# A QUANTITATIVE STUDY OF BRAIN MORPHOMETRY AND SENILE PLAQUE FORMATION IN SDAT

A Study on Heterogeneity

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## DECLARATION

The measurement of the cranial cavity volume and fresh brain volume was performed by Dr. D. O'Donovan and Professor D.I. Graham in the control and SDAT patients respectively. Professor D.I. Graham dissected the brains used in this study and the patients were mentally assessed by Professor Caird and his staff. The rest of the quantitative morphometry and all the technical work involved in this thesis was performed solely by the author. The research of the literature and the write up of the thesis was similarly performed by the author under the supervision of Professor D.I. Graham and Professor J. McCulloch.

## ABBREVIATIONS

SDAT - Senile dementia of the Alzheimer type

AD - Presenile Alzheimer's disease

CCV - Cranial cavity volume

BV - Brain volume

PHF - Anti-paired helical filaments

ChAT - Choline acetyl transferase

MTS - Mental test score

SEM - Standard error of the mean

SD - Standard deviation

PM - Post mortem

NK - Not known

Hrs - Hours

Q10 - Quantiment 10 image analysis system

NS - No significance difference

Abs - The absolute difference in plaque controls regardless of whether positive or negative.

% - $\frac{\text{Count 1 - Count 2}}{\text{mean of Count 1 + 2}} \times \frac{100}{1}$

* - Asymmetric plaque counts and/or a significant difference

GABA - Gamma amino butyric acid

MID - Multi-infarct dementia

AChE - Acetyl cholinesterase

Neuropath- Neuropathological

PET - Positron emission tomography

SPET - Single photon emission tomography

Sup Temp - Superior temporal, Mid-Temp - Middle temporal,

Inf Temp - Inferior temporal

## SUMMARY

Due to a lack of consistency in the literature regarding the methodology of plaque counting, it was necessary to establish a reproducible method for counting plaques. This would allow the quantitative neuropathology to be integrated into the longitudinal study and correlated with various aspects of Alzheimer's disease such as neuropsychology, neuro-imaging and neuropharmacology.

The volume of the brain and the cranial cavity volume (CCV) were determined in cases of senile dementia of the Alzheimer type (SDAT) and age matched controls. This was to provide correction factors for the plaque counts and also to determine whether or not there was any atrophy of the brain in SDAT. The volume of each individual lobe and the amount of cortex, white matter and the size of the ventricles were also measured. There was some loss of tissue in the normal aged brain, but even more in SDAT. There was loss of cerebral cortex in the left temporal, frontal, parietal and occipital lobes, whereas in the right hemisphere only the cortex of the parietal lobe showed any atrophy. When comparing the size of the ventricles it was found that even though the ventricles of the SDAT group were generally larger than the controls, the difference was not statistically significant.

Plaque counts were undertaken on both frozen and paraffin sections and 7 different staining techniques employed to establish which method was the most suitable for demonstrating senile plaques. The highest plaque counts were obtained on the

frozen sections stained by the King's amyloid and the von Braunmuhl silver impregnation techniques. The King's amyloid technique was more reproducible with less variation in staining. It also gave the highest plaque counts in all but a few cases and was therefore employed throughout this study for the quantitative plaque counts. The quantitative plaque counts were corrected for the effects of fixation and atrophy of the brain.

Once it had been established that the King's amyloid was the staining technique which would be employed, the reproducibility of the method of counting plaques had to be evaluated. The number of plaques per $mm^2$ were counted manually using an image analyser at 1, 3 and 6 reference points in each region of the brain being examined and the standard deviation (SD) of the difference in the day to day variability examined. The smaller the SD number, the more reproducible the plaque counts, and the greater the SD number, the less reproducible the plaque counts. By increasing the number of reference points from 1 to 6 in each brain region, the day to day error in the reproducibility of plaque counts was halved in the superficial layers and quartered in the deep layers. The day to day error in the mean plaque count was $\pm$ 0.7 plaques/$mm^2$ ($\pm$ 3.9% of the day 1 count). It was therefore decided that counting plaques at 6 reference points was sufficiently accurate and reproducible for the purpose of this study.

When examining both the number and the area of plaques it was found that there was a significant increase in the number and the area of plaques in the SDAT group compared to the age

matched controls. In fact in 4 control cases there were no plaques at all and in the other 2 there were very few. This suggested that SDAT was not simply a continuation of normal ageing. Since in the controls the vast majority of the plaque counts was zero, the various asymmetric studies on plaque counts were confined to the SDAT cases.

When examining the literature on choline acetyl transferase activity (ChAT) and mental test scores (MTS), it appeared that when a mean plaque count of 10-12 was reached that the ChAT activity and MTS had fallen to approximately 50% of normal. Based on these well established data sets it was decided that a 5 plaque change represented a biologically significant difference. Since a 5 plaque change between 1-6 and 45-50 plaques is a percentage change of between 500% and 10% respectively, it was decided that a second criterion was required. Since ChAT activity was substantially reduced at lower plaque counts (below about 12 plaques) and that a mean plaque count of 12 can segregate dements from non-dements, a 5 plaque change below 12 will give an approximate percentage change of between 40%-500%. Therefore, in this study asymmetric plaque counts would have to fulfil both criteria of a 5 plaque change as well as a minimum of a 40% difference before the counts would be called asymmetric. Having established a method based on biological criteria, the method was then tested on 6 SDAT cases to establish if it was sensitive enough to detect any asymmetries in plaque counts.

When comparing the plaque counts between the left and right

hemispheres of the SDAT brain, it was concluded that some of the interhemispheric plaque counts were asymmetrical. Within each individual brain there was also evidence of intraregional and interregional heterogeneity. The interhemispheric asymmetry was non-directional, i.e. sometimes the highest plaque counts were in the left hemisphere and sometimes in the right. In different cases it was not always the same regions that were aysmmetric.

There was a high degree of positive correlation in the left temporal lobe with the area of plaques. There was also good negative correlation in the right frontal lobe with both the number and area of plaques. There was an excellent positive correlation between the number of plaques and the area of plaques, with the correlation being slightly better in the deep layers of cortex.

Finally, the 6 SDAT brains used in this study showed that each brain was individual. There was no region in either hemisphere that consistently gave the highest plaque count.

# INTRODUCTION

Initially a grant was awarded by the Wellcome Trust to Professors McCulloch and Brooks for research into a longitudinal study of patients with senile dementia of Alzheimer type (SDAT). There was a wish to examine a variety of features whereby neuropsychology, neuro-imaging, quantitative neuropathology and neuropharmacology were correlated and integrated. The literature at that time indicated that by determining the number of senile plaques and/or neurofibrillary tangles, it was possible to provide a measure of the severity of the disease. When the literature was examined in greater depth, it was clear that there was a lack of consistency. Various attempts had been made to correlate the number of plaques with, for example, choline acetyl transferase (ChAT) activity and mental test scores (MTS). However, the literature seemed flawed with a lack of detail and inconsistency, not only in the method used to stain the senile plaques but also in the way in which they were counted. Part of this thesis, therefore, was to establish a quantitative neuropathological method for counting plaques which would be reproducible and could be applied to the longitudinal study.

Alzheimer's disease is the most common cause of dementia and although it is rare in people under 45 years of age, it affects up to 5% of the population over 65 years of age and 20% over the age of 80.[1] Alzheimer's disease accounts for approximately 50% of people diagnosed as being demented and is a contributory factor in a further 20%.[2]

In the past the difference between presenile Alzheimer's disease (AD) and senile dementia of the Alzheimer type (SDAT) used to be based on the age of the demented patient, i.e. under the age of 65 years the patient had AD and over the age of 65 years the patient had SDAT. Nowadays there is evidence that there are clinical, structural and neurochemical differences as well as the age of onset of the disease which distinguish between Alzheimer type I syndrome (late onset, after 70 years: SDAT) and Alzheimer type II syndrome (early onset, before 70 years: AD).[3]

The clinical diagnosis of Alzheimer's disease is reported to have a 70% accuracy[4] and since the clinical diagnosis is not absolute, Alzheimer's disease must be confirmed neuropathologically by the presence of numerous agyrophilic plaques and by neurofibrillary tangle formation. There are well laid down criteria for the diagnosis of Alzheimer's disease,[5] although the staining techniques used to quantify the plaques should be evaluated in each laboratory to determine the most sensitive method.

**Quantitative Morphometry**

Many workers have assessed the volume of the brain over the past two decades to determine whether or not there was any atrophy of the brain in Alzheimer's disease, or whether any atrophy present was due to normal ageing. Tomlinson et al. studied the brains of 28 non-demented[6] and 50 demented old people[7] and found that there was moderate cortical atrophy of only 4 of the 28 non-

demented brains, and in 16 of the 50 demented brains there was generalised atrophy with particular involvement of the temporal lobe. Terry et al. reported that the cortex was 9-10% thinner in SDAT,[8] Prohovnik et al.[9] reported a loss of grey matter, while Brun and Englund reported a loss of white matter in addition to grey matter.[10,11,12]

Davis and Wright devised a balloon method for determining the cranial cavity volume (CCV) and determined that the CCV remains relatively constant with age.[13] Using this method, Hubbard and Anderson[14] determined that in SDAT below the age of 80 there was global loss of brain tissue, whereas above the age of 80 there was selective loss of temporal cortex. The purpose of the quantitative analysis of the brain in this study was two fold. Firstly, to establish exactly where in the SDAT brain this atrophy occurred, i.e. was it the same in both hemispheres, was any particular lobe involved and was it cerebral cortex, white matter or both that were involved in SDAT? Secondly, the BV/CCV ratios of the unfixed and fixed brain would be used to calculate the appropriate correction factors to correct the plaque counts for the effects of fixation and brain atrophy.

We used the balloon method of Davis and Wright to determine the CCV and a modified method of Hubbard and Anderson to calculate the amount of cerebral cortex, white matter and ventricular volume.

**Staining of Senile Plaques**

Since senile plaques were identified in 1892 by Blocq and Marinesco, many different staining methods have been used for the identification of senile plaques, but few attempts have been made to compare the sensitivity of the methods. When Dayan [15] compared the von Braunmuhl technique with the Glees and Marsland method, the more convenient Glees and Marsland on paraffin sections was chosen to quantify plaques. Lamy et al.[16] compared 7 staining techniques, on paraffin sections only, and concluded that the modified Bielschowsky showed the most complete picture of the changes seen in Alzheimer's disease. They stated that since the modified Bielschowsky stained the greatest number of senile plaques it should be considered a reference method in the diagnosis of Alzheimer's disease. However, they also stated that due to serious difficulties with the method, it could not be recommended for routine use. In this study 7 staining techniques were compared employing both frozen and paraffin sections to see which was the most sensitive method for demonstrating senile plaques, i.e. King's amyloid and the von Braunmuhl silver impregnation techniques on frozen sections and the Congo red, sirius red, thioflavine T, Palmgren and an immunocytochemical method using antibodies to paired helical filaments (PHF) on paraffin sections. The paraffin sections were corrected for the effects of paraffin processing and also for the difference in section thickness between the frozen sections cut nominally at 25 microns and the paraffin sections cut nominally at 13 microns. This was to allow a direct

comparison between the number of plaques demonstrated in the frozen sections with those demonstrated in the paraffin sections.

**Quantitation of senile plaques**

Since there was inconsistency in not only the staining method used to quantify plaques but also in the way in which plaques were counted, a suitable method for counting plaques, which was both reproducible and accurate, had to be found. Wilcock and Esiri[17] used the von Braunmuhl technique and took the mean of 10 random fields for the plaque count, Dayan[15] used the Glees and Marsland technique and calculated the lesions per unit volume from 50 random fields, Hubbard and Anderson[14] used the King's amyloid method and a point counting method to determine the percentage of cortex occupied by senile plaques, and Ulrich[18] used the thioflavine S method and graded the plaques between 0-3 where 0 = minimal changes, 1 = slight changes, 2 = moderate changes and 3 = severe changes. This was performed on an unknown number of fields. These are just some of the variable methods that have been used to quantify senile plaques over the years.

Since senile plaques are an important quantitative neuropathological measure of the severity of SDAT which correlate with dementia scores[24] and with deficits in major neurotransmitter systems, e.g. the cholinergic systems,[23] it was important that a standardised method for counting plaques was employed. The method had to be reproducible with as little day

to day variation as possible so that whatever region had the highest plaque count the first time it was quantified, it also had the highest plaque count the next time it was quantified. The variability and reproducibility of the plaque counting method was examined. This was evaluated by measuring the standard deviation of the difference in plaque counts performed on 2 separate days at various reference points on the section. The smaller the standard deviation, the more reproducible the method, i.e. there was less variation between the 2 plaque counts. The plaque counts were made in the superficial (1-3) and deep layers (4-6) of cortex and the number of plaques/$mm^2$ and the area of plaques, in square microns, were measured using a Quantimet 10 image analysing system from Cambridge Instruments (Q10).

**Asymmetry of SDAT**

When quantifying plaques and tangles and correlating them to various neurochemical substances such as choline acetyl transferase (ChAT) activity or to mental test scores (MTS), the majority of centres adopt the procedure of cutting the brain in the mid-sagittal plane and performing the neuropathological studies on one hemisphere and the neurochemical studies on the other. By doing so they are assuming that the disease process and the changes associated with it are symmetrical. Some workers such as Ball[19] and Moossy et al.[20] found no significant difference between the left and right hemispheres when quantifying plaques and tangles, whereas Wilcock and Esiri[21]

found that there was a statistically significant difference between the 2 hemispheres. Arendt et al.[22] found a marked difference in the number of neurons and senile plaques between the 2 hemispheres although the differences failed to reach statistical significance. Arendt et al.[22] say that there was a variable number of plaques in different cortical areas of each case, and the region within which plaque counts were more pronounced varied from case to case. Moossy et al.[20] found no significant difference in the plaque counts between the 2 hemispheres and therefore concluded that the morphological lesions in Alzheimer's disease were bilaterally symmetrical.

If plaque counts were symmetrical, then the difference between them would be zero. If there were 10 plaques in the left hemisphere and 1,000 plaques in the right hemisphere, then these plaque counts would be clearly asymmetric. However, if there were 10.0 plaques in the left hemisphere and either 10.1, 10.01, 10.001 etc. plaques in the right hemisphere, then it could be argued statistically that the null hypothesis was not upheld and that these plaque counts were also asymmetric. The problem was just how small or large a number represented a meaningful asymmetry.

Another problem would be if the left-right asymmetries were non-directional, i.e. sometimes the highest plaque count was obtained in the left hemisphere and sometimes it was obtained in the right, this probably explains why the results obtained by Arendt et al. failed to reach statistical sigificance since the highest plaque counts obtained in certain regions in the left

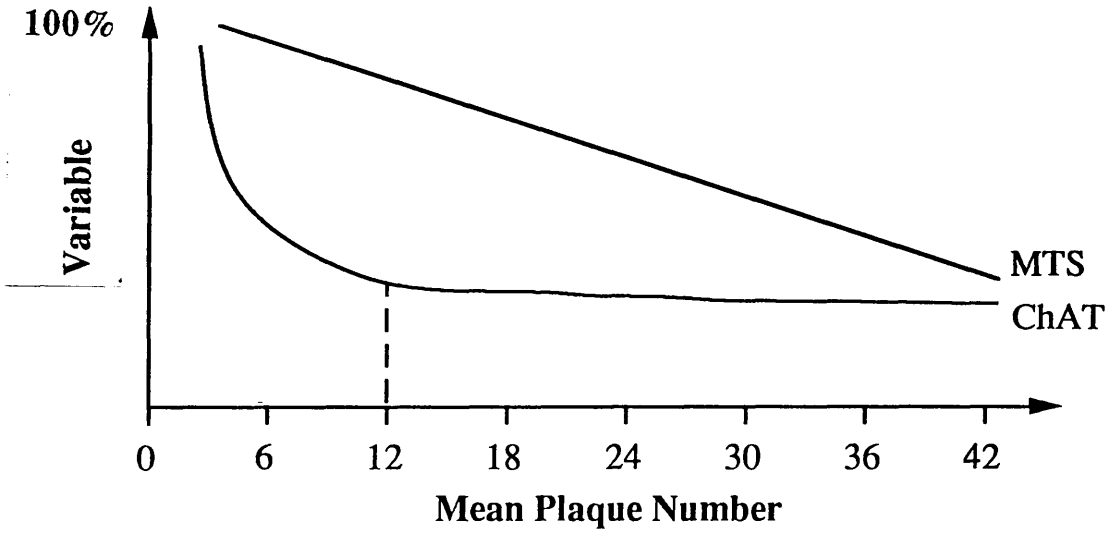


Figure 1 shows a diagramatic representation of the substantially reduced ChAT activity at lower plaque counts (approximately 45% of Normal when a mean plaque count of 12 is reached) and the broadly linear MTS.

MTS = Mental test score
ChAT = Choline acetyl transferase

| Mean Plaque Count | ChAT Activity | MTS |
|---|---|---|
| 1-5 | 75% | 75% |
| 6-10 | 50% | 55% |
| 11-20 | 45% | 30% |

Figure 2 shows the approximate percentage level of ChAT and MTS with the mean plaque count.

MTS = Mental test score
ChAT = Choline acetyl transferase

hemisphere would be cancelled out by the higher plaque counts obtained in other regions in the right hemisphere. A non-statistical method therefore had to be found which had some biological validity and could test the differences, if any, between 2 individual plaque counts. Based on the classical data sets correlating ChAT activity[23] and mental test scores (MTS)[24] with plaque counts (See Fig. 1), it can be seen that approximately 45% of Chat activity was lost at lower plaque counts, i.e. at about 12 plaques per field and that even though the relationship between the mean number of plaques and the MTS was broadly linear, Tomlinson et al. demonstrated that a threshold point of 12 plaques per low power field was found to be able to segregate dements from non-dements with 85% accuracy.[6]

It can also be seen that when a mean plaque count of 5 was reached, the ChAT activity had fallen by about 25% and when a mean plaque count of 10 was reached, the ChAT activity had fallen to about 50% of normal (see Fig. 2). Based on these observations it was decided that a biologically meaningful difference occurred at lower plaque counts, i.e. below about 12 plaques.

## MATERIALS AND METHODS

The materials used in this study were the brains from patients who had been clinically diagnosed as having SDAT. The diagnosis of SDAT was subsequently confirmed by examining frozen sections stained by King's silver impregnation technique for senile plaques and neurofibrillary tangles.

The control brains were obtained from patients who were not alcoholics, who did not have a head injury and who did not have a disease that would affect the brain. As far as possible, the controls were of a similar age to that of the SDAT group.

Both the control group and the SDAT group were mentally assessed and given a Mental Test Score (MTS) between 0 and 10 (0 being the lowest and 10 the highest). The handedness of the patient was also noted if possible (Tables 1 and 2).

### Mental Test Score

A mental test score (MTS) closely based on that of Blessed, Tomlinson and Roth was used to assess mental impairment in 210 patients by Hodkinson.[25] This is an abbreviated test that was 10 questions rather than 34. It was shown that this abbreviated test did not lose any of its discriminatory powers when comparing the results to the full test. The test consisted of the following 10 questions which scored one mark for each correct answer:

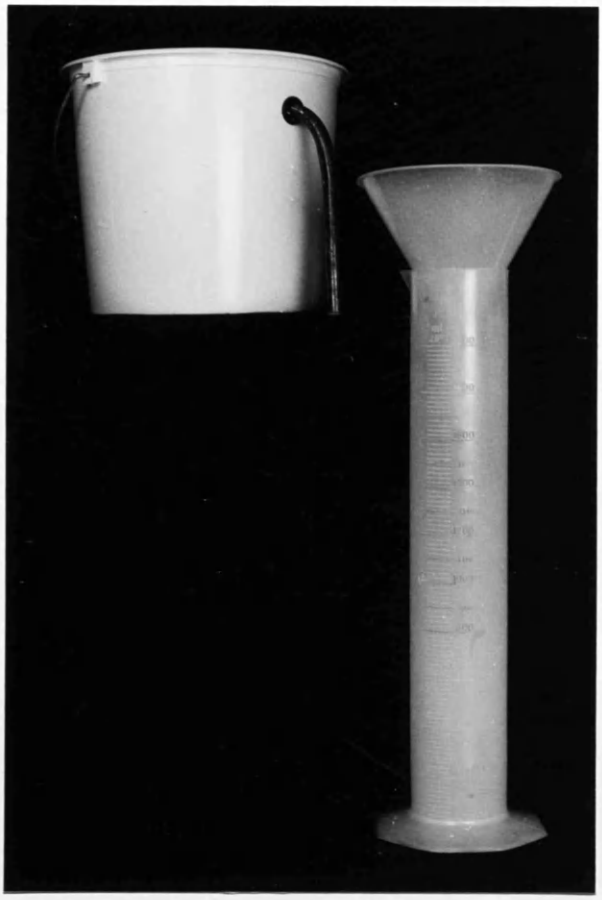

**Figure 3** Archimedes vessel, filter, funnel and measuring cylinder used to determine the volume of the fresh and fixed brain.

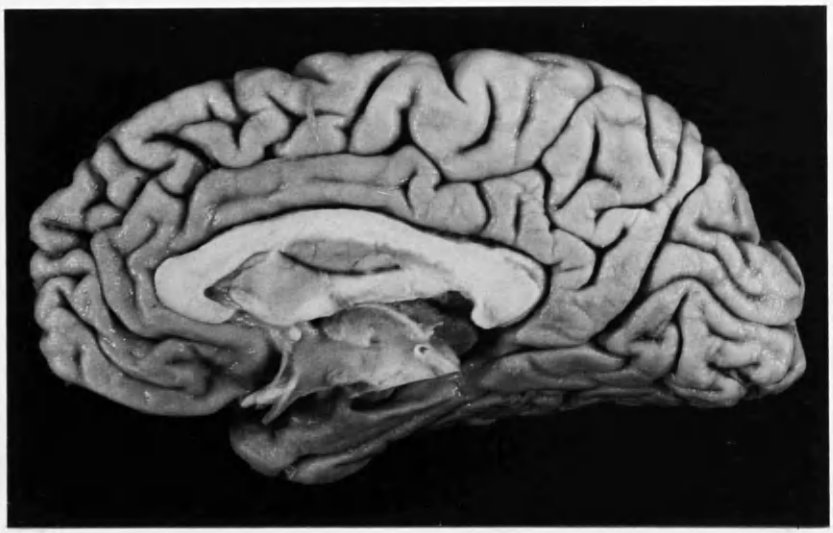

**Figure 4** The right hemisphere of the brain cut in the mid-sagittal plane with the meninges stripped from it.

1) Age
2) Time (to nearest hour)
3) Address for recall at the end of test - this should be repeated by the patient to ensure it has been heard correctly.

4) Year
5) Name of hospital
6) Recognition of 2 persons (doctor, nurse etc.)
7) Date of birth
8) Year of first world war
9) Name of present monarch
10) Count backwards from 20-1

In the full test, a score from 25 to the maximum of 34 could be accepted as the normal range. In this abbreviated test, a score below 7 closely corresponds to those scoring below 25 in the normal test.[25] This abbreviated test was therefore used to mentally assess both the control and SDAT patients used in this study.

**Quantitative Morphometry**

The volumes of each of the frontal, temporal, parietal and occipital lobes were examined to try to determine whether or not there were any lobes which were consistantly affected in SDAT compared to the age matched control group. The grey matter and white matter were examined in each lobe.

Fresh Brain Volume and Cranial Cavity Volume

When the brain was removed at autopsy, it was weighed and the volume of the fresh brain was measured by displacement of isotonic saline from an Archimedes vessel (Fig. 3). The procedure was repeated 4 or 5 times to obtain an average volume for the brain. The cranial cavity volume was then measured

using the balloon method of Davis and Wright.[13] This technique involved placing a rubber balloon inside the skull cavity, replacing the calvaria and holding it in position with a modified coronet clamp. The balloon was then inflated with water to a pressure of 150 mm Hg and tied off. The calvaria was carefully removed and the water content of the balloon taken as the volume of the cranial cavity. This procedure was also repeated 3 or 4 times to obtain an average volume for the cranial cavity. Since the cranial cavity volume does not change significantly with age,[13] changes in brain volume could be assessed by using, as an index, the brain volume expressed as a fraction of the cranial cavity volume.

Fixation and Dissection

The brains were fixed intact by placing each of them separately in a 2 gallon polythene bucket containing 10% formol saline. The brain was suspended in the fixative by passing a paper clip under the basilar artery and hanging it on a piece of string which was tied across the top of the bucket. The fixative was changed after 3 days and again at weekly intervals until the brain was adequately fixed (usually about 3 or 4 weeks). After fixation, the brain was washed in running water for about one hour before it was weighed and the volume measured again by displacement of saline as described. The hindbrain was detached at the level of the midbrain. The brain was then cut mid-sagittally to separate the 2 hemispheres (Fig. 4). The meninges

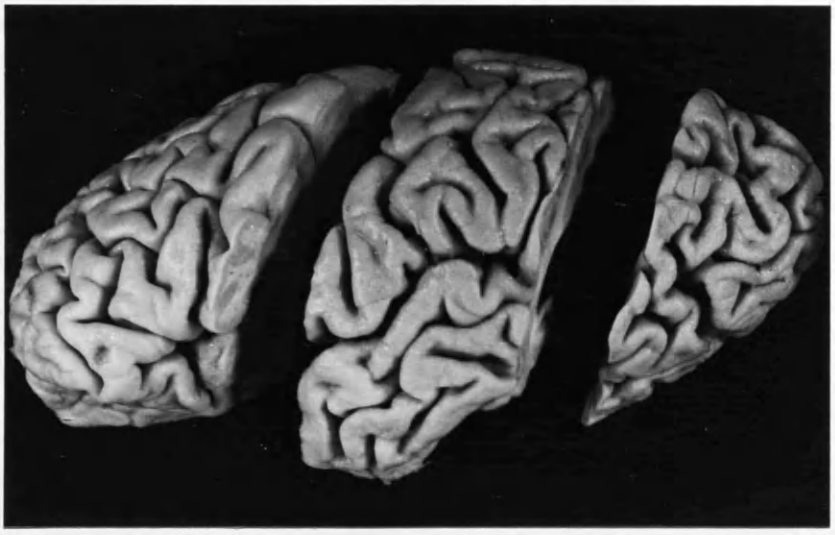

**Figure 5** The right hemisphere cut into 3 pieces, i.e. the frontal + some temporal, the occipital and the parietal + the remainder of the temporal lobe.

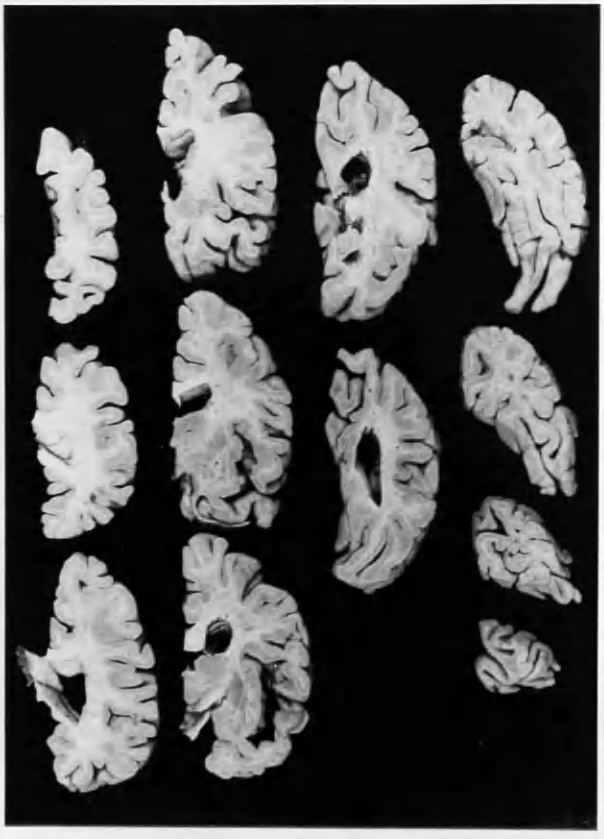

**Figure 6** The right hemisphere cut into 1 cm thick coronal slices.

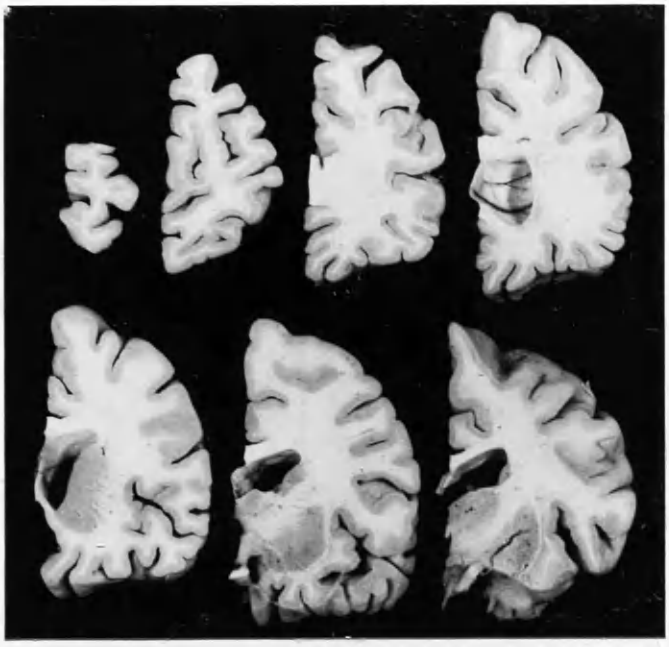

**Figure 7a** Coronal slices of the frontal lobe containing some temporal lobe.

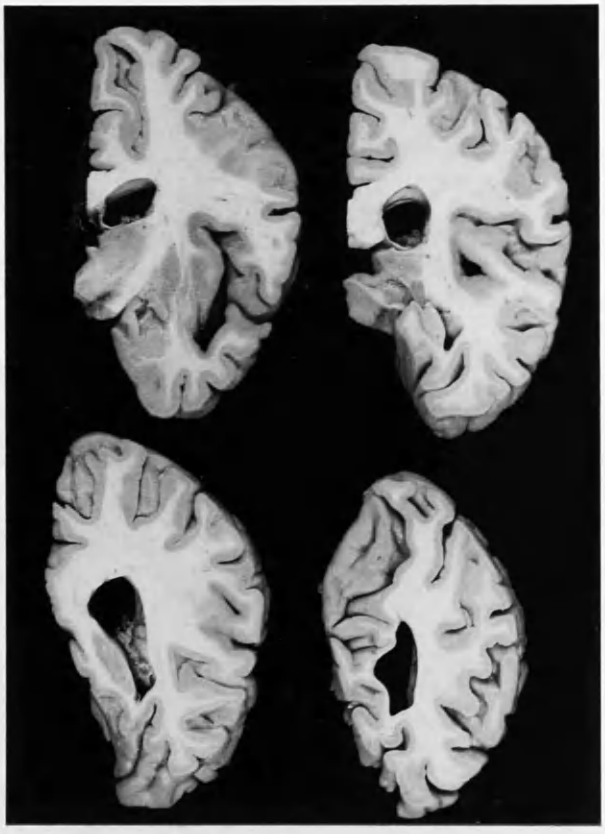

**Figure 7b** Coronal slices of the parietal lobe containing some temporal lobe.

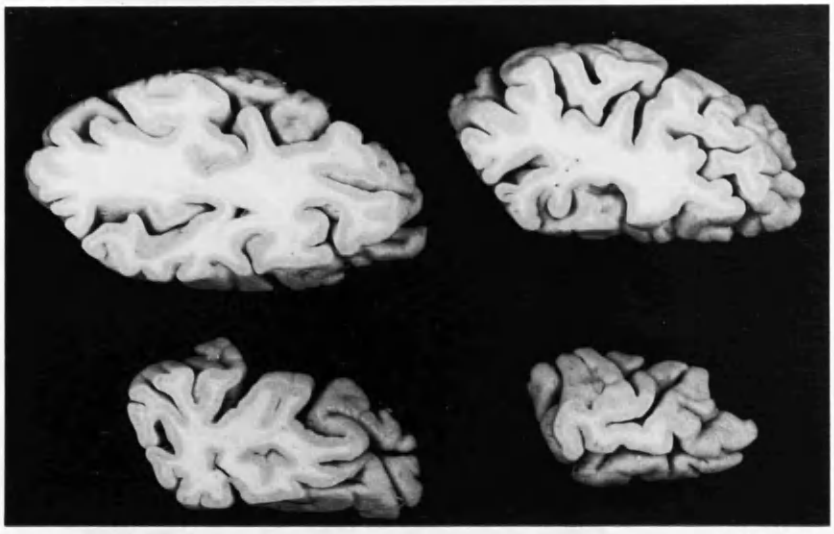

**Figure 8a** Coronal slices of occipital lobe.

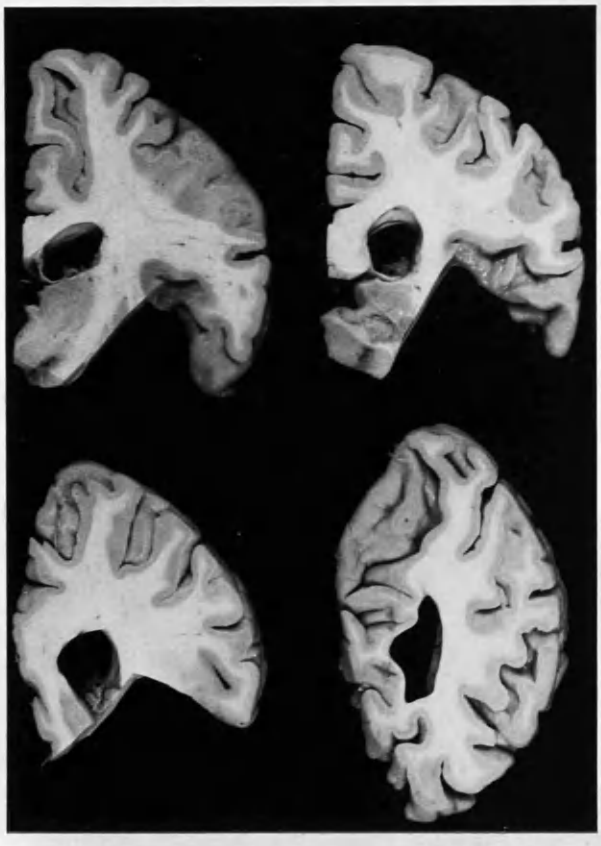

**Figure 8b** Coronal slices of parietal lobe.

**Figure 8c** Coronal slices of temporal lobe.

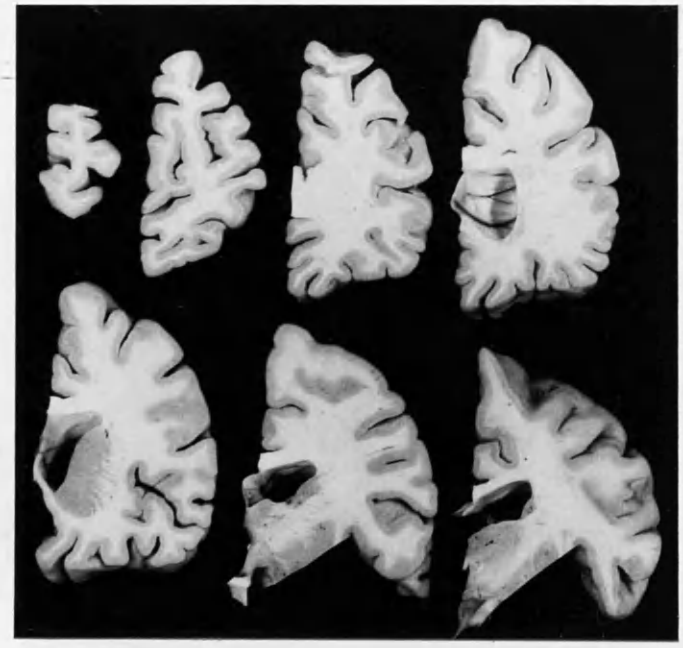

**Figure 8d** Coronal slices of frontal lobe.

were stripped from both hemispheres and an oblique cut made along the central sulcus to the tip of the temporal pole. This separated the frontal lobe along with some temporal lobe. A second cut was then made parallel to the first within the calcarine sulcus to separate the occipital and the parietal lobes with the remainder of the temporal lobe (Fig. 5). The 3 parts of the brain were then cut into 1 cm thick coronal slices parallel to the original cuts, i.e. the central sulcus and the calcarine sulcus (Fig. 6). This left slices containing frontal + some temporal lobe (Fig. 7a) and parietal + some temporal lobe (Fig. 7b). The temporal lobe was separated from the frontal and parietal slices and was taken from the superior pole of the insula to the infero-medial angle of the temporal lobe This separated the hemisphere into the occipital, parietal, temporal and frontal lobes (Figs. 8a-8d respectively).

Point Counting Reproducibility

The volume of the hindbrain (cerebellum and brain stem) was measured and deducted from the volume of the whole brain to give the volume of the cerebral hemispheres and the ventricles. By using the principle put forward by Delesse in 1847, coupled with a point counting technique, the fractional area and fractional volume of the frontal, temporal, occipital and parietal lobes were determined. The amount of grey and white matter, basal ganglia and ventricular volume was also determined. The point counting grid consisted of a lattice of points drawn in a triangular array on a transparent cellulose acetate sheet. The

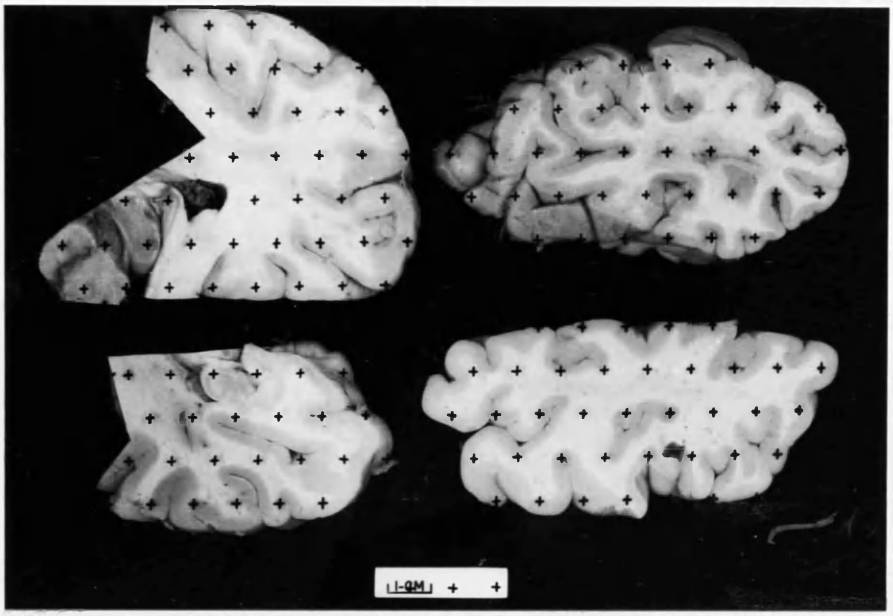

**Figure 9** The point counting grid used to determine the volume of grey matter, white matter, basal ganglia and the size of the ventricles in each of the lobes.

points were at the vertices of an equilateral triangle 10 mm apart. The grid was placed on top of the coronal slices and the number of points falling on the grey matter, white matter, basal ganglia and ventricles in each of the lobes in both left and right hemispheres were recorded (Fig. 9).

On a test brain, the volume and the percentage of each of the cerebral components (white matter, cortex, ventricles and basal ganglia) were determined 3 times in both left and right occipital, parietal, temporal and frontal lobes. This was to determine whether or not the point counting techique was reproducible (Tables 3 and 4). The volume of each of the cerebral components was calculated using the following formula:-

$$\text{Percentage of cerebral component} = \frac{\text{number of points on component}}{\text{total number of points}} \times \frac{100}{1}$$

This gave a percentage of the cerebral hemispheres for each of the cerebral components. Since the volume of the cerebral hemispheres had been determined, the volume of each of the cerebral components could now be calculated.

A paired t-test was performed between the first and second counts, the second and third counts and the first and third counts in both the left and right hemispheres. The results are shown in Tables 3 and 4.

Correction Factors for the Effects of Fixation and Brain Atrophy on the Volume of the Cerebral Components

Even though these volumes were made from fixed tissue, the fresh

volumes of the cerebral hemispheres were calculated using the following method described by Hubbard and Anderson[14]:-

$$\text{Fresh volume of cerebral hemisphere} = \text{Fixed volume of cerebral hemisphere} \times \frac{\text{Fresh volume of brain}}{\text{Fixed volume of brain}}$$

The fresh volumes of the various cerebral components were also calculated in this way:

$$\text{Fresh vol. of cerebral component} = \text{Fixed vol. of cerebral component} \times \frac{\text{Fresh vol. of cerebral hemispheres}}{\text{Fixed vol. of cerebral hemispheres}}$$

This formula will correct the volumes for the effects of fixation. To correct the volumes for the effects of brain atrophy, the fresh components can be expressed as a fraction of the CCV, i.e.

$$\text{Vol. of fresh cerebral component} = \frac{\text{Vol of fixed cerebral component} \times \frac{\text{Fresh vol of cerebral hemispheres}}{\text{Fixed vol of cerebral hemispheres}}}{\text{CCV}}$$

By expressing these various cerebral components as a fraction of the CCV, both males and females can be directly compared with each other since the CCV remains relatively constant with age.[13]

**Staining of Senile Plaques**

Three brains (A, B and C) from patients aged 75, 79 and 93 years old who had been clinically diagnosed as having SDAT, were used to determine which staining method was the most sensitive for demonstrating senile plaques in this Department. The brains were cut into 1 cm thick coronal slices and the following blocks

of tissue were selected from each of the three brains:- left and right superior frontal gyrus, left and right hippocampus and left and right superior parietal lobule.

Frozen Sections

Blocks as large as could be cut on the freezing microtome (4 cm x 3 cm) were taken and free floating frozen sections, nominally, 25 microns thick were cut using a Leitz freezing microtome. The frozen sections were then stained by the King's amyloid and von Braunmuhl silver impregnation methods for senile plaques.

Paraffin Sections

The blocks of tissue that were used to produce the frozen sections were processed to paraffin wax on a 7 day chloroform cycle. Serial sections were cut nominally at 13 microns and stained by the following methods:- thioflavine-T, anti-paired helical filaments, Palmgren, Congo red (Benhold's) and sirius red.

Plaque Counts: Sensitivity of Staining Techniques

These were first undertaken on the frozen sections. The area of cortex (between 15 and 25 $mm^2$) to be counted was marked in ink using a rotring pen to ensure that the boundaries of the area to be counted were easily seen. A grid with one millimetre squares was placed on top of the section, the total number of plaques within the marked area was counted at a magnification of x 25, and the average number of plaques per $mm^2$ calculated. The same

area of cortex was then marked on the serial paraffin sections and the average plaque count per $mm^2$ calculated in the same way.

Correction Factors for Paraffin Processing and Section Thickness

No adjustment was made for the effects of fixation since the same fixed tissue blocks were used for both frozen and paraffin sections. There was, however, some shrinkage of the tissue as it was processed to paraffin wax. The ratio of the area of the paraffin wax sections to the area of the frozen sections gives a processing factor ($p^2$) for this shrinkage. Multiplying the plaque counts on the paraffin sections by this factor should correct the plaque counts for the effects of processing the tissue to paraffin wax.

The areas of the frozen and paraffin sections were calculated using a point counting technique. A grid consisting of a lattice of points drawn in a triangular array (2 mm apart at the vertices of an equilateral triangle) on a transparent cellulose acetate sheet was placed on top of the frozen and corresponding paraffin sections and the number of points falling on each of the sections recorded. This was repeated three times and an average point count obtained for each section. Since the area of the grid is known and the total number of points on the grid is known, then by proportion the area of the sections can be calculated.

The average number of plaques per $mm^2$ was calculated by dividing the total number of plaques counted in each region of the brain by the actual area in $mm^2$ that was counted. The final

plaque counts were expressed as plaques per $mm^3$ to correct for the difference in section thickness between frozen (25 microns) and paraffin (13 microns) sections. The plaque counts on the frozen sections were therefore multiplied by 40 (25 microns x 40 = 1 mm) and the plaque counts from the paraffin sections were multiplied by 77 (13 microns x 77 = 1.001 mm) to give plaque counts per $mm^3$, thus allowing a direct comparison between the frozen and paraffin sections (see Tables 10, 11 and 12).

**Quantitative Plaque Counts**

Once it had been established that in our laboratory the most sensitive method of those tested for demonstrating senile plaques was on frozen sections stained by King's silver impregnation method, and after the fresh volumes of the various cerebral components had been determined using the technique previously described, the following blocks were selected from both the control and SDAT cases for frozen sectioning:-

A. Left and right middle frontal gyrus at level of genu
B. Left and right basal ganglia at level of striatum
C. Left and right globus pallidus
D. Left and right superior temporal gyrus at level of LGB (lateral geniculate body)
E. Left and right middle temporal gyrus at level of LGB
F. Left and right inferior temporal gyrus at level of LGB
G. Left and right hippocampus at level of LGB
H. Left and right amygdaloid nucleus
J. Left and right cingulate at level of LGB


**Figure 10** The Quantimet 10 image analyser system from Cambridge Instruments.

K. Left and right superior parietal lobule

L. Left and right medial occipital 3 cm anterior to occipital pole

M. Left and right cerebellum

N. Midbrain

O. Upper pons

Free floating frozen sections, nominally 25u thick, were cut from each block and stained by King's silver impregnation method for senile plaques and neurofibrillary tangles.

Initially it was decided to do plaque counts in regions A, D, E, F, J, K, and L in both left and right hemispheres, i.e. the frontal, temporal, parietal, occipital lobes and cingulate. To assess how to obtain the plaque counts at various points in each region and indeed how many points in each region to count, a reproducibility study and statistical analysis were undertaken on the first brain to assess not only the reliability of the Quantimet 10, but also the consistency of the operator.

The Quantimet 10

The Quantimet 10 (Q10) image analysis system from Cambridge Instruments (Fig. 10) was used to count the number of plaques and measure the area of the plaques in each of the brains used in this study. Initially, it was hoped to count the number and area of the plaques automatically. This, however, was not practical since the Q10 detects images in 16 different grey levels and the colour of the nuclei was virtually the same as the plaques. Individual nuclei could be discarded by using the

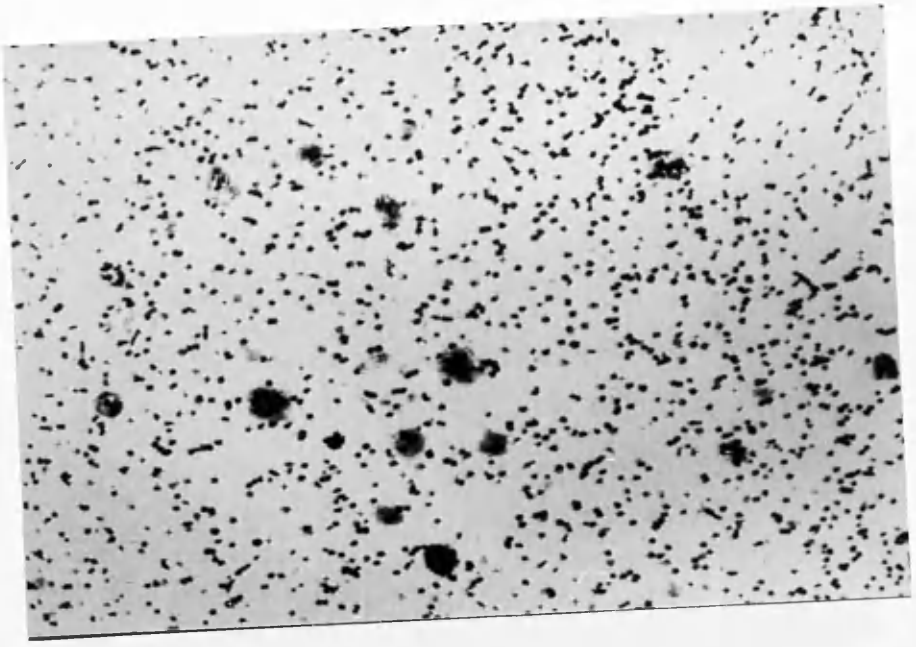

**Figure 11** Senile plaques as seen on the monitor of the Q10.

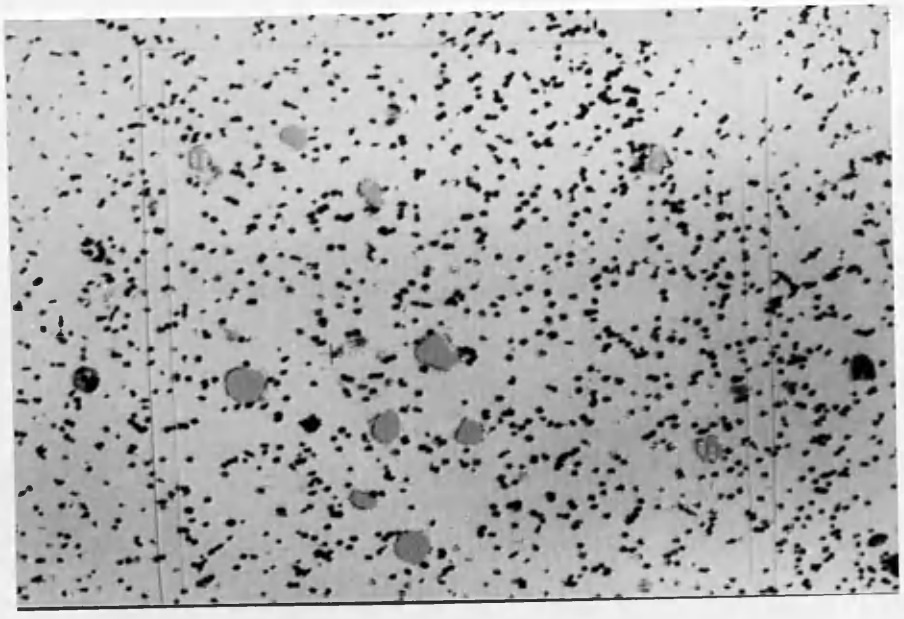

**Figure 12** The same plaques as Figure 11 drawn manually by the operator.

chord size feature which would reject anything smaller than the size (in microns) chosen by the operator. Unfortunately, some of the small 'burnt out' plaques would also be rejected and the image analyser was unable to differentiate between plaques and clumps of nuclei, blood vessels and dirt on the section. In order to have as accurate a plaque count as possible, it was decided to count the plaques manually in the following way.

The image frame and measure frame were set as large as possible on the monitor. As their names imply, the image frame borders the image to be examined and only the features with their lowest point inside the measure frame would be counted. Before any measurements could be made, the Q10 had to be calibrated. The magnification was set at x 200 and a stage micrometer used to calibrate the size of the measure frame. The edges of the frame were adjusted so that they represented a known length (in this case 800 microns) and the Q10 then calculated how many microns represented one pixel (1.75 microns per pixel). The area of any plaques that were measured at x 200 magnification would automatically be converted from pixels into square microns. Since the size of the measure frame was 800 microns x 800 microns, the area of the measure frame was 0.64 $mm^2$.

Once the instrument had been calibrated, the shading correction was set to give an even illumination. When the field to be counted had been selected, the gain and offset keys were used to give the best contrast to allow the maximum detection of plaques (Fig. 11). The field was then examined down the


**Figure 13** The digitiser and mouse used to draw round the plaques.

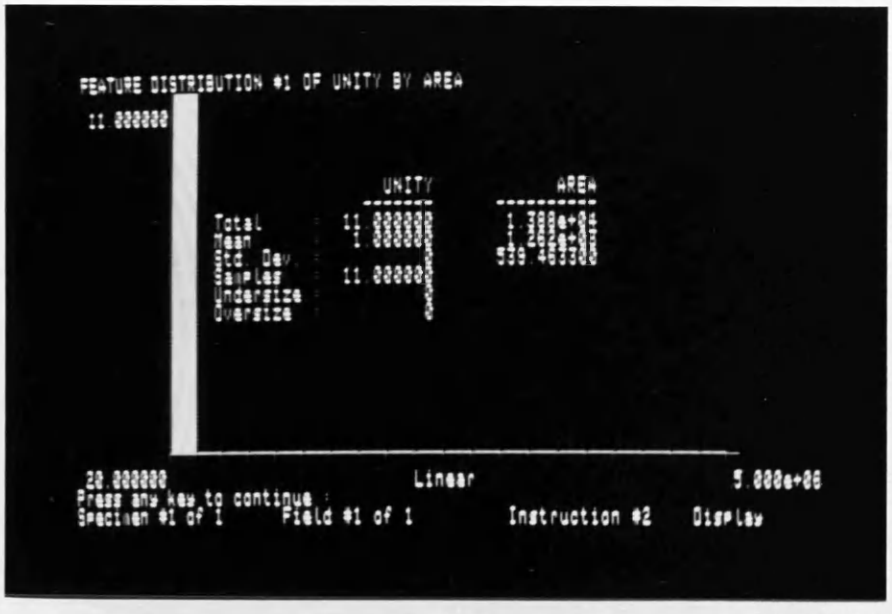


**Figure 14** The number and area of plaques seen in Figure 11 displayed in the form of a histogram.

microscope and the plaques drawn manually on the monitor (Fig. 12) using a digitiser and mouse (Fig. 13). The number of plaques and the area of plaques in square microns was then calculated by the Q10 and the results displayed in the form of a histogram (Fig. 14).

Reproducibility of Plaque Counts

Six reference points were marked in ink on the stained frozen sections and, as far as possible, 3 were put on the crests of the gyri and 3 in the depths of the sulci. Two counts were made at each point, one of which was in the superficial layers and the other in the deep layers (layers 1-3 and 4-6 respectively). The number and area of plaques, in square microns, were counted using the Q10 image analysis system from Cambridge Instruments.

Before comparisons could be made on the plaque counts obtained from different brains and indeed between regions of the same brain, the question of how reproducible were the results and thus the accuracy of the plaque counts had to be examined. This was performed by making two counts at the same points on two different days and examining the variability of the standard deviation in both absolute numbers and the difference in plaque counts (day 2 minus day 1 counts) expressed as a percentage of the day 1 counts (Tables 13-16). This was done both intra-regionally and inter-regionally. The statistical analysis was carried out using a students' paired t-test.

Correction Factors for the Effects of Fixation and Brain Atrophy on Plaque Counts

The plaque counts obtained from the fixed tissue blocks have to be corrected for the effects of fixation. If the brain shrinks, then the cells will be condensed and therefore a falsely high count will have been obtained and vice versa.

The $\frac{\text{Fresh Brain Volume}}{\text{Fixed Brain Volume}}$ will give a fixation factor $f^3$

which will correct the volumes for the effects of fixation. From this the linear factor f can be calculated and also $f^2$ which can be applied to correct the plaque counts obtained in an area (plaques/$mm^2$). The reciprocal of these volume correction factors can be used to convert measurements obtained from fixed tissue into values for fresh tissue.[26] The fixation correction factor would therefore be

$$f^2 = \left(\sqrt[3]{\frac{\text{Fixed Brain Volume}}{\text{Fresh Brain Volume}}}\right)^2$$

Similarly to correct plaque counts due to any atrophy of the brain, the

$\frac{\text{Cranial Cavity Volume}}{\text{Fresh Brain Volume}}$ will give an atrophy factor $a^3$

for volume corrections and, as before, to correct the plaque counts obtained from an area, the following atrophy correction factor should be applied

$$a^2 = \left(\sqrt[3]{\frac{\text{Fresh Brain Volume}}{\text{Cranial Cavity Volume}}}\right)^2$$

Another factor which had to be considered was whether or not the production of the stained frozen section altered the area of the section from the area of the surface of the block. Since the

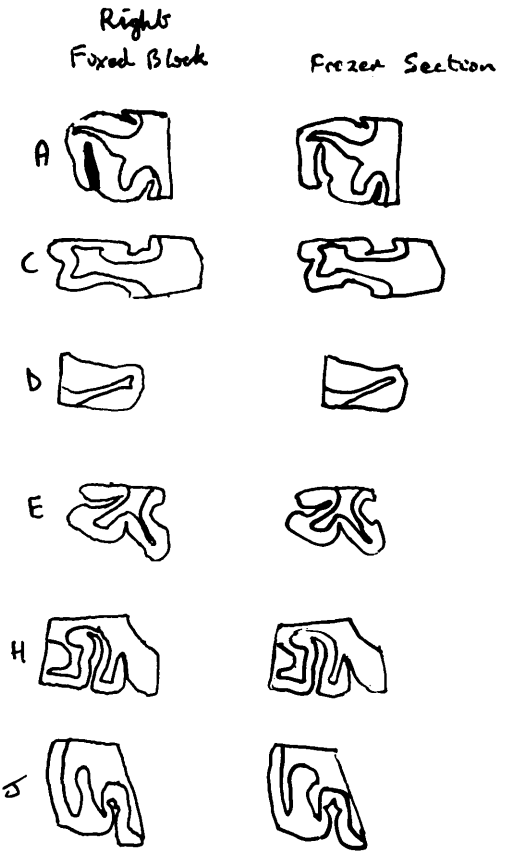


**Figure 15** The cellulose acetate tracings of the fixed tissue blocks and stained frozen sections.

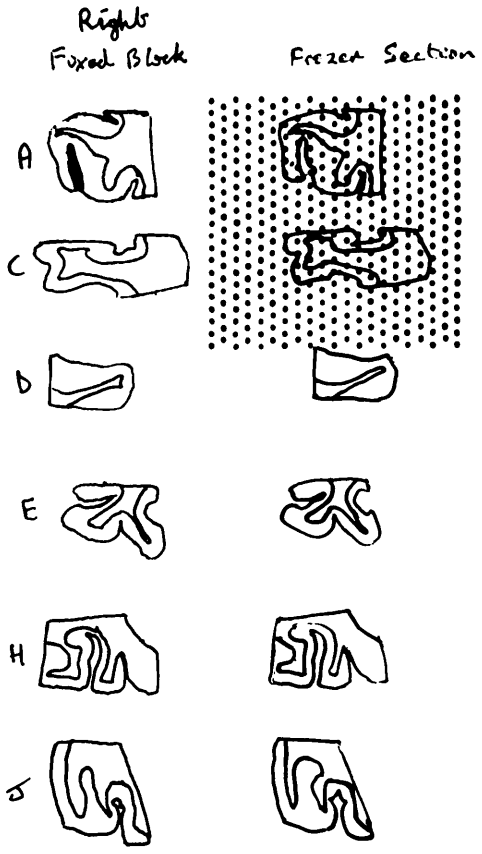


**Figure 16** The point counting grid used to determine the area of cortex in the fixed tissue blocks and stained frozen sections.

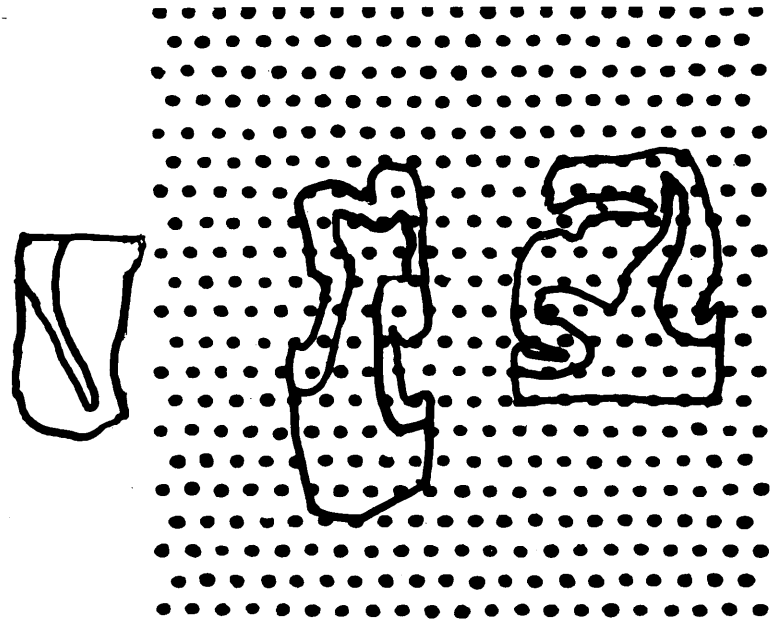

**Figure 17** A higher power of the grid from Figure 16.

plaque counts were made in the cortex, the area of cortex was measured in three cases, firstly in the fixed tissue blocks and then in the corresponding frozen section (Tables 17-19). The area of cortex in the blocks and sections was calculated by placing a piece of cellulose acetate sheet on top of them and drawing round the blocks and sections (Fig. 15). The cortical area was then calculated with a point counting technique using a grid with points at the vertices of an equilateral triangle. The points were 2 mm apart (Figs. 16-17).

**Definition of Asymmetry**

Once the method of plaque counting had been established, the plaque counts had to be assessed to see whether or not the 6 SDAT brains used in this study were symmetrical. If the difference between the plaque counts obtained in the left and right hemisphere (L-R) was not zero, then it could be argued statistically that all the brains were asymmetric. However, the question was are any of the differences biologically meaningful. We therefore had to decide what number of plaques represented a biologically meaningful change.

Many workers when comparing plaque counts to ChAT activity[23] or a mental test score[24] or a variety of other neuropathological and neurochemical correlates[27], usually compare a mean plaque count to whatever deficit they are studying. When examining the data on ChAT activity produced by Perry et al.,[23] it could be seen that by the time a mean plaque count of 1-5 was reached, the ChAT activity had fallen to about 75% and by the time a mean

plaque count of 6-10 plaques was reached, the ChAT activity was about 50% of normal. When a mean plaque count of 11-20 was reached, the ChAT activity had only fallen to about 45%, i.e. when a further 10 plaques were counted the ChAT activity had only fallen another 5%. From the graph shown by Perry et al. it seemed that the rapid drop in ChAT activity began to level off once a mean plaque count of 12 was reached.

Similar results were seen from the Blessed data when comparing the plaque counts to the mental test score (MTS), i.e. when a mean plaque count of 5 was reached the MTS was approximately 75%, and when a mean plaque count of 10 was reached the MTS was approximately 55%.

Based on these well established data sets, a decision was made that a 5 plaque change represented a biologically significant difference. If the relationship between plaque number and whatever the deficit was linear, then a plaque change from 1-6 plaques would have the same effect on e.g. ChAT activity or MTS as a 5 plaque change from 45-50 plaques. However from the literature, regardless of deficit, it could not be said with certainty that the relationship was a linear one. Since the difference between 1-6 plaques is a 5 plaque change and the difference between 45-50 plaques is a 5 plaque change with percentage differences of 500% and 10% respectively, it was decided that a second criterion for asymmetry was required.

Since ChAT activity was substantially reduced at lower plaque counts (below about 12 plaques), and a mean plaque count of 12 can segregate dements from non-dements,[6] a 5 plaque change

below 12 plaques will give an approximate percentage change of between 40% (7-12 plaques) and 500% (1-6 plaques). Therefore in this study asymmetric plaque counts would have to fulfil both criteria of a 5 plaque change as well as a minimum of a 40% change before the counts would be called asymmetric.

The formula used for calculating the percentage difference between the plaque counts was the difference between the plaque counts divided by the mean of the plaque counts x 100%.

**Statistical Analyses**

To test whether or not there was a statistically significant difference between the values obtained in the SDAT brain compared to the age matched controls, a two sample t-test was performed. To test whether or not there was a statistically significant difference between the values obtained in the left hemisphere compared to the values obtained in the right hemisphere (of the same brain), in both control and SDAT cases, a student's paired t-test was used.

When correlating the volume of the various lobes with the number or area of plaques, the Pearson product-moment coefficient of correlation was used (commonly symbolised as r). Again r was calculated when comparing the number of plaques/$mm^2$ to the area of plaques in square microns.

## RESULTS

Controls

These patients scored either 8, 9 or 10 out of 10 for their Mental Test Score (MTS), and six of the seven cases used as controls in this study were diagnosed as having a normal brain. The seventh control brain had a small recent infarct in the right posterior temporal/occipital region. The age of the control group was 81 years old ± 2 years (mean ± SEM), and the time interval between death and post mortem was 47 hours ± 12 hours (mean ± SEM). The age, sex, post-mortem (PM) delay, mental test score (MTS), the handedness (where known) and the neuropathological diagnosis of the control group are shown in Table 1.

**Table 1**

| Case | PM Number | Age | Sex | PM delay | MTS | Handedness | Neuropath. diagnosis |
|---|---|---|---|---|---|---|---|
| 1 | N76/87 | 81 | M | 24 hrs | 10 | NK | Normal brain |
| 2 | N175/87 | 79 | M | 69 hrs | 9 | NK | Normal brain |
| 3 | N181/87 | 77 | M | 24 hrs | 9 | NK | Normal brain |
| 4 | N235/87 | 85 | M | 18 hrs | 8 | NK | Normal brain |
| 5 | N242/87 | 73 | F | 24 hrs | 10 | NK | Small cerebral infarct |
| 6 | N531/87 | 85 | F | 72 hrs | 9 | NK | Normal brain |
| 7 | N819/87 | 89 | M | 96 hrs | 8 | Right | Normal brain |

NK = Not known.
PM = Post mortem
MTS = Mental test score
Neuropath. = Neuropathological

Senile dementia of Alzheimer type (SDAT)

These seven patients all scored 0 out of 10 for their Mental Test Score. The clinical diagnosis of SDAT was confirmed neuropathologically by examining frozen sections stained by King's silver impregnation. The age of the SDAT group was 83 years old ± 2 years (mean ± SEM) and the time interval between death and post mortem was 6 hours ± 1 hour (mean ± SEM). The age, sex, PM delay, MTS, the handedness (where known) and the neuropathological diagnosis of the SDAT group are shown in Table 2.

**Table 2**

| Case | PM number | Age | Sex | PM delay | MTS | Handedness | Neuropath. diagnosis |
|---|---|---|---|---|---|---|---|
| 8 | N216/87 | 87 | F | 3 hrs | 0 | NK | SDAT |
| 9 | N222/87 | 74 | F | 9 hrs | 0 | NK | SDAT |
| 10 | N640/87 | 84 | F | 10 hrs | 0 | Right | SDAT |
| 11 | N641/87 | 83 | F | 4 hrs | 0 | Right | SDAT |
| 12 | N755/87 | 89 | F | 12 hrs | 0 | Right | SDAT |
| 13 | N804/87 | 80 | M | 2 hrs | 0 | Right | SDAT |
| 14 | N201/88 | 87 | F | 6 hrs | 0 | Right | SDAT |

NK = Not known
PM = Post mortem
MTS = Mental test score
Neuropath. = Neuropathological

**Quantitative Morphometry**

The absolute brain volumes of the SDAT group could not be directly compared to the absolute brain volumes of the control

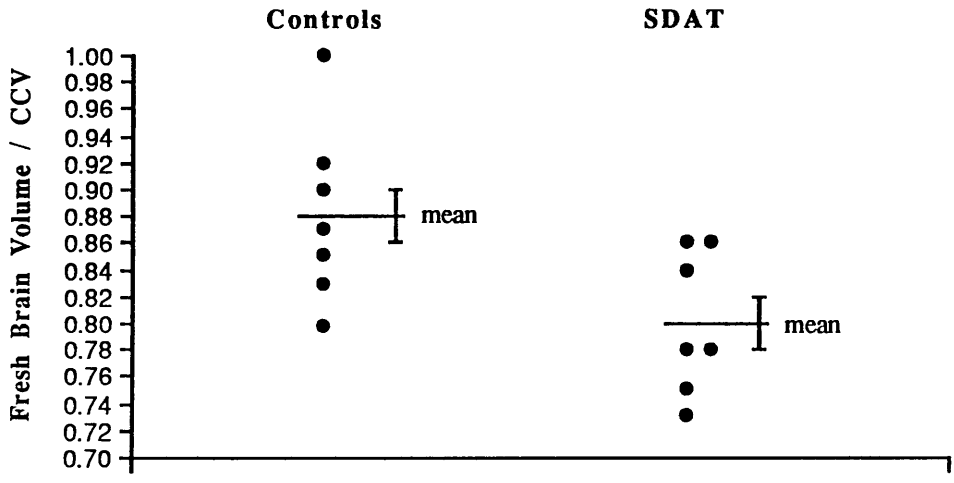


Figure 18 shows the fresh brain volume/CCV ratios of both the control and SDAT patients.

group to see whether or not there was any shrinkage, or loss of tissue, in SDAT compared to the age matched controls. This was because the size and volume of the normal brain varies from individual to individual and, generally speaking, males have slightly larger brains than females. However, if the fresh brain volume (BV) was expressed as a fraction of the cranial cavity volume (CCV), these ratios could be directly compared between SDAT and control (normal) groups since the CCV did not change significantly with age.[13] This also allowed males and females to be grouped together in the same study.

In addition to the whole brain volume, the volume of each individual lobe in both the left and right hemispheres was compared between the SDAT group and the age matched controls. The amount of cortex, white matter and ventricular volume was also compared to see if there was any particular region of the brain which was more atrophic in the SDAT brain.

Fresh brain volume/cranial cavity volume

Any changes that occurred between the SDAT BV/CCV ratio compared to the control BV/CCV ratio could be taken as a change in brain volume. The control group ratios ranged from 0.80-1.0 with a mean value of 0.88 $\pm$ 0.02 (mean $\pm$ SEM), and the SDAT group ratios ranged from 0.73-0.86 with a mean value of 0.80 $\pm$ 0.02 (mean $\pm$ SEM) (see Fig. 18).

As can be seen from Fig. 18, the fresh BV/CCV ratios of the SDAT patients were lower than those of the normal controls. This indicated that there was some loss of brain tissue in

controls but even more in SDAT. There was a statistically significant difference between SDAT and control group (see Table 3).

**Table 3** Total brain, cerebral cortex and white matter volumes

| | Fresh Brain Volume/CCV | | | Fresh Cerebral Cortex/CCV | | | Fresh White Matter Volume/CCV | | |
|---|---|---|---|---|---|---|---|---|---|
| | Mean | SD | P | Mean | SD | P | Mean | SD | P |
| Controls | 0.88 | 0.07 | | 0.43 | 0.05 | | 0.28 | 0.04 | |
| vs | | | 0.028* | | | 0.0024** | | | 0.028* |
| SDAT | 0.80 | 0.05 | | 0.34 | 0.03 | | 0.23 | 0.02 | |

* = $p < 0.05$; ** = $p < 0.01$

Table 3 showing the comparison between the whole fresh brain volume/CCV, the total cerebral cortex volume/CCV and the total white matter volume/CCV of the control brains compared to the SDAT brains.

The next step was to determine where in the brain this tissue loss occurred. First, it was necessary to test the reproducibility of the method to be used.

Reproducibility of point counting technique

The volume and percentage of cortex, white matter and deep grey matter were calculated in both left and right occipital, parietal, temporal and frontal lobes. The volume of the lateral and third ventricles were also determined. All these measurements were repeated three times and the results compared

with each other using a student's paired-t test (Tables 4 and 5).

**Table 4** Reproducibility of point counting in the left cerebral hemisphere of control brain 1.

| | Count 1 | | | Count 2 | | | Count 3 | | |
|---|---|---|---|---|---|---|---|---|---|
| | Vol. (ml) | % | P | Vol. (ml) | % | P | Vol. (ml) | % | P |
| **Occipital** | | | | | | | | | |
| White | 46.74 | 3.8 | | 44.28 | 3.6 | | 43.05 | 3.5 | |
| Cortex | 77.49 | 6.3 | NS | 88.56 | 7.2 | NS | 92.25 | 7.5 | NS |
| Ventricles | 2.46 | 0.2 | | 2.46 | 0.2 | | 2.46 | 0.2 | |
| Total Vol. | 126.7 | 10.3 | | 135.3 | 11.0 | | 137.8 | 11.2 | |
| **Parietal** | | | | | | | | | |
| White | 68.88 | 5.6 | | 67.65 | 5.5 | | 65.19 | 5.3 | |
| Cortex | 76.26 | 6.2 | NS | 81.18 | 6.6 | NS | 84.87 | 6.9 | NS |
| Ventricles | 6.15 | 0.5 | | 7.38 | 0.6 | | 6.15 | 0.5 | |
| Total Vol. | 151.13 | 12.3 | | 156.2 | 12.7 | | 156.2 | 12.7 | |
| **Temporal** | | | | | | | | | |
| White | 25.83 | 2.1 | | 30.75 | 2.5 | | 29.52 | 2.4 | |
| Cortex | 62.73 | 5.1 | | 60.27 | 4.9 | | 63.96 | 5.2 | |
| Ventricles | 2.45 | 0.2 | NS | 1.23 | 0.1 | NS | 2.46 | 0.2 | NS |
| Deep grey | 4.92 | 0.4 | | 6.15 | 0.5 | | 6.15 | 0.5 | |
| Total Vol. | 95.9 | 7.8 | | 98.4 | 8.0 | | 102.1 | 8.3 | |
| **Frontal** | | | | | | | | | |
| White | 104.55 | 8.5 | | 103.32 | 8.4 | | 108.24 | 8.8 | |
| Cortex | 130.38 | 10.6 | | 126.69 | 10.3 | | 129.15 | 10.5 | |
| Ventricles | 9.84 | 0.8 | NS | 7.38 | 0.6 | NS | 8.61 | 0.7 | NS |
| Deep grey | 19.68 | 1.6 | | 24.60 | 2.0 | | 20.91 | 1.7 | |
| Total Vol. | 264.5 | 21.5 | | 262.0 | 21.3 | | 266.9 | 21.7 | |

% = The volume of the cerebral component expressed as a percentage of the whole brain volume.
NS = No significant difference ($p > 0.05$).

Table 4 shows the volumes obtained from the three counts performed in the left occipital, parietal, temporal and frontal lobes from control brain 1. It can be seen there was no significant difference between any of the volumes determined in any of the lobes.

**Table 5** Reproducibility of point counting in the right cerebral hemisphere of control brain 1.

| | Count 1 | | | Count 2 | | | Count 3 | | |
|---|---|---|---|---|---|---|---|---|---|
| | Vol. (ml) | % | P | Vol. (ml) | % | P | Vol. (ml) | % | P |
| **Occipital** | | | | | | | | | |
| White | 30.75 | 2.5 | | 30.75 | 2.5 | | 28.29 | 2.3 | |
| Cortex | 57.81 | 4.7 | NS | 51.66 | 4.2 | NS | 55.35 | 4.5 | NS |
| Ventricles | 0.0 | 0.0 | | 0.0 | 0.0 | | 0 0 | 0.0 | |
| Total Vol. | 88.56 | 7.2 | | 82.41 | 6.7 | | 83.60 | 6.8 | |
| **Parietal** | | | | | | | | | |
| White | 70.11 | 5.7 | | 66.42 | 5.4 | | 63.06 | 5.2 | |
| Cortex | 84.87 | 6.9 | NS | 88.56 | 7.2 | NS | 93.48 | 7.6 | NS |
| Ventricles | 6.15 | 0.5 | | 8.61 | 0.7 | | 9.84 | 0.8 | |
| Total Vol. | 161.10 | 13.1 | | 163.6 | 13.3 | | 167.30 | 13.6 | |
| **Temporal** | | | | | | | | | |
| White | 27.06 | 2.2 | | 23.37 | 1.9 | | 27.06 | 2.2 | |
| Cortex | 44.28 | 3.6 | | 46.74 | 3.8 | | 51.66 | 4.2 | |
| Ventricles | 7.38 | 0.6 | NS | 6.15 | 0.5 | NS | 4.92 | 0.4 | NS |
| Deep grey | 2.46 | 0.2 | | 1.23 | 0.1 | | 1.23 | 0.1 | |
| Total Vol. | 81.20 | 6.6 | | 77.50 | 6.3 | | 84.90 | 6.9 | |
| **Frontal** | | | | | | | | | |
| White | 94.71 | 7.7 | | 100.86 | 8.2 | | 88.56 | 7.2 | |
| Cortex | 129.15 | 10.5 | | 124.23 | 10.1 | | 118.08 | 9.6 | |
| Ventricles | 9.84 | 0.8 | NS | 8.61 | 0.7 | NS | 7.38 | 0.6 | 0.032 |
| Deep grey | 27.06 | 2.2 | | 18.45 | 1.5 | | 17.22 | 1.4 | |
| Total Vol. | 260.80 | 21.2 | | 252.20 | 20.5 | | 231.24 | 18.8 | |

% = the volume of the cerebral component expressed as a percentage of the whole brain volume.
NS = no significant difference ($p > 0.05$)

Table 5 shows the volumes obtained from the three counts performed in the right occipital, parietal, temporal and frontal lobes from control brain 1. It can be seen that there was a statistically significant difference between the first and third counts in the right frontal lobe (see Table 5). Even though the actual differences between these counts is small, to try to reduce this small error even further it was decided to perform 2 point counts on each brain, obtain an average point

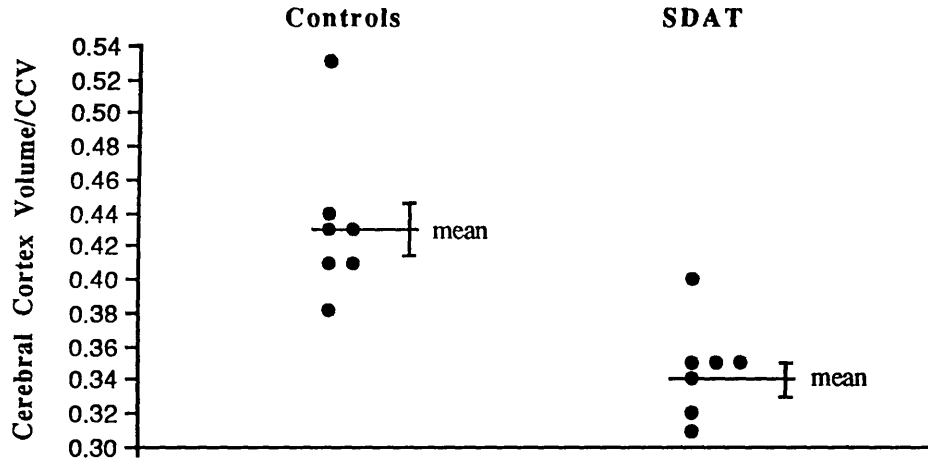


Figure 19 shows the whole brain cortex volume/CCV ratios of both the control and SDAT patients.

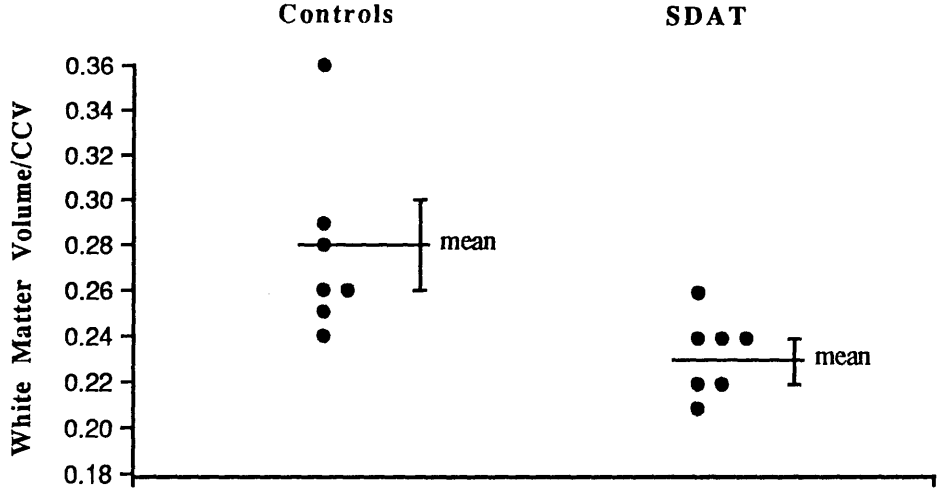


Figure 20 shows the whole brain white matter volume/CCV ratios of both the control and SDAT patients.

count and therefore produce a more accurate volume for each of the cerebral components.

Whole brain cortex volumes/cranial cavity volume

Once it had been established that the point counting technique was reproducible, the total volume of the cortex in each of the brains in the control and SDAT groups was calculated. The cerebral cortex volume/CCV ratios for the control brains ranged from 0.38-0.53 with a mean value of 0.43 ± 0.02 (mean ± SEM) and the cerebral cortex volume/CCV ratios for the SDAT brains ranged from 0.31-0.40 with a mean value of 0.34 ± 0.01 (mean ± SEM) (see Fig. 19).

It can be seen from Fig. 19 that the fresh cortex volume/CCV ratios of the SDAT patients were lower than those of the normal controls. There was a statistically significant difference between the SDAT and control group (see Table 3). This showed that there was a loss of cerebral cortex in SDAT.

Whole brain white matter volumes/CCV

The total white matter in each of the control and SDAT brains was calculated. The cerebral white matter volume/CCV ratios for the control brains ranged from 0.24-0.36 with a mean value of 0.28 + 0.02 (mean ± SEM) and the white matter volume/CCV ratios for the SDAT brains ranged from 0.21-0.26 with a mean value of 0.23 ± 0.01 (mean ± SEM) (see Fig. 20).

It can be seen from Fig. 20 that the fresh white matter volume/CCV ratios of the SDAT patients were lower than those of

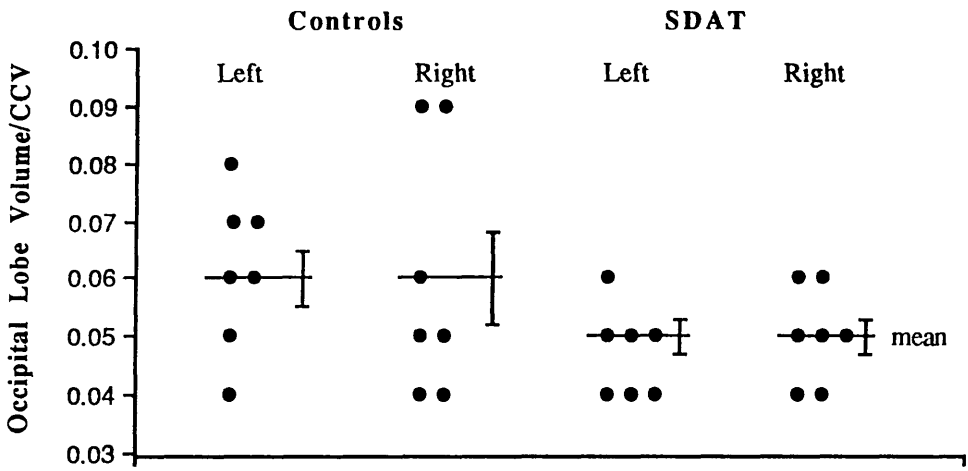


Figure 21 shows the left and right occipital lobe volume/CCV ratios of both the control and SDAT patients.

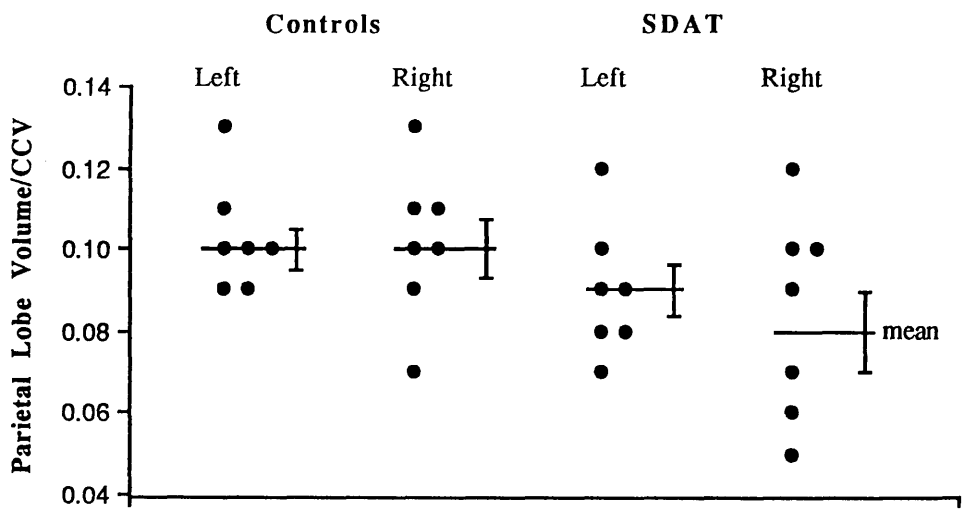


Figure 22 shows the left and right parietal lobe volume/CCV ratios of both the control and SDAT patients.

the normal controls. There was a statistically significant difference between the SDAT and control groups (see Table 3). This showed that there was also a loss of white matter in SDAT.

Volume of individual cerebral lobes/CCV

Since there was an overall reduction in the total volume of cerebral cortex and white matter in SDAT brains compared to the normal controls, it was decided to determine whether or not the atrophy was confined to any particular lobes.

The volume of the occipital, parietal, temporal and frontal lobes in both hemispheres was calculated in each of the control and SDAT brains.

The occipital lobe volume/CCV ratios in the normal brain ranged from 0.04-0.08 with a mean value of 0.06 $\pm$ 0.005 (mean $\pm$ SEM) in the left hemisphere, and ranged from 0.04-0.09 with a mean value of 0.06 $\pm$ 0.008 (mean $\pm$ SEM) in the right hemisphere (see Fig. 21). The occipital lobe volume/CCV ratios in the SDAT brain ranged from 0.04-0.06 with a mean value of 0.05 $\pm$ 0.003 (mean $\pm$ SEM) in the left hemisphere and ranged from 0.04-0.06 with a mean value of 0.05 $\pm$ 0.003 (mean $\pm$ SEM) in the right hemisphere (see Fig. 21).

The parietal lobe volume/CCV ratios in the normal brain ranged from 0.09-0.13 with a mean value of 0.10 $\pm$ 0.005 (mean $\pm$ SEM) in the left hemisphere, and ranged from 0.07-0.13 with a mean value of 0.10 $\pm$ 0.007 (mean $\pm$ SEM) in the right hemisphere (see Fig. 22). The parietal lobe volume/CCV ratios in the SDAT

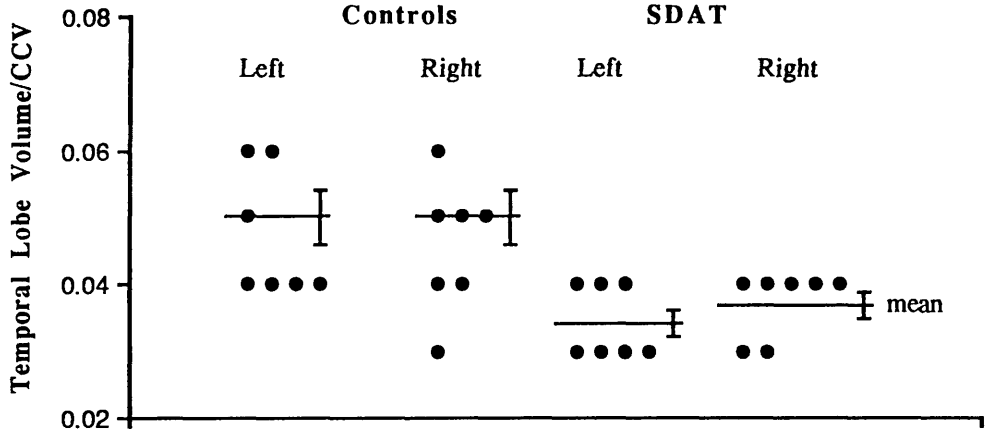


Figure 23 shows the left and right temporal lobe volume /CCV ratios of both the control and SDAT patients.

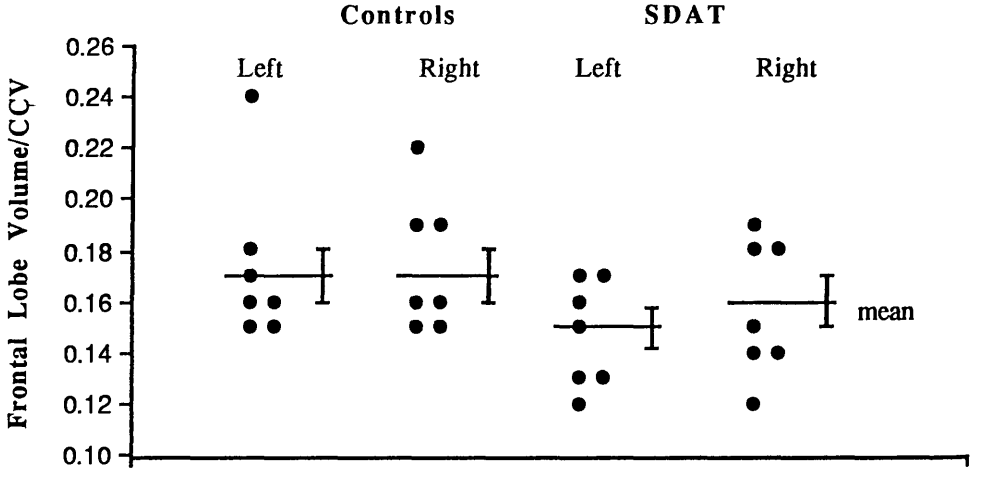


Figure 24 shows the left and right frontal lobe volume /CCV ratios of both the control and SDAT patients.

brain ranged from 0.07-0.12 with a mean value of 0.09 ± 0.006 (mean ± SEM) in the left hemisphere and ranged from 0.05-0.12 with a mean value of 0.08 ± 0.01 (mean ± SEM) in the right hemisphere (see Fig. 22).

The temporal lobe volume/CCV ratios in the normal brain ranged from 0.04-0.06 with a mean value of 0.05 ± 0.004 (mean ± SEM) in the left hemisphere and ranged from 0.03-0.06 with a mean value of 0.05 ± 0.004 (mean ± SEM) in the right hemisphere (see Fig. 23). The temporal lobe volume/CCV ratios in the SDAT brain ranged from 0.03-0.04 with a mean value of 0.03 ± 0.002 (mean ± SEM) in the left hemisphere and ranged from 0.03-0.04 with a mean value of 0.04 ± 0.002 (mean ± SEM) in the right hemisphere (see Fig. 23).

The frontal lobe value/CCV ratios in the normal brain ranged from 0.15-0.24 with a mean value of 0.17 ± 0.01 (mean ± SEM) in the left hemisphere and ranged from 0.15-0.22 with a mean value of 0.17 ± 0.01 (mean ± SEM) in the right hemisphere (see Fig. 24). The frontal lobe volume/CCV ratios in the SDAT brain ranged from 0.12-0.17 with a mean value of 0.15 ± 0.008 (mean ± SEM) in the left hemisphere and ranged from 0.12-0.19 with a mean value of 0.16 ± 0.01 (mean ± SEM) in the right hemisphere (see Fig. 24).

**Table 6** Volume of individual lobes.

| | | Occipital lobe Volume/CCV | Parietal lobe Volume/CCV | Temporal lobe Volume/CCV | Frontal lobe Volume/CCV |
|---|---|---|---|---|---|
| L. Control | Mean diff | 0.001 | 0.001 | 0.001 | 0.010 |
| Vs | SD | 0.018 | 0.009 | 0.017 | 0.020 |
| R. Control | P | NS | NS | NS | NS |
| L. SDAT | Mean diff | 0.003 | 0.017 | 0.003 | 0.001 |
| Vs | SD | 0.011 | 0.015 | 0 008 | 0.013 |
| R. SDAT | P | NS | NS | NS | NS |
| L. Control | Mean | 0.061 | 0.102 | 0.047 | 0.173 |
| Vs | SD | 0.013 | 0.014 | 0.010 | 0.032 |
| L. SDAT | Mean | 0.047 | 0.090 | 0.034 | 0.147 |
| | SD | 0.007 | 0.016 | 0.005 | 0.021 |
| | P | 0.037 | NS | 0.012 | NS |
| R. Control | Mean | 0.060 | 0.101 | 0.046 | 0.174 |
| Vs | SD | 0.022 | 0.019 | 0.010 | 0.026 |
| R. SDAT | Mean | 0.050 | 0.084 | 0.037 | 0.157 |
| | SD | 0.008 | 0.025 | 0.005 | 0.026 |
| | P | NS | NS | NS | NS |

CCV = Cranial cavity volume
Mean diff = Mean difference.
NS = No significant difference ($p > 0.05$)

Table 6 shows the comparison between the left (L) and right (R) control values, the left and right SDAT values, the comparison between the left control and the left SDAT values and the comparison between the right control and right SDAT values in the occipital, parietal, temporal and frontal lobes.

It can be seen from Table 6 that there was a statistically significant difference between the left occipital lobe in controls compared to SDAT patients ($p < 0.05$). There was no significant difference between the right occipital lobes of the controls compared to SDAT patients.

There was no statistically significant difference between the left or right parietal lobes of the controls compared to SDAT patients.

There was a statistically significant difference between the left temporal lobes in the controls compared to the SDAT patients ($p < 0.01$). There was no significant difference between the right temporal lobes of the controls compared to the SDAT patients.

There was no statistically significant difference between the left or right frontal lobes of the controls compared to SDAT patients.

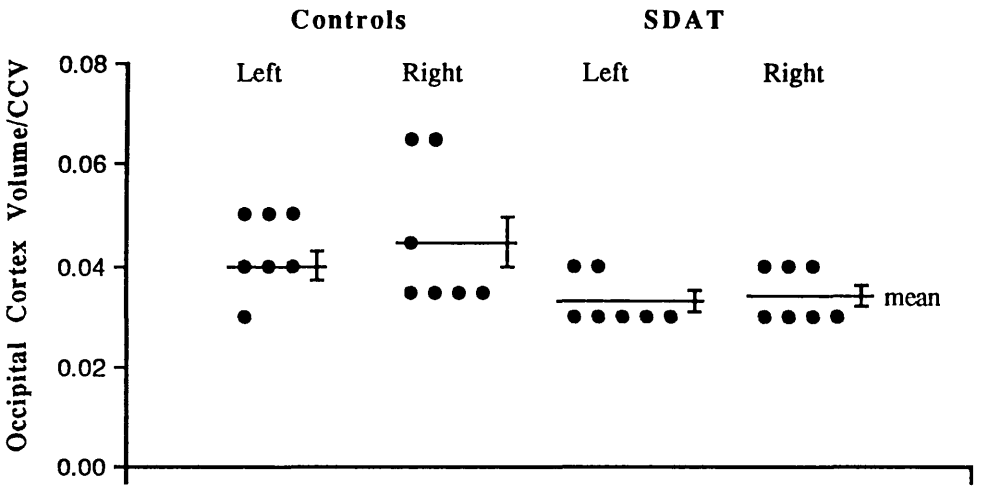


Figure 25 shows the left and right cerebral cortex volumes of the occipital lobe/CCV ratios of both the control and SDAT patients.

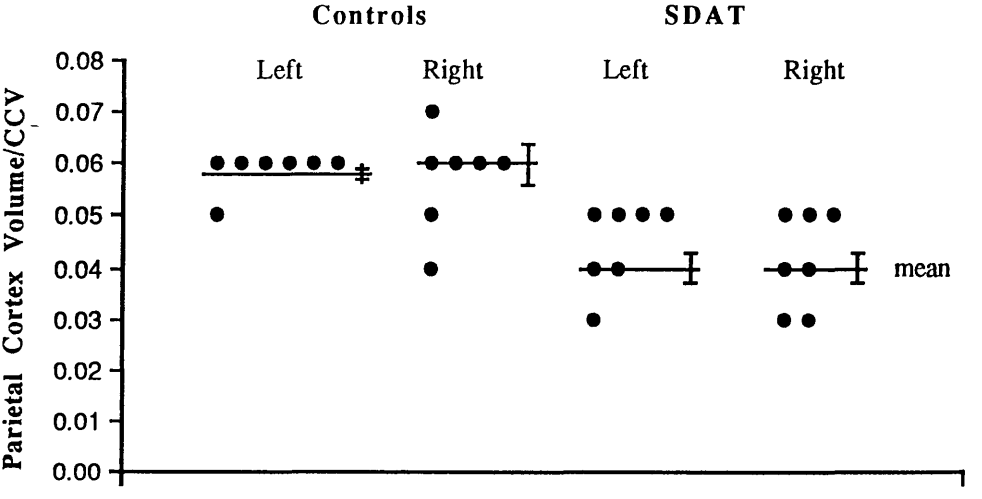


Figure 26 shows the left and right cerebral cortex volumes of the parietal lobe/CCV ratios of both the control and SDAT patients.

Volume of cortex in each lobe/cranial cavity volume

The volume of cerebral cortex in the occipital, parietal, temporal and frontal lobes in both left and right hemispheres was calculated in each of the brains of the control subjects and SDAT patients.

The cerebral cortex volume of the occipital lobe/CCV ratio in the normal brain ranged from 0.03-0.05 with a mean value of 0.04 ± 0.003 (mean ± SEM) in the left hemisphere and ranged from 0.03-0.06 with a mean value of 0.04 ± 0.005 (mean ± SEM) in the right hemisphere (see Fig. 25). The cerebral cortex volume of the occipital lobe/CCV ratio in the SDAT brain ranged from 0.03-0.04 with a mean value of 0.03 ± 0.002 (mean ± SEM) in the left hemisphere and ranged from 0.03-0.04 with a mean value of 0.03 ± 0.002 (mean ± SEM) in the right hemisphere (see Fig. 25).

The cerebral cortex volume of the parietal lobe/CCV ratio in the normal brain ranged from 0.05-0.06 with a mean value of 0.06 ± 0.001 (mean ± SEM) in the left hemisphere and ranged from 0.04-0.07 with a mean value of 0.06 ± 0.004 (mean ± SEM) in the right hemisphere (see Fig. 26). The cerebral cortex volume of the parietal lobe/CCV ratio in the SDAT brain ranged from 0.03-0.05 with a mean value of 0.04 ± 0.003 (mean ± SEM) in the left hemisphere and ranged from 0.03-0.05 with a mean value of 0.04 ± 0.003 (mean ± SEM) in the right hemisphere (see Fig. 26).

The cerebral cortex volume of the temporal lobe/CCV ratio in the normal brain ranged from 0.02-0.04 with a mean value of 0.03 ± 0.002 (mean ± SEM) in the left hemisphere and ranged from 0.02-0.04 with a mean value of 0.03 ± 0.003 (mean ± SEM) in the

right hemisphere (see Fig. 27). The cerebral cortex volume of the temporal lobe/CCV ratios in the SDAT brain was 0.02 in each of the lobes in the left hemisphere and ranged from 0.02-0.03 with a mean value of 0.02 ± 0.002 (mean ± SEM) in the right hemisphere (see Fig. 27).

The cerebral cortex volume of the frontal lobe/CCV ratios in the normal brain ranged from 0.08-0.10 with a mean value of 0.08 ± 0.003 (mean ± SEM) in the left hemisphere and ranged from 0.07-0.10 with a mean value of 0.08 ± 0.004 (mean ± SEM) in the right hemisphere (see Fig. 28). The cerebral cortex volume of the frontal lobe/CCV ratios in the SDAT brain ranged from 0.06-0.08 with a mean value of 0.07 ± 0.004 (mean ± SEM) in the left hemisphere and ranged from 0.06-0.10 with a mean value of 0.08 ± 0.006 (mean ± SEM) in the right hemisphere (see Fig. 28).

**Table 7** Volume of cortex in each lobe

| | | Occipital Cortex Volume/CCV | Parietal Cortex Volume/CCV | Temporal Cortex Volume/CCV | Frontal Cortex Volume/CCV |
|---|---|---|---|---|---|
| L. Control | Mean diff | 0.003 | 0.003 | 0.001 | 0.001 |
| Vs | SD | 0.011 | 0.011 | 0.009 | 0.009 |
| R. Control | P | NS | NS | NS | NS |
| L. SDAT | Mean diff | 0.001 | 0.003 | 0 | 0.004 |
| VS | SD | 0.009 | 0.010 | 0.008 | 0.010 |
| R. SDAT | P | NS | NS | NS | NS |
| L. Control | Mean | 0.043 | 0.058 | 0.030 | 0.084 |
| Vs | SD | 0.008 | 0.004 | 0.006 | 0.009 |
| L. SDAT | Mean | 0.033 | 0.044 | 0.02 | 0.071 |
| | SD | 0.005 | 0.009 | 0 | 0.011 |
| | P | 0.015 | 0.0025 | 0.0038 | 0.026 |
| R. Control | Mean | 0.040 | 0.057 | 0.028 | 0.086 |
| Vs | SD | 0.014 | 0.010 | 0.007 | 0.011 |
| R. SDAT | Mean | 0.034 | 0.041 | 0.023 | 0.076 |
| | SD | 0 005 | 0.009 | 0.005 | 0.015 |
| | P | NS | 0.0088 | NS | NS |

CCV = Cranial cavity volume
NS = No significant difference

Mean diff = Mean difference.

Table 7 shows the comparison of the cerebral cortex values between the left (L) and right (R) control values, the left and right SDAT values, the comparison between the left control and the left SDAT values and the comparison between the right control and right SDAT values in the occipital, parietal, temporal and frontal lobes.

It can be seen from Table 7 that there was a statistically significant difference between the left occipital cortex volume of the controls compared to SDAT patients ($p < 0.02$). There was no significant difference between the right occipital cortex volume of the controls compared to the SDAT patients.

There was a statistically significant difference between the left and right parietal cortex volume of the controls compared to the SDAT patients ($p < 0.01$ in the left and the right).

There was a statistically significant difference between the left temporal cortex volume of the controls compared to the SDAT patients ($p < 0.01$). There was no significant difference between the right temporal cortex volume of the controls compared to the SDAT patients.

There was a statistically significant difference between the left frontal cortex volume of the controls compared to the SDAT patients ($p < 0.05$). There was no significant difference between the right frontal cortex volume of the controls compared to the SDAT patients.

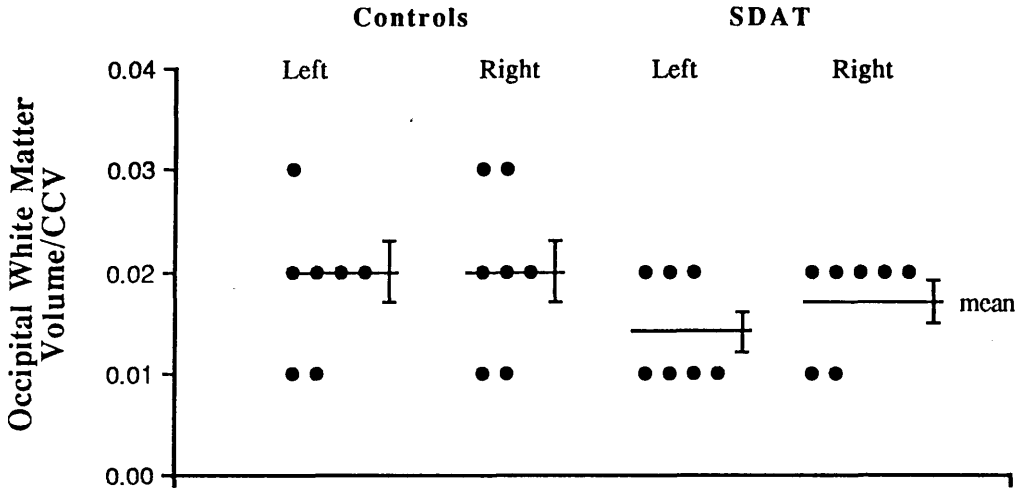


Figure 29 shows the left and right white matter volumes of the occipital lobe/CCV ratios of both the control and SDAT patients.

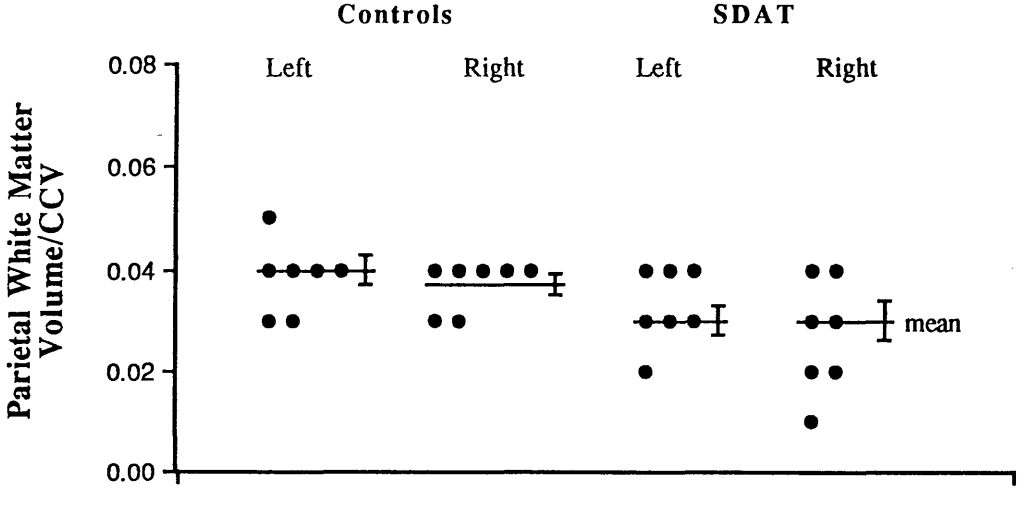


Figure 30 shows the left and right white matter volumes of the parietal lobe/CCV ratios of both the control and SDAT patients.

Volume of white matter in each lobe/cranial cavity volume

The volume of white matter in the occipital, parietal, temporal and frontal lobes in both left and right hemispheres was calculated in each of the control and SDAT brains.

The white matter volume of the occipital lobe/CCV ratio in the normal brain ranged from 0.01-0.03 with a mean volume of 0.02 ± 0.003 (mean ± SEM) in the left hemisphere and ranged from 0.01-0.03 with a mean value of 0.02 ± 0.003 (mean ± SEM) in the right hemisphere (see Fig. 29). The white matter volume of the occipital lobe/CCV ratio in the SDAT brain ranged from 0.01-0.02 with a mean value of 0.01 ± 0.002 (mean ± SEM) in the left hemisphere and ranged from 0.01-0.02 with a mean value of 0.02 ± 0.002 (mean ± SEM) in the right hemisphere (see Fig. 29).

The white matter volume of the parietal lobe/CCV ratio in the normal brain ranged from 0.03-0.05 with a mean value of 0.04 ± 0.003 (mean ± SEM) in the left hemisphere and ranged from 0.03-0.04 with a mean value of 0.04 ± 0.002 (mean ± SEM) in the right hemisphere (see Fig. 30). The white matter volume of the parietal lobe/CCV ratio in the SDAT brain ranged from 0.02-0.04 with a mean value of 0.03 ± 0.003 (mean ± SEM) in the left hemisphere and ranged from 0.01-0.04 with a mean value of 0.03 ± 0.004 (mean ± SEM) in the right hemisphere (see Fig. 30).

The white matter volume of the temporal lobe/CCV ratio in the normal brain ranged from 0.01-0.02 with a mean value of 0.01 ±0.002 (mean± SEM) in the left hemisphere and ranged from 0.01-0.02 with a mean value of 0.01 ± 0.001 (mean ± SEM) in the right hemisphere (see Fig. 31). The white matter volume of the

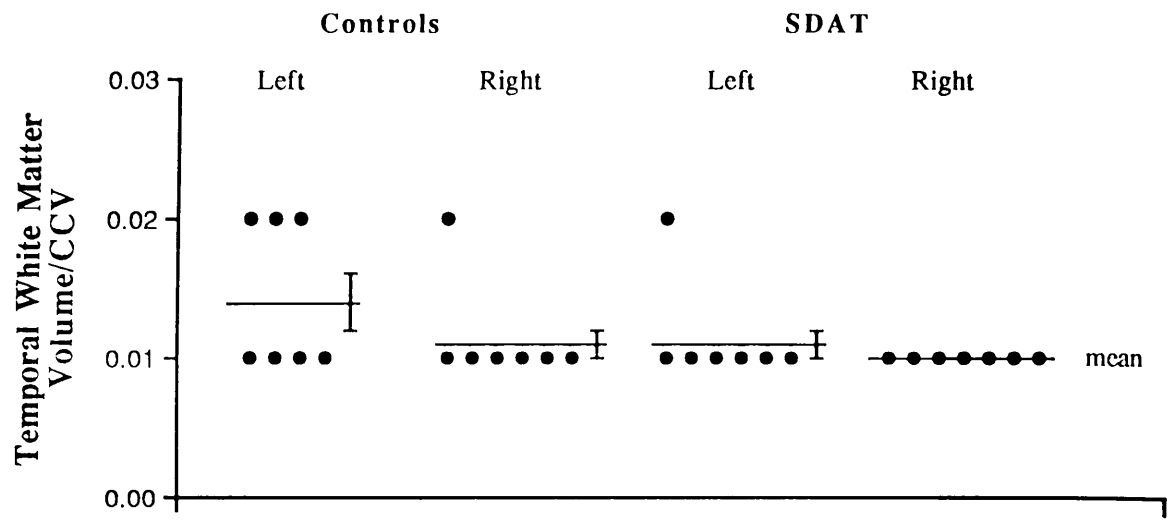


Figure 31 shows the left and right white matter volumes of the temporal lobe/CCV ratios of both the control and SDAT patients.

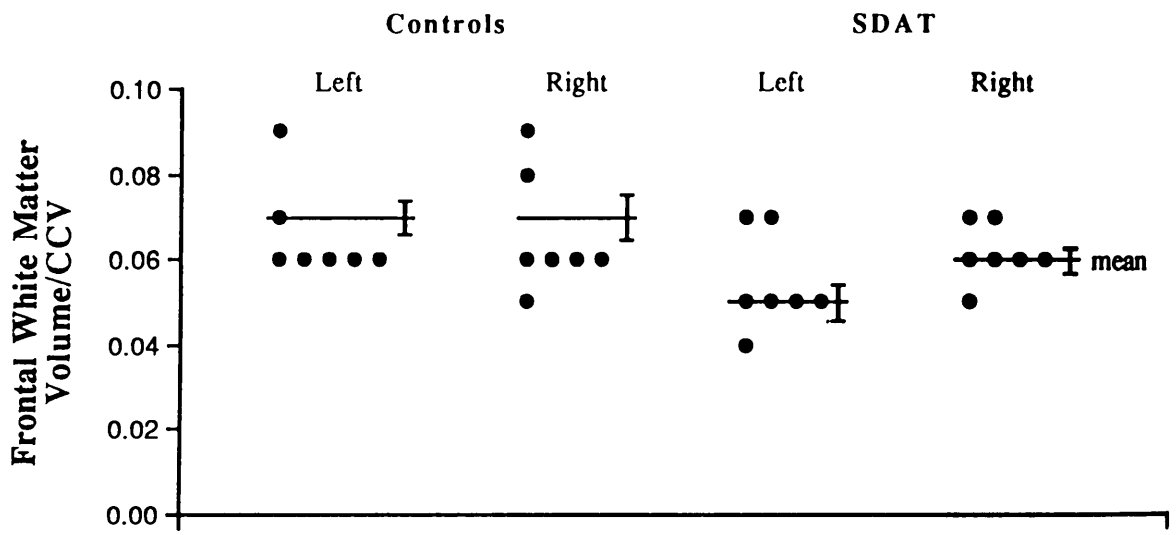


Figure 32 shows the left and right white matter volumes of the frontal lobe/CCV ratios of both the control and SDAT patients.

temporal lobe/CCV ratio in the SDAT brain ranged from 0.01-0.02 with a mean value of 0.01 ± 0.001 (mean ± SEM) in the left hemisphere and was 0.01 in each of the lobes in the right hemisphere (see Fig. 31).

The white matter volume of the frontal lobe/CCV ratio in the normal brain ranged from 0.06-0.09 with a mean value of 0.07 ± 0.004 (mean ± SEM) in the left hemisphere and ranged from 0.05-0.09 with a mean value of 0.07 ± 0.005 (mean ± SEM) in the right hemisphere (see Fig. 32). The white matter volume of the frontal lobe/CCV ratio in the SDAT brain ranged from 0.04-0.07 with a mean value of 0.05 ± 0.004 (mean ± SEM) in the left hemisphere and ranged from 0.05-0.07 with a mean value of 0.06 ± 0.003 (mean ± SEM) in the right hemisphere (see Fig. 32).

**Table 8** Volume of white matter in each lobe.

| | | Occipital white matter/CCV | Parietal white matter/CCV | Temporal white matter/CCV | Frontal white matter/CCV |
|---|---|---|---|---|---|
| L. Control | Mean diff | 0.001 | 0.001 | 0.003 | 0 |
| Vs | SD | 0.007 | 0.004 | 0.005 | 0.006 |
| R. Control | P | NS | NS | NS | NS |
| L. SDAT | Mean diff | 0.003 | 0.006 | 0.001 | 0.007 |
| Vs | SD | 0.005 | 0.008 | 0.004 | 0.011 |
| R. SDAT | P | NS | NS | NS | NS |
| L. Control | Mean | 0.018 | 0.038 | 0.014 | 0.066 |
| Vs | SD | 0.007 | 0.007 | 0.005 | 0.011 |
| L. SDAT | Mean | 0.014 | 0.033 | 0.011 | 0.054 |
| | SD | 0.005 | 0.008 | 0.004 | 0.011 |
| | P | NS | NS | NS | NS |
| R. Control | Mean | 0.020 | 0.037 | 0.011 | 0.066 |
| Vs | SD | 0.008 | 0.005 | 0.004 | 0.014 |
| R. SDAT | Mean | 0.017 | 0.027 | 0 | 0.061 |
| | SD | 0 005 | 0.011 | 0 | 0 007 |
| | P | NS | NS | NS | NS |

CCV = Cranial cavity volume
NS = No significant difference ($p > 0.05$)
Mean diff = Mean difference.

Table 8 shows the comparison of the white matter values between the left (L) and right (R) control values, the left and right SDAT values, the comparison between the left control and the left SDAT values and the comparison between the right control and right SDAT values in the occipital, parietal, temporal and frontal lobes.

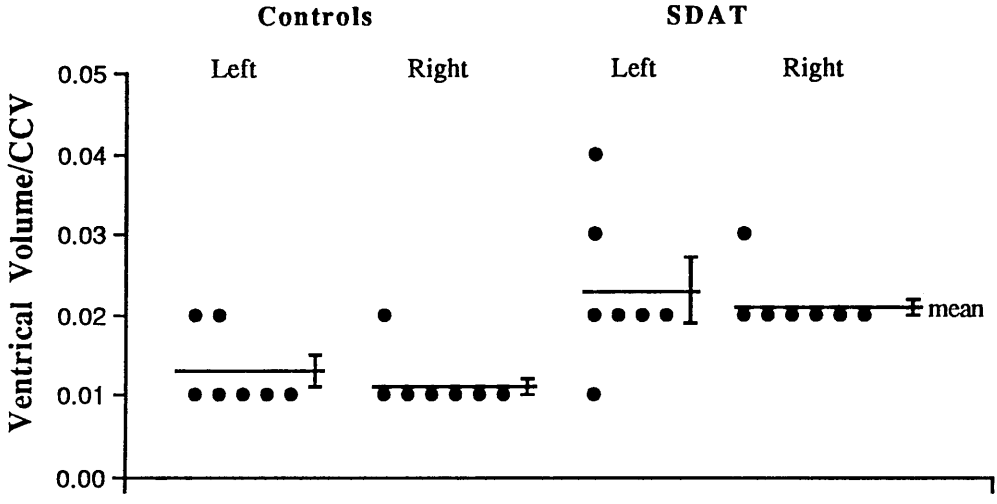


Figure 33 shows the left and right ventricular volume/ccv ratios of both the control and SDAT patients.

It can be seen from Table 8 that there was no statistically significant difference between the left or right occipital white matter volumes of the controls compared to the SDAT patients.

There was no statistically significant difference between the left or right parietal white matter volumes of the controls compared to the SDAT patients.

There was no statistically significant difference between the left or right temporal white matter volumes of the controls compared to the SDAT patients.

There was no statistically significant difference between the left and right frontal white matter volumes of the controls compared to the SDAT patients.

Ventricular volume/CCV

The volume of the ventricles in the left and right hemispheres of the control and SDAT brains was calculated.

The ventricular volume/CCV ratios in the normal brain ranged from 0.01-0.02 with a mean value of 0.01 $\pm$ 0.002 (mean $\pm$ SEM) in the left hemisphere and ranged from 0.01-0.02 with a mean value of 0.01 $\pm$ 0.001 (mean $\pm$ SEM) in the right hemisphere (see Fig. 33). The ventricular volume/CCV ratios of the SDAT brain ranged from 0.01-0.04 with a mean value of 0.02 $\pm$ 0.004 (mean $\pm$ SEM) in the left hemisphere and ranged from 0.02-0.03 with a mean value of 0.02 $\pm$ 0.001 (mean $\pm$ SEM) in the right hemisphere (see Fig. 33).

**Table 9** Ventricular volume.

| | | Ventricular Volume/CCV |
|---|---|---|
| L. Control | Mean diff | 0.001 |
| Vs | SD | 0.007 |
| R. Control | P | NS |
| L. SDAT | Mean diff | 0.001 |
| Vs | SD | 0.007 |
| R. SDAT | P | NS |
| L. Control | Mean | 0.01 |
| Vs | SD | 0.005 |
| L. SDAT | Mean | 0.02 |
| | SD | 0.01 |
| | P | NS |
| R. Control | Mean | 0.01 |
| Vs | SD | 0.004 |
| R. SDAT | Mean | 0.02 |
| | SD | 0.004 |
| | P | NS |
| Control Total | Mean | 0.02 |
| Vs | SD | 0.005 |
| SDAT Total | Mean | 0.04 |
| | SD | 0.01 |
| | P | NS |

CCV = Cranial cavity volume Mean diff = Mean difference.
NS = No significant difference ($p > 0.05$)

Table 9 showing the comparison between the left (L) and right (R) control values, the left and right SDAT values, the comparison between the left control and the left SDAT values, the comparison between the right control and right SDAT values and the comparison between the total ventricular control and total ventricular SDAT values.

It can be seen from Table 9 that there was no statistically significant difference between the left and right ventricular volume of the controls compared to the SDAT patients.

From the quantitative morphometry data it can be seen that there was global loss of cerebral cortex and white matter in the SDAT brain, with more cortex being lost than white matter. There was also selective loss of cortex in the left temporal, frontal, parietal and occipital lobes, whereas in the right hemisphere only the cortex of the parietal lobe showed any atrophy. Even though there was global loss of white matter, there was no significant difference in the white matter between each individual lobe of the SDAT brain compared to the age matched controls. There was also no significant difference in the size of the ventricles between the 2 groups.

**Staining of senile plaques**

In an attempt to evaluate the best method for demonstrating senile plaques in this Department, 7 different staining techniques were employed on both frozen and paraffin sections.

The plaque counts obtained on both frozen and paraffin sections are given in Tables 10, 11 and 12 and are expressed in plaques per $mm^3$ corrected for section thickness and shrinkage due to paraffin processing. The number of plaques in each region of the brain varied considerably, but the highest plaque counts were obtained on the frozen sections stained by the King's amyloid and von Braunmuhl silver impregnation techniques. In Brain A(Table 10) the highest plaque count was obtained in

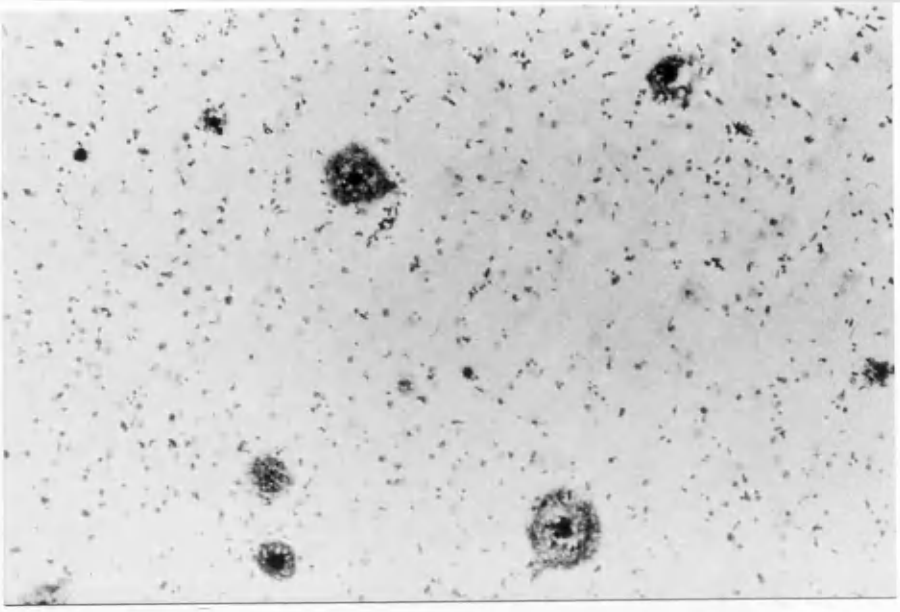

**Figure 34** Senile plaques in the cerebral cortex. King's amyloid x 100.

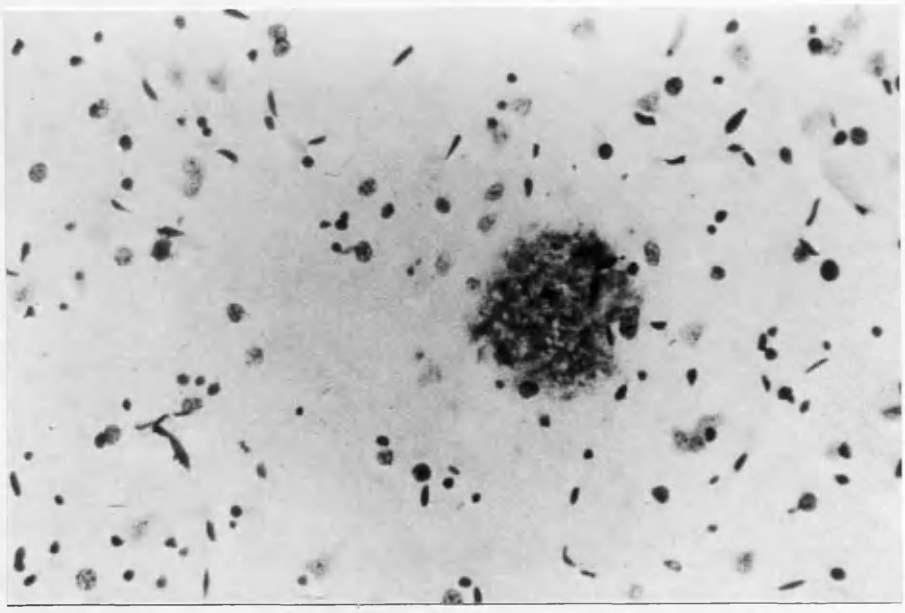

**Figure 35** High power of a primitive senile plaque. King's amyloid x 200.

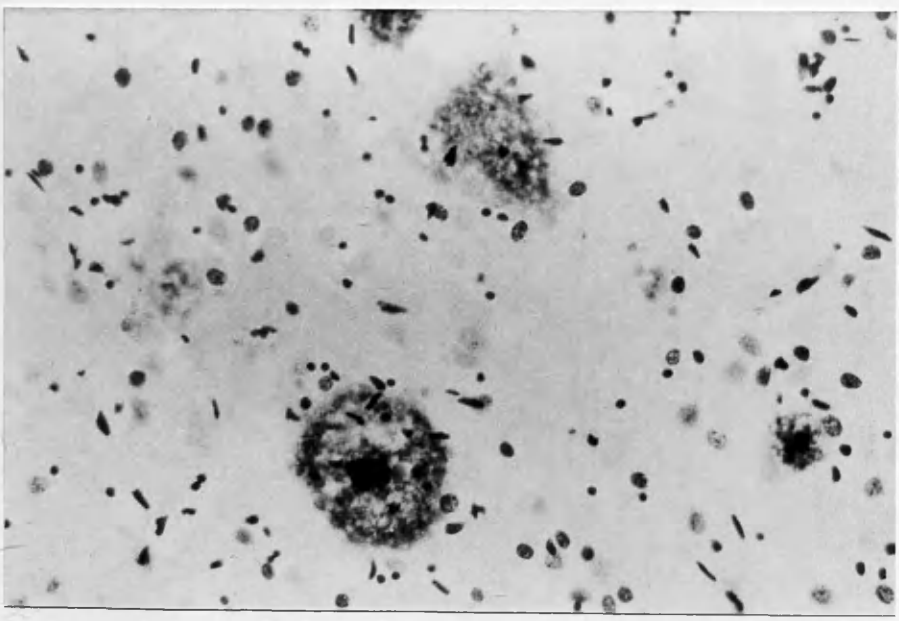

**Figure 36** High power of a classical and burnt out plaque. King's amyloid x 200.

the right parietal lobe (752 plaques/$mm^3$) stained by the King's amyloid method on frozen sections. The highest plaque count obtained from the same block on the paraffin sections was with the thioflavine-T method which gave a plaque count of 357 plaques/$mm^3$ (47% of the plaque count obtained with the King's method). The lowest plaque count (9 plaques/$mm^3$) obtained in the paraffin sections from the right parietal lobe was with the congo red (1.2% of the plaque count obtained with the King's method). The closest comparison in Brain A between the frozen and paraffin techniques was obtained in the left frontal lobe where the highest plaque count was again obtained on frozen sections with the King's method (704 plaques/$mm^3$) and the highest plaque count from the same block on paraffin sections was again obtained on the thioflavine-T (517 plaques/$mm^3$, i.e. 73% of the King's plaque count). Similar results were obtained in Brain B and Brain C.

From the 7 staining techniques used in this study the highest plaque counts were obtained on the frozen sections stained by the King's amyloid and the von Braunmuhl silver impregnation techniques. The King's amyloid technique was more reproducible with less variation in staining. It also gave the highest plaque count in all but a few cases and was therefore employed throughout this study for the quantitative plaque counts (Figs. 34-36).

**Table 10** The number of plaques identified in Brain A expressed as plaques/$mm^3$. The brain was from a 75 year old female.

| Region of brain examined | Staining Techniques Employed | | | | | | |
|---|---|---|---|---|---|---|---|
| | King's | von Braunmuhl | Thioflavine-T | Anti-Paired Helical Filaments | Palmgren | Congo red | Sirius red |
| Left frontal lobe | 704 | 600 | 517 | 146 | 25 | 37 | 31 |
| Right frontal lobe | 588 | 596 | 355 | 48 | 12 | 31 | 31 |
| Left hippocampus | 496 | 484 | 319 | 56 | 99 | 31 | 18 |
| Right hippocampus | 556 | 528 | 328 | 48 | 31 | 28 | 58 |
| Left parietal lobe | 672 | 508 | 386 | 35 | 31 | 111 | 92 |
| Right parietal lobe | 752 | 452 | 357 | 25 | 55 | 9 | 43 |

**Table 11** The number of plaques identified in Brain B expressed as plaques/$mm^3$. The brain was from a 79 year old female.

| Region of brain examined | Staining Techniques Employed | | | | | | |
|---|---|---|---|---|---|---|---|
| | King's | von Braunmuhl | Thioflavine-T | Anti-Paired Helical Filaments | Palmgren | Congo Red | Sirius Red |
| Left frontal lobe | 864 | 792 | 567 | 36 | 0 | 30 | 3 |
| Right frontal lobe | 1032 | 1052 | 535 | 35 | 0 | 18 | 0 |
| Left hippocampus | 1276 | 1200 | 122 | 11 | 0 | 30 | 24 |
| Right hippocampus | 2000 | 1896 | 108 | 31 | 24 | 30 | 18 |
| Left parietal lobe | 392 | 332 | 217 | 38 | 0 | 36 | 30 |
| Right parietal lobe | 772 | 628 | 342 | 20 | 0 | 18 | 34 |

**Table 12** The number of plaques identified in Case 3 expressed as plaques/$mm^3$
The brain was from a 93 year old female.

| Region of brain examined | Staining Techniques Employed | | | | | | |
|---|---|---|---|---|---|---|---|
| | King's | von Braunmuhl | Thioflavine-T | Anti-Paired Helical Filaments | Palmgren | Congo Red | Sirius Red |
| Left frontal lobe | 572 | 564 | 339 | 52 | 6 | 15 | 32 |
| Right frontal lobe | 632 | 436 | 250 | 29 | 0 | 29 | 29 |
| Left hippocampus | 575 | 524 | 341 | 90 | 50 | 50 | 50 |
| Right hippocampus | 580 | 484 | 323 | 74 | 0 | 29 | 38 |
| Left parietal lobe | 436 | 316 | 279 | 55 | 91 | 187 | 178 |
| Right parietal lobe | 500 | 400 | 343 | 55 | 82 | 135 | 123 |

**Quantitative Plaque Counts**

Before plaque counts could be compared between different brains and indeed between different regions with the same brain, the reproducibility and the variability of the plaque counts had to be determined.

The number of plaques/$mm^2$ were counted at 1, 3 and 6 reference points and the standard deviation (SD) of the difference in the day to day reproducibility examined.

Reproducibility of Plaque Counts

The reproducibility of the plaque counts obtained between different regions is obviously important since the results would be meaningless if, for example, the temporal cortex had the highest plaque count on day 1 and the lowest count on day 2. This problem was looked at in three stages to see not only how reproducible the results are, but also how many counts were actually necessary to give an accurate plaque count which can be taken as the average for that brain region. Firstly, all regions had a superficial and deep count made at one reference point in each of the brain regions. This was repeated on day 2 at the same point. Secondly, superficial and deep counts were made at 3 reference points in each of the brain regions and again this was repeated on day 2. Finally, superficial and deep counts were made at all 6 reference points in each of the brain regions and repeated on day 2. See Tables 13 (plaque numbers) and 14 (plaque area).

**Table 13** Reproducibility of plaque counts

| | Standard deviation of the difference in the number of plaques from day 1-day 2. | | | Standard deviation of the difference in the number of plaques expressed as a percentage of the number of plaques counted on day 1 | | |
|---|---|---|---|---|---|---|
| | Superficial (S) | Deep (D) | Total (mean of S+D) | Superficial (S) | Deep (D) | Total (mean of S+D) |
| All Regions, 1 point per region | ±2.5 | ±2.07 | ±2.2 | ±11.3 | ±12.1 | ±9.6 |
| P | <0.02* | NS | <0.05* | | | |
| All Regions, 3 points per region | ±1.4 | ±0.7 | ±0.9 | ± 7.1 | ± 7.6 | ±5.5 |
| P | NS | NS | NS | | | |
| All Regions, 6 points per region | ±1.2 | ±0.5 | ±0.7 | ± 5.1 | ± 6.6 | ±3.9 |
| P | NS | NS | NS | | | |

NS = Not significant
* = P <0.02 and/or P <0.05

**Table 14** Reproducibility of the area of plaques counted in square microns

| | Standard deviation of the difference in the area of plaques from day 1-day 2. | | | Standard deviation of the difference in the area of plaques expressed as a percentage of the area of plaques measured on day 1. | | |
|---|---|---|---|---|---|---|
| | Superficial (S) | Deep (D) | Total (mean of S&D) | Superficial (S) | Deep (D) | Total (mean of S&D) |
| All Regions, 1 point per region | ±5300 | ±3100 | ±3600 | ±25.0 | ±25.8 | ±19.1 |
| P | <0.02* | NS | <0.02* | | | |
| All Regions 3 points per region | ±3800 | ±1900 | ±2400 | ±14.2 | ±25.0 | ±10.2 |
| P | <0.02* | NS | <0.05* | | | |
| All Regions, 6 points per region | ±2100 | ± 800 | ±1400 | ± 5.6 | ± 8.6 | ± 4.8 |
| P | <0.01** | <0.01** | <0.01** | | | |

NS = Not significant
* = P <0.02 or P <0.05
** = P <0.01

**Footnote**
The level of statistical significance increased when more plaque counts were made, presumably due to the compounded error introduced by the neutral density filters (see p 74-75).

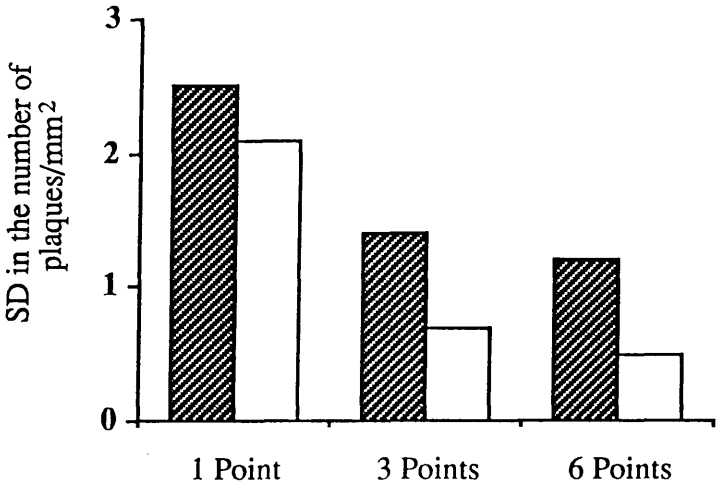


Figure 37 shows the standard deviation of the difference in the number of plaques counted between day 1 and day 2.

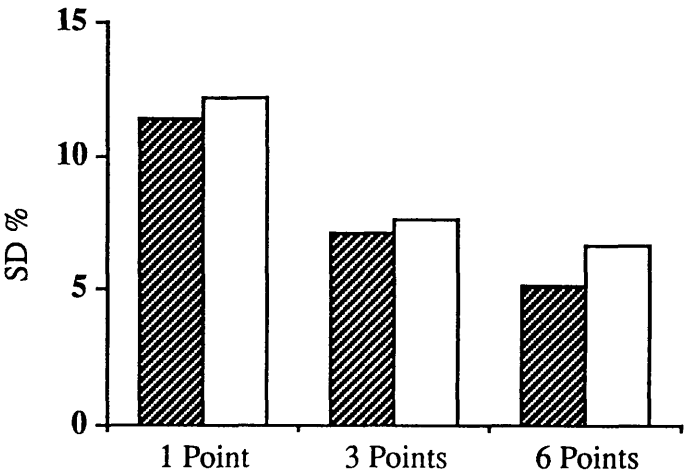


Figure 38 shows the standard deviation of the difference in the number of plaques counted between day 1 and day 2 expressed as a percentage of the day 1 counts.

▨ = superficial layers of cortex
□ = deep layers of cortex
SD = standard deviation

The day to day error was evaluated by examining the SD of the difference between the 2 plaque counts in both absolute and percentage terms. The smaller the SD number, the more reproducible the plaque counts, and the greater the SD number, the less reproducible the plaque counts (see Figs. 37-38 and Tables 13-14).

If plaques were counted at only one reference point per brain region, there was a statistically significant difference between the plaque count obtained on day 1 compared to the plaque count obtained on day 2 ($\pm$ 2.2 plaques and $\pm$ 9.6%). If the number of reference points per brain region was increased to 3, there was no significant difference between the plaque counts on day 1 compared to the plaque counts on day 2 ($\pm$ 0.9 plaques and $\pm$ 5.5%). If the number of reference points per brain region was increased to 6, there was no significant difference between the plaque counts obtained on day 1 compared to the plaque counts obtained on day 2 ($\pm$ 0.7 plaques and $\pm$ 3.9%). It was therefore decided to count the plaques at 6 reference points per brain region.

However, when the area of the plaques was compared between day 1 and day 2, even when 6 reference points per brain region were counted, there was still a statistically significant difference between the area of plaques obtained on day 1 compared to day 2.

On re-examination of the data, it was found that the area of the plaques was consistently lower on day 2 than on day 1. It was therefore necessary to try to find out what was causing

the difference. Since the plaques were drawn free-hand using a cursor, the first thing that was examined for error was the variability of the actual area drawn round each plaque. The small differences obtained by deliberately drawing the plaques slightly larger or smaller than the "normal" size was negligible, therefore another source of error had to be investigated. Neutral density filters had been used to enhance the contrast between the plaques and the background staining. A single field was chosen and there were 55 plaques counted. Without using any neutral density filters, the total area of the 55 plaques was 31846 square microns. When one neutral density filter was used, the same 55 plaques gave a total area of 49615 square microns, and when 2 filters were used, the total area was 71830 square microns. The difference in area between 0 and 1 filter was an increase of 55.8%, between 1 and 2 filters was an increase of 44.8% and the difference between 0 and 2 filters was 125.6%. This was obviously a source of error when measuring the area of the plaques. A counting chamber with a known area ($9mm^2$), which was divided into 9 one $millimeter^2$ squares, was placed in the Quantimet 10 image analysis system and 3 measurements were made of a 1mm ($1,000,000u^2$) square using 0, 1 and 2 filters. The average area for 0 filters was 985547 (-1.4%) square microns: for 1 filter the average area was 1003520 (+0.4%) square microns: and the average area using 2 filters was 1032800 (+3.3%) square microns. It was therefore decided to use one neutral density filter since this gave the most accurate measurement of the area of the square (1,000,000 square microns).

**Table 15** Reproducibility in determining the number of plaques in 7 different cortical regions

| | Standard deviation of the difference in the number of plaques from day 1-day 2. | | | Standard deviation of the difference in the number of plaques expressed as a percentage of the number of plaques counted on day 1. | | |
|---|---|---|---|---|---|---|
| | Superficial (S) | Deep (D) | Total (mean of S+D) | Superficial (S) | Deep (D) | Total (mean of S+D) |
| Middle frontal gyrus | ±3.2 | ±1.7 | ±2.1 | ±13.0 | ±21.0 | ±12.7 |
| P | NS | NS | NS | | | |
| Superior temporal gyrus | ±4.5 | ±3.3 | ±3.7 | ±22.5 | ±63.8 | ±28.8 |
| P | NS | NS | NS | | | |
| Middle temporal gyrus | ±0.8 | ±0.8 | ±0.7 | ± 5.6 | ± 9.8 | ± 6.3 |
| P | <0.01** | NS | NS | | | |
| Inferior temporal gyrus | ±1.0 | ±1.7 | ±0.8 | ± 6.6 | ±21.4 | ± 7.8 |
| P | NS | NS | NS | | | |
| Cingulate | ±2.8 | ±0.8 | ±1.5 | ±24.7 | ± 9.2 | ±16.9 |
| P | NS | NS | NS | | | |
| Superior parietal | ±3.4 | ±3.4 | ±1.3 | ±10 6 | ±24.0 | ±11.2 |
| P | NS | NS | NS | | | |
| Occipital lobe | ±1.8 | ±2.0 | ±1.2 | ±13-0 | ±21.2 | ±10.5 |
| P | NS | NS | NS | | | |

NS = Not significant
** = P <0.01

counted in square microns

**Table 16** Reproducibility in determining the area of plaques in 7 different cortical regions

| | Standard deviation of the difference in the area of plaques from day 1-day 2. | | | Standard deviation of the difference in the area of plaques expressed as a percentage of the area of plaques measured in day 1. | | |
|---|---|---|---|---|---|---|
| | Superficial (S) | Deep (D) | Total (mean of S+D) | Superficial (S) | Deep (D) | Total (mean of S+D) |
| Middle frontal gyrus | ±6706 | ±1610 | ±3734 | ±30.2 | ±13.7 | ±22.9 |
| P | NS | NS | NS | | | |
| Superior temporal gyrus | ±5044 | ±3886 | ±4402 | ±32.8 | ±33.1 | ±32.8 |
| P | NS | NS | NS | | | |
| Middle temporal gyrus | ±4515 | ±2464 | ±3173 | ±15.9 | ±31.6 | ±16 5 |
| P | NS | NS | NS | | | |
| Inferior temporal gyrus | ±3861 | ±3265 | ±2809 | ±21.5 | ±38.3 | ±19.0 |
| P | | | | | | |
| Cingulate | ±4458 | ±1104 | ±2334 | ±28.1 | ±15.1 | ±24.6 |
| P | NS | NS | NS | | | |
| Superior parietal | ±4439 | ±2836 | ±3217 | ±12.2 | ±15.6 | ±12.8 |
| P | <0.01** | NS | <0.01** | | | |
| Occipital lobe | ±5010 | ±4996 | ±3306 | ±19.0 | ±44.2 | ±16.0 |
| P | NS | NS | NS | | | |

NS = Not significant
** = P <0.01

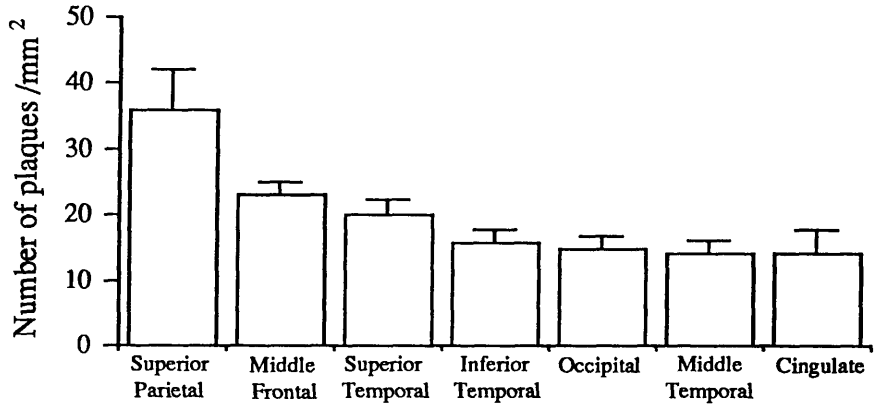


**Figure 39 shows the mean number of plaques/mm 2 (± SE of mean) in the superficial layers of the regions examined in the 6 SDAT cases.**

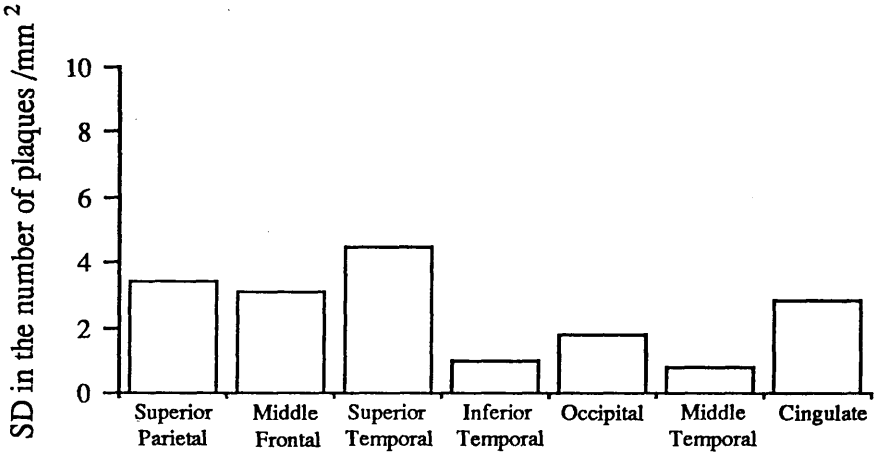


**Figure 40 shows the standard deviation of the difference in the number of plaques between day 1 and day 2 in the superficial layers of cortex. SD = standard deviation**

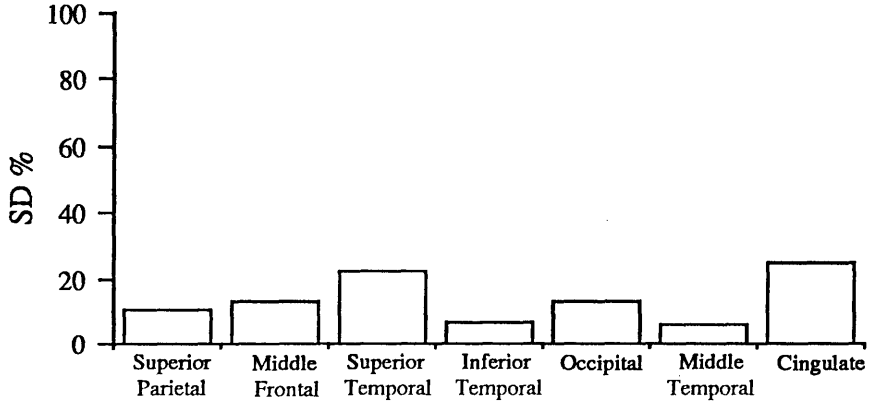


**Figure 41 shows the standard deviation of the difference in the number of plaques between day 1 and day 2 expressed as a percentage of the day 1 plaque counts in the superficial layers of cortex. SD = standard deviation**

Intraregional and interregional reproducibility

All regions were counted and both the superficial and deep counts were repeated on day 2 at all 6 reference points on each of the slides. This was to see if there was a statistically significant difference in the plaque counts obtained in any particular region of the brain (see Tables 15 and 17).

Only the superficial count in the middle temporal gyrus produced a statistically significant difference between the plaque count obtained on day 1 compared to the plaque count obtained on day 2.

When comparing the area of plaques within the same region between day 1 and day 2, there was a statistically significant difference in the superior parietal lobe. The superior parietal lobe had the highest area of plaques on day 1 and it still had the highest area on day 2.

By increasing the number of reference points from 1 to 6 in each brain region, the day to day error in the reproducibility of plaque counts was halved in the superficial layers and quartered in the deep layers. When counting plaques at 6 reference points per brain region, the mean error in the day to day variation was $\pm$ 0.7 plaques/mm$^2$ and $\pm$ 3.9%. The mean number of plaques/mm$^2$ in the superficial layers of each of the regions examined in the 6 SDAT cases are shown in Fig. 39.

In absolute terms, i.e. plaques/mm$^2$, the day to day reproducibility displayed minimal (0.8-4.5) intra- and inter-regional heterogeneity (see Fig. 40 and Table 15). In percentage terms, the day to day reproducibility varied from

5.6-24.7% in the superficial layers and 9.2-63.8% in the deep layers (see Fig. 41 and Table 15).

It can be seen from Figures 39-41 that the day to day error in both absolute and percentage terms was not related to the number of plaques/$mm^2$ counted, i.e. the greater the number of plaques counted did not necessarily mean the greater the error in absolute or percentage terms.

Correction factor between fixed tissue block and stained frozen section

The point counting technique previously described was repeated three times on each tissue block and stained frozen section and the average area for each block and section were compared using a student's paired t-test (see Tables 17-19).

Tables 17-19 show that there was no statistically significant difference between any of the fixed tissue blocks and the corresponding stained frozen section in the 3 brains examined. It was therefore decided that it was not necessary to apply any correction factor for the slight differences that did occur between the tissue blocks and the frozen sections.

**Table 17** Comparison between fixed tissue block and stained frozen section (Case 6).

| | Cortex area in fixed tissue block | Cortex area in stained section | % Difference | P Value |
|---|---|---|---|---|
| Left | | | | |
| Frontal | 211.3mm$^2$ | 180.0mm$^2$ | -14.8 | |
| Sup.temporal | 225.5 | 231.4 | + 2.6 | |
| Mid.temporal | 250.6 | 248.1 | - 1.0 | |
| Inf.temporal | 203.0 | 200.5 | - 1.2 | NS |
| Cingulate | 64.3 | 61.0 | - 5.0 | |
| Parietal | 292.3 | 278.1 | - 4.8 | |
| Occipital | 223.0 | 236.4 | + 6.0 | |
| Right | | | | |
| Frontal | 253.1mm$^2$ | 256.4mm$^2$ | + 1.3 | |
| Sup.temporal | 198.0 | 172.9 | -13.0 | |
| Mid.temporal | 167.0 | 169.6 | + 1.6 | |
| Inf.temporal | 236.4 | 225.5 | - 4.6 | NS |
| Cingulate | 181.2 | 198.0 | + 9.3 | |
| Parietal | 258.9 | 250.6 | - 3.2 | |
| Occipital | 177.9 | 183.8 | + 3.3 | |

NS = No significant difference ($P > 0.05$)

**Table 18** Comparison between fixed tissue block and stained frozen section (Case 10).

| | Cortex area in fixed tissue block | Cortex area in stained section | % Difference | P value |
|---|---|---|---|---|
| Left | | | | |
| Frontal | 192.1mm$^2$ | 189.6mm$^2$ | - 1.3 | |
| Sup.temporal | 208.8 | 225.5 | + 8.0 | |
| Mid.temporal | 144.5 | 139.5 | - 3.5 | |
| Inf.temporal | 256.4 | 242.2 | - 5.5 | NS |
| Cingulate | 102.7 | 106.1 | - 3.3 | |
| Parietal | 292.3 | 298.2 | + 2.0 | |
| Occipital | 219.7 | 208.8 | - 5.0 | |
| Right | | | | |
| Frontal | 248.1mm$^2$ | 248.1mm$^2$ | 0 | |
| Sup.temporal | 183.8 | 181.2 | - 1.4 | |
| Mid.temporal | 158.7 | 164.5 | + 3.6 | |
| Inf.temporal | 225.5 | 203.0 | -10.0 | NS |
| Cingulate | 183.8 | 177.9 | - 3.2 | |
| Parietal | 225.5 | 258.9 | +14.8 | |
| Occipital | 261.4 | 258.9 | - 1.0 | |

NS = No significant difference (P >0.05)

**Table 19** Comparison between fixed tissue block and stained frozen section (Case 11).

| | Cortex area in fixed tissue block | Cortex area in stained section | % Difference | P Value |
|---|---|---|---|---|
| Left | | | | |
| Frontal | 198.0mm$^2$ | 206.3mm$^2$ | + 4.2 | |
| Sup. temporal | 340.0 | 323.2 | - 4.9 | |
| Mid. temporal | 231.4 | 239.7 | + 3.6 | |
| Inf. temporal | 219.7 | 214.7 | - 2.3 | NS |
| Cingulate | 223.0 | 242.2 | + 8.6 | |
| Parietal | 331.6 | 348.3 | + 5.0 | |
| Occipital | 175.4 | 172.9 | - 1.4 | |
| Right | | | | |
| Frontal | 244.7mm$^2$ | 242.2mm$^2$ | - 1.0 | |
| Sup. temporal | 250.6 | 239.7 | - 4.3 | |
| Mid. temporal | 116.9 | 114.4 | - 2.5 | |
| Inf. temporal | 350.8 | 303.2 | -13.6 | NS |
| Cingulate | 161.2 | 158.7 | - 1.6 | |
| Parietal | 314.9 | 356.6 | +13.7 | |
| Occipital | 328.2 | 378.4 | +15.3 | |

NS = No significant difference (P >0.05)

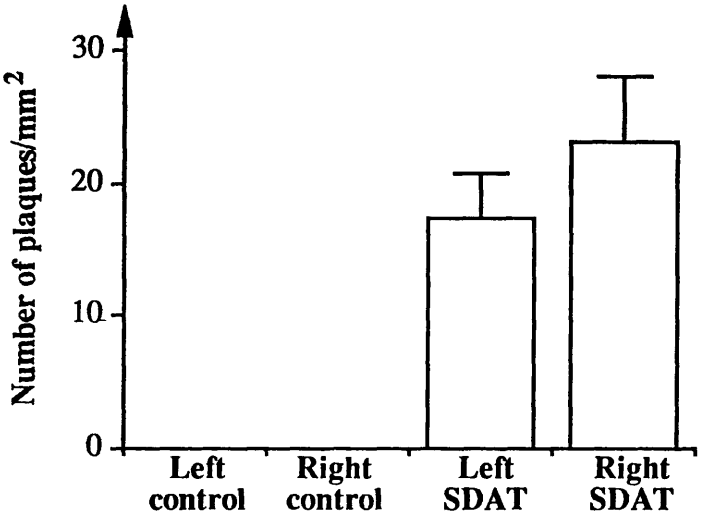


Figure 42 shows the mean superficial plaque count in the superior temporal cortex of the SDAT cases and age matched controls.

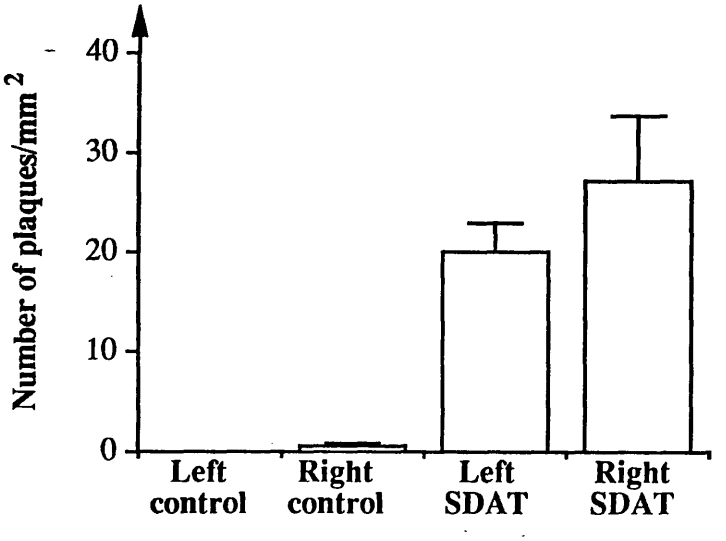


Figure 43 shows the mean superficial plaque count in the frontal cortex of the SDAT cases and age matched controls.

**Asymmetry of the Brain**

When counting the number of plaques in the control cases it was found that there were no plaques in the left or right hemispheres in 4 of the cases (Case 1,3,4 and 5), and only a few plaques in each hemisphere in Case 6. In the middle temporal and inferior temporal cortex in Case 2 there was a mean plaque count of 11.0 and 10.6 respectively in the left hemisphere, and 11.6 and 3.9 respectively in the right hemisphere. The other regions in Case 2 had virtually no plaques present. Figures 42-43 show the mean number of plaques/$mm^2$ in the superficial layers of the superior temporal and frontal cortex of the SDAT cases and the age matched controls.

Since the vast majority of the plaque counts in the control cases was zero, the various studies on plaque counts were confined to the SDAT cases.

The majority of workers studying various aspects of Alzheimer's disease assumed that the disease process was symmetrical. The brain was cut in the mid-sagittal plane and one hemisphere used for neurochemical analyses and the other for neuropathological studies. Part of this study was therefore undertaken to assess whether or not Alzheimer's disease was symmetrical.

Interhemispheric Asymmetry

As previously stated, a 5 plaque change and a 40% difference in plaque number was, by our criteria, a biologically significant difference between the left and right hemispheres. Since it has

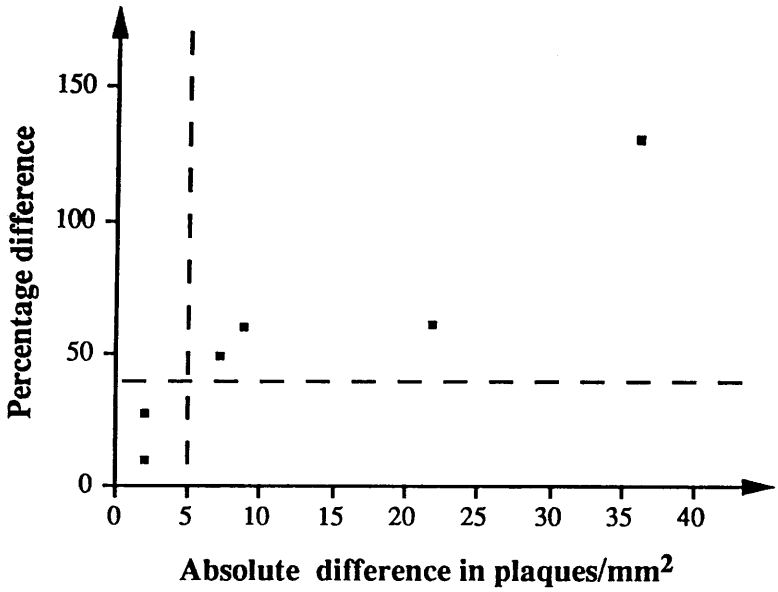


Figure 44 shows the absolute difference in the total number of plaques/mm$^2$ and the percentage difference between the left and right hemispheres of the frontal cortex, in the 6 brains studied

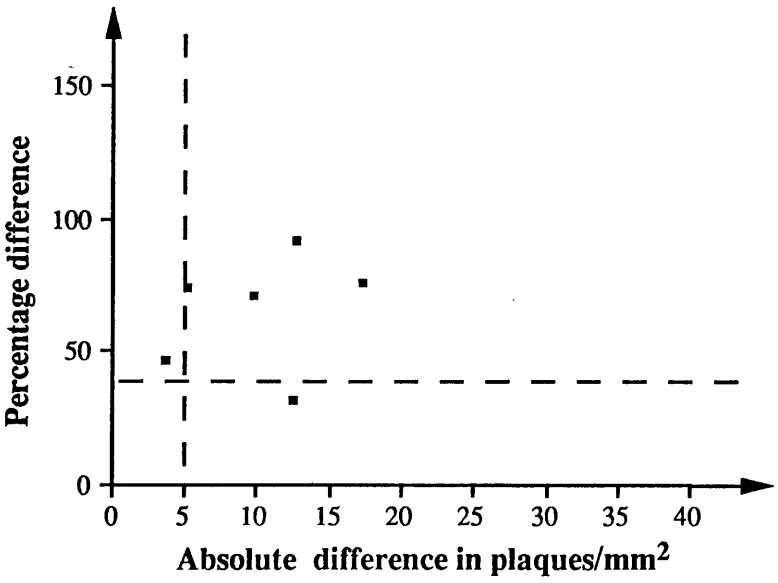


Figure 45 shows the absolute difference in the total number of plaques/mm$^2$ and the percentage difference between the left and right hemispheres of the superior temporal cortex, in the 6 brains studied

been shown in the reproducibility study (Table 13) that the standard deviation between the number of plaques counted on day 1 compared to the same counts on day 2 was ± 1.2 plaques in the superficial layers (± 5.1%), and ± 0.5 plaques in the deep layers (± 6.6%), and ± 0.7 plaques when the total plaque count (mean of superficial + deep) was taken (± 3.9%), then any changes between the hemispheres of 5 plaques with a 40% difference was due to an asymmetry of the disease process and not due to any inaccuracies produced by the Quantimet 10 image analyser or the investigator. The asymmetric plaque counts obtained in the frontal cortex and the superior temporal cortex are shown in Figs. 44 and 45 respectively.

A meaningful difference in plaque area between the hemispheres had also to be determined. This was done by simply calculating the total area of plaques, in square microns, counted in all 7 regions in both left and right hemispheres from the 6 brains used in this study and dividing this by the total number of plaques per $mm^2$ counted to give the average size of a plaque in square microns, i.e. $3,573,530\mu^2 \div 3,204$ plaques = $1,115\mu^2$. Since a 5 plaque change and a 40% difference was decided to be biologically meaningful, a difference of $5575\mu^2$ (5 x $1,115\mu^2$) and a 40% difference is the minimum change required to be biologically significant when examining the difference in the area of plaques between the two hemispheres (see tables 20-33).

It can be seen from Tables 20-33 that all 6 cases had asymmetric plaque counts in at least one region, whether it was

with the superficial, deep or total plaque counts. If the total number of plaques/$mm^2$ was being compared, it can be seen that Case 8 had asymmetric plaque counts in the superior temporal, cingulate and parietal cortex; Case 9 had asymmetric plaque counts in the frontal, superior temporal, cingulate and the occipital cortex; Case 10 had asymmetric plaque counts in the frontal, superior temporal, mid-temporal, cingulate and the parietal cortex; Case 11 had asymmetric plaque counts in the frontal, superior temporal, mid-temporal, cingulate and the parietal cortex; Case 12 had asymmetric plaque counts in the parietal cortex, and Case 13 had asymmetric plaque counts in the frontal, mid-temporal, inferior temporal, cingulate and occipital cortex. It can also be seen that sometimes the left hemisphere had the highest plaque counts (Cases 11 and 12) and sometimes the right hemisphere had the highest plaque counts (Cases 10 and 13). It can also be seen that even within the same brain, some regions had the highest plaque count in the left hemisphere while other regions had the highest plaque count in the right hemisphere (Cases 8 and 9).

When measuring the area of plaques, in square microns, if the total area of plaques was being compared, it can be seen that Case 8 had asymmetric plaque counts in the superior temporal cortex, Case 9 had asymmetric plaque counts in the frontal, superior temporal, mid-temporal and occipital cortex; Case 10 had asymmetric plaque counts in the frontal, superior temporal, mid-temporal, inferior temporal, cingulate, parietal and occipital cortex; Case 11 had asymmetric plaque counts in

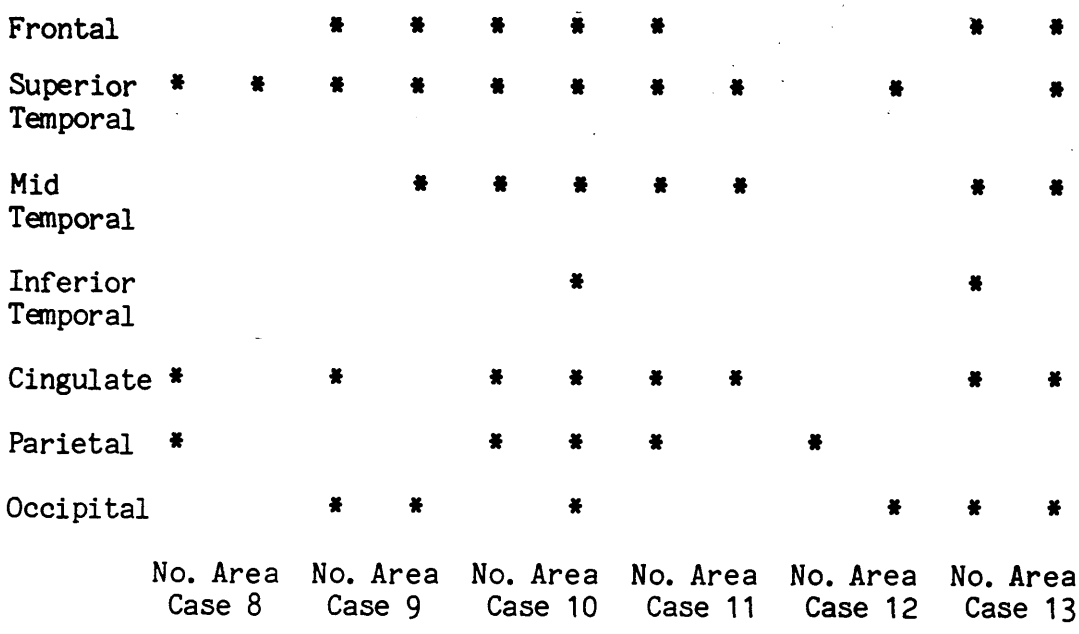


**Figure 46** shows the interhemispheric differences between the various regions of the brain being examined, when counting the number of plaques/$mm^2$ and measuring the area of plaques in square microns.

* = Asymmetric plaque counts between the left and right hemispheres.
No. = Number of plaques/$mm^2$
Area = Area of plaques in square microns

**Footnote**
Since the interhemispheric asymmetry was non directional, an asterisk was used simply to indicate the number of asymmetries in the 6 cases studied. See tables 20 - 33 (p 128-141) to determine whether the left or right hemisphere had the highest plaque count.

the superior temporal, mid-temporal cortex and cingulate; Case 12 had asymmetric plaque counts in the superior temporal and occipital cortex and Case 13 had asymmetric plaque counts in the frontal, superior temporal, mid-temporal, cingulate and occipital cortex.

It can also be seen that sometimes the left hemisphere had the largest plaque area (Case 11) and sometimes the right hemisphere had the largest plaque area (Cases 8, 10, 12 and 13). Even within the same brain, some regions had the largest plaque area in the left hemisphere, while other regions had the largest plaque area in the right hemisphere (Case 9).

It can also be seen that even within the same brain, when counting the number of plaques it was not always the same brain regions that had asymmetric plaque counts when measuring the area of plaques (see Fig. 46), e.g. in Case 9 when counting the number of plaques there was an asymmetric plaque count in the cingulate, but when measuring the area of the plaques there was not. Conversely, when measuring the area of plaques in Case 9, there was an asymmetric plaque count in the mid-temporal cortex and when counting the number of plaques there was not.

It can therefore be concluded that there were inter-hemispheric differences in either the number or area of plaques in each of the regions examined in the 6 SDAT cases used in this study.

**Intraregional Heterogeneity**

Since we have shown that there were interhemispheric differences in all 6 cases examined in this study, it was decided to apply the same criteria of a 5 plaque and a 40% change to the data obtained between the superficial and deep layers within the same region to see if there were any intraregional differences within the brain (see Tables 34-47).

It can be seen from Tables 34-47 that when counting the number of plaques/$mm^2$, there were a few regions which did not have asymmetric plaque counts, i.e. the left superior temporal, left middle temporal and right inferior temporal in Case 9; the right inferior temporal in Case 10; the left frontal, left middle temporal, left and right cingulate in Case 11; and the right frontal in Case 12. When measuring the area of plaques, in square microns, the regions which did not have asymmetric plaque counts were the left frontal and left occipital in Case 8; the left superior temporal, left middle temporal and right inferior temporal in Case 9; the right frontal and right parietal in Case 10; the left frontal, left inferior temporal, left cingulate and right parietal in Case 11; and the left and right frontal in Case 12.

When counting the number of plaques/$mm^2$, the superficial count was highest in all the regions examined in all 6 cases in both left and right hemispheres. When measuring the area of plaques in square microns, again the highest plaque counts were obtained in the superficial layers except for the left frontal, left cingulate and right parietal in Case 11.

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Frontal | * | | * | * | * | * | | | * | | * | * |
| Superior temporal | * | * | | | * | * | * | * | * | * | * | * |
| Middle temporal | * | * | | | * | * | | * | * | * | * | * |
| Inferior temporal | * | * | * | * | * | * | * | | * | * | * | * |
| Cingulate | * | * | * | * | * | * | | | * | * | * | * |
| Parietal | * | * | * | | * | * | * | * | * | * | * | * |
| Occipital | * | | * | * | * | * | * | * | * | * | * | * |
| | No. Area Case 8 | | No. Area Case 9 | | No. Area Case 10 | | No. Area Case 11 | | No. Area Case 12 | | No. Area Case 13 | |

**Figure 47** shows the intraregional variation between the superficial and deep layers of the cerebral cortex, when counting the number of plaques/$mm^2$ and measuring the plaque area, in square microns, in the left hemisphere.
* = Asymmetric plaque count
No. = Number of plaques/$mm^2$
Area = Area of plaques in square microns

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Frontal | * | * | * | * | | | * | * | | | * | * |
| Superior temporal | * | * | * | * | * | * | * | * | * | * | * | * |
| Middle temporal | * | * | * | * | * | * | * | * | * | * | * | |
| Inferior temporal | * | * | | | | * | * | * | * | * | * | * |
| Cingulate | * | * | * | * | * | * | | * | * | * | * | * |
| Parietal | * | * | * | * | * | | * | | * | * | * | * |
| Occipital | * | * | * | * | * | * | * | * | * | * | * | * |
| | No. Area Case 8 | | No. Area Case 9 | | No. Area Case 10 | | No. Area Case 11 | | No. Area Case 12 | | No. Area Case 13 | |

**Figure 48** shows the intraregional variation between the superficial and deep layers of the cerebral cortex, when counting the number of plaques/$mm^2$ and measuring the area of plaques, in square microns, in the right hemisphere.
* = Asymmetric plaque counts
No. = Number of plaques/$mm^2$
Area = Area of plaques in square microns.

When comparing the number of plaques to the area of plaques, it was not always the same regions, even within the same brain, that had asymmetric plaque counts (see Figs. 47 and 48), e.g. in Case 8 when measuring the area of plaques there was an asymmetric plaque count in the left frontal but when counting the number of plaques there was not.

It was found that regardless of whether the number of plaques/$mm^2$ or the area of plaques in square microns was being measured, the greatest concentration of plaques occurred in the superficial layers of the cerebral cortex. It was therefore concluded that there were intraregional differences between the superficial and deep layers in the 6 SDAT cases used in this study.

**Interregional heterogeneity**

Since it has now been shown in this study that there were biologically significant differences between the left and right hemispheres and also between the superficial and deep layers of the same brain region (intraregional differences), the next step was to determine whether or not there were any differences between the various regions being examined in this study (Tables 48-83). This was looked at by examining both the number of plaques per $mm^2$ and the area of plaques in square microns in the superficial and deep layers of the cortex and also comparing the total plaque counts (mean of superficial + deep) between the various regions.

Interregional variation in the number of plaques/$mm^2$ in the superficial layers

When counting the number of plaques/$mm^2$ in the superficial layers of the cortex it can be seen from Tables 48-53 that in both the left and right hemispheres each region examined differed from at least one other region in most of the brains used in this study. There were, however, a few regions in some of the cases which did not differ from the other regions within that case, e.g. case 8, the inferior temporal cortex of the left hemisphere did not differ from any of the other regions examined in the left hemisphere (see Table 48). However, in case 9, the same region i.e. the inferior temporal cortex in the left hemisphere had a different plaque count from all 6 of the other regions (see Table 49).

Interregional variation in the number of plaques/$mm^2$ in the deep layers

When counting the number of plaques/$mm^2$ in the deep layers of the cortex, it can be seen from Tables 54-59 that in all but the right hemisphere of 2 cases, each region differed from between one and 6 of the other regions examined. In Case 9, none of the regions differed from each other in the right hemisphere, whereas in the left hemisphere of Case 9 all 7 regions had asymmetric plaque counts with either 3 or 4 of the other regions, e.g. the frontal cortex did not differ from any of the regions in the right hemisphere whereas in the left hemisphere the frontal cortex differed from the superior temporal, mid-

temporal and inferior temporal cortex (Table 55).

Interregional variation in the total number of plaques/$mm^2$

When counting the total number of plaques/$mm^2$ (mean of superficial + deep), it can be seen from Tables 60-65 that each of the regions differed from at least one other region in both left and right hemispheres of all 6 cases in this study. In some cases there were regions which only differed from one other region in the right hemispheres, whereas the same region in the left hemisphere differed from all 6 of the other regions, e.g. in Case 8 the superior temporal cortex only differed from one other region in the right hemisphere but in the left hemisphere the superior temporal cortex differed from all 6 of the other regions. Within Case 8 the converse was true when examining the parietal cortex, i.e. in the right hemisphere the parietal cortex had asymmetric plaque counts to all 6 of the other regions examined, whereas in the left hemisphere the parietal cortex only differed from one other region (Table 60).

Interregional variation in the area of plaques in square microns in the superficial layers

When measuring the area of plaques in square microns in the superficial layers of the cortex, it can be seen from Tables 66-71 that each of the regions being examined differed from at least one other region in most of the brains in this study. However, like the number of plaques/$mm^2$, the area of plaques in square microns in a few instances did not differ from the area

of plaques in the other regions, e.g. in Case 8 the occipital cortex in the left hemisphere did not differ from any of the other regions, whereas in Case 13 in the left hemisphere the occipital cortex differed from all 6 of the other regions (see Tables 66 and 71 respectively).

Interregional variation in the area of plaques in square microns in the deep layers

When measuring the area of plaques in square microns in the deep layers of the cortex, it can be seen from Tables 72-77 that all of the regions examined in both left and right hemispheres of the 6 SDAT brains used in this study had asymmetric plaque counts with between one and 6 of the other regions examined in that brain. Most of the regions in each of the cases differed from at least 2 of the other regions, whereas in the right hemisphere of Case 9 each of the regions differed only from the parietal cortex, i.e. only one region, and therefore the plaque area in the parietal cortex differed from all 6 of the other regions (see Table 73).

Interregional variation in the total area of plaques in square microns

When measuring the total area of plaques in square microns (mean of superficial + deep), it can be seen from Tables 78-83 that in all but the right hemisphere of Case 10 each region differed from between one and 6 of the other regions examined. In the right hemisphere of Case 10, the mid-temporal, inferior temporal and parietal cortex did not differ from any of the other regions

(see Table 80). It should be noted, however, that the mid-temporal region in the right hemisphere of Case 13 differed from all 6 of the other regions (Table 83) and also that the inferior temporal region in the right hemisphere of Case 11 again differed from all 6 of the other regions (Table 81).

Tables 84-89 show the number of regions that had asymmetric plaque counts in each of the 7 regions examined in both the left and right hemispheres of each brain. It can be seen from these tables that in some cases a few regions did not differ from any of the other regions, whereas the same regions in another brain may have differed from as many as 6 of the other regions. It should also be noted that even though two regions may have had an asymmetric number of plaques per $mm^2$, it did not necessarily follow that the same two regions had asymmetric plaque counts when measuring the area of plaques in square microns. Similarly, for example, the parietal cortex had asymmetric plaque counts with 3 regions in one brain and had asymmetric plaque counts with 3 regions in another brain, it was not necessarily the same 3 regions that it differed from in the 2 separate brains, e.g. the number of plaques counted in the superficial layers of the left parietal cortex in Case 9 differed from the superior temporal, mid temporal and inferior temporal cortex (Tables 49 and 84), whereas in Case 11 the number of plaques counted in the superficial layers of the parietal cortex again differed from 3 regions, only this time it differed from the frontal, occipital cortex and cingulate cortex (Tables 51 and 84).

From the plaque counts obtained from the 6 SDAT cases used in this study, it has been shown that there was interhemispheric asymmetry. Sometimes the left hemisphere had the highest plaque count and other times it was the right hemisphere that had the highest count.

In different cases it was not always the same regions that were asymmetric. If 2 plaque counts were asymmetric when counting the number of plaques, they were not necessarily asymmetric when measuring the area of the plaques and vice versa.

There was evidence of both interregional heterogeneity and intraregional heterogeneity with the highest plaque counts being obtained in the superficial rather than deep layers.

Regardless of whether the number of plaques or the area of plaques was being compared, there was no one region of the brain which consistently gave the same results in each of the brains used in this study. It therefore has to be said that even though there were differences between the regions in each brain, each brain was individual in that it was not the same regions which were consistently different.

Variation in section thickness

It is well known that when cutting free floating sections on a freezing microtome that there can be some variation in thickness of the sections. Since we were trying to show whether or not there was any asymmetry in the plaque counts between the left and right hemispheres, we had to make sure that any asymmetric

counts were due to the disease process and not just the difference in section thickness between the left and right hemispheres.

Three consecutive sections were cut nominally at 20, 25 and 30 microns and stained for senile plaques using King's silver impregnation method for amyloid and neurofibrillary tangles. Although we cannot say that the sections were definitely 20, 25 and 30 microns thick without actually measuring the thickness with a surfometer, it was clear when handling the sections that section 3 (30μ) was thicker than section 2 (25μ), which was thicker than section 1 (20μ). The thicker sections were more opaque than the thinner ones and when handling the sections with a glass rod, transferring them from one solution to the next, it was again apparent which section was the thickest (the thinner ones were much more fragile).

It can be seen from Table 90 that there was no significant difference statistically between the number or area of plaques in any of the sections cut at different thicknesses, either in the superficial or the deep layers of cortex.

Since our criteria for asymmetric plaque counts was a 5 plaque change as well as a 40% difference, the plaque counts obtained on the serial sections, cut at different thicknesses, were examined to see if any of the plaque counts would be called asymmetric simply due to section thickness. None of the plaque counts obtained gave both a 5 plaque and a 40% change between any of the sections examined. Since section thickness (± 20%) did not seem to affect the plaque counts either statistically or

by our criteria of asymmetry, then any asymmetric plaque counts obtained in this study were due to the disease process and not section thickness.

**Table 90** shows the comparison of the number of plaques/$mm^2$ and the area of plaques in square microns between sections cut nominally at 20, 25 and 30 microns thick, in both the superficial and deep layers of the cerebral cortex.

| | 20μ vs 25μ | | 25μ vs 30μ | | 20μ vs 30μ | |
|---|---|---|---|---|---|---|
| | P value | | P value | | P value | |
| Superficial number of plaques | 0.15 | NS | 0.74 | NS | 0.16 | NS |
| Deep number of plaques | 0.17 | NS | 0.065 | NS | 0 23 | NS |
| Superficial area of plaques | 0.61 | NS | 0.62 | NS | 0.72 | NS |
| Deep area of plaques | 0.55 | NS | 0.093 | NS | 0.10 | NS |

NS = no significant difference.

**Correlation between the volume of the lobes, the number of plaques and the area of plaques**

The relationship, if any, between the volume of the frontal. temporal, parietal and occipital lobes/cranial cavity volume (CCV) in both the left and right hemispheres were compared to the number of plaques/$mm^2$ and the area of plaques in square microns using the Pearson product - moment coefficient of correlation, commonly symbolised as r.

The volume of the frontal lobe/CCV was compared with the number and area of plaques in the superficial layers, the deep layers and also with the total plaque counts (mean of

superficial + deep counts) in the left and right hemispheres to see if there was any correlation between the size of the frontal lobe compared to the plaque counts obtained in that lobe. This procedure was repeated with the temporal, parietal and occipital lobes.

Finally, the number of plaques/$mm^2$ was compared to the area of plaques, in square microns, to see if there was any correlation between the numbers of plaques and the area of plaques in each of the 4 lobes of the brain (left and right).

Since all of the SDAT patients scored 0 for their mental test score, it was impossible to calculate any correlation factor.

It can be seen from Table 91 that there was a high degree of positive correlation between the volume of the left temporal lobe/CCV and the area of plaques, in square microns, with the superficial, deep and total plaque counts ($r = 0.921$, 0.960 and 0.941 respectively). This was in contrast with the poor correlation obtained between the right temporal lobe/CCV and the area of plaques in the superficial, deep and total plaque counts ($r = 0.172$, $-0.081$ and 0.079 respectively).

There was also a reasonable negative correlation between the volume of the right frontal lobe/CCV and both the number and area of plaques, although there was a slightly better correlation with the area of plaques ($r = -0.811$, $-0.657$ and $-0.773$ in the superficial, deep and total plaque counts respectively, see Table 91).

There did not seem to be any consistant correlation between

either the number or area of plaques in the left or right parietal and occipital lobes.

When comparing the number of plaques with the area of plaques, there was a good positive correlation in both the superficial and deep layers in the left and right hemispheres of all 4 lobes with the exception of the superficial plaque counts in the right occipital ($r = 0.130$). The correlation between the number and area of plaques was also better in the deep layers than in the superficial layers (see Table 92).

## Discussion

Dementia is a term applied to a diffuse deterioration in mental function resulting from organic disease of the brain.[28] It may be produced by many pathological processes and the clinical picture varies according to the age of onset, the localisation, the rate of progress and the nature of the causal pathological change.[28]

### Pre-senile Alzheimer's disease and senile dementia of the Alzheimer type

Alzheimer's disease is a particular form of dementia where there is a progressive cerebral degeneration, in many ways comparable to accelerated ageing, occurring in middle or late life. In the past it was customary to distinguish between pre-senile dementia occurring in those under 65 years of age and senile dementia developing in those over 65 years of age, but this distinction is now generally accepted as being artificial.[29] Nevertheless, there is evidence that Alzheimer's disease developing in old age (AD-1) may differ from the more rapidly progressive variety (AD-2) which runs a more rapid course and begins in middle age.[30]

Many of the recently discovered cerebral changes associated with Alzheimer's disease (AD) are brought into sharper focus in the light of a comparison between the "early" and "late" onset forms of the disorder. Chronological age alone cannot be the discriminating factor since it fails to separate the syndromes sharply.[3] The terms "early" and "late" onset are therefore imprecise. Onset before the age of 70 years favours the

presence of Alzheimer type II syndrome (presenile AD) but does not decide the issue. Similarly, onset after the age of 70 years favours the presence of Alzheimer type I syndrome (senile dementia of the Alzheimer type -SDAT). As well as clinical differences, there are structural and neurochemical differences between type I and type II Alzheimer's disease. Some of the clinical differences include the presence of early spatial disorientation or visuospatial dysfunction which is in favour of an early onset or type II syndrome, whereas those who fail in every kind of cognitive task generally suffer from type I AD.[3] This is consistent with Lauter, who reported parieto-temporal psychological deficits to be less common and less conspicuous as age of onset increases in AD.[31,32] There are structural variables such as the significant reduction in neurons, mainly the large pyramidal cells, only in the early or type II syndrome, and is confined to the temporal, frontal and cingulate gyri. There is an age-related decline in the neuron count in the well preserved aged brain but in AD of late onset, i.e. type I syndrome, there is no significant reduction in any part of the cortex, even though the neuron counts are consistently less than in the normal aged brain. Some of the neurochemical differences include an extensive reduced ChAT activity in type II AD, whereas reduced ChAT activity is confined to the temporal lobe in type I AD. There is also a significant reduction in noradrenalin and gamma-aminobutyric acid (GABA) in early onset type II AD but not in late onset type I AD.[33]

The combination of widely distributed neurofibrillary tangle

formation in the cortex and the hippocampus and the presence of deficits of ChAT and somatostatin are the only features that differentiate dementia of the Alzheimer type I from normal ageing.[3]

Alzheimer's disease can be diagnosed clinically with an accuracy of about 70%,[34] and a quantitative computed tomographic analysis (CT scan) measuring the 3rd ventricle, bodies of the lateral ventricles and the interhemispheric fissure shows that 77% of the cases studied were correctly diagnosed as having dementia.[35]

Since the Alzheimer patients used in this study had a mean age of 83 ± 2years and were all mentally assessed scoring 0 out of 10 for their mental test score (MTS) compared to the 8, 9 or 10 out of 10 scored by the age matched controls (81 ± 2 years), this would suggest that the brains used in this study are all SDAT brains, i.e. late onset type I Alzheimer's disease.

The clinical diagnosis of Alzheimer's disease, however, is not absolute and can only be diagnosed with certainty by the neuropathological examination of tissue sections for the presence of numerous argyrophilic plaques and neurofibrillary tangles.[5,12,36,37]

The structure of the senile plaque

Since Blocq and Marinesco identified plaques in the human brain in 1892, they have been particularly associated with Alzheimer's disease and the ageing human brain. Plaques accumulate in the cerebral cortex as round or ovoid structures approximately 15-

200 microns in diameter. There are at least 3 main components in a typical plaque, (i) abnormal nerve processes, often termed neurites, (ii) glial processes and (iii) a central or amyloid core.[38] The structure of the plaque can vary considerably but generally there are 3 distinct types of plaque that are recognised:-

a) The primitive or atypical plaque without a central core.

b) The typical or classical plaque with a central core of amyloid.

c) The compact or burnt out plaque.

**The primitive plaque**

This is thought to be in the early stages of develoment when the plaque consists of dystrophic neurites and some glial processes with either no amyloid core or only a few amyloid fibrils which require electron microscopy for their demonstration.

**The classical plaque**

The more mature or typical plaque has a central core of amyloid material surrounded by a peripheral rim of dystrophic neurites. Intermixed with the core and neurites are glial fibres and occasional glial cell bodies.

**The "burnt out" plaque**

The compact or "burnt out" plaque is thought to be at a later, possibly final, stage of development. At this stage the plaque consists almost entirely of a central core of amyloid with either very few or no detectable neurites at the periphery.

More recently a fourth type of plaque has been described. This amyloid plaque stained by a silver impregnation technique

and by A4 protein (amyloid) antibodies was shown to contain no neurites. These amyloid masses varied in shape and size from 15-300 microns in diameter and should not be confused with primitive, mature and burnt out forms of neuritic plaques.[39]

For the purpose of this study, all forms of amyloid and neuritic plaque were counted. If any plaques were touching each other and could quite easily be distinguished from each other, they were counted individually. If the plaques were in a mass where they could not be distinguished from each other, they were counted as one plaque. Since the plaque counts in this study were done manually and not automatically, it was quite easy to count touching plaques individually when they occurred.

Quantitative morphometry

Many workers have examined the volume of the SDAT brain to determine the degree of atrophy present when compared to normal age-matched controls. Only a few of them, however, related the brain volumes to the cranial cavity volume (e.g. Hubbard and Anderson, 1980).[14]

In a study of 28 non-demented old peoples' brains, Blessed, Tomlinson and Roth[50] judged cortical atrophy by examination of the distance between the dura and brain at autopsy (with marked atrophy a gap of 1cm or more may be present), by inspection of the unfixed and fixed brain and by examination of the coronal slices in the latter. There was no case with marked or general atrophy (13 cases showed no atrophy of gyri and 11 cases only slight gyral atrophy). In the latter 11 cases, atrophy was most

visible in the parasagittal gyri of the frontal and parietal lobes with the occipital and temporal convolutions being spared. In 4 cases the atrophy was considered moderate but was not comparable to the atrophy seen in senile dementia. The majority of these normal elderly brains (85%) showed no, or only slight, cortical atrophy which was generally limited to the parasagittal convolutions.[6]

When Tomlinson, Blessed and Roth then examined the brains of 50 demented elderly people they found that many of the brains in the demented group were indistinguishable from the control group, i.e. 20 showed no cortical atrophy at all and 14 had only slight cortical atrophy (10 limited to parasagittal convolutions as in all but 2 of the controls). However, in 16 of the 50 dements there was generalised atrophy present where all convolutions were affected to some degree in the coronal sections. In all 8 demented cases showing slight generalised atrophy the temporal lobes were more severely affected than other areas, and in the 8 cases showing moderate or severe atrophy the temporal convolutions were again markedly involved in 6 of them, i.e. when there was cortical atrophy in the elderly demented brain, there was particular involvement of the temporal lobes.[7]

Terry et al. showed that the cerebral cortex was 9-10% thinner in the SDAT brains compared to the controls when measuring the cortical thickness with a Quantimet 720 image analyser. This, however, was not a statistically significant result. There was also a poor correlation between brain weight

and cortical thickness ($r < 0.37$) in both the SDAT and control groups in both cortical areas examined, i.e. mid-frontal and superior temporal. They also showed that brain weight did not correlate significantly with age in either SDAT or control subjects.[8]

Infarction involving grey and white matter are part of the common multi-infarct dementia syndrome (MID). Brun et al. frequently found a different type of widespread white matter lesion. In addition to complete infarction, large areas of incomplete infarction in the surrounding white matter were found. Similar lesions were found in Alzheimer's pre-senile (AD) and senile dementia (SDAT). These changes were characterised by a partial loss of axons as well as their myelin sheaths and oligodendroglial cells. These structural changes were confined to the white matter and most commonly involved the frontal and parieto-occipital lobes, and often involved central white matter areas in a largely symmetrical fashion. These white matter changes occurred independently of grey matter changes in Alzheimer's disease, therefore it is unlikely that they were only secondary to the cortical changes.[10] These white matter changes were normally invisible to the naked eye. Histopathologically, they consisted of a partial loss of myelin, oligodendroglial cells and axons, a mild fibrillary gliosis and the occurrence of sparse macrophages. These white matter changes occurred in addition to lesions in grey matter,[11] and were present in about 60% of all cases.[40]

Miller et al. used a Quantimet 720 image analyser to measure

the quantity of grey and white matter. With the control cases, only one hemisphere was used in 52 out of 91 cases, and with 12 out of 13 dements only one hemisphere was used. They found that the average hemispheric volume of the SDAT patients was 18% lower than the age-matched controls (statistically significant at the level of $p < 0.001$), but the grey : white matter ratios were identical.[41]

Davis and Wright measured the brain volume and devised a balloon method for measuring the cranial cavity volume (CCV). They showed that the brain volume in healthy young adults bears a constant relationship with the CCV (92.2 $\pm$ SEM 1.6%). As the CCV did not change significantly with age, any changes in brain volume with age could be assessed by using as an index the brain volume expressed as a percentage of the CCV. They also showed that the brain volume did not change significantly for up to 5 days after death. They showed striking and consistent atrophy with age with only 4 out of 33 cases over 70 years old having a BV/CCV % ratio within the normal range of those under 50 years old.[13] These findings are in contrast to those published by Tomlinson et al.[6]

Hubbard and Anderson employed the balloon method of Davis and Wright to measure the CCV and used a point counting technique to measure the volume of cerebral cortex and white matter from the coronal slices of the brain. They showed that the whole brain volume of SDAT patients less than 80 years old generally showed excessive atrophy by comparison to the age-matched controls, sometimes by as much as 18%. They also found

that, in contrast to this, the ratio of BV/CCV in SDAT patients over the age of 80 was not significantly different from controls of the same age. When examining the total volume of cortex and white matter separately, they found that above the age of 80 there was no significant difference from the age-matched controls, but below the age of 80 there was global loss of cortex which was more marked than the white matter deficit. They also found that the temporal lobe was more severely atrophic than other parts of the cerebral hemispheres, and that in SDAT brains over the age of 80 the temporal cortex alone showed a significant difference from the controls.[14]

From computerised measurements of photographs, S. de la Monte showed that there was global atrophy of both grey and white matter (using only one random hemisphere).[42]

Prohovnik et al. showed that the loss of grey matter was significantly related to both the severity and duration of the disease in patients with pre-senile Alzheimer's disease (AD) but not in patients with SDAT.[9]

Since there was disagreement as to whether there was any atrophy in the normal aged brain (Tomlinson et al. showed no or only slight atrophy whereas Davis and Wright showed striking atrophy with age) and that some workers used only one hemisphere (de la Monte, Miller et al. in 52/91 controls and 12/13 dements) for their measurements, it was decided in this study to compare not only fresh whole brain volumes, total cortex volumes and total white matter volumes, but also to compare the volume of cortex and white matter from each individual lobe in both the

left and right hemispheres separately. We used the balloon method of Davis and Wright to determine the CCV and a modified method of Hubbard and Anderson for measuring the amount of grey and white matter using a point counting technique (Delesse principle). We modified the method in that we used a different technique for dissecting the brain.

Our results indicate that there was some loss of tissue in the normal aged brain but there was far more atrophy in the SDAT brain. Both the total cerebral cortex and total white matter volumes of the SDAT brain were significantly different from the volumes obtained in the age-matched controls. When examining each individual lobe (both left and right) there was no significant difference between the frontal or parietal lobes of the SDAT brain compared to the controls. There was, however, a statistically significant difference between the left occipital and the left temporal ($p = 0.037$ and 0.012 respectively). There was no significant difference between either the right occipital or right temporal lobe volumes compared to the controls. The volume of cerebral cortex was significantly different in the left occipital, parietal, temporal and frontal cortex whereas only the right parietal of the SDAT brain was significantly different from the control values. There was no difference in any of the lobes, either left or right, when comparing the volume of white matter between the SDAT brains and controls. These results show that in SDAT there was global loss of cerebral cortex and white matter (more cortex being lost than white). This is in general agreement with most other workers

except Miller et al.[41] who found that the grey : white matter ratios were identical in the SDAT brain compared to the controls. These results also differ from those of Hubbard and Anderson[14] who found that above the age of 80 there was selective loss of temporal cortex. The mean age of our SDAT group was 83 ± 2 years and our relsults show that there was loss of cortex in the left occipital, parietal, temporal and frontal lobes, and also in the right parietal lobe.

Even though this was a small study of only 14 brains (7 controls and 7 SDAT cases) and a larger study such as that undertaken by Hubbard and Anderson (21 controls and 18 dementia cases) may show statistically that there was selective loss of temporal cortex, there are a few differences between their method and ours which may help to explain the differing results. Firstly, we dissected the brain in a different manner and separated it into the four different lobes, i.e. frontal, temporal, parietal and occipital, whereas they measured slices of fronto-parietal, temporal and occipital. Secondly, we kept the left and right hemispheres separate whereas they did not, and thirdly all our patients were mentally assessed and the controls scored either 80% (2 patients), 90% (3 patients) or 100% (2 patients), whereas the SDAT patients all scored 0. This is a very high standard of control material and possibly the control material used in their study was not as "normal" as they thought. It is also interesting to note that it was the cerebral cortex in the left hemisphere which was affected more severely in our patients and even though it was not absolutely

certain, it was thought that they were all right-handed, i.e. it was the dominant hemisphere which was more atrophic.

Even though the size of the ventricles was generally larger in most of the SDAT group, the difference between the SDAT group and the age matched controls failed to reach statistical significance.

Plaque staining and quantitation

Senile plaques can be demonstrated using a wide variety of staining methods such as the King's[14] and von Braunmuhl[6,15,17,21,24,27,43,44] silver impregnation techniques on frozen sections and the modified Palmgren,[45,46,47] Bielschowsky,[48,49] 39 Bodian,[8,49], Glees and Marsland,[15] Congo red,[50] Thioflavin S,[8,50,18] and Thioflavin T[50] on paraffin sections. More recently immunocytochemical methods have been used to demonstrate senile plaques, e.g. anti A-4 protein,[51,52] Amyloid P,[53] Alz-50[54] and anti-paired helical filaments (PHF),[55] but few attempts have been made to compare the various methods.

Dayan compared the von Braunmuhl technique on frozen sections with the Glees and Marsland, congo red and periodic acid Schiff (PAS) on paraffin sections.[15] When Dayan assessed the PAS it was found that even though the plaques were stained magenta by the PAS, in practice many plaques stained very weakly and were so difficult to distinguish from the background staining of cerebral cortex that the method was considered unsuitable for quantitative purposes. Also the congophilia and birefringence properties of the amyloid component of the senile

plaque were exhibited by some of the plaques in some of the cases but none were sufficiently reliable or consistent to be employed for counting. The quantitative plaque counts were therefore compared between the von Braunmuhl and Glees and Marsland silver impregnation techniques. When comparing the frozen and paraffin techniques, Dayan found that there was no significant difference between them and therefore employed the more convenient method of Glees and Marsland on paraffin sections.

More recently Lamy et al. compared 7 different staining methods for demonstrating senile plaques and neurofibrillary tangles in 15 elderly patients.[16] The techniques used were a modified Bielschowsky, a modified Palmgren, Gallyas, Naumenko and Feigin, silver methenamine. Bodian coupled with Luxol fast blue and thioflavine S, all performed on paraffin sections. They found that the modified Bielschowsky stained both the amyloid and neurites, the modified Palmgren, Bodian and Gallyas stained the neurites preferentially and were more sensitive for neurofibrillary tangles than senile plaques, and the silver methenamine revealed amyloid in much the same way as the thioflavine S. The Naumenko and Feigin technique stained only a few senile plaques and neurofibrillary tangles. The highest count of senile plaques was obtained with the modified Bielschowsky.

In the present study the King's amyloid and von Braunmuhl silver impregnation techniques were carried out on free floating frozen sections and were compared to thioflavine T, anti-paired

helical filaments, Palmgren, Congo red and sirius red techniques on paraffin sections. From the results shown in Tables 10-12 it can be seen quite clearly that the best methods for demonstrating senile plaques in this Department were the King's amyloid and the von Braunmuhl silver impregnation techniques on frozen sections.

From the literature it seems that different studies have shown that different staining methods were either better for demonstrating senile plaques, i.e. the modified Bielschowsky,[16] or that the more convenient method of Glees and Marsland should be used.[15] If the actual plaque counts obtained by Dayan are examined it can be seen that in the two regions used in the study to compare the frozen and paraffin sections (frontal and temporal), the highest plaque counts were obtained with the von Braunmuhl technique (frozen sections) in 11 out of 20 counts with a further 2 counts being equal. In the remaining 7 counts the Glees and Marsland (paraffin sections) showed only one or 2 more plaques in 3 of the counts. In other words, it was in only 4 out of the 20 plaque counts that the paraffin sections gave higher plaque counts (5, 7, 12 and 15 more plaques). In 2 of the cases there were as many as 30 more plaques counted with the von Braunmuhl technique on frozen sections. This suggests that even though the more convenient Glees and Marsland technique was employed by Dayan, the method of von Braunmuhl would have been preferable.

When Lamy et al. compared 7 staining methods for demonstrating senile plaques they used paraffin sections only.

Lamy et al. state that the modified Bielschowsky method undoubtedly gave the most complete picture of the changes because it showed both the amyloid and the neuronal processes and it should therefore be considered as a reference technique to which other methods should be compared. However, they also state that the method was expensive, difficult to perform and poorly selective in that it stained a large number of normal structures. The recognition of the lesions was more subjective than with other selective stains and the variability of staining made it difficult to apply to a series of slides and they therefore cannot recommend this technique for routine use. These difficulties and variability in staining should surely exclude this method as a standard reference technique in the diagnosis of Alzheimer's disease. If Lamy et al. found such variation in the method within the same department, there would be even greater variation between the results in different laboratories, both national and international.

In this study the King's and the von Braunmuhl techniques stained both the amyloid and neuritic components of plaques and since the King's amyloid method was more reproducible with less variation in staining and gave the highest plaque counts in all but a few cases, the King's amyloid silver impregnation method on free floating frozen sections can be recommended as a standard reference technique. The King's amyloid technique was therefore employed for the quantitative analysis.

Once it had been established that the King's amyloid was the best method for staining senile plaques, it had to be decided

how the plaques would actually be counted. Since it can be seen from Table 94 that there was inconsistency in the way in which plaques were counted, a reproducibility study was undertaken to see how many counts would have to be done in each brain region so that a consistent count could be obtained which would give an average plaque count for that region wich was both accurate and reproducible. Since it was well known that there are more plaques in the depths of the sulci than there are in the crests of gyri, 6 reference points were marked on each section and as far as possible 3 were in the crests of the gyri and 3 in the depths of sulci. There are also more plaques in the superficial layers of the cerebral cortex (layers 1-3) than there are in the deep layers (layers 4-6). There were therefore 2 counts performed at each reference point, one in the superficial layers and the other in the deep layers. These counts were repeated at the same reference points on a separate day.

It had to be established how many plaque counts had to be performed that would give both an accurate and reproducible plaque count representative of each particular brain region. A student's paried-t test was used to test the variability in the standard deviation of the difference in plaque counts between day 1 and day 2 at 1, 3 and 6 reference points in each brain region being examined. The smaller the standard deviation, the more reproducible the method, i.e. there was less variation between the 2 plaque counts.

It can be seen from Table 13 that when only one count was carried out in each brain region, there was a significant

difference between the counts obtained on day 1 compared to day 2 (± 2.5 plaques in the superficial layers and ± 2.07 plaques in the deep layers). If, however, the number of counts was increased to 3 per brain region, there was no significnat difference between the counts obtained on day 1 and day 2 (± 1.4 plaques in the superficial layers and ± 0.7 plaques in the deep layers). If the number of counts was increased to 6 per brain region, there was no significant difference in the plaque counts between day 1 and day 2 (± 1.2 plaques in the superficial layers and ± 0.5 plaques in the deep layers).

By increasing the number of plaque counts from 1 to 3 reference points, the day to day error was almost halved in the superficial layers and quartered in the deep layers. By increasing the number of reference points from 3 to 6, the day to day error was only marginally improved (± 0.2 plaques in both the superficial and deep layers). Since it was felt that many more plaque counts would have to be performed to improve the accuracy only slightly, it was decided that an accuracy of ± 1.2 and ± 0.5 plaques in the superficial and deep layers respectively was sufficient for the purposes of this study. Therefore 6 superficial and 6 deep counts were performed at X200 magnification recommended by Khachaturian[5] in each brain region examined.

**Asymmetry of plaque counts in the SDAT brain**

As previously stated, most of the work on neurotransmitter and neuropathological abnormalities in Alzheimer's disease have been

performed on only one hemisphere of the brain. It has been the practice in many centres to fix one cerebral hemisphere for histological studies and to freeze the other for neurochemical investigations.[21] The assumption underlying this was that the disease process was symmetrical since the histological changes on one side were compared to the neurochemical changes on the other. Some workers have, however, compared various aspects of Alzheimer's disease in the left and right hemispheres and come to different conclusions. Ball[19] found no significant difference in neurofibrillary tangle formation in the hippocampus between the left and right hemispheres, and Moossy et al. reported bilateral symmetry of the morphologic lesions in Alzheimer's disease.[20] Conversely, Arendt et al. reported a marked difference in the loss of neurons between the left and right hemisphere in 3 of 5 cases with a more pronounced involvement of the left hemisphere.[22] When examining senile plaques there were also marked differences in regional plaque counts between the two hemispheres and in 4 of 5 cases the left hemisphere was most affected.

Wilcock and Esiri found that neither hemisphere consistantly had a higher plaque or tangle count but that there was a statistically significant difference between the two hemispheres in plaque counts in the occipital lobe in 2 cases, and in all lobes in one case (the right side more affected in the parietal and temporal, and the left side more affected in the frontal and occipital lobes).[21]

In a more recent publication, Moossy et al. stated that in

their earlier studies bilateral symmetry was the rule but that there were significant numbers of left-right asymmetries in the number of morphologic lesions and the levels of cholinergic enzymes.[56] In their more recent study they have shown a left-right asymmetry with plaques, tangles, ChAT and AChE, with the plaques and tangles showing more of an asymmetry than the cholinergic variables. They also showed that for both the morphologic and cholinergic variables the number of regions showing a greater effect in the right hemisphere was similar to the number of regions showing a greater effect in the left hemisphere. There was therefore no hemisphere which showed preferential involvement of either morphologic or cholinergic variables.

The problem with trying to test for left-right asymmetries when they are non-directional, i.e. sometimes the left hemisphere had the highest plaque count and at other times the right hemisphere had the highest plaque count, was that the asymmetries may cancel each other out and indicate that there was no statistical difference between them. It was with this in mind that a method for testing the left-right differences had to be devised. The method had to have some biological validity and be able to test each individual plaque count separately so that any left-right asymmetries between individual brain regions would not be masked by testing the mean of the left hemisphere against the mean of the right hemisphere. The question of how many plaques represented a biologically significant change had to be considered. When examining well established data

comparing ChAT activity[23] and mental test scores (MTS)[24] with plaque counts it could be seen that by the time a mean plaque count of 5 plaques was reached, the ChAT activity and MTS had fallen to about 75% of normal. When a mean plaque count of 10 plaques was reached the ChAT activity and MTS had fallen to about 50% of normal. Based on these data sets, it was decided that a change of 5 plaques represented a biologically significant difference. However, a 5 plaque change alone was not sufficient to determine whether or not there was any left-right asymmetry between the plaque counts. If the mean plaque count changed from 1 - 6 plaques or from 45 - 50, this gave percentage changes of between 500% and 10% respectively even though there was only a 5 plaque change in both sets of plaque counts. It was decided that the second criterion for asymmetric plaque counts would therefore be the percentage change between the plaque counts. Since ChAT activity and MTS show the greatest change at lower plaque counts (approximately 45% at a mean plaque count of 12) and since Tomlinson et al. demonstrated that a threshold point of 12 plaques per low power field, using the Newcastle method, was found to define a value which segregated dements from non-dements with 85% accuracy,[7] a 5 plaque change below 12 plaques will give a percentage change between approximately 40% and 500%. Using this criteria, asymmetric plaque counts must have a difference of both a 5 plaque change and a minimum of a 40% difference.

Since it has been shown in the reproducibility study that the accuracy of the plaque counting method was $\pm$ 1.4 plaques in

the superficial layers and ± 0.7 plaques in the deep layers and that by counting plaques in 3 consecutive sections cut nominally at 20, 25 and 30 microns there was no significant difference in the plaque counts due to section thickness, any variation between the plaque counts of a 5 plaque change and a 40% difference was due to the disease process and not any error produced by the operator counting the plaques or any variation in section thickness.

When comparing the plaque counts obtained in the left and right hemispheres, it can be seen from Tables 20-33 that all 6 SDAT cases used in this study had asymmetry in either plaque number or area in at least one of the regions examined. Neither the left nor right hemisphere consistently gave the highest plaque count in any particular region, i.e. sometimes the left hemisphere gave the highest plaque counts and sometimes the right hemisphere gave the highest plaque counts. There was also no particular region which consistently gave the highest plaque counts in either hemisphere, e.g. sometimes the temporal lobe gave the highest plaque counts and sometimes it had the lowest. Even within the same brain some regions had the highest plaque counts in the left hemisphere while other regions had the highest plaque counts in the right hemisphere.

When comparing the plaque counts obtained in the superficial layers with the plaque counts obtained in the deep layers of the cortex, it can be seen from Tables 34-47 that the superficial plaque count was the highest in all of the regions examined in all 6 cases. When applying the criteria of both a 5 plaque

change and a minimum of 40% difference to the plaque counts obtained in the superficial compared to the deep layers, it can be seen that in the majority of cases there was an asymmetric plaque count. In other words, there was intraregional variation in the plaque counts in the various regions examined in this study.

Since it has been shown that there were interhemispheric differences and intraregional differences, the next step was to determine whether or not there were any differences between the various regions being examined. When comparing the number of plaques in the superficial layers, it can be seen from Tables 48-53 that all of the regions examined differed from at least one other region in most of the cases examined in this study. Sometimes there were more asymmetric regions in the left hemisphere and sometimes there were more asymmetric regions in the right hemisphere. It was not always the same regions that differed in both the left and right hemispheres of the same case, e.g. the middle temporal cortex in SDAT Case 8 had asymmetric plaque counts in the right hemisphere but not in the left. If a region did not differ from any other regions within the case, it did not mean that this particular region would not differ from the other regions in other cases, e.g. the left inferior temporal cortex in SDAT Case 8 did not differ from any of the other regions in the left hemisphere of that case, whereas in SDAT Case 9 the left inferior temporal cortex differed from all 6 of the other regions. Similarly when examining the interregional variation of the number of plaques

in the deep cortical layers (Tables 54-59) and the total number of plaques (mean of the superficial and deep counts: Tables 60-65), similar examples could be found. The same was true of the interregional variation in the area of plaques in the superficial layers (Tables 66-71), the deep layers (Tables 72-77) and with the total area of plaques in square microns (mean of superficial + deep counts: Tables 78-83). Even though there were only 6 SDAT brains used in this study, there was sufficient evidence to suggest that SDAT was not a symmetrical process.

The resolution of in vivo imaging such as positron emission tomography (PET) and single photon emission tomography (SPET) is not as accurate as the neuropathological techniques for demonstrating plaques and tangles. However, there is evidence to suggest that brain atrophy in Alzheimer's disease is bilaterally symmetrical.[63] Neary et al. also stated that cerebral imaging by SPET indicated regional differences in the uptake of tracer in patients with different forms of cerebral atrophy. Posterior hemisphere abnormalities were common in the Alzheimer group, suggesting that Alzheimer's disease may not be the uniformly diffuse disorder that had previously been reported, but may exhibit some heterogeneity.[63]

Other workers, however, have demonstrated left-right asymmetries with, for example, glucose metabolism.[64,65,66] However, Loewenstein et al.[64] showed a predominant left rather than right hemisphere reduction in glucose metabolism which was not related to the severity or duration of dementia.[65] Koss et al. showed a greater right rather than left hemisphere

impairment of glucose metabolism in Alzheimer patients under 65 years but not in those over 65 years, and Freidland et al.[66] showed lateral asymmetry of cortical glucose metabolism not favouring any hemisphere. Haxby et al. found that the cerebral glucose metabolic asymmetry was related significantly to asymmetry of language (left parietal and frontal) and visuospatial (right parietal) construction in patients with early Alzheimer's disease, but not in healthy controls.[67]

It seems that the available literature on in vivo imaging is as confused as the methodology and asymmetry literature on plaque counting. Even though there was disagreement as to which hemisphere was predominantly involved in Alzheimer's disease, there was sufficient evidence to show that there were asymmetries in the Alzheimer brain when examining the rate of glucose metabolism,[64,65,66] and that there were neuropsychological differences[67] between the left and right hemispheres. There was also evidence of some heterogeneity in the Alzheimer brain.[63]

Even though there were only 6 SDAT cases used in this study, the method devised for counting plaques seems to be sensitive enough for detecting asymmetries in plaque counts. Similar to the in vivo imaging results, the results of this study have indicated that there were interhemispheric differences and that there was evidence of heterogeneity between the regions examined in the cases used in this study.

**A Comparison of SDAT and Normal Ageing**

The question of whether SDAT is an exaggeration of normal ageing or whether it is a separate disease process has been studied by various workers who have come to different conclusions. Brayne and Calloway found that when using the CAMDEX (Cambridge Mental Disorders of the Elderly Examination) interview to determine mental status there was little evidence to support the view that senile dementia of the Alzheimer type (SDAT) was distinct from the normal ageing process. They also stated that the changes in brain function found in normal ageing, benign senescent forgetfulness and SDAT could be seen as a continuum which may reflect a single underlying process.[58]

In a study of 50 cases of known dementia, Tomlinson, Blessed and Roth showed that the brain weight was, without exception, within the normal range for healthy adults.[7] However, they also showed that there was a statistically significant difference between the demented and control group in relation to cortical atrophy, ventricular dilation, senile plaque formation and Alzheimer's neurofibrillary change.

When comparing the number of senile plaques and neurofibrillary tangles in 40 cases of senile dementia to age matched controls, Dayan found that there was no significant difference in the number of plaques but there was a difference in the number of neurofibrillary tangles between the 2 groups.[57]

Kulmala found that when studying the enkephalin-like immunoreactivity in the neurons of the hippocampus there was no difference in the distribution or number of neurons that could

be attributable to normal ageing or Alzheimer's disease (whether presenile or senile).[59]

Mann et al. showed that there was a loss of neurons in the locus caeruleus of the Alzheimer patient compared to the age matched controls (65% reduction).[60] Mann et al. also showed that there was a significant difference in the number of senile plaques and neurofibrillary tangles between the controls and SDAT brains.[61]

Terry and Hansen counted neurons in the mid-frontal, superior temporal and inferior parietal cortex and found that the number of large neurons decreased significantly with normal old age. They also found that the number of small neurons actually increased with age. In the older group, the mean increase of smaller neurons was equal to the average decrease of large neurons. They therefore concluded that the larger neurons had shrunk and that the total number of neurons did not change as a function of normal ageing.[62] When they compared the number of neurons, plaques, tangles and level of ChAT activity between SDAT patients and normal age matched controls, they found that even after the age of 80 years significant differences still remained between the two groups.

In this study when comparing the number of plaques found in the various regions examined, there was a significant difference between the SDAT cases and the age matched controls. In fact the majority of the control cases showed no senile plaques, or very few plaques at all. This is in agreement with Terry and Hansen[62] and Mann et al.[60,61] that there were significant

differences in the number of plaques between the SDAT brain compared to normal age matched controls. In this study there was also a significant difference between the brain volume, the cerebral cortex volume and the white matter volume of the SDAT cases compared to the age matched controls. Therefore SDAT does not seem to be a continuation of normal ageing as suggested by Brayne and Calloway,[58] but a disease per se.

## CONCLUSION

From the results obtained in this study it can be concluded that in SDAT there was global loss of cerebral cortex and white matter (more cortex being lost than white). There was also selective loss of cortex in the left temporal, frontal, parietal and occipital lobes, whereas in the right hemisphere only the cortex of the parietal lobe showed any atrophy. There was no significant difference between the ventricles of the SDAT group compared to the age matched controls.

From the 7 stains evaluated in this study, the King's amyloid on frozen sections was found to be the most sensitive for demonstrating senile plaques. By increasing the plaque counts from 1 to 6 greatly improved the reproducibility and accuracy of the plaque counts by reducing the day to day error from a mean plaque count of $\pm 2.2$ plaques ($\pm 9.6\%$) to $\pm 0.7$ plaques ($\pm 3.9\%$). Compared to the age matched controls there was a significant increase in the number and area of plaques in the SDAT brain. There was also evidence of interhemispheric asymmetry, intraregional and interregional heterogeneity in the SDAT brain.

Since there was a significant difference both in the volume of the brain and the number of senile plaques observed in the cortex of the SDAT brain compared to the age matched controls, it could be concluded that SDAT was not a continuation of normal ageing.

There was a high degree of positive correlation between the volume of the left temporal lobe and the area of plaques. There

was also a good negative correlation between the volume of the right frontal lobe and both the number and area of plaques. Finally, there was an excellent positive correlation between the number of plaques and the area of plaques with the correlation being slightly better in the deep layers of the cortex.

## APPENDIX

**Tables 20-33** Interhemispheric differences in both the number of plaques/$mm^2$ and the area of plaques in square microns.

**Tables 34-47** Intraregional differences in both the number of plaques/$mm^2$ and the area of plaques in square microns.

**Tables 48-53** Interregional variation in the number of plaques/$mm^2$ in the suerficial layers of cortex.

**Tables 54-59** Interregional variation in the number of plaques/$mm^2$ in the deep layers of cortex.

**Tables 60-65** Interregional variation in the total number of plaques/$mm^2$.

**Tables 66-71** Interregional variation in the area of plaques in square microns in the superficial layers of cortex.

**Tables 72-77** Interregional variation in the area of plaques in square microns in the deep layers of cortex.

**Tables 78-83** Interregional variation in the total area of plaques in square microns.

**Tables 84-89** The number of regions that had asymmetric plaque counts when counting the number of plaques/$mm^2$ and measuring the area of plaques in square microns.

**Table 91** Correlation values (r) between the volume of each lobe/CCV and the number and area of plaques.

**Table 92** Correlation values (r) between the number of plaques and the area of plaques.

**Table 93** Variation in the methods used to quantify senile plaques.

**Table 20** Interhemispheric differences in the number of plaques/$mm^2$ demonstrated in the left and right hemispheres with the superficial, deep and total plaque counts in the fontal cortex.

| | Superficial (S) | | Abs | % | Deep (D) | | Abs | % | Total (mean of S+D) | | Abs | % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case | Left | Right | | | Left | Right | | | Left | Right | | |
| 8 | 28.8 | 28.6 | 0.2 | 0.7 | 15.4 | 11.4 | 4.0 | 29.8 | 22.1 | 20.0 | 2.1 | 10.0 |
| 9 | 27.4 | 16.8 | 10.6 | 48.0* | 10.8 | 3.8 | 7.0 | 95.9* | 19.1 | 10.3 | 8.8 | 59 9* |
| 10 | 15.5 | 53.5 | 38.0 | 110.0* | 3.8 | 38.0 | 34.2 | 163.6* | 9.6 | 45.8 | 36.2 | 130.7* |
| 11 | 17.4 | 17.4 | 0 | 0 | 18.9 | 4.6 | 14.3 | 121.7* | 18.2 | 11 0 | 7.2 | 49.3* |
| 12 | 10.5 | 9.5 | 1.0 | 10.0 | 2.0 | 6.8 | 4.8 | 109.1 | 6.2 | 8.2 | 2.0 | 27.8 |
| 13 | 20.7 | 37.2 | 16.5 | 57.0* | 3.9 | 9.3 | 5.4 | 81.8* | 24.6 | 46.5 | 21.9 | 61.6* |

Abs. = The absolute difference in plaque counts between the left and right hemispheres.

% = The percentage change between the left and right hemisphere

* = Asymmetric plaque counts

**Table 21** Interhemispheric differences in the area of plaques in square microns demonstrated in the left and right hemispheres with the superficial, deep and total plaque counts in the frontal cortex.

| | Superficial (S) | | Abs | % | Deep (D) | | Abs | % | Total (mean of S+D) | | Abs | % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case | Left | Right | | | Left | Right | | | Left | Right | | |
| 8 | 22,304 | 30,478 | 8,174 | 31.0 | 15,477 | 13,175 | 2,302 | 16.1 | 18,890 | 21,826 | 2,936 | 14.0 |
| 9 | 33,705 | 17,536 | 16,169 | 63.1* | 11,832 | 4,576 | 7,256 | 88.4* | 22,768 | 11.056 | 11,712 | 69.2* |
| 10 | 10,892 | 62,009 | 51,117 | 140.2* | 3,939 | 43,072 | 39,133 | 166.5* | 7,416 | 52,540 | 45,125 | 150.0* |
| 11 | 29,191 | 35,030 | 5,839 | 18.0 | 32,457 | 8,542 | 23.915 | 117.0* | 30.824 | 21.786 | 9,038 | 34.0 |
| 12 | 8,652 | 9,278 | 626 | 7.0 | 3,463 | 9,230 | 5,767 | 91.0* | 6,058 | 9,254 | 3,196 | 42.0 |
| 13 | 23,478 | 37,070 | 13,592 | 45.0* | 4,135 | 11,264 | 7,129 | 93.0* | 13,806 | 24.167 | 10.360 | 54.0* |

Abs = The absolute difference in plaque counts between the left and right hemispheres

% = The percentage change between the left and right hemisphere

* = Asymmetric plaque counts

**Table 22** Interhemispheric differences in the number of plaques/$mm^2$ in the left and right hemispheres with the superficial, deep and total plaque counts in the superior temporal cortex.

| | Superficial (S) | | Abs | % | Deep (D) | | Abs | % | Total (mean of S+D) | | Abs | % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case | Left | Right | | | Left | Right | | | Left | Right | | |
| 8 | 14.1 | 24.9 | 10.8 | 55.4* | 3.5 | 12.2 | 8.7 | 110.8* | 8.8 | 18.6 | 9.8 | 71.5* |
| 9 | 6.1 | 13.3 | 7.2 | 74.2* | 2.8 | 5.8 | 3.0 | 69.8 | 4.4 | 9.6 | 5.2 | 74.3* |
| 10 | 22.8 | 40.8 | 18.0 | 56.6* | 5.1 | 21.8 | 16.7 | 124.2* | 14.0 | 31.3 | 17.3 | 76.4* |
| 11 | 27.0 | 13.0 | 14.0 | 70.0* | 13.1 | 1.8 | 11.3 | 151.7* | 20.0 | 7.4 | 12.6 | 92.0* |
| 12 | 9.7 | 13.2 | 3.5 | 30.6 | 2.4 | 6.1 | 3.7 | 87.0 | 6.0 | 9.6 | 3.6 | 46.2 |
| 13 | 23.9 | 34.8 | 10.9 | 37.1 | 9.3 | 10.8 | 1.5 | 14.9 | 33.2 | 45 6 | 12.4 | 31.5 |

Abs = The absolute difference in plaque counts between the left and right hemispheres.

% = The percentage change between the left and right hemispheres

* = Asymmetric plaque counts

**Table 23** Interhemispheric differences in the area of plaques in square microns demonstrated in the left and right hemispheres with the superficial, deep and total plaque counts in the superior temporal cortex.

| | Superficial (S) | | Abs | % | Deep (D) | | Abs | % | Total (mean of S+D) | | Abs | % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case | Left | Right | | | Left | Right | | | Left | Right | | |
| 8 | 14,860 | 25,491 | 10,631 | 52.7* | 5,299 | 16,417 | 11,118 | 102.4* | 10.080 | 20,954 | 10,874 | 70.0* |
| 9 | 5,170 | 17,860 | 12,690 | 110.2* | 3,055 | 6,900 | 3,845 | 77.2 | 4 112 | 12 380 | 8,268 | 100.2* |
| 10 | 16,000 | 43,698 | 27,698 | 92.8* | 4,603 | 22,822 | 18,219 | 132.9* | 10,302 | 33,260 | 22,959 | 105.0* |
| 11 | 49,289 | 32,455 | 16,834 | 41.0* | 29,339 | 5,621 | 23,718 | 136.0* | 39,314 | 19,038 | 20.276 | 69.0* |
| 12 | 12,498 | 20,566 | 8,068 | 49.0* | 2,772 | 8,304 | 5,532 | 100.0 | 7,635 | 14,435 | 6,800 | 62.0* |
| 13 | 23,899 | 38,364 | 14,465 | 46.0* | 10,721 | 13.570 | 2,849 | 23.0 | 17,310 | 25.967 | 8,657 | 40.0* |

Abs = The absolute difference in plaque counts between the left and right hemispheres

% = The percentage change between the left and right hemispheres

* = Asymmetric plaque counts

**Table 24** Interhemispheric differences in the number of plaques/mm$^2$ in the left and right hemispheres with the superficial, deep and total plaque counts in the middle temporal cortex.

| | Superficial (S) | | Abs | % | Deep (D) | | Abs | % | Total (mean of S+D) | | Abs | % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case | Left | Right | | | Left | Right | | | Left | Right | | |
| 8 | 20.2 | 17.8 | 2.4 | 12.6 | 7.9 | 8.9 | 1.0 | 11.9 | 14.0 | 13.4 | 0.6 | 4.4 |
| 9 | 3.5 | 10.8 | 7.3 | 102.1* | 1.2 | 5.1 | 3.9 | 123.8 | 4.4 | 8.0 | 3.6 | 58.1 |
| 10 | 32.3 | 44.6 | 12.3 | 32.0 | 5.8 | 25.6 | 19.8 | 126.1* | 19.0 | 35.1 | 16.1 | 59.5* |
| 11 | 30.9 | 23.2 | 7.7 | 28.5 | 20.8 | 4.6 | 16.2 | 127.6* | 25.8 | 13.9 | 11.9 | 59.9* |
| 12 | 14.4 | 18.1 | 3.7 | 22.8 | 4.1 | 9.5 | 5.4 | 79.4* | 9.2 | 13.8 | 4.6 | 40.0 |
| 13 | 21.2 | 43.1 | 21.9 | 68.1* | 9.7 | 21.4 | 11.7 | 75.2* | 30.7 | 64.6 | 33.8 | 71.0* |

Abs = The absolute difference in plaque counts between the left and right hemispheres.

% = The percentage change between the left and right hemispheres

* = Asymmetric plaque counts

**Table 25** Interhemispheric differences in the area of plaques in square microns demonstrated in the left and right hemispheres with the superficial, deep and total plaque counts in the middle temporal cortex.

| | Superficial (S) | | Abs | % | Deep (D) | | Abs | % | Total (mean of S+D) | | Abs | % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case | Left | Right | | | Left | Right | | | Left | Right | | |
| 8 | 19,073 | 26,390 | 7,317 | 32.2 | 7,343 | 9,876 | 2,533 | 29.4 | 13,208 | 18,133 | 4,925 | 31.0 |
| 9 | 3,160 | 10,381 | 7,671 | 109.6* | 546 | 4,824 | 4,278 | 159.3 | 1.853 | 7,828 | 5,974 | 121.6* |
| 10 | 33,065 | 54,968 | 21,903 | 49.8* | 5,157 | 28,177 | 23,020 | 138.1* | 19,111 | 41,572 | 22,462 | 74.0* |
| 11 | 62,193 | 37,616 | 24,577 | 49.0* | 32,269 | 7,883 | 24,386 | 121.0* | 47,231 | 22.750 | 24.482 | 70.0* |
| 12 | 19,619 | 28,254 | 8,635 | 36.0 | 9,440 | 14,337 | 4,897 | 41.0 | 14,530 | 21,296 | 6,766 | 38.0 |
| 13 | 36,836 | 54,278 | 17,442 | 38.0 | 15,098 | 33.843 | 18,745 | 77.0* | 25,967 | 44 060 | 18,094 | 52.0* |

Abs = The absolute difference in plaque counts between the left and right hemispheres

% = The percentage change between the left and right hemispheres

* = Asymmetric plaque counts

Table 26 Interhemispheric differences in the number of plaques/$mm^2$ demonstrated in the left and right hemispheres with the superficial, deep and total plaque counts in the inferior temporal cortex.

| | Superficial (S) | | Abs | % | Deep (D) | | Abs | % | Total (mean of S+D) | | Abs | % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case | Left | Right | | | Left | Right | | | Left | Right | | |
| 8 | 23.3 | 19.7 | 3.6 | 16.7 | 7.5 | 8.3 | 0.8 | 10.1 | 15.4 | 14.0 | 1.4 | 9.5 |
| 9 | 12.8 | 8.0 | 4.8 | 46.2 | 2.1 | 4.2 | 2.1 | 66.7 | 7.4 | 6.1 | 1.3 | 19.2 |
| 10 | 37 | 40.1 | 3.1 | 8.0 | 10.5 | 28.4 | 17.9 | 92.0* | 23.8 | 34.2 | 10.4 | 35.9 |
| 11 | 34.9 | 38.0 | 3.1 | 8.5 | 22.6 | 18.6 | 4.0 | 19.4 | 28.8 | 28.3 | 0.5 | 1.8 |
| 12 | 26.1 | 24.9 | 1.2 | 4.7 | 12.9 | 10.8 | 2.1 | 17.7 | 19.5 | 17.8 | 1.7 | 9.1 |
| 13 | 19.7 | 31.2 | 11.5 | 45.4* | 6.6 | 12.9 | 6.3 | 64.6* | 26.3 | 44.1 | 17.8 | 50.6* |

Abs = The absolute difference in plaque counts between the left and right hemispheres

% = The percentage change between the left and right hemispheres

* = Asymmetric plaque counts

**Table 27** Interhemispheric differences in the area of plaques in square microns demonstrated in the left and right hemispheres with the superficial, deep and total plaque counts in the inferior temporal cortex.

| | Superficial (S) | | Abs | % | Deep (D) | | Abs | % | Total (mean of S+D) | | Abs | % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case | Left | Right | | | Left | Right | | | Left | Right | | |
| 8 | 25,522 | 22,131 | 3,391 | 14.2 | 9,213 | 8,418 | 795 | 9.0 | 17,368 | 15,274 | 2,093 | 13.0 |
| 9 | 14,627 | 6,920 | 7,707 | 71.5* | 2,607 | 4,743 | 2,136 | 58.1 | 8,617 | 5,832 | 2,786 | 38.6 |
| 10 | 38,112 | 48,764 | 10,652 | 24.5 | 8,076 | 29,899 | 21,823 | 114.9* | 23,094 | 39,332 | 16,238 | 52.0* |
| 11 | 77,512 | 77,014 | 498 | 1.0 | 60,052 | 38,470 | 21,582 | 44.0* | 68,782 | 57,742 | 11.040 | 17.0 |
| 12 | 46,349 | 37,401 | 8,948 | 21.0 | 24,846 | 23,494 | 1,352 | 6.0 | 35,598 | 30,448 | 5,150 | 16.0 |
| 13 | 27,985 | 36,268 | 8,283 | 26.0 | 7.342 | 16,443 | 9,101 | 76.0* | 17,664 | 26,356 | 8,692 | 39.0 |

Abs = The absolute difference in plaque counts between the left and right hemispheres

% = The percentage change between the left and right hemispheres

* = Asymmetric plaque counts

**Table 28** Interhemispheric differences in the number of plaques/$mm^2$ demonstrated in the left and right hemispheres with the superficial, deep and total plaque counts in the cingulate cortex.

| | Superficial (S) | | Abs | % | Deep (D) | | Abs | % | Total (mean of S+D) | | Abs | % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case | Left | Right | | | Left | Right | | | Left | Right | | |
| 8 | 27.4 | 17.6 | 9.8 | 43.6* | 11.2 | 7.7 | 3.5 | 37.0 | 19.3 | 12.6 | 6.7 | 42.0* |
| 9 | 29.9 | 21.7 | 8.2 | 31.8 | 12.8 | 5.4 | 7.4 | 81.3* | 21.4 | 13.6 | 7.8 | 44.6* |
| 10 | 12.7 | 45.8 | 33.1 | 113.2* | 1.4 | 20.9 | 19.5 | 174.9* | 7.0 | 33.4 | 26.4 | 130.7* |
| 11 | 13.4 | 8.8 | 4.6 | 41.4 | 12.7 | 4.4 | 8.3 | 97.1* | 13.0 | 6.6 | 6.6 | 65.3* |
| 12 | 15.8 | 15.8 | 0 | 0 | 3.4 | 6.1 | 2.7 | 56.8 | 9.6 | 11.0 | 1.4 | 13.6 |
| 13 | 20.5 | 30.2 | 9.7 | 38.3 | 2.7 | 10.5 | 7.8 | 118.2* | 20.5 | 2.7 | 17.8 | 153.4* |

Abs = The absolute difference in plaque counts between the left and right hemispheres

% = The percentage change between the left and right hemispheres

* = Asymmetric plaque counts

**Table 29** Interhemispheric differences in the area of plaques in square microns demonstrated in the left and right hemispheres with the superficial, deep and total plaque counts in the cingulate cortex.

| | Superficial (S) | | Abs | % | Deep (D) | | Abs | % | Total (mean of S+D) | | Abs | % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case | Left | Right | | | Left | Right | | | Left | Right | | |
| 8 | 21,350 | 18,513 | 2,837 | 14.2 | 10,027 | 9,318 | 709 | 7.3 | 15,688 | 13,916 | 1,773 | 12.0 |
| 9 | 26,659 | 28,590 | 1,931 | 7.0 | 11,718 | 7,068 | 4,650 | 49.5 | 19,188 | 17,829 | 1,360 | 7.3 |
| 10 | 9,773 | 38,487 | 28,714 | 119.0* | 1,375 | 18,850 | 17,475 | 172.8* | 5,574 | 28,668 | 23,094 | 135.0* |
| 11 | 20,564 | 14,700 | 5,864 | 33.0 | 27,856 | 5,641 | 22,215 | 133.0* | 24,210 | 10.170 | 14,040 | 82.0* |
| 12 | 17,962 | 20,351 | 2,389 | 12.0 | 5,802 | 9,129 | 3,327 | 44.0 | 11,882 | 14,740 | 2,858 | 21.0 |
| 13 | 19,665 | 33,757 | 14,092 | 53.0* | 2,045 | 8,723 | 6,678 | 124.0* | 10,855 | 21,240 | 10,385 | 65.0* |

Abs = The absolute difference in plaque counts between the left and right hemispheres

% = The percentage change between the left and right hemispheres

* = Asymmetric plaque counts

**Table 30** Interhemispheric differences in the number of plaques/$mm^2$ demonstrated in the left and right hemispheres with the superficial, deep and total plaque counts in the parietal cortex.

| | Superficial (S) | | Abs | % | Deep (D) | | Abs | % | Total (mean of S+D) | | Abs | % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case | Left | Right | | | Left | Right | | | Left | Right | | |
| 8 | 21.8 | 44.8 | 23.0 | 69.1 | 9.2 | 19.3 | 10.1 | 70.9* | 15.5 | 32 | 16.5 | 69.5* |
| 9 | 23.9 | 31.8 | 7.9 | 28.4 | 14.0 | 7.0 | 7.0 | 66.7* | 19 0 | 16.2 | 2.8 | 15.9 |
| 10 | 32.6 | 41.3 | 8.7 | 23.5 | 12.7 | 27.2 | 14.5 | 72.7* | 22.6 | 34.2 | 11.6 | 40.8* |
| 11 | 33.8 | 18.9 | 14.9 | 56.5* | 14.9 | 11.6 | 3.3 | 24.9 | 24.4 | 15.2 | 9.2 | 46.5* |
| 12 | 23.4 | 11.4 | 12.0 | 69.0* | 9.3 | 3.6 | 5.7 | 88.4* | 16.4 | 7.5 | 8.9 | 74.5* |
| 13 | 20.0 | 23.7 | 3.7 | 16.9 | 1.7 | 3.6 | 1.9 | 71.7 | 21.7 | 27.3 | 5 6 | 22.8 |

Abs = The absolute difference in plaque counts between the left and right hemispheres

% = The percentage change between the left and right hemispheres

* = Asymmetric plaque counts

**Table 31** Interhemispheric differences in the area of plaques in square microns demonstrated in the left and right hemispheres with the superficial, deep and total plaque counts in the parietal cortex.

| | Superficial (S) | | Abs | % | Deep (D) | | Abs | % | Total (mean of S+D) | | Abs | % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case | Left | Right | | | Left | Right | | | Left | Right | | |
| 8 | 28,145 | 43,156 | 15,011 | 42.1* | 14,903 | 20,320 | 5,417 | 30.8 | 21,524 | 31,738 | 10,214 | 38.0 |
| 9 | 32,978 | 26,643 | 6,335 | 21.2 | 25,382 | 13,420 | 11,962 | 61.6* | 29.180 | 20,032 | 9,148 | 37.2 |
| 10 | 32,036 | 44,710 | 12,674 | 33.0 | 15,019 | 30,345 | 15,326 | 67.6* | 23,528 | 37,528 | 14,000 | 46.0* |
| 11 | 50,358 | 31,113 | 19,245 | 47.0* | 18,474 | 32,037 | 13.563 | 54.0* | 34,416 | 31,575 | 2,841 | 9.0 |
| 12 | 20,757 | 15,055 | 5,702 | 32.0 | 11,463 | 6,201 | 5,262 | 60.0 | 16,110 | 10,628 | 5,482 | 41.0 |
| 13 | 20,630 | 27,649 | 7,019 | 29.0 | 2.402 | 4,843 | 2,441 | 67.0 | 11,516 | 16.246 | 4,730 | 34.0 |

Abs = The absolute difference in plaque counts between the left and right hemispheres

% = The percentage change between the left and right hemispheres

* = Asymmetric plaque counts

**Table 32** Interhemispheric differences in the number of plaques/mm$^2$ demonstrated in the left and right hemispheres with the superficial, deep and total plaque counts in the occipital cortex.

| | Superficial (S) | | Abs | % | Deep (D) | | Abs | % | Total (mean of S+D) | | Abs | % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case | Left | Right | | | Left | Right | | | Left | Right | | |
| 8 | 26.0 | 18.5 | 7.5 | 33.7 | 13.9 | 8.7 | 5.2 | 46.o* | 20.0 | 13.6 | 6.4 | 38.1 |
| 9 | 29.9 | 23.6 | 6.3 | 23.6 | 11.9 | 3.2 | 8.7 | 115.2* | 20.9 | 13 4 | 7.5 | 43.7* |
| 10 | 26.3 | 27.9 | 1.6 | 5.9 | 10.5 | 8.2 | 2.3 | 24.6 | 18.4 | 18.0 | 0.4 | 2.2 |
| 11 | 18.6 | 14.5 | 4.1 | 24.8 | 4.8 | 8.1 | 3.3 | 51.2 | 11.7 | 11.3 | 0.4 | 3.5 |
| 12 | 13.2 | 9.5 | 3.7 | 32.6 | 1.7 | 4.6 | 2.9 | 92.1 | 7.4 | 7.0 | 0.4 | 5.6 |
| 13 | 8.0 | 23.7 | 15.7 | 99.0* | 0 | 0.5 | 0.5 | 200.0 | 8 | 24.2 | 16.2 | 100.6* |

Abs = The absolute difference in plaque counts between the left and right hemisphere

% = The percentage change between the left and right hemispheres

* = Asymmetric plaque counts

Table 33 Interhemispheric differences in the area of plaques in square microns demonstrated in the left and right hemispheres with the superficial, deep and total plaque counts in the occipital cortex.

| | Superficial (S) | | Abs | % | Deep (D) | | Abs | % | Total (mean ofS+D) | | Abs | % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Left | Right | | | Left | Right | | | Left | Right | | |
| 8 | 21,548 | 26,943 | 5,395 | 22.2 | 15,679 | 10,544 | 5,135 | 39.2 | 18,614 | 18,744 | 130 | 0.7 |
| 9 | 45,095 | 28,672 | 16.423 | 44.5* | 19,994 | 5,505 | 14,489 | 113.6* | 32.544 | 17 088 | 15.456 | 62 3* |
| 10 | 22,517 | 50,418 | 27,901 | 76.0* | 11,147 | 15,531 | 4,384 | 32.9 | 16,832 | 32,974 | 16,142 | 65.0* |
| 11 | 33,722 | 24,969 | 8,753 | 30.0 | 11,304 | 14 492 | 3,188 | 25 0 | 22,513 | 19,730 | 2,782 | 13.0 |
| 12 | 20,663 | 41,069 | 20,406 | 66.0* | 2,410 | 6,139 | 3,729 | 87.0 | 11,536 | 23,604 | 12,068 | 69.0* |
| 13 | 9,086 | 22,040 | 12,954 | 83.0* | 0 | 438 | 438 | 200.0 | 4,543 | 11 239 | 6,696 | 85.0* |

Abs = The absolute difference in plaque counts between the left and right hemispheres

% = The percentage change between the left and right hemispheres

* = Asymmetric plaque counts

**Table 34** Intraregional differences in the number of plaques/$mm^2$ between the superficial and deep layers of the frontal cortex.

| | Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|---|
| Case | Superficial | Deep | | | Superficial | Deep | | |
| 8 | 28.8 | 15.4 | 13.4 | 60.6* | 28.6 | 11.4 | 17.2 | 86.0* |
| 9 | 27.4 | 10.8 | 16.6 | 86.9* | 16.8 | 3.8 | 13.0 | 125.6* |
| 10 | 15.5 | 3.8 | 11.7 | 121.2* | 53.5 | 38.0 | 15.5 | 33.9 |
| 11 | 17.4 | 18.9 | 1.5 | 8.3 | 17.4 | 4.6 | 12.8 | 116.4* |
| 12 | 10.5 | 2.0 | 8.5 | 136.0* | 9.5 | 6.8 | 2.7 | 33.1 |
| 13 | 20.7 | 3.9 | 16.8 | 136.6* | 37.2 | 9.3 | 27.9 | 120.0* |

Abs = The absolute difference in plaque counts between the superficial and deep layers
% = The percentage change between the superficial and deep layers
* = Asymmetric plaque counts.

**Table 35** Intraregional differences in the area of plaques, in square microns, between the superficial and deep layers of the frontal cortex.

| | Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|---|
| Case | Superficial | Deep | | | Superficial | Deep | | |
| 8 | 22,304 | 15,477 | 6,827 | 36.1 | 30,478 | 13,175 | 17.303 | 79.3* |
| 9 | 33,705 | 11,832 | 21,873 | 96.1* | 17,536 | 4,576 | 12,960 | 117.2* |
| 10 | 10,892 | 3.939 | 6,953 | 93.8* | 62,009 | 43,072 | 18.937 | 36.0 |
| 11 | 29,191 | 32,457 | 3,266 | 10.0 | 35,030 | 8,542 | 26,488 | 122.0* |
| 12 | 8,652 | 3,463 | 5,189 | 86.0 | 9,278 | 9,230 | 48 | 0.5 |
| 13 | 23,478 | 4,135 | 19,343 | 140.0 | 37,070 | 11,264 | 25,806 | 107.0* |

Abs = The absolute difference in plaque counts between the superficial and deep layers
% = The percentage change between the superficial and deep layers
* = Asymmetric plaque counts

**Table 36** Intraregional differences in the number of plaques/$mm^2$ between the superficial and deep layers of the superior temporal cortex.

| | Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|---|
| Case | Superficial | Deep | | | Superficial | Deep | | |
| ♂ | 14.1 | 3.5 | 10.6 | 120.4* | 24.9 | 12.2 | 12.7 | 68.5* |
| 9 | 6.1 | 2.8 | 3.3 | 74.2 | 13.3 | 5.8 | 7.5 | 78.5* |
| 10 | 22.8 | 5.1 | 17.7 | 126.9* | 40.8 | 21.8 | 19.0 | 60.7* |
| 11 | 27.0 | 13.1 | 13.9 | 69.3* | 13.0 | 1.8 | 11.2 | 151.4* |
| 12 | 9.7 | 2.4 | 7.3 | 120.7* | 13.2 | 6.1 | 7.1 | 73.6* |
| 13 | 23.9 | 9.3 | 14.6 | 88.0* | 34.8 | 10.8 | 24.0 | 105.3* |

Abs = The absolute difference in plaque counts between the superficial and deep layers.
% = The percentage change between the superficial and deep layers.
* = Asymmetric plaque counts.

Table 37 Intraregional differences in the area of plaques, in square microns, between the superficial and deep layers of the superior temporal cortex.

| | Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|---|
| Case | Superficial | Deep | | | Superficial | Deep | | |
| 8 | 14,860 | 5,299 | 9,561 | 94.8* | 25,491 | 16,417 | 9,074 | 43.3* |
| 9 | 5,170 | 3,055 | 2,115 | 51.4 | 17,860 | 6,900 | 10,960 | 88.5* |
| 10 | 16,000 | 4,603 | 11,397 | 110.6* | 43,698 | 22.822 | 20.876 | 63.0* |
| 11 | 49,289 | 29,339 | 19,950 | 51.0* | 32,455 | 5,621 | 26,834 | 141.0* |
| 12 | 12,498 | 2,772 | 9,726 | 127.0* | 20,566 | 8,304 | 12,262 | 85.0* |
| 13 | 23,899 | 10,721 | 13,178 | 76.0* | 38,364 | 13,570 | 24,794 | 95.0* |

Abs = The absolute difference in plaque counts between the superficial and deep layers
% = The percentage change between the superficial and deep layers
* = Asymmetric plaque counts

**Table 38** Intraregional differences in the number of plaques/$mm^2$ between the superficial and deep layers of the middle temporal cortex.

| | Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|---|
| Case | Superficial | Deep | | | Superficial | Deep | | |
| 8 | 20.2 | 7.9 | 12.3 | 87.5* | 17.8 | 8.9 | 8.9 | 66.7* |
| 9 | 3.5 | 1.2 | 2.3 | 97.9 | 10.8 | 5.1 | 5.7 | 71.7* |
| 10 | 32.3 | 5.8 | 26.5 | 139.1* | 44.6 | 25.6 | 19.0 | 54.1* |
| 11 | 30.9 | 20.8 | 10.1 | 39.1 | 23.2 | 4.6 | 18.6 | 133.8* |
| 12 | 14.4 | 4.1 | 10.3 | 111.4* | 18.1 | 9.5 | 8.6 | 62.3* |
| 13 | 21.2 | 9.7 | 11.5 | 74.4* | 43.1 | 21.4 | 21.7 | 67.3* |

Abs = The absolute difference in plaque counts between the superficial and deep layers.
% = The percentage change between the superficial and deep layers
* = Asymmetric plaque counts

Table 39 Intraregional differences in the area of plaques, in square microns, between the superficial and deep layers of the middle temporal cortex.

| | Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|---|
| Case | Superficial | Deep | | | Superficial | Deep | | |
| 8 | 19,073 | 7,343 | 11,730 | 88.8* | 26,390 | 9,876 | 16,514 | 91.1* |
| 9 | 3,160 | 546 | 2,614 | 141.1 | 10,381 | 4,824 | 5,557 | 73.1* |
| 10 | 33,065 | 5,157 | 27,908 | 146.0* | 54,968 | 28,177 | 26,791 | 64.0* |
| 11 | 62,193 | 32,269 | 29,924 | 63.0* | 37,616 | 7,883 | 29,733 | 131.0* |
| 12 | 19,619 | 9,440 | 10.179 | 70.0* | 28,254 | 14,337 | 13,917 | 65.0* |
| 13 | 36,836 | 15,098 | 21,738 | 84.0* | 54,278 | 33,843 | 20,435 | 46.0* |

Abs = The absolute difference in plaque counts between the superficial and deep layers
% = The percentage change between the superficial and deep layers
* = Asymmetric plaque counts

**Table 40** Intraregional differences in the number of plaques/$mm^2$ between the superficial and deep layers of the inferior temporal cortex.

| | Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|---|
| Case | Superficial | Deep | | | Superficial | Deep | | |
| 8 | 23.3 | 7.5 | 15.8 | 102.6* | 19.7 | 8.3 | 11.4 | 81.4* |
| 9 | 12.8 | 2.1 | 10.7 | 143.6* | 8.0 | 4.2 | 3.8 | 62.3 |
| 10 | 37.0 | 10.5 | 26.5 | 111.6* | 40.1 | 28.4 | 11.7 | 34.2 |
| 11 | 34.9 | 22.6 | 12.3 | 42.8* | 38.0 | 18.6 | 19.4 | 68.6* |
| 12 | 26.1 | 12.9 | 13.2 | 67.7* | 24.9 | 10.8 | 14.1 | 79.0* |
| 13 | 19.7 | 6.6 | 13.1 | 99.6* | 31.2 | 12.9 | 18.3 | 83.0* |

Abs = The absolute difference in plaque counts between the superior and deep layers
% = The percentage change between the superficial and deep layers
* = Asymmetric plaque counts

**Table 41** Intraregional differences in the area of plaques, in square microns, between the superficial and deep layers of the inferior temporal cortex.

| | Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|---|
| Case | Superficial | Deep | | | Superficial | Deep | | |
| 8 | 25,522 | 9,213 | 16.309 | 93.9* | 22,131 | 8,418 | 13,713 | 89.8* |
| 10 | 38,112 | 8,076 | 30,036 | 130.1* | 48,764 | 29,899 | 18,865 | 48.0* |
| 11 | 77,512 | 60,052 | 17,460 | 25.0 | 77,014 | 38,470 | 38.544 | 67.0* |
| 12 | 46,349 | 24,846 | 21,503 | 60.0* | 37,401 | 23,494 | 13,907 | 46.0* |
| 13 | 27,985 | 7,342 | 20,643 | 117.0* | 36,268 | 16,443 | 19,825 | 75.0* |

Abs = The absolute difference in plaque counts between the superficial and deep layers
% = The percentage change between the superficial and deep layers
* = Asymmetric plaque counts

**Table 42** Intraregional differences in the number of plaques/$mm^2$ between the superficial and deep layers of the cingulate cortex.

| | Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|---|
| Case | Superficial | Deep | | | Superficial | Deep | | |
| 8 | 27.4 | 11.2 | 16.2 | 83.9* | 17.6 | 7.7 | 9.9 | 78.3* |
| 9 | 29.9 | 12.8 | 17.1 | 80.1* | 21.7 | 5.4 | 16.3 | 120.3* |
| 10 | 12.7 | 1.4 | 11.3 | 160.3* | 45.8 | 20.9 | 24.9 | 74.7* |
| 11 | 13.4 | 12.7 | 0.7 | 5.4 | 8.8 | 4.4 | 4.4 | 66.7 |
| 12 | 15.8 | 3.4 | 12.4 | 129.2* | 15.8 | 6.1 | 9.7 | 88.6* |
| 13 | 20.5 | 2.7 | 17.8 | 153.4 | 30.2 | 10.5 | 19.7 | 96.8* |

Abs = The absolute difference in plaque counts between the superficial and deep layers
% = The percentage change between the superficial and deep layers
* = Asymmetric plaque counts

**Table 43** Intraregional differences in the area of plaques, in square microns, between the superficial and deep layers of the cingulate cortex.

| | Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|---|
| Case | Superficial | Deep | | | Superficial | Deep | | |
| 8 | 21,350 | 10,027 | 11,323 | 72.2* | 18,513 | 9,318 | 9,195 | 66 1* |
| 9 | 26,659 | 11,718 | 14,941 | 77.9* | 28,590 | 7,068 | 21,522 | 120.7* |
| 10 | 9,773 | 1,375 | 8,398 | 150.6* | 38,487 | 18,850 | 19,637 | 68.0* |
| 11 | 20,564 | 27,856 | 7,292 | 30.0 | 14,700 | 5,641 | 9,059 | 89.0* |
| 12 | 17,962 | 5,802 | 12,160 | 102.0* | 20,351 | 9,129 | 11,222 | 76.0* |
| 13 | 19,665 | 2,045 | 17,620 | 162.0* | 33,757 | 8,723 | 25,034 | 118.0* |

Abs = The absolute difference in plaque counts between the superficial and deep layers
% = The percentage change between the superficial and deep layers
* = Asymmetric plaque counts

**Table 44** Intraregional differences in the number of plaques/$mm^2$ between the superficial and deep layers of the parietal cortex.

| | Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|---|
| Case | Superficial | Deep | | | Superficial | Deep | | |
| 8 | 21.8 | 9.2 | 12.6 | 81.3* | 44.8 | 19.3 | 25.5 | 79.6* |
| 9 | 23.9 | 14.0 | 9.9 | 52.2* | 31.8 | 7.0 | 24.8 | 127.8* |
| 10 | 32.6 | 12.7 | 19.9 | 87.8* | 41.3 | 27.2 | 14.1 | 41.2* |
| 11 | 33.8 | 14.9 | 18.9 | 77.6* | 18.9 | 11.6 | 7.3 | 47.9* |
| 12 | 23.4 | 9.3 | 14.1 | 86.2* | 11.4 | 3.6 | 7.8 | 104.0* |
| 13 | 20.0 | 1.7 | 18.3 | 168.7* | 23.7 | 3.6 | 20.1 | 147.2* |

Abs = The absolute difference in plaque counts between the superficial and deep layers.
% = The percentage change between the superficial and deep layers.
* = Asymmetric plaque counts.

**Table 45** Intraregional differences in the area of plaques, in square microns, between the superficial and deep layers of the parietal cortex.

| | Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|---|
| Case | Superficial | Deep | | | Superficial | Deep | | |
| 8 | 28,145 | 14,903 | 13,242 | 61.5* | 43,156 | 20,320 | 22-836 | 72.0* |
| 9 | 32,978 | 25,382 | 7,596 | 26.0 | 26,643 | 13,420 | 13,223 | 66.0* |
| 10 | 32,036 | 15,019 | 17,017 | 72.0* | 44,710 | 30,345 | 14,365 | 38.0 |
| 11 | 50,358 | 18,474 | 31,884 | 93.0* | 31,113 | 32,037 | 924 | 3.0 |
| 12 | 20,757 | 11,463 | 9,294 | 58.0* | 15,055 | 6 201 | 8,854 | 83.0* |
| 13 | 20,630 | 2,402 | 18,228 | 158.0* | 27,649 | 4,843 | 22,806 | 140.0* |

Abs = The absolute difference in plaque counts between the superficial and deep layers
% = The percentage change between the superficial and deep layers
* = Asymmetric plaque counts

**Table 46** Intraregional differences in the number of plaques/$mm^2$ between the superficial and deep layers of the occipital cortex.

| | Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|---|
| Case | Superficial | Deep | | | Superficial | Deep | | |
| 8 | 26.0 | 13.9 | 12.1 | 60.6* | 18.5 | 8.7 | 9.8 | 72.0* |
| 9 | 29.9 | 11.9 | 18.0 | 86.1* | 23.6 | 3.2 | 20.4 | 152.2* |
| 10 | 26.3 | 10.5 | 15.8 | 85.9* | 27.9 | 8.2 | 19.7 | 109.1* |
| 11 | 18.6 | 4.8 | 13.8 | 117.9* | 14.5 | 8.1 | 6.4 | 56.6* |
| 12 | 13.2 | 1.7 | 11.5 | 154.4* | 9.5 | 4.6 | 4.9 | 69.5* |
| 13 | 8.0 | 0 | 8.0 | 200.0* | 23.7 | 0.5 | 23.2 | 191.7* |

Abs = The absolute difference in plaque counts between the superficial and deep layers
% = The percentage change between the superficial and deep layers
* = Asymmetric plaque counts

**Table 47** Intraregional differences in the area of plaques, in square microns, between the superficial and deep layers of the occipital cortex.

| | Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|---|
| Case | Superficial | Deep | | | Superficial | Deep | | |
| 8 | 21,548 | 15,679 | 5,869 | 31.5 | 26,943 | 10,544 | 16,399 | 87.5* |
| 9 | 45,095 | 19,994 | 25,101 | 77.1* | 28,672 | 5,505 | 23,167 | 135.6* |
| 10 | 22,517 | 11,147 | 11,370 | 68.0* | 50,418 | 15.531 | 34,887 | 106.0* |
| 11 | 33,722 | 11,304 | 22,418 | 100.0* | 24,969 | 14,492 | 10,477 | 53.0* |
| 12 | 20,663 | 2,410 | 18,253 | 158.0* | 41,069 | 6 139 | 34.930 | 148.0* |
| 13 | 9,086 | 0 | 9,086 | 200.0* | 22,040 | 438 | 21,602 | 192.0* |

Abs = The absolute difference in plaque counts between the superficial and deep layers
% = The percentage change between the superficial and deep layers
* = Asymmetric plaque counts

**Table 48.** Interregional variation in the number of plaques/mm$^2$ in the superficial layers of SDAT Case 8

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 28.8 | 14.1 | 14.7 | 68.5* | 28.6 | 24.9 | 3.7 | 13.8 |
| | Mid Temp | | | | Mid Temp | | |
| | 20.2 | 8.6 | 35.1 | | 17.8 | 10.8 | 46.6* |
| | Inf Temp | | | | Inf Temp | | |
| | 23.3 | 5.5 | 21.1 | | 19.7 | 8.9 | 36.8 |
| | Cingulate | | | | Cingulate | | |
| | 27.4 | 1.4 | 5.0 | | 17.6 | 11.0 | 47.6* |
| | Parietal | | | | Parietal | | |
| | 21.8 | 7.0 | 27.7 | | 44.8 | 16.2 | 44.1* |
| | Occipital | | | | Occipital | | |
| | 26.0 | 2.8 | 10.2 | | 18.5 | 10.1 | 42.9* |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 14.1 | 20.2 | 6.1 | 35.6 | 24.9 | 17.8 | 7.1 | 33.2 |
| | Inf Temp | | | | Inf Temp | | |
| | 23.3 | 9.2 | 49.2* | | 19.7 | 5.2 | 23.3 |
| | Cingulate | | | | Cingulate | | |
| | 27.4 | 13.3 | 64.1* | | 17.6 | 7.3 | 34.4 |
| | Parietal | | | | Parietal | | |
| | 21.8 | 7.7 | 42.9* | | 44.8 | 19.9 | 57.1* |
| | Occipital | | | | Occipital | | |
| | 26.0 | 11.9 | 59.4* | | 18.5 | 6.4 | 29.5 |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 20.2 | 23.3 | 3.1 | 14.2 | 17.8 | 19.7 | 1.9 | 10.1 |
| | Cingulate | | | | Cingulate | | |
| | 27.4 | 7.2 | 30.2 | | 17.6 | 0.2 | 1.1 |
| | Parietal | | | | Parietal | | |
| | 21.8 | 1.6 | 7.6 | | 44.8 | 27.0 | 86.3* |
| | Occipital | | | | Occipital | | |
| | 26.0 | 5.8 | 25.1 | | 18.5 | 0.7 | 3.8 |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 23.3 | 27.4 | 4.1 | 16.2 | 19.7 | 17.6 | 2.1 | 11.3 |
| | Parietal | | | | Parietal | | |
| | 21.8 | 1.5 | 6.6 | | 44.8 | 25 1 | 77.8* |
| | Occipital | | | | Occipital | | |
| | 26.0 | 2.7 | 11.0 | | 18.5 | 1.2 | 6.3 |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 27.4 | 21.8 | 5.6 | 22.8 | 17.6 | 44.8 | 27.2 | 87.2 |
| | Occipital | | | | Occipital | | |
| | 26.0 | 1.4 | 5.2 | | 18.5 | 0.9 | 5.0 |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 21.8 | 26.0 | 4.2 | 17.6 | 44.8 | 18.5 | 26.3 | 82.8* |

* = Asymmetric plaque counts between the regions.

**Table 49.** Interregional variation in the number of plaques/mm$^2$ in the superficial layers of SDAT Case 9.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 27.4 | 6.1 | 21.3 | 127.2* | 16.8 | 13.3 | 3.5 | 23.2 |
| | Mid Temp | | | | Mid Temp | | |
| | 3.5 | 23.9 | 154.7* | | 10.8 | 6.0 | 43.5* |
| | Inf Temp | | | | Inf Temp | | |
| | 12.8 | 14.6 | 72.6* | | 8.0 | 8.8 | 71.0* |
| | Cingulate | | | | Cingulate | | |
| | 29.9 | 2.5 | 8.7 | | 21.7 | 4.9 | 25.4 |
| | Parietal | | | | Parietal | | |
| | 23.9 | 3.5 | 13.6 | | 31.8 | 15.0 | 61.7* |
| | Occipital | | | | Occipital | | |
| | 29.9 | 2.5 | 8.7 | 16.8 | 23.6 | 6.8 | 33.7 |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 6.1 | 3.5 | 2.6 | 54.2 | 13.3 | 10.8 | 2.5 | 20.7 |
| | Inf Temp | | | | Inf Temp | | |
| | 12.8 | 6.7 | 70.9* | | 8.0 | 5.3 | 49.8* |
| | Cingulate | | | | Cingulate | | |
| | 29.9 | 23.8 | 132.2* | | 21.7 | 8.4 | 48.0* |
| | Parietal | | | | Parietal | | |
| | 23.9 | 17.8 | 118.7* | | 31.8 | 18.5 | 82.0* |
| | Occipital | | | | Occipital | | |
| | 29.9 | 23.8 | 132.2* | | 23.6 | 13.3 | 72.1* |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 3.5 | 12.8 | 9.3 | 114.1* | 10.8 | 8.0 | 2.8 | 29.8 |
| | Cingulate | | | | Cingulate | | |
| | 29.9 | 26.4 | 158.1* | | 21.7 | 10.9 | 67.1* |
| | Parietal | | | | Parietal | | |
| | 23.9 | 20.4 | 148.9* | | 31.8 | 21.0 | 98.6* |
| | Occipital | | | | Occipital | | |
| | 29.9 | 26.4 | 158.1* | | 23.6 | 12.8 | 74.4* |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 12.8 | 29.9 | 17.1 | 80.1* | 8.0 | 21.7 | 13.7 | 92.2* |
| | Parietal | | | | Parietal | | |
| | 23.9 | 11.1 | 60.5* | | 31.8 | 23.8 | 119.6* |
| | Occipital | | | | Occipital | | |
| | 29.9 | 17.1 | 80.1* | | 23.6 | 15.6 | 98.7* |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 29.9 | 23.9 | 6.0 | 22.3 | 21.7 | 31.8 | 10.1 | 37.8 |
| | Occipital | | | | Occipital | | |
| | 29.9 | 0 | 0 | | 23.6 | 1.9 | 8.4 |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 23.9 | 29.9 | 6.0 | 22.3 | 21.7 | 31.8 | 10.1 | 37.8 |

* = Asymmetric plaque counts between the regions.

**Table 50.** Interregional variation in the number of plaques/mm$^2$ in the superficial layers of SDAT Case 10.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 15.5 | 22.8 | 7.3 | 38.1 | 53.5 | 40.8 | 12.7 | 26.9 |
| | Mid Temp | | | | Mid Temp | | |
| | 32.3 | 16.8 | 70.3* | | 44.6 | 8.9 | 18.1 |
| | Inf Temp | | | | Inf Temp | | |
| | 37.0 | 21.5 | 81.9* | | 40.1 | 13.4 | 28.6 |
| | Cingulate | | | | Cingulate | | |
| | 12.7 | 2.8 | 19.8 | | 45.8 | 7.7 | 15.5 |
| | Parietal | | | | Parietal | | |
| | 32.6 | 17.1 | 71.1* | | 41.3 | 12.2 | 25.7 |
| | Occipital | | | | Occipital | | |
| | 26.3 | 10.8 | 51.7* | | 27.9 | 25.6 | 62.9* |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 22.8 | 32.3 | 9.5 | 34.5 | 40.8 | 44.6 | 3.8 | 8.9 |
| | Inf Temp | | | | Inf Temp | | |
| | 37.0 | 14.2 | 47.5* | | 40.1 | 0.7 | 1.7 |
| | Cingulate | | | | Cingulate | | |
| | 12.7 | 10.1 | 56.9* | | 45.8 | 5.0 | 11.5 |
| | Parietal | | | | Parietal | | |
| | 32.6 | 9.8 | 35.4 | | 41.3 | 0.5 | 1.2 |
| | Occipital | | | | Occipital | | |
| | 26.3 | 3.5 | 14.2 | | 27.9 | 12.9 | 37.6 |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 32.3 | 37.0 | 4.7 | 13.6 | 44.6 | 40.1 | 4.5 | 10.6 |
| | Cingulate | | | | Cingulate | | |
| | 12.7 | 19.6 | 87.1* | | 45.8 | 1.2 | 2.6 |
| | Parietal | | | | Parietal | | |
| | 32.6 | 0.3 | 0.9 | | 41.3 | 3.3 | 7.7 |
| | Occipital | | | | Occipital | | |
| | 26.3 | 6.0 | 20.5 | | 27.9 | 16.7 | 46.1* |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 37.0 | 12.7 | 24.3 | 97.8* | 40.1 | 45.8 | 5.7 | 13.3 |
| | Parietal | | | | Parietal | | |
| | 32.6 | 4.4 | 12.6 | | 41.3 | 1.2 | 2.9 |
| | Occipital | | | | Occipital | | |
| | 26.3 | 10.7 | 33.8 | | 27.9 | 12.2 | 34.8 |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 12.7 | 32.6 | 19.9 | 87.8* | 45.8 | 41.3 | 4.5 | 10.3 |
| | Occipital | | | | Occipital | | |
| | 26.3 | 13.6 | 69.7* | | 27.9 | 17.9 | 48.6* |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 32.6 | 26.3 | 6.3 | 21.4 | 41.3 | 27.9 | 13.4 | 38.7 |

* = Asymmetric plaque counts between the regions.

**Table 51.** Interregional variation in the number of plaques/mm$^2$ in the superficial layers of SDAT Case 11.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 17.4 | 27.0 | 9.6 | 43.2* | 17.4 | 13.0 | 4.4 | 28.9 |
| | Mid Temp | | | | Mid Temp | | |
| | 30.9 | 13.5 | 55.9* | | 23.2 | 5.8 | 28.6 |
| | Inf Temp | | | | Inf Temp | | |
| | 34.9 | 17.5 | 66.9* | | 38.0 | 10.6 | 38.3 |
| | Cingulate | | | | Cingulate | | |
| | 13.4 | 4.0 | 26.0 | | 8.8 | 8.6 | 65.6* |
| | Parietal | | | | Parietal | | |
| | 33.8 | 16.4 | 64.1* | | 18.9 | 1.5 | 8.3 |
| | Occipital | | | | Occipital | | |
| | 18.6 | 1.2 | 6.7 | | 14.5 | 2.9 | 18.2 |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 27.0 | 30.9 | 3.9 | 13.5 | 13.0 | 23.2 | 10.2 | 56.4* |
| | Inf Temp | | | | Inf Temp | | |
| | 34.9 | 7.9 | 25.5 | | 38.0 | 25.0 | 98.0* |
| | Cingulate | | | | Cingulate | | |
| | 13.4 | 13.6 | 67.3* | | 8.8 | 4.2 | 38.5 |
| | Parietal | | | | Parietal | | |
| | 33.8 | 6.8 | 22.4 | | 18.9 | 5.9 | 37.0 |
| | Occipital | | | | Occipital | | |
| | 18.6 | 8.4 | 36.8 | | 14.5 | 1.5 | 10.9 |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 30.9 | 34.9 | 4.0 | 12.2 | 23.2 | 38.0 | 14.8 | 48.4* |
| | Cingulate | | | | Cingulate | | |
| | 13.4 | 17.5 | 79.0* | | 8.8 | 14.4 | 90.0* |
| | Parietal | | | | Parietal | | |
| | 33.8 | 2.9 | 9.0 | | 18.9 | 4.3 | 20.4 |
| | Occipital | | | | Occipital | | |
| | 18.6 | 12.3 | 49.7* | | 14.5 | 8.7 | 46.2* |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 34.9 | 13.4 | 21.5 | 89.0* | 38.0 | 8.8 | 29.2 | 124.8* |
| | Parietal | | | | Parietal | | |
| | 33.8 | 1.1 | 3.2 | | 18.9 | 19.1 | 67.1* |
| | Occipital | | | | Occipital | | |
| | 18.6 | 16.3 | 60.9* | | 14.5 | 23.5 | 89.5* |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 13.4 | 33.8 | 20.4 | 86.4* | 8.8 | 18.9 | 10.1 | 72.9* |
| | Occipital | | | | Occipital | | |
| | 18.6 | 5.2 | 32.5 | | 14.5 | 5.7 | 48.9* |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 33.8 | 18.6 | 15.2 | 58.0* | 18.9 | 14.5 | 4.4 | 26.3 |

* = Asymmetric plaque counts between the regions

**Table 52.** Interregional variation in the number of plaques/mm$^2$ in the superficial layers of SDAT Case 12.

| **Left** | | Abs | % | **Right** | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 10.5 | 9.7 | 0.8 | 7.9 | 9.5 | 13.2 | 3.7 | 32.6 |
| | Mid Temp | | | | Mid Temp | | |
| | 14.4 | 3.9 | 31.3 | | 18.1 | 8.6 | 62.3* |
| | Inf Temp | | | | Inf Temp | | |
| | 26.1 | 15.6 | 85.2* | | 24.9 | 15.4 | 89.5* |
| | Cingulate | | | | Cingulate | | |
| | 15.8 | 5.3 | 40.3* | | 15.8 | 6.3 | 49.8* |
| | Parietal | | | | Parietal | | |
| | 23.4 | 12.9 | 76.1* | | 11.4 | 1.9 | 18.2 |
| | Occipital | | | | Occipital | | |
| | 13.2 | 2.7 | 22.8 | | 9.5 | 0 | 0 |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 9.7 | 14.4 | 4.7 | 39.9 | 13.2 | 18.1 | 4.9 | 31.3 |
| | Inf Temp | | | | Inf Temp | | |
| | 26.1 | 16.4 | 91.6* | | 24.9 | 11.7 | 61.4* |
| | Cingulate | | | | Cingulate | | |
| | 15.8 | 6.1 | 47.8* | | 15.8 | 2.6 | 17.9 |
| | Parietal | | | | Parietal | | |
| | 23.4 | 13.7 | 82.8* | | 11.4 | 1.8 | 14.6 |
| | Occipital | | | | Occipital | | |
| | 13.2 | 3.5 | 30.6 | | 9.5 | 3.7 | 32.6 |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 14.4 | 26.1 | 11.7 | 57.8* | | 24.9 | 6.8 | 31.6 |
| | Cingulate | | | | Cingulate | | |
| | 15.8 | 1.4 | 9.3 | | 15.8 | 2.3 | 13.6 |
| | Parietal | | | | Parietal | | |
| | 23.4 | 9.0 | 47.6* | | 11.4 | 6.7 | 45.4* |
| | Occipital | | | | Occipital | | |
| | 13.2 | 1.2 | 8.7 | | 9.5 | 8.6 | 62.3* |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 26.1 | 15.8 | 10.3 | 49.2* | 24.9 | 15.8 | 9.1 | 44.7* |
| | Parietal | | | | Parietal | | |
| | 23.4 | 2.7 | 10.9 | | 11.4 | 13.5 | 74.4* |
| | Occipital | | | | Occipital | | |
| | 13.2 | 12.9 | 65.6* | | 9.5 | 15.4 | 89.5* |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 15.8 | 23.4 | 7.6 | 38.8 | 15.8 | 11.4 | 4.4 | 32.4 |
| | Occipital | | | | Occipital | | |
| | 13.2 | 2.6 | 17.9 | | 9.5 | 6.3 | 49.8* |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 23.4 | 13.2 | 10.2 | 55.7* | 11.4 | 9.5 | 1.9 | 18.2 |

* = Asymmetric plaque counts between the regions.

**Table 53.** Interregional variation in the number of plaques/mm$^2$ in the superficial layers of SDAT Case 13.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 20.7 | 23.9 | 3.2 | 14.3 | 37.2 | 34.8 | 2.4 | 6.3 |
| | Mid Temp | | | | Mid Temp | | |
| | 21.2 | 0.5 | 2.4 | | 43.1 | 5.9 | 14.7 |
| | Inf Temp | | | | Inf Temp | | |
| | 19.7 | 1.0 | 5.0 | | 31.2 | 6.0 | 17.5 |
| | Cingulate | | | | Cingulate | | |
| | 20.5 | 0.2 | 1.0 | | 30.2 | 7.0 | 20.8 |
| | Parietal | | | | Parietal | | |
| | 20.0 | 0.7 | 3.4 | | 23.7 | 13.5 | 44.3* |
| | Occipital | | | | Occipital | | |
| | 8.0 | 12.7 | 88.5* | | 23.7 | 13.5 | 44.3* |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 23.9 | 21.2 | 2.7 | 12.0 | 34.8 | 43.1 | 8.3 | 21.3 |
| | Inf Temp | | | | Inf Temp | | |
| | 19.7 | 4.2 | 19.3 | | 31.2 | 3.6 | 10.9 |
| | Cingulate | | | | Cingulate | | |
| | 20.5 | 3.4 | 15.3 | | 30.2 | 4.6 | 14.2 |
| | Parietal | | | | Parietal | | |
| | 20.0 | 3.9 | 17.8 | | 23.7 | 11.1 | 37.9 |
| | Occipital | | | | Occipital | | |
| | 8.0 | 15.9 | 99.7* | | 23.7 | 11.1 | 37.9 |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 21.2 | 19.7 | 1.5 | 7.3 | 43.1 | 31.2 | 11.9 | 32.0 |
| | Cingulate | | | | Cingulate | | |
| | 20.5 | 0.7 | 3.4 | | 30.2 | 12.9 | 35.2 |
| | Parietal | | | | Parietal | | |
| | 20.0 | 1.2 | 5.8 | | 23.7 | 19.4 | 58.1* |
| | Occipital | | | | Occipital | | |
| | 8.0 | 13.2 | 90.4* | | 23.7 | 19.4 | 58.1* |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 19.7 | 20.5 | 0.8 | 4.0 | 31.2 | 30.2 | 1.0 | 3.2 |
| | Parietal | | | | Parietal | | |
| | 20.0 | 0.3 | 1.5 | | 23.7 | 7.5 | 27.3 |
| | Occipital | | | | Occipital | | |
| | 8.0 | 11.7 | 84.5* | | 23.7 | 7.5 | 27.3 |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 20.5 | 20.0 | 0.5 | 2.5 | 30.2 | 23.7 | 6.5 | 24.1 |
| | Occipital | | | | Occipital | | |
| | 8.0 | 12.5 | 87.7* | | 23.7 | 6.5 | 24.1 |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 20.0 | 8.0 | 12.0 | 85.7* | 23.7 | 23.7 | 0 | 0 |

* = Asymmetric plaque counts between the regions.

**Table 54.** Interregional variation in the number of plaques/mm$^2$ in the deep layers of SDAT Case 8.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 15.4 | 3.5 | 11.9 | 125.9* | 11.4 | 12.2 | 0.8 | 6.8 |
| | Mid Temp | | | | Mid Temp | | |
| | 7.9 | 7.5 | 64.4* | | 8.9 | 2.5 | 24.6 |
| | Inf Temp | | | | Inf Temp | | |
| | 7.5 | 7.9 | 69.0* | | 8.3 | 3.1 | 31.5 |
| | Cingulate | | | | Cingulate | | |
| | 11.2 | 4.2 | 31.6 | | 7.7 | 3.7 | 38.7 |
| | Parietal | | | | Parietal | | |
| | 9.2 | 6.2 | 50.4* | | 19.3 | 7.9 | 51.5* |
| | Occipital | | | | Occipital | | |
| | 13.9 | 1.5 | 10.2 | | 8.7 | 2.7 | 26.9 |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 3.5 | 7.9 | 4.4 | 77.2 | 12.2 | 8.9 | 3.3 | 31.3 |
| | Inf Temp | | | | Inf Temp | | |
| | 7.5 | 4.0 | 72.7 | | 8.3 | 3.9 | 38.0 |
| | Cingulate | | | | Cingulate | | |
| | 11.2 | 7.7 | 104.8* | | 7.7 | 4.5 | 45.2 |
| | Parietal | | | | Parietal | | |
| | 9.2 | 5.7 | 89.8* | | 19.3 | 7.1 | 45.1* |
| | Occipital | | | | Occipital | | |
| | 13.9 | 10.4 | 119.5* | | 8.7 | 3.5 | 33.5 |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 7.9 | 7.5 | 0.4 | 5.2 | 8.9 | 8.3 | 0.6 | 7.0 |
| | Cingulate | | | | Cingulate | | |
| | 11.2 | 3.3 | 34.6 | | 7.7 | 1.2 | 14.4 |
| | Parietal | | | | Parietal | | |
| | 9.2 | 1.3 | 15.2 | | 19.3 | 10.4 | 73.8* |
| | Occipital | | | | Occipital | | |
| | 13.9 | 6.0 | 55.0* | | 8.7 | 0.2 | 2.3 |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 7.5 | 11.2 | 3.7 | 39.6 | 8.3 | 7.7 | 0.6 | 7.5 |
| | Parietal | | | | Parietal | | |
| | 9.2 | 1.7 | 20.4 | | 19.3 | 11.0 | 79.7* |
| | Occipital | | | | Occipital | | |
| | 13.9 | 6.4 | 59.8* | | 8.7 | 0.4 | 4.7 |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 11.2 | 9.2 | 2.0 | 19.6 | 7.7 | 19.3 | 11.6 | 85.9* |
| | Occipital | | | | Occipital | | |
| | 13.9 | 2.7 | 21.5 | | 8.7 | 1.0 | 12.2 |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 9.2 | 13.9 | 4.7 | 40.7 | 19.3 | 8.7 | 10.6 | 75.7* |

* = Asymmetric plaque counts between the regions.

**Table 55.** Interregional variation in the number of plaques/mm$^2$ in the deep layers of SDAT Case 9.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 10.8 | 2.8 | 8.0 | 117.6* | 3.8 | 5.8 | 2.0 | 41.7 |
| | Mid Temp | | | | Mid Temp | | |
| | 1.2 | 9.6 | 160.0* | | 5.1 | 1.3 | 29.2 |
| | Inf Temp | | | | Inf Temp | | |
| | 2.1 | 8.7 | 134.9* | | 4.2 | 0.4 | 10.0 |
| | Cingulate | | | | Cingulate | | |
| | 12.8 | 2.0 | 16.9 | | 5.4 | 1.6 | 34.8 |
| | Parietal | | | | Parietal | | |
| | 14.0 | 3.2 | 25.8 | | 7.0 | 3.2 | 59.2 |
| | Occipital | | | | Occipital | | |
| | 11.9 | 1.1 | 9.7 | | 3.2 | 0.6 | 17.1 |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 2.8 | 1.2 | 1.6 | 80.0 | 5.8 | 5.1 | 0.7 | 54.5 |
| | Inf Temp | | | | Inf Temp | | |
| | 2.1 | 0.7 | 28.6 | | 4.2 | 1.6 | 32.0 |
| | Cingulate | | | | Cingulate | | |
| | 12.8 | 10.0 | 82.2* | | 5.4 | 0.4 | 7.1 |
| | Parietal | | | | Parietal | | |
| | 14.0 | 11.2 | 133.3* | | 7.0 | 1.2 | 18.8 |
| | Occipital | | | | Occipital | | |
| | 11.9 | 9.1 | 123.8* | | 3.2 | 2.6 | 57.8 |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 1.2 | 2.1 | 0.9 | 54.5 | 5.1 | 4.2 | 0.9 | 19.4 |
| | Cingulate | | | | Cingulate | | |
| | 12.8 | 11.6 | 165.7* | | 5.4 | 0.3 | 5.7 |
| | Parietal | | | | Parietal | | |
| | 14.0 | 12.8 | 168.4* | | 7.0 | 1.9 | 31.4 |
| | Occipital | | | | Occipital | | |
| | 11.9 | 10.7 | 163.4* | | 3.2 | 1.9 | 45.8 |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 2.1 | 12.8 | 10.7 | 143.6* | 4.2 | 5.4 | 1.2 | 25.0 |
| | Parietal | | | | Parietal | | |
| | 14.0 | 11.9 | 147.8* | | 7.0 | 2.8 | 50.0 |
| | Occipital | | | | Occipital | | |
| | 11.9 | 9.8 | 140.0* | | 3.2 | 1.0 | 27.0 |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 12.8 | 14.0 | 1.2 | 9.0 | 5.4 | 7.0 | 1.6 | 25.4 |
| | Occipital | | | | Occipital | | |
| | 11.9 | 0.9 | 7.3 | | 3.2 | 2.2 | 51.2 |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 14.0 | 11.9 | 2.1 | 16.2 | 7.0 | 3.2 | 3.8 | 74.5 |

* = Asymmetric plaque counts between the regions.

**Table 56.** Interregional variation in the number of plaques/mm$^2$ in the deep layers of SDAT Case 10.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 3.8 | 5.1 | 1.3 | 29.2 | 38.0 | 21.8 | 16.2 | 54.2* |
| | Mid Temp | | | | Mid Temp | | |
| | 5.8 | 2.0 | 41.7 | | 25.6 | 12.4 | 39.0 |
| | Inf Temp | | | | Inf Temp | | |
| | 10.5 | 6.7 | 93.7* | | 28.4 | 9.6 | 28.9 |
| | Cingulate | | | | Cingulate | | |
| | 1.4 | 2.4 | 92.3 | | 20.9 | 17.1 | 58.1* |
| | Parietal | | | | Parietal | | |
| | 12.7 | 8.9 | 107.9* | | 27.2 | 10.8 | 33.1 |
| | Occipital | | | | Occipital | | |
| | 10.5 | 6.7 | 93.7* | | 8.2 | 29.8 | 129.0* |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 5.1 | 5.8 | 0.7 | 12.8 | 21.8 | 25.6 | 3.8 | 16.0 |
| | Inf Temp | | | | Inf Temp | | |
| | 10.5 | 5.4 | 69.2* | | 28.4 | 6.6 | 26.3 |
| | Cingulate | | | | Cingulate | | |
| | 1.4 | 3.7 | 113.8 | | 20.9 | 0.9 | 4.2 |
| | Parietal | | | | Parietal | | |
| | 12.7 | 7.6 | 85.4* | | 27.2 | 5.4 | 22.0 |
| | Occipital | | | | Occipital | | |
| | 10.5 | 5.4 | 69.2* | | 8.2 | 13.6 | 90.7* |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 5.8 | 10.5 | 4.7 | 57.7 | 25.6 | 28.4 | 2.8 | 10.4 |
| | Cingulate | | | | Cingulate | | |
| | 1.4 | 4.4 | 122.2 | | 20.9 | 4.7 | 20.2 |
| | Parietal | | | | Parietal | | |
| | 12.7 | 6.9 | 74.6* | | 27.2 | 1.6 | 6.1 |
| | Occipital | | | | Occipital | | |
| | 10.5 | 4.7 | 57.7 | | 8.2 | 17.4 | 103.0* |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 10.5 | 1.4 | 9.1 | 152.9* | 28.4 | 20.9 | 7.5 | 30.4 |
| | Parietal | | | | Parietal | | |
| | 12.7 | 2.2 | 19.0 | | 27.2 | 12 | 4.3 |
| | Occipital | | | | Occipital | | |
| | 10.5 | 0 | 0 | | 8.2 | 20.2 | 110.4* |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 1.4 | 12.7 | 11.3 | 160.3* | 20.9 | 27.2 | 6.3 | 26.2 |
| | Occipital | | | | Occipital | | |
| | 10.5 | 9.1 | 152.9* | | 8.2 | 12.7 | 87.3* |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 12.7 | 10.5 | 2.2 | 19.0 | 27.2 | 8.2 | 19.0 | 107.3* |

* = Asymmetric plaque counts between the regions.

**Table 57.** Interregional variation in the number of plaques/mm$^2$ in the deep layers of SDAT Case 11.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 18.9 | 13.1 | 5.8 | 36.2 | 4.6 | 1.8 | 2.8 | 87.5 |
| | Mid Temp | | | | Mid Temp | | |
| | 20.8 | 1.9 | 9.6 | | 4.6 | 0 | 0 |
| | Inf Temp | | | | Inf Temp | | |
| | 22.6 | 3.7 | 17.8 | | 18.6 | 14.0 | 120.7* |
| | Cingulate | | | | Cingulate | | |
| | 12.7 | 6.2 | 39.2 | | 4.4 | 0.2 | 4.4 |
| | Parietal | | | | Parietal | | |
| | 14.9 | 4.0 | 23.7 | | 11.6 | 7.0 | 86.4* |
| | Occipital | | | | Occipital | | |
| | 4.8 | 14.1 | 119.0* | | 8.1 | 3.5 | 55.1 |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 13.1 | 20.8 | 7.7 | 45.4* | 1.8 | 4.6 | 2.8 | 87.5 |
| | Inf Temp | | | | Inf Temp | | |
| | 22.6 | 9.5 | 53.2* | | 18.6 | 16.8 | 164.7* |
| | Cingulate | | | | Cingulate | | |
| | 12 7 | 0.4 | 3.1 | | 4.4 | 2.6 | 83.9 |
| | Parietal | | | | Parietal | | |
| | 14.9 | 1.8 | 12.8 | | 11.6 | 9.8 | 146.3* |
| | Occipital | | | | Occipital | | |
| | 4.8 | 8.3 | 92.7* | | 8.1 | 6.3 | 127.3* |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 20.8 | 22.6 | 1.8 | 8.3 | 4.6 | 18.6 | 14.0 | 120.7* |
| | Cingulate | | | | Cingulate | | |
| | 12.7 | 8.1 | 48.4* | | 4.4 | 0.2 | 4.4 |
| | Parietal | | | | Parietal | | |
| | 14.9 | 5.9 | 33.0 | | 11.6 | 7.0 | 86.4* |
| | Occipital | | | | Occipital | | |
| | 4.8 | 16.0 | 125.0* | | 8.1 | 3.5 | 55.1 |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 22.6 | 12.7 | 9.9 | 56.1* | 18.6 | 4.4 | 14.2 | 123.5* |
| | Parietal | | | | Parietal | | |
| | 14.9 | 7.7 | 41.1* | | 11.6 | 7.0 | 46.4* |
| | Occipital | | | | Occipital | | |
| | 4.8 | 17.8 | 129.9* | | 8.1 | 10.5 | 78.6* |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 12.7 | 14.9 | 2.2 | 15.9 | 4.4 | 11.6 | 7.2 | 90.0* |
| | Occipital | | | | Occipital | | |
| | 4.8 | 7.9 | 90.3* | | 8.1 | 3.7 | 59.2 |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 14.9 | 4.8 | 10.1 | 102.5* | 11.6 | 8.1 | 3.5 | 35.5 |

* = Asymmetric plaque counts between the regions.

**Table 58.** Interregional variation in the number of plaques/mm$^2$ in the deep layers of SDAT Case 12.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 2.0 | 2.4 | 0.4 | 18.2 | 6.8 | 6.1 | 0.7 | 10.8 |
| | Mid Temp | | | | Mid Temp | | |
| | 4.1 | 2.1 | 68.8 | | 9.5 | 2.7 | 33.1 |
| | Inf Temp | | | | Inf Temp | | |
| | 12.9 | 10.9 | 146.3* | | 10.8 | 4.0 | 45.4 |
| | Cingulate | | | | Cingulate | | |
| | 3.4 | 1.4 | 51.8 | | 6.1 | 0.7 | 10.8 |
| | Parietal | | | | Parietal | | |
| | 9.3 | 7.3 | 129.2* | | 3.6 | 3.2 | 61.5 |
| | Occipital | | | | Occipital | | |
| | 1.7 | 0.3 | 16.2 | | 4.6 | 2.2 | 38.6 |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 2.4 | 4.1 | 1.7 | 52.3 | 6.1 | 9.5 | 3.4 | 43.6 |
| | Inf Temp | | | | Inf Temp | | |
| | 12.9 | 10.5 | 137.2* | | 10.8 | 4.7 | 55.6 |
| | Cingulate | | | | Cingulate | | |
| | 3.4 | 1.0 | 34.5 | | 6.1 | 0 | 0 |
| | Parietal | | | | Parietal | | |
| | 9.3 | 6.9 | 117.9* | | 3.6 | 2.5 | 51.5 |
| | Occipital | | | | Occipital | | |
| | 1.7 | 0.7 | 34.1 | | 4.6 | 1.5 | 28.0 |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 4.1 | 12.9 | 8.8 | 103.5* | 9.5 | 10.8 | 1.3 | 128.1 |
| | Cingulate | | | | Cingulate | | |
| | 3.4 | 0.7 | 18.7 | | 6.1 | 3.4 | 43.6 |
| | Parietal | | | | Parietal | | |
| | 9.3 | 5.2 | 77.6* | | 3.6 | 5.9 | 90.1* |
| | Occipital | | | | Occipital | | |
| | 1.7 | 2.4 | 82.8 | | 4.6 | 4.9 | 69.5 |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 12.9 | 3.4 | 9.5 | 116.6* | 10.8 | 6.1 | 4.7 | 55.6 |
| | Parietal | | | | Parietal | | |
| | 9.3 | 3.6 | 32.4 | | 3.6 | 7.2 | 100.0* |
| | Occipital | | | | Occipital | | |
| | 1.7 | 11.2 | 153.4* | | 4.6 | 6.2 | 80.5* |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 3.4 | 8.3 | 5.9 | 92.9* | 6.1 | 3.6 | 2.5 | 51.5 |
| | Occipital | | | | Occipital | | |
| | 1.7 | 1.7 | 66.7 | | 4.6 | 1.5 | 28.0 |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 9.3 | 1.7 | 7.6 | 138.2* | 3.6 | 4.6 | 1.0 | 24.4 |

* = Asymmetric plaque counts between the regions.

**Table 59.** Interregional variation in the number of plaques/mm$^2$ in the deep layers of SDAT Case 13.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 3.9 | 9.3 | 5.4 | 81.8* | 9.3 | 10.8 | 1.5 | 14.9 |
| | Mid Temp | | | | Mid Temp | | |
| | 9.7 | 5.8 | 85.3* | | 21.4 | 12.1 | 78.8* |
| | Inf Temp | | | | Inf Temp | | |
| | 6.6 | 2.7 | 51.4 | | 12.9 | 3.6 | 32.4 |
| | Cingulate | | | | Cingulate | | |
| | 2.7 | 1.2 | 36.4 | | 10.5 | 1.2 | 12.1 |
| | Parietal | | | | Parietal | | |
| | 1.7 | 2.2 | 78.6 | | 3.6 | 5.7 | 88.4* |
| | Occipital | | | | Occipital | | |
| | 0 | 3.9 | 200.0 | | 0.5 | 8.8 | 179.6* |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 9.3 | 9.7 | 0.4 | 4.2 | 10.8 | 21.4 | 10.6 | 65.8* |
| | Inf Temp | | | | Inf Temp | | |
| | 6.6 | 2.7 | 34.0 | | 12.9 | 2.1 | 17.7 |
| | Cingulate | | | | Cingulate | | |
| | 2.7 | 6.6 | 110.0* | | 10.5 | 0.3 | 2.8 |
| | Parietal | | | | Parietal | | |
| | 1.7 | 7.6 | 138.2* | | 3.6 | 7.2 | 100.0* |
| | Occipital | | | | Occipital | | |
| | 0 | 9.3 | 200.0* | | 0.5 | 10.3 | 182.3* |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 9.7 | 6.6 | 3.1 | 38.0 | 21.4 | 12.9 | 8.5 | 49.6* |
| | Cingulate | | | | Cingulate | | |
| | 2.7 | 7.0 | 112.9* | | 10.5 | 10.9 | 68.3* |
| | Parietal | | | | Parietal | | |
| | 1.7 | 8.0 | 140.4* | | 3.6 | 17.8 | 142.4* |
| | Occipital | | | | Occipital | | |
| | 0 | 9.7 | 200.0* | | 0.5 | 20.9 | 190.9* |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 6.6 | 2.7 | 3.9 | 83.9 | 12.9 | 10.5 | 2.4 | 20.5 |
| | Parietal | | | | Parietal | | |
| | 1.7 | 4.9 | 118.1 | | 3.6 | 9.3 | 112.7* |
| | Occipital | | | | Occipital | | |
| | 0 | 6.6 | 200.0* | | 0.5 | 12.4 | 185.1* |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 2.7 | 1.7 | 1.0 | 45.4 | 10.5 | 3.6 | 6.9 | 97.9* |
| | Occipital | | | | Occipital | | |
| | 0 | 2.7 | 200.0 | | 0.5 | 10.0 | 181.8* |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 1.7 | 0 | 1.7 | 200.0 | 3.6 | 0.5 | 3.1 | 151.2 |

* = Asymmetric plaque counts betweem the regions.

**Table 60.** Interregional variation in the total number of plaque/mm$^2$ in SDAT Case 8.

| **Left** | | Abs | % | **Right** | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 22.1 | 8.8 | 13.3 | 86.1* | 20.0 | 18.6 | 1.4 | 7.2 |
| | Mid Temp | | | | Mid Temp | | |
| | 14.0 | 8.1 | 44.9* | | 13.4 | 6.6 | 39.5 |
| | Inf Temp | | | | Inf Temp | | |
| | 15.4 | 6.7 | 35.7 | | 14.0 | 6.0 | 35.3 |
| | Cingulate | | | | Cingulate | | |
| | 19.3 | 2.8 | 13.5 | | 12.6 | 7.4 | 45.4* |
| | Parietal | | | | Parietal | | |
| | 15.5 | 6.6 | 35.1 | | 32.0 | 12.0 | 46.2* |
| | Occipital | | | | Occipital | | |
| | 20.0 | 2.1 | 10.0 | | 13.6 | 6.4 | 38.1 |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 8.8 | 14.0 | 5.2 | 45.6* | 18.6 | 13.4 | 5.2 | 32.5 |
| | Inf Temp | | | | Inf Temp | | |
| | 15.4 | 6.6 | 54.5* | | 14.0 | 4.6 | 28.2 |
| | Cingulate | | | | Cingulate | | |
| | 19.3 | 10.5 | 74.7* | | 12.6 | 6.0 | 38.5 |
| | Parietal | | | | Parietal | | |
| | 15.5 | 6.7 | 55.1* | | 32.0 | 13.4 | 53.0* |
| | Occipital | | | | Occipital | | |
| | 20.0 | 11.2 | 77.8* | | 13.6 | 5.0 | 31.0 |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 14.0 | 15.4 | 1.4 | 9.5 | 13.4 | 14.0 | 0.6 | 4.4 |
| | Cingulate | | | | Cingulate | | |
| | 19.3 | 5.3 | 31.8 | | 12.6 | 0.8 | 6.2 |
| | Parietal | | | | Parietal | | |
| | 15.5 | 1.5 | 10.2 | | 32.0 | 18.6 | 81.9* |
| | Occipital | | | | Occipital | | |
| | 20.0 | 6.0 | 35.3 | | 13.6 | 0.2 | 1.5 |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 15.4 | 19.3 | 3.9 | 22.5 | 14.0 | 12.6 | 1.4 | 10.5 |
| | Parietal | | | | Parietal | | |
| | 15.5 | 0.1 | 0.6 | | 32.0 | 18.0 | 78.3* |
| | Occipital | | | | Occipital | | |
| | 20.0 | 4.6 | 26.0 | | 13.6 | 0.4 | 2.9 |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 19.3 | 15.5 | 3.8 | 21.8 | 12.6 | 32.0 | 19.4 | 87.0* |
| | Occipital | | | | Occipital | | |
| | 20.0 | 0.7 | 3.6 | | 13.6 | 1.0 | 7.6 |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 15.5 | 20.0 | 0.5 | 2.8 | 32.0 | 13.6 | 18.4 | 80.7* |

* = Asymmetric plaque counts between the regions.

**Table 61.** Interregional variation in the total number of plaques/$mm^2$ in SDAT Case 9.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 19.1 | 4.4 | 14.7 | 125.1* | 10.3 | 9.6 | 0.7 | 7.0 |
| | Mid Temp | | | | Mid Temp | | |
| | 4.4 | 14.7 | 125.1* | | 8.0 | 2.3 | 25.1 |
| | Inf Temp | | | | Inf Temp | | |
| | 7.4 | 11.7 | 88.3* | | 6.1 | 4.2 | 51.2 |
| | Cingulate | | | | Cingulate | | |
| | 21.4 | 2.3 | 11.4 | | 13.6 | 3.3 | 27.6 |
| | Parietal | | | | Parietal | | |
| | 19.0 | 0.1 | 0.5 | | 16.2 | 5.9 | 44.5* |
| | Occipital | | | | Occipital | | |
| | 20.9 | 1.8 | 9.0 | | 13.4 | 3.1 | 26.2 |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 4.4 | 4.4 | 0 | 0 | 9.6 | 8.0 | 1.6 | 18.2 |
| | Inf Temp | | | | Inf Temp | | |
| | 7.4 | 3.0 | 50.8 | | 6.1 | 3.5 | 44.6 |
| | Cingulate | | | | Cingulate | | |
| | 21.4 | 17.0 | 131.8* | | 13.6 | 4.0 | 34.5 |
| | Parietal | | | | Parietal | | |
| | 19.0 | 14.6 | 124.8* | | 16.2 | 6.6 | 51.2* |
| | Occipital | | | | Occipital | | |
| | 20.9 | 16.5 | 130.4* | | 13.4 | 3.8 | 33.0 |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 4.4 | 7.4 | 3.0 | 50.8 | 8.0 | 6.1 | 1.9 | 27.0 |
| | Cingulate | | | | Cingulate | | |
| | 21.4 | 17.0 | 131.8* | | 13.6 | 5.6 | 51.8* |
| | Parietal | | | | Parietal | | |
| | 19.0 | 14.6 | 124.8* | | 16.2 | 8.2 | 67.8* |
| | Occipital | | | | Occipital | | |
| | 20.9 | 16.5 | 130.4* | | 13.4 | 5.4 | 50.5* |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 7.4 | 21.4 | 14.0 | 97.2* | 6.1 | 13.6 | 7.5 | 76.1* |
| | Parietal | | | | Parietal | | |
| | 19.0 | 11.6 | 87.9* | | 16.2 | 10.1 | 90.6* |
| | Occipital | | | | Occipital | | |
| | 20.9 | 13.5 | 95.4* | | 13.4 | 7.3 | 74.9* |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 21.4 | 19.0 | 2.4 | 11.9 | 13.6 | 16.2 | 2.6 | 17.4 |
| | Occipital | | | | Occipital | | |
| | 20.9 | 0.5 | 2.4 | | 13.4 | 0.2 | 1.5 |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 19.0 | 20.9 | 1.9 | 9.5 | 16.2 | 13.4 | 2.8 | 18.9 |

* = Asymmetric plaque counts between the regions

**Table 62.** Interregional variation in the total number of plaques/mm$^2$ in SDAT Case 10.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 9.6 | 14.0 | 4.4 | 37.3 | 45.8 | 31.3 | 14.5 | 37.6 |
| | Mid Temp | | | | Mid Temp | | |
| | 19.0 | 9.4 | 65.7* | | 35.1 | 10.7 | 26.4 |
| | Inf Temp | | | | Inf Temp | | |
| | 23.8 | 14.2 | 85.0* | | 34.2 | 11.6 | 29.0 |
| | Cingulate | | | | Cingulate | | |
| | 7.0 | 2.6 | 31.3 | | 33.4 | 12.4 | 31.3 |
| | Parietal | | | | Parietal | | |
| | 22.6 | 13.0 | 80.7* | | 34.2 | 11.6 | 29.0 |
| | Occipital | | | | Occipital | | |
| | 18.4 | 8.8 | 62.8* | | 18.0 | 27.8 | 87.1* |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 14.0 | 19.0 | 5.0 | 30.3 | 31.3 | 35.1 | 3.8 | 11.4 |
| | Inf Temp | | | | Inf Temp | | |
| | 23.8 | 9.8 | 51.8* | | 34.2 | 2.9 | 8.8 |
| | Cingulate | | | | Cingulate | | |
| | 7.0 | 7.0 | 66.7* | | 33.4 | 2.1 | 6.5 |
| | Parietal | | | | Parietal | | |
| | 22.6 | 8.6 | 47.0* | | 34.2 | 2.9 | 8.8 |
| | Occipital | | | | Occipital | | |
| | 18.4 | 4.4 | 27.2 | | 18.0 | 13.3 | 54.0* |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 19.0 | 23.8 | 4.8 | 22.4 | 35.1 | 34.2 | 0.9 | 2.6 |
| | Cingulate | | | | Cigulate | | |
| | 7.0 | 12.0 | 92.3* | | 33.4 | 1.7 | 5.0 |
| | Parietal | | | | Parietal | | |
| | 22.6 | 3.6 | 17.3 | | 34.2 | 0.9 | 2.6 |
| | Occipital | | | | Occipital | | |
| | 18.4 | 0.6 | 3.2 | | 18.0 | 17.1 | 64.4* |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 23.8 | 7.0 | 16.8 | 109.1* | 34.2 | 33.4 | 0.8 | 2.4 |
| | Parietal | | | | Parietal | | |
| | 22.6 | 1.2 | 5.2 | | 34.2 | 0 | 0 |
| | Occipital | | | | Occipital | | |
| | 18.4 | 5.4 | 25.6 | | 18.0 | 16.2 | 62.1* |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 7.0 | 22.6 | 15.6 | 105.4* | 33.4 | 34.2 | 0.8 | 2.4 |
| | Occipital | | | | Occipital | | |
| | 18.4 | 11.4 | 89.8* | | 18.0 | 15.4 | 59.9* |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 22.6 | 18.4 | 4.2 | 20.5 | 34.2 | 18.0 | 16.2 | 62.1* |

* = Asymmetric plaque counts between the regions.

**Table 63.** Interregional variation in the total number of plaques/mm$^2$ in SDAT Case 11.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 18.2 | 20.0 | 1.8 | 9.4 | 11.0 | 7.4 | 3.6 | 39.1 |
| | Mid Temp | | | | Mid Temp | | |
| | 25.8 | 7.6 | 34.5 | | 13.9 | 2.9 | 23.3 |
| | Inf Temp | | | | Inf Temp | | |
| | 28.8 | 10.6 | 45.1* | | 28.3 | 17.3 | 88.0* |
| | Cingulate | | | | Cingulate | | |
| | 13.0 | 5.2 | 33.3 | | 6.6 | 4.4 | 50.0 |
| | Parietal | | | | Parietal | | |
| | 24.4 | 6.2 | 29.1 | | 15.2 | 4.2 | 32.1 |
| | Occipital | | | | Occipital | | |
| | 11.7 | 6.5 | 43.5* | | 11.3 | 0.3 | 2.7 |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 20.0 | 25.8 | 5.8 | 25.3 | 7.4 | 13.9 | 6.5 | 61.0* |
| | Inf Temp | | | | Inf Temp | | |
| | 28.8 | 8.8 | 36.1 | | 28.3 | 20.9 | 117.1* |
| | Cingulate | | | | Cingulate | | |
| | 13.0 | 7.0 | 42.4* | | 6.6 | 0.8 | 11.4 |
| | Parietal | | | | Parietal | | |
| | 24.4 | 4.4 | 19.8 | | 15.2 | 7.8 | 69.0* |
| | Occipital | | | | Occipital | | |
| | 11.7 | 8.3 | 52.4* | | 11.3 | 3.9 | 41.7 |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 25.8 | 28.8 | 3.0 | 11.0 | 13.9 | 28.3 | 14.4 | 68.2* |
| | Cingulate | | | | Cingulate | | |
| | 13.0 | 12.8 | 66.0* | | 6.6 | 7.3 | 71.2* |
| | Parietal | | | | Parietal | | |
| | 24.4 | 1.4 | 5.6 | | 15.2 | 1.3 | 8.9 |
| | Occipital | | | | Occipital | | |
| | 11.7 | 14.1 | 75.2* | | 11.3 | 2.6 | 20.6 |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 28.8 | 13.0 | 15.8 | 75.6* | 28.3 | 6.6 | 21.7 | 124.4* |
| | Parietal | | | | Parietal | | |
| | 24.4 | 4.4 | 16.5 | | 15.2 | 13.1 | 60.2* |
| | Occipital | | | | Occipital | | |
| | 11.7 | 17.1 | 84.4* | | 11.3 | 17.0 | 85.8* |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 13.0 | 24.4 | 11.4 | 61.0* | 6.6 | 15.2 | 8.6 | 78.9* |
| | Occipital | | | | Occipital | | |
| | 11.7 | 1.3 | 10.5 | | 11.3 | 4.7 | 52.5 |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 24.4 | 11.7 | 12.7 | 70.4* | 15.2 | 11.3 | 3.9 | 29.4 |

* = Asymmetric plaque counts between the regions.

**Table 64.** Interregional variation in the total number of plaques/mm$^2$ in SDAT Case 12.

| **Left** | | Abs | % | **Right** | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 6.2 | 6.0 | 0.2 | 3.3 | 8.2 | 9.6 | 1.4 | 15.7 |
| | Mid Temp | | | | Mid Temp | | |
| | 9.2 | 3.0 | 39.0 | | 13.8 | 5.6 | 50.9* |
| | Inf Temp | | | | Inf Temp | | |
| | 19.5 | 13.3 | 103.5* | | 17.8 | 9.6 | 73.8* |
| | Cingulate | | | | Cingulate | | |
| | 9.6 | 3.4 | 43.0 | | 11.0 | 2.8 | 29.2 |
| | Parietal | | | | Parietal | | |
| | 16.4 | 10.2 | 90.3* | | 7.5 | 0.7 | 8.9 |
| | Occipital | | | | Occipital | | |
| | 7.4 | 1.2 | 17.6 | | 7.0 | 1.2 | 1.6 |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 6.0 | 9.2 | 3.2 | 42.1 | 9.6 | 13.8 | 4.2 | 35.9 |
| | Inf Temp | | | | Inf Temp | | |
| | 19.5 | 13.5 | 105.9* | | 17.8 | 8.2 | 59.8* |
| | Cingulate | | | | Cingulate | | |
| | 9.6 | 3.6 | 46.2 | | 11.0 | 1.4 | 13.6 |
| | Parietal | | | | Parietal | | |
| | 16.4 | 10.4 | 92.8* | | 7.5 | 2.1 | 2.4 |
| | Occipital | | | | Occipital | | |
| | 7.4 | 1.4 | 20.9 | | 7.0 | 2.6 | 31.3 |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 9.2 | 19.5 | 10.3 | 71.8* | 13.8 | 17.8 | 4.0 | 25.3 |
| | Cingulate | | | | Cingulate | | |
| | 9.6 | 0.4 | 4.2 | | 11.0 | 2.8 | 22.6 |
| | Parietal | | | | Parietal | | |
| | 16.4 | 7.2 | 56.2* | | 7.5 | 6.3 | 59.2* |
| | Occipital | | | | Occipital | | |
| | 7.4 | 1.8 | 21.7 | | 7.0 | 6.8 | 65.4* |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 19.5 | 9.6 | 9.9 | 68.0* | 17.8 | 11.0 | 6.8 | 47.2* |
| | Parietal | | | | Parietal | | |
| | 16.4 | 3.1 | 17.3 | | 7.5 | 10.3 | 81.4* |
| | Occipital | | | | Occipital | | |
| | 7.4 | 12.1 | 90.0* | | 7.0 | 10.8 | 87.1* |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 9.6 | 16.4 | 6.8 | 52.3* | 11.0 | 7.5 | 3.5 | 37.8 |
| | Occipital | | | | Occipital | | |
| | 7.4 | 2.2 | 25.9 | | 7.0 | 4.0 | 44.4 |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 16.4 | 7.4 | 9.0 | 75.6* | 7.5 | 7.0 | 0.5 | 6.9 |

* = Asymmetric plaque counts between the regions.

**Table 65.** Interregional variation in the total number of plaques/mm$^2$ in SDAT Case 13.

| **Left** | | Abs | % | **Right** | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 24.6 | 33.2 | 8.6 | 29.8 | 46.5 | 45.6 | 0.9 | 2.0 |
| | Mid Temp | | | | Mid Temp | | |
| | 30.7 | 6.1 | 22.1 | | 64.5 | 18.0 | 32.4 |
| | Inf Temp | | | | Inf Temp | | |
| | 26.3 | 1.7 | 6.7 | | 44.1 | 2.4 | 5.3 |
| | Cingulate | | | | Cingulate | | |
| | 23.2 | 1.4 | 5.8 | | 40.7 | 5.8 | 13.3 |
| | Parietal | | | | Parietal | | |
| | 21.7 | 2.9 | 12.5 | | 27.3 | 19.2 | 52.0* |
| | Occipital | | | | Occipital | | |
| | 8.0 | 16.6 | 101.8* | | 24.2 | 22.3 | 63.1* |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 33.2 | 30.7 | 2.5 | 7.8 | 45.6 | 64.5 | 18.9 | 34.3 |
| | Inf Temp | | | | Inf Temp | | |
| | 26.3 | 6.9 | 23.2 | | 44.1 | 1.5 | 3.3 |
| | Cingulate | | | | Cingulate | | |
| | 23.2 | 10.0 | 35.5 | | 40.7 | 4.9 | 11.4 |
| | Parietal | | | | Parietal | | |
| | 21.7 | 11.5 | 41.9* | | 27.3 | 18.3 | 50.2* |
| | Occipital | | | | Occipital | | |
| | 8.0 | 25.2 | 122.3* | | 24.2 | 21.4 | 61.3* |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 30.7 | 26.3 | 4.4 | 15.4 | 64.5 | 44.1 | 20.4 | 37.6 |
| | Cingulate | | | | Cingulate | | |
| | 23.2 | 7.5 | 27.8 | | 40.7 | 23.8 | 45.2* |
| | Parietal | | | | Parietal | | |
| | 21.7 | 9.0 | 34.4 | | 27.3 | 37.2 | 81.0* |
| | Occipital | | | | Occipital | | |
| | 8.0 | 22.7 | 117.3* | | 24.2 | 40.3 | 90.9* |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 26.3 | 23.2 | 3.1 | 12.5 | 44.1 | 40.7 | 3.4 | 8.0 |
| | Parietal | | | | Parietal | | |
| | 21.7 | 4.6 | 19.2 | | 27.3 | 16.8 | 47.0* |
| | Occipital | | | | Occipital | | |
| | 8.0 | 18.3 | 106.7* | | 24.2 | 19.9 | 58.3* |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 23.2 | 21.7 | 1.5 | 67 | 40.7 | 27.3 | 13.4 | 39.4 |
| | Occipital | | | | Occipital | | |
| | 8.0 | 15.2 | 97.4* | | 24.2 | 16.5 | 50.8* |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 21.7 | 8.0 | 13.7 | 92.2* | 27.3 | 24.2 | 3.1 | 12.0 |

* = Asymmetric plaque counts between the regions.

**Table 66.** Interregional variation in the area of plaques in square microns in the superficial layers of SDAT Case 8.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 22304 | 14860 | 7444 | 40.1* | 30478 | 25491 | 4987 | 17.8 |
| | Mid Temp | | | | Mid Temp | | |
| | 19073 | 3231 | 15.6 | | 26390 | 4088 | 14.4 |
| | Inf Temp | | | | Inf Temp | | |
| | 25522 | 3218 | 13.4 | | 22131 | 8347 | 31.7 |
| | Cingulate | | | | Cingulate | | |
| | 21350 | 954 | 4.4 | | 18513 | 11965 | 48.8* |
| | Parietal | | | | Parietal | | |
| | 28145 | 5841 | 23.2 | | 43156 | 12678 | 34.4 |
| | Occipital | | | | Occipital | | |
| | 21548 | 756 | 3.4 | | 26943 | 3535 | 12.3 |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 14860 | 19073 | 4213 | 24.8 | 25491 | 26390 | 899 | 3.5 |
| | Inf Temp | | | | Inf Temp | | |
| | 25522 | 10662 | 52.8* | | 22131 | 3360 | 14.1 |
| | Cingulate | | | | Cingulate | | |
| | 21350 | 6490 | 35.8 | | 18513 | 6978 | 31.7 |
| | Parietal | | | | Parietal | | |
| | 28145 | 13285 | 61.9* | | 43156 | 17665 | 51.5* |
| | Occipital | | | | Occipital | | |
| | 21548 | 6688 | 36.7 | | 26943 | 1452 | 5.5 |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 19073 | 25522 | 6449 | 28.9 | 26390 | 22131 | 4259 | 17.6 |
| | Cingulate | | | | Cingulate | | |
| | 21350 | 2277 | 11.3 | | 18513 | 7877 | 35.1 |
| | Parietal | | | | Parietal | | |
| | 28145 | 9072 | 38.4 | | 43156 | 16766 | 48.2* |
| | Occipital | | | | Occipital | | |
| | 21548 | 2475 | 12.2 | | 26943 | 553 | 2.1 |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 25522 | 21350 | 4172 | 17.8 | 22131 | 18513 | 3618 | 17.8 |
| | Parietal | | | | Parietal | | |
| | 28145 | 2623 | 9.8 | | 43156 | 21025 | 64.4* |
| | Occipital | | | | Occipital | | |
| | 21548 | 3974 | 16.9 | | 26943 | 4812 | 19.6 |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 21350 | 28145 | 6795 | 27.4 | 18513 | 43156 | 24643 | 79.9* |
| | Occipital | | | | Occipital | | |
| | 21548 | 198 | 0.9 | | 26943 | 8430 | 37.1 |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 28145 | 21548 | 6597 | 26.6 | 43156 | 26943 | 16213 | 46.2* |

* = Asymmetric plaque counts between the regions.

**Table 67.** Interregional variation in the area of plaques in square microns in the superficial layers of SDAT Case 9.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 33705 | 5170 | 28535 | 146.8* | 17536 | 17860 | 324 | 1.8 |
| | Mid Temp | | | | Mid Temp | | |
| | 3160 | 30545 | 165.7* | | 10831 | 6705 | 47.3* |
| | Inf Temp | | | | Inf Temp | | |
| | 14627 | 19078 | 78.9* | | 6920 | 10616 | 86.8* |
| | Cingulate | | | | Cingulate | | |
| | 26659 | 7046 | 23.3 | | 28590 | 11054 | 47.9* |
| | Parietal | | | | Parietal | | |
| | 32978 | 727 | 2.2 | | 26643 | 9107 | 41.2* |
| | Occipital | | | | Occipital | | |
| | 45095 | 11390 | 28.9 | | 28672 | 11136 | 48.2* |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 5170 | 3160 | 2010 | 48.2 | 17860 | 10831 | 7029 | 49.0* |
| | Inf Temp | | | | Inf Temp | | |
| | 14627 | 9457 | 95.5* | | 6920 | 10940 | 88.3* |
| | Cingulate | | | | Cingulate | | |
| | 26659 | 21489 | 135.0* | | 28590 | 10730 | 42.6* |
| | Parietal | | | | Parietal | | |
| | 32978 | 27808 | 145.8* | | 26643 | 8783 | 39.5 |
| | Occipital | | | | Occipital | | |
| | 45095 | 39925 | 158.8* | | 28672 | 10812 | 46.5* |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 3160 | 14627 | 11467 | 128.9* | 10831 | 6920 | 3911 | 44.1 |
| | Cingulate | | | | Cingulate | | |
| | 26659 | 23499 | 157.6* | | 28590 | 17759 | 90.1* |
| | Parietal | | | | Parietal | | |
| | 32978 | 29818 | 165.0* | | 26643 | 15812 | 84.4* |
| | Occipital | | | | Occipital | | |
| | 45095 | 41935 | 173.8* | | 28672 | 17841 | 90.3* |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 14627 | 26659 | 12032 | 58.3* | 6920 | 28590 | 21670 | 122.0* |
| | Parietal | | | | Parietal | | |
| | 32978 | 18351 | 77.1* | | 26643 | 19723 | 117.5* |
| | Occipital | | | | Occipital | | |
| | 45095 | 30468 | 102.0* | | 28672 | 21752 | 122.0* |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 26659 | 32978 | 6319 | 21.2 | 28590 | 26643 | 1947 | 7.0 |
| | Occipital | | | | Occipital | | |
| | 45095 | 18436 | 51.4* | | 28672 | 82 | 0.3 |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 32978 | 45095 | 12117 | 31.0 | 26643 | 28672 | 2029 | 7.3 |

* = Asymmetric plaque counts between the regions.

**Table 68.** Interregional variation in the area of plaques in square microns in the superficial layers of SDAT Case 10.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 10892 | 16000 | 5108 | 38.0 | 62009 | 43698 | 18311 | 34.6 |
| | Mid Temp | | | | Mid Temp | | |
| | 33065 | 22173 | 100.9* | | 54968 | 7041 | 12.0 |
| | Inf Temp | | | | Inf Temp | | |
| | 38112 | 27220 | 111.1* | | 48764 | 13245 | 23.9 |
| | Cingulate | | | | Cingulate | | |
| | 9773 | 1119 | 10.8 | | 38487 | 23522 | 46.8* |
| | Parietal | | | | Parietal | | |
| | 32036 | 21144 | 98.5* | | 44710 | 17299 | 32.4 |
| | Occipital | | | | Occipital | | |
| | 22517 | 11625 | 69.6* | | 50418 | 11591 | 20.6 |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 16000 | 33065 | 17065 | 69.6* | 43698 | 54968 | 11270 | 22.8 |
| | Inf Temp | | | | Inf Temp | | |
| | 38112 | 22112 | 81.7* | | 48764 | 5066 | 11.0 |
| | Cingulate | | | | Cingulate | | |
| | 9773 | 6227 | 48.3* | | 38487 | 5211 | 12.7 |
| | Parietal | | | | Parietal | | |
| | 32036 | 16036 | 66.8* | | 44710 | 1012 | 2.3 |
| | Occipital | | | | Occipital | | |
| | 22517 | 6517 | 33.8 | | 50418 | 6720 | 14.3 |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 33065 | 38112 | 5047 | 14.2 | 54968 | 48764 | 6204 | 12.0 |
| | Cingulate | | | | Cingulate | | |
| | 9773 | 23292 | 108.7* | | 38487 | 16481 | 35.3 |
| | Parietal | | | | Parietal | | |
| | 32036 | 1029 | 3.2 | | 44710 | 10258 | 20.6 |
| | Occipital | | | | Occipital | | |
| | 22517 | 10548 | 38.0 | | 50418 | 4550 | 8.6 |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 38112 | 9773 | 28339 | 118.4* | 48764 | 38487 | 10277 | 23.6 |
| | Parietal | | | | Parietal | | |
| | 32036 | 6067 | 17.3 | | 44710 | 4054 | 8.7 |
| | Occipital | | | | Occipital | | |
| | 22517 | 15595 | 51.4* | | 50418 | 1654 | 3.3 |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 9773 | 32036 | 22263 | 106.5* | 38487 | 44710 | 6223 | 15.0 |
| | Occipital | | | | Occipital | | |
| | 22517 | 12744 | 78.9* | | 50418 | 11931 | 26.8 |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 32036 | 22517 | 9519 | 34.9 | 44710 | 50418 | 5708 | 12.0 |

* = Asymmetric plaque counts between the regions.

**Table 69.** Interregional variation in the area of plaques in square microns in the superficial layers of SDAT Case 11.

| Left | | Abs | % | Right | | Abs | * |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 29191 | 49289 | 20098 | 51.0* | 35030 | 32455 | 2575 | 8.0 |
| | Mid Temp | | | | Mid Temp | | |
| | 62193 | 33022 | 72.0* | | 37616 | 2586 | 7.0 |
| | Inf Temp | | | | Inf Temp | | |
| | 77512 | 48321 | 90.0* | | 77014 | 41984 | 75.0* |
| | Cingulate | | | | Cingulate | | |
| | 20564 | 8627 | 35.0 | | 14700 | 20330 | 82.0* |
| | Parietal | | | | Parietal | | |
| | 50358 | 21167 | 53.0* | | 31113 | 3917 | 12.0 |
| | Occipital | | | | Occipital | | |
| | 33722 | 4531 | 14.0 | | 24969 | 10061 | 34.0 |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 49289 | 62193 | 12904 | 23.0 | 32455 | 37616 | 5161 | 15.0 |
| | Inf Temp | | | | Inf Temp | | |
| | 77512 | 28223 | 44.0* | | 77014 | 44559 | 81.0* |
| | Cingulate | | | | Cingulate | | |
| | 20564 | 28725 | 82.0* | | 14700 | 17755 | 75.0* |
| | Parietal | | | | Parietal | | |
| | 50358 | 1069 | 2.0 | | 31113 | 1342 | 4.0 |
| | Occipital | | | | Occipital | | |
| | 33722 | 15567 | 38.0 | | 24969 | 7486 | 26.0 |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 62193 | 77512 | 15319 | 22.0 | 37616 | 77014 | 39398 | 69.0* |
| | Cingulate | | | | Cingulate | | |
| | 20564 | 41629 | 101.0* | | 14700 | 22916 | 88.0* |
| | Parietal | | | | Parietal | | |
| | 50358 | 11835 | 21.0 | | 31113 | 6503 | 19.0 |
| | Occipital | | | | Occipital | | |
| | 33722 | 28471 | 59.0* | | 24969 | 12647 | 40.0* |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 77512 | 20564 | 56948 | 116.0* | 77014 | 14700 | 62314 | 136.0* |
| | Parietal | | | | Parietal | | |
| | 50358 | 27154 | 42.0* | | 31113 | 45901 | 85.0* |
| | Occipital | | | | Occipital | | |
| | 33722 | 43790 | 79.0* | | 24969 | 52045 | 102.0* |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 20564 | 50358 | 29794 | 84.0* | 14700 | 31113 | 16413 | 72.0* |
| | Occipital | | | | Occipital | | |
| | 33722 | 13158 | 48.0* | | 24969 | 10269 | 52.0* |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 50358 | 33722 | 16636 | 40.0* | 31113 | 24969 | 6144 | 22.0 |

* = Asymmetric plaque counts between the regions.

**Table 70.** Interregional variation in the area of plaques in square microns in the superficial layers of SDAT Case 12.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 8652 | 12498 | 3846 | 36.0 | 9278 | 20566 | 11288 | 76.0* |
| | Mid Temp | | | | Mid Temp | | |
| | 19619 | 10967 | 78.0* | | 28254 | 18976 | 101.0* |
| | Inf Temp | | | | Inf Temp | | |
| | 46349 | 37697 | 137.0* | | 37401 | 28123 | 120.0* |
| | Cingulate | | | | Cingulate | | |
| | 17962 | 9310 | 70.0* | | 20351 | 11073 | 75.0* |
| | Parietal | | | | Parietal | | |
| | 20757 | 12105 | 82.0* | | 15055 | 5777 | 47.0* |
| | Occipital | | | | Occipital | | |
| | 20663 | 12011 | 82.0* | | 41069 | 31791 | 126.0* |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 12498 | 19619 | 7121 | 44.0* | 20566 | 28254 | 7688 | 31.0 |
| | Inf Temp | | | | Inf Temp | | |
| | 45349 | 33851 | 115.0* | | 37401 | 16835 | 58.0* |
| | Cingulate | | | | Cingulate | | |
| | 17962 | 5464 | 36.0 | | 20351 | 215 | 1.0 |
| | Parietal | | | | Parietal | | |
| | 20757 | 8259 | 50.0* | | 15055 | 5511 | 31.0 |
| | Occipital | | | | Occipital | | |
| | 20663 | 8165 | 49.0* | | 41069 | 20503 | 66.0* |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 19619 | 46349 | 26730 | 81.0* | 28254 | 37401 | 9147 | 28.0 |
| | Cingulate | | | | Cingulate | | |
| | 17962 | 1657 | 9.0 | | 20351 | 7903 | 32.0 |
| | Parietal | | | | Parietal | | |
| | 20757 | 1138 | 6.0 | | 15055 | 13199 | 61.0* |
| | Occipital | | | | Occipital | | |
| | 20663 | 1044 | 5.0 | | 41069 | 12815 | 37.0 |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 46349 | 17962 | 28387 | 88.0* | 37401 | 20351 | 17050 | 59.0* |
| | Parietal | | | | Parietal | | |
| | 20757 | 25592 | 76.0* | | 15055 | 22346 | 85.0* |
| | Occipital | | | | Occipital | | |
| | 20663 | 25686 | 77.0* | | 41069 | 3668 | 9.0 |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 17962 | 20757 | 2795 | 14.0 | 20351 | 15055 | 5296 | 30.0 |
| | Occipital | | | | Occipital | | |
| | 20663 | 2701 | 14.0 | | 41069 | 20718 | 67.0* |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 20757 | 20663 | 94 | 0.4 | 15055 | 41069 | 26014 | 93.0* |

* = Asymmetric plaque counts between the regions.

**Table 71.** Interregional variation in the area of plaques in square microns in the superficial layers of SDAT Case 13.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 23478 | 23899 | 421 | 2.0 | 37070 | 38364 | 1294 | 3.0 |
| | Mid Temp | | | | Mid Temp | | |
| | 36836 | 13358 | 44.0* | | 54278 | 17208 | 38.0 |
| | Inf Temp | | | | Inf Temp | | |
| | 27985 | 4507 | 18.0 | | 36268 | 802 | 2.0 |
| | Cingulate | | | | Cingulate | | |
| | 19665 | 3813 | 18.0 | | 33757 | 3313 | 9.0 |
| | Parietal | | | | Parietal | | |
| | 20630 | 2848 | 13.0 | | 27649 | 9421 | 29.0 |
| | Occipital | | | | Occipital | | |
| | 9086 | 14392 | 88.0* | | 22040 | 15030 | 51.0* |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 23899 | 36836 | 12937 | 43.0* | 38364 | 54278 | 15914 | 34.0 |
| | Inf Temp | | | | Inf Temp | | |
| | 27985 | 4086 | 16.0 | | 36268 | 2096 | 6.0 |
| | Cingulate | | | | Cingulate | | |
| | 19665 | 4234 | 19.0 | | 33757 | 4607 | 13.0 |
| | Parietal | | | | Parietal | | |
| | 20630 | 3269 | 15.0 | | 27649 | 10715 | 32.0 |
| | Occipital | | | | Occipital | | |
| | 9086 | 14813 | 90.0* | | 22040 | 16324 | 54.0* |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 36836 | 27985 | 8851 | 27.0 | 54268 | 36268 | 18010 | 40.0* |
| | Cingulate | | | | Cingulate | | |
| | 19665 | 17171 | 61.0* | | 33757 | 20521 | 47.0* |
| | Parietal | | | | Parietal | | |
| | 20630 | 16206 | 56.0* | | 27649 | 26629 | 65.0* |
| | Occipital | | | | Occipital | | |
| | 9086 | 27750 | 121.0* | | 22040 | 32238 | 84.0* |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 27985 | 19665 | 8320 | 35.0 | 36268 | 33757 | 2511 | 7.0 |
| | Parietal | | | | Parietal | | |
| | 20630 | 7355 | 30.0 | | 27649 | 8619 | 27.0 |
| | Occipital | | | | Occipital | | |
| | 9086 | 18899 | 102.0* | | 22040 | 14228 | 49.0* |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 19665 | 20630 | 965 | 5.0 | 33757 | 27649 | 6108 | 20.0 |
| | Occipital | | | | Occipital | | |
| | 9086 | 10579 | 74.0* | | 22040 | 11717 | 42.0 |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 20630 | 9086 | 11544 | 78.0* | 27649 | 22040 | 5609 | 23.0 |

* = Asymmetric plaque counts between the regions.

**Table 72.** Interregional variation in the area of plaques in square microns in the deep layers of SDAT Case 8.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 15477 | 5299 | 10178 | 98.0* | 13175 | 16417 | 3242 | 21.9 |
| | Mid Temp | | | | Mid Temp | | |
| | 7343 | 8134 | 71.3* | | 9876 | 3299 | 28.6 |
| | Inf Temp | | | | Inf Temp | | |
| | 9213 | 6264 | 50.7* | | 8418 | 4757 | 44.1* |
| | Cingulate | | | | Cingulate | | |
| | 10027 | 5450 | 42.7 | | 9318 | 3857 | 34.3 |
| | Parietal | | | | Parietal | | |
| | 14903 | 574 | 3.8 | | 20320 | 7145 | 42.7* |
| | Occipital | | | | Occipital | | |
| | 15679 | 202 | 1.3 | | 10544 | 2631 | 22.2 |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 5299 | 7343 | 2044 | 32.3 | 16417 | 9876 | 6541 | 49.8* |
| | Inf Temp | | | | Inf Temp | | |
| | 9213 | 3914 | 53.9 | | 8418 | 7999 | 64.4* |
| | Cingulate | | | | Cingulate | | |
| | 10027 | 4728 | 61.7 | | 9318 | 7099 | 55.2* |
| | Parietal | | | | Parietal | | |
| | 14903 | 9604 | 95.1* | | 20320 | 3903 | 21.2 |
| | Occipital | | | | Occipital | | |
| | 15679 | 10380 | 99.0* | | 10544 | 5873 | 43.6* |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 7343 | 9213 | 1870 | 22.6 | 9876 | 8418 | 1458 | 15.9 |
| | Cingulate | | | | Cingulate | | |
| | 10027 | 2684 | 30.9 | | 9318 | 558 | 5.8 |
| | Parietal | | | | Parietal | | |
| | 14903 | 7560 | 68.0* | | 20320 | 10444 | 69.2* |
| | Occipital | | | | Occipital | | |
| | 15679 | 8336 | 72.4* | | 10544 | 668 | 6.5 |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 9213 | 10027 | 814 | 8.5 | 8418 | 9318 | 900 | 10.1 |
| | Parietal | | | | Parietal | | |
| | 14903 | 5690 | 47.2* | | 20320 | 11902 | 82.8* |
| | Occipital | | | | Occipital | | |
| | 15679 | 6466 | 52.0* | | 10544 | 2126 | 22.4 |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 10027 | 14903 | 4876 | 39.1 | 9318 | 20320 | 11002 | 74.2* |
| | Occipital | | | | Occipital | | |
| | 15679 | 5652 | 44.0* | | 10544 | 1226 | 12.3 |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 14903 | 15679 | 776 | 5.1 | 20320 | 10544 | 9776 | 63.3* |

* = Asymmetric plaque counts between the regions.

**Table 73.** Interregional variation in the area of plaques in square microns in the deep layers of SDAT Case 9.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 11286 | 2509 | 8777 | 127.2* | 4576 | 6900 | 2324 | 40.0 |
| | Mid Temp | | | | Mid Temp | | |
| | 1 | 11285 | 200.0* | | 4824 | 248 | 5.0 |
| | Inf Temp | | | | Inf Temp | | |
| | 2061 | 9225 | 138.0* | | 4743 | 167 | 4.0 |
| | Cingulate | | | | Cingulate | | |
| | 11172 | 114 | 1.0 | | 7068 | 2492 | 43.0 |
| | Parietal | | | | Parietal | | |
| | 24836 | 13550 | 75.0* | | 13420 | 8844 | 98.0* |
| | Occipital | | | | Parietal | | |
| | 19448 | 8162 | 53.0* | | 5505 | 929 | 18.0 |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 2509 | 1 | 2508 | 200.0 | 6900 | 4824 | 2076 | 35.0 |
| | Inf Temp | | | | Inf Temp | | |
| | 2061 | 448 | 20.0 | | 4743 | 2157 | 37.0 |
| | Cingulate | | | | Cingulate | | |
| | 11172 | 8663 | 127.0* | | 7068 | 168 | 2.0 |
| | Parietal | | | | Parietal | | |
| | 24836 | 22327 | 163.0* | | 13420 | 6520 | 64.0* |
| | Occipital | | | | Occipital | | |
| | 19448 | 16939 | 154.0* | | 5505 | 1395 | 22.0 |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 1 | 2061 | 2060 | 200.0 | 4824 | 4743 | 81 | 2.0 |
| | Cingulate | | | | Cingulate | | |
| | 11172 | 11171 | 200.0* | | 7068 | 2244 | 38.0 |
| | Parietal | | | | Parietal | | |
| | 24836 | 24835 | 200.0* | | 13420 | 8596 | 94.0* |
| | Occipital | | | | Occipital | | |
| | 19448 | 19447 | 200.0* | | 5505 | 681 | 13.0 |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 2061 | 11172 | 9111 | 138.0* | 4743 | 7068 | 2325 | 39.0 |
| | Parietal | | | | Parietal | | |
| | 24836 | 22775 | 169.0* | | 13420 | 8677 | 96.0* |
| | Occipital | | | | Occipital | | |
| | 19448 | 17387 | 162.0* | | 5505 | 762 | 15.0 |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 11172 | 24836 | 13664 | 76.0* | 7068 | 13420 | 6352 | 62.0* |
| | Occipital | | | | Occipital | | |
| | 19448 | 8276 | 54.0* | | 5505 | 1563 | 25.0 |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 24836 | 19448 | 5388 | 24.0 | 13420 | 5505 | 7915 | 84.0* |

* = Asymmetric plaque counts between the regions.

**Table 74.** Interregional variation in the area of plaques in square microns in the deep layers of SDAT Case 10.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 3939 | 4603 | 664 | 15.5 | 43072 | 22822 | 20250 | 61.5* |
| | Mid Temp | | | | Mid Temp | | |
| | 5157 | 1218 | 26.8 | | 28177 | 14895 | 41.8* |
| | Inf Temp | | | | Inf Temp | | |
| | 8076 | 4137 | 68.9 | | 29899 | 13173 | 36.1 |
| | Cingulate | | | | Cingulate | | |
| | 1375 | 2564 | 96.5 | | 18850 | 24222 | 78.2* |
| | Parietal | | | | Parietal | | |
| | 15019 | 11080 | 116.9* | | 30345 | 12727 | 34.7 |
| | Occipital | | | | Occipital | | |
| | 11147 | 7208 | 95.6* | | 15531 | 27541 | 94.0* |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 4603 | 5157 | 554 | 11.4 | 22822 | 28177 | 5355 | 21.0 |
| | Inf Temp | | | | Inf Temp | | |
| | 8076 | 3473 | 54.8 | | 29899 | 7077 | 26.8 |
| | Cingulate | | | | Cingulate | | |
| | 1375 | 3228 | 108.0 | | 18850 | 3972 | 19.1 |
| | Parietal | | | | Parietal | | |
| | 15019 | 10416 | 106.2* | | 30345 | 7523 | 28.3 |
| | Occipital | | | | Occipital | | |
| | 11147 | 6544 | 83.1* | | 15531 | 7291 | 38.0 |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 5157 | 8076 | 2919 | 44.2 | 28177 | 29899 | 1722 | 5.9 |
| | Cingulate | | | | Cingulate | | |
| | 1375 | 3782 | 115.8 | | 18850 | 9327 | 39.7 |
| | Parietal | | | | Parietal | | |
| | 15019 | 9862 | 97.8* | | 30345 | 2168 | 7.4 |
| | Occipital | | | | Occipital | | |
| | 11147 | 5990 | 73.5* | | 15531 | 12646 | 57.9* |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 8076 | 1375 | 6701 | 141.8* | 29899 | 18850 | 11049 | 45.3* |
| | Parietal | | | | Parieta | | |
| | 15019 | 6943 | 60.1* | | 30345 | 446 | 1.5 |
| | Occipital | | | | Occipital | | |
| | 11147 | 3071 | 32.0 | | 15531 | 14368 | 63.2* |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 1375 | 15019 | 13644 | 166.4* | 18850 | 30345 | 11495 | 46.7* |
| | Occipital | | | | Occipital | | |
| | 11147 | 9772 | 156.1* | | 15531 | 3319 | 19.3 |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 15019 | 11147 | 3872 | 29.6 | 30345 | 15531 | 14814 | 64.6* |

* = Asymmetric plaque counts between the regions.

**Table 75.** Interregional variation in the area of plaques in square microns in the deep layers of SDAT Case 11.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 32457 | 29339 | 3118 | 10.0 | 8542 | 5621 | 2921 | 41.0 |
| | Mid Temp | | | | Mid Temp | | |
| | 32269 | 188 | 0.5 | | 7883 | 659 | 8.0 |
| | Inf Temp | | | | Inf Temp | | |
| | 60052 | 27595 | 60.0* | | 38470 | 29928 | 127.0* |
| | Cingulate | | | | Cingulate | | |
| | 27856 | 4601 | 15.0 | | 5641 | 2901 | 41.0 |
| | Parietal | | | | Parietal | | |
| | 18474 | 13983 | 55.0* | | 32037 | 23495 | 116.0* |
| | Occipital | | | | Occipital | | |
| | 11304 | 21153 | 97.0* | | 14492 | 5950 | 52.0 |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 29339 | 32269 | 2930 | 10.0 | 5621 | 7883 | 2262 | 34.0 |
| | Inf Temp | | | | Inf Temp | | |
| | 60052 | 30713 | 69.0* | | 38470 | 32849 | 149.0* |
| | Cingulate | | | | Cingulate | | |
| | 27856 | 1483 | 5.0 | | 5641 | 20 | 0.4 |
| | Parietal | | | | Parietal | | |
| | 18474 | 10865 | 45.0* | | 32037 | 26416 | 140.0* |
| | Occipital | | | | Occipital | | |
| | 11304 | 18035 | 89.0* | | 14492 | 8871 | 88.0* |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 32269 | 60052 | 27783 | 60.0* | 7883 | 38470 | 30587 | 132.0* |
| | Cingulate | | | | Cingulate | | |
| | 27856 | 4413 | 15.0 | | 5641 | 2242 | 33.0 |
| | Parietal | | | | Parietal | | |
| | 18474 | 13795 | 54.0* | | 32037 | 24154 | 121.0* |
| | Occipital | | | | Occipital | | |
| | 11304 | 20965 | 96.0* | | 14492 | 6609 | 59.0* |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 60052 | 27856 | 32196 | 73.0* | 38470 | 5641 | 32829 | 149.0* |
| | Parietal | | | | Parietal | | |
| | 18474 | 41578 | 106.0* | | 32037 | 6433 | 18.0 |
| | Occipital | | | | Occipital | | |
| | 11304 | 48748 | 137.0* | | 14492 | 23978 | 90.0* |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 27856 | 18474 | 9382 | 40.0* | 5641 | 32037 | 26396 | 140.0* |
| | Occipital | | | | Occipital | | |
| | 11304 | 16552 | 84.0* | | 14492 | 8851 | 88.0* |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 18474 | 11304 | 7170 | 48.0* | 32037 | 14492 | 17545 | 75.0* |

* = Asymmetric plaque counts between the regions.

**Table 76.** Interregional variation in the area of plaques in square microns in the deep layers of SDAT Case 12.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 3463 | 2772 | 691 | 22.0 | 9230 | 8304 | 926 | 10.0 |
| | Mid Temp | | | | Mid Temp | | |
| | 9440 | 5977 | 93.0* | | 14337 | 5107 | 43.0 |
| | Inf Temp | | | | Inf Temp | | |
| | 24846 | 21383 | 151.0* | | 23494 | 14264 | 87.0* |
| | Cingulate | | | | Cingulate | | |
| | 5802 | 2339 | 50.0 | | 9129 | 101 | 1.0 |
| | Parietal | | | | Parietal | | |
| | 11463 | 8000 | 107.0* | | 6201 | 3029 | 3.9 |
| | Occipital | | | | Occipital | | |
| | 2410 | 1053 | 36.0 | | 6139 | 3091 | 40.0 |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 2772 | 9440 | 6668 | 109.0* | 8304 | 14337 | 6033 | 53.0* |
| | Inf Temp | | | | Inf Temp | | |
| | 24846 | 22074 | 160.0* | | 23494 | 15190 | 96.0* |
| | Cingulate | | | | Cingulate | | |
| | 5802 | 3030 | 71.0 | | 9129 | 825 | 9.0 |
| | Parietal | | | | Parietal | | |
| | 11463 | 8691 | 122.0* | | 6201 | 2103 | 29.0 |
| | Occipital | | | | Occipital | | |
| | 2410 | 362 | 14.0 | | 6139 | 2165 | 30.0 |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 9440 | 24846 | 15406 | 90.0* | 14337 | 23494 | 9157 | 48.0* |
| | Cingulate | | | | Cingulate | | |
| | 5802 | 3638 | 48.0 | | 9129 | 5208 | 44.0 |
| | Parietal | | | | Parietal | | |
| | 11463 | 2023 | 19.0 | | 6201 | 8136 | 79.0* |
| | Occipital | | | | Occipital | | |
| | 2410 | 7030 | 119.0* | | 6139 | 8198 | 80.0* |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 24846 | 5802 | 19044 | 124.0* | 23494 | 9129 | 14365 | 88.0* |
| | Parietal | | | | Parietal | | |
| | 11463 | 13383 | 74.0* | | 6201 | 17293 | 116.0* |
| | Occipital | | | | Occipital | | |
| | 2410 | 22436 | 165.0* | | 6139 | 17355 | 117.0* |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 5802 | 11463 | 5661 | 66.0* | 9129 | 6201 | 2928 | 38.0 |
| | Occipital | | | | Occipital | | |
| | 2410 | 3392 | 83.0 | | 6139 | 2990 | 39.0 |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 11463 | 2410 | 9053 | 130.0* | 6201 | 6139 | 62 | 1.0 |

* = Asymmetric plaque counts between the regions.

**Table 77.** Interregional variation in the area of plaques in square microns in the deep layers of SDAT Case 13.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 4135 | 10721 | 6586 | 89.0* | 11264 | 13570 | 2306 | 18.0 |
| | Mid Temp | | | | Mid Temp | | |
| | 15098 | 10963 | 114.0* | | 33843 | 22579 | 100.0* |
| | Inf Temp | | | | Inf Temp | | |
| | 7342 | 3207 | 56.0 | | 16443 | 5179 | 37.0 |
| | Cingulate | | | | Cingulate | | |
| | 2045 | 2090 | 68.0 | | 8723 | 2541 | 25.0 |
| | Parietal | | | | Parietal | | |
| | 2402 | 1733 | 53.0 | | 4843 | 6421 | 80.0* |
| | Occipital | | | | Occipital | | |
| | 0 | 4135 | 200.0 | | 438 | 10826 | 185.0* |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 10721 | 15098 | 4377 | 34.0 | 13570 | 33843 | 20273 | 86.0* |
| | Inf Temp | | | | Inf Temp | | |
| | 7342 | 3379 | 37.0 | | 16443 | 2873 | 19.0 |
| | Cingulate | | | | Cingulate | | |
| | 2045 | 8676 | 136.0* | | 8723 | 4847 | 43.0 |
| | Parietal | | | | Parietal | | |
| | 2402 | 8319 | 127.0* | | 4843 | 8727 | 95.0* |
| | Occipital | | | | Occipital | | |
| | 0 | 10721 | 200.0* | | 438 | 13132 | 187.0* |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 15098 | 7342 | 7756 | 69.0* | 33843 | 16443 | 17400 | 69.0* |
| | Cingulate | | | | Cingulate | | |
| | 2045 | 13053 | 152.0* | | 8723 | 25120 | 118.0* |
| | Parietal | | | | Parietal | | |
| | 2402 | 12696 | 145.0* | | 4843 | 29000 | 150.0* |
| | Occipital | | | | Occipital | | |
| | 0 | 15098 | 200.0* | | 438 | 33405 | 195.0* |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 7342 | 2045 | 5297 | 113.0 | 16443 | 8723 | 7720 | 61.0* |
| | Parietal | | | | Parietal | | |
| | 2402 | 4940 | 101.0 | | 4843 | 11600 | 109.0* |
| | Occipital | | | | Occipital | | |
| | 0 | 7342 | 200.0* | | 438 | 16005 | 190.0* |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 2045 | 2402 | 357 | 16.0 | 8723 | 4843 | 3880 | 57.0 |
| | Occipital | | | | Occipital | | |
| | 0 | 2045 | 200.0 | | 438 | 8285 | 181.0* |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 2402 | 0 | 2045 | 200.0 | 4843 | 438 | 4405 | 167.0 |

* = Asymmetric plaque counts between the regions.

**Table 78.** Interregional variation in the total area of plaques in square microns in SDAT Case 8.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 18890 | 10080 | 8811 | 60.8* | 21826 | 20954 | 872 | 4.1 |
| | Mid Temp | | | | Mid Temp | | |
| | 13208 | 5682 | 35.4 | | 18133 | 3694 | 18.5 |
| | Inf Temp | | | | Inf Temp | | |
| | 17368 | 1523 | 8.4 | | 15274 | 6552 | 35.3 |
| | Cingulate | | | | Cingulate | | |
| | 15688 | 3202 | 18.5 | | 13916 | 7911 | 44.3* |
| | Parietal | | | | Parietal | | |
| | 21524 | 2634 | 13.0 | | 31738 | 9912 | 37.0 |
| | Occipital | | | | Occipital | | |
| | 18614 | 277 | 1.5 | | 18744 | 3083 | 15.2 |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 10080 | 13208 | 3128 | 26.9 | 20954 | 18133 | 2821 | 14.4 |
| | Inf Temp | | | | Inf Temp | | |
| | 17368 | 7288 | 53.1* | | 15274 | 5680 | 31.4 |
| | Cingulate | | | | Cingulate | | |
| | 15688 | 5609 | 43.5* | 13916 | 13916 | 7038 | 40.4* |
| | Parietal | | | | Parietal | | |
| | 21524 | 11444 | 72.4* | | 31738 | 10784 | 40.9* |
| | Occipital | | | | Occipital | | |
| | 18614 | 8534 | 59.5* | | 18744 | 2210 | 11.1 |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 13208 | 17368 | 4160 | 27.2 | 18133 | 15274 | 2858 | 17.1 |
| | Cingulate | | | | Cingulate | | |
| | 15688 | 2480 | 17.2 | | 13916 | 4218 | 26.3 |
| | Parietal | | | | Parietal | | |
| | 21524 | 8316 | 47.9* | | 31738 | 13605 | 54.6* |
| | Occipital | | | | Occipital | | |
| | 18614 | 5406 | 34.0 | | 18744 | 610 | 3.3 |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 17368 | 15688 | 1679 | 10.2 | 15274 | 13915 | 1359 | 9.3 |
| | Parietal | | | | Parietal | | |
| | 21524 | 4156 | 21.4 | | 31738 | 16464 | 70.0* |
| | Occipital | | | | Occipital | | |
| | 18614 | 1246 | 6.9 | | 18744 | 3469 | 20.4 |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 15688 | 21524 | 5836 | 31.4 | 13916 | 31738 | 17822 | 78.1* |
| | Occipital | | | | Occipital | | |
| | 18614 | 2925 | 17.0 | | 18744 | 4828 | 29.6 |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 21524 | 18614 | 2910 | 14.5 | 31738 | 18744 | 12994 | 51.5* |

* = Asymmetric plaque counts between the regions.

**Table 79.** Interregional variation in the total area of plaques in square microns in SDAT Case 9.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 22768 | 4112 | 18656 | 138.8* | 11056 | 12380 | 1324 | 11.3 |
| | Mid Temp | | | | Mid Temp | | |
| | 1853 | 20916 | 169.9* | | 7828 | 3228 | 34.2 |
| | Inf Temp | | | | Inf Temp | | |
| | 8617 | 14152 | 90.2* | | 5832 | 5224 | 61.9 |
| | Cingulate | | | | Cingulate | | |
| | 19188 | 3580 | 17.1 | | 17829 | 6773 | 46.9* |
| | Parietal | | | | Parietal | | |
| | 29180 | 6412 | 24.7 | | 20032 | 8976 | 57.7* |
| | Occipital | | | | Occipital | | |
| | 32544 | 9776 | 35.3 | | 17088 | 6032 | 42.9 |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 4112 | 1853 | 2259 | 75.8 | 12380 | 7828 | 4552 | 45.0 |
| | Inf Temp | | | | Inf Temp | | |
| | 8617 | 4504 | 70.8 | | 5832 | 6548 | 71.9* |
| | Cingulate | | | | Cingulate | | |
| | 19188 | 15076 | 129.4* | | 17829 | 5449 | 36.1 |
| | Parietal | | | | Parietal | | |
| | 29180 | 25068 | 150.6* | | 20032 | 7652 | 47.2* |
| | Occipital | | | | Occipital | | |
| | 32544 | 28432 | 155.1* | | 17088 | 4708 | 32.0 |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 1853 | 8617 | 6764 | 129.2* | 7828 | 5832 | 1996 | 29.2 |
| | Cingulate | | | | Cingulate | | |
| | 19188 | 17336 | 164.8* | | 17829 | 10002 | 78.0* |
| | Parietal | | | | Parietal | | |
| | 29180 | 27327 | 176.1* | | 20032 | 12204 | 87.6* |
| | Occipital | | | | Occipital | | |
| | 32544 | 30692 | 178.4* | | 17088 | 9261 | 74.3* |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 8617 | 19188 | 10572 | 76.0* | 5832 | 17829 | 11998 | 101.4* |
| | Parietal | | | | Parietal | | |
| | 29180 | 20563 | 108.8* | | 20032 | 14200 | 109.8* |
| | Occipital | | | | Occipital | | |
| | 32544 | 23928 | 116.3* | | 17088 | 11257 | 98.2* |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 19188 | 29180 | 9992 | 41.3* | 17829 | 20032 | 2202 | 11.6 |
| | Occipital | | | | Occipital | | |
| | 32544 | 13356 | 51.6* | | 17088 | 740 | 4.2 |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 29180 | 32544 | 3364 | 10.9 | 20032 | 17088 | 2943 | 15.8 |

* = Asymmetric plaque counts between the regions.

**Table 80.** Interregional variation in the total area of plaques in square microns in SDAT Case 10.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 7416 | 10302 | 2886 | 32.6 | 52540 | 33260 | 19280 | 44.9* |
| | Mid Temp | | | | Mid Temp | | |
| | 19111 | 11696 | 88.2* | | 41572 | 10968 | 23.3 |
| | Inf Temp | | | | Inf Temp | | |
| | 23094 | 15678 | 102.8* | | 39332 | 13209 | 28.8 |
| | Cingulate | | | | Cingulate | | |
| | 5574 | 1842 | 28.4 | | 28668 | 23872 | 58.8* |
| | Parietal | | | | Parietal | | |
| | 23528 | 16112 | 104.1* | | 37528 | 15013 | 33.3 |
| | Occipital | | | | Occipital | | |
| | 16832 | 9416 | 77.7* | | 32974 | 19566 | 45.8* |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 10302 | 19111 | 8810 | 59.9* | 33260 | 41572 | 8312 | 22.2 |
| | Inf Temp | | | | Inf Temp | | |
| | 23094 | 12792 | 76.6* | | 39332 | 6072 | 16.7 |
| | Cingulate | | | | Cingulate | | |
| | 5574 | 4728 | 59.6 | | 28668 | 4592 | 14.8 |
| | Parietal | | | | Parietal | | |
| | 23528 | 13226 | 78.2* | | 37528 | 4268 | 1.2 |
| | Occipital | | | | Occipital | | |
| | 16832 | 6530 | 48.1* | | 32974 | 286 | 1.0 |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 19111 | 23094 | 3983 | 18.9 | 41572 | 39332 | 2241 | 5.5 |
| | Cingulate | | | | Cingulate | | |
| | 5574 | 13537 | 109.7* | | 28668 | 12904 | 36.7 |
| | Parietal | | | | Parietal | | |
| | 23528 | 4416 | 20.7 | | 37528 | 4045 | 10.2 |
| | Occipital | | | | Occipital | | |
| | 16832 | 2279 | 12.7 | | 32974 | 8598 | 23.1 |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 23094 | 5574 | 17520 | 122.2* | 39332 | 28668 | 10663 | 31.4 |
| | Parietal | | | | Parietal | | |
| | 23528 | 434 | 1.9 | | 37528 | 1804 | 4.7 |
| | Occipital | | | | Occipital | | |
| | 16832 | 6262 | 31.4 | | 32974 | 6357 | 17.6 |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 5574 | 23528 | 17954 | 123.4* | 28668 | 37528 | 8859 | 26.8 |
| | Occipital | | | | Occipital | | |
| | 16832 | 11258 | 100.5* | | 32974 | 4306 | 14.0 |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 23528 | 16832 | 6696 | 33.2 | 37528 | 32974 | 4553 | 12.9 |

* = Asymmetric plaque counts between the regions.

**Table 81.** Interregional variation in the total area of plaques in square microns in SDAT Case 11.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 30824 | 39314 | 8490 | 24.0 | 21786 | 19038 | 2748 | 13.0 |
| | Mid Temp | | | | Mid Temp | | |
| | 47231 | 16407 | 42.0* | | 22750 | 964 | 4.0 |
| | Inf Temp | | | | Inf Temp | | |
| | 68782 | 37958 | 76.0* | | 57742 | 35956 | 90.0* |
| | Cingulate | | | | Cingulate | | |
| | 24210 | 6614 | 24.0 | | 10170 | 11616 | 73.0* |
| | Parietal | | | | Parietal | | |
| | 34416 | 3592 | 11.0 | | 31575 | 9789 | 37.0 |
| | Occipital | | | | Occipital | | |
| | 22513 | 8311 | 31.0 | | 19730 | 2056 | 10.0 |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 39314 | 47231 | 7917 | 18.0 | 19038 | 22750 | 3712 | 18.0 |
| | Inf Temp | | | | Inf Temp | | |
| | 68782 | 29468 | 54.0* | | 57742 | 38704 | 101.0* |
| | Cingulate | | | | Cingulate | | |
| | 24210 | 15104 | 48.0* | | 10170 | 8868 | 61.0* |
| | Parietal | | | | Parietal | | |
| | 34416 | 4898 | 13.0 | | 31575 | 12537 | 50.0* |
| | Occipital | | | | Occipital | | |
| | 22513 | 16801 | 54.0* | | 19730 | 692 | 4.0 |
| Mid Temp | vs Inf Temp | | | Sup Temp | vs Inf Temp | | |
| 47231 | 68782 | 21551 | 37.0 | 22750 | 57742 | 34992 | 87.0* |
| | Cingulate | | | | Cingulate | | |
| | 24210 | 23021 | 64.0* | | 10170 | 12579 | 76.0* |
| | Parietal | | | | Parietal | | |
| | 34416 | 12815 | 31.0 | | 31575 | 8826 | 32.0 |
| | Occipital | | | | Occipital | | |
| | 22513 | 24718 | 71.0* | | 19730 | 3019 | 14.0 |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 68782 | 24210 | 44572 | 96.0* | 57742 | 10170 | 47572 | 140.0* |
| | Parietal | | | | Parietal | | |
| | 34416 | 34366 | 67.0* | | 31575 | 26167 | 58.0* |
| | Occipital | | | | Occipital | | |
| | 22513 | 46269 | 101.0* | | 19730 | 38012 | 98.0* |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 24210 | 34416 | 10206 | 35.0 | 10170 | 31575 | 21404 | 102.0* |
| | Occipital | | | | Occipital | | |
| | 22513 | 1697 | 7.0 | | 19730 | 9560 | 64.0* |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 34416 | 22513 | 11903 | 42.0* | 31575 | 19730 | 11844 | 46.0* |

* = Asymmetric plaque counts between the regions

**Table 82.** Interregional variation in the total area of plaques in square microns in SDAT Case 12.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 6058 | 7635 | 1578 | 23.0 | 9254 | 14435 | 5181 | 44.0 |
| | Mid Temp | | | | Mid Temp | | |
| | 14530 | 8472 | 82.0* | | 21296 | 12042 | 79.0* |
| | Inf Temp | | | | Inf Temp | | |
| | 35598 | 29540 | 142.0* | | 30448 | 21194 | 107.0* |
| | Cingulate | | | | Cingulate | | |
| | 11882 | 5824 | 65.0* | | 14740 | 5486 | 46.0 |
| | Parietal | | | | Parietal | | |
| | 16110 | 10052 | 91.0* | | 10628 | 1374 | 14.0 |
| | Occipital | | | | Occipital | | |
| | 11536 | 5479 | 62.0 | | 23604 | 14350 | 87.0* |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 7635 | 14530 | 6894 | 62.0* | 14435 | 21296 | 6860 | 38.0 |
| | Inf Temp | | | | Inf Temp | | |
| | 35598 | 27962 | 129.0* | | 30448 | 16012 | 71.0* |
| | Cingulate | | | | Cingulate | | |
| | 11882 | 4247 | 44.0 | | 14740 | 305 | 2.0 |
| | Parietal | | | | Parietal | | |
| | 16110 | 8475 | 71.0* | | 10628 | 3807 | 30.0 |
| | Occipital | | | | Occipital | | |
| | 11536 | 3902 | 41.0 | | 23604 | 9169 | 48.0* |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 14530 | 35598 | 21068 | 84.0* | 21296 | 30448 | 9152 | 35.0 |
| | Cingulate | | | | Cingulate | | |
| | 11882 | 2648 | 20.0 | | 14740 | 6556 | 36.0 |
| | Parietal | | | | Parietal | | |
| | 16110 | 1580 | 10.0 | | 10628 | 10668 | 67.0* |
| | Occipital | | | | Occipital | | |
| | 11536 | 2993 | 23.0 | | 23604 | 2308 | 10.0 |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 35598 | 11882 | 23716 | 100.0* | 30448 | 14740 | 15708 | 70.0* |
| | Parietal | | | | Parietal | | |
| | 16110 | 19488 | 75.0* | | 10628 | 19820 | 97.0* |
| | Occipital | | | | Occipital | | |
| | 11536 | 24061 | 102.0* | | 23604 | 6844 | 25.0 |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 11882 | 16110 | 4228 | 30.0 | 14740 | 10628 | 4112 | 32.0 |
| | Occipital | | | | Occipital | | |
| | 11536 | 346 | 3.0 | | 23604 | 8864 | 46.0* |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 16110 | 11536 | 4574 | 33.0 | 10628 | 23604 | 12976 | 76.0* |

* = Asymmetric plaque counts between the regions

**Table 83.** Interregional variation in the total area of plaques in square microns in SDAT Case 13.

| Left | | Abs | % | Right | | Abs | % |
|---|---|---|---|---|---|---|---|
| Frontal | vs Sup Temp | | | Frontal | vs Sup Temp | | |
| 13806 | 17310 | 3504 | 22.0 | 24167 | 25967 | 1800 | 7.0 |
| | Mid Temp | | | | Mid Temp | | |
| | 25967 | 12160 | 61.0* | | 44060 | 19894 | 58.0* |
| | Inf Temp | | | | Inf Temp | | |
| | 17664 | 3857 | 24.0 | | 26356 | 2189 | 9.0 |
| | Cingulate | | | | Cingulate | | |
| | 10855 | 2952 | 24.0 | | 21240 | 2927 | 13.0 |
| | Parietal | | | | Parietal | | |
| | 11516 | 2290 | 18.0 | | 16246 | 7921 | 39.0 |
| | Occipital | | | | Occipital | | |
| | 4543 | 9264 | 101.0* | | 11239 | 12928 | 73.0* |
| Sup Temp | vs Mid Temp | | | Sup Temp | vs Mid Temp | | |
| 17310 | 2596 | 8657 | 40.0* | 25967 | 44060 | 18094 | 52.0* |
| | Inf Temp | | | | Inf Temp | | |
| | 17664 | 354 | 2.0 | | 26356 | 389 | 1.0 |
| | Cingulate | | | | Cingulate | | |
| | 10855 | 6455 | 46.0* | | 21240 | 4727 | 20.0 |
| | Parietal | | | | Parietal | | |
| | 11516 | 5794 | 40.0* | | 16246 | 9721 | 46.0* |
| | Occipital | | | | Occipital | | |
| | 4543 | 12767 | 117.0* | | 11239 | 14728 | 79.0* |
| Mid Temp | vs Inf Temp | | | Mid Temp | vs Inf Temp | | |
| 25967 | 17664 | 8304 | 38.0 | 44060 | 26356 | 17705 | 50.0* |
| | Cingulate | | | | Cingulate | | |
| | 10855 | 15112 | 82.0* | | 21240 | 22820 | 70.0* |
| | Parietal | | | | Parietal | | |
| | 11516 | 14451 | 77.0* | | 16246 | 27814 | 92.0* |
| | Occipital | | | | Occipital | | |
| | 4543 | 21424 | 140.0* | | 11239 | 32821 | 119.0* |
| Inf Temp | vs Cingulate | | | Inf Temp | vs Cingulate | | |
| 17664 | 10855 | 6808 | 48.0* | 26356 | 21240 | 5116 | 21.0 |
| | Parietal | | | | Parietal | | |
| | 11516 | 6148 | 42.0* | | 16246 | 10110 | 47.0* |
| | Occipital | | | | Occipital | | |
| | 4543 | 13120 | 118.0* | | 11239 | 15117 | 80.0* |
| Cingulate | vs Parietal | | | Cingulate | vs Parietal | | |
| 10855 | 11516 | 661 | 6.0 | 21240 | 16246 | 4994 | 27.0 |
| | Occipital | | | | Occipital | | |
| | 4543 | 6312 | 82.0* | | 11239 | 10001 | 62.0* |
| Parietal | vs Occipital | | | Parietal | vs Occipital | | |
| 11516 | 4543 | 6973 | 87.0* | 16246 | 11239 | 5007 | 36.0 |

* = Asymmetric plaque counts between the regions

**Table 84.** When counting the number of plaques/$mm^2$ in the superficial layers of cortex, this table shows the number regions that had asymmetric plaque counts in the left and right hemispheres in each of the regions examined.

| | SDAT | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Case 8 | | Case 9 | | Case 10 | | Case 11 | | Case 12 | | Case 13 | |
| | Left | Right | Left | Right | Left | Right | Left | Right | Left | Right | Left | Right |
| Frontal | 1 | 4 | 3 | 3 | 4 | 1 | 4 | 1 | 3 | 3 | 1 | 2 |
| Superior Temporal | 4 | 1 | 5 | 4 | 1 | 0 | 2 | 2 | 3 | 1 | 1 | 0 |
| Middle Temporal | 0 | 2 | 5 | 4 | 2 | 1 | 3 | 4 | 2 | 3 | 1 | 2 |
| Inferior Temporal | 0 | 1 | 6 | 5 | 2 | 0 | 3 | 5 | 5 | 5 | 1 | 0 |
| Cingulate | 1 | 2 | 3 | 3 | 5 | 1 | 4 | 5 | 3 | 3 | 1 | 0 |
| Parietal | 1 | 6 | 3 | 4 | 2 | 0 | 3 | 2 | 4 | 2 | 1 | 2 |
| Occipital | 1 | 2 | 3 | 3 | 2 | 3 | 3 | 3 | 2 | 3 | 6 | 2 |

**Table 85.** When counting the number of plaques/$mm^2$ in the deep layers of cortex, this table shows the number of regions that had asymmetric plaque counts in the left and right hemispheres in each of the regions examined.

| | SDAT | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Case 8 | | Case 9 | | Case 10 | | Case 11 | | Case 12 | | Case 13 | |
| | Left | Right | Left | Right | Left | Right | Left | Right | Left | Right | Left | Right |
| Frontal | 4 | 1 | 3 | 0 | 3 | 3 | 1 | 2 | 2 | 0 | 2 | 3 |
| Superior Temporal | 4 | 1 | 4 | 0 | 3 | 2 | 3 | 3 | 2 | 0 | 4 | 3 |
| Middle Temporal | 2 | 1 | 4 | 0 | 1 | 1 | 3 | 2 | 2 | 1 | 4 | 6 |
| Inferior Temporal | 2 | 1 | 4 | 0 | 3 | 1 | 4 | 6 | 5 | 2 | 1 | 3 |
| Cingulate | 1 | 1 | 3 | 0 | 3 | 2 | 3 | 2 | 2 | 0 | 2 | 3 |
| Parietal | 2 | 6 | 3 | 0 | 4 | 1 | 2 | 5 | 5 | 2 | 2 | 5 |
| Occipital | 3 | 1 | 3 | 0 | 3 | 6 | 6 | 2 | 2 | 1 | 3 | 5 |

**Table 86.** When counting the total number of plaques/$mm^2$, this table shows the number of regions that had asymmetric plaque counts in the left and right hemispheres in each of the regions examined.

| | SDAT | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Case 8 | | Case 9 | | Case 10 | | Case 11 | | Case 12 | | Case 13 | |
| | Left | Right | Left | Right | Left | Right | Left | Right | Left | Right | Left | Right |
| Frontal | 2 | 2 | 3 | 1 | 4 | 1 | 2 | 1 | 2 | 2 | 1 | 2 |
| Superior Temporal | 6 | 1 | 4 | 1 | 3 | 1 | 2 | 3 | 2 | 1 | 2 | 2 |
| Middle Temporal | 2 | 1 | 4 | 3 | 2 | 1 | 2 | 3 | 2 | 3 | 1 | 3 |
| Inferior Temporal | 1 | 1 | 4 | 3 | 3 | 1 | 3 | 6 | 5 | 5 | 1 | 2 |
| Cingulate | 1 | 2 | 3 | 2 | 6 | 1 | 4 | 3 | 2 | 1 | 1 | 2 |
| Parietal | 1 | 6 | 3 | 4 | 3 | 1 | 2 | 3 | 5 | 2 | 2 | 4 |
| Occipital | 1 | 1 | 3 | 2 | 2 | 6 | 5 | 1 | 2 | 2 | 6 | 5 |

**Table 87.** When measuring the area of plaques in square microns in the superficial layers, this table shows the number of regions that had asymmetric plaque counts in the left and right hemispheres in each of the regions examined.

| | SDAT | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Case 8 | | Case 9 | | Case 10 | | Case 11 | | Case 12 | | Case 13 | |
| | Left | Right | Left | Right | Left | Right | Left | Right | Left | Right | Left | Right |
| Frontal | 1 | 1 | 3 | 5 | 4 | 1 | 4 | 2 | 5 | 6 | 2 | 1 |
| Superior Temporal | 3 | 1 | 5 | 4 | 4 | 0 | 3 | 2 | 4 | 3 | 2 | 1 |
| Middle Temporal | 0 | 1 | 5 | 5 | 3 | 0 | 3 | 3 | 3 | 2 | 5 | 4 |
| Inferior Temporal | 1 | 1 | 6 | 5 | 4 | 0 | 5 | 6 | 6 | 4 | 1 | 2 |
| Cingulate | 0 | 2 | 4 | 4 | 5 | 1 | 5 | 6 | 2 | 3 | 2 | 2 |
| Parietal | 1 | 5 | 3 | 3 | 3 | 0 | 4 | 2 | 3 | 4 | 2 | 1 |
| Occipital | 0 | 1 | 4 | 4 | 3 | 0 | 4 | 3 | 3 | 4 | 6 | 5 |

**Table 88.** When measuring the area of plaques in square microns in the deep layers, this table shows the number of regions that had asymmetric plaque counts in the left and right hemispheres in each of the regions examined.

| | SDAT | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Case 8 | | Case 9 | | Case 10 | | Case 11 | | Case 12 | | Case 13 | |
| | Left | Right | Left | Right | Left | Right | Left | Right | Left | Right | Left | Right |
| Frontal | 3 | 2 | 5 | 1 | 2 | 4 | 3 | 2 | 3 | 1 | 2 | 3 |
| Superior Temporal | 3 | 4 | 4 | 1 | 2 | 1 | 3 | 3 | 3 | 2 | 4 | 3 |
| Middle Temporal | 3 | 2 | 4 | 1 | 2 | 2 | 3 | 3 | 4 | 4 | 5 | 6 |
| Inferior Temporal | 3 | 3 | 4 | 1 | 2 | 2 | 6 | 5 | 6 | 6 | 2 | 4 |
| Cingulate | 1 | 2 | 5 | 1 | 3 | 3 | 3 | 3 | 2 | 1 | 2 | 3 |
| Parietal | 3 | 5 | 5 | 6 | 5 | 2 | 6 | 5 | 5 | 2 | 2 | 5 |
| Occipital | 4 | 2 | 5 | 1 | 4 | 4 | 6 | 5 | 3 | 2 | 3 | 4 |

**Table 89.** When measuring the total area of plaques in square microns, this table shows the number of regions that had asymmetric plaque counts in the left and right hemispheres in each of the regions examined.

| | SDAT | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Case 8 | | Case 9 | | Case 10 | | Case 11 | | Case 12 | | Case 13 | |
| | Left | Right | Left | Right | Left | Right | Left | Right | Left | Right | Left | Right |
| Frontal | 1 | 1 | 3 | 2 | 4 | 3 | 2 | 2 | 4 | 3 | 2 | 2 |
| Superior Temporal | 5 | 2 | 4 | 2 | 4 | 1 | 3 | 3 | 3 | 2 | 4 | 3 |
| Middle Temporal | 1 | 1 | 5 | 3 | 3 | 0 | 3 | 2 | 3 | 2 | 5 | 6 |
| Inferior Temporal | 1 | 1 | 5 | 4 | 3 | 0 | 5 | 6 | 6 | 4 | 3 | 3 |
| Cingulate | 1 | 3 | 5 | 3 | 4 | 1 | 3 | 6 | 2 | 2 | 4 | 2 |
| Parietal | 2 | 5 | 4 | 4 | 3 | 0 | 2 | 4 | 3 | 3 | 4 | 3 |
| Occipital | 1 | 1 | 4 | 2 | 3 | 1 | 4 | 3 | 1 | 4 | 6 | 5 |

**Table 91.** Correlation values (r) between the volume of each lobe/CCV and the number and area of plaques

| | Frontal | | Temporal | | Parietal | | Occipital | |
|---|---|---|---|---|---|---|---|---|
| | Left | Right | Left | Right | Left | Right | Left | Right |
| Number of plaques (Superficial) | -0.054 | -0.675 | 0.561 | -0.087 | -0.205 | 0.226 | -0.008 | 0.355 |
| Number of plaques (Deep) | -0.538 | -0.614 | 0.809 | 0.008 | 0.165 | 0.076 | -0.169 | -0.663 |
| Number of plaques (Total) | 0.093 | -0.692 | 0.253 | -0.306 | -0.730 | 0.200 | -0.056 | 0.279 |
| Area of plaques (Superficial) | -0.180 | -0.811 | 0.921 | 0.172 | -0.471 | 0.025 | 0.363 | 0.450 |
| Area of plaques (Deep) | -0.574 | -0.657 | 0.960 | -0.081 | -0.181 | -0.168 | 0.115 | -0.499 |
| Area of plaques (Total) | -0.434 | -0.773 | 0.941 | 0.079 | -0.226 | -0.080 | 0.282 | 0.141 |

**Table 92** Correlation values (r) between the number of plaques and the area of plaques

| | Frontal | | Temporal | | Parietal | | Occipital | |
|---|---|---|---|---|---|---|---|---|
| | Left | Right | Left | Right | Left | Right | Left | Right |
| Superficial | 0.710 | 0.921 | 0.804 | 0.833 | 0.799 | 0.892 | 0.698 | 0.130 |
| Deep | 0.934 | 0.997 | 0.935 | 0.982 | 0.904 | 0.775 | 0.906 | 0.935 |
| Total | 0.592 | 0.771 | 0.549 | 0.765 | 0.385 | 0.655 | 0.728 | -0.286 |

**Table 93** Variation in methods used to quantify senile plaques.

| Reference | Hemisphere | Method | Magnification | Number of fields | Quantification |
|---|---|---|---|---|---|
| 24 | Left | von Braunmuhl | x 80 | 10 random | Mean |
| 38 | Right | Glees & Marsland | x 80 | 50 random | Lesions/unit volume |
| 27 | Left + right (mean) | von Braunmuhl | 1.3mm (field area) | 5 random | Mean plaque count for for each brain |
| 74 | NK | King's | x 250 | Point count on minimum 2,500 points | % cortex occupied by plaques |
| 109 | NK | Thioflavine S | x 20 | NK | Graded 0-3<br>0 = minimal changes<br>1 = slight<br>2 = moderate<br>3 = severe |
| 110 | Left | Modified Palmgren | x 10 | NK | Graded 0-3<br>0 = absent<br>1 = max 2 plaques/field<br>2 = 3-10 plaques/field<br>3 = > 10 plaques/field |
| 175 | Left + right separately | Bielschowsky | x 200 | 5 adjacent fields | Mean plaque count per field |

NK = Not known

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