Brains were fixed in Carnoy's solution and embedded in paraffin. Five micron coronal sections through the head of the caudate-putamen nucleus (rostral to the anterior commissure) were stained with cresyl violet (pH 3.5). Staining was monitored microscopically. Slides remained in the cresyl violet staining solution from 15 min to as long as 24 h, with tissue from older animals requiring longer times to be considered adequately stained. Five sections were selected for detailed analysis from each animal. Four sections were rostral to the crossing of the anterior commissure and the fifth section at the level of crossing of the anterior commissure (Sidman et al. 1971, atlas plates 25 through 28). A camera lucida projection drawing of each selected section was made. Based upon previous work (Mensah 1977), the mediolateral extent of each section was divided into three zones - a lateral peripheral (LP) zone, a CORE or central region, and a medial peripheral (MP) zone. Each of the selected sections contained all three zones. All large cells with abundant Nissl substance were plotted on the drawings and counted, giving a total count of the number of large cells occurring per tissue section and per zone within each section. Age means for all tables are based upon the total number of large neurons per tissue section.

A second quantitative procedure was designed to ascertain possible changes in large cell-medium cell clusters. In individual sections, the proximity of large cells to medium-sized neurons was classified according to one of four categories (Mensah 1980): (1) Cluster + Periphery: a large neuron that occupies a peripheral position in a group of smaller neurons; (2) Center + Cluster: a large cell that occupies a central position in the cell cluster; (3) Cell Pair: A large cell that occurs adjacent to a smaller neuron, but the pair is not part of a cell cluster; and (4) No Cluster: A large cell that has no neighboring neurons within 5 \( \mu \)m of its soma. In each of the five selected sections, the percentage of large neurons occurring in each configuration was tabulated for each of the three zones of the nucleus, with the total number of large cells per section representing 100%. This data was used to test the hypothesis that changes in the alignment of neuronal cell groupings might occur during aging.

As can be seen from Table 1, there is no statistically significant difference in the number of large neurons throughout the timespan represented in this study. In animals of all ages, the only significant variation in large cell number occurs with respect to the predominant presence of this cell type in the CORE or central zone of the nucleus, an observation that is highly significant \( (p < 0.001) \) and was established for the adult mouse neostriatum in an earlier report (Mensah 1977).

The question of age-related changes in medium-sized cell number was approached in this study by restricting the population of medium-sized neurons being considered to include only those forming large cell-medium cell clusters. An analysis of variance was performed separately for the Cluster + Periphery (Table 2) and for the No Cluster patterns. In neither case did age affect the incidence of occurrence of these two patterns. So few large cells occur in the Cell Pair and Center + Cluster configurations that these percentages were combined: age also did not affect the probability of occurrence of these configurations. Significant interanimal variation \( (p < 0.05) \) occurred only in the Cluster + Periphery analysis; therefore, the results of this analysis (Table 2) are included for inspection.

Results

The first analysis was confined to the large striatal neuron with abundant Nissl substance and characterized by a maximal pole-to-pole diameter of 25 \( \mu \)m.