Aging of the Human Nervous System: What Do We Know?

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LEARNING OBJECTIVES

Demonstrate the ability to identify and use in clinical care:

1. Nervous system changes with age
2. Differences between pure aging in the NS and the effects of common diseases
3. Age-related changes in key domains:
   a. Cognition/Memory
   b. Special senses
   c. Strength
   d. Balance
   e. Somatic sensation

OVERVIEW: AGING IN 21ST CENTURY AMERICA

Americans have gained >25 years of average life expectancy during the 20th century, and there is no evidence of slowing in the 21st. Although clinical and public health interventions have allowed gains in healthy life expectancy (average age of disability onset) to keep pace with the striking gains in longevity, the sheer numerical increases of older persons portend a burden of disease and disability that will overwhelm the social and financial capacity of our technologically advanced society to manage older persons' health and health care. And Congress dabbles by trying to trim 1-2% from the current Medicare growth rate. The tools to meet these care needs are biomedical science coupled with strategic changes in health care delivery for the very old and vulnerable; neurological problems of aging are a major contributor to the morbidity and healthcare costs for older adults.

NEUROLOGY OF AGING

There is no greater fear among most Americans than loss of brain function—whether the loss of the very persons from dementia (usually Alzheimer's disease), the multiple other neurodegenerative conditions that are increasingly common with age (e.g., Parkinson's disease, ALS) or the sudden devastation of stroke.

WHAT IS OBLIGATORY WITH AGING?

As we age, many neurological disorders become common. What are the changes occurring in the nervous system that are inevitable with age in the healthiest adults, even those who exhibit all known risk-reducing behaviors? Using the term Pure Aging Syndrome makes clear that no disease, environmental, lifestyle or behavioral risk factor plays a role in the change. These are brain function changes that are inevitable, irreversible with current technology, and while mostly decremental, do not cause symptoms on their own. Although there is much in the literature about decrease in brain size and weight with age, secular trends of increasing size of humans and longer years. There is a decline with age, mostly in free recall; recognition is well preserved. The universal temporary decline in the ability to retrieve names generally begins early in middle age, and worsens over time. The lost name is almost always retrieved soon after the episode. This phenomenon is not predictive of any neurodegenerative disorder (e.g., Alzheimer's disease).

I. COGNITION

A. Attention

- There is a mild decline in overall accuracy, beginning in the 60s that progresses slowly, but sustained attention very good in healthy older adults. Older adults are more easily distracted, especially if irrelevant information is presented concurrent with important material.

Clinical point: When giving crucial information to older patients, stick to core data, repeat it and write it down.

B. Learning and memory

1. Sensory memory is the earliest stage (visual, auditory, tactile); it is inherently unstable and decays rapidly. There is no age-related change.
2. Primary (short-term) memory is the stage after transfer of sensory memory. There is no loss with age.
3. Secondary (long-term) memory persists for hours, days and years. There is a decline with age, mostly in free recall; recognition is well preserved. The universal temporary decline in the ability to retrieve names generally begins early in middle age, and worsens over time. The lost name is almost always retrieved soon after the episode. This phenomenon is not predictive of any neurodegenerative disorder (e.g., Alzheimer's disease).
4. Encoding strategies help retrieval - mnemonics, mental hierarchies, clusters—but they are used less by older persons. Training gives long-lasting improvements.
5. Distraction interferes with learning more in older persons than in young.
6. Clinical point: Give instructions directly and simply, encourage encoding strategies, refer to reputable memory training.

C. Language

- Vocabulary increases well into the 50s and 60s, and shows no decline with age in those who continue to be engaged in complex language use. Similarly, syntactic skills—the ability to combine words in meaningful sequences—show no decline with pure aging.
D. Intelligence, as measured by the Wechsler Adult Intelligence Scale, declines with age, but the biggest, earliest losses were reported in flawed studies. Cohort differences underlined these cross sectional studies, causing selection bias regarding education, gender, race, occupation and income. Summary scores of "intelligence" per se are less useful in adults. Measuring specific intellectual functions has become usual.

1. Crystallized intelligence (learning and experience) remains stable or improves with age until the late 70s or beyond, especially in those who remain healthy and engaged in cognitively demanding activities.
2. Fluid intelligence (problem-solving with novel material requiring complex relations) declines rapidly after adolescence.
3. Perceptual motor skills (timed tasks) decline with age.

Special Senses
E. Vision
1. Pure aging includes decline in accommodation (presbyopia), low-contrast acuity, glare tolerance, adaptation, color discrimination and attentional visual field. Changes occur in components of the eye itself and in central processing. These numerous changes affect reading, balance and driving, but compensatory glasses and behavior can maintain safety.
2. The common eye diseases in old age (glaucoma, macular degeneration, cataracts, diabetic retinopathy) are superimposed upon these pure aging changes.

F. Hearing
1. Conductive and sensory hearing losses (presbycusis) occur with age; losses are primarily high tones, making consonants in speech difficult to discriminate.
2. Although impairment is defined as an auditory threshold greater than 25 decibels, the nearly half of Americans > 80 who don't reach the clinical threshold of 25 decibels still have diminution in acuity – pure aging effects.
3. Consequences include difficulty in localizing sound and understanding speech, usually accompanied by hypersensitivity to loudness.
4. Common diseases in old age are superimposed upon these changes, often resulting in worsening hearing impairment (e.g., cerumen impaction, otosclerosis, 8th N drug toxicity).

G. Taste buds don't diminish, but salt detection declines; perception of sweet is unchanged, and bitter is exaggerated. The volume and quality of saliva diminish. All changes combine to make eating less interesting. These aging changes are compounded by common diseases (periodontal) and medications.

H. Smell acuity declines with aging. There is atrophy of olfactory bulb neurons, and central processing is altered. The result is decreased perception and less interest in food. Again, these age-related changes are compounded by disease (e.g., AD and PD have diminution and alteration of smell).

II. Strength
A. Muscle – Disuse and disease, as in many systems, are major confounders of age effect.
1. Age-related changes include loss of muscle mass, though strength loss can be relatively preserved by exercise. Reduction in muscle fiber size occurs primarily in Type II ('fast') fibers, which are highly anaerobic; Type I ('slow') fibers, which are aerobic, tend to retain their size during aging.
2. Muscle wasting in frail older persons, a disorder known as sarcopenia, leads to higher incidence of falls and fractures and functional decline.

B. Spinal reflex changes include decline in amplitude of the spinal stretch reflex with normal aging, due in part to stiffness of tendons.

D. Motor cortex changes with age include decrease in the number of neurons and synapses; one hypothesis is that disuse atrophy occurs, arguing for a "use it or lose it" construct.

E. Basal Ganglia – Age-related changes in the striatum include decline in dopamine D1 receptor density in the caudate and putamen. Age-related loss of dopamine neurotransmission may play a role in vulnerability of older adults to extrapyramidal disorders. In the substantia nigra, pigmented neurons drop out; their loss is associated with motor dysfunction, including bradykinesia, stooped posture and gait disturbance. These aging changes mimic parkinsonian features, and may account for the increase in prevalence of PD with age.

III. Balance
Balance function declines with increasing age, but is rarely the sole cause of falls in older persons. Strength, cerebellar integrity, vestibulo-cochlear function, hearing and vision all play a role in maintaining balance. Degeneration of the otoconia (granules of the otolith) is a mechanism for vestibulo-cochlear decline with aging. Many diseases affect the vestibular portion of the 8th N, and it is also sensitive to drugs. Finally, proprioception also contributes to maintenance of balance. Muscle spindle and mechanoreceptor functions decline with pure aging, further interfering with balance. Clinical position sense does not decline with age.

IV. Sensation
A. Pain – Typically painful disorders are often less or not at all painful in elders.
1. Some cortical processing capacity for pain sensation appears to decline with age. When functional magnetic resonance imaging (fMRI) was used to compare cortical nociceptive responses to painful contact heat in healthy young and older subjects, older subjects had significantly smaller pain-related fMRI responses in anterior insula (aINS), primary somatosensory cortex (S1), and supplementary motor area. Gray matter volumes in S1 and aINS were significantly smaller in the elders, suggesting reduced processing capacity in these regions, perhaps accounting for smaller pain-related fMRI responses.
The Mini-Cog assessment instrument combines an unceded 3-item recall test with a clock-drawing test (CDT) that serves as a recall distractor. The Mini-Cog can be administered in about 3 min, requires no special equipment, and is relatively unaffected by level of education or language differences.

ADMINISTRATION — The test is administered as follows:

1. Make sure you have the patient’s attention. Instruct the patient to listen carefully to and remember 3 unrelated words and then to repeat the words back to you (to be sure the patient heard them).
2. Instruct the patient to draw the face of a clock, either on a blank sheet of paper, or on a sheet with the clock circle already drawn on the page. After the patient puts the numbers on the clock face, ask him or her to draw the hands of the clock to read a specific time (11:10 and 8:20 are most commonly used and more sensitive than some others). These instructions can be repeated, but no additional instructions should be given. If the patient cannot complete the CDT in 3 min, move on to the next step.
3. Ask the patient to repeat the 3 previously presented words.

SCORING — Give 1 point for each recalled word after the CDT distractor. Score 0–3 for recall. Give 2 points for a normal CDT, and 0 points for an abnormal CDT. The CDT is considered normal if all numbers are depicted, once each, in the correct sequence and position, and the hands readably display the requested time. Add the recall and CDT scores together to get the Mini-Cog Score:

- 0–2 indicates positive screen for dementia.
- 3–5 indicates negative screen for dementia.

2. Endogenous pain inhibition is reduced with aging. Opioid-mediated endogenous analgesic systems are particularly susceptible to functional decline with aging. Additionally, older age is associated with reduced beta-endorphin levels.
3. Some pain thresholds show age-related changes. Although sensitivity to heat pain is decreased with age (above), sensitivity to pressure pain is enhanced.
4. Both Substance P and calcitonin gene-related peptide (CGRP), major neurotransmitters of primary afferent nociceptive fibers, are decreased with aging, likely reflecting reduction in density or function of nociceptive nerves. The rate of CGRP axonal transport also decreases with advancing age.

B. Sensory nerves lose myelin selectively, perhaps predisposing to neuropathy. Vibrational sensation perception diminishes with aging, especially in the legs. Since position sense is carried in the same tracts as vibration, diminished vibratory sense should be followed up by position sense testing.

REFERENCES

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