

# 1 Introduction

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Many illnesses have a historical course. Diseases described in antiquity no longer exist and diseases apparently not present in the past are currently with us. The “black plague” no longer exists, but HIV-AIDS or AIDS-related complex (ARC) infection was never observed or identified before recent times. Other illnesses, while observed and described from ancient times until the present, have been understood differently over time, having been repeatedly reconceptualized. Stroke was described by Hippocrates in his writings as apoplexy (Greek for “struck down with violence”) and was then of unknown cause, but the term had possible religious implications – at one time there was a belief that stroke was a punishment by God for wrongdoing. It was recognized during the 17th century that it involved bleeding in the brain, an idea that led to our eventual understanding of it as a cerebrovascular disorder. Thus, there are new illnesses and old illnesses that are thought of differently now from how they were considered in the past. In this book we consider new neurobehavioral disorders that apparently did not exist before the beginning of the 20th century, as well as disorders that have been known for long periods of time but have been reconceptualized after the beginning of the 20th century. A neurobehavioral disorder is a condition associated with some abnormality of the brain that produces mainly behavioral symptoms. A new illness is a condition in which case reports appear that reflect the presence of a disorder that was never previously observed. A reconceptualization occurs when an illness thought to be produced by a particular cause is no longer considered so, and credible evidence has been provided that it is produced by a different cause.

There are numerous reasons for the appearance of new illnesses. Evolutionary changes may result in mutations that are not desirable and that produce pathological conditions rather than adaptive changes. Perhaps schizophrenia evolved as one of these unfortunate genetic transformations. Evolutionary changes may occur not in humans but in the environment, when a new life form emerges that has harmful, often infectious, effects on humans. The HIV virus may be such a case. Other new illnesses may appear because of human activity. Most notable is the production of toxic substances in products that did not exist in the past. Environmental pollution is one broad example of this phenomenon, but there have been specific substances produced or placed in environments that have toxic effects on humans, either by accident or chronic exposure. Exposures to organophosphates or mercury are examples of this phenomenon. Sometimes purely behavioral matters can produce new disorders. Posttraumatic stress disorder (PTSD) is probably the best example here. A

adequate social support – and possibly genetic factors apparently produced PTSD. There is now evidence that PTSD is different from previously noted traumatic neuroses and related stress disorders. PTSD is of interest to us here because it apparently has neurobehavioral implications.

New disorders are sometimes unique combinations of old disorders. The best example is “Persian Gulf” or “Balkan” syndrome in which veterans coming back from wars in these areas had a combination of psychiatric and medical disorders that seemed to have different characteristics from what was observed previously in combat veterans. They had a combination of stress disorders and a variety of physical symptoms, sometimes associated with infection that involved multiple systems as well as reproductive capacities. The individual disorders themselves, while often undiagnosable, were not considered to be new diseases, but a combination of numerous diseases sometimes involving exposure to organisms not found outside of the areas to which they were located, or to the often unknown effects of some form of toxic exposure such as from depleted uranium or organophosphates. This pattern was characterized by some as a new illness called “Persian Gulf” or “Balkan” syndrome and what we characterize in a general way in this book as “deployment syndromes.” The weight of evidence now suggests that these conditions are not new diseases but various combinations of previously identified diseases. However, exposure to certain specific agents, such as depleted uranium, initiated new lines of investigation into the medical consequences of as yet unstudied substances.

A known disorder may also not be new but may be newly discovered in a population different from where it was observed in the past. The best example of this is attention deficit hyperactivity disorder (ADHD). Initially this condition was thought to be present only in children, and was outgrown. There is now impressive evidence based upon abundant research that ADHD extends into adulthood, and there are adults with diagnosed ADHD where the symptomatology is not based upon the existence of some other disorder.

Reconceptualization occurs when an illness that has been observed for some time is found to have a different cause from what was previously thought. The clinical phenomenology and course remain the same, but the conditions thought to produce the illness are often remarkably changed. Autism is probably the clearest example and its reconceptualization is described in Chapter 3 of this book. Leo Kanner, who wrote the first paper on autism, was a psychoanalyst who described the cause of autism as resulting from early experience with emotionally impoverished parents with whom infants could not bond. Kanner’s description of the disorder was quite precise and essentially provides the basis for its current description in the *Diagnostic and Statistical Manual of the American Psychiatric Association IV* (DSM-IV), but autism has been completely reconceptualized as a neurobiological disorder produced by abnormal brain function and is probably genetically based. Further reconceptualization of the autism spectrum will probably appear in the forthcoming DSM-V manual. Thus, we have the same disorder with an entirely changed basis.

Another important reconceptualization is in the area of dementias of the elderly. Until recently, it was thought that these disorders were mostly produced by vascular disease, notably arteriosclerosis (hardening of the arteries), and that Alzheimer’s

rare condition. Essentially that view has been reversed and it is now thought that Alzheimer’s disease is relatively common and cerebral arteriosclerosis, or vascular dementia, is relatively rare, largely occurring in individuals with histories of small strokes. This view has been supported by vastly increased knowledge of the neuropathology of Alzheimer’s disease and several related disorders, such as dementia with Lewy bodies, as described in this volume, and their identification in the brain by newly developed staining and neuroimaging methods.

Another aspect of recent changes in how illness is viewed is the increasing interest in the fact that many individuals have more than one illness, and that multiple illnesses in an individual interact in ways that produce health problems typically not associated with each illness when it occurs by itself. Thus, there has been extensive study of comorbidity in recent years and the model of producing the best science by studying illnesses in patients who only have a single disorder has been modified to some extent. There is now increasing scientific investigation of patients with co-occurring disorders. In the neurobehavioral and neuropsychiatric area, the emphasis has been on comorbidity between mental and substance use disorders (e.g., depression and alcoholism) but other combinations have been studied as well (e.g., PTSD and depression). There is particular interest in comorbidity involving bipolar disorder, or schizophrenia, and alcoholism. These considerations have been associated with the development of a new paradigm in diagnosis in which disorders are not diagnosed by presence or absence of individual clinical signs but by empirically derived dimensions established through the application of statistical methods such as cluster and factor analysis or various taxonomic methods.

Another change in approaches to the theory of illness involves a developing understanding of precursors of illness or risk factors. Two such developments are reviewed in this book. In one of them the neurobehavioral consequences of preterm birth are considered, and in the other the effects in children that exposure during the mother’s pregnancy to toxic agents may have on cognitive outcome are described. Epidemiological and developmental studies have been conducted that provide impressive scientific evidence that some neurobehavioral disorders may be associated with health-impairing outcomes related to events that took place in the course of development, extending from the prebirth period. Such matters as women who eat fish with high methylmercury levels and go on to have children born prematurely have become objects of intensive study in recent years. In other cases, there has been recognition that what were previously viewed as physical health disorders may have neurobehavioral implications. There appears to be a development of the view that general health status may have neurobehavioral consequences, and such illnesses as diabetes, cardiovascular disease, and nutritional disorders may be associated with changes in cognitive function. The area of respiratory disorders is reviewed in this book as an illustration of this phenomenon.

In many cases, issues related to new or reconceptualized disorders have raised extensive scientific controversy, as well as public concern. As an extreme example, it has been proposed that autism could be caused by routine vaccination in some individuals. Following extensive investigation of this proposal the idea was rejected, but it generated extensive controversy in the scientific and public communities.

disorder and, more recently, whether there is really such a thing as "Persian Gulf syndrome." There were at one time remaining advocates of Kanner's original opinion regarding the etiology of autism, but an abundant multidisciplinary scientific literature has essentially eliminated acceptance of that view. The reality of "sick building syndrome" has also been questioned. These controversies have generally been productive because they promoted extensive research, much of which generated reasonably definitive answers to the questions that were debated. Regarding these examples, there is now common acceptance of the views that: vaccination does not cause autism; PTSD is a diagnosable disorder accepted by the scientific and clinical community; Persian Gulf syndrome, while real, incorporates a number of different disorders; autism is in fact a neurobiological disorder; and sick building syndrome is a complex matter that can involve both toxic exposure and emotionally driven behaviors. We therefore provide discussion of controversies, where relevant, in several chapters of this book.

## Overview

In what follows we give an overview of the contents of the book. When topics were selected, our decisions were based on whether we agreed that the disorders chosen were in fact new or reconceptualized during the 20th century, and whether there was a substantial literature containing scientific investigation of the new disorder or its reconceptualization. There was extensive consideration of how a new disorder was defined. Perhaps the clearest cases of truly new illnesses were some of the toxicological disorders in which the toxic substance, such as depleted uranium, did not exist before the 20th century. Persian Gulf syndrome is obviously new because the Gulf War took place in the 20th century. The situation is less clear in some of the other disorders. For example, historians have been concerned with whether autism or related conditions such as Asperger's disorder existed in the past. Efforts have been made to build a case that there were some individuals with well documented biographies who would have been described in the 20th century as having autism or Asperger's disorder. PTSD may have existed but was not called that in situations in which people were exposed to trauma.

Neurasthenia has been described in the past, but not the specific conditions of fibromyalgia or chronic fatigue syndrome. Thus the term "new" is perhaps best understood as implying newly diagnosed rather than engaging in often difficult to resolve speculations about whether some disorder actually existed in the past or is a product of the 20th century.

Lynda Katz was asked to write a chapter on ADHD in adults (Chapter 4). The new aspect of that condition is that it was previously considered to be a disorder of children but there is now compelling evidence that it persists into adulthood in many cases. The formerly held belief that it is only present in children is reflected in a previous name for the disorder: "hyperkinetic reaction of children." While the disorder can be diagnosed in adulthood, the clinical phenomenology is somewhat different from what is seen in children. There is less hyperactivity, and inattentiveness is more prominent — described in DSM-IV as the predominantly inattentive

orders. Distinguishing between it and bipolar disorder is often difficult, but criteria have been developed that help in accomplishing that task. The DSM diagnostic criteria were originally mainly child oriented, but new assessment methods have been developed that are more appropriate for adults. This identification of the disorder in adults has been accompanied by major developments in the neurobiology and genetics of the disorder, and several candidate genes have been designated. Therefore, what is new about ADHD is not only the discovery of its extension into adults but its conceptualization as a neurobiological disorder associated with specific cognitive characteristics, neurochemical variations, and genetics. This development has been fortunate because it was found that adults with ADHD often respond as well as children to psychostimulant treatment that might not have been considered if an ADHD diagnosis was not made.

Leslie Griebling and collaborators (Chapter 3) assert from the beginning that autism and autism spectrum disorders are neurodevelopmental disorders, and proceed to review what is known about their neurobiology. The history of autism before the 20th century is unclear, and mention is made of only a small number of cases that in retrospect might have had autism: the classic case of the "wild boy of Aveyron," reported in 1798 by Jean Itard, a French physician; the case of Hugh Blair, who demonstrated severe deficits in social relations and mental retardation, appearing in print in 1747 for a decision on his mental capacity; and a case reported by Martin Luther's notetaker of a 12-year-old boy who may have had severe autism. However, there is no documentation in psychiatric texts written before the 20th century of the clinical syndrome of autism. We are therefore left with an unanswered question as to whether autism existed from antiquity or evolved as a separate entity in the early 20th century. However, it is clearer that there has been a still changing reconceptualization of the disorder since Kanner's original work.

The intensive neurobiological work in autism is reviewed by Griebling and her collaborators in the areas of brain structure, neuropathology, head circumference, imaging (including structural and functional MRI), magnetic resonance spectroscopy (MRS), infant research, genetics, longitudinal research, neuropsychology, and clinical neurology. There are findings of interest in all of these areas, supporting the view that autism is a neurobiological disorder. Developmental and longitudinal studies address the crucial issue of how the brain changes with age in autism and how these changes are associated with the progression of the disorder. The introduction of neuropsychological research to the field of autism has shown how cognitive impairment can contribute to the dysfunctions associated with the disorder. Recently developed techniques, notably functional MRI, are showing how the brain in autism processes information differently from normally developing individuals.

The chapter by James Becker and collaborators (Chapter 5) contributes to our understanding of the dementia disorders of the elderly. It is pointed out that Alzheimer's disease is the most common form of senile dementia, followed by cerebrovascular disease, but there is also a relatively less frequently occurring disorder characterized by fluctuating cognition, hallucinations, and extrapyramidal signs occurring early in the course of the illness. There is a significant impairment of attentional processes, also seen early in the course of the illness. It is called dementia with Lewy

that were called Lewy bodies because their existence was first reported by Dr. Lewy (originally seen in the substantia nigra of patients with Parkinson's disease). Diagnostic efforts are now made to separate this disorder from Alzheimer's disease. DLB is probably not a new illness, but what is new is its identification as a separate disorder from Alzheimer's disease. There are complexities involved because as the disorder progresses it increasingly resembles Alzheimer's disease. There are also complexities associated with the relationship with Parkinson's disease when dementia is present.

As in the case of autism, the description of a new or reconceptualized disease is not only a matter of delineating a new clinical syndrome but may also involve extensive knowledge of the characteristics and etiology of the disorder based upon extensive research with new technologies and methods. As a notable example, the new neuroimaging techniques have substantially increased our understanding of the pathology of numerous neurobehavioral disorders. This process has been particularly productive in the area of the dementias, in which great strides have been made in recent years to identify pathological processes and the role of particular brain structures and functions. As Becker and colleagues indicate, autopsy studies have identified neurochemical differences between Alzheimer's disease and DLB. Structural imaging studies have found that hippocampal volume is greater in DLB than in Alzheimer's disease. Neurobiological findings of this type support the construct validity of different disorders, and help to justify separating them as different syndromes. Such separation is often useful in planning, management, and treatment. While the disorders are probably not new, distinctions within a previously considered single disorder are a new scientific development.

Several actual new disorders appear to have been produced by toxicity, while others that have existed for some time are now understood as being associated with toxins long present in the environment. These occurrences are covered in Chapter 9 by Shemansky and Goldstein under the heading of behavioral toxicological disorders. These illnesses are produced by exposure, including exposure in unborn infants, to a variety of toxins. They use the examples of depleted uranium, methylmercury, and sick building syndrome to illustrate how toxins were suspected and sometimes definitively found to produce neurobehavioral disorders. In some cases, such as depleted uranium exposure, following intensive research the neuropsychological consequences of exposure were not found to be extensive. The opposite was true for methylmercury where exposure, particular in human embryos, was clearly associated with developmental cognitive abnormalities. Sick building syndrome was found to be a complex disorder that was clarified by a distinction between it and what was called building-related illness. In building-related illness there is a known pathogen existing in the involved buildings. The classic example is legionnaire's disease, in which the specific organism responsible for the illness was identified. Sick building syndrome has been associated with the recently emerged field of multiple chemical sensitivity (MCS), involving the sensitivities of some individuals to substances in particular environments that produce multiple deficits, often involving unpleasant reactions to odors. Much research has been devoted to separating the emotional from the toxicological aspects of this disorder. MCS may in fact be a new syndrome since we know of no report of it prior to recent times. Legionnaire's disease also appears

Study of the behavioral toxicological disorders has been particularly relevant to public health concerns. It has led to the implementation or at least the recommendation of adopting preventive procedures. Some examples include discouraging women from eating fish with high methylmercury content, especially during pregnancy, checking for the safety of materials used in the construction of buildings, inspecting heating and ventilation facilities for organisms such as the legionella virus, and disposing of toxic substances such as mercury in water. Many of these disorders are eminently preventable through health education and environmental management.

One could question the characterization of PTSD as a neurobehavioral disorder since it is a stress-related condition associated with experiencing a serious traumatic event. Chapter 7 by Julie Alvarez and colleagues reviews this matter, elaborating on the point that numerous lines of investigation, including neurochemical studies, and structural and functional imaging procedures, electrophysiological studies, and cognitive assessment, suggest that the characterization is appropriate. PTSD as a diagnosis did not appear until 1980 but, as these authors point out, it has historical antecedents going back at least to the 19th century. As they report, Kraepelin recognized stress reactions to traumatic events such as serious accidents and fires. Also, literature going back to the 17th century makes reference to "terrors of the great fire" associated with the Great Fire of London. As in the case of other disorders, we cannot be certain that these individuals had PTSD as currently defined, but there is certainly no question that people apparently have experienced stress reactions related to trauma. What is new in the 20th century is information concerning the neurobiological correlates of these disorders. Apparently, these correlates may be divided into those that produce predispositions associated with acquisition of the disorder and those that are consequences of the traumatic experience.

Can a historic event produce a new illness? Gerald Goldstein deals with this question in Chapter 6 on deployment syndromes. Soldiers deployed to foreign countries often returned ill, however the illness was often not a readily diagnosable disease but a mysterious symptom complex of often undiagnosable conditions. In the case of the Gulf War that took place during 1990 and 1991 in Iraq and Kuwait, many veteran soldiers returned with this symptom complex and, although it had numerous manifestations, its uniqueness led to its characterization as "Gulf War" syndrome. The Gulf area was clearly a hostile environment to these veterans, including the presence of organisms to which they lacked resistance, oil clouds produced by burning oil fields, and possibly weaponized toxins, including depleted uranium aerosols, organophosphates, and possibly poison gases. Stress levels were high and some veterans returned home with PTSD or PTSD-like conditions. Upon return, evaluations indicated that a percentage of these veterans, excluding those who sustained traumatic brain injury, had cognitive and other neurological deficits.

The extensive research done suggests that some aspects of Gulf War syndrome do not reflect a new illness but a combination of illnesses, some rarely acquired by Americans. Expertise in tropical medicine was required to identify some of the infectious diseases acquired by American and other non-indigenous people in Iraq and Kuwait. What is new is primarily reflected in the work of the Haley group that identified an apparently verified high risk of developing amyotrophic lateral sclerosis

acquiring this neurological illness associated with toxic exposure have not been reported in the past. Thus, an aspect of newness is the acquisition of a known illness under conditions not associated with each other in the past. The neurobehavioral consequences of such matters as exposure to oil clouds and possible exposure to unidentified poison gases are still under active investigation. In general, it would appear that events, notably wars that involve the movement of individuals to strange and often hostile environments, can produce not only well understood illnesses but also new syndromes and risk factors that people would not acquire had they not been deployed to these new environments.

Chapter 2 by Natalie Barre and colleagues deals with the specific risk factor of preterm birth. The important point is made that while poor health outcomes associated with preterm birth or low birth weight are not new, the number of children with poor behavioral and medical outcomes may have actually increased in recent years because of advances in healthcare that have increased the survival rates of such individuals. Thus mortality has decreased but morbidity has not. Behaviorally these individuals may have numerous cognitive deficits involving the major domains of function that may persist or may be outgrown. These individuals are at relatively high risk for acquiring ADHD and at increased risk for autism and other psychiatric disorders. As in the case of prenatal exposure to toxins, preterm birth consequences do not produce new disorders, but their study has made us aware of a variety of neurobehavioral disorders that are acquired on a developmental basis, often produced by an interaction between medical complications and environmental factors such as maternal health and socio-economic status. The understanding of these disorders is greatly enhanced by developmental longitudinal studies because of the complexities of outcome involved. Some disorders may be present from birth and persist throughout life, some may not appear until a critical period is reached, and some may disappear with growth.

John DeLuca and his colleagues (Chapter 11) introduce us to a series of illnesses that clearly became diagnosed only during the latter half of the 20th century: fibromyalgia, chronic fatigue syndrome, multiple chemical sensitivity (MCS), irritable bowel syndrome, and mitral valve prolapse. Earlier, all of these disorders had been described as neurasthenia, and all involve fatigue in some way. In recent years all of these new syndromes have generated substantial bodies of research. They do not have well established causes, and there are no specific diagnostic tests or definitive treatments. They may involve pain, severe fatigue, intestinal distress, heart-related symptoms, and, in the case of MCS, multiple physical and psychiatric symptoms. Fatigue and pain are the major features of these conditions. These disorders have generated substantial scientific controversy, notably MCS. Diagnostic criteria are mainly based upon subjective report and have frequently been revised. These disorders are of neurobehavioral interest because there have been positive neuroimaging findings and indications of impaired information processing.

DeLuca and colleagues indicate that fatigue syndromes have been recognized for more than 200 years and were known as neurasthenia – a condition involving nervous exhaustion, nervousness, and depression – but chronic fatigue syndrome, as we now characterize it, was not recognized before close to the end of the 20th century. The

been divided into various anxiety disorders. Thus chronic fatigue syndrome, fibromyalgia, and other neurasthenic disorders appear to characterize symptoms that have been noted for some time but only recently have become identified as a group of specific disorders, all having neurobehavioral aspects.

Illnesses traditionally viewed as physical conditions have recently become understood as having behavioral implications. In Chapter 10 by Krug and Puente a clear connection is made between a particular class of physical disorders and cognitive function. Respiration provides a blood supply to the brain as well as other organs, and reduction of the blood supply can significantly alter brain function. Furthermore, rate and pattern of respiration may influence sleeping, with serious health consequences for individuals who have sleep apnea or related disorders. The cycle therefore involves a respiratory disturbance associated with sleep that may reduce blood flow to the brain, thereby impairing cognitive function. There are also interactions between sleep disturbance and other disorders, such as traumatic brain injury (TBI), that may exacerbate cognitive impairment. Sleep apnea is not a new disorder, but what is new is the recognition of its possible effect on cognitive function.

As indicated in Chapter 10, there are now numerous publications concerning neurological function in sleep apnea and chronic obstructive pulmonary disease. The evidence is impressive that deficits occur in children and adults, and there is preliminary evidence for specific cell loss in the prefrontal cortex and hippocampus. It is possible that we are working toward the development of a newly defined syndrome based on memory and executive function deficits associated with pathology of these areas. As a general point, future development of neurobehavioral science may involve the discovery in identified illnesses of previously unidentified syndromes elicited by cognitive assessment and advanced neurodiagnostic procedures. Clinically, neuro-psychologists may productively increase their alliances with primary care medicine, taking an interest in patients with general, systemic illnesses as well as neurological and psychiatric disorders.

It has always been recognized that an individual may have more than one illness either historically or at the same time. However, from the point of view of science, it has traditionally been the common wisdom that disease can be best studied in individuals who only have the disorder that is the target of the investigation under study. Indeed, vigorous efforts are frequently made to provide assurance that the patient being studied does not have any illness other than the one being studied. Individuals found to have other illnesses are typically excluded from participation in the research being undertaken. The “clean case” has been the ideal. While this view has its merits, it greatly discourages scientific investigation of individuals who have multiple illnesses. As we now know, this condition is quite frequently more the rule rather than the exception. There are numerous examples. Elderly individuals with well diagnosed Alzheimer’s disease frequently have health conditions, including vascular, respiratory, infectious, or neoplastic disease, that would rule them out of research studies. The otherwise healthy individual with Alzheimer’s disease is not exceptionally common. Bipolar disorder is very frequently accompanied by substance abuse. Individuals with PTSD often have diagnosable depression. The point is not that these individuals should not be excluded from research involving particular disorders, but

conditions that require separate study. The patient with schizophrenia is different from the patient with schizophrenia and alcoholism. Chapter 8 on comorbidity by Goldstein, López, and Puente deals with that issue.

From a clinical standpoint, patients with comorbid disorders often have different treatment and management needs from patients with single disorders. The requirement is heightened for integrated treatment so that, for example, patients with bipolar disorder and alcoholism need to have both matters addressed, ideally within the framework of a coordinated case management program. In clinical neuropsychological assessment, results for patients with schizophrenia alone may be different from those for patients with schizophrenia and a long history of alcoholism. Concerning the theme of this book, there are the beginnings of delineation of new syndromes associated with a number of comorbidities, such that there may evolve a cognitive profile for individuals with TBI and PTSD different from what is seen in each disorder separately. The same may be true for bipolar disorder and alcoholism, dementia and depression, and numerous other comorbidities. Scientific investigation is clearly needed to characterize these commonly occurring comorbidities.

### **Concluding remarks**

As can be seen, the title "Contemporary Neurobehavioral Syndromes" has been interpreted in numerous ways. There are new illnesses that did not exist before the 20th century, most of them related to recently developed toxins and possibly newly evolved microorganisms. Other illnesses, notably autism spectrum disorders, may or may not have existed before the 20th century but clearly have been reconceptualized in recent years. Illnesses such as stroke have been known since antiquity, but have been repeatedly reconceptualized. Some new syndromes have appeared apparently as a matter of circumstance when particular individuals were placed in a particular environment. PTSD is an example, but the so-called deployment syndromes are clearer cases in which people sent to a strange environment returned with a complex of difficult-to-diagnose illnesses in addition to the acquisition of risk factors for illnesses they may or may not acquire. Increased risk of getting ALS associated with being in the Persian Gulf region during the Gulf War is a good example of that problem.

The identification of neurobehavioral difficulties associated with risk factors is another recently undertaken area of investigation. The illustrations used here are methylmercury exposure and preterm birth. What is new here is the study of disorders that are not acquired in the environment postnatally but that have precursors existing before birth and also have developmental implications. There are also new concepts about the developmental course of some disorders. ADHD was originally thought to be a disorder of childhood that is outgrown, but we now know that it may persist into adulthood. In a way, the boundaries have disappeared between child and adult neurobehavioral science and clinical neuropsychology, since there now appear to be several developmental disorders, notably ADHD and the autism spectrum disorders, that begin during childhood but persist through adulthood. The adult with ADHD and possibly the adult with autism or Asperger's disorder present new diagnostic challenges. The disorders are the same, but the clinical

Our understanding of dementias of the elderly has changed in recent years in several respects. The epidemiology has changed, with a shift to relatively higher prevalence of Alzheimer's disease and lower prevalence of cerebrovascular disease. Within the dementias of the elderly we have separated out several specific disorders – in this book we used the example of DLB. These are not new diseases in the sense that they did not exist before the recent past, but they are newly diagnosable diseases because of scientific and technological developments. The capability of diagnosing these disorders has led to more refined behavioral assessments, and both cognitive and psychiatric symptom patterns specific to these disorders may be identified, at least at some point during their course. The presence, for example, of hallucinations or severe attentional dysfunction may be specifically characteristic of DLB.

The neuroathletic disorders are clearly new to clinical neuropsychologists, although they may have been identified in some form in the past. The more elderly members of our profession will probably not recall receiving referrals during the early part of their careers for evaluation of patients with such conditions as fibromyalgia, chronic fatigue syndrome, sick building syndrome, or MCS. Obviously physicians in the past have recognized the signs of fatigue or toxic exposure, and were aware of chronic pain conditions. However, these new terms connote recently discovered or appearing disorders, with specific but generally as yet unknown causes. Some critics of "medical" explanations of these disorders have ascribed them to stress or other behavioral causes, and have questioned their construct validities. However, in some cases there was evidence of cognitive impairment apparently unrelated to functional matters, and laboratory evidence of pathology. The truth appears to lie somewhere in-between, as there is some evidence of an association between flu-like onset and chronic fatigue syndrome, and the identification of a "real" sick building syndrome in the case of legionnaire's disease. However, apparently most cases go unexplained.

We would note two general matters that make neurobehavioral syndromes at the present time different from what was the case in the past. Looking at textbooks written about these disorders in the past suggests that the term was restricted to relatively pure brain diseases, with the emphasis on identifying the regions of the brain involved and the interruption of connections among those regions. Most notably, we had extensive descriptions of aphasia syndromes with detailed neuroanatomic identification of the structures and pathways involved in those subtypes. Thus, for example, we had the syndrome of alexia without agraphia or conduction aphasia. While interest in these disorders continues, there has been a broad extension of clinical neurobehavioral science and practice to conditions outside of the brain and to more general aspects of health status. In simple terms, the idea that the brain is a part of the body has been implemented and there is now great interest in neuro-psychological aspects of more general pathological conditions such as cancer or heart disease in patients who do not necessarily have a brain tumor or who sustained a stroke. Clinical neuropsychologists now have formed alliances with primary care physicians, internists, oncologists, and members of other medical specialties. As part of this movement there has been an increasing interest in prevention and developmental disorders, with growing science and clinical practice involving the assess-

occurring around the perinatal period. Indeed, one of the major areas of newness in the neuropsychology of the late 20th century is its increased application to general health matters.

The second point of emphasis concerns the matter of comorbidity. In many clinical settings patients have more than one illness, and as age increases, the chance of having more than one illness increases. The scientific paradigm that has espoused the desirability of investigating one disorder ruling out others remains, but progress has been made allowing for rigorous scientific investigation of comorbid disorders. Several common co-occurring illnesses have been identified and are being studied. These conditions are not necessarily characterized as having specific syndromes, but the two disorders in combination may have differing cognitive profiles from what is demonstrated when only a single disorder is present. Thus, there has been substantial neuropsychological research in comorbid dementia and depression in the elderly, substance use disorders and schizophrenia, and alcoholism and bipolar disorder.

Aside from the matter of clinical utility, the consideration of comorbid disorders may be part of a process presaging a change in our entire concept of syndromes. Syndromes have traditionally been defined as unique combinations of clinical signs, but dimensional approaches to classification have challenged that practice and have encouraged the making of classifications and diagnoses on a quantitative basis using continuous variables. Syndromes then become established on the basis of statistical techniques such as factor and cluster analysis, and various taxonomic methods as developed by Paul Meehl. The statistical technique of latent class analysis is now frequently used to find subtypes that have taxon-like characteristics. In this manner, syndromes are empirically determined and, as an example, bipolar disorder with alcoholism may become a single separate disorder, as established by falling into a separate cluster or taxon. Thus, what would now be viewed as a comorbid condition combining two illnesses may become a single empirically established condition. Thus, where appropriate, the next review of contemporary neurobehavioral syndromes may not have separate chapters on individual disorders such as PTSD, but chapters on various dimensions of psychopathology and perhaps pathology in general, reviewing empirically derived illnesses based on dimensional methods.