Alterations in cortical thickness and neuronal density in the frontal cortex of Albert Einstein

Britt Anderson a,b,*, Thomas Harvey

aDepartment of Neurology, University of Alabama at Birmingham, Birmingham, AL 35294-0007, USA
bNeurology Service, Birmingham Department of Veterans Affairs Medical Center, Birmingham, AL, USA

Received 11 March 1996; revised version received 26 April 1996; accepted 26 April 1996

Abstract

Neuronal density, neuron size, and the number of neurons under 1 mm² of cerebral cortical surface area were measured in the right pre-frontal cortex of Albert Einstein and five elderly control subjects. Measurement of neuronal density used the optical dissector technique on celloidin-embedded cresyl violet-stained sections. The neurons counted provided a systematic random sample for the measurement of cell body cross-sectional area. Einstein's cortex did not differ from the control subjects in the number of neurons under 1 mm² of cerebral cortex or in mean neuronal size. Because Einstein's cortex was thinner than the controls he had a greater neuronal density.

Keywords: Intelligence; Brain; Einstein; Neurons; Cerebral cortex

Humanity is fascinated by the brains of geniuses [6,9, 16,19,21] and scientists have measured brain size and gyri to explain the intellectual bounty of great men. While such neumorphologic investigations may now seem quaint, at odds with politically popular beliefs of general intellectual parity and the modularity of mental operations, these prejudices deserve re-examination. Intelligence is not a mystical psychological process which confers smartness in proportion to its presence [7], but a psychometric index for the effects of neurobiological features which affect the efficiency of neural operations [1,23]. The presence of such biological features is indicated by the anatomical and physiological correlations between brain and intelligence, e.g. the brain volume-IQ correlations [2,10,15,22,24–26].

Studying the brain of a genius can play a small and titillating role in the quest to identify these neurobiological features. Single case studies, while not definitive, may point the way towards solutions and have a long history in cognitive research [4]. These considerations prompted us to undertake precise quantitative measurements of the cerebral cortex of Albert Einstein, our most renowned genius. Using the optical dissector technique neuronal density, the number of neurons under 1 mm² of cortex, and the cross-sectional area of a random selection of cortical neurons were measured and compared to five elderly men.

Einstein died in 1955, at age 76 years, of a ruptured abdominal aortic aneurysm. An autopsy was performed 7 h postmortem. The brain was fixed in formalin for several months. After fixation the cerebral cortex was divided into numbered blocks and embedded in celloidin. The brain region from which the Einstein block was taken is shown in the diagram in Fig. 1. The fact that the block is no. 9 and probably includes brain tissue from Brodmann area 9 is coincidental. This diagram was prepared at the time of the original processing of Einstein’s tissue for celloidin embedding. The celloidin blocks were kept in alcohol until use.

The control subjects were all men, ages 63, 63, 64, 71, and 79 years. All died non-neurological deaths and routine neuropathologic examinations were unremarkable. The area of cortex studied for each subject was right middle frontal gyrus midway between the frontal tip and the central sulcus and corresponded topographically with the available area of Einstein’s prefrontal cortex. Similar to Einstein’s tissue, all control blocks were immersion
fixed in formalin, followed by celloidin embedding and maintenance of the celloidin blocks in 80% ethanol. Most of the control tissue was kept in 80% ethanol for only weeks whereas Einstein's tissue had been maintained in this way for decades.

Sections were cut at a thickness of 40 μm using a sliding microtome and stained with cresyl violet. Under microscopic examination and using the Neurolucida computer program (MicroBrightField, Colchester, VT) four measurements of cortical thickness were made on a single section at 200 μm intervals (see Fig. 2).

With a 100x objective each mark, as illustrated in Fig. 2, was sequentially moved to. A grid of 20 × 20 μm was overlaid and neurons counted while focusing down through the section. Neurons in focus at the start of the section were not counted, nor were any neurons counted that touched the lower and left grid exclusion lines. Neurons were counted when their cellular and nuclear membranes came into sharpest focus. A nucleolus was not required for a neuron to be counted. Neurons were differentiated from glia based on size and staining patterns. The number of neurons per dissector was recorded as was the depth of the dissector. Most dissectors contained zero or one neuron. The maximum was four. For all brains except one it was necessary to make four passes through the cortex to count the 100 neurons that was the study goal. In one brain, because of a thicker cortex, a sufficient number of neurons was achieved with only three passes through the cortex. This approach is basically the optical dissector [8,12,20].

While these cells were being counted the cell tracing software of Neurolucida was used to trace each cell body area at the cell's greatest diameter to provide the cross-sectional areas of a systematically random selection of neurons.

Neuron density was computed by dividing the number of neurons counted by the area of the grid square multiplied by the total dissector depth (measured from the microscopic section) for all dissectors on each pass through the cortex. The reliability of these estimates was high (>0.95 by Cronbach's α). To calculate the number of neurons under 1 mm² of cerebral cortex the neuron density was multiplied by the cortical depth.

The neuron density for each of the passes through Einstein's cerebral cortex was compared to similar measures for the control group by the Mann–Whitney U-test. The same test was used to compare the estimates of the number of neurons under 1 mm² of cortex and the size of the cerebral cortical neurons.

A non-parametric test was used because the normality of the data could not be established with this small sample size. The reason for using multiple measurements from Einstein's and the controls' tissues as individual 'samples' was to strengthen the conclusion that Einstein's greater results for some measures were not due to chance. With only six specimens the odds that Einstein would have had, for example, a greater measured neuronal density was 1/6 by chance alone. However, if Einstein's neuronal density was truly the same as the control population, the odds that repeated assessments of neuronal density would have been consistently greater than the controls should have grown smaller with each repetition. By using each measure as an individual 'sample' and applying the Mann–Whitney U-test it was possible to quantitate the odds for such results.

Einstein's cortex was thinner than the controls and more densely populated with neurons. The mean distance through the right frontal cortex of Einstein was 2137 μm and for the control population it was 2659 μm (P = 0.002, \( U = 0.0, n's 20/4 \)). Einstein had more neurons per mm³ of cortex.
cortex with a mean for the four dissector paths through the cortex of 46,995 neurons/mm\(^3\) compared to the mean for the control population of 34,962 neurons/mm\(^3\) (P = 0.015, U = 8, n's 19/4).

Einstein's cortex did not differ in the size of the neurons' somas or in the number of neurons contained within a column of cortex 1 mm\(^2\) at the surface. The mean cross-sectional area of the neurons in Einstein's right frontal cerebral cortex was 63 \(\mu\)m\(^2\) (35 SD), and 68 \(\mu\)m\(^2\) (46 SD) for the control population (P = 0.85, U = 32,713, n's 501/132). The mean number of neurons in a column of cortex 1 mm\(^2\) at the cortical surface was 98,654 for Einstein and 87,364 for the controls (P = 0.26, U = 24, n's 19/4).

Studies performed on Einstein's brain tissue in the early years after his death were only qualitative, and not showing any important differences from normal subjects, were not published. One prior study of Einstein's cerebral tissue has been formally reported. Diamond et al. [5] measured the ratio of neurons to glia in the frontal and parietal cerebral cortex. Diamond and colleagues reported a greater glia/neuron ratio for Einstein's tissue. Since they reported neither the absolute numbers of neurons nor their size, their results cannot be directly compared with this study. The results for neuron density and neuron number obtained from this investigation are in general agreement with prior estimates [13,27].

The differences between Einstein's tissue and the control tissue is primarily due to Einstein having the same number of neurons packed into a thinner cortex. Age or dementia-related atrophy are not explanations for this finding since Einstein's cortex was compared to elderly controls and because there is no history that Einstein suffered from cognitive decline.

The thinner cortex is not due to technical factors. Both Einstein's tissue and the controls' were embedded in celloidin, sectioned, and stained similarly. As the brain tissue is completely dehydrated in an alcohol-ether solution as part of the celloidin embedding process, the subsequent duration of the storage in 80% ethanol should not result in greater tissue shrinkage with longer storage. A precise measure of the size of the tissue block for Einstein prior to its embedding was not available to quantitate tissue shrinkage. In general, celloidin embedding is felt to result in less tissue distortion than paraffin techniques, and probably frozen sections that are subsequently dehydrated.

Could the difference in cortical packing density in any way account for Einstein's superior intellectual skills? An increase in neuronal density could translate to an overall increase in the total number of cortical neurons if Einstein's brain volume was equal to or greater than the control cases. Unfortunately, it is not currently possible to provide an accurate measurement of total cerebral cortical volume or surface area for Einstein. This measure is necessary to translate a neuronal density measure into an absolute neuronal number measure. While it is not possible to provide a measure of total cerebral cortical volume the available data does not suggest that Einstein's cerebral cortical volume was greater than controls. Einstein's brain weight was 1230 g, which is within the average range, but below the mean, for men of his age [11,14]. In addition, the length of the hemispheres (17.2 cm left/16.4 cm right) and the width of the hemispheres (7.5 cm left/7.5 cm right) are not significantly different from 'eminent' and non-eminent men born in the 1800s [21].

An alternative consideration would be that an increase in neuronal density might be advantageous by decreasing interneuronal conduction time. Interneuronal conduction time has been posited as a limiting feature of the development of brain size and cortical connectivity [17,18]. An increase in neuronal density has been implied as a possible mechanism to explain how women and men may achieve comparable IQ's [27] even though women's brains are smaller when corrected for body size [3].

This work would not have been possible without the superb technical assistance of Valisa Rutledge.


