neurodegenerative disorder, autosomal recessive juvenile parkinsonism, is caused by a genetic defect in a component of that system, parkin.[7]

The causes of the abnormal folding are various and still poorly understood. Obvious causes are genetic defects producing a single amino acid substitution or expansion of a repeating amino acid tract, as occurs in the strongly familial forms of many neurodegenerative diseases.[8 9] However, for most neurodegenerative disorders that occur sporadically or in non-Mendelian familial fashion, other causes of abnormal folding lie at the source of the pathogenetic cascade.

For example, again in the case of non-familial Parkinson's disease, exposure to pesticides,[10] certain metals,[11] or oxidative stress (probably via mitochondrial defects)[12] can cause abnormal α-synuclein folding and subsequent aggregation. Genetically determined variation in the ability to degrade exogenous toxins enzymatically or compensate for oxidative stress may be central to susceptibility to disease and to determination of the age of onset.

Introducing the concept of protein aggregation into our thinking will also allow us to transcend the classic rubric of clinical and anatomical pathology. An excellent example is the obsolescence of the term olivopontocerebellar atrophy. The sporadic form of olivopontocerebellar atrophy has been found to harbour cytoplasmic inclusions in oligodendrocytes consisting chiefly of α-synuclein. The same is true for Shy-Drager syndrome and striatonigral degeneration.[13] These three entities have now been combined into a pathogenetically based rubric called multiple system atrophy. The familial form of olivopontocerebellar atrophy has been subsumed into the various forms of spinocerebellar ataxia, which are differentiated by their genetic defects and by the nature of their protein aggregates. The term olivopontocerebellar atrophy has therefore proved useless and has virtually disappeared from the literature.

As we consider the pathogenesis and classification of neurodegenerative disease, we must consider the identity of the abnormally aggregating protein, the cause of its misfolding, causes of protein aggregation other than misfolding, the causes of failure of the ubiquitin-proteasome system to dispose of the abnormally folded or aggregated protein, and the mechanism by which abnormally aggregated protein causes cellular damage. This framework will bring a more rational classification of disease and a very high probability of specific treatments or prevention.

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The wall between neurology and psychiatry

Advances in neuroscience indicate it's time to tear it down

For more than 2000 years in the West, neurology and psychiatry were thought to be part of a single, unified branch of medicine, which was often designated neuropsychiatry. Charcot, Freud, Jackson, Bleuler, among many others, thought in terms of a unified study of the brain and the mind, irrespective of special clinical and research interests. During the 20th century, however, a schism emerged as each of these fields went its separate way. Neurologists focused on those brain disorders with cognitive and behavioural abnormalities that also presented with somatic signs—stroke, multiple sclerosis, Parkinson's, and so forth—while psychiatrists focused on those disorders of mood and thought associated with no, or minor, physical signs found in the neurological examination of the motor and sensory systems—schizophrenia, depression, anxiety disorders, and so on. For certain disorders, conflicting theories emerged about their aetiology and pathogenesis, at times engendering negative attitudes among workers in one or the other field, including derision and incivility. In academic medical centres, separate departments were formed in neurology and psychiatry that had little interest in collaboration in research, teaching, or patient care.[1] Those specialists who supported a more holistic view of these disciplines were in full retreat by midcentury.[2]

Clearly, recent advances in neuroscience make it untenable at this time to know precisely where to draw the line between neurological and psychiatric disorders. For example, it is well known that many patients with Parkinson's disease and stroke manifest depression and, in some, dementia. Is there a substantive difference between a toxic psychosis (psychiatry) and a metabolic encephalopathy with delirium (neurology)? We have known of these examples for several years. More recent and dramatic evidence has come largely

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through functional magnetic resonance imaging and positron emission tomography. Obsessive-compulsive disorder is characterised by recurrent, unwanted, intrusive ideas, images, or impulses that seem silly, weird, nasty, or horrible (obsessions) and by urges to carry out an act (compulsions) that will lessen the discomfort due to the obsessions. Increasing the levels of brain serotonin with selective reuptake inhibitors may control the symptoms and signs of this disorder. Evidence of a genetic basis in some patients, structural abnormalities of the brain on magnetic resonance imaging in others, and abnormal brain function on functional magnetic resonance imaging and positron emission tomography collectively suggest that schizophrenia is a disorder of the brain.[3]

Nor does all of the neuroscientific evidence linking neurology and psychiatry arise from study of patients. Learning to read by braille can enlarge the brain region responding to fingertip stimulation. Brain imaging research shows that several brain areas are larger in adult musicians than in non-musicians. The primary motor cortex and the cerebellum, which are involved in movement and coordination, are bigger in musicians than in people who don't play musical instruments, as is the corpus callosum. Discontinuing the use of braille or the violin can reverse the functional neuroanatomic connections.[4]

Because of the vast increase in neurobiological knowledge in recent years, and the ever increasing number of disorders (including those referred to above) once thought to be psychopathological yet now known to be neuropathological, some neurologists might cling to the view that their specialty has now emerged alone as the reigning queen of the medical sciences. If they do, we do not agree with them. The concept of mental health as much more than the mere absence of brain disease is, we suggest, indispensable for neurological and psychiatric practice and care. From our angle of vision, the fundamental alliance between mental health and brain illness (devoid of the confounding terms brain health and mental illness[5]) as the basis of care derives in the first instance from Aristotle's distinction between efficient causes and final causes. (An efficient cause, or mechanism, is that by means of which something happens; a final cause, or teleological cause, is that for the sake of which something happens.) Neurologists and psychiatrists must have a suitably broad perspective, for theirs is the domain of purposeful behaviour and intentionality (final causes) that is no less a brain/mind function than sense perception and movement. Clearly, the education of future generations of neurologists and psychiatrists must be grounded in neuroscience, but must equally be focused on those dimensions of professional activity that quintessentially define the work of medical doctors from the neck up.[6]

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Demystifying neurology

Phenomenology can help

See Reviews p 1528

Muhammad Ali, Dudley Moore, Ronald Reagan, and Christopher Reeve have in common that they suffered from degenerative and traumatic disorders of the nervous system, the prevalence of which will increase greatly during the next 20 years.[1] Although neurological and psychiatric disorders account for only 1.4% of all deaths, they account for a remarkable 28% of all years of life lived with a disability. Thus all doctors must be prepared to meet the needs of patients with such disorders and refer appropriately for specialised care and investigations, bearing in mind that neurologists often function as consultants for other physicians. Yet do medical students and house officers believe they are being adequately prepared for independent practice, and do general doctors have confidence in their ability to diagnose and treat patients with disorders of the nervous system?

Apparently not. Schon et al recently surveyed medical students, senior house officers, and general practitioners about such matters, and the results merit serious attention.[2] Compared with their knowledge of other organ systems, their knowledge of disorders of the nervous system was said to be poorest. Moreover, basic neuroscience and clinical neurology ranked at the top of the list for difficulty in learning and complexity. Practising doctors likewise averred that they had less confidence in practical clinical situations in neurology than in other system disorders. When respondents to the survey were asked to identify the causes of their difficulties in neurological education, they cited insufficient, poor, irrelevant, or poorly coordinated teaching, and intimidation by neurology's reputation as a tough grind, among other considerations. Although the survey was carried out in the United Kingdom, few neurologists and educators elsewhere would doubt the universality of these disturbing findings, which were in fact identified in the United States and Canada a generation ago.[3 4]

Many groups, including the World Federation for Medical Education, the Royal College of Physicians of

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