Dean Liddon and a Catholic priest. In the end, as not infrequently happens in such cases, he found himself unable to accept any system of dogmatic religion. He, however, retained an interest in the affairs of the Church of England, and stoutly as he maintained his own views, respected those of others. He believed that beyond man's finite understanding there is an Infinite Purpose. As he surveyed the future untiring and confident, he looked back upon a life of high endeavour and solid achievement, honoured by his own profession; honoured, too, by those others with whom he had laboured for so many years. Need man wish more? Need more be said?

W. NORWOOD EAST.

Part I.—Original Articles.

*The Beattie Smith Lectures on Insanity for 1926.** By RICHARD J. A. BERRY, M.D., F.R.C.S., F.R.S.Edin., Professor of Anatomy, including Histology, in the University of Melbourne; Honorary Psychiatrist to the Children's Hospital, Melbourne; Honorary Consulting Psychiatrist to the Melbourne Hospital, and Member of the Royal Medico-Psychological Association.

LECTURE I.—THE PRINCIPLES OF NEUROLOGY.

THE nervous system of all vertebrates is built up of long conducting, specialized cells, termed *neurons*. In order to function, these neurons, or nerve-cells, must be linked together in chains or arcs. Each neuron in the chain or arc is structurally separated from other neurons by a break termed a *synapse*. The structural elements of a neuronic arc are, therefore, as follows:

1. A sensitive receiving organ—the *receptor* or sense-organ.
2. A centrally conducting receptor bipolar neuron.
3. One or more short connector or *internuncial* neurons.
4. A peripherally conducting *effector* multipolar neuron.
5. An *effector* apparatus—for example, a muscle or a gland.

The phenomena of the nervous system are much more easily understood if the terms "receptor" and "effector" are uniformly utilized instead of the older "sensory or afferent" and "motor or efferent." In fact, the older terms are frequently quite inaccurate,

* The late Dr. W. Beattie Smith, of Melbourne, in the expressed belief that "both the Profession and the Public were in need of education on the nationally important problem of Insanity," bequeathed to the University of Melbourne the necessary funds for the establishment of an annual course of lectures. The 1926 series, in the regrettable absence through illness of Professor Sir John Macpherson, were delivered by Professor Berry, in December, 1926, in Melbourne, and in April–May, 1927, in New York, U.S.A., at the Cornell University.

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inasmuch as many effector neurons, for example, are not concerned in motor phenomena. Further, the great clinical importance of endeavouring to refer all nerve phenomena to their appropriate sides of the neuronic arc may be shown as follows:

1. Receptor neurons		Locomotor ataxia.
2. Internuncial neurons	Normal	Psychology
	Abnormal	Psychiatry.
3. Effector neurons		Hemiplegia.

As regards the *receptor* or "*sense*"-*organs* of the neuronic arc, these vary from simple structures like naked axons, to complex pieces of apparatus, like the organ of Corti. It is a mistake, for it leads to confusion, to term these receptors "nerve-endings" or "peripheral terminations of axons," because they really mark the commencing point of nerve stimulation.

The receptor organs of viscera, arousing enteroceptive impulses, are usually naked axons themselves. They respond to chemical, mechanical, physical, or other minimal stimuli.

The receptor organs of the locomotory system, arousing proprioceptive impulses, comprise muscle spindles, corpuscles of Golgi, corpuscles of Pacini, and the semicircular canals. Enteroceptive and proprioceptive impulses are thus concerned only with the body itself.

Exteroceptive impulses, on the other hand, are conveyed to the brain from the physical world around and outside the body, and are largely concerned in arousing consciousness. They comprise, in the skin, receptor organs for touch, temperature and pressure; the relatively feebly developed (in man) olfactory organ of smell; the rods and cones for vision; the organ of Corti for hearing, and many others. It is thus a serious mistake to speak and think only of the "five senses" of man. Man possesses about twenty "senses," but even these "senses" are limited, and only put man into conscious touch with a limited part of the physical world around him. As regards the long conducting receptor and effector neurons of the neuronic arc, medical attention has for the most part been chiefly, and for too long a time, devoted solely to these elements of the nervous system. In the phenomena of mind and its aberrations, it is the shorter, internuncial neurons which are of supreme importance, and to these an insufficient amount of attention has been paid, and yet the evolution of this most important nerve element of the neuronic arc is most instructive.

According to Ramon y Cajal, the nervous system has passed through five stages, which, from the standpoint of its structural element, the neuron, are as follows:

1. The epoch of irritability.
2. The epoch of the reflex arc.

3. The epoch of the inter-segmental reflex neuron.
4. The epoch of the supra-segmental reflex neuron.
5. The epoch of the psycho-associational neuron.

In the last two evolutionary stages the internuncial neuron is the dominating factor.

The epoch of irritability.—Here a receptor cell receives a chemical or physical stimulus, and transmits it direct to an adjacent effector or contractile (motor) cell. Examples of this primitive type of nervous system are seen in the Sponges, and may exist in the myenteric or gut-wall reflexes of man.

The epoch of the reflex arc.—The receptor and effector cells are here elongated to form a simple neuronic reflex arc. A receptor stimulus, from a limited area, is transferred, through the now elongated cells, to an extensive area of reaction, over several effector cells. The nervous system of Cœlenterates is of this type and doubtfully the patellar reflex of man.

The epoch of the intersegmental reflex neuron.—Here there is introduced, for the first time in the evolution of a nervous system, a third, interpolated, or *internuncial*, neuron, between the receptor and effector limbs of the neuronic arc. It is this third, or internuncial, neuron which is eventually utilized by Nature, to give those phenomena which we term "mind." The neuropile of the earthworm contains the internuncial or third neurons in a primitive form, and most of the spinal cord reflexes of man are compounded of neuronic arcs of this order. It is important to note and remember that the type of internuncial neuron differs in the segmented portions of the neuraxis, from the more recently added supra-segmental additions. In all segmented animals, such as most vertebrates lower than the mammal, the reflex neuronic arc and the inter-segmental internuncial neuron suffice to regulate the motor reactions in the behaviour of the animal. All the bodily motions are *immediate* responses to the stimulus—that is, there is no delay in the motor response to the stimulus, and the nature of that response can be predicted with certainty. The reactions of such animals to their environment will always be the same, and the combinations of these stereotyped performances will be limited in scope and rigid also in form. Up to this time in the development and evolution of a nervous system there is, therefore, no appreciable interval between the receipt of a stimulus and the despatching of the motor or effector impulse, so that the reflex arc has an immediate consummation in motion. In the higher animals such immediate response to the stimulus would be disadvantageous. A *period of latency* is necessary, and consequently there are introduced

between the receptor and effector limbs of the neuronic arc a number of short interpolated or internuncial neurons.

There are two great types of internuncial neurons—segmental and supra-segmental. In the *segmental* portions of the neuraxis the internuncial neurons are of the association and commissural orders, as seen in most animals lower than mammals, and in the spinal cord, medulla oblongata (exclusive of the pyramids), the dorsal pons, and the tegmentum of the mid-brain in man.

In the *supra-segmental* neuraxis, the internuncial neurons are usually of the " granular " or Golgi Type II order, and are found in man in the tectum or roof of the mid-brain, the cerebellum, the inter-brain, and the cerebrum.

The general plan of the neuronic construction of the *segmented* portions of the neuraxis is practically constant in all vertebrates, and is relatively simple. There are comparatively few interposed or internuncial neurons between the receptor and effector limbs of the neuronic arcs, and such a form of neuraxis controls, in all vertebrates, the fixed and fundamental organic reactions, that is, those which are usually reflex, unconscious, and essential to the maintenance of life. A segmented neuraxis is obviously incapable of much increase in the numbers of its interposed or internuncial neurons, because the grey matter is situated in the interior, is everywhere surrounded by white matter, and is thus incapable of extension.

The *supra-segmental* portions of the neuraxis, on the other hand, are much later evolutionary additions to the neuraxis. They serve the purpose of some special additional functions for which the segmental neuraxis does not provide. As the grey matter is situated on the exterior in all supra-segmental additions, there is ample room for additions to the numbers of interpolated or internuncial neurons, and thus the animal is adapted to much more complex correlations of nerve impulses. In those lower animals with a segmented neuraxis only, the reactions to the environment, or the behaviour, will be fixed, constant, and innate (instinct), whereas in animals with a supra-segmental cerebral cortex (mammals and man) the reactions to the environment, or the behaviour, will vary, and, in their higher manifestations, constitute reason or " mind."

These differences in the behaviour of the lower animals and man, that is, the reactions to the environment, are entirely brought about by a progressive increment, at the cephalic end, in the numbers of internuncial neurons interposed between the receptor and effector limbs of the neuronic arcs. Contrast, first, the segmental spinal cord and the supra-segmental cerebellum. In the *spinal cord*, the internuncial neurons are comparatively few in

numbers, are of some length, their axons are not confined to the grey matter, and their purpose is clearly to pass on the nerve impulses as quickly as possible. They are either associational or commissural in character. In the *cerebellum* the internuncial neurons are enormous in numbers, have no length, the whole of the neuron—dendrons, cell bodies and axons—is strictly confined to the grey matter, and their function is clearly to arrest the flow of nerve impulse through the cerebellum—that is to say, the function of such supra-segmental internuncial neurons is to store up nerve energy. Clinically, the cerebellum is known to be a store-house of such energy. It is *constantly* receiving proprioceptive impulses from all parts of the locomotory apparatus of the body, and is thus constantly storing up nerve energy. It is a significant fact that the structure of the cerebellum is practically the same in all animals. From without inwards there are:

1. A grey, molecular layer, receptor in function, and containing very numerous basket and cortical cells.
2. A middle layer, composed of a single row of Purkinjë effector cells.
3. An internal granular layer, receptor in function, containing granular and Golgi type II neurons.

Within the three layers of this cerebellar cortex are also found medullated axons, known as moss fibres, climbing fibres, and Purkinjë cell axons. Now this mass of nomenclature disguises the truth. Stripped of this nomenclature, cerebellar cortical histology simply teaches once more the great principles of the neuronic arc, thus:

Receptor axons.—The moss and climbing fibres are the axons of proprioceptive neurons pouring into the cerebellum impulses from muscles, joints, semicircular canals, etc.

Internuncial neurons.—All the basket, stellate, cortical, and Golgi type II cells described in the cerebellar cortex are internuncial in character, and serve to arrest, or store up, the impulses constantly poured into the cerebellum.

Effector neurons.—The cells of Purkinjë, very much less numerous than the internuncial cells of the cerebellum.

The relative fewness of the effector or Purkinjë cells of the cerebellum, as compared with the proprioceptive axons and the internuncial cells of the cerebellum, affords a natural proof that nerve impulses must be stored up in the cerebellum. Further, the wide-spreading antler-like dendrons of the cells of Purkinjë are admirably adapted for the collection of impulses from the numerous internuncial cells of the cerebellar cortex; and lastly, as cortico-cerebellar connections are far more numerous than cortico-spinal,

the cerebellum obviously discharges its accumulated nerve energy under control from the cerebrum.

The mammalian cerebellum is thus an excellent example of Cajal's fourth stage in the evolution of a nervous system—that is, of the *epoch of the supra-segmental reflex neuron*. The introduction of the innumerable internuncial neurons between the receptor and effector limbs of the neuronic arcs furnishes the machinery by which the *period of latency*, or the delay between the receipt of the stimulus and its translation into action, is brought about. The nervous system has thus clearly come under the guidance of a new influence, and has now acquired the far-reaching quality of being able to withhold action until it is most opportune or profitable. Behaviour is thus no longer a matter of instantaneous impulse, but is made subject to a certain degree of supervision. *This marks the beginnings of psychic life.*

The final stage in the fashioning of an organ of mind is reached with the mammal, and culminates in man. In the *mammal* there is, for the first time, a true neo-pallial cerebral hemisphere, with three main cortical layers and primitive and limited undifferentiated areas foreshadowing the huge association areas of the "mighty brain of man" (Gaskell). In the *higher mammals* and *anthropoid apes* there are five histological cortical layers and rudimentary association areas. In *man* there is a fully developed five-layered histological cerebral cortex with large association areas. The chief structural differences between the brain of man and that of any other mammal is that the former contains an infinitely greater number of internuncial neurons.

If the brains of any of the *lowest mammals* and *man* be looked at with the naked eye, the *mammal* will be seen to have a small, smooth brain, about equally divided into an archi-pallium or smell brain and a neo-pallial brain, with practically no association areas. *Man* possesses a large, convoluted or gyrencephalic brain, with the archi-pallium or smell brain relatively suppressed. The neo-pallial brain is enormously increased, the functional areas being exactly as in the mammal, though separated from each other by large, well-developed, association areas. These naked-eye differences between the brain of the mammal and man are largely due to an enormous increase in the numbers of cortical internuncial neurons. It has been estimated that these number 9,280 millions, and no other animal possesses even a third of this number.

It is to be particularly noted that in many human beings these brain-cells do not all reach maturity, and consequently the individual's mental reactions to his environment are on an altogether lower plane, and it is this fact which explains many anti-social

phenomena, for a one-cylindered motor car cannot possibly do the same work as a six, or even a four, though the external differences may be slight. Before anyone is entitled to formulate theories concerning the phenomena of mind, or its aberrations, it is surely essential to know something of the histological construction of the cerebral cortex, and yet this appears to be what most theorists ignore, for human cortical histology is, to most students, a repellant subject, to be forgotten as soon as the exigencies of examinations permit. But the truth of the matter is that cortical histology is an extremely important subject. Its teachings are of the utmost significance in the study of the reaction of the individual to his social surroundings, in the practice of medicine, and in the phenomena of everyday life.

Pavlov states that he was struck by the fact that when the physiologist leaves the study of the simpler parts of the central nervous system, which he has investigated by the observation of the reflexes, and proceeds to the higher parts, especially to the cerebral cortex, his methods suddenly change. He gives up, says Pavlov, observations of the relation between external phenomena and the reaction of the organism to them, and introduces psychological ideas, derived from his own internal consciousness. This changed attitude can only arise either from neglect of structural studies, or from an inability to realize that the cerebral cortex is constructed on exactly the same principles as all other portions of the nervous system—that is, of neuronic arcs, but with enormous numbers of internuncial neurons between the receptor and effector limbs. When one looks at the primitive diagrams which still profess to illustrate cerebral cortical histology in current medical text-books, it is, perhaps, not surprising that the fact that mind results from a multiplicity of internuncial neurons is not understood, and that if the individual does not possess his average share of such neurons he must perforce be of less than average intelligence. Under an unsuitable environment he may further become a social menace.

The *cerebral cortex* fulfils functions so different from those of either spinal cord or cerebellum as to suggest the employment of a different construction. Yet such does not appear to be the case, for the cerebral cortex is once more compounded of neuronic arcs, the main components of which are as follows:

Receptor axons.—The thalamo-cortical and other receptor neurons.

Internuncial neurons.—

Spinal cord type: The associational and commissural neurons with cell stations in both the polymorphic and pyramidal cortical layers.

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Cerebellar type: The granular (Golgi type II) cells of the third cortical layer.

Effector neurons.—The giant and other pyramidal cells, and possibly other projection systems.

All the evidence seems to warrant the only reasonable conclusion that it is the presumably internuncial cortical neurons which, by storing up those numerous nerve impulses which continually bombard the brain from birth to death, act as the physical basis of memory, and, therefore, of speech, reason, judgment, and of all other mental phenomena. If one's ideas are not in the brain-cells, where are they, and for what are the extraordinarily numerous brain-cells, if not for this purpose? Again, why is it that the human microcephalic idiot is so hopelessly devoid of ideas if it is not because he is so grossly lacking in brain-cells? Why is all human progress the result of the work of the multi-neuronic genius, and not of the cerebral ament, who is usually responsible only for much human suffering, disease and financial loss? And lastly, why is it that the late acquisition of speech by a child is such a significant clinical sign of cerebral amentia? It is surely of the first importance to study the construction, development and functions of the cerebral cortex.

The *mammalian cerebral cortex* is primarily built up on an infra-granular basis (Watson), but in man there is a fully formed five-layered cortex, the intermediate transitions between the early mammalian cortex and the human being represented by many living mammalian forms. These five primary layers of the human cerebral cortex are named by Bolton and Watson respectively:

Bolton.	*Watson.*
The outer fibre lamina.	The supra-granular cortex.
The outer pyramidal cell lamina.	
The middle or granular cell lamina.	The granular cortex.
The inner fibre lamina.	The infra-granular cortex.
The inner polymorphic cell lamina.	

It is thus clear that the chief difference between the human brain and that of any other mammal is not so much a difference of construction, as of enormously increased numbers of brain-cells or neurons, and that these increments mainly concern the internuncial neurons interposed between the receptor and effector limbs of the cortical neuronic arcs. These increments of cortical neurons are brought about in several ways. There is, first, an actual increase in linear size, for the brain of man exceeds that of any other mammal —that is, it contains more neurons. Next, the complexity of the fissuring of the surface still further increases the numbers of neurons.

The presence of association areas adds more neurons, and to all these there is added an outer pyramidal-celled layer, containing far more neurons than in any other mammalian brain, and providing the human being with the power of inhibition. With all these increases in size, prominence and complexity, the nervous system has become gradually transformed from an instrument of reflex activities into a brain of intelligence and mind, but the structural process by which this is accomplished is always the same, namely, a constant increase in numbers of neurons combined into arcs and chiefly involving the interpolated or internuncial neurons between the receptor and effector limbs of the arcs.

The *human cerebral cortex*, with its millions of receptive or granular cells (cerebellar type of internuncial neurons), and its even more numerous associational and commissural polymorphic and pyramidal cells (spinal cord type of internuncial neurons), represents the last stage in the evolution of a primitive nervous system from one of reaction to physical stimuli into one of intelligence and mind—that is, Cajal's *epoch of the psycho-associational neuron*. This attains its highest development in man, but does *not* attain equal development in all human beings. There are consequently many who are not always able to react normally to the human environment described as normal by normally developed individuals. Such a highly developed brain, when its development is really normal, makes possible numerous associations between the various types of sensibility out of which the individual is constructed, and upon which the foundations of all the higher faculties rest, but it is to be particularly noted that even this complex brain is still built up of neuronic arcs.

The *key to cortical histology* is, then, the fact that the human brain is made up of receptor axons, joined functionally to the effectors, by a complex mass of internuncial neurons of the segmental and supra-segmental orders, and interposed, like a rheostat, between the main long conducting neurons. Within the nerve elements of this rheostat, incoming nerve impulses become arrested, stored up, dissipated or discharged, and thus the properties of "mind" are the special functions of these cortical internuncial neurons. The human cerebral cortex is thus, as Howell has suggested, a vast collection of neuronic arcs, and its main components would appear to be :

Receptor.—Thalamo-cortical and other receptor axons, which run into the cerebral cortex as radial bundles, and turn thence at right angles to form the lines of Baillarger, running parallel to the surface. These discharge on to—

Internuncial neurons, comprising the granular cells of the third

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cortical layer, and thence on to the polymorphic and pyramidal association and commissural axons, proceeding to all parts of the cortex, in which the incoming impulses are stored up for immediate or future use.

Effector.—The projection systems, such as the cortico-spinal and cortico-ponto-cerebellar, and possibly others.

If, from developmental errors, lack of use, or other cause, these numerous cortical internuncial neurons do not continue their development, as they should do, from neuroblast to neuron, there will be a proportionate diminution in intellect. But further, if, after a correct development from neuroblast to neuron, the latter becomes subsequently impaired by disease (toxæmia, or other poison) or injury, there must also result a corresponding impairment of intellect. When the numbers of properly functioning cortical neurons fall, from either of these two great causes, below a certain proportion, the reactions to the environment may depart so markedly from what normal people call normal, as to constitute a legal insanity, but the minor degrees of lunacy usually pass quite unnoticed. Cortical histology thus ceases to be a repellant subject, but becomes intelligible, interesting and of the utmost importance.

Cerebral function.—Medical and other diagrams purporting to display areas of known cortical function, such as the somæsthetic, Rolandic motor, visual, hearing, etc., are correct so far as they go, but, as they only show cortical function in vertical projection spheres, they disguise the important fact that the cerebral cortex also functions in horizontal planes. There must, therefore, be considered the functions of the granular receptive cortex, the infra-granular, and the supra-granular.

The *granular cortex* is always well developed in known receptive cortical areas. This layer thus primarily subserves the reception of nerve impulses, whether these arrive directly from the lower receptor neurons, or, indirectly, from other cortical regions. It has been shown that the first type of internuncial neuron introduced into the neuraxis is of the associational and commissural varieties. Why, then, are granular internuncial neurons introduced into the later supra-segmental additions? Clearly, as in the cerebellum, for the reception and storage of receptor nerve impulses, and the association of present with past impulses. Therefore, such neurons must play an important part in memory. In the visuo-sensory area, that is, the cortical area where visual impulses are first received, the granular neurons are so numerous as to form a double band around the incoming visual medullated axons (stria of Gennari) conveying such impulses. It is even more instructive to note that

in cases of congenital blindness, where visual impulses have never been transmitted or received, the stria of Gennari and that part of the granular layer lying superficial to it are diminished in depth, by sometimes as much as 50% (J. Shaw Bolton). Clearly, then, cortical neuroblasts not stimulated do not develop.

As regards the functions of the *infra-granular*, *polymorphic* or *instinctive cortex*, the researches of Bolton on the human brain, and of Watson on the mammalian brain, show that the infra-granular cortex is concerned with the performance of the instinctive, in contradistinction to the reasoned and inhibitory (supra-granular) or receptive (granular) activities. It is, therefore, in the human being, the brain of those purely animal instincts which are inherent in every human individual, and are essential for the preservation of the individual and the species. It presides over those bodily functions which require, for their fulfilment, no experience or education. These actions form the basis of many complex reflexes necessary for the preservation of the individual and the species, such as the acquisition of food, the quest of the opposite sex, and other actions necessary to life. (Watson.) Such being the functions of the infra-granular cortex, what is its structure? The layer is apparently composed of polymorphic cells, whose axons form association and commissural fibres—that is, of neuronic arcs. Bolton finds that the layer is of extremely constant depth in the adult, which means that its contained cells are also fairly constant. In cases of high-grade amentia and of chronic insanity with moderate dementia, the thickness of the infra-granular cortex is slightly decreased. In low-grade aments and in gross dements, who are unable to carry on the ordinary animal functions, such as attending to their own wants, the thickness of the infra-granular cortex is considerably decreased. The behaviour of the individual, that is, his reactions to his environment, are thus correspondingly altered.

The pyramidal cells of the *supra-granular cortex* are a recent evolutionary addition to the mammalian brain, and attain their highest development and largest numbers in man. The supra-granular cortex is, indeed, the most prominent histological feature of the human brain, and constitutes a higher level basis for the carrying on of cerebral and mental functions. It is the last cortical cell layer to be evolved, and is the first to undergo retrogression. It is the only cortical cell layer which varies definitely in measurable depth in normal brains, and is under-developed to different degrees, according to the mental capacity of the individual exhibiting various grades of mental sub-evolution. It undergoes degrees of retrogression which correspond to the amount of dementia existing in cases which permanently suffer from diminution or loss

of their mental powers. Except for the fact that the contained cells are pyramidal in outline, that is, of the effector type, instead of polymorphic, the supra-granular cortex is an exact repetition of the infra-granular. That some essential functional meaning attaches to these structural differences of form is certain, and lends support to the views of Bolton, Watson and Mott, of the important differences in function of these two great cortical layers.

In view of the already suggestive evidence of the functions of the horizontal layers of the cerebral cortex, it is regrettable that *post-mortem* examiners continue to neglect even the simplest estimation of the thickness of the cerebral cortex, whilst a systematic microscopic examination of the cortical cells themselves is practically never made outside the mental hospital laboratory, and even there not always as a systematic procedure. Yet even older and largely forgotten observations show the necessity for such systematic examination. Thus Conti and Franceschi found the average thickness of the normal human cerebral cortex to be 2·25 and 2·47 mm. respectively, whilst Bucknill and Tuke, and Cionini, found the thickness in the insane to be reduced to 1·88 and 1·83 mm. respectively.

Conclusions.

As a result of this study of the comparative anatomy and minute structure of the vertebrate nervous system, and of the functioning of cortical brain-cells in horizontal layers, there begins to emerge the highly significant fact that in every human individual there is an inner or infra-granular brain of the animal instincts and activities and an outer or supra-granular brain of control, inhibition and educability. Bolton has shown that the neurons of the latter develop late and are extremely variable in numbers in different individuals; hence it follows that some will react to their social environment on a more nearly animal basis than others, and there thus appears to be an established physical or structural basis for many social problems, such as certain crimes, prostitution and general inefficiency, as well as for many of the insanities.

In cases of mental affection, grading from idiots and imbeciles, through various types of amentia, great differences in the thickness and numbers of neurons of the supra-granular cortex have been quite definitely established, both macroscopically and microscopically. In *amentia* the condition is one of under-development of the cortical layers, particularly the supra-granular, whilst in *dementia* there has been a destruction of such cells, and the destruction affects the layers in the reverse order to that of their development, the most affected being the latest developed, and the least

affected being the earliest developed. It is thus clear that cortical histology is an extremely important subject, and that its teachings are of the utmost significance in the study of the reaction of the individual to his social surroundings—that is, his behaviour; in the practice of medicine and jurisprudence; in the study of normal and abnormal mentality, and in the phenomena of everyday life—that is, in all industrial and social welfare work.

Lecture II.—Application of the Principles of Neurology to the Insanities.

The *development of the normal human brain* occupies a long period, which may be best examined at three stages—the prenatal nine months, at birth, and the eighteen (more or less) post-natal years to adolescence.

During the *pre-natal nine months* the single-celled ovum becomes converted, by repeated subdivision, into the multi-celled embryonic nervous system. During this stage the future functional brain-cell passes through several developmental phases. There is, first the germinal cell, which becomes changed into the indifferent cell; then follows the mitotic indifferent cell, which divides into the neuroblast and the spongioblast. At birth the brain is largely in this neuroblastic-spongioblastic condition, hence the child's apparent idiocy. The neuroblast eventually becomes converted into the nerve-cell or neuron. The spongioblast forms the supporting or neuroglial cell. If neuroblastic development exceeds spongioblastic, there may result the multi-neuronic genius. If, on the other hand, spongioblastic development predominates, there may result the large, heavy brain and big head of the unintelligent. These developmental facts are usually ignored by those who altogether deny any correlation between head size and developmental state of the brain.

At *birth* the brain is, as just stated, in a largely non-functional neuroblastic condition, and only those axons are fully medullated which are necessary for the maintenance of life (Flechsig).

During the *first eighteen years* (more or less) of *post-natal life*, the embryonic, non-functional neuroblasts become converted, under suitable exteroceptive and other stimuli, into fully developed, functional neurons, linked together in neuronic arcs.

But nerve-cells, or neurons, are not the only cells formed from the fertilized ovum. There are three great types of bodily cells so formed, as follows:

Somatic or bodily cells, such as those of bone, muscle, etc.
Reproductive cells—the spermatozoon or ovum.
Nerve-cells or neurons.

All three types pass, developmentally, through several stages, and they may be arrested in their development at any stage. Thus developmental failure of somatic cells may produce hare-lip, cleft palate, club-foot and the like. Failure of the reproductive cells may subsequently result in impotence. Similarly, though it does not appear to be as generally recognized or admitted, neuronic cell failure of normal development may occur, and if pronounced, must result in some subsequent display of mental aberration or unintelligence.

If the development of the neuron becomes arrested at, or about, the *eighth month of pre-natal life*, whilst somatic and reproductive development proceeds fairly normally, the subsequent mental aberration, or inability to react to the environment in a normal manner, may be so pronounced that legal certification will be demanded, and the individual branded as an idiot or an imbecile. Thus a microcephalic idiot, æt. 23, was unable to talk, but could fetch or carry and perform simple routine tasks, and the *post-mortem* examination revealed the fact that the brain was small and lissencephalic and weighed only 568 grm.—clearly a form of insanity entirely due to a prematurely arrested neuronic brain development.

As regards the *causes* of these prematurely early developmental neuronic failures it is not always possible to speak with certainty, because, though some are definitely known, others are only conjectural. Amongst the known causes may be mentioned heredity, syphilis, and birth injuries to the brain. Amongst the conjectural are alcoholism, tuberculosis, etc., in the parents. It is unnecessary here to stress the enormous influence of *heredity* as a cause of the developmental insanities, because the records of every properly conducted mental hospital contain thousands of examples. So long as civilized communities refuse to recognize the developmental mental disorders and to pay more attention to the good breeding of dogs and domestic animals than to human beings, it is to be feared that the developmental insanities will tend to increase rather than diminish. The effect of *congenital syphilis* in arresting brain growth, or at least seriously retarding it, has been made painfully obvious at the Psychiatric Clinic of the Melbourne Children's Hospital, and most mental hospitals can furnish the adult examples. Whatever the cause of this pre-natal failure or arrest of brain development may have been, there results a diminution of the numbers of the cortical neurons and almost as frequently an imperfect construction of these only partially formed neurons, with a corresponding inability to react to the environment in a normal manner. The histological thinning of the cortex is abundantly

demonstrated in the researches of Bolton, Tredgold, and many others.

The consequence of these developmental structural errors, whether diminishing the numbers of cortical neurons, or affecting the cell bodies themselves, is that the individual passes on into adult life with an imperfectly developed brain, which is incapable of reacting to the environment in the manner regarded as normal by normal people. The latter thus regard the former as being dangerous to themselves and to society, and civilized usage demands certification as insane, but it is clear that some of these so-called lunacies are not diseases at all, but result from errors of development. To give a normal reaction to the environment, there must be a sufficiency of normally developed functioning neurons, and every mental hospital contains numerous living examples of the results of insufficiency. Many cases of so-called lunacy are, therefore, due to a partial or total cessation of brain development prior to birth, and are not the result of post-natal disease or micro-organisms.

The human brain at birth.—Assuming that pre-natal development has proceeded normally, then at birth the brain should have attained about 25% of its total adult volume. The infra-granular cortex should have developed to 82% of its adult thickness, but the inhibiting supra-granular cortex has only reached half to two-thirds of its total adult thickness (Bolton). This means that the majority of the infra-granular neuroblasts have been converted into neurons, whereas approximately only half of the supra-granular pyramidal cells have completed their development. The actual condition of the brain at birth may be shown from *camera lucida* drawings of the numbers of neuroblasts and neurons in the supra-granular cortex; from a study of the micrometric thickness of the cortical layers (Watson), and from a study of the percentage volume (Berry and Porteus). (These several methods and their results were shown upon the screen.) At birth the human brain is, therefore, in a embryonic or undeveloped state, and the newborn child is an unconscious, reflex organism. Only those neurons are fully matured which are necessary for the maintenance of life. The act of defæcation, for example, is, at first, purely reflex, automatic and unconscious, because the neurons governing the *voluntary* control of the act are, as yet, undeveloped and non-myelinated.

Brain development during the first four years of life.—During these early and important years brain development should increase rapidly, so that by the fourth birthday the volume should be about 80% of the adult size. This increment is naturally brought about by the conversion of the embryonic neuroblasts into fully functioning

neurons and the medullation of their axons, and the necessary stimulus to the conversion is supplied by exteroceptive stimuli from many sources, particularly those of hearing and sight, and the increment chiefly affects the supra-granular cortex. If the child be totally deprived of these important incoming exteroceptive stimuli there results *idiocy from deprivation of the senses*, and there is a corresponding diminution in numbers of cortical neurons and of brain volume. If the child be deprived of only one of these stimuli, say hearing, there will be no speech, and brain volume, at least in so far as neurons are concerned, will be diminished, and this diminution in head size can often be detected by the use of calipers and percentiles of standard brain volume. That a congenital deprivation of certain exteroceptive impulses, such as sight or hearing, which play such an important part in brain education and growth, leads in many cases to an appreciable diminution in head size and cubic capacity of brain is shown by the following observations carried out in Melbourne on many hundreds of children :

13-year-old normal boys	1,352 c.c.
13-year-old deaf and dumb boys . .	1,307 c.c.
13-year-old mentally deficient boys . .	1,292 c.c.

It is therefore probable that for the correct development of brain growth during the first four years of life there must be no interference with the access to the brain of exteroceptive impulses. But unfortunately there are, in addition, quite a large number of other conditions, pathological as well as physiological, which may check, or totally arrest, the growth and development of the delicate neuroblasts and neurons, and so lay the foundations of some, at least, of those mental aberrations which, ultimately, are recognized as insanity. Among these may be mentioned encephalitis, head injuries, syphilis, tuberculosis, hookworm and many others. The general effect of these disorders during the first four years of life is to arrest the growth and development of the neuron, particularly of the pyramidal cells of the cortex, and thus that condition termed by Bolton "amentia" is produced, and this under-development or amentia is, particularly in the high-grade amentias, the unquestionable basis of many of the later developed insanities.

The brain at puberty.—From the fourth year until about the age of puberty, brain growth proceeds, in the normal, steadily and regularly along the lines of the biometrically smooth curve. But just prior to the onset of puberty, measurements, compiled from about 10,000 Australian (Victorian) boys and girls, appear to show a slight resting phase in the otherwise regular development of brain

growth. The actual percentages of brain volume were found to be as follows:

	Boys.		Girls.
11th year .	Brain volume, 91·3%	. 88·8%.	Pre-puberty.
12th ,, .	,, ,, 0·6%	. 0·6%.	Resting.
14th ,, .	,, ,, 3·4%	. 2·2%.	Puberty.
20th ,, .	,, ,, 4·7%	. 8·4%.	Post-puberty.

Differently expressed, these figures show that by the end of the fourteenth year the brain has completed 95·3% of its adult growth in boys and 91·6% in girls, leaving 4·7% to be completed in boys and 8·4% in girls. This post-pubescent increment must be almost entirely concerned with the final development of the supra-granular pyramidal controlling cells, for the simple reason that the polymorphic infra-granular cortex is almost completely developed soon after birth. If, therefore, an adult only possesses a brain capacity of an 11- or 12-year-old child, it is a justifiable inference that his brain development has been arrested, and it is equally probable that the under-development concerns chiefly the supra-granular pyramidal-celled cortex. There are quite a large number of individuals who pass into adult life with a cerebral growth arrested at or about the 12-year-old level—that is, with an under-developed supra-granular brain of control over the animal instincts. Quite apart from other abundant scientific proofs of the statement, the American army tests, crude though they were, were equally convincing. Placed in the relatively simple environment for which their brain development is thus clearly designed, these under-developed individuals may pass through life without harm to themselves or to others. They will, however, tend to break down under the stresses of life earlier and oftener than the more normally constructed individual—that is, they are predisposed to insanity. Placed under wrong environmental conditions, such high-grade aments may become criminals, prostitutes and social pests. Two Australian examples may suffice. Deeming, the notorious Australian wife murderer, was found to have had a cubic capacity of brain of 1,358 c.c., or 18 c.c. less than the true mean capacity of brain of the normal 13-year-old schoolboy. The brain of Ned Kelly, the Australian bushranger and robber, had a cubic capacity of 1,405 c.c., or 13 c.c. less than the true mean brain capacity of a normal 14-year-old schoolboy. Of 33 criminals hanged for murder in Melbourne, only 7 had head sizes within the normal range of variation. In another criminal condemned for murder, *post-mortem* examination of the brain showed the occipital region with a shrivelled appearance and a divergence of the lobes. The supra-granular cortex was shallow, but the infra-granular cortex was increased in depth.

Microscopic examination showed that the frontal area was particularly barren of pyramidal cells; the visuo-psychic area was reduced in thickness and its supra-granular cells were again reduced in numbers, but the infra-granular cortex was here also thicker than usual. Dr. Wilson, who made the examination, adds, "It is a scientific corroboration of my dictum, that the criminal has only the control of a child. It is due to *the natural development of the brain being arrested before birth.*" In view of more recent work and research since Wilson wrote the foregoing, the words "before birth" should here read "before puberty."

None of these examples, Deeming, Kelly, or the condemned murderer, would be accepted in modern law as "insane," because the legal conception of insanity has not yet been amended to include, even if it were thought advisable to do so, those social, rather than clinical, abnormal reactions to the environment which result from mal-developments of the brain, but there can be no room for doubt that all three were fairly gross examples of amentia or under-development of the brain.

Summary of brain development.—If brain development be arrested prior to birth, *microcephalic idiocy* is the probable result, with perhaps absence of speech, and other human attributes so pronounced as to require legal segregation.

During the first four years of life, brain volumes increase from 20% to 80%. Arrest of brain development at this stage results in some of the many clinical forms of *low-grade amentia*, which may, or may not, require legal segregation.

The remaining 20% increment may, or may not, take place. If little or none of this development occurs, some form of *high-grade amentia* results, with more or less anti-social or "insane" reactions according to the environment and the degree of the amentia. This variety of aberrant mentality is the most dangerous, as it usually passes quite unnoticed. Even to-day it is the almost invariable practice to regard all individuals who are not actually certified lunatics as being sane. The public generally refuses to recognize any inequalities in mental abilities, apart, perhaps, from a grudging and unwilling one of sanity, feeble-mindedness, and insanity. But there are many more degrees than these.

Amentia is here used to connote an under-development of cortical neurons from any cause whatsoever, in consequence of which the individual is unable to react to his environment in the manner regarded as normal. Tredgold says the brain of the ament is characterized by a numerical deficiency of cortical neurons, an irregular development of such neurons and an imperfect development of the individual cells of the cortex. He adds that the

amount of the change discoverable by the microscope is directly proportionate to the degree of mental deficiency during life. In many cases this paucity of cells produces a decrease in the thickness of the cortical grey matter which is obvious to the naked eye—always assuming, of course, that it is looked for, which is but seldom the case.

It is quite commonly supposed that amentia only includes certain easily recognizable mental hospital types of a gross physical kind, such as idiots, imbeciles, cretins and the like. Many other forms are apparently regarded as being merely "backward," and the parents are led to believe that the child "will grow out of it"—which is seldom the case. It is the unrecognized cerebral ament who so often becomes the social menace, and his diagnosis demands special methods based on a sound neurology, a knowledge of which is not always a part of the average medical man's armamentarium. Bolton divides the amentias into two great grades, low- and high-grade amentia, and clinical experience leads one to support this classification. *Low-grade amentia* includes idiots, imbeciles, and those other cases where brain growth is largely arrested before birth. Among the *high-grade amentias*, Bolton places the moral, unstable, excited cases, recurrent cases, hysteria, epilepsy, some criminals, and so on, and these are usually the result of an arrested or partially unequal development of the brain between the ages of birth and puberty. It should not be assumed that the high-grade ament is thus only a thinly disguised mental hospital case, because this clinical division of high-grade amentia includes many others who would not legally be certifiable, though medically they would probably be the better for a temporary or permanent segregation in some institution other than the existing mental hospital. Many of these high-grade aments are not recognizable as such by the ordinary methods of medical examination, but special neurological methods can usually be relied upon for their accurate diagnosis. In all these cases, which include many criminals, quacks, paranoiacs and the like, there is either under-development, or irregular development of the cortical cells, particularly of the supra-granular pyramidal cells, with a consequent irregular or disordered reaction to the environment. These cases of high-grade amentia have certain other features in common, besides these deficiencies of pyramidal cells. They are usually developmental in origin, and there is not usually any naked-eye change visible in the cerebral cortex, though the microscope, as Tredgold has remarked, reveals some of the cellular shortage. As it is usually the inhibiting pyramidal cell layer which is at fault, the reactions to the environment are on the more animal basis of the infra-granular cortex—that is,

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uncontrolled sexual or acquisitive activities. Many of these individuals depart so far from the normal reactions of man as to leave doubts even in the minds of those not specially skilled in their diagnosis as to their sanity, hence many of the disputes in courts of law, and the difficulties of the present legal requirements of certification.

The high-grade ament of both sexes is liable, on account of his lack of pyramidal cortical neurons and lowered powers of neuronic resistance, to break down mentally, both earlier and oftener, than normal individuals, and is thus an early prospective victim of such disorders as dementia præcox, hysteria, neuroses of various kinds, and of psycho-neuroses. Some of these commoner periods of breakdown are at puberty, transference from school life to employment, periods of domestic squabbling or stress, sexual evolution, periods of financial worry, illegitimate pregnancies, abnormal menstrual disorders, abnormal parturitions, and others.

Summary of the developmental amentias.—It is clear that the word " amentia " is here used to denote a developmental state, and not a clinical syndrome. In this sense the amentias may be summarized as follows :

Clinical types.	Histological condition.
Low-grade amentia—	
Idiots.	Deficiency of cortical neurons in both the supra-granular and infra-granular cortices. The higher the clinical type, the less the numerical deficiency of brain-cells.
Imbeciles.	
Mental defectives.	
High-grade amentia—	
Morons.	Deficiency of neurons is here apparently chiefly confined to the supra-granular cortex of the pre-frontal region, but more evidence is required.
Moral, unstable cases.	A deficiency of neurons in some regions, and an excess in others.
Cranks.	
Psychopaths.	
Recurrent types.	? Amentia, *plus* dementia.
Hysteria.	
Epileptic insanity.	
Paranoia.	

Dementia or cerebral dissolution.—" It is clearly wrong," says Sir Maurice Craig, " to describe dementia as a distinct malady." Yet it would appear to be a not uncommon practice to regard dementia as a disease or a clinical syndrome, instead of a physiological

process which may occur in every individual who lives long enough. It is merely a question of whether the individual outlives his cortical neurons (senile dementia), or whether the durability of the neuron is such that it cannot last during even the period of reproductive life, in which case we seem to regard the condition as a disease, and speak of a complex of phenomena as dementia præcox. Amentia thus denotes a feeble mind from a lack of neurons. Dementia is a state brought about by a destruction of cortical neurons, and thus again leads to a feebleness of mind. As Tredgold happily puts it, the ament has never had a banking account; the dement has become bankrupt. As thus used, the term "dementia" denotes a local death or destruction of previously fully formed neurons. It may occur in almost every human individual who lives long enough, because the durability of exceedingly delicate cells, like cortical neurons, is distinctly limited, and still more so in persons of weak heredity. Speaking very broadly, it would perhaps be better to regard dementia as pathological when it precedes sexual involution. If it does, there is usually some underlying cause which it is not always possible or easy to ascertain. Amongst these possible causes for premature dissolution of cortical neurons are heredity, amentia, alcoholism, the spirochæte (general paralysis of the insane), toxæmias, and possibly many others.

In Victoria, official figures would appear to show an increase in the numbers of the certified insane. If so, it is not impossible that this increase is due to the inability of the ament to withstand the stresses of an increasingly complex civilization. The environment is becoming altogether too severe for his insufficient and defective neurons. He breaks down, develops a precocious psychosis and thus swells the numbers in mental hospitals. Were the diagnosis of an under-developed cerebral cortex made earlier, as it now can be, the individual could be placed, under suitable laws, in the simpler environment of a segregation home or colony where he could be made happy and self-supporting.

Chromatolysis of the cell body and its effects on the mind.—In these developmental studies of mental disorder stress has so far been entirely laid upon the structural basis, because that appears to be both the most important and the most neglected. But there remain other causes for those deviations from normal reactions to the environment which are rather badly termed the insanities. Even in the individual with a fully developed nervous system, there may still result the most pronounced reactions to the environment, including many for which the law demands certification. But in these cases the cause is quite different. Physiological exhaustion of the cell body of the neuron, the result of fatigue, is a perfectly

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well-known phenomenon. The exhausted neuron cannot function properly, and there is a more or less disordered reaction to the environment. Insomnia is a physiological manifestation of this state of affairs, and the so-called puerperal insanity is another more serious example of greatly exhausted and poisoned neurons. The underlying cause is a temporary diminution in, or destruction of, the chromatin material in the cell body of the neuron, and this alteration is termed *chromatolysis*. Provided the cause of the chromatolysis be removed in time, the cell body of the neuron will recover. If it be not, the neuron will die. Many examples of cells, the actual changes in the Nissl bodies, and the effects of over-fatigue, even to destruction of the cell-body, are furnished in almost every modern laboratory and text-book.

The *causes of chromatolysis* would appear, even with our imperfect knowledge, to be very numerous, and amongst them may be mentioned toxins, the products of disease, insufficient oxygen, fevers and febrile conditions, insufficient sleep, worries, excessive strains on receptor organs and many others. When these causes of chromatolysis are persistent, the individual may pass into a stage of such completely disordered reaction to the environment as to call, under existing legislation, for certification—a matter of great difficulty, for it is clear that this group includes many of the recoverable insanities, and legal procedure is not always in harmony with scientific knowledge.

As every normal human individual of more than average longevity commences and ends his life in a state so closely simulating insanity as to be almost indistinguishable from it, its medical, public and legal conception would appear to require considerable revision. Insanity would be better termed "disordered reaction to the environment." If persons exhibiting disordered reactions to environment become dangerous to themselves or to others, a temporary or permanent segregation, in their own interests, as well as that of others, is clearly indicated.

These disordered reactions to the environment may result from the following:

1. An insufficient number of cortical neurons—that is, a developmental amentia. Such an under-development necessarily leads to an altered reaction to the environment. Every living animal is provided with a nervous system which is strictly adapted to its requirements—that is, provision is made for those reactions to the animal's environment which best adapt it to the struggle for existence. When these reactions effect their purpose, they are *normal*. When they fail to effect their purpose, they are *abnormal*. When, in man, defects of cerebral construction give reactions to the

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environment of such an abnormal character as to be noticeable, we call it insanity.

2. Actual disease of the brain-cells in a formerly normal individual, as when general paralysis of the insane follows syphilis. Here, as the cortical neurons become slowly destroyed by the spirochæte, or its products, there is a gradually increasing abnormal reaction to the environment, and the clinical condition, when sufficiently obvious, is called insanity.

3. The natural destruction of cortical neurons—that is, their gradual death, as occurs in the physiological dementia of the aged.

4. Temporary condition of "ill-health" of the cortical neurons—that is, an evanescent chromatolysis, in otherwise normal individuals, as in delirium from acute fevers, acute delirium after chloroform, delirium tremens, uræmic convulsions and other examples.

5. Any of the foregoing in combination, which are probably the commonest basal factors underlying the certifiable insanities.

Present-day conceptions of insanity, both medical and legal, present inconsistencies and errors which can be eliminated only by knowledge based on the sure foundation of structure and function. There is probably no system in the body where normal functioning is so dependent on normal structure as in the nervous system. Hence the key to the pathology of insanity lies in the study of structure quite as much, maybe more, than in that of clinical phenomena. All the phenomena presented by the functioning of the nervous system, normal and abnormal, and whether regarded as belonging to psychology, psychiatry or diseases of the nervous system, from the clinical standpoint, fall into four great groups—namely absence, diminution, perversion or exaggeration—of the functions of the three great structural divisions of the central nervous system:

Structure and function.		Phenomena.
Receptor neurons.	Sensations.	Absence.
Cortical internuncial neurons.	Thought.	Diminution.
Effector neurons.	Actions.	Perversion.
		Exaggeration.

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