Chapter 1

The Prolific Years

In the life of every scientist who contributes something of importance to his field there must have been a long period of intense devotion to experimentation, reading, study, and thinking, being the patrimony of a dear wife who would find it difficult to understand the sudden shifts in the husband's moods from distant solitude and absentmindedness to moments of obvious elation depending upon intellectual problems difficult to share with others. In Sherrington's life 1900 to 1913, the years at Liverpool, were such a period of intense creation and study. So far only those aspects of his work at Liverpool have been presented that became normative for the future development of theoretical neurophysiology as we know it today, but he accomplished even indeed many other things which Anne would have made a lesser man satisfied with his day of labour.

During these years Sherrington wrote *Integrative Action*, he was responsible for some of the best chapters in Schäfer's *Text-book of Physiology*, issue on the spinal cord, the brain stem, cerebellum and medulla oblongata, on cutaneous sensations, and on the muscular sense; all of which are still highly readable, forward-looking products of well-digested experimental experience and vast reading; he taught, even physiological chemistry, sat on committees, and published reports as professor-in-charge in this then new, he built (and organ of a new laboratory, and wrote much of the poetry in the *Anything of Moderation* not to mention the experimental papers, from which only some leading ideas can be extracted here. He wrote too much, said Cushing, but life was exciting and life was full.

What would Sherrington have retorted, had he known of Cushing's remark? Possibly what he said to me once when we were talking about John Fulton's biography of Harvey Cushing: "You know, the life of a great surgeon is not really exciting, except, of course, from the patient's point of view." We discussed the subject at some length and Sherrington began to recall names of surgeons whom he would respect as surgeons. The two he mentioned were Lord Lister and Wilder Penfield, both also scientists and physiologists.

In those days professors did not have secretaries but Sherrington's wife took upon herself the secretarial duties needed in the laboratory and also for his international work, because at the time and for fifteen years Sherrington was Anglo-American secretary of the *International Congresses of Physiologists*. Sherrington and Athel Wright of Pearson, Sheffield, had been instrumental in 1901 in setting up the Professor Superintendent of the Brown Institution.

There was no laboratory when Sherrington arrived in Liverpool. He described it to me as 'almost a shed'. But the University Council, in addition to the Rev. R. A. Thompson Yates and in October 1904 the new laboratory for physiology and pathology, besides Sherrington's nurse, are built by Messrs. A. Waterhouse & Son, were opened with a solemn set. Several eminent guests were present, among them Lord Lister and the pathologist, Professor Virchow, in whose laboratory in Berlin Sherrington had worked (and he remained from Paglia. The dinner gave an opening Address published in the *Thompson-Yates Laboratories Papers*, volume 1, edited by the two professors (Lister, Sir) Robert Boyce (1863–1911) and Sherrington. In this volume of 400 pages, issue on the spinal cord, the brain stem, cerebellum and medulla oblongata, on cutaneous sensations, and on the muscular sense, all of which are still highly readable, forward-looking products of well-digested experimental experience and vast reading; he taught, even physiological chemistry, sat on committees, and published reports as professor-in-charge in this then new, he built (and organ of a new laboratory, and wrote much of the poetry in the *Anything of Moderation* not to mention the experimental papers, from which only some leading ideas can be extracted here. He wrote too much, said Cushing, but life was exciting and life was full.

What would Sherrington have retorted, had he known of Cushing's remark? Possibly what he said to me once when we

As a consequence the grime and soot of sixty-four years were now been removed from the relief and the young charming wives, attired à la Gretjen, can be admired in their original beauty, possibly somewhat falsified.

In the opening address by the Rev. Thompson Yates there were some words which Sherrington at least would have found to with appreciation: '. . . I would urge you all, whatever your profession, not to be satisfied with knowledge merely professional. You will make better doctors, better men of Science, better citizens, and be of greater use to your fellow creatures if you know something of the size of human thought expressed in the words Philosophy, Poetry, History, Literature. You have not time? Then make it somehow. I believe we all can do so, and make ourselves better men and women by the wholesome influence in the manufacture.'

The *Lesions of Spinal Disorder* published in January 1900 an extract from the *Memoirs of Sherrington* by his son, C. E. H. Sherrington, which is worth quoting:

Writing to his mother in October, 1896, from Grove Park, Liverpool, he described the house as in many ways like his devoted home at Ashtead, adding: 'In the study hangs the dinner-bell, and the tale manifested, and the alcove too.'

He was pleased with the climate which was bright and sunny compared with that of London; and he was well received both by his colleagues and the great Merseyside families, the young nurse, the housekeeper and nursery maid, on occasion, also proved willing to support his experiments.

One of Sherrington's early students, an analog at and surgeon, H. V. Forster, in a brief address to the Laboratory at Liverpool (1961) has some interesting reminiscences of the young professor, worth putting on record:

I can see him now, coming through that door on my left in his black gown (1896). There was nothing of the dilettante about him, but much humility and enquiry . . . We had heard with much curiosity that at Liverpool when working with Grünbaum, Sherrington had mapped out areas of function in the motor cortex of the chimpanzee and even the gorilla, and he also time after instruction upon the conjugated action of antagonistic muscles we were translated to the reversal in the leg also from . . . both in myoclonus and tetanus

tetanus. . . . It is not surprising that we were especially attentive to Mr. Hunt on the predominance of the brain and the local in physiologically transferred.

Forster had some old lecture notes on this:

"The organism, living at the leading pole of the animal, senses as they are with the great "distance" sense-organs, constitutes what is termed the "head". [Thus he goes on to enquire whether this dominance of the leading segments refers to transmitter in the inspiration of the nervous system. Half applies to the field of reception which is termed the proprioceptive.] The labyrinth (*See* example) is the chief proprioceptive of the leading segment of the body which is the head. The labyrinth keeps the world right side up for the organism by keeping the organism right side up to the external world.'

Sherrington was on the side of proprioceptive, the labyrinth and the cerebellum in mammalian now has already acquired their genesis here. Sherrington's use of the cerebellum (in *De Forster's notes*) at the head ganglion of the proprioceptive system, as he was wont to do in the end. The cerebellum was the ganglion of the distance receptors. He liked to generalize in conjunction to the 'two poles', the nothing by 'last' conjunction covering, an emblem of antiseptical rigidity' built up clearly on mechanical. Now the eyes with their capacity for binocular vision. His master's voice is also vividly there in the notes on the much out in the Pitter Ring of all vertebrates, the young nurse: 'The knock-on knee where the knee joint contains cartilages to the meniscus, reduces is a moment a spasmodic adjuster to an unstrung bolt of flesh whose weight alone determines its activity, if indeed a reactionless non-cart, be done fixed in proceeding attitude at all.'

A. S. F. Grünbaum (1860–1932) under Forster mentioned is better known under the name of Leyton (after 1905, by deed poll). He was Sherrington's assistant at Liverpool and later became Professor of Pathology at Leeds. After Sherrington he was a Cassville and Cabin man scholar; also began at St. Thomas's Hospital. In 1896 Leyton had worked in Vienna where he devised the agglutination test in typhoid fever but this that he had not few cases and so could not publish it. Wilde then, on two cases, pointed him by a few weeks (Sherrington). Leyton

and Sherrington carried out work, still quoted today, on the motor cortex of the chimpanzee, orang-utan, and gorilla. Other members of the group were T. Graham Brown, F. W. Mott, and L. Schaver. In 1901 Cushing joined them for a month. A young American, R. S. Woodworth, proved good and was accepted to stay on after having studied with Sherrington a 'pseudo-affective reflex' in the decerebrate preparation, recently taken up again by R. S. Lee, but finally returned to the States to become Professor of Psychology at Columbia University and live in a great age as the revered Nestor of the American psychologists. In a letter to me (January 27, 1961) outlining some reminiscences from Liverpool, Woodworth among other things pointed out that Sherrington began his day with exercise, and too, as most professors, with minor matters of administration and instruction. Prominent among foreign guest workers at Liverpool were Rudolf Magnus (see below), H. K. Hering, discoverer of the carotid baroreceptor reflexes, and the American, Alfred Fröhlich, well known for his description of the so-called adiposo-genital syndrome. In his Sherrington Lecture of 1956 Fulton has some extracts from Cushing's diary and concludes: 'Gay and busy days these were, says the Charles and Alfred Fröhlich still recall them with a lively sense of pleasure, as did Harvey Cushing while he lived.'

'Cleaning back in perspective', says C. R. B. Sherrington in the *Liverpool Recorder*, the years at Liverpool were, I believe, the happiest in his life, and my mother's too,' and well wonder. Prize-presented in the vertical axis work in the new laboratory was exciting. Guest workers came and stayed on to experienced under Sherrington's guidance, visitors from the United States and Canada in those days took the route by Liverpool, and international contacts with the European continent were developed, officially, by his work as Anglo-American secretary of the congresses, unofficially as well, by travel for pleasure during holidays. The young couple loved Paris, the wife, being partly of French origin, spoke the language fluently but may not have shared her husband's taste for browsing among the *bouquiniste* stalls on the Rive Gauche and hunting up incunabula and old books in libraries so big the groundwork for his study of Jean Fernel and the ancient history of the Latin Quarter. For this

The extremely detailed map of localization in the motor cortices of primates which Sherrington and Leyton published become the accepted standard for many years, but equally important were the cortexes they showed. They established the functional instability and deviation of the response that became evident as soon as the explored cortex was sufficiently small and stimul often enough over some time. A cortical point representing, say, movement of the ankle flexor is replaced by a number of other points (cells) which represent various combinations in which this movement is obtained. A comparison of a particular frontal muscle may take part in chewing, in mimetic acts, in the production of sound. Also in the motor cortex this showed 'representation' or small local loss of movement, each slightly overdistorted with others yet separately efficiable, instead of between less evident with assent to the higher types of locomotion, between mimic to. Thus, it is more evident in man and dog than is rabbit, more evident in the Macaque than in cat or dog, in baboon than in Macaque, in gibbon than in baboon, and in the chimpanzee, orang, and gorilla than in gibbon. . . . Phenomena such as "reversal of response" (from one type of movement to its opposite), "facilitation", and "deviation of response" prominent in cortical response, and accounting for the functional instability of cortical motor points, are indicative of the enormous wealth of mutual associations existing between the separable motor cortical points. These associations must also be a characteristic part of the mechanism by which the synthetic powers of their circles are made possible.

We have not since found it necessary to alter in any substantial way the picture Leyton and Sherrington gave of the functional organization of the motor cortex even though the number of sites in the motor cortex which motor effects can be elicited has since increased.

Localization of function has always been a field in which physiologists, anatomists, neurologists, and neuropsychiatrists have a common interest. It is hardly necessary to dwell upon the need for functional maps in clinical work. One example may suffice. Hughlings Jackson, from studies of focal epileptogenic fits, had predicted the localization of the motor area one year before Fritsch and Hitzig discovered it by direct electrical stimulation.

Sherrington followed this work through with great interest, and when Penfield discovered places in the brain of man which on stimulation during operations made the patients recall long-forgotten events in their lives, he did indeed dwelled in him with a quizzical smile and said: 'It must be nice to hear the proposition speak to you.'

To this time at Liverpool belongs a story that he often been told but which he assured me was false of his that I must recall it, in spite of my intention to indulge very little of the well-known anecdotal lore of Sherrington's persona. The problem was presented in *The Daily Mail* as having said to a lecture: 'One day after a night I turned back, pondering what the chimpanzee might do when I left them. I started down and looked through the keyhole, and there the chimpanzee sat—I mean the chimpanzee's eye—met mine. The same thought had struck us both, but the chimpanzee, being a lady, had got there first.'

With some justification one might say that much of this work that Sherrington did on the supraspinal sensorium was of the kind that in itself would not have given him the unique position he now occupies in the history of neurophysiology and neurology. It was important enough to win him to place him in the front rank among those who influenced progress in these fields, and probably it was more reliable than most of many of his laboratory contemporaries. Why then did he spend so much time experimenting on the brain when the real *harvest* lay in the spinal cord with the conjugated actions that the heterodyneous organization of their circuitry made possible, as explained above?

The answer has already been indicated in the extracts from De Forster's lecture notes. The spinal cord is a servant of that great master, the brain. It may be an exaggerated metaphor to compare the cord with a portal plane monitoring by 'supraspinal' stimuli, but the truth is useful in order to explain why Sherrington and many of his successors neglected or later have been irresistibly drawn towards the higher centres, mostly, I suppose, coming to the conclusion that to use and the reflective problem of work in the lower portion of the neuraxis provides greater satisfaction. On the other hand, experiment with the organs of expression control is required by any one interested in neurology

and the spinal cord. Without it, the integrative action of the central nervous system can never be fully appreciated.

Thus with Sherrington, who on Goltz's advice had 'left from the side-streams of medical pathology into the relative daylight that study of the spinal cord secretes to promise, was forced to his main work of departure by observations and circumstances which should now be briefly reviewed in order to illustrate the development of his experimental and thinker.

During his visits to Goltz's laboratory, Sherrington had become acquainted with the general symptoms exhibited by the spinal dog and so was familiar with the fact that control of supraspinal control led to a state of shock characterized by great depression of response to stimulation in the immediate before the earlier. This was a striking demonstration of the importance of the higher centres. It may explain this condition was known to develop in different ways in cog and in man where it was familiar, as a result of accidents for instance. Sherrington had recourse to monkeys and soon found that her's persistent damage and relief. Goltz are disappointingly greater in monkeys than in cat and dog, and following out his case he separated 'shock' as such from the latter effects of isolation-Gyrophy. He found monkey and man more similar in their symptoms than man and dog. The symptoms of shock, in many monkeys, parallel for days instead of hours and minutes, as in man and dog' (Marshall Hall Prize Address 'On the spinal animal', 1889). This is in keeping with the law of decreasing sensitivities of these systems, made possible, as explained above (von Monakow).

Sherrington studied the spinal state with his customary attention to every detail of behaviour, sensory, motor, vegetative, and his work became normative both for Sherrington and the laboratory. Several of his pupils have continued this work (Barcroft, Brown, Fulton, Liddell, McCouch, Hinde), and for thirty years the spinal or the spinalized, concentrate attend has been a favourite preparation to which to study the spinal cord, physiology of central control, especially in work on problems of synaptic transmission. For such problems is a clean necessary to simplify the neural circuit. Thus, for instance, Lloyd in his analysis of monosynaptic transmission in the flexion focus this preparation a valuable tool.

In a similar way other supraspinal structures were drawn into Sherrington's sphere of interest. In tests yet be made the fundamental observation that decerebrate rigidity could be abolished by stimulating the anterior portion of the cerebellum, unilaterally, if only one side of it was stimulated. This work was developed by one of his best pupils, Frédéric Bremer (1892), professor at Brussels, one of the best-known neurologists and neurophysiologists of the present day. Sherrington reported his findings in 1908 and published it in 1907. One month later the same mind, was reported by Ransonoff and Hinsey. Sherrington went on to describe in considerable detail a number of other sites from which decerebrate rigidity could be abolished.

In some other ways the problem of supraspinal control engaged Sherrington's attention, in connection with tone, tonicity, and postural reflexes in general. The matter seemed to him very important, and rightly so, because tonicity all movements have a postural component. The importance of posture is sometimes emphasized by saying that, in the starting-point and point of every movement. But posture, as Barnay Hurst remarked, accompanies 'movement like a shadow'. Stanley Cobb (another Sherrington disciple) writes that 'they coalesce and often cannot be separated. As an example, Sherrington said, 'one might take the arousal reflex elicited by an "artificial flea" in the form of a hair-brush stroked lightly on skin behind the ear. The dog executes a most complex series of postural reflexes to balance itself while scratching. An array of muscles is co-ordinated or integrated in this act'.

If one were to check the very fundamental observations Sherrington made on posture, they would fill this book. Alongside his experimental and conceptual advance towards the definition of properties of synaptic action at neuromuscular single neurons, his work on tone, or posture as he preferred to call it, stands as a monument any pioneer in a field whose third component is the analysis of neuronal transmission. I place these in this order but we have see that Sherrington himself put neuronal transmission first, probably because to him it must have been the great open-prize for the general problem of inhibition. And to this particular concept of his youth became surrounded by an aura of delight that never vanished

When we now call the Sherrington type of decerebrate

rigidity discussed above, it is idiot of extensor spasm or exaggerated tone dependent upon tonic influents from the rigid muscles. But it is not the only form of extensor rigidity, as Sherrington very well understood. Abolition of the cerebellum will also cause rigidity, and *sometimes* this state with the one existing upon intercollicular section Sherrington with preservation tonicity remained. 'That the two conditions are identical I am not convinced' (1908). Later, but in his *Decline*, Fulton, and Dow contributed experiments which make it clear that cerebellar rigidities did not vanish upon decerebration. Sherrington himself showed that rigidity in the forelimbs followed when the spinal cord was sectioned at some lower level. This finding is known as the Sherrington phenomenon because Sherrington had made a similar observation on the frog (1910). In 1908 it was taken up again by T. C. Ruch. Today we know a great and more about the various factors determining muscular tone (see later) and they have been well analysed by Merritt in his important monography with Dow, the latter responsible for the clinical part (*Physiology and pathology of the cerebellum*, 1958).

The restricted space available for discussion of such subjects should not lead to the mistaken conclusion that nothing was known about supraspinal factors influencing tone before Sherrington entered on the stage. He had had great predecessors, especially in the field of cerebellar physiology, and at least two names must be mentioned, Luciani of Bologna (1891–1907), in perspective one of the greatest of all French physiologists, and Jolyot (1862–1905), particularly a monumentary, who has published his thirteen book, *Il Cervelletto*, in 1901. Would, when Sherrington knew well, had printed on a clear demonstration of the vestibular organs reduces the tone of the viscera, mentioned on the side of the operation. Sherrington's standpoint that the cerebellum might be regarded as the central station for the control of proprioceptive reflexes therefore had road support in both old and contemporary experimentation.

In this section still total? There are those who deny this, basing themselves upon what Bikman has called the 'unexpected discovery' that the cerebellum receives no proprio proposition from exteroceptive senses such as the eye, the ear, and, in particular, the ear. This was found almost simultaneously in

independent electrophysiological experiments by Adrian, and also by Dow and by Bishop (1942 to) and co-workers. But why need such findings indicate the contrary? Even from the cerebellum proprioceptive head ganglion? It seems reasonable that an organ for proprioceptive control would need all that information from exteroceptive sense organs, after all, is part of every movement and movements taken place in surroundings continuously measured by our exteroceptive sense aided by its vestibular organs of balance and its endings in muscles and joints. The cerebellum, we might say today, in expanding Sherrington's concept, integrates sensory information for the purpose of postural control. Space does not permit us to discuss other tasks allotted to this organ (cf. the Dow and Moruzzi monograph, mentioned above).

Sherrington's work on muscular tone had led him to the final conclusion that, in mammals, tone was due to postural reflexes, just as Bronchgeest, at Utrecht (1896) had found it to be the case in frogs and toadies. Bronchgeest's work had unfortunately been repeated and confirmed by Dr Bloomfield in the laboratory of Dr Rein-Raymond, who added more to this effect in his *Archives* where Dr Dumb worker had published his findings. These professors accepted Sherrington's view that in the case (in 1908) when Magnus arrived in Liverpool and possibly the latter had been impressed by the 'tonic reflexes' which the decerebrate animals assumed when stimulated in various ways (Fig. 7). So that as it may, when Magnus with his co-worker de Kleijn demonstrated that cutting of the head set up characteristic posture of tonic extension (*tonic*), Sherrington was also anxious to bind this theme over to them even though, two years before, he had written in his *summary study of stepping and standing*: 'Again, unless or passive rotation of neck or its long axis in the decerebrate preparation inhibits extensor tonus in hind-limb on the side of the lowered pieces and causes active flexion of knee; and does so also extensor in hind crural; this and both extra.' Indeed, Magnus and de Kleijn were urged by Sherrington to pursue their work and in this and they made a monumental contribution to our knowledge of neuronal reflexes. In one course Magnus and de Kleijn receive medical and later for our Nobel prize (*Allgemeines*) but Magnus' untimely death (1927) put an end to such proposals

The work of Magnus and de Kleijn is a model of just investigative physiology. It describes a large number of automatic reflex adjustments of posture which are mainly 'figures' or the sequences of coordinated acts, the most interesting being the righting reflexes analysed in the labyrinth which and those arising from the labyrinthine organs and the neck receptors (or, rather, their ligaments. McCouch) which lead to characteristic postural effects from the head upon body and limbs. These involve our long spinal paths which Liddell and Sherrington had studied (1924). Magnus and de Kleijn were also impressed by their own findings to make a fundamental analysis of the neural mimesis in which the vestibular organs are sensitive, a field in which another pupil of Sherrington's, the late Mario Ghinis, professor at Parma, had made serious, his excellent monograph *The Physiology of the Vestibular Apparatus*, was translated into English by R. S. Creed in 1929.

The integrative line and Sherrington's work on the cortex appealed particularly to pupils of certain temperaments and interests especially, of course, to those who wanted to devote themselves to clinical work; the spinal cord work, as the years went by, tended to become more theoretical and analytic and this line therefore had not great appeal for the physiologists and the theoretically minded. To the former group belonged John Fulton (1899–1960), professor at Yale University, who defined a great role as an inspiring force in brain physiology. 'The contributions of the first laboratory of primate physiology in the U.S.A. was a signal triumph' (or Fulton, wrote Earl Walker in his obituary and continuing, expressions of the great nations of the past were repeated three under more ideal conditions and with statistical controls so that they yielded more "meaningful" results. In the thirties Fulton's laboratory attracted a large number of younger biologists and neurons opens from all over the world and many more have sought information about the intricate functions of the brain from his *Physiology of the Nervous System*. Throughout his life, Fulton looked upon the Oxford years and the guidance of Sherrington as his main source of inspiration.

The most important clinical schools which owe allegiance to Sherrington are the Montreal Neurological Institute, Wilder Penfield's creation, where he and Herbert Jasper have for years played a leading role in world neurosurgery, and the department of Dusseldorf in Bonn, combining experimental neurology with clinical work.

A large part of the influence of a teacher, and the most difficult part to assess, is the Certain from the example he sets in trying to realize his ideals scientific, personal, moral, aesthetic, and in his happy towards them. A sense of idealism and the pursuit of goals must perhaps be accepted as an expression of their attempts in the endless valid kinds of the ones, aimed to carry them through disappointment and setbacks. In this wider sense Sherrington was a teacher of many young men who knew in life remembered him with gratitude and paid homage to his influence. There are difficulty to name others they were actual, somewhere or have since made a name for themselves in the wider sphere of influence. It is impossible to mention more than a few, neurologists such as Russell (Sam, Lord) Brain, Stanley Cobb, W. G. Gibson, Gordon Holmes, Sir C. Jefferson, S. Ormiston, Henry Head, F. M. R. Walshe, physiologists, as H. C. Bazett, S. S. Dresser, Lord Florey, the brothers H. S. and E. C. Hoff, Grayson McCouch, Ian Munro, Karl Mashin, F. R. Miller, J. M. D. Olmsted, H. W. Holt, H. E. Hoff, T. C. Ruch, E. Sarra, S. C. M. Sherrin, F. M. Toner, and many others.

Graham Brown, representing an older generation of co-workers, is here chosen as their spokesman: 'It was to those who worked in his laboratory that Sherrington gave and showed most. The research effected would enter in, finally, with a second volume of the author of his *Integrative Action* to a man who was in itself in a sphere of his own making, difficult to attain or to travel to . . . a man necessarily aloof and out of common reach, "academic", coldly intellectual. But his discerning spirit of equality with which the student was received at once dissipated a natural barrier which could not in any case have for long withstood the sympathetic friendship which was offered by Sherrington and turned in return. . . . The laboratory life was a continuing adventure with always widening horizons . . . he would be moved . . . by the beauty of an experiment or of an ingenious technical method. And always there was originality and delight.'