Neuropsychological Disorders Across the Lifespan: Overview and Implications

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ABSTRACT

Neuropsychological disorders vary in prevalence, base rates, types of impairments, and functional changes over the course of a person's lifespan, with different immediate and late effects as well as expected outcomes. This article provides an overview of the important issues, concepts, and processes involved in a lifespan approach to understanding and managing neurobehavioral disorders from birth to death. Brief case examples of children and adults with attention-deficit/hyperactivity disorder and traumatic brain injury illustrate the effects and needs of patients with developmental and acquired disorders at different ages and phases in life. It is hoped that practitioners can benefit from using a lifespan perspective whether the focus is on pediatric, adult, or geriatric conditions.
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From the moment of conception, through birth, development, and aging, and to the end of life, there are multiple factors affecting people and they are always changing. The human lifespan sees many influences—good and bad, internal and external—during its development and functioning. Disorders of the nervous system and resulting neurobehavioral conditions are dynamic and can affect people differently at various times of their life. Many people with early-life neurological or psychiatric conditions survive for lengthy periods with the repercussions of their disorder (see Mucci and Torno[1] for the example of childhood cancer); these manifestations and their needs vary and change over time. In addition, people with later-life neurological disorders may have unique early developmental factors or conditions that are comorbid or influence the expression of their later dysfunction. In any case, the manifestations of neurobehavioral difficulties vary with time (due to age and other developmental or physiological mechanisms); therefore, people with neuropsychological disorders have a variety of health care needs that may change over time.

This article provides a brief overview of lifespan developmental issues

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for neuropsychologists, neurologists, psychiatrists, and similar providers, and touches on some of the major concepts underlying our understanding of these issues and ideas to date. Two major neuropsychological disorders, one typically developmental in nature and one acquired, are used to illustrate some of the differences seen across the lifespan based on age, developmental status, and severity of each disorder.

A LIFESPAN PERSPECTIVE

All humans have individual and dynamic life histories. Development of biological systems, cognitive and behavioral functioning, and personal characteristics occurs throughout a person's lifespan, and all people are all subject to environmental and social influences.[2-4] In health care, pediatric practitioners focus on children, adult practitioners focus on adults, and geriatric practitioners focus on the elderly, which is a system that usually works well. However, when dealing with people with brain dysfunction and related conditions, it is usually best to have a more encompassing developmental perspective that is not cross-sectional but longitudinal in nature. Such a model assists practitioners in their ability to predict expected outcomes of either developmental or acquired disorders, and also helps practitioners manage persisting developmental issues sometimes seen in older adults or better understand the comorbid difficulties they present.

Major advances in the understanding and treatment of medical and neurological disorders have contributed to improved survival and reduced morbidity compared to the past. As a consequence, people with conditions whose prognosis was once poor now face a range of potential late-life neuropsychological effects. Some of the major lifespan issues for researchers and practitioners include how to specify prognosis of either static or changing neurological disorders;[5] the idea that brain dysfunction is generally a chronic disorder; consideration of maturational factors, including "growing into" or "out of" deficits (called "heterology" by Goldman[6]); the increased or cumulative risk for dementia or other disorders later in life with chronic or repetitive conditions; the fact that cerebral/neural plasticity varies by age and across the lifespan;[7-9] and how early-life dysfunction is often a precursor for later health problems (**Table 1**).

Examples of some of the neurobehavioral disorders in which a lifespan or chronic disease perspective has been shown to be useful include multiple sclerosis,[10] attention-deficit/hyperactivity disorder (ADHD), traumatic brain injury (TBI), chronic kidney disease, cancer, and liver disease. There are clearly different trajectories and perturbations of biology and behavior for each of these disorders. Lifespan development can take many forms,[11] including both adaptive and maladaptive continuous development, discontinuous development, accumulated lesions, maladaptive development emerging in aging, and parallel childhood and aging-based factors. Developmental differences in clinical presentation (phenotypic variability) can result in age-related differences in diagnosis and instability in subtyping of disorders.[12-13] Neuropsychological heterogeneity is also seen in a number of neurobehavioral disorders. Pediatric disorders are generally different than adult disorders, which are different than older adult disorders, although much overlap and comorbidity is present.

As shown in **Table 1**, there are many important developmental concepts and processes that underlie a lifespan perspective. Multiple cerebral systems change dramatically during both childhood and adult development,[14-16] as does the organization of cognitive abilities.[17] Age is only a proxy for the developmental mechanisms, and development is not entirely an age-related or steady process.

TABLE 1.

Lifespan Issues, Concepts, and Processes

- **Issues**
  - Age of onset of a disorder
  - Developmental vs acquired dysfunction
  - Brain dysfunction as a chronic illness/disorder
  - Brain-related changes in disorders during development and aging (all ages)
  - How to specify prognosis?
  - Effects of ongoing neurocognitive limitations, cerebral changes, or repeated injuries
  - Early life dysfunction as a precursor for later health problems
- **Concepts and Processes**
  - Maturation and developmental mechanisms
    - Windows of opportunity
    - Critical periods
  - Neural plasticity
    - Cerebral/neural plasticity varies by age
  - Differential expression of early life deficits (heterology)
  - Base rate differences of neuropsychological disorders across age
  - Trajectories and transitions
  - Cumulative risk at older ages
  - Cognitive and biological/brain reserve

Functional brain development in humans has commonly been characterized as an unfolding of a maturational sequence; however, present models indicate that postnatal functional brain development is a more dynamic process of emerging patterns of interactions between different brain regions.[18,19] To fully appreciate the human organism, it is important to understand the processes underlying and contributing to its maturation, and how related processes continue to shape brain structure and function until death.[20] For example, intellectual ability is generally associated with brain development, organization, integrity, and functional efficiency, and engagement in intellectual

activities across the lifespan contributes to higher brain reserves that buffer normal cognitive decline or pathological brain dysfunction in late life.[21-22] Interestingly, childhood assessments of intelligence have been linked in longitudinal research to aspects of physical health, such as smoking, obesity, alcoholism, hypertension, and lung function, even after controlling for psychosocial and behavioral factors; similarly, childhood intellectual functioning has been associated with survival or longevity at advanced ages (see Smith and Infurna[23] for other precursors of later health).

For young people, maturational and developmental mechanisms during critical periods (ie, frontal lobe maturation occurs throughout adolescence) and "windows of opportunity" for the acquisition of skills are prominent. Neural plasticity is thought to be at its greatest in the young and developing child,[7] but if critical cerebral regions are disturbed, lifelong disabilities may result. Also, similar levels and types of plasticity may not be available in later years.

For older people, long-term outcomes of both childhood and adult-onset, brain-based conditions may be affected by other health risk factors, and thus there is the potential for cumulative risk. The interrelated notions of cognitive (brain, cerebral) and biological reserve have been applied as mechanisms indicating that people have thresholds for expression of deficits and that, if enough positive historical and innate ability factors are present, a person can be protected from serious deleterious effects of a disorder compared to people who have less protective abilities.[22]

Persisting disorders change form and have varied needs over the course of a person's life. Important transitional phases when growing up with a chronic brain condition include moving from childhood into adolescence, from adolescence into early adulthood, and from working adulthood into retirement. In people with these conditions, particular attention needs to be paid to the changing patterns and requirements for health care in these transitions.[24,25] Outcome and recovery paths of neurobehavioral disorders are often difficult to predict; therefore, further development of predictive outcome and chronic care models for neurological disorders is sorely needed.[24,26]

THE LIFE COURSE OF NEUROBEHAVIORAL DISORDERS

This section briefly discusses two major neurobehavioral disorders that are examples of developmental and acquired conditions. A lifespan neuropsychological perspective is used in discussing these two categories of disorders, using brief, descriptive case examples. This overview does not include progressive neurological conditions, although consideration of lifespan factors in these types of disorders is still relevant.

Broadly and simplistically speaking, there are two primary sources or etiologies of pathology for neurobehavioral disorders: (1) neurodevelopmental abnormalities and (2) acquired disorders or changes to an otherwise functioning organism. Neurodevelopmental disorders (or neurobehavioral disorders related to developmental causation) include such etiologies as chromosomal abnormalities (eg, Down, Turner, Prader-Willi, Huntington, or fragile X syndromes), complex genetic and congenital syndromes (autism, dyslexia,[27] ADHD,[28] or specific language impairments), and structural abnormalities of the nervous system (congenital hydrocephalus, cerebral palsy, or cardiac malformations).[29] Later-life effects of all these developmental diseases have been well articulated.[24] Later-life but "inborn" developmental abnormalities may include such conditions as Alzheimer's or Parkinson's diseases, assuming that an ultimate causative genetic or pathophysiological factor can be confirmed in these conditions. In that sense, some progressive neurological disorders occurring with aging can also be considered both developmental and acquired disorders. More traditional acquired disorders include traumatic conditions such as injuries from motor vehicle accidents or falls, cerebrovascular accidents or strokes, development of chronic medical conditions that affect the brain such as kidney, liver, or cardiac disease, brain infections, tumors, or anoxia.[30]

Attention-Deficit/Hyperactivity Disorder

Viewed from a lifespan developmental perspective, ADHD is a highly prevalent, heterogeneous, and lasting neurodevelopmental disorder that results in considerable functional impairment.[31] Historically, ADHD has been conceptualized as a disorder of childhood or early adolescence, typically beginning during the preschool years and initially diagnosed in childhood or soon thereafter.[32-34] The combined presentation of ADHD includes problems with sustained attention, behavioral inhibition, motor restlessness, and high activity levels, and includes temperamental issues such as negative emotionality and elevated novelty seeking; whereas the inattentive presentation of ADHD involves poor focus and poor planning, as well as inattention in sustained situations. A variety of different presentations and courses are possible, with motor restlessness being an early symptom in a toddler, inattentive and overactive characteristics present and identifiable during school age, and potentially worsening self-regulatory problems throughout education and into adulthood. Although ADHD is typically relatively stable in severity through development, some people have a worsened course with antisocial and other comorbid issues. Patients are often diagnosed with the inattentive presentation of ADHD later in adolescence or early adulthood when

demands for greater focus and academic coursework are increased. A substantial proportion of children and adolescents remain relatively affected into adulthood.[35] In addition, diagnosis of ADHD in adulthood also occurs, potentially due to more overt manifestations of symptoms when greater demands are present in social, collegiate, or occupational contexts, or perhaps due to a lack of diagnosis earlier in life.

There are a number of functional consequences of ADHD throughout the lifespan.[13] Neuropsychological functioning varies across age in people with ADHD, although impaired executive functioning and issues with the brain's reward system are prominent.[36] There is a real lack of longitudinal studies that track the specific neurocognitive changes in ADHD through all stages of life. Usually, ADHD is associated with reduced school performance and academic attainment, as well as elevated issues with interpersonal conflicts and negative social interactions. Children with ADHD, particularly those with impulsive-hyperactive characteristics, are more likely than their peers without ADHD to develop conduct disorder in adolescence, as well as antisocial personality disorders with frequent comorbid substance use disorder.[37] Adults with persisting ADHD show less schooling, poorer occupational performance, higher probability of unemployment, more frequent traffic accidents and violations as drivers (especially when impulsivity is prominent), and disrupted peer relationships.[33,35] Throughout the lifespan, mortality is increased in all people with ADHD.[38,39]

Turgay et al.[40] (as part of the ADHD Transition Phase Model Working Group) have presented a life transition model of ADHD and discussed its application. These authors emphasize that ADHD is a chronic illness and that ADHD persists from childhood into later life in at least two-thirds of patients. In addition, optimal management requires an understanding of the symptoms and impairments within developmental phases and with changing environmental demands. The ADHD Life Transition Model, proposed as a guiding framework by these authors, is aimed at raising awareness of phase-specific presentations (eg, childhood into adolescence, and adolescence into young adulthood) of ADHD and providing a basis for developing prospective approaches to the issues at each transition phase. For example, the authors describe potential resource-demand imbalances across the lifespan of people with ADHD and emphasize that when functional demands tax available resources, both internal (eg, working memory, sustaining focus) and external (supportive people and objects/interventions), then functional impairments will continue to be evident. In all phases, timely diagnosis, recognition and treatment of symptoms, and ongoing external supports are critical, with particular emphasis on the need for formal transition planning and psychotherapeutic assistance.

Illustrative case 1. The patient is a 16-year-old diagnosed with ADHD-inattentive presentation at age 10 years based on limited cognitive testing and questionnaires completed by parents and teachers, as well as by self-report. She was initially diagnosed by a child psychiatrist with the inattentive type of ADHD due to the presence of many of the criterion symptoms listed in the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (*DSM-IV*),[41] including not following through on homework, difficulty sustaining attention in and out of school, problems with organizational skills on projects and other assignments, and easy distractibility in class. The patient was otherwise an intelligent (IQ = 108) and inquisitive child with no significant problems in interpersonal relationships or affect. In fact, she was able to maintain good grades in school with the support of a 504 Accommodation plan initiated in 6th grade, which provided extra time for test and assignment completion, as well as tutoring after school to assist with organizing and planning activities. Her parents, who were college-educated professionals, did not want her to use medication if at all possible.

The patient was given a brief neuropsychological evaluation again at age 16 years (at the beginning of 11th grade) to assist in documenting her functioning and needs, in preparation for college and post-high school planning. She was found to show strong intellectual skills with no major cognitive impairments except for mild inefficiency in initial encoding and learning of information (retention and recall was fully average), inattentiveness, and mild variability on a computerized measure of sustained attention, and clinically significant but mild difficulties with planning and organizational skills as noted on self, parent, and teacher ratings. No clinically significant psychoemotional issues were noted, and her family and social situations were stable and supportive. It was felt that the patient was being supported adequately with use of the 504 Accommodation plan in her current educational program, and that continued use of those interventions and strategies should occur in her senior year of high school and thereafter. She was recommended to contact her planned college's student disability office with regard to continuing the accommodations, and that she should consider either re-evaluation or additional support services toward the end of her college career, when she begins pursuing employment.

Illustrative case 2. The patient is a 37-year-old who was diagnosed with ADHD-combined type as an adult at another facility, so complete diagnostic details are not known. However, he reported a complex past history that included probable learning disabilities as a child (he stopped school initially in

the 11th grade), substance abuse (approximately 10 years of regular use of cocaine and methamphetamine before success in a drug treatment program) during adolescence and young adulthood, and drug-related legal offenses, but greater stability and improved functioning in his life beginning in his late 20s when he remained drug free, got married, and worked in manual labor jobs. The patient received little formal intervention, although his ADHD diagnosis approximately 10 years prior to presentation did lead to subsequent psychiatric medication management with an antidepressant, which has been effective in helping him remain stable and cope with life demands as an adult.

The patient completed a brief neuropsychological evaluation to help clarify differential diagnosis, as he was contemplating a return to school to complete a general educational development degree and perhaps get additional job training. He was found to demonstrate low-average intellectual skills (IQ = 87) with specific academic weaknesses in spelling and reading (approximately third to fourth grade levels) and with quite good memory and visuospatial skills, but with relative weaknesses in complex and sustained attention (impulsivity and variability prominent). He also had rating scale results indicating moderate but clinically significant levels of inattention, impulsivity, and executive (working memory, organizational skills) problems, and mild anxiety and depression. He was felt to meet criteria for ADHD-combined type (which was likely developmental in nature), and also was felt to show evidence for a specific language-based learning disability, but no other overt neurocognitive dysfunction. He was recommended to consider remedial educational assistance for preparation for his GED, and tutoring for any further training. It was noted that he was fairly functional in his living situation, but that his ADHD likely was affecting his job performance, or at least his stability in jobs once obtained, so ongoing psychiatric care for the ADHD and social/vocational supports for his work situation were recommended.

Traumatic Brain Injury

TBI is one of the most common causes of acquired disability throughout the lifespan.[42] Traumatic injuries to the head and brain are a common problem and affect a significant proportion of the population every year. Approximately 1.5 million cases of TBI occur every year in the United States, primarily due to motor vehicle crashes and falls, and most commonly affect people between ages 15 and 24 years and those older than age 64 years.[43] Sports-related mild TBIs (ie, concussions) and blast-related TBIs in military conflicts are currently among the most studied injuries in health care. TBI is a chronic disorder that can happen to anyone. TBI varies in severity and spontaneous recovery is generally expected, particularly in mild injuries, although the extent and pattern of recovery depends on the severity and type and localization of injury sustained.[44] The consequences of TBI are well established, with findings indicating significant potential physical, cognitive, psychological, educational, and vocational difficulties, even several decades after the injury. The most common neurobehavioral problems for people with TBI include impairments of attention, speed of information processing, learning and memory, self-regulation, and psychoemotional functioning, including self-awareness.[45]

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TBI is a lifespan risk factor, whether the injury occurred at younger or older ages. Most survivors of significant pediatric TBI show ongoing, long-term cognitive impairments, although they tend to manage adequately through their school years with social supports and special educational assistance. Social maladjustment and vocational problems, as well as persisting physical sequelae, are often seen in moderate and severe injuries (see Kirkwood et al.[46] for a review). Transitions between grades or schools and from adolescence to adulthood tend to be particularly important phases for support and intervention in cases of pediatric TBI. Cumulative risk from recurrent mild TBIs when young may diminish cognitive resources when older, with less compensation for deficits available. Limited plasticity with aging is noted and cognitive reserve may be reduced.[7,21] When severe TBI affects children, some sequelae may not become fully manifest until many years after the injury; there is also concern about the possible acceleration of onset of degenerative diseases in older adults who sustained moderate or severe TBI decades earlier. Moderating variables for outcome can include socioeconomic adversity, family dynamics, and possibly genetics.[47]

Illustrative case 3. This patient was involved in a significant motor vehicle crash at age 6 years, in which she was a restrained back seat passenger in a car struck by a truck on her side of the vehicle. The patient suffered a complicated mild TBI that included brief loss of consciousness and impact to the left side of her head resulting in a left temporal depressed skull fracture. She underwent surgical elevation of the fracture while hospitalized and also underwent brief neuropsychological and speech-

language pathology evaluation as an inpatient. The patient showed a moderate mixed receptive-expressive aphasia initially, which improved quite rapidly, so that by the time of the evaluations (approximately 6-7 days after injury) she was able to communicate at a functional level but clearly still showed problems with verbal expression and fluency. In the brief inpatient neuropsychological evaluation, she showed mild impairment in verbal learning and memory along with a slight motor asymmetry in favor of better functioning on her nondominant (left) hand, all of which was consistent with the localization and severity of her cerebral injury. The patient demonstrated minimal right-sided motor weakness but responded well to physical therapy and showed rapid and progressive improvement in her ambulation and motor skills. A computed tomography (CT) scan of her head close to her time of discharge showed minimal parenchymal damage in the left temporo-parietal region. She was ultimately discharged home, with outpatient speech-language pathology therapy services for several months and several additional physical therapy outpatient visits. In all, the patient demonstrated a good physical and motor recovery over a short period of time, and her communication skills rapidly improved.

The patient was then seen for repeat neuropsychological evaluation approximately 10 months later, toward the end of her year in second grade, when she was age 7 years. She was reported to have shown minimal difficulties in academic re-entry and school performance, and she had been able to continue good academic progress from first into second grade. She showed no obvious problems functioning in everyday life activities, her family circumstances had not changed, and she demonstrated good interpersonal capabilities with family and friends, both in school and away from school. On the repeat neuropsychological evaluation, the patient demonstrated continued improvement in language and other cognitive skills, such that the only measurable impairment present at that time in her recovery was a mild expressive fluency and word retrieval difficulty. It was felt that she would continue to demonstrate slight spontaneous recovery in the future, and she would likely not show obvious lasting functional consequences, except in rapid communication situations and a "measurable" fluency deficit that could be detected in any future objective language evaluations. She was considered to have made an excellent recovery from a complicated mild TBI, and her strong family support, solid innate intellectual and other cognitive potential, and neurosurgical and rehabilitative interventions were felt to be factors associated with her improvement and generally good prognosis.

Illustrative case 4. The patient, a 62-year-old, fell off a horse and was kicked in the head and face by the horse, causing her to lose consciousness for an unknown but presumably brief period of time. She was taken to a local hospital where a CT scan showed right maxillary and facial fractures, as well as a presumed mild complicated TBI with right frontal contusions. She underwent surgical repair of the fractures, which required 1 week of hospitalization. She demonstrated good physical recovery from the fractures. The patient did have a medical history that included hypertension, diabetes, and previous mild heart attack, all of which were being followed medically and treated with medications and diet. The patient worked as a legal secretary at a law firm, but she remained away from work through the entire time she received formal neurocognitive evaluation (approximately 3 months after injury). During this time, she was noted to have had increased and problematic interactions with her husband, who described her as irritable, impulsive, and unable to multitask, leading to significant concerns about her ability to be on her own and to perform cooking activities safely (something she previously enjoyed and a skill in which she was proficient).

In the neuropsychological evaluation, the patient reported only minimal current difficulties and good recovery physically and mentally. Self- and family inventory reports showed significant discrepancy in reporting of disinhibition and executive characteristics, with the patient denying any changes over time while her husband endorsed high levels of problems with inhibitory and organizational skills. Her test findings indicated mild to moderate objective executive dysfunction, including problems with working memory, new learning efficiency, planning skills, and impulsivity, as well as perseverative tendencies. Other cognitive impairments in free recall, nonverbal problem solving, and complex visual attention were also described. The results were felt to be consistent with the persisting effects of her right frontal lobe injury with prominent executive and memory impairment, as well as indications of moderate changes in her personality, probably associated with orbitofrontal damage. Recommendations included probable need for disability determination, as it was thought that she could not return to her previous employment due to the performance demands (eg, need for multitasking, appropriate interactions with attorneys and others) required in that setting. She was recommended for formal brain injury rehabilitation in a local outpatient program, which included work on not only cognitive capabilities but also her insight/awareness and psychoemotional adjustment to the persisting changes (which she downplayed).

Her prognosis for further functional recovery was guarded, due to not only her deficits and reduced awareness, but

also to her history of prior medical issues that could affect cerebrovascular functioning and limit her overall cognitive reserve.

IMPLICATIONS

It must be remembered that all people with neuropsychological and neuropsychiatric disorders have a history with a past, a present, and a future. Considering the lifespan issues discussed in this article can help practitioners be sensitive to the important transitions and needs of people as they age. Human development is a lifelong process and there are factors in each phase of life that are the foundations or precursors for subsequent development and outcomes later in life. The relative importance of the factors in each life phase, the mechanisms underlying their influence, and the potential to modify or intervene in the resulting pathways and trajectories are more difficult to specify but necessary for full understanding.

Integrated biopsychosocial models incorporating a lifespan approach are needed to provide sound theoretical guidance for future research and practice. Many models of neuropsychological functioning focus on a restricted age range and do not offer a more complete lifespan perspective. It also needs to be appreciated that "outcome" is a multidimensional construct and that different predictors, moderators, and mediators are likely to be found for various dimensions of development and for the outcome of various disorders.

Most neurobehavioral disorders extend throughout the lifespan; we are only gaining incremental knowledge about how they change and how best to prognosticate. Knowledge of childhood disorders can help adult practitioners understand some characteristics of their adult patients, and knowledge of adult outcomes (and predisposing factors) can help pediatric practitioners understand how to better predict outcomes and expectations from childhood conditions. In general, all practitioners should develop some expertise in understanding the factors and mechanisms that affect maturation, transitions, and developmental change in neurobehavioral functioning for people with brain-based disorders.

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