1. Clinical Overview

Primary care physicians are often asked to recommend behavioral changes that might improve an older person’s chance for successful aging. The primary care physician can use insights from clinical, basic science, and pathological research to recommend intellectual, physical, and psychosocial stimulation as part of their cognitive wellness program for middle aged and older patients. The definition of successful aging can be divided into three domains including physical, social, and psychocognitive (1). In one study, 20% of older individuals reported poor physical functioning, 40% reported problems with social function, and 36% were identified as having psychiatric or severe cognitive disability. Only 13% achieved optimal scores for high overall functioning and 10% met all criteria for successful aging. Although elders experience many types of physical, mental, and social stressors, the majority continue to endorse a sense of wellbeing. This sense of accomplishment can become a major support for the successful aging of an older person (1).

2. Defining Intellectual Reserve in Humans

The interplay between lifetime intellectual achievement and late life cognitive function has been scrutinized by numerous scientists. Recently, the concept of “brain reserve” has achieved greater validity in the scientific community (2), (3). Brain reserve implies that a patient has sufficient functional capacity or redundancy to compensate for brain injury of subclinical functional loss. Some scientist would argue that there are three types of human brain reserve: 1) the number of neurons and synapses or the sophistication of synaptic connectivity, as well as the resilience of neurotransmitters or trophic factors, 2) the number of backup cognitive strategies to solve specific types of neuropsychological tasks presented to elders, and 3) the quantity or speed of brain tissue loss with advancing age.

Several studies support the role of early life intellectual achievement on later life intellectual function (4), (5), (6), (7), (8). Early and mid life intellectual achievement may predict enhanced metabolic activity on brain imaging in later life (9), (10). The Nun Study was first to suggest that individuals with greater,
early life intellectual achievement experienced a diminished risk for developing dementia, even when the brain demonstrated significant Alzheimer-type pathology (11), (12). Subsequent studies have examined the role of early life intellectual function and late life cognitive function. Childhood mental ability appears related to the risk of late-onset dementia (13), as well as enhanced late-life function (14). Other studies suggest that the rate of cognitive decline in later life may be dose-dependent upon the intensity of academic achievement in early life (15). Other variables related to late life cognitive function include the number of siblings and rural location of childhood that predicts socioeconomic strata (16). A similar phenomenon is seen in other types of diseases or conditions that may produce intellectual decline, including cognitive loss following coronary artery bypass surgery and risk for HIV-related dementia (17). About 10% of postmortem brains from intellectually normal individuals will demonstrate Alzheimer pathology at death. Individuals with higher academic achievements are less likely to demonstrate cognitive decline, even with Alzheimer’s pathology in the brain (39).

3. Animal Models for Intellectual Reserve

Animal models of early life intellectual achievement are difficult to interpret. Environmental or physical enrichment paradigms involve more complex activities than simple learning. Rodent environmental enhancement includes intellectual stimulation as well as opportunities for exercise. Animal models of environmental enrichment suggest enhanced neural production, glial proliferation, trophic factor production and enhancement of neurotransmitters (18). The brains of animals raised in enhanced environments demonstrate enhanced production of neurons in the hippocampus and accelerated production of dendrites and synapses in both the hippocampus and the occipital lobe. The production of glia and blood vessels also appear to be enhanced in these animal models. Environmental enrichment also appears to increase the levels of certain trophic factors such as nerve growth factors or brain derived neurotrophic factors as well as specific neurotransmitters such as serotonin or acetylcholine. Transgenic models of amyloid-producing mice appear to exhibit diminished quantities of brain amyloid and enhanced cognitive function when those animals are raised in enhanced environments.

4. Leisure Activities as Promoters of Cognitive Reserve in Older Persons

A surrogate activity for intellectual stimulation in elders is leisure activities. Passive intellectual activities, such as watching television, demonstrate no significant benefit on cognitive loss. Other stimulating late-life activities, such as writing letters or social interactions, appear to diminish the risk for cognitive decline in elders. One activity during any particular day of the week reduces this risk by 7%. A 63% diminished risk of cognitive decline is detected in those elders in the top third of late life intellectual activity (19). Numerous other studies
suggest a similar positive impact of leisure activities on cognitive abilities inferring that other types of intellectual or emotional stimulation may preserve intellect with aging (19), (20), (21), (22). For instance, loneliness will almost double the risk of developing dementia in older persons (40).

Rodent models of environmental enrichment appear to benefit rodents subjected to a variety of other brain disorders to include stroke, trauma, and epilepsy. The mechanisms of environmental enhancement for rodent models of brain damage are similar to those seen with rodent aging brain, i.e., improving neural plasticity or neurogenasis (23), (24).

5. Physical Exercise as a Promoter of Cognitive Reserve in Older Persons

Long-term physical exercise appears to exert a protective effect against clinical symptoms of dementia in humans (41). Older individuals who exercise on a regular basis, such as three or more times per week, appear to have an enhanced sense of wellbeing and a diminished risk for developing cognitive decline in later life or a delay in onset of symptoms (35). Walking and bicycling appears to have many beneficial effects to these individuals when done on a daily basis for 30 minutes or more (26), (27), (33). Physical exercise reduces the impact of age-related neuronal reproduction (36).

Rodent models of high exercise environments suggest that physical stimulation promotes neurological resilience and enhancement of vascular networks in rat brain (23), (24). Transgenic rodent models with high levels of exercise demonstrate diminished amyloid load in the neocortex. The cerebral brain mechanism that diminishes brain amyloid content is unclear but appears linked to overall brain function within the affected mouse (25), (27), (28).

Late-life, human cognitive decline appears related to mid-life obesity (29) and perhaps the metabolic syndrome that includes obesity, insulin resistance, diabetes, and elevated lipids (30). Central obesity appears to be a risk factor for hypertension and excessive insulin secretion which may be harmful to long-term neurological function. Obesity is related to life-time exercise which may correlate with relative risks for developing dementia. CLICK HERE FOR ADDITIONAL INFORMATION ON THE METABOLIC SYNDROME – 2513.91

The newest scientific data suggests that the brain is a use-it or lose-it organ with regards to physical and intellectual stimulation (16). Newer data suggests that exercise and cognitive stimulation exert benefits beyond maintaining synaptic resilience. Long-term effects from stimulation may actually diminish disease-specific changes based in rodent models. This second benefit remains
unsubstantiated in human models; however, this scientific assumption appears reasonable based on other information. Mechanisms of synaptic plasticity detected in rodent brain appear present in human brain based on human surgical specimens (31).

6. Impact of Cognitive Training on Age-Related Changes in Function or Brain Imaging

Cognitive training may slow age-related cognitive decline for over five years for individuals using computer-based, training systems that included ten sessions with four booster sessions (37). Functional imaging shows enhancement in markers of neuronal plasticity in the brains of aged individuals who engage in “cognitive conditioning” (38).

A variety of commercial and free cognitive activity programs are available to promote “mental gymnastics”. Programs conducted by the individual, in groups, and on-line show significant promise for improving cognition and promoting cognitive longevity.

Each person has individualized tastes for intellectual or social activity. The clinician should encourage selection of an appropriate intervention and continued participation. Novel intellectual activities are preferred to repetition of already over-learned tasks; for example, learning a new language or discovering the computer.

7. Possible Conclusions Based on Available Science about the Role of Education, Exercise and Psychosocial Factors on the Risk of Developing Late-life Dementia in Humans

Comprehensive, prospective studies have not been performed on the role of physical, intellectual or environmental stimulation in preventing dementia. These studies will not likely be performed because of technical obstacles. No intervention provides an insurance policy against the development of dementia, especially in those individuals with a high genetic risk for Alzheimer’s disease. The available studies in humans indicate that lifetime exercise enhances overall physical wellbeing, cardiovascular fitness and cognitive wellness. Three mechanisms might explain this benefit including: 1) enhanced angiogenesis in the brain, 2) enhanced synaptic reserve, and 3) diminished amyloid load. A second issue is the role of midlife obesity and hypertension that may reflect diminished exercise and the increased risk for dementia in those individuals who may suffer from metabolic syndrome.
The second “protective” issue is the role of lifetime intellectual achievement on risks for cognitive decline. Synaptic reserve, neuroplasticity, and perhaps other factors such as neurotransmission, trophic factor, and neurogenesis may be impacted by lifetime intellectual achievement. The role of late-life intellectual stimulation is less compelling than early and midlife intellectual achievement (42), (43), (44). The relationship of leisure activities or other forms of intellectual stimulation such as social interactions to diminished risk for dementia suggests several mechanisms including stress reduction and overall cognitive stimulation. These interventions are difficult to quantitate and therefore, the beneficial consequence of these activities are more difficult to define than other variables such as blood pressure or homocysteine levels.

The combined package of intellectual, physical, and social stimulation appears to be the optimal recommendation by primary care clinicians for patients in mid to later life.

**Recommendations to Primary Care Clinicians**

1. Encourage middle aged patients to develop a regular physical exercise schedule.
2. Encourage all age groups to maintain normal body weight to reduce risk of dementia in later life.
4. Promote social and intellectual activity in older patients.
5. Encourage participation in “mental gymnastic” programs that appeal to the individual.
6. Identify lonely elders and encourage social reconnection.
7. Screen for depression in lonely or isolated elders.
References


