

# The Integration of Neurology, Psychiatry, and Neuroscience in the 21st Century

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**Objective:** This article examines the historical basis for the divergence of neurology and psychiatry over the past century and discusses prospects for a rapprochement and potential convergence of the two specialties in the next century.

**Method:** The author presents a brief historical overview of developments in neurology and psychiatry from the late 19th century. The histories of research and prevailing scientific opinion on two neuropsychiatric disorders, Alzheimer's disease and Tourette's syndrome, are compared to illustrate the effects of viewing a disease process from, respectively, the neurologic/organic and psychiatric/functional perspectives.

**Results:** Research on Alzheimer's disease, because of its early pathologic demonstration, moved rapidly toward identification of associated synaptic abnormalities and genetic mutations. In Tourette's syndrome, the absence of evident brain pathology resulted in vacilla-

tion between organic and functional explanations and persistent controversy about the nature of the illness.

**Conclusions:** Neurology and psychiatry have, for much of the past century, been separated by an artificial wall created by the divergence of their philosophical approaches and research and treatment methods. Scientific advances in recent decades have made it clear that this separation is arbitrary and counterproductive. Neurologic and psychiatric research are moving closer together in the tools they use, the questions they ask, and the theoretical frameworks they employ. The interests of neurology and psychiatry converge within the framework of modern neuroscience. Further progress in understanding brain diseases and behavior demands fuller collaboration and integration of these fields. Leaders in academic medicine and science must work to break down the barriers between disciplines.

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As we enter the 21st century, it is appropriate to pause and reflect on the accomplishments of the past century in our understanding of the brain and mind and of neurologic and psychiatric disorders. Remarkable advances were made at the end of the 20th century in understanding the genetic basis of many diseases affecting the brain and the special senses. New drugs have been developed, and new theories have been espoused. It is increasingly difficult to distinguish scientifically between the disciplines of neurology and psychiatry.

## Neuroscience and Neurology Circa 1900

We begin this reflection by looking back to the last turn of the century to examine the emerging fields of neuroscience, neurology, and psychiatry. Ramon y Cajal (1) had just proposed the neuron doctrine, the idea that the functions of the nervous system are best understood by analysis of individual neurons, which, when connected by synapses (a term first coined in 1897 by Charles Sherrington [2]), produce the neuronal networks that subservise function. This was a challenge to Golgi's contention (3) that the

nervous system functioned as a "neurosyncytium," in that it lacked discrete units. Golgi's and Nissl's methods of using silver and gold impregnation, combined with other histochemical techniques, revealed the morphology of individual cells.

For neurology, too, it was a time of considerable optimism. During the 19th century, neurologists used post-mortem and microscopic techniques to make clinical correlations between neurologic syndromes and neuropathologic changes. Notable progress was made by the London school, focused at University College and the National Hospital at Queen Square; the Paris school at the Salpêtrière; and the North American school, focused primarily at Harvard, the University of Pennsylvania, and Columbia-Presbyterian Hospital.

In 1817 James Parkinson (4) described the condition of shaking palsy or *paralysis agitans*. An inveterate London walker, Parkinson discovered a group of patients who were disabled by difficulties with walking and posture associated with tremulousness. Striking pictures of these patients are found in his monograph (4). As the century unfolded, neurologists in London and elsewhere focused on epilepsy and a variety of other disorders, as described in

detail by W.R. Gowers (5) in his 1888 handbook of clinical neurology.

In France, Charcot and his group at the Salpêtrière made landmark descriptions of multiple sclerosis, spinal cord and peripheral nerve disorders, and many other conditions. Charcot's colleague, Georges Gilles de la Tourette (6), described the "maladie des tics" that bears his name and differentiated it from Sydenham's chorea, which had first been described in 1604. Charcot distinguished two syndromes characterized by tics. One he considered to be "degenerate," meaning not neurodegeneration as we think of it today, but producing a brain that was structurally and functionally abnormal and incapable of full neural functioning. He distinguished this from a form associated with hysteria and believed that hypnosis was capable of separating the two syndromic disorders.

The origins of neurology in North America date to mid-19th-century work by pioneers such as Silas Weir Mitchell, who described peripheral nerve and brain injuries incurred by soldiers during the Civil War. The American Neurological Association was founded in 1874, with an initial membership of 28 physicians. In 1872 George Huntington (7) described the hereditary chorea that now carries his name and established the principle of direct inheritability of neurologic disorders, in which a rather precise phenotype occurred in one generation after another. (The Boston Psychological Society was formed in 1880 by eight psychiatrists. Not until a decade later were neurologists included in its membership. The name was changed to the Boston Society of Neurology and Psychiatry in 1901. Ironically, in January 1998, the historic 900th meeting of the society was attended by only four psychiatrists. The room was filled with neurologists, neuroscientists, and other scholars of the brain.) At Harvard, neuropsychiatry was promoted by neurological leaders, including James Jackson Putnam, who founded one of the country's first neurologic clinics at Massachusetts General Hospital in 1872 (8, pp. 145–146). After the turn of the century, Putnam became interested in psychoanalysis and played a crucial role in the acceptance of Sigmund Freud's theories in the United States. Putnam and his associates enjoyed a cross-disciplinary collegiality that we might well try to emulate today. Putnam's Boston "school" was notable for the informal cooperation of psychologists, philosophers, neurologists, and psychiatrists, and "developed the most sophisticated and scientific psychotherapy in the English-speaking world" (9, p. 237).

Stanley Cobb, who retired as Bullard Professor of Neuro-pathology at Harvard in 1954, made important contributions in several areas during the first half of the 20th century. His early work did much to define the neurophysiology of the human nervous system (8, p. 385). He demonstrated that increased brain function is associated with increased blood flow to the brain. In the field of epilepsy research, he was the first to demonstrate that a given type of retinal stimulation can induce seizures. He also made

significant discoveries regarding the role of vitamin B deficiencies in neurologic diseases and alcoholism.

"Cobb refused to entertain the notion that neuropathology and psychiatry could be divided into two compartments," a commentator noted (9, p. 62). "The mind," he maintained, "is the living brain in action, and the brain is subject to physical and chemical changes just as any other cell or tissue in the body" (9, p. 237). The Neurological Institute in New York was founded in 1909 and grew to be an enormously successful enterprise during the 20th century.

## 19th Century Origins of Psychiatry

Psychiatry has a long, distinguished, and controversial history in North America. The American Psychiatric Association was founded in 1844, and the *Journal* began publication with Amariah Brigham as editor (10). Before that, Benjamin Rush, a renowned Philadelphia physician who was a signatory to the Declaration of Independence and a founder of the University of Pennsylvania, published in 1812 an important treatise on mental illness, *Medical Inquiries and Observations Upon Diseases of the Mind*. He suggested that mental illness, like physical illness, was caused by abnormal body processes. In a letter to former President John Adams (11), he wrote, "I have endeavored to bring [diseases of the mind] down to the level of all other diseases of the human body, and to show that the mind and body are moved by the same causes and subject to the same laws." Although he expected a rebuff from his colleagues, Rush added that he hoped "time...will do my opinions justice. I believe them to be true and calculated to lessen some of the greatest evils of human life. If they are not, I shall console myself of having aimed well and erred honestly."

In late-19th-century America, neurology was practiced primarily in the great inner-city hospitals among the poor and indigent. Psychiatry, by contrast, was isolated almost entirely in sanatoriums and insane asylums scattered throughout the country, usually in rural areas isolated from the rest of the medical world. In a scathing attack on psychiatry addressed to the American Medico-Psychological Association in 1894, S. Weir Mitchell derided this isolationism and the failure of psychiatrists to see their patients in the setting of real life. He stated that he could not

cease to lament the day when the treatment of the insane passed too completely out of the hands of the profession at large, and into those of a group of physicians who constitute almost a sect apart from our more vitalized existence. What evil has this wrought, what harm it has done to us and to you I shall try to show. Why it has been so much more grave in its results here than in Europe is not clear to me. (10, p. 29)

In Europe, Freud, trained as a neurologist, worked in the Viennese laboratory of Ernst Brucke to define the structural basis of neurologic functions. His anatomic descriptions of the lamprey's spinal ganglia were a major contri-

bution. But after 8 years he became discouraged with his lack of progress and inability to support himself in research. He decided to enter clinical neurology and went to Paris to study under Charcot (12). It was at the Salpêtrière that Freud became acquainted with the study of hysteria, the experience that set him on the trajectory that was to become his life's work.

Freud turned his attention to in-depth interviews of patients, and at the turn of the century, well into his theories of repression and infantile predisposition to disease, he separated himself from the German school led by Emil Kraepelin. Samuel Barondes (13), in his 1998 book *Mood Genes*, wrote that

Throughout the twentieth century, attempts to understand manic-depressive illness have themselves swung between poles established by the two great founders of modern psychiatry. Born in the same year, 1856, trained in medicine at a time when it was just beginning to establish itself on a scientific footing, they have each left a rich legacy. So great was their influence that both are included in a recent book on the hundred most influential scientists: one of them, Emil Kraepelin, ranked 92 (of *all* scientists, *ever*) and the other, Sigmund Freud, a stratospheric 6.

Freud and Kraepelin became the two most influential figures in psychiatry in the early 20th century. An extensive search failed to uncover any evidence of correspondence between the two, although they frequently considered and wrote about the same problems. A biographer of Freud noted that Kraepelin "largely ignored Freud when he did not malign him for ideas he no longer held" (14).

Kraepelin and his students and followers (including Alzheimer) had trained in neuropsychiatry and were qualified to see patients as psychiatrists. But they hoped to discover the basis of psychiatric disease using new histologic methods to examine brain tissue and to correlate neuropathologic lesions with clinical syndromes. Kraepelin embarked on studies of a condition he labeled "dementia praecox," which led subsequently to Eugen Bleuler's description of schizophrenia. To his dismay, Kraepelin was unable to find any pathologic markers to distinguish the illness from other conditions. At the turn of the century, then, neuropsychiatry was an emerging discipline engaging the interests of many students of the pathological brain, particularly in the German-speaking world.

## Divergence of Neurology and Psychiatry

Two conditions, Alzheimer's disease and Tourette's syndrome, serve as prototypes of how research in neurology and psychiatry diverged over the century. A consideration of how these disorders were historically viewed suggests lessons that might caution us as to the perils of assuming extreme positions about the causation and etiopathogenesis of disease. They illustrate the hazards of trying to link

scientific hypotheses to clinical symptom profiles and of assuming doctrinaire attitudes toward mental illness.

### *Alzheimer's Disease*

The neuropathologic hallmarks of Alzheimer's disease—neuronal loss, senile plaques, and neurofibrillary tangles—were described by Alois Alzheimer, who was born in 1864 in Marktbreit, Germany. In describing the first recognized case in 1906, Alzheimer presented his findings of the behavioral and neuropathological changes in a woman, Frau Auguste D., who died at age 51 after developing a rapidly progressive dementia (15). This patient's clinical course, which Alzheimer described as unique, was a rapid deterioration in mental competence accompanied by paranoia, confusion, disorientation, severe memory loss, and difficulty understanding language. Alzheimer wrote that the patient

had as initial prominent presentation jealousy against the husband. Soon, a rapidly progressive weakness of memory became noticeable. She was unable to find herself oriented about her apartment. She moved objects from one place to the other, hid them, at times she believed one intended to murder her and she began to shout loudly....She was completely disoriented as to time and place. Occasionally, she remarked that she did not understand anything any more, that she was at a complete loss. The physician she greeted like a visitor and excused herself that she had not completed her work. Before long she shouted loudly that he wanted to cut her or she sends him away incensed with remarks which indicate that she is concerned about him regarding her female honor. At times, she is delirious, moves her bed around, calls for her husband and daughter, and appears to have auditory hallucinations.

Her ability to observe is severely disturbed. If one shows objects to her, she names these usually correctly, but immediately thereafter she has forgotten everything. When reading, she drifts from one line to another, reads by spelling or with senseless intonation; when writing, she repeats individual syllables repeatedly, drops others, and bogs down rather quickly. When speaking, she often uses phrases of embarrassment, some paraphasic expressions (creamier instead of cup), sometimes she gets stuck (in speaking). Some questions she obviously does not understand. She does not comprehend anymore the usage of certain objects. The neurological examination except for mental status was unrevealing of a focal neurological deficit. Her gait is undisturbed, she uses her hands equally well. The patellar reflexes are present. The pupils react. (15)

(I thank Prof. Walter Rosenau of the University of California, San Francisco, for providing this literal translation.)

The neurofibrillary tangles accompanying the disease were later defined by Robert Terry and his colleagues (16) as paired helical filaments made up of a microtubular protein called "tau," which becomes hyperphosphorylated, resulting in neuronal dysfunction and death (p. 360). Eventually, as Alzheimer observed, this cellular change becomes very extensive, leading to a severe loss of neurons in the cerebral cortex. In 1984 Glenner and Wong (17)

showed that the plaques contain a protein fragment,  $\beta$  amyloid, which appears to cause degeneration of nerve terminals, loss of normal brain architecture, and inflammation. These changes create thousands of microscopic scars in the cerebral cortex. The issue of which comes first, plaques or tangles, and whether the abnormalities in amyloid metabolism are the primary factor causing disease remain the focus of intense investigation.

Progress in understanding the molecular and genetic basis of Alzheimer's disease advanced slowly until the mid-1980s, when clinical observations combined with new techniques in biochemistry and molecular biology opened the door to significant discoveries. Patients with Down's syndrome, if they live beyond about 35 to 40 years, invariably develop plaques and tangles and often suffer intellectual deterioration. These findings demonstrated that Down's syndrome, caused by an extra copy of genes on chromosome 21 (trisomy 21), induces pathological changes in the brain identical to those of Alzheimer's disease. The observation that 3%–5% of Alzheimer's disease cases appear early in life with a Mendelian pattern of autosomal-dominant inheritance made possible linkage studies to locate the genes involved. In 1987 St. George-Hyslop and colleagues (18) showed positive linkage to the long arm of chromosome 21 in four families, in a region close to that duplicated in Down's syndrome. (It was later shown that Alzheimer's disease in these families actually linked more robustly to chromosome 14, but the initial observation triggered an explosion in genetic research.)

Other researchers searched for the gene for  $\beta$  amyloid. In 1987 four separate laboratories in North America and Europe reported that the amyloid gene was also on the long arm of chromosome 21 (19). These findings revealed that  $\beta$  amyloid is a fragment of a large protein called amyloid precursor protein. Encouraged by this result, other investigators examined additional pedigrees of familial Alzheimer's disease for mutations of the amyloid precursor protein gene. Eventually, an amyloid precursor protein mutation that was segregated with dementia was described in two families (20). Since then, others have found more than 20 amyloid precursor protein mutations. Most mutations are close to, but outside, the  $\beta$  peptide region. The vast majority of Alzheimer's disease families have no amyloid precursor protein mutations; however, it is now evident that multiple genetic loci are involved in causing the disease. A second locus, found on chromosome 14q, encodes the presenilin 1 protein. More than 75 mutations of this gene have been reported (21), and it is estimated to account for approximately 25% to 40% of the cases with early onset. A third locus, presenilin 2, was identified on chromosome 1 in two kindreds with an early onset of dementia (22, 23). The functions of amyloid precursor protein and the presenilins are unknown, but the latter is involved in signal transduction. A fourth locus, on chromosome 19q, is important in late-onset Alzheimer's disease, in which genes encode three isoforms of apolipoprotein E,

first identified for its role in transporting cholesterol in the blood. Although no mutations have been found in apolipoprotein E, one of its three alleles, E4, substantially increases the risk for Alzheimer's disease, with onset about 7 years earlier in patients who are homozygous for E4 (16, p. 341). Other gene loci have been identified on chromosomes 10 and 12 (24, 25).

Although Alzheimer's disease's pathologic description placed the disorder firmly into the discipline of neurology, it was more than 70 years later that scientists and clinicians came to realize that efforts to separate presenile from senile dementia were fruitless. And only later, in the past two decades, has the high prevalence of the disorder been fully appreciated.

In an important way, Alzheimer's disease defined some of the territorial rifts between neurology and psychiatry. The observations made by Alzheimer occurred in a psychiatric institute. Once seen under the microscope, however, Alzheimer's disease was assigned to the neurological category of disease, despite the fact that many of Frau Auguste D.'s symptoms were "psychiatric." As the disease progresses, its manifestations include deepening dementia, paranoia, depression, and cognitive defects in speech and language. Clearly, a conjoined effort of neurologists and psychiatrists is necessary to understand how a disease of the brain results in an illness of the mind. Clinical attempts to categorize diseases as "organic" or "functional" become somewhat arbitrary.

### *Gilles de la Tourette's Syndrome*

In the second condition, Gilles de la Tourette's syndrome, it is even more obvious that attempts to separate "neurologic" from "psychiatric" disease have been counterproductive. Tourette's syndrome usually begins in childhood with symptoms of verbal and motor tics and a constellation of behavioral problems. The initial description of what later became known as Tourette's syndrome was made in 1825 by the French physician Jean Marc Gaspard Itard (26). The patient was a young aristocratic woman, the Marquise de Dampierre. From childhood until her death in 1884, the marquise exhibited convulsive tics and scandalous cursing that became the talk of Paris.

To better understand the history of Tourette's syndrome, we need to begin before the syndrome got that name. Goodman and Murphy (27) noted,

The earliest historical account of Tourette syndrome may be from a treatise on witchcraft, *Malleus Maleficarum* (or *The Evildoer's Hammer*), about a 15th century individual: "When he passed any church, and genuflected in honor of the Glorious Virgin, the devil made him thrust his tongue far out of his mouth; and when he was asked whether he could not restrain himself from doing this, he answered: 'I cannot help myself at all, for so he uses all my limbs and organs, my neck, my tongue, and my lungs, whenever he pleases, causing me to speak or to cry out; and I hear the words as if they were



spoken myself, but I am altogether unable to restrain them.”

Itard, who first described Madame Dampierre's disturbing behavior, believed her symptoms reflected an underdeveloped will, probably a consequence of her remaining childless and thus lacking the moral fortitude conferred by maternity. Although he never treated the marquise, Itard sensibly recommended “moral” treatments for her “moral” deficiency.

Other French physicians weighed in with their own interpretations of the marquise's symptoms, though none had personally examined her. One, David Didier Roth, placed her in a category with other cases involving “muscle tics of speech and the larynx” and asserted that the cause was organic muscular pathology. Another, Théodule Ribot, attributed it to hereditary psychological degeneration, caused by unsavory habits, such as alcoholism, poor diet, and immoral behavior, in preceding generations. Thus, even before Tourette published his articles describing other patients with tic disorders, the leading physicians of the day were debating the etiology of the syndrome that bears his name.

When Tourette's articles were published, Charcot claimed they established the basis for a new diagnostic category. Like Ribot, Charcot and Tourette believed the symptoms were the result of hereditary insanity. Although hysterical patients also frequently displayed tics, they insisted the two categories could be distinguished through hypnosis, since only true hysterics could be hypnotized. Many of their colleagues at the Salpêtrière disagreed, arguing that the “maladie des tics” was simply one manifestation of hysteria. At the same time other critics outside the Salpêtrière circle maintained that Tourette's syndrome could not reliably be distinguished from Sydenham's chorea, a condition that had first been described in the early 1600s, and thus they reasoned that the two shared a common etiology in rheumatic fever brought on by microbial infection.

As Kushner (28) noted, “By the early twentieth century, physicians who attempted to diagnose and treat patients presenting with tics and involuntary vocalizations were forced to draw from a confusing array of contradictory claims.” Over the past century, the understanding of this illness has continued to bounce back and forth between neurology and psychiatry, between organic causes and psychodynamic explanations. In 1995 Oliver Sacks (29) described the remarkable talents of a Canadian surgeon who suffered from severe symptoms of Tourette's syndrome. The symptoms disappeared, astonishingly, while he was performing surgery. Sigmund Freud described only a single case of tic disorder, in 1889, before he had fully formulated his psychoanalytic theory (28). Freud essentially subscribed to the idea that tics were a hysterical symptom, and he claimed to have successfully treated his patient with hypnosis, although no proof has been found about whether the patient actually improved. In 1921 Freud's

Hungarian disciple, Sandor Ferenczi (30) outlined what became the standard psychoanalytic explanation for tics. Ferenczi had never examined a single patient with Tourette's syndrome, but drawing on published cases, he reasoned that the tics and verbal outbursts were a symbolic expression of masturbation in patients whose repression of their sexual urges rendered them incapable of acting them out. (He believed that the same psychodynamic conflicts were expressed in other patients as catatonia—the opposite of ticcing.) The much more common occurrence of Tourette's syndrome in boys than in girls reinforced this hypothesis of sexual repression, an idea that still persists in parts of the world, particularly in France.

### *Evolving Concepts of Tourette's Syndrome*

After World War II, when the first neuroleptic drugs were developed, tics, aberrant vocalizations, and cursing were all shown to respond to these agents, leading to the hypothesis of abnormalities in dopaminergic neurotransmission. Studies, principally by Arthur and Elaine Shapiro and colleagues (31), showed that haloperidol and other antipsychotics were more effective than psychotherapy in the treatment of Tourette's syndrome. The Tourette Syndrome Association was founded in 1972 by patients of the Shapiros and their families who were frustrated by psychoanalytic interpretations of the etiology of Tourette's syndrome that implicitly or explicitly blamed inadequate parenting. The association raised awareness of the disease's true prevalence and argued for the separation of Tourette's syndrome from obsessive-compulsive disorder (OCD).

The development of selective serotonin reuptake inhibitors (SSRIs) led to a further improvement in the treatment of Tourette's syndrome and to a chaotic redefinition of the overlap between Tourette's syndrome and OCD. The search for genetic loci accounting for a familial predisposition to Tourette's syndrome and OCD has, to date, been unfruitful. The results of the first systematic genome analysis in sibling pairs with Tourette's syndrome failed to show any loci with statistically significant lod scores, although multipoint maximum-likelihood scores greater than 2.0 were suggested in two regions (4q and 8p).

In 1956 Taranto and Stollerman (32) made the unequivocal clinical association between  $\beta$ -hemolytic streptococcal infections and the occurrence of Sydenham's chorea. The speculation that Tourette's syndrome might be founded on a similar pathophysiologic mechanism has received considerable support. Treatment with plasmapheresis is reported to be beneficial for children with severe tic disorder (33). The analogy between Sydenham's chorea and Tourette's syndrome deserves further study. It is very possible that some cases of Tourette's syndrome represent an autoimmune state not unlike, for example, multiple sclerosis, which has a familial incidence and appears to involve the interplay of multiple predisposing genes.

The early onset, male preponderance, and familial tendency of Tourette's syndrome and OCD strongly suggest a genetic predisposition to these conditions. Expressivity, penetrance, predisposing and epigenetic factors, environment, autoimmunity, and nurture may interact in complex ways that are at present only possible to imagine but that will likely yield to further careful study.

At a 1985 symposium in Paris marking the 100th anniversary of the naming of the syndrome, the divisiveness among participants was startling. The American contingent presented evidence in support of an organic basis, while many in the French academy clung to the explanation that held sway for the first 70 years of the century—that although there might be a familial tendency toward tics, the underlying cause was a psychopathologic release of repressed tendencies.

As Kushner (28) summed it up, “The rise and fall of each successive explanation for and treatment of Tourette syndrome has been as much a story of the power of a shared set of beliefs of a professional faction as it has been a vindication of either rigorous scientific testing or carefully analyzed clinical results.”

### **A Century of Research**

I have used these two disorders, Alzheimer's disease and Tourette's syndrome, to illustrate the contradictions and difficulties of attempting to label diseases as organic versus functional or as pathologically or genetically based versus sporadic or as experience-based phenomena. The separation of the two categories is arbitrary, often influenced by beliefs rather than proven scientific observations. And the fact that the brain and mind are one makes the separation artificial anyway.

Research in Alzheimer's disease, based on demonstration of pathologic brain lesions, moved apace using the tools of electron microscopy, biochemistry, and molecular genetics to emerge as one of the areas of brain disease study most likely to yield specific treatments. For Tourette's syndrome, however, the absence of either a specific unifying phenotype or evidence of brain pathology resulted in vacillation between organic versus functional explanations and continuing controversy regarding its etiology. As with schizophrenia and bipolar affective disorder, the failure to identify specific genetic loci has slowed progress in elucidating a biological mechanism.

Nevertheless, it seems likely that genetic predisposition and environmental factors interact in the pathogenesis of Alzheimer's disease, particularly in cases that arise sporadically (perhaps as many as 50% of the total). Environmental and aberrant hormonal, physiological, or inflammatory events likely influence the timing of onset and the progression of the illness. For example, higher educational level is associated with a lower risk, head trauma with a greater risk. Estrogen may influence progression, and nonsteroidal antiinflammatory drugs and vitamin E are

prospects for protection from a cascade of inflammatory events.

Neurology has always been premised on observational correlation—linking a symptom to a structural change, a disorder to a pathology. Neurologists have at the same time often been unyielding to notions of plasticity, regeneration, and recovery, a bias reflected in a skepticism about the efficacy of physical, occupational, and speech and language therapy. Many genetic disorders are seen phenotypically as complex mixtures of physical, intellectual, and emotional difficulties. Even diseases like myotonic dystrophy, ataxia telangiectasia, and Duchenne's muscular dystrophy are associated with deficiencies in mental functioning.

### **Neurology, Psychiatry, and Neuroscience**

After World War II, the division between neurology and psychiatry became explicit. The *Archives of Neurology and Psychiatry* was separated into two journals. The American Academy of Neurology was founded in 1948, and departments of neurology sprung up across the United States, diverting neurologic research and practice into a separate realm. Neurology and psychiatry have remained separate to this day. The training programs of students in the two fields were initially separated by an artificial division between disorders that were considered either organic or functional. Those with identifiable brain lesions were readily identified as having neurologic disorders. But it has become vividly clear that the major diseases treated by psychiatry, such as bipolar affective disorder and schizophrenia—for which the organic basis was more elusive—are also brain diseases, with accompanying changes in brain structure and function.

Since the 1960s the evolution in the understanding of neuropharmacology and the identification of neurotransmitters have led to the emergence of biological psychiatry. At first psychiatric research focused on measuring neurotransmitter levels in the brain, spinal fluid, or urine and identifying receptor modifications associated with disease. Now, as we emerge from the “Decade of the Brain,” neurologic and psychiatric research are moving closer together in the tools they use, the questions they ask, and the theoretical frameworks they employ. The development of functional imaging techniques, including magnetic resonance imaging, positron emission tomography, and computerized tomography with rapid infusion, are now used not only by neurologists and psychiatrists but also by psychologists and cognitive neuroscientists. Recent developments using transcranial magnetic stimulation have provided impressive methods to temporarily interrupt cognitive functions, such as attention (34), as well as providing promising new approaches besides ECT for the treatment of depression (35).

As the Society of Neuroscience has grown from a few hundred scientists in 1970 to nearly 30,000, it has become difficult to distinguish the research reported by neurologists and psychiatrists at the society's annual meeting. This meeting has become the principal forum in which the two disciplines meet and discuss their mutual interests in diseases such as Parkinson's (with its tendency for depression and dementia), Alzheimer's disease (with its disorders of mood as well as cognitive function), and other disorders now recognized as either genetic (for example, Tourette's syndrome) or as having a strong neurochemical basis.

A principal lesson to be learned from surveying neuroscience, neurology, and psychiatry in the past century has been how often predictions have proven wrong. Meanwhile, issues of turf persist. One might liken neurology and psychiatry to Winston Churchill's characterization of the United States and Great Britain—two countries separated by a common language. For us, that common language is neuroscience.

Kandel (36) wrote perceptively of psychiatry and neuroscience:

The details of the relationship between the brain and mental processes—precisely how the brain gives rise to various mental processes—is understood poorly, and only in outline. The great challenge for biology and psychiatry at this point is to delineate that relationship in terms that are satisfying to both the biologist of the brain and the psychiatrist of the mind....

As a result of advances in neural science...both psychiatry and neural science are in a new and better position for a rapprochement...that would allow the insights of the psychoanalytic perspective to inform the search for a deeper understanding of the biological basis of behavior.

With the advent of psychopharmacology, psychiatry was changed, and that change brought it back into the mainstream of academic medicine....When it comes to studying mental function, biologists are badly in need of guidance. It is here that psychiatry, and cognitive psychology, as guide and tutor, can make a particularly valuable contribution to brain science....[They] can define for biology the mental functions that need to be studied for a meaningful and sophisticated understanding of the human mind.

James Jackson Putnam told the members of the Massachusetts Medical Society in 1899 to "Remember, when you go to see your patients, that it is after all the man, not the disease, that you are called upon to treat" (9, p. 238). Physicians and scientists now accept that brain chemistry plays a role in mental illness, since medications for it are effective. But we also recognize that the best therapeutic responses seem to come from combining treatment modalities—both administering medication and talking to the patient.

## Toward a 21st-Century Revolution

What are we to do? In a recent article (37), Price et al. analyzed the persistent rift between neurology and psychiatry and came up with a series of recommendations. The most important, perhaps, is that

The education of future psychiatrists and neurologists should be redesigned....Both disciplines should emphasize basic neuroscience, genetics, neuroanatomy, neuropathology, neuroimaging, neuropsychology, cognitive neuroscience, behavioral phenomenology, neuropsychopharmacology, and psychological interventions. Neurologists in training should be given a rich clinical exposure to patients suffering from major mental and neuropsychiatric diseases. Psychiatrists in training should be given more exposure to patients with neurologic syndromes, particularly those that are likely to be accompanied by psychiatric symptoms.

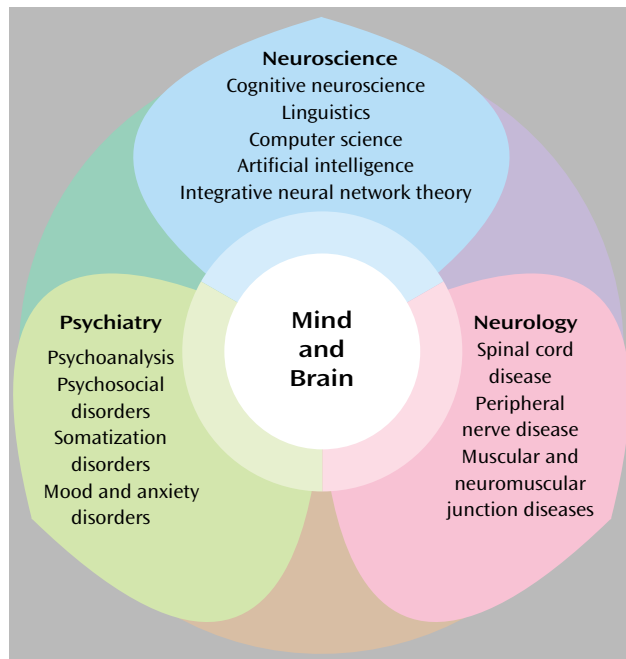
Introducing the rapidly accumulating neuroscientific knowledge along with other programmatic changes in neurology and psychiatry training programs will be a challenge....Ultimately, given the delicate balance and growing disparities between our rapidly accumulating scientific knowledge and social policies, we need to include perspectives from social scientists, ethicists, philosophers, religious representatives, patient advisory groups, and the legal community. (37)

It seems appropriate to consider whether radical changes should be taken to place neurology and psychiatry in direct juxtaposition. One major concern for academic leaders in neurology and psychiatry is the paucity of interest among medical students and residents in pursuing careers in the clinical neurosciences. As reviewed by Iverson (38), fewer than half of all U.S. neurology and psychiatry residency positions nationwide are filled by U.S. medical school graduates. The acceptance rate for U.S. graduates who apply to residency programs in neurology or psychiatry is close to 97%, with a 70% acceptance rate for foreign medical school graduates. At a time when neuroscience research promises so much to our understanding of the brain in its normal and abnormal conditions, it comes as a shock that we have failed to instill more excitement in our students. Statistics from 2000 (39) show that 46% of neurology residency slots were filled by foreign medical graduates; in the case of psychiatry, the number was 41%.

A more specific set of recommendations might be based on the scientific and clinical interfaces among neurology, psychiatry, and neuroscience. The model I propose places mind and brain at the center of a circle, surrounded by three zones of convergence, represented, respectively, by the broader disciplinary motifs of psychiatry, neurology, and neuroscience (Figure 1).

In psychiatry, lying beyond the center of convergence are the fields of psychoanalytic theory, psychosocial disorders, and many somatoform, mood, and anxiety disorders. Training in psychiatry must include the theoretical constructs, diagnostic terminology, and treatment approaches for these conditions. In neurology, diseases of

**FIGURE 1. The Relationship of Neuroscience, Neurology, and Psychiatry and Their Subtopics to Mind and Brain**



the spinal cord, peripheral nerves, and the neuromuscular junction and muscle are outside the bounds of neuropsychiatry. Specific areas aligned to varying degrees with neuroscience are cognitive neuroscience and the allied fields of computer science, artificial intelligence, and integrative neural network theory.

To prepare students for a career informed by the convergence of these disciplines, universities should introduce the common core concepts of neuroscience in the undergraduate curriculum. It is amazing how many students in our best colleges and universities adopt an interest in brain science. We need to strengthen their experience through a conjoined approach to neuropsychiatry in the early years of medical school and provide an integrated clinical experience in the overlapping areas in the last 2 years of medical school. At Harvard Medical School, an integrated preclerkship curriculum in neuroscience, psychiatry, and neurology has been implemented in the form of a course on the human nervous system and behavior for second-year students; there is coordination of course content with other relevant learning experiences, such as neurological and mental status examinations and psychiatric interviewing (40). Students have overwhelmingly endorsed this curriculum, consistently ranking the course as one of their best and stating that it has greatly increased their interest in the subject matter. In the postdoctoral years, residents who have selected brain disease as a focus should be given continuing opportunities to take part in experimental approaches to understanding mind, brain, and behavior.

To implement these goals, the postgraduate experience might be reconfigured into 2 or 3 years of basic and clinical

education on the brain in health and disease—the core area in which the disciplines converge—followed by subspecialty training that extends beyond the core.

To take full advantage of the enormous opportunities for elucidating the causes of neuropsychiatric disorders and seeking effective treatments for them, bold, revolutionary planning and experimentation will be required. Progress will also depend on overcoming social and psychological obstacles, including ingrained, dualistic concepts of brain and mind, rigid educational traditions, and protective instincts with regard to professional turf.

I do not share the perspective of Hobson and Leonard (41), who set out to protect psychiatry from the inroads of neurology. They argued defensively, and not persuasively, that psychiatry needs to strengthen its base and protect itself from a takeover by neurology, which, they noted, nearly occurred in the latter part of the 19th century. I argue instead that we need to join forces and create a seamless interconnection in training and in clinical practice.

In a recent article on prospects for neurology and psychiatry, Cowan and Kandel (42) expressed optimism that the decades ahead will “be remembered as the time when, at long last, neurology and psychiatry came into their own, as among the major beneficiaries of the revolution in biological science that began in the early 1950s.” They predict that

We will see a new degree of cooperation between neurology and psychiatry. This cooperation is likely to have its greatest impact on patients for whom the two approaches, neurological and psychiatric, overlap, such as in the treatment of autism, mental retardation, and the cognitive disorders associated with Alzheimer and Parkinson diseases. We therefore believe that with further growth, neuroscience will most likely serve to bring neurology and psychiatry even closer together. (42)

In conclusion, two points need to be made. First, I want to urge some humility as we begin the 21st century. Although we must acknowledge the power and seduction of science, we need at the same time to be aware that much of what we do today will in 10 to 20 years seem foolish—naive, oversimplified, and self-promoting. The “brain problem” is arguably the most difficult we will ever encounter. It is a challenge that will excite and test the limits of our creativity and imagination. We need all the help we can marshal, which leads to the second point.

The success of our endeavors will increasingly depend, as I have already implied, on interdisciplinary, interdepartmental research: chemists, physicists, engineers, and computer scientists working in close collaboration with neuroscientists, physicians, and psychologists. The reductionist approach to biomedical research has been a powerful and enormously fruitful one. But in the 21st century, we must focus on putting Humpty Dumpty back together again, which will require the collaboration of scientists from diverse disciplines.



Koch and Laurent (43) argued that further progress in neuroscience will depend on the integration of a number of distinct and complementary approaches to studying brain and behavior. "Advances in the neurosciences have revealed the staggering complexity of even 'simple' nervous systems," they wrote. "This is reflected in their function, their evolutionary history, their structure, and the coding schemes they use to represent information. These four viewpoints need all play a role in any future science of 'brain complexity.'" They concluded that

Perhaps the most obvious thing to say about brain function from a 'complex systems' perspective is that continued reductionism and atomization will probably not, on its own, lead to fundamental understanding. Each brain is a tremendously heterogeneous patchwork. Understanding the function of any of its parts requires a precise knowledge of its constituents but also of the context in which this part operates. (43)

Leaders in academic medicine and the sciences at each of our institutions and at a national and international level must work to break down the barriers between disciplines to remove the obstacles to fuller collaboration and integration. We must move beyond the turf battles of the past to a recognition that the ground we are now breaking in the science of brain and mind is common ground.

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