Chapter 1: Education
Section 2: The Aging Spectrum

I. Normal Aging May Not Feel So Normal To You

Life Becomes More Complicated

The truth is that as we get older, life just becomes more complicated. Normal aging will result in subtle though important cognitive changes, such as delays in speed of information processing, susceptibility to distraction and limitations in active memory. These three factors alone can account for the majority of attention failures, a.k.a. “senior moments”.

Cognitive Functions Affected by Aging

A. Neurocognitive Changes Associated with Normal Aging

Delays in Information Processing Speed

Delays in motor speed are an accepted part of advanced aging. Attend any number of sporting events such as a golf tournament or marathon and you will find a masters division which allows equitable comparison of skills among similar age groups. Why should we not expect similar changes in cognitive speed?

Our environment bombards us with data which requires us to rapidly process, rehearse and consolidate information in order to create new memories. Information that is not rapidly encoded,
sorted and rehearsed will not be retained. Decline in information processing speed can be as gradual as changes in vision and hearing, with similar need for accommodation in lifestyle.

**Working Memory**

Delays in processing speed can easily overload the limits on working memory. Active or working memory is like a conveyer belt in a mail room. It is limited to 7 bits of information, or about the size of a telephone number, and remains on the belt for about 10 seconds before something new crowds it out. It is inaccurate to say information was forgotten. In fact, the memory was still under construction and was not fully consolidated and stored.

**Attention Failures**

Not only must we turn over new information at a high rate of speed, we have to simultaneously sort and file new information into different bins so it can be easily accessed at a later time. To ensure information is accurately encoded we have to actively listen and rehearse it. Attention is like a guard whose job it is to keep irrelevant information out, while at the same time allowing us to focus on a limited amount of key information.

A frequent side effect of inattention is intentional memory loss, or forgetting to perform a task that one intends to do. When one is *just about to do something*, then one does not make an active effort to remember it. Anything that places additional demands on active memory, such as mental fatigue or cognitive slowing, will make future retrieval more difficult.

Inattentive errors can occur at any age, although susceptibility to mental fatigue, distraction and reduced stamina can become more apparent with aging. Mindfulness is a skill that teaches us to quiet our mind, focus in the moment and aides in creating accurate memories.

**Forgetfulness**

Problems rapidly processing and manipulating information can affect our ability to organize a systematic plan for encoding, rehearsing and recalling information. In other words, we “forget to remember”. We have to accept that retrieval of new information will no longer be effortless. The more effort that we put into developing a strategy to recall it later the less likely that we will experience annoying episodes of forgetfulness.

The most common form of forgetfulness is failure to remember future events. Prospective memory is different than other types of memory. It is especially difficult because it requires you to remember out of the ordinary events without prompts. For example, remembering to return a book to the library, defrost the chicken for dinner or to take medications. In contrast, immediate memory is more easily called to mind by the appearance of a trigger, whereas prospective memory lacks such a prompt.

**Problems with Executive Function**

Executive function involves the ability to anticipate future events, set goals, develop a strategy and the sequential steps in order to successfully carry out a task. Strategic problem-solving is essential to live and thrive independently in the home. Reliant on processing speed, working memory and divided
attention, executive function is susceptible to failure with advanced aging. Lucky for us executive function is a skill that can be practiced to offset changes in aging.

Sensory Loss
Complicating matters further, everyday functions which we once took for granted such as vision, hearing and physical stamina, no longer operate with the same degree of reliability. How can we recall information without an accurate record?

B. An Individual Equation for Aging
Recognizing that normal aging will require some adjustment on our part is the first step to maintaining a high quality of life. Lucky for us, we can level the playing field as we age by working smarter, not harder. Contrary to popular belief, strategic problem-solving is not a gift. Organization and planning, like remembering, is a skill; a skill you can learn, relearn or improve at any age.

The degree to which individuals will experience observable changes in their day to day functioning depends upon numerous factors, such as overall mental and physical health, prior education, and whether they are continuing to engage in challenging cognitive pursuits and/or have a purpose to get up every day.

Factors Which Reduce Risk of Normal Aging

It really is an individual equation for each person, with risk factors being offset by a healthy lifestyle. For example, recent research indicates that every one year in higher education is associated with about 10% reduced risk of being overweight or obese, and 8% decreased risk of dementia.

II. A Continuum of Cognitive Changes
Changes associated with aging are best thought of as belonging on a continuum and can range from annoying episodes of absentmindedness to more severe memory loss.
AAMI: Age Associated Memory Impairment
MCI: Mild Cognitive Impairment
DAT: Dementia of the Alzheimer’s Type
PD: Picks Disease/FTL: Frontal Temporal Lobe
PDD: Parkinson’s Disease Dementia
LBD: Lewy Body Dementia

HD: Huntington’s Disease
IPD: Idiopathic Parkinson’s Disease
SVID: Small Vessel Ischemic Disease
TIA: Transient Ischemic Attack
CVD: Cerebral Vascular Dementia
CAA: Cerebral Amyloid Angiopathy
A. Cortical Cognitive Changes

1. Age Associated Memory Impairment (AAMI)

Approximately 30-40% of adults over 65 years will show some degree of Age Associated Memory Impairment (AAMI). This statistic increases up until age 90 when decline levels out.

Cognitive Changes Related to Age Associated Memory Impairment (AAMI)

Software

Delays in speed of information processing can rapidly overload the limits of working memory. Capacity of working memory is between 5 - 7 bits of information; factors such as length, complexity and novelty tend to decrease our capacity levels.

Hardware

Expect changes in visual, auditory and sensory motor skills.

Attention

Reduced levels of the neurochemical acetylcholine are related to attention failures. Attention requires staying consciously focused on the information we want to remember as well as actively attempting to reduce competing and irrelevant stimuli in the environment that distract us from learning.

Given likelihood for the mind to wander, expect more absentminded errors such as misplacing keys, a wallet or a purse. While attention failures can occur at any age, they occur more frequently with aging because of cognitive slowing.

Memory

Expect prospective memory loss, or actions which need to be recalled in the future, such as an upcoming doctor appointment or errand.

Self-awareness

Generally speaking, age-related memory changes are first recognized by the individual experiencing the problem. For example, an uncharacteristic need to make lists to overcome inattentive errors. In contrast, those suffering from Alzheimer’s dementia often present as unaware, oblivious, pleasantly confused or are in denial of the deficits.

Language

Tip of the tongue experiences, or mild word finding problems, with decreased verbal fluency are considered part of the normal aging process. One could expect difficulty with names and low frequency words. In contrast, older adults show little problems with high frequency words such as “spoon”, family and close friends’ names or overall sentence structure.
2. Mild Cognitive Impairment (MCI)

Next on the aging continuum is Mild Cognitive Impairment (MCI). At this stage, individuals demonstrate disproportionately severe memory problems for their age as well as deficits in other cognitive functions. However, these occurrences are not enough to warrant diagnosis of dementia. Symptoms of MCI include those previously mentioned with AAMI. Additional symptoms include trouble with multitasking and difficulty solving problems. MCI doesn’t significantly interfere with activities of daily living, but it may make those activities more effortful or challenging for you.

On average, individuals diagnosed with MCI progress to dementia at the rate of 10% per year (DeCarli, 2003, Bruscoli, 2004, Peterson, 2004, Panza, 2005). Given a linear rate of progression, research indicates that after 6 years, a significant amount of the mild cognitive impairment group had progressed to dementia with the assumption that the rate continues up to 80-90% in ongoing years (Peterson, 2003).

However, results from more recent studies using a representative general population who are 75 years or older suggest that people with mild cognitive impairment develop clinical dementia during their lifetime at a rate closer to 60-65% (Busse, 2006).

Why such a difference in probability rates for development of dementia following onset of MCI? Conversion rates to dementia are time dependent. The risk of developing dementia is actually highest during the first 2-3 years following diagnosis, with about 20% of individuals going on to exhibit signs of dementia. However, rates level off and reduce after the first several years.

Undoubtedly, people with mild cognitive impairment are at increased risk for developing dementia. On the other hand, it is premature to assume that once you have been diagnosed with MCI in your 70’s it is a given you will develop dementia in your lifetime.

Remember, your risk for developing dementia is an individual equation. Depending on age when diagnosed, as well as various lifestyle factors, the actual rate and progression will vary. Factors such as diet, exercise, leading a purpose-driven life and having an absence of vascular disease could tip the scales in your favor.

Cognitive Changes Related to Mild Cognitive Impairment (MCI)

Software

Expect changes in thought monitoring, or the tendency to lose one’s train of thought during conversation, when reading or watching movies. Increased problems with conceptual shift of set, or mental flexibility, inability to consider different alternatives or tending to perseverate, or ask the same question over and over.

Problems with executive functioning are common. Strategic problem solving skills are needed to perform various Independent Activities of Daily Living (IADL), such as medication management, scheduling doctor’s appointments, home finances, investment planning and preparation of nutritious meals. Executive functioning is required to live and thrive independently.
Memory
Expect problems with episodic memory, for example, recalling the details of a conversation you had yesterday, rather than procedural recall, or the how to” memory that involves dressing, turning on a light or operating the coffee maker. Changes may be observed with spatial agnosia and geographical orientation, or the ability to follow maps and driving directions, even on familiar routes.

Attention
Expect problems with divided attention, or the ability to rapidly shift attention between two activities to complete a task. This skill is essential to driving, multitasking, paying bills and even balancing a checkbook.

Learning
Expect difficulty with effort demanding memory, or the ability to learn complex, lengthy and/or new information. For example, learning how to program a VCR, playback messages on a cell phone or use any new technology these days. In contrast, consolidated learning, or the ability to comprehend and remember new information when presented in a well-organized, concise and written format as well as recognition recall, or spontaneous recovery of a memory with a verbal hint, remains intact.
Responding well to prompts and cues indicates problems are likely in the retrieval phase of memory rather than the encoding phase. This is good news. It indicates that the ability for learning is still intact; however, the information will need to be broken down into small chunks, repeated frequently and accompanied by a visual prompt. In contrast, Alzheimer’s dementia results in deficits in the encoding and consolidation phase of learning.

Behavior
Expect increased desire for security and routine. Traveling may be too much of a challenge. Difficulty with making decisions may be observed as noted by stacks of mail, correspondence or bills, indicating problems with divided attention and sequential problem solving or inability to decide what to keep or throw away. Finally, changes in routines may result in uncharacteristic irritability, anxiety, impulsivity or poor judgment at times.

Language
Expect the tendency to misspeak or make the wrong choice of word. Speech has a vague, unelaborative quality, lacking facts and details. Expect moderate difficulty with word finding, struggling to name moderate to common words such as family names and common objects.

Myth Buster: Age Associated Memory Impairment (AAMI) and Mild Cognitive Impairment (MCI) are an inevitable part of aging.

Truth: The severity of age-related cognitive changes can be mitigated by adopting a brain health lifestyle based on the 5 core brain health lifestyle goals: physical activity, nutrition, brain fitness, socialization and mental restoration.
While amyloid plaques and neurofibrillary tangles both may be associated with the development of Alzheimer’s disease, their presence alone is not always sufficient in development of the disease. Up to 20 percent of people who demonstrated no major memory problems throughout the course of their life are discovered to evidence signs of plaques and tangles upon autopsy (Stern, 2005). How does the brain continue to function efficiently despite the presence of known markers for Alzheimer’s disease? The answer comes down to a combination of innate abilities, emotional resiliency, and cognitive reserve. Engaging in diverse, mentally stimulating activities can build up additional brainpower to offset or bypass age-related or even disease-related damage to the brain. The more reserve you have in your mental bank, the better your ability to overcome the inevitable challenges of aging.

Another factor that appears to tip the scales pertaining to whether someone will demonstrate the debilitating symptoms of Alzheimer’s is the presence of vascular risk factors such as high cholesterol, hypertension, diabetes mellitus and atherosclerotic disease. The presence of lacunar infarcts (mini strokes), in combination with telltale plaques and tangles signaling abnormal protein development in the brain, is being evaluated as one of the culprits of Alzheimer’s disease (Snowden, 1996).

Research suggests that stroke free brains can compensate for Alzheimer’s lesions to some extent and mute the symptoms of the disease. Thus, while we don’t yet know how to prevent plaques and tangles, we do have effective strategies for reducing cerebral vascular disease and stroke.

A longitudinal study of nuns (Snowden, 2001) found that nuns tend to suffer Alzheimer’s at a rate less than the general population. This is likely related to their rigorous lifestyle filled with exercise, mental stimulation and lifelong learning, good nutrition, spiritual devotion and service to others.

**Diagnosis of Dementia**

So how does one determine whether one has dementia or a milder form of cortical or vascular impairment? Depending on your definition, dementia is an acquired and persistent impairment in three or more neurocognitive domains of function, including memory, language, visuospatial, judgment or abstract reasoning, thinking, emotion or personality.

From a more practical standpoint, dementia involves inability to learn new behavior. In effect, the person is flying on autopilot: relying on information stored in remote memory prior to onset of the disease process. The inability to incorporate new information into everyday decision-making places one at great risk for failure to thrive and self-neglect.

For people and their families that are experiencing signs of dementia, coping techniques are the key. Compensatory strategies which encourage the habit of referring to calendars and day planners, as well as use of reminder systems for medications, will provide practical help as the dementia symptoms progress. While we may not be able to change the underlying course of brain changes, we can teach compensation strategies to help maintain a person’s functional independence for as long as possible.

**3. Dementia of the Alzheimer’s Type (DAT)**

Alzheimer’s disease is a type of cortical dementia. It preferentially affects the corticolimbic connections including the basal forebrain and medical dorsal nucleus, critical for registration, consolidated learning and storage of new information. Neurofibrillary tangles located in medial temporal regions
compromise the hippocampus, entorhinal cortex and the amygdala resulting in accelerated rate of forgetting, intrusive errors, confabulation as well as poor recognition recall.

Onset is gradual with course described as slow and progressive. Although eventually deterioration is global, initially Alzheimer’s may spare motor, somatosensory and visual functions, which can remain intact until later in its course. Alertness, drive, sequential attention and procedural recall can remain well intact for a number of years.

In the initial stages, Alzheimer’s presents with characteristic loss of immediate memory, decline in verbal reasoning and general knowledge. Perhaps the single most telling indicator of Alzheimer’s is early loss of subjective awareness, social engagement and judgment. As self-insight lags well behind that of family and friends, self-referral is very rare in cases of Alzheimer’s. Later in the disease, expect one may forget how to perform routine habits and simple tasks, becoming increasingly dependent upon others for their daily care.

Alzheimer’s is by far the most common type of degenerative memory loss, accounting for a full 65% of new cases diagnosed each year. In 2010, 5.1 million Americans age 65 and above were diagnosed with Alzheimer’s disease, which breaks down to 1 in 8, or 13% of this age group. The prevalence of Alzheimer’s increases sharply with increasing age, with more than 50% of over 85 years old affected.

No Longer a Catch All Diagnosis

The diagnosis of Alzheimer’s has been confounded by the fact that its’ pathological features, proteins in the brain associated with extracellular amyloid plaques and intracellular neurofibrillary tangles, are invisible to traditional neuroimaging techniques and can only be confirmed during an autopsy.

Plaques are a result of abnormal protein deposits called beta-amyloid or β-amyloid that can build up in the spaces between nerve cells in cerebral cortex of the brain. Tangles are twisted fibers of another protein called tau that can build up inside cells.

In prior years Alzheimer’s disease had become a diagnosis of exclusion, a “catch all” diagnosis, made after other considerations potentially contributing to behavioral change or cognitive impairment had been ruled out. At the present time, this may be changing.

Detection During the Preclinical Stage

In April of 2011, the National Institute on Aging (NIA) updated its diagnostic guidelines for Alzheimer’s disease for the first time in nearly 30 years. The updated NIA guidelines describe three stages of Alzheimer’s disease, including a new Preclinical Alzheimer’s Stage where brain changes may be in progress, but significant clinical symptoms are not yet evident. The following two stages include the familiar signs of Mild Cognitive Impairment (MCI), followed by the final stage of the disease in which symptoms of Alzheimer’s are significant enough to impair a person’s ability to function independently.

Biological markers are reliable predictors and indicators of a disease process. Various biomarkers are emerging to detect preclinical symptoms of Alzheimer’s disease. They include proteins in blood or spinal fluid, genetic variations (mutations) or brain changes detectable by head neuroimaging.

In April of 2011, the National Institutes of Health (NIH) funded the largest genome-wide association study (GWAS) ever conducted in Alzheimer’s research. Investigators studied DNA samples from more
than 56,000 participants and analyzed shared data sets to detect gene variations that may have subtle
effects on the risk for developing Alzheimer’s disease.

Scientists have confirmed one gene variant, Apolipoprotein E-e4 (APOE-e4), as a significant risk factor
gene for the common form of Late-Onset Alzheimer’s Disease (LOAD), which typically occurs after age
60 as does an increased risk for arteriosclerosis.

But carrying this allele by itself does not mean a person has or will develop Alzheimer’s dementia.
Nearly 40% of patients without dementia tested positive for the protein biomarkers. Therefore, genetic
testing for APOE e4 is not recommended outside of research settings.

In absence of neuromotor, auto immune, cardiovascular, dymyelinating or CNS disease, early signs of
recent memory loss at or before age 65 may indicate early onset or autosomal dominant alzheimer’s
dementia. Early-Onset Alzheimer’s Disease (EOAD) is a rare type of genotype, found in certain families
caused by mutations in the amyloid precursor protein, Presenilin 1 or Presenilin 2 genes. A person
who inherits any of these mutations from a parent will almost surely develop Alzheimer’s dementia
before age 65. Genetic testing for the disease is common in families with a history of EOAD.

The Role of Vascular Disease in Developing Alzheimer’s

While Alzheimer’s disease (AD) is often cited as the most common cause of dementia, cerebral vascular
disease is very common in Alzheimer’s disease, with dual pathology thought to have an additive or
synergistic effect, that not only lowers the threshold for developing Alzheimer’s dementia but
increases the risk of developing either disorder independently. In fact, the frequency of pure
Alzheimer’s disease in U.S. population study varied from 21% -56.5 %, with 45% exhibiting mixed
Alzheimer’s and vascular lesions.

Going back to Snowden’s research and The Nun Study, the expression of dementia in elderly nuns with
Alzheimer’s pathology found on autopsy was markedly influenced by deep white matter ischemic
disease and lacunar infarcts in thalamus and basal ganglia region. The coexistence of strokes increased
the likelihood of dementia with Alzheimer’s pathology from 57% to 75% and the presence of smaller
lacunar infarcts or TIA’s increased the likelihood to 93%, so times the odds!

Increasingly, Alzheimer's research has identified the role of oxidative damage, inflammation and
hypertensive disease in the accumulation of beta-amyloid in the vasculature system of the brain.
Cerebral amyloid angiopathy (CAA) is a type of vascular disease that is associated with the deposit of β-
amyloid in the small and medium cerebral blood vessels that irrigate the cortical region of the brain.

CAA can be observed on head MRI scans as scattered microbleeds or punctate areas of high T2 signal
throughout the periventricular white matter region of the brain. The presence of microvascular disease
in the frontal lobe region, in absence of history of hypertension, cardiovascular disease or
demyelinating disorder such as Multiple Sclerosis can be telling for CAA. When additional cortical risk
factors are present on the MRI as well, such as enlarged ventricles, sulci and atrophy, likelihood for
Alzheimer’s disease is markedly increased.

Like certain genotypes, the presence of β-amyloid appears to be an important risk factor associated
with Alzheimer’s disease. However, it does not appear to be sufficient in determining who will
ultimately demonstrate the more disabling symptoms of the disease. While virtually everyone with the

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ailment has these plaques in their brains, many people have amyloid buildup and never show any signs of cognitive impairment.

More important than the presence of amyloid plaques in the cerebral cortex is the appearance of β-amyloid in the vasculature system underlying the cerebral cortex, which dramatically increases the risk for the development of Alzheimer’s type symptoms. In fact, cerebral amyloid angiopathy has been associated with the genotype Apolipoprotein E (APOE) e4 and APOE- e2. Its presence has been confirmed in 90% of Alzheimer’s patients upon autopsy.

How important is maintaining vascular health in protecting against Alzheimer’s disease? Huge! In the absence of approaches to detect and treat late stage Alzheimer’s disease, targeting vascular risk factors and improving cerebrovascular health offers the best opportunity for the near future. Lifestyle factors such as diet and exercise and their role in brain health cannot be understated.

Cognitive Changes Related to Dementia of the Alzheimer’s Type (DAT)

Software
During early stages may appear very alert and attentive. While perceptual processing speed may remain well intact, could exhibit problems with spatial navigation and geographical orientation resulting in getting lost in familiar places. Drive and energy remains intact aiding in strategic planning although goal directed behavior may increasingly lack rationale.

Hardware
Motor speed and physical stamina are excellent. Risk of elopement may be high, with extra care paid toward ensuring a secure living environment.

Memory
Severe episodic memory loss or frank inability to learn new information, sometimes referred to as anteriograde or amnestic memory loss, can occur. Could expect accelerated rate of forgetting, intrusive errors and confabulation. As a result, retention is not only very sparse, but it may include misinformation and self-generated stories to filling in missing gaps. Consolidated learning remains flat with poor response to recognition recall indicating that frequent of information will not aid in retrieval. Remote memory and procedural memory are initially resistant to change; however, expect difficulty in later stages performing rote Activities of Daily Living (ADL) like dressing, cooking and housekeeping as well as recalling autobiographical history.

Language
Expect anomic aphasia associated with inability to recall familiar or common words such as family names and common objects. Misspeaks may occur as well. Also common is alogia or derailed, repetitive, empty and impoverished speech, lacking in details and facts. Written expression mirrors language problems. Gradually may exhibit signs of agnosia and apraxia or loss of ability to identify the meaning of objects or how to use them.
Behavior

Expect loss of subjective insight, objective reasoning, social judgment and withdrawal from social activities. Symptoms of anxiety, emotional reactivity and insomnia may occur. One should also be alert for uncharacteristic signs of disinhibition, agitation or paranoia. Frank psychosis associated with visual and auditory hallucinations can be expected in about 20% of the cases, late in the disease process.

Myth Buster: Forgetfulness is an early sign of Alzheimer’s disease.

Truth: The incidence of dementia increases with age and the prevalence increases with every decade after 65 years of age. While Dementia of the Alzheimer’s type (DAT) is the most familiar and prevalent type of dementia, not all changes in memory represent signs of a disorder. Furthermore, not all disorders are related to a dementia and certainly not all dementia is an example of Alzheimer’s disease.

Forgetfulness, or absentmindedness, is a form of attention failure rather than an actual deficit in memory. While absentmindedness can occur at any age, it occurs more frequently as we get older because of age-related cognitive slowing and increased risk for distractibility.

When one experiences episodes of forgetfulness, the most sensible strategy is to do a personal inventory of factors that reduce our attention, including physical or emotional problems, multitasking, distraction in the environment or poor learning habits, and see what is appropriate in the situation.

Remember; if you want to overcome a memory or any other kind of deficit, you will need to target the skill or ability which is at the root of the problem, choose a specific strategy and tool to hone the skill, and learn to practice the new skill until it becomes a habit.

Performing a crossword puzzle can be helpful in improving verbal fluency and preventing tip of the tongue experiences, but it will not be particularly effective in helping you find your car keys. Playing Sudoku, brain teasers or computer games may be helpful in increasing speed and efficiency of information processing, working memory and fluid reasoning, but should never be substituted for an automatic pill dispenser box if one can’t take blood pressure medications as directed.

4. Other Cortical Degenerative Disorders

Although Alzheimer’s disease is the most common form of degenerative dementia, several other types of cortical dementia include Frontal Temporal Lobe and Pick’s disease. In general, both involve early and marked changes in personality, deterioration in social behavior and judgment. Pick’s disease may also present with significant emotional blunting and altered dietary preferences.

B. Subcortical Cognitive Changes and Extrapyramidal Disorders

1. Vascular Cognitive Impairment (VCI)

The prevalence of life style disease has come to play a very important role in shaping the symptoms we have come to expect as part of normal cognitive aging. Ischemic vascular disease can result from lifestyle diseases, such as smoking, obesity, high serum cholesterol and LDL levels, elevated homocysteine, Type 2 diabetes, arteriosclerosis, hypertension, heart disease and sleep apnea. While
Ischemic disease is often considered benign, its presence can magnify the normal process of aging and increase the scope and severity of functional loss.

**Ischemic Vascular Disease**

Subcortical Ischemic Vascular Disease (SIVD) or small vessel ischemic disease is a subtype of vascular cognitive impairment associated with hypertension and characterized by extensive white matter lesions, multiple lacunar infarcts and damage to subcortical structures. Subcortical ischemic vascular disease is typically localized to the dorsolateral prefrontal pathway, and includes various mid brain regions such as the basal ganglia as well as the basal forebrain and dorsal medial nucleus of the thalamus.

Ischemic change to the basal ganglia can adversely affect motor skills and result in a number of extrapyramidal symptoms including lower extremity weakness, broad based short stepped gait, imbalance, falls, incontinence, mental inertia and motor slowing as well as deficits in visuospatial and perceptual motor skills. Alternately the thalamus can be affected, including the basal forebrain and mediodorsal nucleus, the core brain regions involved in immediate memory and contributing to problems with encoding, working memory and information retrieval. Pattern is one of forgetfulness which tends to rebound with cueing.

The frontal subcortical loop connects these midbrain regions to the dorsolateral prefrontal cortex and frequently results in a patchy pattern of deficits involving alertness, initiation, language fluency, speed of information processing, attention regulation and shift of set.

Inability to rapidly manipulate information frequently results in higher order executive problem solving required for planning, sequencing and abstraction. Executive dysfunction can likewise impede memory retrieval, unable to organize a systematic plan for encoding, rehearsing and recalling information. Neuropsychiatric symptoms often reflect executive dyscontrol, including mental inflexibility and perseverative thinking, depression and apathy as well as response disinhibition, loss of tact and emotional lability.

In contrast, preservation of insight as well as anterior temporal lobe abilities involving long term autobiographical memory, verbal reasoning, general knowledge and procedural recall required to perform routine activities of daily living would remain intact, although may be performed a bit slower and less efficiently.

Expect a slow, gradual progressive decline in cognitive function, particularly executive function. As a result could expect decreased efficiency with strategic thinking and dependency in various Independent Activities of Daily Living (IADS), such financial planning and medication management. Course can fluctuate from day to day and throughout the day, with nocturnal exacerbation of confusion.

While individuals diagnosed with Mild Cognitive Impairment or Vascular Cognitive Impairment do not meet criteria for dementia, they can experience significant problems performing functional activities of daily living. Changes which may still be considered “normal for one’s age” can nonetheless result in an inability to drive safely or live independently without assistance.
Rate and progression is generally determined by ability to manage vascular risk factors, such as blood pressure, heart disease and diabetes. Dependent upon degree of ischemic involvement, white matter change can also be noted in the medial temporal lobe, adversely affecting the hippocampus, and resulting in impaired learning and consolidation of information. If poorly controlled, ischemic disease can also result in transient ischemic attack (TIA), stroke, heart attack and/or vascular dementia.

Binswangers Disease

In some cases, the addition of hypotensive disease, associated with smoking, obesity, high cholesterol Type 2 diabetes, coronary artery disease, AF and obstructive sleep apnea can lead to ischemic white matter change in the periventricular region, tending accelerate neuronal loss and overall cognitive slowing. Diffuse periventricular white matter disease as identified on brain MRI can decrease central processing speed and working memory as much as 2 SD from normal age peers. The presence of periventricular region in addition to deep white matter change and lacunar infarcts can result in dense cortical atrophy, the single best indicator of degenerative cortical dementia and can accelerate transition from independent living to residential care.

2. Idiopathic Parkinson’s Disease

Parkinson’s disease is the most common neurodegenerative movement disorder, affecting more than 1 million Americans, and diagnosed at a rate of 60,000 cases a year. Similar to ischemic vascular disease, Parkinson’s disease results in atrophy to the substantia nigra and the depletion of dopamine, a type of neurotransmitter, required for mental initiation and motor movement.

However, the atrophic process is much more dramatic, occurring at a cellular level rather than as a side effect of arteriosclerosis and diminished blood flow. Lewy bodies, composed of abnormal alpha – synuclein proteins, infiltrate the forebrain and brainstem region and result in extrapyramidal symptoms commonly associated with Parkinson’s’ disease. Typical motor problems include resting tremor, psychomotor slowing, cogwheel rigidity and postural instability.

Spectrum Parkinson’s Dementia

It is estimated that 20-60% of Parkinson’s cases will progress to Parkinson’s disease with dementia (PDD). The range of symptoms is dependent upon whether lewy bodies remain localized to the basal ganglia and brainstem region. In this case, presentation resembles more of a vascular dementia with deficits in retrieval and higher order problem solving associated with delays in perceptual processing speed.

Should lewy bodies infiltrate the cerebral cortex of the brain, with the addition of senile plaques and neurofibrillary tangles, then the cognitive presentation resembles the later stages of Alzheimer’s disease. In this case, could expect pronounced spatial motor problems, fluctuations in arousal, amnestic type memory loss, late afternoon confusion, with occasional hallucinations and delusions.

When cortical dementia develops after primary motor disorder and diagnosis of Parkinson’s disease, it is referred to as PDD with cortical lewy bodies. In contrast, the presence of “Parkinsonian” like features, in absence of resting tremor as well as telltale psychotic symptoms that predate cognitive decline, warrant a diagnosis of Lewy Body Dementia (LBD).
However, for all practical purposes, advanced stage PDD with cortical lewy bodies and LBD are much more similar than they are different and for that reason are frequently seen as being on a continuum of a similar disease process rather than as two distinct entities.

**Cognitive Changes Related to Vascular Cognitive Impairment (VCI) and Idiopathic Parkinson’s Disease**

**Software**
Small vessel ischemic disease as well as Parkinson’s disease, is associated with deterioration to the basal ganglia of the brain resulting in physical, mental and behavioral changes. Signs of mental inertia, inattention, delays in speed of information processing, or cognitive slowing, associated with problems in working memory and executive functioning.

**Hardware**
Increase in extrapyramidal symptoms, including lower extremity weakness, imbalance and risk for falls, urinary incontinence and fatigue.

**Memory**
Expect signs of forgetfulness and impaired episodic recall due to mental fatigue while consolidated learning remains generally intact. Procedural learning as well as ability to perform basic activities of daily living is limited by generalized weakness and delays in psychomotor skills.

**Intellectual**
Verbal problem solving, general knowledge, social comprehension and judgment remain generally intact. In contrast, executive function is limited by inattention and results in problems with strategic planning, organization, task monitoring and self-correction.

**Behavior**
Signs of apathy syndrome associated with abulia, lack of motivation, drive and spontaneous problem solving. Presentation may appear similar to depression; however, individuals will deny psychiatric symptoms such as feeling sad, blue, hopeless, despair or tearful. It is important to make this distinction as treatment will involve use of a prefrontal cortex enhancer, such as Aricept or Namenda rather than an antidepressant. Likewise, evidence of reactive anxiety disorder is common, especially in presence of heart disease, with signs of lowered frustration tolerance, marked anxiety and irritability.

**C. Mixed Type Cognitive Changes**
It is well established that the major risk factors for dementia is a combination of ischemic vascular lesions and Alzheimer’s disease. Mixed dementia will result in characteristics shared by cortical type dementias such as Alzheimer’s disease and frontotemporal lobe dementias (FTD), as well as subcortical types such as small vessel ischemic disease, Idiopathic Parkinson’s Disease (IPD) and stroke.
1. Lewy Body Dementia (LBD)

Lewy Body Dementia (LBD) is the second most prevalent form of dementia, preceded by Alzheimer’s disease and followed by vascular dementia. LBD accounts for a full 15-20 % of all diagnosed cases of dementia. Like dementia of the Alzheimer’s type, LBD is associated with abnormal protein deposits in the cerebral cortex and is diagnosed upon autopsy.

While LBD and Idiopathic Parkinson’s disease (IPD) are both associated with abnormal alpha –synuclein proteins or lewy bodies, their location determines the expression of the symptoms. Lewy bodies found in the substantia nigra result in characteristic motor impairments associated with IPD, while their presence in the cerebral cortex increases the risk of Alzheimer’s disease and LBV.

Typical clinical features of LBD include signs of cortical type dementia, “Parkinsonian” like symptoms, prominent visual hallucinations early in the course of the disease as well as extremely poor response to dopamine based antipsychotics. LBD is rarely inherited; however, underlying vascular risk factors have an obvious genetic component. The prevalence of lifestyle diseases such as diabetes and heart disease and severity of extrapyramidal symptoms seems to hasten the rate and progression of the disease.

Cognitive Changes Related to Lewy Body Dementia (LBD)

Software

Expect fluctuating course, associated with autonomic imbalance, hypotension, daytime drowsiness and episodes of abrupt confusion or pseudementia. Rapid changes in arousal level and mental status can be observed throughout the day and from day to day.

Hardware

Like Parkinson’s disease, LBV presents with numerous extrapyramidal or “Parkinsonian” like symptoms, although of a less severe nature. Expect signs of psychomotor slowing, postural imbalance, muscle rigidity, blacking out and repeated falls. Distinguishing features include restless limb movement during sleep, myoclonus, absence of resting tremor, with poor response to dopamine replacement medication.

Behavioral

Expect signs of treatment resistant delirium, prominent delusions and visual hallucinations in as many as 80% of the cases during the early stages of the disease. In contrast, frank psychosis is observed in only 20% of the cases diagnosed with Alzheimer’s, and usually in the advanced stages of the disease.

Another distinguishing characteristic, reality testing or subject awareness remains grossly intact in LBV cases, able to discuss the delusions with some degree of objectivity, which is completely absent in later stages of Alzheimer’s or primary psychotic disorder.

Systemized delusions usually present as non-threatening in nature, such as small children or phantom boarders living in the home and hence the term “boarder delusions”. However, cases can include dark or malevolent delusions, suspiciousness and paranoia. Due to underlying vascular disease, use of typical antipsychotic medications should be expressly avoided. Dopamine based atypical antipsychotics such
Zyprexa and Risperdal may worsen extrapyramidal symptoms as well. Consider small amount of serotonin based antipsychotic such as Seroquel in the evening.

2. Cerebral Amyloid Angiopathy (CAA)

Like ischemic based microvascular degenerative disease, cerebral amyloid angiopathy (CAA) results in vascular inflammation, vessel breakdown and characteristic pattern of microbleeds as visible on brain MRI’s. In addition, CAA can increase the risk of spontaneous intracranial hemorrhage (ICH) in the cerebral and cerebellar regions, as well as in cases associated with head trauma and in combination with medications that clear blocked arteries and reduce chance of blood clots.

In the case of CAA, β-amyloid protein is deposited in the small and medium sized cerebral blood vessels irrigating the cortical and periventricular region of the brain, and can be detected on brain MRI’s by the presence of high T2 signal in the area surrounding the lateral ventricles. In contrast, small vessel ischemic disease is generally localized to the deep white matter, forebrain and brainstem regions, with microbleeds noted in the thalamus, basal ganglia, cerebellum and pons.

Cerebral amyloid angiopathy can be detected in its earliest stages on brain MRI’s by the presence of small microbleeds in the peripheral white matter region, in combination with cortical atrophy, leukomalacia, or softening of the brain, enlarged lateral and third ventricles and sulci. History of spontaneous intracranial hemorrhage resulting subdural hematoma in absence of trauma or hemorrhagic stroke in absence of vascular disease can be a tip off as well.

The prevalence of β-amyloid angiopathy increases with age and is highly associated with the Alzheimer’s APO-E2 / APO-E4 genotype. Early detection and diagnosis of cerebral amyloid angiopathy is critical as a full 90% of patients with confirmed diagnosis of Alzheimer’s dementia demonstrate signs of cerebral amyloid angiopathy upon autopsy. Progression of dementia can be further hastened by the additional presence of ischemic small vessel ischemic disease, TIA and stroke.

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