J.G. Dusser de Barenne *1885-1940*

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Joannes Gregorius Dusser de Barenne was born on June , in the village of Brielle in the Dutch province of Zeeland, the son of Dorothea Vogelzang and Elize M. Dusser de Barenne. His father was the chief of police in Brielle from , and in Amsterdam from . He studied medicine at the University of Amsterdam, graduating in . On October , he married Kate Snellen, daughter of the well-known Dutch ophthalmologist Snellen, who succeeded the great ophthalmic surgeon Frans C. Donders as professor of Ophthalmology at the University of Utrecht. They had three daughters. Mrs. Dusser de Barenne died suddenly in Ithaca, New York, on the May , , while accompanying her husband on a lecture trip. Four years later (in June), he married a former student of his at Yale, Emily Lockwood Greene; they had one daughter.

Figure .
Johannes Gregorius Dusser de Barenne.

His professional career began in as teaching assistant in the Physiology laboratory in Amsterdam, where he started his work on the effect of strychnine on the reflex activity of invertebrate ganglia. These initial studies concerned the effect of local application of strychnine on the reflexes of the spinal cord. ' Seven of the nine papers he published during the period - dealt with the effects of strychnine on various parts of the nervous system. Magendie had already used strychnine ( ) to substantiate his findings concerning the motor function of the dorsal spine roots. In Dusser's hands, the procedure entailed application of small pieces of absorbent paper soaked in a solution of strychnine on to a - mm area of the exposed spinal cord of the cat or, later, the cerebral cortex of that animal, which rendered the associated cutaneous and deep pressure receptors hypersensitive, thus defining the function of the 'strychninised' area of the cerebral cortex ( ). "Dusser de Barenne quickly grasped the potentialities of the drug as a tool for investigations of the activity of the nervous system, and, in later years he used the alkaloid in connection with many of his most fundamental studies of nervous function" (Fulton and Garol). Further details of these studies are given below. His wide use of this compound as a research tool "won him the nickname he enjoyed - Strychnine" (McCulloch).

He was appointed psychiatrist at the Meerenberg psychiatric institute, north of Amsterdam, in September . He remained there until the outbreak of World War I, engaged in the physiological analysis of decerebrate rigidity , earlier described by Sherrington and others, and also of tonic neck and labyrinthine reflexes. Among

other things, he established the fact that well-defined action currents can be detected in muscles exhibiting the rigidity of the decerebrate state.

During World War I he served as a medical officer in the Dutch Army in Delft (August , - April ,). Despite his military duties, he managed to continue research on the tonic contraction of skeletal muscle, publishing fourteen papers in this period, including one on the functional localisation of sensory phenomena in the cerebral cortex and one with J. Boeke on the sympathetic innervation of skeletal muscle.

The fourth phase of his scientific career started in , when he became assistant to Rudolf Magnus at Utrecht. He participated actively in the work of Magnus's team for twelve years, helping to develop the physiological concept of 'Körperstellung' (posture), which earned the Utrecht school international recognition. In addition, between May and September , he published papers on a variety of subjects including the action of insulin, the metabolism of muscles during decerebrate rigidity, the influence of the vagus nerves on action currents of the diaphragm, and several papers on nystagmus, as well as one with Magnus on righting reflexes in the decerebrate cat and dog. His most important contribution during this period was the result of a few months stay at the laboratory of Sir Charles Sherrington in Oxford in the spring of where he studied the sensory symptoms produced by local application of strychnine to the cerebral cortex of rhesus monkeys (Fig.). The paper describing the results of this investigation became a classic of neurophysiology within five years.

While there, he demonstrated for the first time the major functional subdivisions of the sensory cortex, viz. the areas for the leg, arm and face. This paper was the first of an important series on functional localisation in the cerebral cortex. During , in collaboration with Sager – a scientist who had come over from Bucharest – he used the same approach in experiments on the cat to explore the last relay station of sensation, the thalamus opticus. Thus, by , he had delineated the entire central system subserving bodily sensation with the aid of the technique of local strychninization that he had developed. He had thus clearly and largely anticipated the famous explorations at McGill University and later at the Montreal Neurological Institute by Wilder Graves Penfield (-), who identified the cortical areas, mild stimulation of which elicited motor or sensory

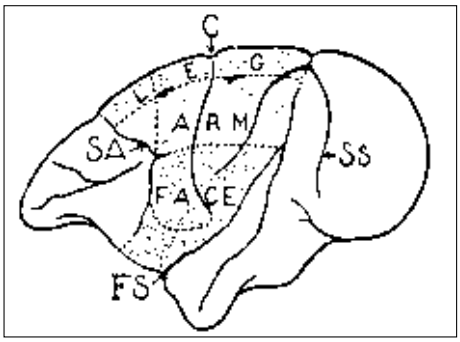

Figure .
Map of somatosensory cortex in macaque as outlined by method of strychnine stimulation. Abbreviations used are: C., central fissure; FS., sylvian fissure; SA., arcuate sulcus; and SS., simian sulcus (external parieto-occipital sulcus). (After Dusser de Barenne, Proc. Roy. Soc. B ( ), -).

responses, changes in speech and vocalisation, memory of past experience, and visual and auditory effects. Penfield did not start these experiments until , after having returned from Breslau where he had seen for the first time the human electrocorticograms taken from conscious patients in Otfrid Foerster's clinic.

The year became a turning point in Dusser de Barenne's career. By this time he had, according to Fulton and Garol, "become the foremost of the younger generation of Dutch physiologists." In this year, the physiologists Rudolf Magnus in Utrecht and Nobel Prize winner Willem Einthoven in Leiden both died and a third professor of Physiology, Hendrik Zwaardemaker, retired. The three most important chairs of Physiology and Pharmacology in the Netherlands thus became vacant almost simultaneously. Although second on the list in Leiden, the chairs were for extraneous reasons again occupied by others. "And so it came to pass that the Netherlands allowed the United States to claim one of the most distinguished physiologists the continent of Europe has ever produced" (McCulloch). After some initial hesitation, Dusser de Barenne was persuaded to come to the Yale School of Medicine at New Haven to establish a neurophysiology research laboratory there.

He arrived in Yale with his family on September , . His first research collaborator was Clyde Marshall, neuroanatomist, well acquainted with the work of Magnus and Rademaker, with whom Dusser described a release phenomenon induced by isolating a locus of the motor cortex from adjacent cortical areas. The second was Stephen Brody, with whom he studied the effects of hyperventilation on the excitability of the cerebral cortex. These two papers inaugurated a whole series of key-studies on the functional organisation of the cerebral hemispheres in primates. A fruitful collaboration was begun in with Warren S. McCulloch, , who was his devoted and congenial colleague in research for six years. With the subsequent arrival of Leslie Nims and others a team was built that demonstrated the reciprocal relationships between the activity of the cortex and its hydrogen-ion concentration. The research programme inaugurated by Dusser de Barenne at Yale thus proceeded in the most logical manner from the study of the release phenomenon with Marshall via the investigation of the effects of hyperventilation on cortical excitability with Brody, the development of thermocoagulation (a new technique for selective laminar destruction of the cerebral cortex which proved to be a powerful tool for mapping the function of this organ) with Zimmerman, and the study of excitability cycles with McCulloch, to its culmination in - when Dusser de Barenne worked with Nims and McCulloch to show how the above-mentioned phenomena were correlated with changes in the hydrogen-ion concentration of the cerebral neuropil.

In his physiological work Dusser de Barenne developed many new techniques such as the strychnine method for localisation of sensory function, laminar thermocoagulation for analysis of the cortical layers, and adaptation of electrical techniques for study of the interaction between specific cortical areas. J.F. Fulton and H.W. Garol, two friends and colleagues, in an obituary in the pages of the *Journal of Neurophysiology*, of which Dusser de Barenne was co-founder and co-editor, stated:

> "He will be remembered for his unyielding faith in the experimental method and for his utter intolerance of those who placed the armchair ahead of the experimental table for solving the problems of physiology. He was a man of strong personality and strong loyalties, and he had a number of heroes. Among those was Claude Bernard, whose portrait was always before him on his desk; another was Carl Ludwig; and the third was his chief at Utrecht, Rudolph Magnus. These were men of action, men of experiment, men who never allowed their deduction to exceed their evidence [...] Although he did not have a formal obligation to teach he offered each year one or two electives, either on the sense organs, or on special phases of the physiology of the central nervous system. Almost invariably he illustrated the lectures by experimental demonstrations into which he had put much time and thought, and usually he ended these amusing and informative discussions in a fever heat of perspiration. The students responded with great warmth of appreciations, for these were lectures unique in their medical experience."

W.S. McCulloch also cast light on these lectures in the obituary he wrote for the *Yale Journal of Biology and Medicine*:

> ."... these lectures combined a continental dignity with amusing turns in phrase and turns of the dynamic lecturer, which were a source of unending delight to the class. No one can, for example, forget his demonstration of nystagmus in the cat, during which he pirouetted around with a cat in his arms, and would stagger back to the blackboard, saying his semicircular canals were more affected than those of the cat. It was great teaching, great devotion to an ideal - the creed of experimental physiology which the students at Yale will not soon forget... "

Any league table of the centres of excellence for experimental physiology in the years - worldwide would have placed Dusser de Barenne's neurophysiology laboratory at the Yale School of Medicine high in the top ten. Known as the 'father of chemical neuronography', Dusser de Barenne showed in subsequent experiments that the electrical disturbance produced by the simultaneous firing of the underlying cells, could be recorded at the nerve fibre endings. This method provided a physiological cross-check of the connections found by the anatomists on dissection of dead brains, but divulged nothing about the pathways traversed from origin to destination; its major benefit was in demonstrating the multiplicity of corticocortical links. Dusser de Barenne demonstrated the wide-ranging extent of such links in the frontal cortex by application of strychnine on either side of the central (rolandic) sulcus, thus greatly intensifying the sensitivity of the organism to somatic sensory stimulation. This was shown first in the cat ( ) and later in the monkey ( ). As soon as the sensory cortex subdivisions were mapped in the monkey he turned to the chimpanzee to discover the finer differentiations of this structure and to obtain a better indication of what might be expected in man. Experiments on the chimpanzee were well under way when Dusser de Barenne died on June , . Several unpublished

and almost completed manuscripts, and others, for which his notes and conclusions exist, are preserved in the Dusser de Barenne archives at the Yale Medical Library. Chemical neuronography led to the discovery of hitherto unsuspected fibre connections and projections (chiefly nonmyelinated). Some neurophysiologists fostered doubts about the method. The absence of clear-cut findings in some cases could cause confusion about the interpretation of the experimental results. Others, such as Adrian and Moruzzi in England in , elaborated the technique and examined the strychnine-evoked potential with the aid of loudspeaker effects (dramatically described by Moruzzi many years later). After a number of preliminary investigations of the electrical activity of the cortex in - , "he [D de B] finally gave permission to put on strychnine" – as McCulloch recalls – "and watch the oscillograph. His face when he saw the first record is as unforgettable as the strychnine spike itself…."

The method of laminar thermocoagulation ' came to him in a dream, as he recalled later during a conversation with his friends Fulton and McCulloch. The sudden death of his wife in had depressed him to such an extent that he thought of quitting science. He lay awake night after night, worrying about the impasse in his laboratory work for lack of a method to determine which layers of a cortex were requisite for sensation. Finally, in the middle of one long lonely night he thought of getting up and having breakfast, but dozed off. In his dream, he saw an egg cooking slowly. He jumped from his bed, rushed to the laboratory, heated a brass rod in boiling water, and applied it to the cortex of an experimental animal. Within twenty minutes, the method of laminar thermocoagulation was at his fingertips (McCulloch). "It was equally characteristic of the man that he used that insomnia which never left him as an opportunity to become most erudite," McCulloch goes on to say.

During the s, voluminous evidence accumulated for what came to be termed the 'feedback' of information between cortex and thalami. In a presentation on this topic to the Boston Society of Psychiatry and Neurology, B. Brouwer ( ) from Amsterdam embellished his talk with slides, drawings and glass models, then much in vogue, depicting centrifugal and centripetal brain systems. He acknowledged the key role that Dusser de Barenne's neuronographic techniques had played in his researches, and reported: "A very remarkable fact is this, that many fibers descending from various parts of the cerebral cortex, go back to all their [thalamic] nuclei."

Dusser de Barenne argued that the bilateral 'thalamic syndrome' of acute cutaneous hypersensitivity after application of strychnine to a small area of the sensory cortex, despite the novocain decortication of the surrounding areas, must be due to "setting on fire the cortex of the whole sensory arm area and… those [representational] portions of the optic thalamus" (p.). This was Dusser de Barenne's contribution to an elucidation of a syndrome that had long baffled clinicians. In his assumption of a close functional relationship between cortex and thalamus (Fig.), Dusser de Barenne joined the company of those clinical investigators, among them Head and Holmes, von Monakow and Dejerine, who entertained the idea of an interactive information flow between cortex and thalamus.

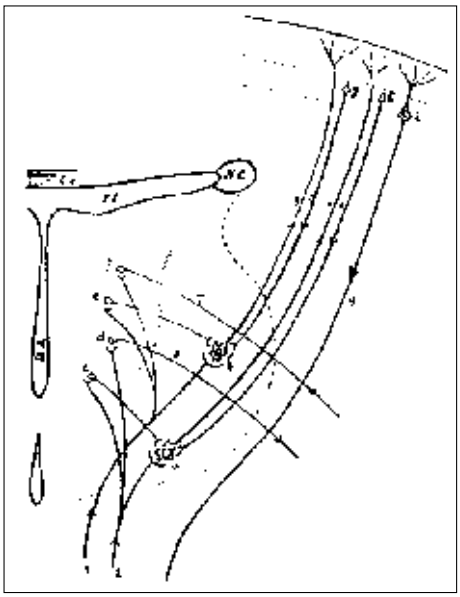

Figure. .
The scheme of reciprocal action between cerebral cortex and thalamus, as sketched by the 'father of neuronography'.
a, b - ventrolateral thalamic nuclei; c, d, e, f - medial thalamic nuclei; g, h - corticothalamic neurons; , - afferents from the periphery; , - corticopetal fibers to sensory cortex; , - corticothalamic fibers; , - extrapyramidal fibers; i, - corticifugal, pyramidal fibers.
(From Dusser de Barenne ( ) , Fig. , x .)

At that time, the ground was ready for an entirely new approach to the understanding of neural networks. The benefits derived from the method permitting demonstration of the wide-ranging corticocortical, corticothalamic and other connections developed at Dusser de Barenne's laboratory elicited great public interest. A front-page article in the New York Times of December brought readers the news on this topic under the headline '"Inside telephones" in Brain': "Dusser de Barenne, interviewed, claimed the new 'brain circuit' might be likened to an 'interoffice' communicating system which linked the cerebral cortex with the thalamus. Thus he said a mutual exchange of messages goes on constantly between the old (the seat of emotions) and the new brain (seat of intellect) on the one hand, and the sense organs and the muscles on the other hand...."

By , the concepts of thalamic cytoarchitecture and cortico-thalamic connections were fairly well established, the former in part through the work of Cajal and the latter equally so through neuronography as elaborated by Dusser de Barenne and McCulloch. The occipital cortex occupies a position of prominence in the history of the human brain – anatomically, physiologically and behaviourally – because it is the primary cortical projection of the most extensively studied of the senses. In , he stated that vision "is, I think, the function which in the higher mammals has become most corticalized" (Dusser de Barenne , p.). Dusser based his opinion on the fact that vision has a distinct and stable localisation, in contrast to other functions, which are more diffuse and may show marked repair of lost function. "His statement was made prior to discovery of many additional cortical centres concerned with vision whose relation to the phylogenetic response to evolutionary influence is still not understood."

Hughling Jackson (-), the conceptualist, a man of few words and often with second thoughts of what he had published but with emphasis on the non-existence of sharp boundaries around cerebral functional areas, would have nodded his

assent hearing Dusser's views on 'corticalisation'. He would have been comfortable with Dusser's warning ( ) "about the parochialism of designating" localisation "for a function that so patently takes place in many parts and levels of the brain." Dusser preferred 'corticalisation' as the more accurate term. ' -

The close collaboration with Warren S. McCulloch (-) has been mentioned several times above. Further details of McCulloch's life are given by Marshall and Magoun ( ). From an early interest in philosophy, McCulloch trained as a psychiatrist; his attainments eventually gained him memberships in an unusually broad array of professional societies, representing the fields of neurology, anatomy, physiology, mathematics, biological psychiatry, arts and sciences. Such diversity was lodged in a man who was dubbed a "rebel genius" (Gerard) and whose intense eyes, unfashionable beard and abrupt manner did not inspire general confidence. Nonetheless, he was a magnet to those neuroscientists who could conceptualise beyond impulse conduction and the neuromuscular junction. The collaboration between Dusser de Barenne and McCulloch bore the richest fruits during the last six years of the former's life, due to the synergy of their different mind-sets and their unusual friendship. It would thus seem appropriate to conclude this portrait by citing McCulloch ( ) once more: "To succeed at all any man so heartily kind and trusting must carry a shield. To the outsider he appeared suspicious and as blunt as only those can afford to be who are completely humble to the fact. But once past that guard all were compelled, by his very openness, to give him their best."

Fulton, another friend, wrote later from New Haven: "The sudden death of Professor Dusser de Barenne on June , , occurred at a time when international communications were seriously disrupted, and many of his colleagues in Europe were therefore long unaware that his brilliant career had been brought to a premature close when he was but fifty-five years of age and at the height of his powers..."

Acknowledgements

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Extensive use has been made of the obituaries written by Dusser de Barenne's close friends and colleagues J. F. Fulton and H. W. Garol (Fulton and Garol) and W. S. McCulloch ( ) in the preparation of this biographical note.

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