Is there anything so extravagant as the imaginations of men’s brains? Where is the head that has no chimeras in it? (John Locke, 1690) 

NEUROSCIENCE AND THE HISTORY AND THEORY OF SCIENCE

The ideal of inexorable scientific progress, characterized by expanding knowledge and increased sophistication and complexity, is a defining characteristic of the modern self-image of the natural sciences and can even be objectively quantified. Rider (1944) and de Solla Price (1963), the founders of bibliometrics and scientometrics, noted many years ago that from the 17th century onward the number of scientific publications has been doubling every 10–20 years, while at the same time citations of earlier literature have fallen off markedly. This finding seems also to be confirmed by publishing developments in the fields of basic psychiatric and neurobiological research. A rough estimate based on the medical subject headings gathered in the National Library of Medicine’s Medline Database shows that in the four decades from 1966 to 2005 the number of essays on psychiatric disorders published in magazines increased from 5400 to 32 000 per year, and in the entire field of neuroscience from 35 000 to 144 000 per year.

Does this increase of approximately 4% per year actually reflect inexorable and continuous progress in neuroscience and psychiatry? Among contemporary historians and philosophers of science, this traditional image of progressive scientific development is considered to be naive. This is not to deny that research is shaped markedly by concepts and issues inherent to specific scientific fields – concepts such as “neuron” (Waldeyer-Hartz, 1891), “nerve growth factor” (Cohen and Levi-Montalcini, 1957), or “manic-depressive illness” (Kraepelin, 1899). Yet such ideas are by no means the result of simple linear growth in knowledge. Instead, scientific consensus derives from complex historical processes that involve political attitudes, prevailing scientific beliefs, or academic career trajectories, just as much as more “objective” criteria like the research methodology or the structures of decision-making processes in research groups. Furthermore, medical science does not exist simply for its own sake; instead, it is practiced in institutes and clinics that are financed by state organizations or private enterprises (Fig. 1.1). Consequently, it is shaped by political and administrative decisions and must respond to social needs. The results of a scientific inquiry are deemed “facts” only after they have been published in professional, peer-reviewed journals, presented at conferences, and accepted as worthy of discussion by the “scientific community.”

This “constructivist” understanding of science evolved within the history of the neurosciences. It can be traced back to the work of the Polish microbiologist Ludwik Fleck who, in 1935, after working in the laboratory of August von Wassermann, used the successful serological identification of syphilis to study the factors that influence scientific innovation and knowledge growth. Fleck spoke of “styles of thought” (Denkstile) to describe the comprehensive concepts and hypotheses that influence the questions and methodologies of any given scientific community. Subsequently, in his study on the Scientific Revolution, Thomas Kuhn (1962) coined the phrase “paradigm” to describe the underlying idea that any kind
of research is affected by such antecedent styles of thought. For example, the classification of mental diseases as “psychogenic neuroses” and as “organically induced psychoses” was an important characteristic of the psychiatric style of thought in the middle of the 20th century, and until recently the “one gene – one protein” hypothesis dominated the field of molecular biology. Scientists doing research in this field know from their own experience how rapidly almost all neuroscientific disciplines deemed “safe” since the 1950s are subject to change: the growing influence of epigenetics (Allis et al., 2006) is but one typical example of such a change in the style of thought.

The medical specialties we now call “psychiatry” and “neurology” are also historical constructions (Hirschmüller, 1999). They resulted not from ineluctable scientific progress, but from the negotiations of 19th-century practitioners who managed to redefine some neuroses away from Cullen’s old class of “disorders of general sensation and movement, without idiopathic pyrexia and local lesion” (Cullen, 1803). So-called “neurological diseases” were thus constructed on the basis of two criteria: salient disorders of motor and sensory function, and the possibility of being related to a “focal” brain lesion. On the belief that a putative etiological link existed between “focal lesion” and symptoms as dictated by the clinicopathological model of disease, it was further claimed that the said motor and sensory changes were “primary” and that all other complaints, e.g., mental symptoms and cognitive deficits, were “occasional” or “secondary.” Huntington’s disease, Parkinson’s disease, and multiple sclerosis were constructed in this way (Berrios and Porter, 1995). This maneuver created two independent clinical spaces: on the one hand the brand new space of clinical neurology and on the other the obscure space of alienism that was occupied by conditions which were definable only in terms of mental symptoms or behavioral complaints and which could not be plausibly linked to a “focal brain lesion.”

Although critics have advanced many valid arguments against such constructivist models, the ensuing debates in the history and philosophy of science have insured that it is no longer possible to view science as a closed system, isolated from society, politics, and economics and governed by its own inherent rules of knowledge acquisition (Golinski, 1998). Scientists working in the field of psychiatry and neuroscience should be especially aware of this fact, because in public discourse their concepts always affect human self-interpretation in a very particular way. For example, the 20th century has been called the “psychiatric century” (Porter, 2002). Culturally and historically, it has been shaped decisively not just by psychoanalysis and “biological psychiatry” or psychopharmacology, but also by the antipsychiatry movement in the 1960s and 1970s and by psychiatric genetics in both its racist guise under National Socialism and its arguably progressive contemporary guise.

Given the abundance of knowledge at the disposal of contemporary psychiatrists and neurobiologists, they can hardly keep up with current literature in their own field, let alone with the history of their discipline. Given the international nature of biomedical research today, historical accounts that stress national traditions – as the introduction to volume one of this handbook (Zülch, 1968) did – no longer seem relevant. Instead, to understand long-term developments in neuroscience, it now seems more appropriate to focus on several core themes that have recurred in debates throughout history. More precisely, two key questions seem worthy of consideration: first, the material localization of the psyche, and second, the significance of hereditary transmission in the etiology of mental disorders.

THEORIES AND CONCEPTS OF LOCALIZATION AND GENETICS

The localization of the psyche as a function of the brain is anything but self-evident. In Greek antiquity, especially in the well-known paper on epilepsy in the Corpus Hippocraticum, disturbances in the brain were believed to cause mental illness. Yet this belief should not be taken to imply that the idea of the psyche being localized in the blood/heart system, i.e., in the body fluids, became obsolete. Although today the brain is often described
using the metaphors of computer science and information technology, contemporary theories that are indebted to classical humor pathology have played a decisive role in neuroendocrinology and research on depression (Holsboer, 2001). Not until after the Enlightenment did the brain finally become the “organ of the soul” (Sömmering, 1796). Most of the neuroscientific studies conducted during the past two centuries can be understood as attempts to specify mental functions ever more precisely, to record them quantitatively, and to allocate them to ever more “individual” morphological structures of the central nervous system along the lines of a pragmatic, psychophysical parallelism.

From this perspective, the 18th-century phrenology of Franz Joseph Gall, which today is ridiculed as “unscientific,” was of no less importance than the mapping of the cortex by Oskar Vogt or the identification of the central visual system of the vertebrates by David Hubel (1982) and Torsten Wiesel in the second half of the 20th century. Moreover, there have always been competitive models, especially in neurophysiology, in which the overall function of the brain was considered more important than a sophisticated topology. Such concepts were advocated by Pierre Flourens (1824) and Charles Sherrington (1906), for example. In addition, the paradigm of localization illustrates the fact that certain concepts, although successful in basic research, do not necessarily result in clinical progress. A neuropathologically oriented psychiatry that traced its roots to the work of Theodor Meynert (1884), Carl Wernicke, or Paul Flechsig was replaced by the nosologies of Emil Kraepelin, who emphasized the clinical observation and diagnosis of psychopathological states (Burgmair et al., 2003).

Like the allocation of psychic functions to brain structures, the observation that similar psychopathological conditions recur in families over several generations and are therefore connected to procreative and hereditary processes dates back to Greek antiquity (Lesky, 1950). Plato’s Politeia, for example, demonstrates that ideas about heredity have also always produced concepts that quickly extend beyond specific disease prevention and often assume the character of utopian (or dystopian) directives. For centuries, the hereditary transmission or “familiar taint” was only one of numerous somatic and psychological factors that medical writers recognized as causing mental illness. It was only after the emergence of “degeneration theory” – first in France around 1850 (Morel, 1857) and later in Germany and England thanks to Richard von Krafft-Ebing and Henry Maudsley – that hereditary transmission of pathogenic traits came to be seen as the most important etiological factor behind nearly all mental diseases.

Degeneration theory’s quick dissemination was due not only to the fact that the new science of biology seemed to confirm traditional moral/religious ideals, but also that it “fit” the political climate in France and Germany in the second half of the 19th century (Dowbiggin, 1985). While both Darwin’s theory of evolution and scientific genetics emerged independently of degeneration theory, against the backdrop of the political and social milieu around 1900 these concepts combined to bring forth social darwinism in England and racial hygiene in Germany (Weber, 1993). Eventually the latter served as justification for forced sterilizations and the murder of some hundred thousand individuals suffering from mental illness under the National Socialist regime.

Since the identification of DNA as the basis of hereditary transmission by James Watson and Francis Crick in the 1950s, psychiatry and neurogenetics have looked increasingly to molecular biology. The social utopias of early geneticists no longer seemed plausible, not least because of Mendel’s law which, itself being quite simple, was replaced by ever more complex ideas of biological gene–environment interactions. Despite the enormous quantity of data produced using modern, genome-wide scans and elaborate biostatistical analysis, identification of the genetic components of mental disorders remains a daunting task, and there is no telling what consequences genetic research harbors for psychiatric nosology and therapy.

The history localization theories and psychiatric genetics thus show that methodological and conceptual changes do not necessarily resolve fundamental questions. Instead, more often than not, they simply reformulate those basic, underlying questions.

**HISTORICAL EPISTEMOLOGIES OF NEUROSCIENCE – PICTURING THE BRAIN**

The relative stability of theoretical frameworks such as cerebral localization and heredity points to a distinctly anticipatory or proleptic structure of the neurosciences (Borck and Hagner, 1999). That is, although the theoretical problems have remained relatively stable, the solutions which the neurosciences have offered up throughout history have been chronically anticipatory, perpetually holding out the prospect of solving ultimate questions of human life and consciousness. It is not so much the basic theoretical assumptions of localization or heredity that have managed to keep this anticipatory engine in gear, but rather the successive waves of new technologies and instruments that generate fascinating new perspectives and invasive possibilities. History can help us recognize and appreciate this proleptic structure and the conditions that support it.
Among the most pervasive and revolutionary technologies that have come to inform contemporary neuroscience are the new imaging techniques. Researchers now have at their disposal an array of instruments that enable them to study the brain in vivo, including most prominently positron emission tomography (PET), functional magnetic resonance imaging (fMRI), and electro- and magnetoencephalography (EEG, MEG). These techniques hold out the promise of a new scientific psychopathology that can visualize the functional organization of the brain and ultimately link it to the workings of the human mind (Andreasen, 1997). By delivering a “cartography” of neural connections, analyzing “abnormal prefrontal activation,” or studying the systemic effects of “symptom provocation,” these methods sustain hopes not only of drawing together an eclectic mix of disciplines such as neuropathology, neuroendocrinology, neuropsychology, and psychopharmacology, but also of replacing clinically grounded diagnostic systems with nosologies based on etiology and pathophysiology.

Brain images have a unique and complex epistemological status. For one, the knowledge that they mediate is conditional upon the very material apparatus that generates them (Brown, 2001; Baird, 2004; Wise, 2006). Today pictures are above all products of complex scanning and computing devices, and their development parallels the history of these technologies. They derive from highly manipulative interactions, protocols, and procedures of data collection, and their material reality is anchored in the processing of electronic data using various filters, statistical algorithms, “black-box” software packages, and representational conventions rather than on some putatively “pure” observation of physical phenomenon (Eddy et al., 1999).

The electronic and statistical manipulation that lies behind these images is just the most obvious example of the “packed significance” (Tucker, 2006) of images. For they are also socially and culturally formed. They demand the cultivation of the observer (“viewing culture”) and become incomprehensible if divorced from the signifying systems and cultural machinery (theories, interpretive contexts) that surround them and in which they are embedded. They require institutions that can coordinate and support the requisite technical and scientific skills (Lenoir, 1997). Pointing to such epistemological constraints fosters a greater awareness of visual images as material and sociocultural artefacts (Tucker, 2006). Images and their content are produced and decisively modulated by the various material, social, institutional, and cultural conditions that support their generation and dissemination. Historical analysis of the “packed significance” of images provides a reflexive platform on which we can critique the epistemological status of contemporary technologies and explore the proleptic dynamics they generate.

Contemporary imaging techniques and the claims that accompany them are only the most recent artefacts in a long tradition of picturing the brain. Indeed, the history of psychiatry and neurology contains a plethora of different imaging technologies. Most famously, Franz Joseph Gall’s phrenological pictures mapped mental function on to the human skull and in doing so created an entire iconography that decisively shaped early 19th-century discourse and understanding. The staining and photographic techniques developed by Camillo Golgi exposed the neuroanatomic networks that undergirded consciousness and simultaneously exploited the enormous excitement unleashed by the exploration of hitherto unimaginable microscopic worlds. Wernicke’s schematic drawings were crucial in interpreting aphasic symptoms as breakdowns within brain centers and their connections, so much so that clinical protocols were tailored to fit the diagrams (Jacyna, 2000). The graphic representations produced by Hans Berger’s EEG captured not only traces of underlying physiological processes in the brain, but also the imaginations of spectators for whom cultural metaphors of mental energy and of the human body as an electric motor were commonplace (Rabinbach, 1990; Bork, 2005). All of these visual media and the proleptic fascination that has accompanied them have played a crucial role in the development of the neurosciences. The respective historical images and the technological systems and cultural machinery in which those images were embedded have informed what scientists knew, how they came to know it, and what questions have been (able to be) asked (Kosslyn, 1999).

One of the most striking aspects of neuroimaging is the fact that its very material and cultural embeddedness belies the rhetoric of objectivity that has enveloped it throughout much of history. Successive technologies of visualization (e.g., microscope, EEG, fMRI) have, in their own specific ways, mediated the relationships between observers and objects, straddling the divide between “trust and depth” and evoking at once both distance and proximity in what can be described as a “paradox of transparency” (Bork, 2001; Brown, 2001; Wise, 2006). On the one hand, the pictures are the products of increasingly complex technical manipulations that distinguish them as characteristically human artefacts. On the other hand, however, they seem to make claims to represent natural phenomena objectively and to reveal fundamental truths about the working of the human brain (Sargent, 1996; Perini, 2005). What links early efforts to visualize brain function with contemporary imaging techniques is their ability to fascinate observers and to sustain scientific and public discourse.
They underscore a tradition of using and managing pictures with the help of a “rhetoric of self-evidence” (Borck, 2001) that transforms pictures into transparent representations of nature, unsullied by human activities. Although obviously contested, various historical images of the brain have been able to muster discursive credibility and support broad claims about the nature of the mind–body relationship.

**NEUROSCIENCE AND PSYCHIATRIC DISORDERS – DEMENTIA AS A MODEL FOR THE INTERDEPENDENCE OF BASIC AND CLINICAL SCIENCE**

Clinical pictures in general result from the convergence of a name (word, term), a concept (i.e., the explanatory narratives anchoring the process to a given historical period), and a set of behavioral forms or captured subjectivities. This third component of the convergence, the behavioral forms, has proven to be the most complex and elusive. For example, on the one hand, it can be regarded as ontologically stable and independent from the language of description, and on the other as a construct whose structure is fully dependent upon the concepts and descriptions involved in the convergence. Each of these polarities gives rise to an entirely different approach to the history and philosophy of psychiatry. A viable standpoint is somewhere between the two extremes: the language of description provides the opaque object of inquiry with form and meaning (Berrios and Marková, 2006). Convergences can be successful (lasting) or unsuccessful. Success should be primarily defined as a social, political, and economic category.

The history of dementia can be envisaged as a loose concatenation of convergences. We shall pick up the definition of dementia that appears in Pinel’s (1809) classification. The six conceptual pressures listed above, accompanied by much etiological speculation, brought about changes in the definition and classification of the dementias. The syndromatic concept was jettisoned and specific dementias – with or without specific clinical profiles – were defined according to known or putative neuropathology. The differentiation between degenerative, traumatic, toxic, infectious, and atherosclerotic dementias provided the opportunity to seek differential biological markers (Berrios and Freeman, 1991). This notwithstanding, it can also be said that the “cognitive paradigm” did set back research. This was very much the case in relation to the diagnostic value of psychiatric symptoms, such as hallucinations, delusions, obsessions, depression, confusion, and behavioral disorder. Early enough, theoreticians had chosen to introduce an auxiliary hypothesis, e.g., “superimposed delirious state,” to explain these symptoms away and protect the cognitive paradigm. It has only been during the last 30 years that they have been accepted as “primary” components of some of the dementias.

Early enough, theoreticians had chosen to introduce an auxiliary hypothesis, e.g., “superimposed delirious state,” to explain these symptoms away and protect the cognitive paradigm. It has only been during the last 30 years that they have been accepted as “primary” components of some of the dementias.
The last 20 years of the 19th century show an interaction between research in the basic sciences and changes in the concept of dementia. In addition to the psychological research into the concept of memory noted above, there were important advances in bacteriology and in brain neuroanatomy, particularly in the development of the concepts of neuron and synapse, and the completion of the mapping of both cortical and subcortical functions. By the time Pick and Alzheimer started their research, robust correlations were being established between clinical profile and neuropathology (Berrios, 1990). Arnold Pick was an acute clinician and his observations on the relationship between linguistic and behavioral disorders and temporal and then frontal brain atrophy became a model of analysis (Kertesz and Kalvach, 1996).

The construction of so-called Alzheimer’s disease is far more complicated. It was undertaken by Kraepelin with little or no participation from Alzheimer himself, who only lent his name to the enterprise and was rather unconvinced that his report of the case of Auguste D constituted the beginning of a new disease (Berrios, 1990). The fact that this 51-year-old woman had marked visual hallucinations, delusions, agitation, and other behavioral disturbances and that the neuropathological report showed marked vascular changes, and that these features were to disappear in the idealized final definition of the disease is illuminating of the process of disease construction. Equally illuminating is the finding that the additional “case” found by young Perusini at the request of Kraepelin was worryingly similar and that the existence of such a case has not yet been independently ascertained.

Although Alzheimer’s disease became the flagship of, and model for, the rest of the dementias, it did not attract a great amount of interest from researchers and clinicians until in the late 1970s the strange claim was made that there was in the offing a “silent epidemic” of dementia. This has led to a disproportionate investment of money and time to find a magic bullet, which, in general, has not paid off. But this is not the only problem. The important concept of arteriosclerotic dementia was challenged in the 1970s and a famous neurological instrument was introduced to rule out vascular involvement and identify “pure” cases of Alzheimer’s disease. In due course, the Hachinski score proved to be a very bad instrument – it only detected the presence of stroke — which means that a great deal of the research results based on the analysis of “pure” Alzheimer’s disease are invalid. Be that as it may, major advances in neurogenetics have led to the fragmentation of whatever “Alzheimer’s disease” happens to be. This process, just started, also involves conditions such as Parkinson’s disease.

What is happening to Alzheimer’s disease and the other dementias cannot just be explained away as the result of understandable “scientific” error. It is also the result of faulty conceptualization, boundary disputes between medical specialisms, and the disproportionate influence of certain social groups in the apportioning of research funds (Ballenger, 2006). This can be seen in the way in which Alzheimer’s disease and Parkinson’s disease are mentioned as the “only and final” objectives every time a new – controversial – line of research is to be introduced. Research into the dementias is now part of the new rhetoric of power and it has become impossible to talk rationally about their relative clinical importance.

The example of the dementias illustrates that the development of neurobiological research is highly dependent on conceptual, political, social, and technical factors that are not directly related to scientific or clinical priorities. Although neuroscientists cannot escape these dependencies, they should at least be aware of them.

REFERENCES


