SOME OBSERVATIONS ON THE DEPTH AND NERVE-CELL CONTENT OF THE SUPRAGRANULAR CORTEX IN NORMAL AND MENTALLY DEFECTIVE PERSONS

BY

R. M. NORMAN

Burden Mental Research Trust, Stoke Park Colony, Bristol

(RECEIVED 12TH APRIL, 1938)

Introduction

THE observations recorded in this paper have been made to test the validity of certain statements made by writers on mental deficiency as to the changes present in the cerebral cortex of the mental defective of no particular pathological type. While a small group of pathological rareties has received intensive study by neuropathologists, as regards the less distinctive cerebral abnormalities in the majority of institutional defectives the histologist is still in somewhat the same position as was the psychologist before the introduction of the Binet Scale of tests ; the frontiers of abnormality are as yet ill-defined. Nevertheless, in this latter group many microscopical abnormalities have been noted by various investigators, and to some of these findings reference may be made. According to Tredgold (1929), the nerve cells of the primary ament when compared with those of the normal cerebral cortex are characterized by : (1) numerical deficiency ; (2) irregular arrangement ; and (3) imperfect development of individual cells. These changes, he pointed out, are most obvious in the small and medium-sized pyramidal nerve cells. Bolton (1914), on the basis of micrometric measurements of three cortical areas in four ament and three normal brains, concluded that amentia is associated with " sub-evolution " of that part of the cerebral cortex which phylogenetically and ontogenetically is the last to develop, namely the supragranular layers, this sub-evolution being demonstrable by measurement of the cortical depth. Later observers have, however, failed to demonstrate such generalized reduced cortical depth in aments. In collaboration with Professor Berry (1934) I examined eight cortical areas in each of four defective brains from the point of view of depth of cell layers and numbers of nerve cells. The result of this investigation supported in the main Tredgold's views and not Bolton's. More recently Ashby and Stewart (1934) studied the depth of supra- and infra-

granular cortex in 62 defective and nine normal brains and were unable to demonstrate any statistically significant relationship between depth of cortex and mental ability.

During the last few years there has been accumulating at Stoke Park Colony a large collection of defective and normal brains. It has thus become possible to re-investigate some of the issues raised in the foregoing discussion, and observations have been made to provide, if possible, answers to the following questions : (1) Is thinness of the supragranular nerve cell layers a common feature of defective cortices ? (2) Is the average nerve-cell count in these layers reduced in defectives ? (3) Is the distribution of nerve cells throughout the section less uniform in defective than in normal brains examined by identical methods ? It is obvious that a statistical approach has advantages over an impressionistic one in evaluating the results of such an investigation.

Method of selecting Brains and Cortical Areas for Examination

Measurements of depth of supragranular cortex and counts of nerve-cell bodies in the supragranular cortex have been carried out in groups of some 30 ament and 30 normal brains. The ament brains were selected from the general collection at Stoke Park Colony in the following manner. All brains showing obvious macroscopic abnormalities, such as porencephaly, hydrocephalus, tuberosc sclerosis ; lobar sclerosis and microgyria were excluded. Certain less obvious pathological types that had been encountered during routine microscopical examination, such as juvenile amaurotic idiocy and meningo-vascular and parenchymatous syphilis, were also excluded. According to this method of selection, therefore, Mongolian brains were included in the group to be examined. The majority of these ament brains came from defectives of the imbecile and idiot classes.

Three cortical areas from the left cerebral hemisphere have been examined in the normal and defective groups. They were from :

1. Bolton's " visuo-psychic " area (Area O.A. of von Economo). The part of this area which was examined lay immediately posterior to the point where the parieto-occipital fissure indents the convexity of the hemisphere.
2. The Frontal Pole (Area F.E. of von Economo). In this area the part selected for examination came from the convexity of the hemisphere at a point approximately half an inch equidistant from the great longitudinal fissure and the extremity of the frontal pole.
3. The Supramarginal Gyrus (Area P.F. of von Economo). The anterior and dorsal part of the gyrus was selected.

All these are examples of von Economo's six-layered type of isocortex. They all have a well-marked granular layer (L.IV) and the extent of the pyramidal cell layers of the supragranular cortex (L.II and L.III) may be clearly demarcated. It is in such association areas that Bolton and Tredgold have observed the most pronounced abnormalities which they have described as characteristic of the ament brain.

These areas have been taken from a total group of 39 normal and 54 defective brains. For reasons given later in this paper it was not found practicable to examine all three areas in every one of these individual brains. The smaller groups in which measurements and cell counts were made differed therefore among themselves as regards the constituent brains from which sections had been prepared. Since, however, the age distribution of these smaller groups did not materially differ from those of the main series given in Table I, this information has not been repeated in the subsequent detailed account of the findings in the three areas selected.

TABLE I

Age (yrs.) . .	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	TOTAL
Normals . .	1	3	4	5	7	3	2	5	6	2	0	1	39
Defectives	1	5	14	14	9	5	3	3	0	0	0	0	54

Age distribution of total normal and defective groups.

Mean age of normals : 27 years. Mean age of defectives : 18 years.

Sex distribution : normals : ♂ 24, ♀ 15. Defectives : ♂ 27, ♀ 27.

Mental grade of defectives : feeble-minded 5, imbecile 30, idiots 19.

Technique

Method of preparing sections.—Both normal and defective brains were fixed in 10 per cent. formol-saline solution. In the case of the defectives, formol-saline solution was injected into the skull through the orbit as a routine procedure immediately after death. The time occurring between death and autopsy in the normal group was about 24 hours and in the defective group 24 to 48 hours. In removing blocks of tissue from the fixed brain the incisions dividing the gyrus were made as far as possible at right angles to the surface and also to the direction of the gyrus. The blocks of cortex so removed were stored in 5 per cent. formol-saline. Sections 25μ in thickness were cut on a freezing microtome and received into distilled water. The sections were then mounted on albuminized slides and allowed almost to dry in a warm atmosphere so that they adhered to the slide. They were then stained either with 1 per cent. aqueous Toluidin blue or 1 per cent. aqueous Cresyl violet, differentiated with Gothard's solution and absolute alcohol, cleared in xylol, and mounted in Mersol. In the event of a section becoming partially detached from the slide, this preparation was rejected and another stained. It was sometimes found that while satisfactory sections could be prepared in this way from one area, the sections cut from another area of the same brain were unsatisfactory, either because of œdema or poor staining of the nerve cells or because of the appearance of small holes in the glial ground substance. Such artefacts, which were encountered more frequently in the defective group, made accurate cell counting impossible. All sections exhibiting these appearances were therefore rejected and replaced by others from brains that proved

to be satisfactory. It thus came about that the constitution of the groups of normal and defective brains varied somewhat according to the cortical area examined.

Method of measuring depth of supragranular cortex.—Measurements were confined to the crowns of the gyri. The area of the section in which measurements were to be taken was determined in the following manner. The lines of demarcation between cortex and central core of white matter on either side of the section, corresponding to the walls of the gyrus, were marked on the back of the slide with a blue pencil. These two lines were then extended so as to mark off an area in the crown of the section. The slide was then transferred to the movable stage of the microscope (Leitz objective No. 3, draw tube at 170 mm.), and a number of measurements taken of the combined depths of layers II and III in the previously demarcated area of the cortex, a Leitz "Schraubenmikrometer" being used (eyepiece $\times 10$). The left-hand blue line having been recognized, a measurement was taken in a vertical direction between the most superficial point of the external granular layer (L.II) and the base of the deepest large pyramidal cell of L.III. The slide was then moved slightly to the left and another measurement made, this time working from below upwards. In this way a number of estimations of the combined depth of these two layers of the cortex were made until the right-hand blue-pencil line came into view. The extent of the demarcated area of the crown of the gyrus necessarily varied between sections, so that a varying number of these measurements (on the average 15) were made per section. The individual measurements were recorded in units of the scale of the micrometer eyepiece. At the magnification used one division of the scale = 41.66μ .

Method of cyton counting.—After preliminary trials on small groups of normal and defective sections, it was decided to adopt the following method. The cyton counts were confined to the supragranular cortex and to the middle of the pyramidal nerve cell layers. The depth of L.II and L.III was first estimated as described above and the midpoint of this depth of cortex brought into the centre of the microscopical field. The micrometer eyepiece was then exchanged for a Leitz Ehrlich ocular $\times 6$ set at position 6. The objective of the microscope was then changed for a No. 6 and the number of nerve-cell bodies visible in the square field counted. The side of this square measured 200μ . All neuroncytons, whether large or abnormally small, were counted. In some of the defective sections difficulty was occasionally experienced in deciding whether a cyton belonged to a minute neurone with little stainable cytoplasm or to a glial cell. In such cases the shape and character of the nucleus was taken as distinguishing features, a nucleus having a nucleolus being considered as identifying a neuroncyton. Seven such cell counts were made in the crown of the section. Owing to the method adopted it was impossible to tell beforehand whether one was going to count in an area of the cortex possessing numerous or few nerve cells. Any bias in the selection of microscopic fields was therefore avoided. If the area contained a large blood vessel a count was not made, and another position found. This rule was adopted in both normal and defective sections.

In examining the parietal area (P.F.), in addition to the method of cyton counting described above, a more extensive survey of the crown of the section was made. Instead of seven counts using a large square, 20 counts per section were made using a smaller square in the eyepiece. The sides of this square microscopic field measured 100μ . Apart from this difference, precisely the same method of counting in the middle part of L.II and L.III was adopted.

Measurement of Depth of Layers II and III in Normal and Defective Cortices

In none of the three selected areas has measurement of the supragranular cell layers demonstrated a significant difference in mean between normals and defectives.

TABLE II

	AREA O.A.	AREA F.E.	AREA P.F.
No. of normal sections	29	27	32
No. of defective sections	34	27	32
Normal mean	22.50	23.78	26.51
Defective mean	21.09	23.64	25.94
Difference in mean	1.41	0.14	0.57
Standard error of difference ..	± 0.74	± 0.99	± 0.93
Difference $\div$ S.E.	1.90	0.14	0.61
Significance	—	—	—

Comparison of mean depth of cortex.

It will be seen in Table II that only in the visuo-psychic area O.A. was a difference approaching significance discovered. While it is possible that with much larger numbers of cases a result in favour of the normals would have been obtained, such small differences would have little meaning from the neurological point of view. In any case, such differences may well be regarded as the expression of the fact that normal brains are on the average considerably larger than those of defectives. Thus the hypothesis that amentia is associated with a specific reduction in depth of the supragranular cortex receives no confirmation from these findings.

Cyton Counts in the Middle of Layers II-III in Normal and Defective Cortices

Comparison of mean cyton counts.—In contrast to the measurements of cortical depth, the method of cell counting revealed an important difference between the two groups of brains.

TABLE III

	AREA O.A.	AREA F.E.	AREA P.F.
No. of normal sections	30	27	30
No. of defective sections	38	27	32
Normal mean	21.19	16.71	16.62
Defective mean	25.23	18.68	15.08
Difference in mean	4.04	1.97	1.54
Standard error of difference ..	± 1.23	± 1.16	± 1.01
Difference $\div$ S.E.	3.28	1.70	1.52
Significance	++	—	—

Comparison of mean cyton counts.

It will be seen in Table III—area O.A.—that the number of neuroncytons per unit area in the defective sections significantly exceeded the normal figure. To avoid any possible misconception as to the meaning of this observation it may be emphasized that the nerve cells counted in the defective sections included many examples of small cell types, that this crowding together of defective cytons is to be regarded as an indication of cerebral inferiority and is in marked contrast to the well-developed, well-spaced-out cells of the normal cortex.

Variability of cyton counts.—The most striking and constant differences between the two groups of brains were found when the results of the cell counts were analysed for differences in variance (i.e. a measure of variability, the mean square deviation from the mean or standard deviation squared). The total variance may be split into two parts: the “variance within sections,” which gives a measure of the amount by which the separate cell counts made in the same section vary among themselves; and the “variance between sections,” which gives a measure of the amount by which the average cell counts of sections vary between themselves from section to section, i.e. in this series from brain to brain. The former variance thus indicates whether the nerve cells are distributed with more or less uniformity throughout the part of the gyrus sampled by the cell counts. The variances of the cell counts, having been calculated in the normal and defective series, were then compared using Fisher’s *z* method (1934). The term *z* is derived from the difference between half the Napierian logarithm of each variance. The significance of the difference between the variances was then ascertained either by using the table of *z* or, when the number of observations was large and not very unequal, by calculating the standard error of *z*.

Tables IV, V, and VI show that the variance between sections was significantly greater in all three areas among the defectives than among normals. This may be taken as an indication that certain cortical areas from a series of defective brains such as those examined in this investigation show a greater variability in the average nerve-cell content of the supragranular cortex as compared with normal brains. While it is true that on the average there were more cytons per unit area in the defective group, the defective series differed from the normal not only in providing sections in which the nerve cells were more crowded together than in any normal, but also in showing examples of greater sparseness of nerve cells than did any normal.

TABLE IV

			DEGREES OF FREEDOM	SUMS OF SQUARES	MEAN SQUARE	$\frac{1}{2} \log_e$
Defectives	{	Normals				
		Within sections	180	2,544.00	14.13	1.3242
		Between sections	29	1,801.76	62.13	2.0647
		Defectives				
{	Within sections	228	5,495.17	24.10	1.5911	
	Between sections	37	12,036.4	325.3	2.8924	

Analysis of variance. (Area O.A.)

			z	S.E.	z/S.E.	SIGNIFICANCE
Within sections			0.2669	0.07	3.81	++
Between sections			0.8277	0.18	4.60	++

Comparison of variance of normals and defectives.

TABLE V

			DEGREES OF FREEDOM	SUMS OF SQUARES	MEAN SQUARE	$\frac{1}{2} \log_e$
Defectives	Normals	{ Within sections	162	1,519.99	9.383	1.1195
		{ Between sections	26	1,923.04	73.96	2.1518
		{ Within sections	162	2,403.42	14.84	1.3487
		{ Between sections	26	4,635.75	178.3	2.5918

Analysis of variance. (Area F.E.)

			z	S.E.	z/S.E.	SIGNIFICANCE
Within sections			0.2292	0.079	2.90	++
Between sections			0.4400	0.196	2.24	+

Comparison of variance of normals and defectives.

TABLE VI

			DEGREES OF FREEDOM	SUMS OF SQUARES	MEAN SQUARE	$\frac{1}{2} \log_e$
Normals	Within sections		180	2,610.53	14.50	1.3371
	Between sections		29	1,914.58	66.02	2.0949
Defectives	Within sections		192	3,007.99	15.67	1.3759
	Between sections		31	4,846.56	156.3	2.5259

Analysis of variance. (Area P.F.)

			z	S.E.	z/S.E.	SIGNIFICANCE
Within sections			0.0388	0.073	0.53	—
Between sections			0.4310	0.183	2.36	+

Comparison of variance of normals and defectives.

The most important finding, however, was that in two areas the variance within sections was significantly greater in the defective group, while in the third area the difference though non-significant was in the same direction. This means that within a single section the cytons tended to be more irregularly grouped in the defectives than in the normals. This abnormal and irregular arrangement of nerve cells is often easily distinguishable in defective sections by ordinary microscopical inspection and has been reported by other observers. To reduce this qualitative observation to terms of measurement is not an easy task, and while it is probable that many different methods carried out upon sufficient numbers would yield a significant difference between defectives and normals, the actual magnitude of the difference found would depend upon how accurately such methods estimated the greater irregularities of the defective group. This point is well illustrated in the following re-examination of area P.F., using in this case a counting square of smaller dimensions and counting more fields (see Technique).

It will be seen in Table VII that the new method of counting has yielded highly significant differences between the two groups as regards variances between and within sections. The magnitude of such observed differences thus depends largely on the refinement of the technique employed, and no doubt further research would improve the arbitrary methods employed in this investigation—which have, nevertheless, sufficed to detect significant differences between the two groups of brains.

A comparison of the results of cyton counts in Mongolian, non-Mongolian defective and normal sections.—The foregoing analyses have demonstrated differences between normal cortices and those of a mixed group of defectives including Mongols. It was considered profitable to analyse the results of the cell counts in area O.A. for the three groups separately in order to discover

to what extent the abnormalities of the defective group were due to the admixture with Mongols. The results of this comparison are given in Table VIII.

TABLE VII

Area P.F. (Smaller counting square.)

Comparison of mean cyton counts : normals 3·8891 ; defectives 3·9266. Difference $0\cdot0375 \pm 0\cdot2112$ ($0\cdot18 \times \text{S.E.}$) non-significant.

				DEGREES OF FREEDOM	SUMS OF SQUARES	MEAN SQUARE	$\frac{1}{2} \log$
Normals	Within sections	..	..	608	1,697·25	2·792	0·5134
	Between sections	..	..	31	179·87	5·802	0·8791
Defectives	Within sections	..	..	608	2,441·25	4·015	0·6950
	Between sections	..	..	31	704·29	22·72	1·5617

Analysis of variance. (Area P.F.)

				z	S.E.	z/S.E.	SIGNIFICANCE
Within sections	..	..		0·1816	0·041	4·43	++
Between sections	..	..		0·6826	0·180	3·79	++

Comparison of variance of normals and defectives.

TABLE VIII

				NORMAL	MONGOL	NON-MONGOLIAN DEFECTIVES
No. of sections	..	..	..	30	11	27
Mean	..	..	..	21·19	24·45	25·55
Difference in mean	..	..	..	3·26		1·10
S.E. of difference	..	..	..	$\pm 0\cdot76$		$\pm 1\cdot51$
Difference $\div$ S.E.	..	..	..	4·29		0·73
Significance	..	..	..	++		—

Comparison of mean cyton counts in normal, Mongolian and non-Mongolian defective cortices. (Area O.A.)

The results of this analysis indicate that the number of cytons per unit area in the Mongol sub-group significantly exceeded the normal figure but did not differ significantly from that of the non-Mongolian defective group. Thus the relative crowding together of nerve cells was a feature common to both groups of defectives. The analysis of variance of cell counts in the three groups is shown in Table IX.

TABLE IX

				DEGREES OF FREEDOM	SUMS OF SQUARES	MEAN SQUARE	$\frac{1}{2} \log_e$
Non-Mongolian defectives	Normals	Within sections		180	2,544.00	14.13	1.3242
		Between sections		29	1,801.76	62.13	2.0647
	Mongols	Within sections		66	1,463.45	22.17	1.5494
		Between sections		10	2,155.66	215.6	2.6868
	defectives	Within sections		162	4,031.73	24.89	1.6073
		Between sections		26	9,815.05	377.5	2.9668

Analysis of variance. (Area O.A.)

				z	1 PER CENT. POINT	5 PER CENT. POINT	SIGNIFICANCE
Within sections	..	..		0.2252	0.226	0.161	++
Between sections	..	..		0.6221	0.538	—	++

Comparison of variance of normals and Mongols.

				z	1 PER CENT. POINT	5 PER CENT. POINT	SIGNIFICANCE
Within sections	..	..		0.0579	—	0.178	—
Between sections	..	..		0.2800	—	0.501	—

Comparison of variance of Mongols and non-Mongolian defectives.

It will be seen that, as in the total defective group, the variance of counts within and between sections was significantly greater in the Mongol group than in the normal. When, however, the Mongol and non-Mongol defective groups were compared, no significant differences in variability of counts either within or between sections was discovered. The greater variability of the total defective group compared with the normal cannot, therefore, be attributed to the inclusion of Mongols.

Discussion

This investigation has shown that in a representative group of institutional defectives of no particular pathological type abnormalities of cortical structure may be demonstrated by a relatively simple and arbitrary technique. The main negative finding was that micrometric measurements of the depth of the supragranular cortex failed to reveal any appreciable difference between normal and defective sections. Bolton's conclusion, that as a general rule this part of the cortex is thinner in mental defectives, was not, therefore, con-

firmed. The results of the neuroncyton counts, on the other hand, indicated that, in the main, two processes making for abnormality had been operative in the defective brains: the one producing an excessive crowding together of the nerve-cell bodies, the other producing the opposite effect, an undue sparseness leading to a low cell count. These effects were to be seen not only in the average cyton content (variability between sections), but also in the patchy distribution of cytons within the section itself (variability within the sections).

Before discussing the neurological significance of these abnormalities it may be pointed out that in the development of the normal cerebral cortex several factors governing the number and arrangement of the constituent neurones come into play. As is well known, the development of the crowded foetal cortex into the adult state, where the nerve cells are well spaced out, is associated primarily with the rapid surface expansion of the growing cerebral hemispheres (Donaldson, 1895). Besides this general and largely mechanical process, there are inherent factors which produce the final organization of the numerous cortical areas appropriate to the species. In man von Economo and Koskinas (1925) have distinguished 52 principal cortical areas, each with a characteristic structure which may be defined in terms of depth of layers and size and number of the neuroncytons composing these layers. There are also other, less easily measured, differences between these areas. For example, in the deeper part of L.III in area O.A. the nerve-cell bodies are normally arranged in short columns, while in area F.E. this columnar distribution is much less evident. That the appearances of anatomically identical areas from presumably normal brains may vary considerably in ordinary post-mortem material is evident from the results of the present investigation, but it is noteworthy that in defective brains this variability is considerably greater. The conclusion may legitimately be drawn that some at any rate of the differences in mentality existing between normal and mentally defective persons are due to the greater frequency and degree of such structural abnormalities in the defective group.

As has already been stated, the increased variability of the cyton counts in defectives may be attributed to the operation of two processes, one making for sparseness, the other for crowding together of the nerve-cell bodies. Taking the group as a whole, the latter factor appears to be the more common and may be interpreted as a sign of inhibited development of the ament brain. This relative crowding together of cytons may thus be regarded as the microscopical counterpart of the small size of the majority of these defective brains as compared with the normal. In this respect, then, the defective brains show signs of retarded neurone development.

With regard to situations in the defective brains in which a paucity of nerve cells per microscopic field was found, it may be said that the problem of pathogenesis is much more complex. There is no analogy here with the foetal state. The wider separation from each other of the normal adult nerve-cell bodies is due in part to the greater development of their processes, the cell bodies and nuclei being larger as a general rule in pyramidal nerve cells the processes of which traverse a longer course in the nervous system (Bok, 1936).

It was certainly not the case that the widely separated cytons in those sections from defectives which exhibited nerve-cell paucity were better developed than those present in more normally populated areas. Thus the low cyton counts per microscopic field cannot be attributed to a compensatory hyper-development of the nerve cells. Areas of relative nerve-cell poverty were not uncommonly encountered in some of the normal brains, and as is well known the middle of the third layer of the cortex seems to be peculiarly liable to exhibit such changes. The patchy "areas of clearing" in the defective cortex cannot, therefore, be considered to be a change peculiar to mental defectives, but merely occur more frequently and often to a greater degree than in the normal series. It is probable that many ætiological factors are operative in setting up this picture of relative nerve-cell deficiency. Some of the less conspicuous areas devoid of nerve cells may have resulted from a malformation of the cortical pattern: that is to say, in the final stage of organization less than the appropriate number of nerve cells may have developed in that part of the cortex. It will be recalled that in the middle and inferior temporal convolutions of the normal brain the nerve cells in L.III are arranged in a patchy way that would constitute an abnormality if found in other parts of the cortex. Thus microscopic fields poorer in nerve cells than fields in the immediate vicinity may arise in a gyrus without the intervention of destructive influences. Some of the patchy "areas of clearing" in the defective cortices may thus result from faulty development. On the other hand, in several instances the poverty of nerve cells was too gross and generalized to admit of this explanation, quite extensive fields having the appearance of cortical devastation being sometimes observed in the present series of defective brains; and this even though the method of selecting the brains was calculated to exclude cases where such changes might have been expected. It is by no means clear what significance is to be attached to such presumably degenerative phenomena, since it is difficult to assess their chronological onset. If such lesions occur during the developmental stages of the cortex they may well play a primary part in the complex ætiology of amentia; if, on the other hand, they are merely coincidental and appear in later life as the expression of the less effective resistance on the part of a poorly developed organ to environmental stress, their ætiological significance is of secondary importance. Only a detailed examination of individual cases can be expected to throw light on this problem.

Finally, it may be pointed out that while the micrometric measurements of cortical depth recorded in this paper have not confirmed Bolton's views as to the anatomical basis of amentia, the abnormalities which have been demonstrated in these defective brains lend support to the spirit if not to the letter of his thesis: namely, that mental deficiency is commonly associated with structural anomalies in those parts of the nervous system which phylogenetically and ontogenetically are of recent acquisition.

Summary

A microscopic examination of sections from three cortical areas (O.A., F.E., and P.F. of von Economo) has been carried out in groups of some 30

normal and 30 mentally defective brains. Brains exhibiting gross pathological macroscopic appearances were excluded. The combined depth of layers II and III of the supragranular cortex has been measured and a series of neuron cyton counts made in the middle of this pyramidal cell lamina.

No significant difference in mean depth of cortex was demonstrated between normals and defectives.

There was no indication that a general poverty of nerve cells was an important characteristic of this group of ament brains. On the contrary, in the visuopsychic area the average number of cytons per microscopic field in the series from defectives significantly exceeded the normal figure. This diminution of normal spacing between poorly developed nerve cells is highly characteristic of the defective cortex. Cellular richness *per se* is not, therefore, in this case to be equated with functional superiority.

Microscopic fields poor in nerve cells were more often found in ament than in normal cortices, but the general effect of such cases was not sufficiently marked in the present investigation to reduce the average nerve-cell count below the normal level.

The distribution of neuron cytons throughout the middle portion of the supragranular cortex in defectives was significantly less uniform than in the normals. This irregular arrangement of nerve cells in the mental defective, suspected from the qualitative observations of earlier observers, finds confirmation in the results here presented.

The average nerve-cell content of sections was significantly more variable in the defective group than in the normal.

No significant differences were found between Mongol and non-Mongolian defectives as regards mean cell content or variability of nerve-cell distribution.

This investigation supports the view that amentia is commonly associated with structural abnormalities of those parts of the neopallium which have been most recently acquired.

It is a pleasure to record my indebtedness to Professor R. J. A. Berry, Director of Medical Services at Stoke Park Colony and Chairman of the Burden Mental Research Trust, for much valuable advice and encouragement; to Dr. J. A. Fraser Roberts, Principal Investigator to the Burden Mental Research Trust, for his advice and assistance in carrying out the statistical analysis; and to Dr. A. L. Taylor, Pathologist to the Bristol General Hospital and to Stoke Park Colony, who provided the collection of normal brains and has taken an active interest in the investigation.

REFERENCES

- Berry, R. J. A., and Norman, R. M. (1934). *J. Neurol. Psychopath.*, **14**, 289.
 Bok, S. T. (1936). *Verhandelingen der Koninklijke Akademie van Wetenschappen te Amsterdam Afdeling Natuurkunde* (tweede sectie), Deel XXXV, No. 2.
 Bolton, J. S. (1914). *The Brain in Health and Disease*, Chapter 6. London: Edward Arnold.
 Donaldson, H. H. (1895). *The Growth of the Brain*, p. 238. London: Walter Scott.
 Economo, C. von, and Koskinas, G. N. (1925). *Die Cytoarchitektonik der Hirnrinde des erwachsenen Menschen*. Wien u. Berlin: Julius Springer.
 Fisher, R. A. (1934). *Statistical Methods for Research Workers*. 5th ed. Edinburgh: Oliver and Boyd.
 Stewart, R. M. (1934). *Proc. roy. Soc. Med.*, **28**, 1, 786.
 Tredgold, A. F. (1929). *Mental Deficiency*. 5th ed., p. 78. London: Baillière, Tindall and Cox.