Perspective

Executive dysfunction, brain aging, and political leadership

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ABSTRACT. **Decision-making is an essential component of executive function, and a critical skill of political leadership. Neuroanatomic localization studies have established the prefrontal cortex as the critical brain site for executive function. In addition to the prefrontal cortex, white matter tracts as well as subcortical brain structures are crucial for optimal executive function. Executive function shows a significant decline beginning at age 60, and this is associated with age-related atrophy of prefrontal cortex, cerebral white matter disease, and cerebral microbleeds. Notably, age-related decline in executive function appears to be a relatively selective cognitive deterioration, generally sparing language and memory function. While an individual may appear to be functioning normally with regard to relatively obvious cognitive functions such as language and memory, that same individual may lack the capacity to integrate these cognitive functions to achieve normal decision-making. From a historical perspective, global decline in cognitive function of political leaders has been alternatively described as a catastrophic event, a slowly progressive deterioration, or a relatively episodic phenomenon. Selective loss of executive function in political leaders is less appreciated, but increased utilization of highly sensitive brain imaging techniques will likely bring greater appreciation to this phenomenon. Former Israeli Prime Minister Ariel Sharon was an example of a political leader with a well-described neurodegenerative condition (cerebral amyloid angiopathy) that creates a neuropathological substrate for executive dysfunction. Based on the known neuroanatomical and neuropathological changes that occur with aging, we should probably assume that a significant proportion of political leaders over the age of 65 have impairment of executive function.**

Key words: Executive function, presidential disability, brain aging, cerebral microbleeds, frontal lobe, prefrontal cortex

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Decision-making is critically important for political leadership, and it might be assumed that this capacity increases as one ages. Indeed, wisdom is generally thought to be a key attribute of older individuals. In the United States, presidential and vice presidential candidates in their late-60s and early-70s have become increasingly common. The negative impact of aging on political leaders is typically viewed from the perspective of either catastrophic illness such as cancer or heart attack, or slowly progressive but fairly obvious deterioration, as seen with Alzheimer's Disease.[1] However, there are alternate scenarios of brain aging and political leadership that are as insidious as they are common. This paper examines a common but relatively unexplored syndrome in the realm of politics: age-related deterioration of decision-making abilities.

From a neuropsychological perspective, decision-making capacity is an essential element of executive function. Executive function is a multifaceted cognitive process that enables goal-directed behavior that integrates and coordinates subordinate cognitive skills, the latter including task and goal selection, task- and self-monitoring, planning and organization, cognitive flexibility, impulse control, and problem solving.[2] Neuroanatomically, the frontal lobes are traditionally viewed as critical to executive function, with particular reference to prefrontal cortex.

A detailed neuroanatomic delineation of executive function is beyond the scope of this paper. However, some basic features should be emphasized. The prefrontal cortex (the far front of the brain) has three major components: orbitofrontal cortex, anterior cingulate cortex, and dorsolateral prefrontal cortex. Orbitofrontal cortex is considered essential for emotion-based decisions, inhibition, and rewards processing, while anterior cingulate cortex is important in assessing conflicting options, and dorsolateral prefrontal cortex integrates information arising from multiple sources.[3] All three regions (orbitofrontal, anterior cingulate, and dorsolateral prefrontal cortex) communicate via cortico-cortical connections (see Figure 1).

While the prefrontal cortex is critically important for executive function, it must be emphasized that connecting fibers (or white matter tracts or pathways) are essential for providing the necessary connections for prefrontal cortex. These white matter tracts are subcortical, that is, below the gray matter (cortex/cortical) surface of the brain. These pathways connect elements of the prefrontal cortex with each other, connect prefrontal cortex with similar structures on the opposite (contralateral) side of the brain, and allow for communication between these prefrontal cortex regions and important subcortical structures such as thalamus, basal ganglia, and cerebellum. Injury to any of these three components (prefrontal cortex, white matter tracts, and key subcortical regions) can impact decision making and lead to executive dysfunction.

Decision-making is thus a complex task, one in which differing perspectives may focus on the underlying neuroanatomy, neuropsychological testing, or neurological illness and its relevant neuropathology. This paper will address these elements, including the common impact of age-related disease of white matter, and offer some historical perspective emphasizing the enduring relevance of the issue to decision-making and political leadership.

Historical perspectives

Historical evidence for isolated impairment of executive functioning is limited. In contrast, the historical record is replete with examples of a more generalized cognitive impairment of political leaders, which would include a decline in decision-making capability. Among these are the cases of at least three American presidents. These illnesses can be categorized as catastrophic, slowly progressive, or episodic.

Catastrophic

President Woodrow Wilson developed severe disability after suffering a major stroke on October 2, 1919 during an American political trip taken to generate support for the League of Nations. Wilson had a history of hypertension dating to at least 1906, and there has been extensive debate in the literature over whether his widely noted rigid and inflexible behavior was a psychologically-driven character trait or a consequence of chronic cerebrovascular disease.[4,5] By the fall of 1919 when Wilson returned from the Paris Peace Talks that followed World War I, he was described as exhausted and complaining of severe headaches; this led both his White House physician, Cary Grayson, and the White House chief of staff, Joseph Tumulty, to strongly recommend that he cancel

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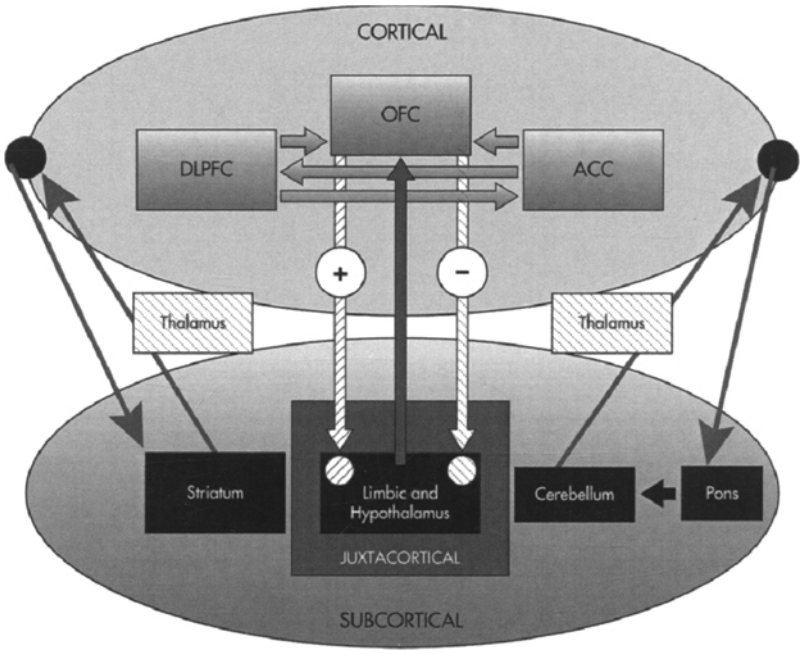


Figure 1. The neuroanatomy of decision-making, with interactions between cortical and subcortical brain regions. OFC: orbitofrontal cortex; ACC: anterior cingulate cortex; DLPFC: dorsolateral prefrontal cortex. Reprinted with permission from Michael H. Rosenbloom, Jeremy D. Schmahmann, and Bruce H. Price, "The functional neuroanatomy of decision-making," *Journal of Neuropsychiatry and Clinical Neurosciences*, 2012, 24:266-277.

his upcoming trip.[6,7] Wilson overrode their objections, and in September began to experience transient stroke symptoms.[8] This was followed, on October 2, by a massive ischemic stroke in the distribution of the right internal carotid artery, resulting in the left side of his body becoming paralyzed and severe speaking difficulties. Wilson was totally incapacitated. During his recuperation only Joseph Tumulty, Grayson, and his Wilson's wife Edith had access to the disabled president and knew the extent of his disability. These three individuals basically made presidential decisions in the name of the President following his stroke.[9]

Slowly progressive

Franklin Delano Roosevelt's battle with poliomyelitis is well known, but it was cerebrovascular disease that led to his death at age 63. Roosevelt's blood pressure was recorded as in the normal range in 1935 but progressively severe hypertension was noted by 1941, with an ominously elevated blood pressure of 188/105 (140/80 is considered normal). By 1944, blood pressure readings were alarmingly high: 230/126 (April), 230/130 (August), and 260/150 (November).[10] Note that in contemporary medical management, these blood pressure readings would be considered in the range for malignant hypertension, a medical emergency warranting hospital admission to the intensive care unit. In addition to stroke and cardiac insufficiency, poorly treated or untreated hypertension puts the patient at high risk for white matter disease and cerebral microbleeds (see below). Roosevelt experienced congestive heart failure and chronic pulmonary disease as a consequence of his hypertension and smoking. He may even have had episodes of hypertensive encephalopathy, consisting of transient periods of major cognitive dysfunction, including frank unresponsiveness.[11]

When President Roosevelt participated in the crucial Yalta summit in early 1945 with British Prime Minister Winston Churchill and Soviet leader Josef Stalin, Churchill's physician Lord Moran was struck by the deterioration in Roosevelt's condition: "The President...sat looking straight ahead with his mouth open, as if he were not taking things in... He intervened very little in the discussions..." Moran commented that "I doubt...whether he is fit for his job here," noting that

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he "has all the symptoms of hardening of the arteries of the brain in an advanced stage."[12] The "sick man of Yalta" died shortly thereafter, of a massive intracerebral hemorrhage.[13]

Episodic

President Ronald Reagan experienced at least two major episodes of transient cognitive dysfunction. The first of these occurred in the aftermath of his attempted assassination in April 1981. Reagan's disability was far greater than publicly acknowledged at the time. The Twenty-Fifth Amendment, which addresses the consequences of Presidential disability, was not invoked, and executive decisions were made by an unelected group of senior political appointees.[14]

When President Ronald Reagan underwent surgery for colon cancer in 1985, the Twenty-Fifth Amendment was again not officially invoked. The surgery lasted nearly three hours, and Reagan was noted to be disoriented upon awakening from the operation. The immediate issue was whether and when the President was competent to resume official duties. Remarkably, the President was not given a mental status examination or any test of cognitive functioning. Rather, he was given a two sentence letter to sign that was drafted by three men, none of whom had a medical background: White House Press Secretary Larry Speakes, White House Counsel Fred Fielding, and Chief of Staff Donald Regan. Some medical input, however minimal, was obtained from the President's attending surgeon, who agreed that this letter was sufficient to determine when Reagan could resume his duties. No other physicians, including the White House medical staff, were involved in this matter, which appears to have been treated as a political decision rather than a medical issue.[15,16] As it turned out, the Iran-Contra scandal developed while Reagan was recovering from surgery.[17]

Neuropsychological features of executive dysfunction

There are numerous methods for identifying deficits in the frontal regions of the brain, including brain imaging and neuropsychological testing. Neuropsychology is a clinical specialty concerned with the cognitive, behavioral, and emotional problems that may arise from known or suspected brain dysfunction. There are well-known neuropsychological testing instruments that focus primarily on the skills that incorporate the cognitive domain of executive functioning. These tests include the Wisconsin Card Sorting Test, the Trail Making Part B, and the Stroop Color/Word Test.

The Wisconsin Card Sorting Test is one of the most utilized measures of executive functioning, with approximately 70 percent of neuropsychologists using this assessment on a frequent basis.[18] This test requires each individual to match *response* cards to four *key* cards that are based on the constructs of color, form, and number. Each individual is required to sort the cards according to these principles. This is a measure of mental flexibility (the ability for an individual to switch when required to complete a task) and problem-solving ability. It has been hypothesized via positron emission tomography (PET) and single photon emission computerized tomography (SPECT) that the Wisconsin Card Sorting Test activates the dorsolateral prefrontal cortex as well as the ventromedial and orbitofrontal cortices.[19] However, other nonfrontal regions have been found to be important when performing this test, including inferior parietal cortex, basal ganglia, temporal-parietal association cortex, and occipital cortices.[20] Individuals who demonstrate difficulty with this test will struggle in moving from one construct to the next, an indication of cognitive rigidity and thus executive dysfunction.

The Trail Making Test Part B is another well-known neuropsychological assessment frequently used to assess executive functioning. This task requires each individual to draw lines from a number to a letter and then to another number, in numerical and alphabetical order. The numbers are spaced randomly across the page. This is a measure of mental flexibility, but in a timed fashion as compared to the Wisconsin Card Sorting Test (which is not timed). Less time required to complete the test and fewer errors are consistent with less difficulty in efficiently switching. This is also a measure of working memory, as the individual is asked to hold and manipulate information very quickly.[21]

Executive dysfunction is also measured using the Stroop Color/Word Test. This is a three-part test, in which each task is divided into 45 seconds. The first task involves reading aloud words that describe colors, but with the words printed in black. For example, the

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individual would read aloud the word *brown* or *purple* printed in black ink, as fast as possible. The second task requires the individual to say aloud the color of an object, e.g., if an item is in the color brown, the individual would be required to say aloud *brown*. The last task, the Stroop Color/Word Test also known as the *Stroop Effect*, requires the individual to say aloud the color of a printed word, rather than reading the word itself; the word is a color, but the color in which the word is printed is different than the word itself. For example, if the word *purple* is printed in brown ink, the individual first sees the word *purple* and may attempt to read the word out loud instead of identifying the color in which the word is printed. For this example, the individual must say aloud *brown,* instead of *purple*. Functional neuroimaging studies find that the anterior cingulate, orbitofrontal cortex, and middle frontal gyrus are important for this task. Moreover, other nonfrontal regions are also implicated for this task, including the parietal and temporal lobe regions.[22]

Aging and executive function

Executive function has been observed to substantially deteriorate after age 60, in otherwise normal and healthy individuals. Notably, this deterioration appears to occur with relative preservation of verbal fluency and memory.[23] Thus, while an individual may appear to be normal from the perspective of overall cognitive function, that same individual may have an impaired ability to integrate basic cognitive skills such as language and memory, in order to achieve normal decision-making capacity. The brain changes underlying these findings are of considerable interest.

Brain volume declines with normal aging, and the frontal lobes are particularly susceptible to this change. Frontal cortex has demonstrably greater volume loss compared with other cortical regions (occipital, parietal, or temporal).[24] This has obvious implications for executive function, which is heavily reliant on prefrontal cortex and its principal connections. And prefrontal cortex has been identified as the specific brain region showing the greatest age-related volume-loss in healthy individuals.[25] The prefrontal cortex is thus considered the brain region most sensitive to the aging process, with volume loss of approximately 5 percent per decade.[26] There is evidence that within the prefrontal cortex, the dorsolateral region may be preferentially affected.[27]

But volume loss of prefrontal cortex is only the beginning of age-related brain changes. White matter changes are demonstrable by brain magnetic resonance imaging (MRI) techniques in more than 95 percent of individuals age 65 or older.[28] The majority of these white matter changes are trivial. However, one-third of subjects in this age group show white matter change of Grades 3-8 (see Figure 2). These changes are not insignificant, and are probably sufficient to be characterized as white matter disease of aging.

There is considerable, if not overwhelming, evidence that presence of white matter disease significantly contributes to executive dysfunction. This has been reported so frequently that there appears to be little reason to question this relationship.[29,30,31,32,33,34,35,36,37,38] The consensus of these reports is that, while other cognitive domains may be involved, executive dysfunction is impacted in a relatively selective manner. The mechanism of effects of white matter disease on executive dysfunction has been linked to disruption of the integrity of neuroanatomic connections within prefrontal cortex or between prefrontal cortex and subcortical structures.[39,40]

Cerebral microbleeds are another feature of brain aging identifiable with brain imaging techniques. Microbleeds are small regions of brain bleeding (microscopic hemorrhages) that have specific MRI features (see Figure 3) and are clearly age-dependent, with prevalence in the general population approaching 20 percent by age 60 and 40 percent by age 80.[41] Microbleeds are often associated with chronic hypertension and the degenerative brain vascular disorder known as cerebral amyloid angiopathy. Importantly, microbleeds and cerebral white matter disease have a strong association, suggesting a common etiology.[42] Cognitive changes have been widely reported with cerebral microbleeds, and relatively selective impairment of executive function appears to be an important feature.[43] As is the case with white matter disease of aging, it appears that microbleeds contribute to disrupted connections of prefrontal cortex.[44]

In summary, there is a substantial decline in executive function after age 60. This deterioration appears to be linked to enhanced age-related volume loss of prefrontal cortex. Notably, white matter disease appears present in about one-third of the population age 65 and older, and is associated with accentuated

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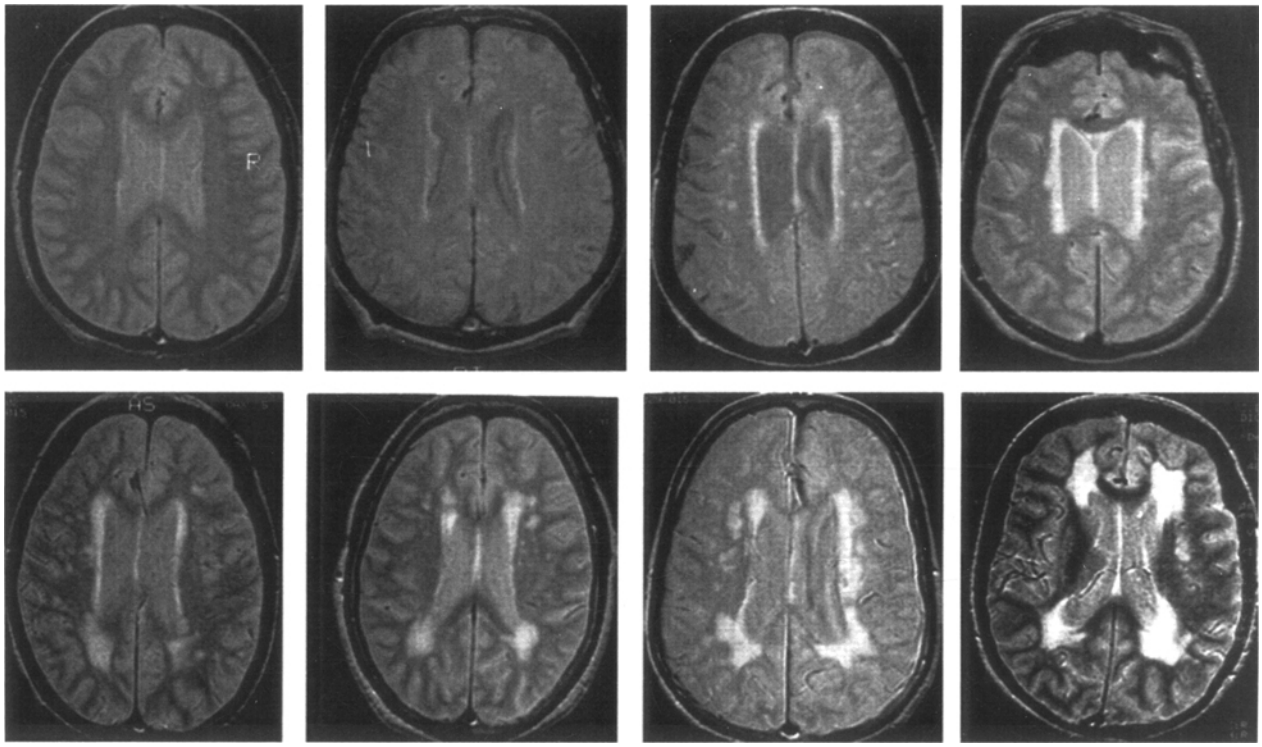


Figure 2. From top left to bottom right, examples of white matter changes Grades 1-8 are illustrated by single slices of magnetic resonance imaging (MRI) from subjects aged 65 and older. Note that Grade 3 (subcortical disease in scattered patches with relatively thick periventricular rim) and above represent 33 percent of the study population. Reprinted with permission from W.T. Longstreth, Jr., Teri A. Manolio, Alice Arnold et al., "Clinical correlates of white matter findings on cranial magnetic resonance imaging of 3301 elderly people. The Cardiovascular Health Study," *Stroke*, 1996, 27:1274-1282.

decline of executive dysfunction. Thus, approximately one-third of the aging population may have increased susceptibility to enhanced deterioration of executive function. Remarkably, this decline appears to be relatively selective, as it can occur with preservation of language, memory, and other cognitive functions, thus resulting in a deficit that may not be obvious. Cerebral microbleeds, strongly associated with white matter disease, also have high age-dependent prevalence and are similarly associated with executive dysfunction. These findings would appear to have implications for decision-making in aged political leaders.

Executive dysfunction and Ariel Sharon

While global deterioration in intellectual functioning of political leaders is fairly well-documented, there is only limited evidence for political leaders having deterioration of executive function. Given the advances in neurological diagnosis and vast improvements in brain imaging capabilities in recent years, this is likely to substantially change as we move forward. A recent and instructive example is the case of former Israeli Prime Minister Ariel Sharon (1928-2014).

From a medical perspective, Sharon was at high risk for developing cognitive impairment in his last few years as Prime Minister. By late 2005, he was obese at 5′ 7" with an estimated weight of at least 260 lbs.[45] In December 2005 he sustained minor stroke symptoms that were thoroughly evaluated, including performance of brain MRI, and a cardiac condition was thought to be the cause. He was placed on anticoagulants (powerful blood thinners) prior to a planned procedure to correct the cardiac condition. However, while on anticoagulants he developed a massive, catastrophic, and ultimately fatal intracerebral hemorrhage. It was

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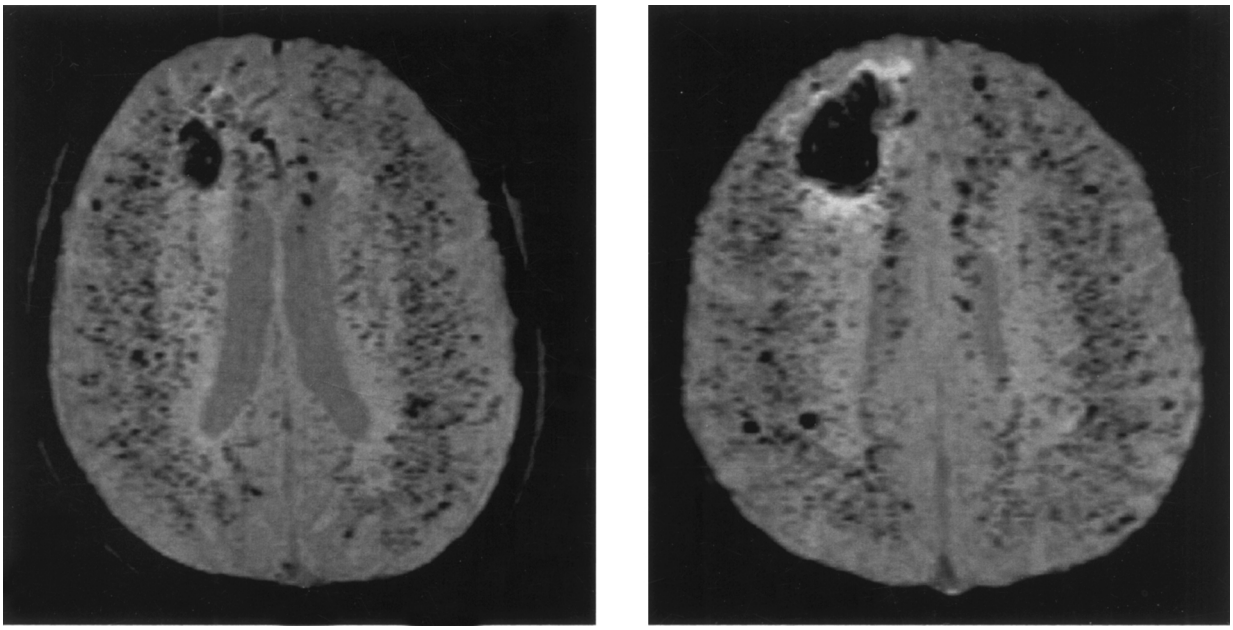


Figure 3. Magnetic resonance imaging (MRI) of cerebral microbleeds in a patient. The many black dots are microbleeds, while the larger lesion in the frontal lobe (top left of image) is an intracerebral hemorrhage.

later revealed that Sharon had cerebral amyloid angiopathy,[46] a degenerative disorder of brain blood vessels that produces extensive cerebral white matter disease and cerebral microbleeds.[47] The latter predisposes one to brain hemorrhage, particularly under conditions of anticoagulation.

Given the presence of Sharon's cerebral amyloid angiopathy, what is the evidence for executive dysfunction? It is notable that during the last years of his political leadership (2003-2006), a notable change was evident in his political decisions. Most prominent was the decision to unilaterally withdraw from the Gaza Strip, a policy at odds even with his own Likud Party. In addition, nearly 10,000 settlers were expelled from Gaza and the West Bank in August 2005. Sharon's political behavior was characterized as an "about-face." He was accused by a former political ally of "undergoing a mutation into a leftist" and that "his moral duty" was to resign.[48]

Of course, we cannot say with assurance how much of Sharon's decision-making during these later years was a manifestation of executive dysfunction due to his underlying cerebral amyloid angiopathy and any related (and presumed) cerebral white matter disease and microbleeds. However, Sharon's change in political direction was notable. One certainly cannot rule out that a cool-headed pragmatism was at work, with Sharon seeking a lasting legacy. However, it seems at least as likely that Sharon's brain disorder had a substantial impact on some of his critical decisions toward the end of his tenure as Prime Minister.

Conclusions

Executive function is a cognitive domain encompassing decision-making capacity and is neuroanatomically based in the prefrontal cortex. White matter connections for elements of the prefrontal cortex provide additional sites for potential disruption. Volumetric analysis has demonstrated that the prefrontal cortex is perhaps the cortical brain region most susceptible to age-related volume loss.

Deterioration of executive function is a prominent feature of aging, and this is associated with prefrontal cortex volume loss as well other features of brain aging. These age-related changes include cerebral white matter disease and cerebral microbleeds, both of which have been associated with relatively selective decline in executive function while sparing language and memory. These brain changes are easily defined by contemporary brain imaging studies, especially magnetic resonance imaging (MRI).

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Deterioration of cognitive function in political leaders is historically well-described, but usually in the context of global cognitive loss such as dementia. These deteriorations may be sudden and catastrophic, as in the massive stroke experienced by President Woodrow Wilson; slowly progressive, as seen in President Franklin Roosevelt; or relatively episodic, as noted in President Ronald Reagan. Each of these historical cases occurred during the pre-MRI era. Former Israeli Prime Minister Ariel Sharon is an example of a political leader who showed major changes in political decision-making while experiencing an important neurodegenerative condition (cerebral amyloid angiopathy) diagnosed by MRI, in which white matter disease and cerebral microbleeds are prominent. The degree to which executive dysfunction was manifest in Sharon's later decisions is unclear. Nevertheless, it appears reasonable to assume that his political decisions were to some degree impacted by his neurological condition. Based on the known neuroanatomic localization of executive function and its well-described age-dependent changes, a significant proportion of political leaders over the age of 65 are likely subject to executive dysfunction.

The practical implications of executive dysfunction in older political leaders are difficult to assess at this point. It is unlikely that political leaders and candidates for high office will routinely submit to neuropsychological testing or subject themselves to brain imaging any time soon. Perhaps the most workable near-term solution is to educate the electorate about this phenomenon, and let the public evaluate candidates accordingly. The relative spontaneity of news conferences and political debates may confer new value on these venues as helpful contexts for assessing a candidate's executive function. An appropriately informed electorate may thus be able to better balance the anticipated wisdom of aging versus age-related deterioration of cognitive functioning.

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