Available online at www.sciencedirect.com
SCIENCE DIRECT®
NeuroImage
NeuroImage 20 (2003) S2–S7
www.elsevier.com/locate/ynimg

Cerebral localization, then and now

John C. Marshall[a,b,*] and Gereon R. Fink[c,d]

[a] University Department of Clinical Neurology, Radcliffe Infirmary, Oxford, UK
[b] Department of Psychology, University of Hertfordshire, Hatfield, UK
[c] Institut für Medizin, Forschungszentrum Jülich, Germany
[d] Neurologische Klinik, RWTH Aachen, Germany

Received 5 September 2003; accepted 5 September 2003

Abstract

We review some of the progress made in understanding the nature of functional specialization in the human brain, beginning with the anatomical claim that all mental faculties have their own distinct material substrate in different regions of the brain and the psychological claim that each mental faculty is characterized by the content domain with which it deals. This conceptual framework led behavioral neurologists to show how discrete brain lesions provoked different types of language, praxic, gnostic, spatial, and memory disorders. The simplest way of interpreting these anatomoclinical associations was to conjecture that the normal function (now impaired by brain damage) was localized within that lesioned region. It was also realized that cognitive impairments could arise from lesions that spared the functional centers themselves but disconnected them from other centers. Nonetheless, many neuroscientists remained skeptical of the entire paradigm. Accordingly, in the late 19th century functional localization began to be studied in the intact human brain by such techniques as measuring the temperature of different brain regions when different cognitive tasks were performed. During the 20th century these crude techniques gave way to positron emission tomography, functional magnetic resonance imaging, and magnetoencephalography. The relatively precise spatial and temporal resolution of modern methods now raises a crucial question: Do the functional localizations obtained by the anatomoclinical method converge with those implied by the functional neuroimaging of cognition in healthy volunteers? We then conclude with some recent suggestions that functional specialization is not such a fixed property of brain regions as previously supposed.

Keywords: Anatomoclinical method; Functional neuroimaging; Functional brain specialization; Functional brain integration; Phrenology

From organology to anatomo-clinical methods

Hippocrates (460?–377 BCE) was well aware that the brain was the material substrate underlying all cognitive, affective, and conative powers and processes:

> It ought to be generally known that the source of our pleasure, merriment, laughter, and amusement, as of our grief, pain, anxiety, and tears, is none other than the brain. It is specially the organ which enables us to think, see, and hear, and to distinguish the ugly and the beautiful, the bad and the good, pleasant and unpleasant. . . .It is the brain too which is the seat of madness and delirium, of the fears and frights which assail us, often by night, but sometimes even by day; it is there where lies the cause of insomnia and sleep-walking, of thoughts that will not come, forgotten duties, and eccentricities" (Gross, 1998, p. 13)

But another two millennia were to pass before a paradigm was proposed that could guide a research program on the nature of functional specialization in the human brain. This framework was first advanced by Franz Joseph Gall (1758–1828). Gall put forward two bold conjectures, one anatomical and one psychological, that would guide most 19th- and 20th-century attempts to understand the relationship of mind to brain.

Gall's anatomical claim was that all mental faculties have their own distinct material substrate in punctate regions of the brain; his psychological claim was that each

* Corresponding author. Neuropsychology Unit, University Department of Clinical Neurology, Radcliffe Infirmary, Woodstock Road, Oxford OX2 6HE, UK. Fax: +44-1865-556164.
E-mail address: john.marshall@clneuro.ox.ac.uk (J.C. Marshall).

1053-8119/$ – see front matter © 2003 Elsevier Inc. All rights reserved.
doi:10.1016/j.neuroimage.2003.09.001

mental faculty or organ is characterized by the content domain with which it was concerned (Gall, 1822–1825). The cerebral cortex is thus seen as a mosaic of organs specialized to deal with, for example, language, number, music, and color. The characterization of these organs has nothing in common with the earlier cognitive powers of scholastic philosophy: attention, perception, abstraction, reasoning, and memory. There the faculties were defined primarily by what they do, that is, by the processes they carry out, irrespective of what was being processed. By contrast, Gall's organs are defined by the type of material that they analyze and produce (Marshall, 1984).

The distinction is very clear in the way that the two systems dealt with memory. For the Scholastics, memory was a primitive unitary faculty of mind deployed in remembering all manner of information, verbal, spatial, visual, auditory, and so on. For Gall, "memory" in the scholastic sense is merely an abstraction that conceals the true biological proliferation of different, domain-specific memory systems. Gall himself differentiated between "memory for facts" (now known as declarative memory), "memory for words" (now known as semantic memory), and "sense of place" (now known as topographic memory). Furthermore, Gall argued that it was reasonable to expect that related, but distinct, functions would be found in close spatial proximity. "Memory of words" and "sense of language and speech," organs 14 and 15 in Gall (1822–1825), were placed adjacently in the posterior region of the orbital area of the inferior surface of the frontal lobes. Later phrenologists, such as Spurzheim, reported that the organs responsible for the analysis of shape, size, and color are clustered together, as are the organs of order and calculation. The idea, presumably, is that communication between specialized but congeneric cognitive modules would be facilitated by contiguity of their physical substrates. Although Gall did not discuss what we would now call disconnection syndromes due to white matter lesions, his status as the greatest neuroanatomist of his day (according to Flourens, 1846) would have left him in no doubt that an anatomical basis for information transfer between related cognitive modules was in place.

Gall made the mistake of thinking that the relative sizes (and hence the differential efficiency) of the cortical organs he postulated could be inferred from the size of the overlying area of the skull. Indeed, this erroneous assumption was the basis on which he had originally "discovered" the cerebral locus of those mental functions that could be so variably developed within and between individuals. Nonetheless, Gall was aware that craniology may be an unreliable guide to the brain structures that were his primary concern. Crucially, however, Gall's craniological localizations could be confirmed (or refuted) on the basis of the patterns of impaired and preserved cognitive performance that followed relatively discrete brain lesions. Gall had initially localized memory for words in prefrontal cortex on the basis of the (purported) fact that people who were especially good at memorizing verbal passages had protruding foreheads and large bulging eyes. Confirmation was then obtained when Edouard de Rampan, a patient referred to Gall by Napoleon's surgeon, sustained a fencing injury to the left frontal lobe that resulted in right-sided paralysis and an isolated but severe loss of memory for words. There remained the problem of explaining why a unilateral lesion could give rise to such a profound impairment: All mental organs in Gall's scheme were bilaterally represented. But it did not seem unreasonable to argue that a sudden insult to one hemisphere could "upset the balance between the two hemispheres, thus affecting the faculties on both sides" (Finger, 2000).

More importantly, the stage was set for physicians to deploy what became known as the anatomoclinical method: brain autopsy at death reveals the pathological changes responsible for the patient's acquired cognitive impairment in life. This method would eventually uncover the fact that the two cerebral hemispheres had their own functional specializations.

The classic anatomoclinical method and its critics

The false parts of Gall's doctrine—reading competence and character from bumps on the skull—rapidly became a joke in most medical circles. But organology or phrenology (the latter term was created by Gall's one-time assistant, Spurzheim), in the sense of deploying the anatomoclinical method to elucidate mind–brain relationships, rapidly became established across the entire Western world. As Paul Broca was eventually to phrase the issue, "I had thought that if there were ever a phrenological science, it would be the phrenology of convolutions [in the cortex], and not the phrenology of bumps [on the head]" (Broca, 1861). The evidence for relevant anatomoclinical associations rapidly accumulated from the 1820s onward. Both explicitly phrenological journals and more mainstream medical journals reported a steady flow of case reports in which different types of language disorder, praxic disorder, gnostic disorder, spatial disorder, and memory disorder had resulted from a moderately discrete, well-localized brain lesion, with relative sparing of other cognitive functions.

Language loss was the first disorder to be studied systematically. In 1825, the Parisian physician Jean-Baptiste Bouillaud published the first of his many papers on impaired speech after frontal lobe damage in explicit support of Gall's localization of "l' organe du langage articulé" (Bouillaud, 1825). Eventually, Broca (1865) realized that it was unilateral lesions of the left third frontal convolution (and not the right) that typically resulted in loss of "the memory of the procedure that is employed to *articulate* language." A little later, Carl Wernicke (1874) remarked on the association between injury to left temporal cortex and a pattern of behavioral impairment that included fluent but paraphasic speech allied to considerable difficulty in language comprehension.

After Broca (1865) the floodgates opened. Harlow (1868) described "enfeebled" intellectual faculties and uninhibited "animal passions" after bilateral frontal damage. Jackson (1876) observed that higher visuospatial abilities were differentially impaired by right hemisphere lesions and conjectured that right posterior cortex played the major role in visual "mentation." Lissauer (1890) began to describe different forms of visual recognition disorder, including apperceptive and associative agnosia, after occipito-temporal lesions. Liepmann (1900) began to analyze the different forms of praxic disturbance seen after left parietal lesions. Dejerine (1892) produced the first convincing disconnection model of alexia without agraphia after lesion of the left angular gyrus and the splenium of the corpus callosum. Alzheimer (1907) described a patient with rapidly progressive memory loss who suffered from a neurodegenerative disease that is now known to disproportionately affect the medial temporal lobes in many cases.

We will not continue with this listing. A glance at any current textbook of neuropsychology or behavioral neurology will confirm how throughout the 20th century more and more cognitive impairments were described and putatively associated with specific lesion loci. It is, however, equally clear that, from the very inception of the anatomoclinical paradigm, critics have voiced two very different objections to the entire enterprise. The first objection is simple to state, if difficult to address in a principled fashion: There have always been substantial numbers of apparent counterexamples to particular anatomoclinical associations. With respect to language impairments, heated discussions of problematic cases have a long history (see, for example, Moutier, 1908). More recently, similar issues have arisen with respect to the relationship between different types of left visuospatial neglect and their anatomical substrates (Halligan et al., 2003). Visual neglect can fractionate as a function of task (e.g., line bisection vs cancellation), spatial domain (e.g., peripersonal vs extrapersonal), spatial frame of reference (e.g., egocentric vs allocentric), response mode (e.g., left hand vs right hand), and representational type (e.g., perceptual vs imaginal). Anatomically, visual neglect is most usually seen after lesions of the right inferior parietal lobule (Mort et al., 2003) but is also found after lesions of the right superior temporal gyrus, right lateral premotor cortex, thalamus, basal ganglia, and cerebellum. One might accordingly have hoped that the different subtypes of neglect would map onto different lesion sites in the distributed circuit that underlies spatial cognition. But, so far, this hope has not been realized.

In general, the problem here is not that the textbook localizations are false. It is rather that they give a somewhat idealized picture of the primary data on which they are based. There are, of course, well-known escape routes. Naturally occurring brain lesions may impair many distinct functions; disruption of white matter fiber tracts can result in malfunction of regions that are far distant from the primary lesion site; and both cortical and subcortical gray matter lesions can give rise to distance effects ("diaschisis") as reflected by hypoperfusion and hypometabolism in the absence of any structural damage. In addition, there may be genuine biological differences in gross structure–function relationships between individuals. These complications do not render the anatomoclinical method invalid, but they do indicate how it is fraught with practical difficulties even in the age of computed tomography and structural magnetic resonance imaging. It is little wonder that in both the 19th (Lichtheim, 1885) and 20th (Marshall and Newcombe, 1973) centuries some neuropsychologists would choose to construct models of cognitive functions from the patterns of impaired and preserved performance seen after brain damage but give little thought to the location of that damage.

The second objection to the anatomoclinical method was not an objection to the method per se but rather to the *functional* interpretation of the results obtained thereby. Few neurologists and neuropsychiatrists were content merely to state that there was an association between such and such a lesion site and such and such a symptom or symptom complex. From Gall onward, the temptation seemed almost irresistible to postulate that (1) particular mental functions had been impaired by brain damage; and (2) each of these (normal) functions was localized in the region that, when damaged, gave rise to the symptoms. The observant reader will have noted that we followed this convention in some, but not all, of our descriptions of classic findings. But, when the convention is baldly stated, it is obvious that the inference from localized symptoms to localized (normal) functions is anything but straightforward. As Jackson (1874) originally phrased the point, "To locate the damage which destroys speech and to locate speech are two different things."

Von Monakow (1911) took up the same theme when he argued that many behavioral neurologists "employed (at least) three quite distinct concepts of localization: genuine anatomical localization of nerve tracts and specified cell types; correlations between (grossly) localized pathology and manifest symptoms; localization of basic psychological functions." Von Monakow (1911) concluded that "Nothing has so obscured the problems of cerebral localization or led it so far astray as the confusion between these three different modes."

Assume for the sake of argument that "basic psychological functions" (whatever they may be) are localized in a punctate fashion and that complex psychological functions are constituted from many such basic functions joined together in distributed circuits. It still would not follow that the symptoms that resulted from localized lesions to such a circuit necessarily enabled one to localize psychological functions. Rather, the symptoms may have arisen from a reconfiguration of the entire circuit in response to damage. As Goldstein (1948) wrote, the correct question may not be "where is a definite function or symptom localized?" but rather "how does a definite lesion modify the function of the brain so that a definite symptom comes to the fore?" It is only recently that neuroscientists have explored the latter possibility in a computationally precise manner (see, for example, Young et al., 2000). One might also argue that pathological inquiries must be complemented by investigations of the entire neural circuit that underlies particular cognitive functions in the *healthy* human brain. It is to this topic that we now turn.

The development of functional neuroimaging

In the closing decades of the 19th century, it was widely recognized that new techniques were needed to study the neurophysiology of the living, structurally intact brain. From a clinical standpoint, Jean-Martin Charcot and his group at the Salpêtrière had become deeply concerned with how patients without any apparent structural injury to the brain could nonetheless manifest symptoms that mimicked organic paralysis, sensory loss, or cognitive disorders such as aphasia. Charcot (1889) conjectured that in such cases there would be "dynamic" or "functional" lesions in the regions in which structural damage could give rise to the same symptomatology. The physical basis for these functional lesions was hypothesized to be localized anemia or hyperemia "of which no trace is found after death" (Freud, 1893). It would not be possible to adequately test such neurophysiological accounts of "hysterical" disorder for another hundred years (Marshall et al., 1997; Vuilleumier et al., 2001). Nonetheless, early attempts to associate cognitive and affective states with local measures of cerebral physiology in healthy individuals cast an interesting light on current concerns.

One modest but elegant technique worked as follows: "The subject to be observed lay on a delicately balanced table which could tip downward either at the head or at the foot if the weight of either end were increased. The moment emotional or intellectual activity began in the subject, down went the balance at the head end, in consequence of the redistribution of blood in his system" (James, 1890). Ingenious as this method was for measuring the hemodynamic response function, its limitations with respect to localization within different regions of the brain are all too obvious. By contrast, the most advanced technique deployed in the late 19th century (and the most widely used)—multichannel cerebral thermometry—gave remarkably precise information (Broca, 1879).

The method involved placing thermometers or more sensitive thermoelectric piles on different regions of the scalp and measuring the differential temperatures thereon in response to well-defined stimuli and tasks. Raichle (1988) notes that Paul Broca, Angelo Mosso (the inventor of the balanced table), and Hans Berger (who later developed the electroencephalogram) were all devotees of the method. The real king of cerebral thermometry, however, was J.S. Lombard, M.D., formerly Assistant Professor of Physiology in Harvard University, U.S.A. In his 1879 monograph on "Experimental Researches on the Regional Temperature of the Head under Conditions of Rest, Intellectual Activity and Emotion," Lombard set out a research program that even now looks strangely sophisticated. Furthermore, the care with which he executed a very large number of experiments can rarely have been equaled. A few examples must suffice to give the flavor of Lombard's work.

Lombard decided "not to examine a great number of heads taken at random, but to limit the observations to a thorough and minute examination of a small number of heads, which could be accurately measured, and compared one with another." The thermopiles were placed in well defined frontal, temporal, parietal regions "in symmetrically situated spaces on the two sides" of the head. In these regions, Lombard first measured absolute and relative temperatures "in the quiescent mental state." He reported that "the anterior region shows the highest percentage of occurrence of superiority of temperature for the right side, and the lowest percentage for the left side: that the posterior region shows the highest percentage of occurrence of superiority of temperature for the left side, and the lowest percentage for the right side." The temperature of central ("middle") regions was intermediate between those of anterior and posterior regions and showed no clear between-hemisphere differences.

Next Lombard considers the "effect of different kinds of intellectual work on the temperature of the three regions." The tasks performed included making mathematical calculations, "making notes of subjects requiring considerable reflection," and "putting into writing ideas which were difficult of expression." Each task was undertaken for 90 min, during which time span a steady rise in temperature was observed in all three regions. In all tasks the "degree and rapidity of rise of temperature" were greatest in the anterior regions, with the largest effect observed for composition ("writing ideas which were difficult of expression"). All regions also showed a greater rise in temperature in the left hemisphere compared with the right, although the differential was again larger in anterior regions.

To examine the consequences of affective variables, Lombard chose "the reading or recitation aloud, or to one's self, of poetical or prose productions of an emotional character," having previously established that "mere mechanical reading or recitation . . . produced no effect." As in the studies of "intellectual work," Lombard reported that the most pronounced rises in temperature were in left anterior regions. More interestingly, there was a "greater effect of recitation to one's self than of recitation aloud." Lombard interpreted this finding in terms of the "conservation of force," arguing that "in internal recitation an additional portion of energy, which in recitation aloud was converted into nervous and muscular force, now appears as heat." By contrast, James (1890) argues that "the *simple* central process is to *speak* when we think; to think silently involves a check in addition." He accordingly argues that Lombard's finding of a "surplus of heat in recitation to one's self is due to inhibitory processes which are absent when we recite aloud."

Reading Lombard's monograph is a somewhat uncanny experience. In many ways, Lombard's general concerns and, indeed, some of his specific questions seem to have quite direct reflections in modern work with positron emission tomography (PET) and functional magnetic resonance imaging (fMRI). Like Lombard, we too recognize that "a baseline or control state is fundamental to the understanding of most complex systems" (Raichle et al., 2001) and attempt to characterize that "organized, baseline default mode of brain function that is suspended during specific goal-directed behaviors" (Raichle et al., 2001). Like Lombard, we are still concerned with understanding the neural bases of arithmetical computation by imaging the brains of healthy volunteers (Dehaene et al., 1996). The neuroimaging of word generation (Warburton et al., 1996) and reading (Price and Friston, 1997) also remain topics of considerable interest.

In other ways, Lombard's monograph seems very alien. Tasks are not described in sufficient detail to allow replication, considerations of statistical significance are conspicuous by their absence, the experimental designs are crude, and no effort is made to give any kind of theoretical interpretation of the results. Furthermore, Lombard does not consider his results in relation to what was already known about the localization of language and reading from anatomoclinical studies. But before we are too critical we should always remember that a hundred years from now our experiments and theories may well seem equally primitive to the neuroscientists of that time. Be that as it may, there is now a vast literature on the cerebral localization of cognitive functions derived from lesion studies and from functional neuroimaging of the healthy brain. The current special issue examines how the two methods can complement each other and also the extent to which the two data sets converge on the same functional localizations.

But already there are suggestions from recent work that functional localization is not such a fixed property of brain regions as either lesion studies or early neuroimaging work might have suggested. Rather, "the *neural context* in which an area is active may define the cognitive function" that it is carrying out (McIntosh, 2000). The point can be illustrated by reference to Broca's area. Initially, this region (which includes Brodmann area 44) was regarded as the center that coordinated articulatory movements (but see Wise et al., 1999). Yet neuroimaging of healthy volunteers has suggested that the region also plays a role in natural language syntactic processing (Caplan et al., 2000; Heim et al., 2003), in processing musical syntax (Maess et al., 2001), in the perception of rhythmic motion (Schubotz and von Cramon, 2001), in imaging movement trajectories (Binkofski et al., 2000), and in local visuospatial search (Manjaly et al., 2003). It is difficult to see how a single common function (localized in Broca's area) could underlie such a disparate collection of effects. A more reasonable conjecture is that "BA 44 as part of Broca's area receives its functional specification by its particular interaction with different neural networks" (Heim et al., 2003). Exactly how the functional specialization of a cortical area is determined by its extrinsic anatomical connections (Passingham et al., 2002) and its intrinsic cytoarchitecture (Hutsler and Geluske, 2003) remains to be seen. New methods of measuring the functional integration of different brain regions in terms of effective connectivity may yet yield a picture of cerebral organization that is distinct from any 19th- and 20th-century models of the brain. As Friston (2002) writes: "Functional specialization is only meaningful in the context of functional integration and vice versa."

Acknowledgments

J.C. Marshall is supported by the (UK) Medical Research Council. G.R. Fink is supported by the Deutsche Forschungsgemeinschaft. Additional support from the VolkswagenStiftung is also gratefully acknowledged.

References

Alzheimer, A., 1907. Über eine eigenartige Erkrankung der Hirnrinde. Allegemein Z. Psychiatrie Psychisch-Gerichtliche Med. 64, 146–148.
Binkofski, F., Amunts, K., Stephan, K.M., Posse, S., Schormann, T., Freund, H.J., Zilles, K., Seitz, R.J., 2000. Broca's region subserves imagery of motion: a combined cytoarchitectonic and fMRI study. Hum. Brain Mapp. 11, 273–285.
Bouillaud, J.B., 1825. Recherches cliniques propres à demontrer que la perte de la parole correspond à la lésion des lobules antérieurs du cerveau et à confirmer l'opinion de M Gall, sur le siège de l'organe du langage articulé. Arch. Gen. Med. 6, 25–45.
Broca, P., 1861. Nouvelle observation d'aphémic produite per une lesion de la moité postérieur des deuxième et troisième circonvolutions frontales. Bull. Soc. Anat. Paris 36, 398–407.
Broca, P., 1865. Sur le siège de la faculté du langage articulé. Bull. Soc. Anthropol. Paris 6, 377–393.
Broca, P., 1879. Sur les températures morbides locale. Bull. Acad. Med. 8, 1331–1347.
Caplan, D., Alpert, N., Waters, G., Olivieri, A., 2000. Activation in Broca's area by syntactic processing under conditions of concurrent articulation. Hum. Brain Mapp. 9, 65–71.
Charcot, J.M., 1889. Clinical Lectures on Diseases of the Nervous System. New Sydenham Society, London.
Dehaene, S., Tzourio, N., Frak, V., Raynaud, L., Cohen, L., Mehler, J., Mazoyer, B., 1996. Cerebral activations during number multiplication and comparison: a PET study. Neuropsychologia 34, 1097–1106.
Dejerine, J., 1892. Contribution à l'étude anatomoclinique et clinique des differentes varietes de cécité verbale. Mem. Soc. Biol. 4, 61–90.
Finger, S., 2000. Minds behind the brain: a history of the pioneers and their discoveries. Oxford University Press, Oxford.
Flourens, P., 1846. Phrenology examined. Hogan & Thompson, Philadelphia.
Freud, S., 1893. Quelques considerations pour l'étude comparative des paralysies motrices organiques et hystériques. Arch. Neurol. 26, 29–43.

Friston, K., 2002. Beyond phrenology: what can neuroimaging tell us about distributed circuitry? Annu. Rev. Neurosci. 25, 221–250.

Gall, F.J., 1822-1825. Sur les Fonctions du Cerveau et sur celles de chacune de ses Parties. Baillière, Paris.

Goldstein, K., 1948. Language and Language Disturbances. Grune & Stratton, New York.

Gross, C.G., 1998. Brain, Vision, Memory. MIT Press, Cambridge, MA.

Halligan, P.W., Fink, G.R., Marshall, J.C., Vallar, G., 2003. Spatial cognition: evidence from visual neglect. Trends Cogn. Sci. 7, 125–133.

Harlow, J.M., 1869. Recovery from the passage of an iron bar through the head. Publ. Mass. Med. Soc. 2, 327–347.

Heim, S., Opitz, B., Friederici, A.D., 2003. Distributed cortical networks for syntax processing: Broca's area as the common denominator. Brain Lang. 85, 402–408.

Hutsler, J., Galuske, R.A.W., 2003. Hemispheric asymmetries in cerebral cortical networks. Trends. Neurosci. 26, 429–435.

Jackson, J.H., 1874. On the nature of the duality of the brain. Med. Press Circ. 1, 19–41.

Jackson, J.H., 1876. Case of large cerebral tumour without optic neuritis and with left hemiplegia and imperception. R. London Ophthal. Hosp. Rep. 8, 434–441.

James, W., 1890. The Principles of Psychology. Macmillan, London.

Lichtheim, L., 1885. On aphasia. Brain 7, 433–484.

Liepmann, H., 1900. Das Krankheitsbild der Apraxie ("motorischen asymbolie"). Monatsch. Psychiatrie Neurol. 8, 15–44.

Lissauer, H., 1890. Ein Fall von Seelenblindheit nebst einen Beitrage zur Theorie derselben. Arch. Psychiatrie Nervenkrankheiten 21, 222–270.

Lombard, J.S., 1879. Experimental Researches on the Regional Temperature of the Head under Conditions of Rest, Intellectual Activity, and Emotion. H.K. Lewis, London.

Maess, B., Kölsch, S., Gunter, T.C., Friederichi, A.D., 2001. Musical syntax is processed in Broca's area: an MEG study. Nat. Neurosci. 4, 540–545.

Manjaly, Z.M., Marshall, J.C., Stephan, K.E., Gurd, J.M., Zilles, K., Fink, G.R., 2003. In search of the hidden: an fMRI study with implications for the study of patients with autism and with acquired brain injury. NeuroImage 19, 674–683.

Marshall, J.C., 1984. Multiple perspectives on modularity. Cognition 17, 209–242.

Marshall, J.C., Halligan, P.W., Fink, G.R., Wade, D.T., Frakowiak, R.S.J., 1997. The functional anatomy of a hysterical paralysis. Cognition 64, B1–8.

Marshall, J.C., Newcombe, F., 1973. Patterns of paralexia: a psycholinguistic approach. J. Psycholinguistic Res. 2, 175–199.

McIntosh, A.R., 2000. Towards a network theory of cognition. Neural Networks 13, 861–870.

Mort, D.J., Malhotra, P., Mannan, S.K., Rorden, C., Pambakian, A., Kennard, C., Husain, M., 2003. The anatomy of visual neglect. Brain 126, 1986–1997.

Moutier, F., 1908. L'Aphasie de Broca. Steinheil, Paris.

Passingham, R.E., Stephan, K.E., Kötter, R., 2002. The anatomical basis of functional localization in the cortex. Nat. Rev. Neurosci. 3, 606–616.

Price, C.J., Friston, K.J., 1997. The temporal dynamics of reading: a PET study. Proc. R. Soc. London Ser. B 264, 1785–1791.

Raichle, M.E., 1988. Behind the scenes of functional brain imaging: a historical and physiological perspective. Proc. Nat. Acad. Sci. 95, 765–772.

Raichle, M.E., MacLeod, A.M., Snyder, A.Z., Powers, W.J., Gusnard, D.A., Shulman, G.L., 2001. A default mode of brain function. Proc. Nat. Acad. Sci. 98, 676–682.

Schubotz, R.I., von Cramon, D.Y., 2001. Interval and ordinal properties of sequences are associated with distinct premotor areas. Cereb. Cortex 11, 210–222.

Von Monakow, C., 1911. Die Lokalisation im Grosshirn. J. Psychol. Neurol. 17, 185–200.

Vuilleumier, P., Chicherio, C., Assal, F., Schwartz, S., Slosman, D., Landis, T., 2001. Functional neuroanatomical correlates of hysterical sensorimotor loss. Brain 6, 1077–1090.

Warburton, E., Wise, R.J.S., Price, C.J., Weiller, C., Hadar, U., Ramsay, S., Frakowiak, R.S.J., 1996. Noun and verb retrieval by normal subjects: studies with PET. Brain 119, 159–179.

Wernicke, C., 1874. Der aphasische Symptomenkomplex. Cohn & Weigart, Breslau.

Wise, R.J.S., Greene, J., Büchel, C., Scott, S.K., 1999. Brain regions involved in articulation. Lancet 353, 1057–1061.

Young, M.P., Hilgetag, C.-C., Scannell, J.W., 2000. On imputing function to structure from the behavioural effects of brain lesions. Philos. Trans. R. Soc. London Ser. B. 355, 147–161.