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Cognition, Aging and Disabilities: Conceptual Issues

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Introduction

Cognitive impairment is the primary determinant of disability in late life (1), and at all ages, cognitive function is the foundation of individuals' capacity to meet the challenges of disabling conditions. In this chapter, we review normative changes in cognition that are observed across the adult life span and consider how specific disabilities may interact with aging processes to increase functional decline in later life. Disabling conditions that directly affect the brain are contrasted with those that do not, using specific exemplars to illustrate these points. We consider that while some cognitive aging processes may impair the capacity of disabled persons to cope with their lives, others may enhance it. The goal of the approach taken here is two-fold: to create a framework for thinking about how cognitive changes, aging, and disability may interact to help explain individual differences in coping, and to promote the inclusion of cognition in a comprehensive approach to assessment and care.

What is cognition?

"Cognition" refers to a broad range of largely invisible activities carried out by the human brain. Perceiving, thinking, knowing, reasoning, remembering, analyzing, planning, paying attention, generating and synthesizing ideas, creating, judging, being aware, having insight – all these, and more, are aspects of cognition. The following is a working definition: cognition includes any and all process by which a person becomes aware of his/her situation, needs, goals, and required actions, and uses this information to implement problem solving strategies for optimal living. Motivation, usually considered a quality of affect rather than of thought, would, by this definition, be an aspect of cognition and we include it as such here.

How does cognition change with age?

Recent critical reviews of cognitive aging distinguish between processes showing gradual declines across the life-span and those that remain stable until advanced age (2). Basic mechanisms common to many cognitive processes, including perceptual and thinking speed, numerical ability, working memory, and encoding and retrieval of new information, appear to

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show small but continuous, more or less linear declines across the entire adult life span from the early 20's through the 80's, though the magnitude and precise trajectory of these normal changes is debated. Most functions that depend on stable knowledge stores and well-practiced tasks remain stable into old age, and some – including 'wisdom', the superior judgment and insight born of life experience and resulting strategic efficiencies – improve with age. When cognitive decline departs from its relatively linear path to follow an accelerated pattern of loss, the influence of disease processes must be suspected and makes distinctions between pathology and normal aging very difficult to disentangle. The pathologies that account for much of the accelerated cognitive decline that may be observed in old people include both systemic diseases with cerebral effects, such as cardiovascular disease and diabetes, and diseases manifested primarily by their cognitive signs and symptoms, such as Alzheimer's disease. Though studies of brain integrity, for example those based on neuroimaging technologies, such as structural and functional MRI, PET and SPECT, and MR spectroscopy, provide additional insight into normal versus pathological aging, it is likely that these distinctions will remain somewhat blurred (3).

Brain aging: the substrate of cognitive change

A concise review of the evidence regarding neural changes associated with brain aging (2) provides a useful working model emphasizing two critical systems subserving cognitive processes. The first component involves changes in the frontostriatal system, broadly associated with executive abilities and adaptation to new environmental inputs and changes in one's physical and mental self, and the second, changes in the medial temporal lobes and the bidirectional relays that link the hippocampus and association cortices. By and large, neurobiological data are generated and interpreted through the one-way glass of a 'deficit' model of aging: progressive decay of neural tissues, based on 'toxic hits' to vulnerable macromolecules, cumulative oxidative stress, diminished bioreparative mechanisms, subtle disease processes, and disuse, produces impairment in cognitive abilities. The deficit model is the basis for investment in brain aging research aimed at identifying preventive and therapeutic interventions that can delay the onset of a particular disease (e.g. Alzheimer's dementia) or mitigate the decline that results. Findings from basic and clinical neurobiology can be most broadly informative if separated, to the extent possible, from specific disease categories, as progress in research has found overlapping molecular mechanisms across a broad spectrum of clinical diagnostic entities. Such findings support a reorientation of research toward locating factors that retard or accelerate brain aging and account for wide variations among individuals in the rate at which brain systems age. The reader is referred to the excellent review cited earlier (2) for a detailed discussion and citation of extensive data supporting a two-component model of brain aging, sketched below. Note that any disease process or injury that affects these age-vulnerable systems is likely to intensify, and be made more disabling as a result of, the age related changes described here.

Frontostriatal systems—The prefrontal cortex is particularly expressive of age related changes, which, like a number of cognitive abilities, shows a linear decline in volume detectable by the 20's (possibly at first the result of extensive synaptic pruning that occurs during the transition from adolescence to early adulthood). Similar volume changes occur in the striatum, to which the prefrontal cortex is linked by a series of parallel pathways that have been associated with cognitive, affective, and motor functions. Not surprisingly, since these pathways use signature neurotransmitters (most prominently, but not limited to, dopamine) as part of their communication systems, neurochemical changes also occur (e.g. reductions in dopamine transmission, affecting frontal activation, movement, and motivation). Volumetric changes in frontostriatal systems have been associated with reduced cognitive flexibility, working memory, suppression of unwanted or irrelevant responses, and strategic encoding of time-

linked episodic memories. All of these are elements of cognition that underpin everyday multitasking, behavioral regulation, and adaptive functioning.

Medial temporal lobes, hippocampus, and associated neocortical systems—To a far smaller extent than the frontostriatal systems, the volume of medial temporal lobe structures tends to decline a little across the lifespan, but there are few cognitive correlates of such changes until later midlife (e.g. age 60) and beyond, when explicit (declarative) memory performance tends to correlate with hippocampal volumes. However, in the healthy aging hippocampus and elsewhere, dendritic branching still occurs and new neural connections form in response to experience (neural plasticity). Functional imaging techniques have shown reductions in hippocampal and corresponding changes in the pattern of prefrontal activation during specific kinds of cognitive tasks in healthy older persons, suggesting altered pathways for at least some information management tasks. The significance of many of the observed changes for everyday function have not been specifically queried, but very likely they relate to the gradual declines and shifts in motivation, overall cognitive and motor activity, and efficiency of learning that have been recognized as part of late life throughout history.

What accounts for the decreased volume of some aging brain structures?—The clearest answer to this question from existing neurobiological research is that brain cells decrease in size (rather than die out) and that the communication highways between regions, the long myelinated white matter tracts, undergo gradual thinning and reduced efficiency. Damage to white matter has been extensively attributed to vascular ischemia associated with reduced small-caliber vessel perfusion and the size of the cerebrovascular bed during aging, as well as to pathological changes caused by vascular occlusive disease, hypertension and other cerebrovascular risk factors, and even a form of vascular disease most often recognized as part of Alzheimer's disease, known as amyloid angiopathy. Amyloid angiopathy is receiving renewed research interest due to the development of neuroimaging techniques capable of identifying its presence and consequences in living patients. Other mechanisms for both white matter and neuronal cell body and axonal damage are also under investigation.

Individual differences, choices, and training matter—Despite good evidence for some decline in many cognitive functions, reductions in brain tissue volumes, and changes in tissue composition that occur with apparently normal aging, there are large individual differences that increase after late midlife, with the mechanisms responsible for these differences remaining largely unaccounted for (4). Among the factors that may account for some individual differences are two that can be potentially modified by choice and are prompting revisions in the deficit model of brain and cognitive aging. The two are aerobic fitness and specific cognitive training. Six months of sustained aerobic fitness training increases the volume of both gray and white matter in older persons, reducing or reversing tissue losses previously thought to be inevitable (5). Is sustaining the level of activity required to bring fitness to the effective level practical for most older adults? Can its brain effects be realized for 'average' older people, and its benefits be maintained over prolonged periods of time? These questions have yet to be explored.

Specialized cognitive training has also been shown, first in uncontrolled studies and more recently in randomized controlled trials, to improve a variety of cognitive processes, including memory, speed, and reasoning and problem solving, among others. "Strategy training", based on identification of weaker abilities to be targeted for training and teaching of explicit strategies for improving performance, describes a variety of training models and successful approaches. Most improvements resulting from training paradigms are modality-specific, showing little or no transfer or generalization to other cognitive abilities; reasoning training, however, has been found to cross modalities more effectively than memory and speed of processing training and to be associated with less decline in instrumental activities of daily living over a prolonged (5

year) period of follow up (6). The reader is referred to a recent comprehensive review of both mental and physical training approaches to sustaining cognitive abilities in ‘normally aging’ individuals (7).

Application of brain aging principles to specific disabilities

Recent discoveries that age-related structural and functional brain changes can be mitigated or reversed by aerobic and cognitive training point to a crucial dilemma for persons aging with a disability. Conditions that directly impair the function of the brain, and/or the large muscle groups needed to enhance fitness and forestall age-related losses, may prevent successful participation in either aerobic conditioning or cognitive training, or both. Many disabling conditions affect both brain and neuromuscular control mechanisms, including multiple sclerosis (MS), cerebral palsy, and many traumatic brain injuries, while others have no recognized cognitive (e.g. post-polio syndrome) or neuromotor (e.g. permanent amnesia in survivors of herpes encephalitis) component. While a full review of the emerging evidence about cognitive and physical training for individuals aging with disabilities is beyond the scope of this chapter, the high prevalence of MS, and the extensive literature on the heterogeneity of both cognitive and motor aspects of the disease, make it a useful exemplar of how aging principles may be applied to a specific condition.

Multiple sclerosis—Impairment in complex attention, processing speed and efficiency, executive functioning, and memory are increasingly appreciated as features of MS that may occur with the first recognized neurological episode, independent of the more familiar motor and neuropsychiatric signs, and in a wide variety of clinical types and symptom arrays that differ from person to person and over time (8). While overt dementia has been considered a rare outcome in MS, deficits consistent with an MS form of ‘mild cognitive impairment’ are not, and evolution in the concept of what constitutes dementia – and a concomitant shift away from using the features of Alzheimer’s disease as the paradigm for all dementias – may prompt increased attention to cognitive impairment as a source of disability in MS in the future. Such a shift has already occurred in thinking about Parkinson’s disease (PD), another neurological condition which, like MS, was initially defined solely by its hallmark motor features. Somewhat later, depression and anxiety disorders came to be recognized as much more common in PD than could be accounted for by psychological factors alone, and depression, anxiety, and neurobehavioral disturbances have now been incorporated into the standardized approach to staging PD and rating the disability it causes; still later, cognitive impairment of some degree was discovered to occur in most patients with PD who live two decades or more with disease, and it too has become part of the standard way of assessing PD as a motor/neuropsychiatric/cognitive syndrome. In MS, impaired processing speed, learning and memory, impulse sorting and suppression, self-appraisal, and executive function (occurring variably in 10–70% of patients depending on clinical form and duration of disease) are common enough to indicate that cognitive dysfunction should be considered a core feature of the MS syndrome. Cognitive impairments are more frequent and chronic among persons classified as having primary or secondary progressive MS than those with relapsing-remitting forms of disease. Secondary progressive MS increases in prevalence with age, as remissions become shorter and less complete. The reasons for this change in course are not fully understood, but likely result both from accumulation of permanent CNS damage over time, age-related diminution in brain repair mechanisms, and overall loss of both brain and body fitness.

Cognitive deficits are associated with functional impairment in everyday life, independent of the effects of depression, fatigue, and motor disability (8). These deficits can impair day to day decision making, motivation, and new learning sufficient to affect self-care in both higher order and basic activities of daily living as well as to impact capacity for gainful employment and promote the transition to permanent disability status. As data accrue and thinking continues to

evolve about cognition and its relationship to functionality, and as the clinical course of MS is modified by newer treatments and those still to be developed, cognitive function will likely come to be incorporated into standard methods for assessing and staging MS disability, as it has in PD.

What cognitive abilities are central to aging well with a disability?

Many cognitive abilities, such as remembering important conversations (auditory and verbal memory) and balancing a checkbook (arithmetic skills), are convenient, time-saving skills that make everyday life work more efficiently. However, many such skills have acceptable substitutes (voice recorders, written notes, calculators), and most cognitive measures are poor predictors of everyday functioning. In a comprehensive review published by a working group of the American Neuropsychiatric Association (9), very few specific cognitive abilities were associated with everyday functional capacity; measures that accounted for the largest amount of variance were tests of general cognitive ability and executive control. Broadly, executive control functions encompass many “general purpose mechanisms for goal-oriented organization and manipulation of information stored in working memory” (2). Executive function encompasses those cognitive activities that relate to making plans, thinking ahead, suppressing irrelevant sensory, cognitive, and emotional intrusions, imagining, evaluating, and comparing possible consequences of alternative actions, managing time and space, changing or correcting behavior in light of its results, organizing and sequencing tasks in service to specific goals, and sustaining the necessary motivation to follow through to their accomplishment. In health care, impaired executive function is most easily appreciated ‘in the breach’ – when a patient unintentionally omits a necessary medication several days a week, resulting in a relapse of a treatable chronic condition, or a young adult in rehabilitation for a traumatic brain injury neglects to practice his problem-solving and impulse management exercises. Patients with impaired executive control functions cope poorly with many other disabilities, and when impairment is not recognized, such patients may be considered ‘bad’, ‘intentionally non-compliant’, ‘passive aggressive’, or just plain frustrating to their families, partners, providers, and even themselves.

Executive function, representing an integrated composite of many related elemental cognitive activities, is most often linked in common clinical parlance and neuroscience research to the frontal lobes – which, as we have seen earlier, are particularly vulnerable to age related changes: across the human lifespan, the frontal lobes are last to finish their development and first to decay. However, the extensive synaptic connections that link various sub regions of the frontal lobes to other cortical and sub cortical structures, imply that brain lesions occurring outside the frontal lobes may have exaggerated impact on frontal functioning as individuals age. This mechanism is recognized in certain stroke syndromes, where damage to one area of the brain causes functional deficits in otherwise normal tissue that is synaptically linked to the region of the stroke (referred to as diaschisis), but is also seen commonly in subcortical vascular ischemic disease of the brain, which affects executive function and cognitive speed to a greater extent than it does formal memory processing. The same can occur in MS and other brain diseases with distributed lesion foci.

Future perspectives: finding opportunities to preserve or improve cognition in aging people with disabilities

Uniform assessments

A key step toward improving the recognition of the cognitive components of disability in aging individuals is a core set of assessment tools that can be applied across a broad range of ages, disorders, and conditions, and supplemented with disease-specific measures when needed. Progress toward that goal is represented by the NIH Toolbox Initiative, to be completed by

2011, which aims to offer “efficient, flexible, and responsive assessment of cognitive functions such as learning, memory, executive function, language/lexical retrieval, visuospatial abilities, attention, and speed of processing” (10) in addition to similarly uniform assessments of emotion and motor and sensory function.

Testing and adapting emerging anti-aging strategies for persons with disabilities

The most promising avenues currently identified for preserving cognitive health in aging are physical and cognitive fitness training. Their goals are to maximize and support the function of healthy brain, and despite some research there is currently no convincing evidence that they can delay or prevent any specific disease that causes cognitive decline. In persons with chronic disabilities, studies showing the potential of cognitive and physical training to improve important dimensions of functionality yield inconsistent results, at least partly because of the variability inherent between persons and conditions. While one study reported better ‘cortical and cognitive plasticity’ in relapsing-remitting MS patients with higher baseline cardiorespiratory fitness (11), other work finds cognitive impairment a limiting factor in the success of exercise-based approaches to rehabilitation (12). A new pilot trial of intensive, computer-assisted cognitive training for relapsing-remitting patients with MS, relatively low levels of disability, and deficits in attention, information processing, and executive function, found significant improvements in all domains, and in depressive symptoms, after three months of training, compared to a usual-care, non-matched control group (13). As the value, limitations, and necessary adaptations of both physical and neuropsychological training approaches are better defined by research in specific disabled populations, the case for incorporating them into standard care will become more compelling.

Pharmacological approaches to enhancing cognition

Alzheimer’s disease has led the way in drug development for cognitive impairments of late life and remains the principal condition for which cognitive enhancing medications have received an FDA indication. The recognized antidementia medications, which are known by their pharmacological actions as inhibitors of acetylcholinesterase or glutamate in the brain, do not affect basic etiological processes and do not have significant disease-modifying effects in Alzheimer’s disease or other disorders. Donepezil, an acetylcholinesterase inhibitor approved for treating all stages of Alzheimer’s disease, has shown some promise for improving memory processing and subjective cognition in MS, in a small randomized placebo-controlled trial of moderate quality (14). Other pharmacological agents, generally classed as stimulants and alerting, rather than cognitive enhancing, drugs, can have cognitive benefits in persons with suitable conditions. Such conditions span a broad range of diagnoses, including attention deficit disorder in children and adults, attention deficits in MS, and disorders of wakefulness such as narcolepsy and sleep apnea). Drugs in the stimulant/alerting class generally act on dopaminergic and noradrenergic brain systems, both of which provide strong neurochemical inputs to the frontal lobes. No fundamentally new molecular entities having cognitive impairment as their principal target have been approved for use in over six years, despite large worldwide investment in drug discovery and development and a willing and eager aging population. Such facts encourage (and demand) enduring respect for the many secrets still held by the aging brain and the dysfunctions that come with living long.

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