EXPERIMENTAL NEUROLOGY 88, 198–204 (1985)

On the Brain of a Scientist: Albert Einstein

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Received September 25, 1984

Neuron:glial ratios were determined in specific regions of Albert Einstein's cerebral cortex to compare with samples from 11 human male cortices. Cell counts were made on either 6- or 20-μm sections from areas 9 and 39 from each hemisphere. All sections were stained with the Klüver–Barrera stain to differentiate neurons from glia, both astrocytes and oliogdendrocytes. Cell counts were made under oil immersion from the crown of the gyrus to the white matter by following a red line drawn on the coverslip. The average number of neurons and glial cells was determined per microscopic field. The results of the analysis suggest that in left area 39, the neuronal: glial ratio for the Einstein brain is significantly smaller than the mean for the control population ($t = 2.62$, df 9, $p < 0.05$, two-tailed). Einstein's brain did not differ significantly in the neuronal:glial ratio from the controls in any of the other three areas studied.

INTRODUCTION

Albert Einstein is generally conceded to have had one of the greatest scientific minds that ever existed. Whereas neuroscientists may have no idea what characterized the brains of an Aristotle, Galileo, or Newton aside from the extraordinary quality and prodigous quantity of their work, we are fortunate when we turn to a consideration of Einstein. We recently had the privilege of access to sufficient tissue from Einstein's brain to make certain quantitative measures. Because of the method used for preparing the tissue for histological examination, we were limited in the kind of analysis we could make.

[1] Appreciation is extended to Ruth E. Johnson and E. Rosalie Greer, Ph.D. for their excellent technical assistance and to Doug Coe for his editorial critique. Dr. Harvey's current address is Weston, MO 64098.

0014-4886/85 $3.00

The French mathematician, Jacques Hadamard, was interested in determining the nature of the mental processes of mathematicians. He conducted a psychological survey of the mental images or internal words which mathematicians use . . . "whether they are motor, auditory, visual or mixed." When queried by Hadamard, Einstein replied that written and spoken words did not seem to play any role in his mechanism of thought. He felt that "a combinatory play of certain signs and more or less clear images" seemed to be the essential features in productive thought. Einstein stated it was clear the desire to arrive finally "at logically connected concepts was the emotional basis of a rather vague play of visual and some muscular types" (10).

It is doubtful whether any single region of the brain mediates all cross modal interactions. When studying Einstein's brain, we found it necessary to choose regions which seemed to follow the lead provided by his introspection. We decided to examine cortical association regions of the superior prefrontal and inferior parietal lobes in the right and left hemispheres. Neuronal:glial ratios in these areas were calculated as representing one valid measure of the status of neuronal activity (4).

METHODS

A control base of male human brains had been obtained during the last few years from the Veteran's Administration Hospital in Martinez, California. These included 11 brains from individuals 47 to 80 years of age who had died from nonneurologically related diseases. The average age was 64 years; Einstein was 76 at the time of death. (Chronological age is not necessarily a useful indicator in measuring biological systems. Environmental factors also play a strong role in modifying the condition of the organism. One major problem in dealing with human specimens is that they do not come from controlled environments.)

From the Formalin-fixed brains of former VA Hospital patients, blocks of cerebral cortex about 1.25 cm^2 were removed from area 9 (superior frontal gyrus on the dorsal lateral surface) and area 39 (inferior parietal lobule, including the anterior lip of the angular gyrus surrounding the termination of the superior temporal sulcus) from both right and left hemispheres (see Fig. 1). The blocks were cut as close to perpendicular to the surface as possible and deeply enough to include the underlying white matter. Of this group of 11 brains, frozen sections cut at 20 μm were taken from 8 brains and celloidin sections at 6 μm were obtained from 3 brains.

The Einstein brain blocks from areas 9 and 39 from the right and left hemispheres arrived in the laboratory already embedded in celloidin. Six-micrometer sections were taken from Einstein's brain. Four to six sections

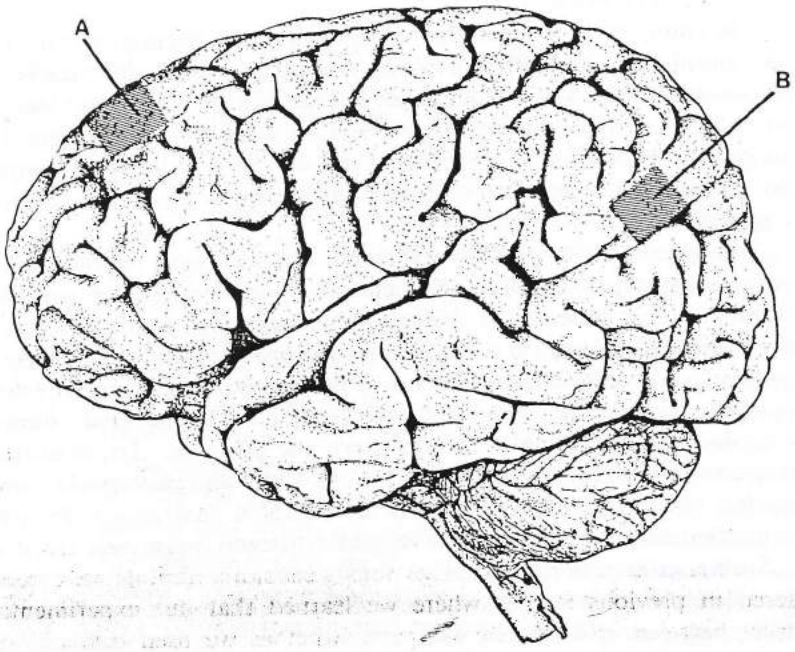

FIG. 1. A lateral view of the human brain indicating the position of the samples removed for cell counts. A represents the sample from area 9 and B, area 39.

were cut from each block, Einstein's and the controls'. All brain sections were stained with the Klüver–Barrera, luxol fast blue cresyl echt violet stain, to differentiate neurons from glia. After staining, one of the six sections from each block was chosen for study. To assure the vertical orientation of the cell counts, a straight line, perpendicular to the crown of the gyrus, was drawn with a red pen on the coverslip. This ruled line was kept just out of the field of vision as the cell counts were made, beginning at layer II and extending into the subcortical white matter. Cell counts were made with the aid of an oil immersion lens (100×) and an eyepiece (10×), with a ruled graticule placed in the eyepiece.

Since the demarkation between cortical gray matter and the underlying white is not as clear in the human brain as in the rodent brain (3, 5), the number of microscopic fields sampled was more arbitrary. Counts were made into the white–gray boundary for one or two fields depending on the density of the myelinated fibers, which are clearly demonstrated with this stain. Two vertical columns were counted in the brain sections and the average number of both neurons and glial cells per microscopic field was determined.

The counts were made in the following manner: Beginning at the junction of layer I with layer II, the purple-stained neurons with clearly defined nuclei and nucleoli were counted in a single microscopic field. The position of each neuron in the field was marked on a ruled sheet of paper identical in format to the grid within the eyepiece. In this way the investigator could be certain which neurons were tabulated thereby preventing oversight or duplication.

Two types of glia fulfilling a standard criterion were counted: astrocytes with large, clear, blue-stained nuclei and oligodendrocytes with smaller, deeply stained, blue nuclei. Visual differentiation of astroglial nuclei from those of small neurons is a frequently cited problem in neurocytologic work of this type. Previous studies attest to the effectiveness of cresyl echt violet in distinguishing between these cell types (6, 8). The glial counts were recorded on the same sheets as were the neurons. To determine the neuronal:glial ratios, the counts of the astrocytes and oligodendrocytes were pooled from each section to provide a single glial count. In addition, neuronal:astrocytic and neuronal:oligodendrocytic ratios were calculated.

Shrinkage factors for frozen sections versus celloidin sections have been considered in previous studies where we learned that our experimental differences between groups were the same whether we used celloidin or frozen sections (3).

RESULTS

To test whether the Einstein brain differed significantly from the population from which the 11 control brains were sampled, the mean and the standard deviation for the sample were taken as estimates of the population parameters μ and σ. Then, the deviation of the neuronal:glial ratio for Einstein's brain from the mean neuronal:glial ratio for the sample was computed in standard deviation units. This score was referred to a Student's t distribution with nine degrees of freedom, because two degrees of freedom were lost in estimation, one for the mean and one for the standard deviation. The results of this analysis suggested that in left area 39, the neuronal:glial ratio for the Einstein brain was significantly smaller than the mean for the control population ($t = 2.62$, df 9, $P < 0.05$, two-tailed). Einstein's brain did not differ significantly in the neuronal:glial ratio from the controls in any of the other three areas studied (see Table 1).

Neither the neuronal:astrocytic nor the neuronal:oligodendrocytic ratios by themselves were significantly different in any of the areas studied, comparing Einstein's brain with the control brains. It was necessary to pool all glial cells counted to attain statistically significant differences, but the data indicated that one glial cell type alone was not responsible for the difference noted.

TABLE 1

Neuron:Glial Ratios between Einstein's Brain and Those from 11 Males (47 to 80 Years of Age)

Region	$N:G_{\bar{x}}$ (11 males)	SD	$N:G_{\bar{x}}$[a] Einstein	% Δ	*P*
Left area 9	1.849	0.661	1.04	77	NS
Right area 9	1.754	0.755	1.16	51	NS
Left area 39	1.936	0.312	1.12	73	0.05
Right area 39	2.026	0.588	0.92	120	NS

[a] In every area Einstein had a smaller N:G ratio, but by comparing one brain with 11 having relatively large SDs, the results showed only one area to be significantly different.

DISCUSSION

We studied the prefrontal and inferior parietal association areas of Einstein's brain because such areas are known to be concerned with "higher" neural functions. These regions do not directly receive primary sensory information, but rather, as their name implies, "associate" or analyze inputs from other brain regions. The association cortices are the last domains of the cortex to myelinate, indicating their comparatively late development. It is not possible at present to identify with a high degree of specificity the independent functions of these zones. Characterizing the modes of function of the cortical association regions may prove to be one of the most elusive of all neurobiological tasks.

Considering the fact that the tissue blocks were already embedded in celloidin when they became available for histological study (thereby making Golgi or other more revealing studies impossible), we decided that differential cell counts constituted a potentially meaningful measure of the functional status of the brain. Not only is the cerebral cortex rich in its distribution of nerve cell bodies, but glial cell types also constitute a large fraction of the mammalian cerebral cortex. Bass *et al.* (2) reported that neuronal:glial ratios decrease as the phylogenetic scale is ascended from mouse to man. On the other hand, Rockel *et al.* (16) demonstrated remarkable consistency in the absolute number of nerve cells in cortical strips from pial surface to white matter, regardless of the mammalian species or cortical thickness. Such uniformity in number was found, for instance in the motor cortex (area 4) and in the somatosensory cortex (area 3b), although not in the visual cortex (area 17) which has about two-and-one-half times as many neurons as other cortical areas.

The thicker cortices of large mammals seems to be primarily a function of large nerve cell bodies, more extensive dendritic and axonal systems, and concomitantly, more numerous glial cells. Furthermore, environmental

enrichment and other augmented neural inputs in the rat increase all these neuronal measures of enhanced cell activity together with an increase in the number of glial cells (1, 3, 5, 7, 8, 11).

An increase in the number of glial cells without a significant increase in the neuronal population suggests a response by glial cells to greater neuronal metabolic need. All these data suggest that neuronal:glial ratios in selected regions of Einstein's brain might reflect the enhanced use of this tissue in the expression of his unusual conceptual powers in comparison with control brains.

The rationale for choosing the prefrontal and infraparietal regions was based on the speculations of several investigators. Comparative anatomical studies indicate that the parietal lobe expands progressively to crowd the motor, auditory, and visual cortices forward, downward, and backward, respectively. Studies of endocasts by von Bonin (17) comparing parietal and frontal lobes led him to conclude that it was this expansion of the parietal lobe which was most characteristic of the human brain. According to Passingham (15), on the other hand, the prefrontal cortex is thought to subserve in unique fashion those activities and qualities which distinguish man from other mammals and primates. The anterior portion of the frontal lobe appears to be engaged in the temporal organization of behavior, e.g., the planning and establishment of behavioral strategies (13). From lesion studies in animals and human beings, it has been shown that the prefrontal cortex is involved in mechanisms of attention, recent memory, capacity for abstracting and categorizing information, and the formulation and initiation of actions. The parietal lobe has been associated with the integration of visual, auditory and tactile modalitities and with problems of self-awareness, imagery, memory, and attention (14). Lesions in the inferior parietal region (area 39), especially of the dominant side, result in inability to read words or letters, and in gross impairment in writing, spelling, and calculation [(12), for recent review see (9)].

One mathematician with a lesion in area 39 found it difficult to draw or write formulae and could not use a slide rule. However, at night he could visualize the correct construction of the formulae (3). A mathematician at the University of California, Berkeley, Calvin Moore, stated that he develops a feeling of reality for abstract concepts. They exist in his brain and can be manipulated like real objects. It is the interplay of these objects which may contribute to mathematical insight. It has also been reported that in the educated individual, lesions in the inferior parietal lobule of the dominant hemisphere result in the loss of versatility of imagery and the capability for complex thinking (3).

The possible relationship of these phenomena to Einstein's intellectual gifts served as a guide for the selection of our tissue samples. It therefore seemed conceivable that area 9 of the prefrontal cortex and/or area 39 of

the inferior parietal cortex on the left and/or right sides might be characterized by smaller than normal neuronal:glial ratios.

Our data suggest that the neuronal:glial ratio in area 39 of the left hemisphere in Einstein's brain is significantly lower than that of the control subjects, or of the other regions in which measurements were made (e.g., area 39, right; area 9, left and right). Mental activities ascribed to area 39 fit many of the comments that Einstein himself made about his conceptual processes.

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