PSYCHOLOGICAL MECHANISMS OF SELF-CONTROL

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THE ROLE OF EXECUTIVE FUNCTION IN NEUROPSYCHOLOGICAL HEALTH AND DISEASE

Consider the constant cognitive work you, and most of the people you know, undertake everyday: scheduling every hour, changing behavioral modes and goals between various involvements, and maneuvering through many different social worlds. All of these tasks require a few key skills. One must be able to redirect one's focus, track useful information, and avoid distractions. In other words, much of our everyday functioning, as well as the occasional extraordinary successes, depends on our capacity to correctly analyze new situations and respond in a controlled manner. These abilities are encompassed by the broad term "executive function" (EF), which refers to working memory, planning, and cognitive flexibility.[1]

Although these are rather complex cognitive skills, they are fundamental to living with purpose, and their dysfunction is nothing short of disastrous for the average cognitively healthy adult. Consequently, executive function is often tracked in cases of neuropsychological disorders. Common tests of executive function challenge the subject to change focus, adjust habitual physical motor responses, correctly respond to conflicting experiences or directions (interference tasks), and focus on long term goals.

One interference task, which takes several forms, is called "set-shifting." Set-shifting requires the subject to switch a goal, and the corresponding set of behavioral responses, in the middle of a task. As this goes against the subject's previous habits, successful completion of the task demands flexible thinking. More specifically, set-shifting tasks force the subject to choose one correct response when presented with cues that would elicit different responses if they appeared separately, thus producing an interference condition. Set-shifting tasks exist for a surprising number of different animals, including humans, rats, and monkeys.

THE ROLE OF THE PREFRONTAL CORTEX

How is it that monkeys can ever successfully complete tests of executive function? The answer lies in brain structure. In primate, and especially human, evolution, the development of one area of the brain particularly stands out: the prefrontal cortex (PFC). The PFC refers to the furthest forward, or "anterior," part of the frontal cortex, located below our foreheads. As we look at various members of the animal kingdom, the complexity of an animal's PFC is inversely related to its evolutionary distance from *Homo sapiens*. That is, the human PFC is more complex than that of other primates - denser with neurons and their interconnections - while the primate PFC is, in turn, more complex than that of other non-human mammals. Meanwhile, mammals are the largest category of animals that have any PFC whatsoever - although some other animals have analogous, but simpler, brain structures. Therefore, it is reasonable

that the PFC is responsible for many of the neurological functions which form the "crucial aspect[s] of what we think of as "human" cognition."[1,4] These include direction of spoken and written language, conscious response to emotions, and various social behaviors, in addition to executive function.[14]

Notably, the PFC is one of the latest brain areas to develop in humans, and the dorsolateral area of the PFC (the DLPFC) is especially delayed in development. The DLPFC is also the most directly implicated anatomical structure in executive function. This correlates to the very slow timeline for cognitive development in humans, where more complex cognitive skills are picked up later on in development. With regards to executive function, a recent study demonstrated that normal adults naturally respond more to tasks which engage their executive functions (EF) than children, while older children respond more than younger ones, indicating that people pay increasing amounts of attention towards tasks that require usage of EF as they grow into adulthood.[13] Some researchers suggest the PFC has a notable role in psychological disorders through its late development and role in executive function.[14]

We know the PFC is involved in executive function partially because its activation is observed, in both humans

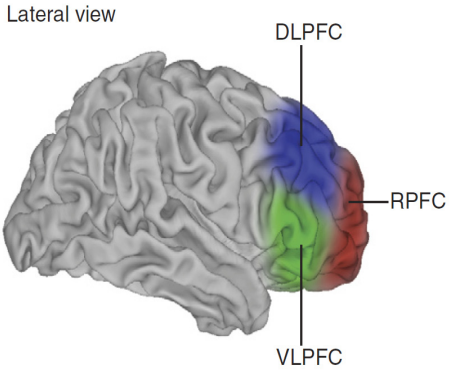

FIgure 1. Anatomy of the prefrontal cortex (PFC) from a lateral (side) view. Dorsolateral PFC (DLPFC), rostral PFC (RPFC), and ventrolateral PFC (VLPFC) are highlighted.

and monkeys, during set-shifting tasks.[10] In monkeys and humans, loss of function in the DLPFC keeps subjects from correctly adapting to "conflict" in behavioral goals, as in the set-shifting task.[10] Other parts of the PFC - rostral (RPFC), ventrolateral (VLPFC), and medial (MPFC) - are also consequential in EF. The VLPFC is related to working memory functions, although not directly responsible. It aids in short-term memory storage before information is called into use to adapt to some situation, and thus moved into working memory.[4] The RPFC seems important to even higher-level processes that may be more specific to humans than non-human primates, such as multitasking or imagining "what other people are thinking," otherwise known as theory of mind.[4] The MPFC contains the anterior cingulate cortex (ACC), which, while still controversial in terms of function,[10] is highly connected to the DLPFC and appears to be related to proper EF, perhaps by helping alert the DLPFC to potential behavioral conflicts.[4] However, the ACC is not as essential to EF as the DLPFC, since human patients with ACC lesions, or damage, still perform adequately on tests like the Wisconsin Card Sorting Test (WCST.)[4,10] Therefore, researchers tend to look at the PFC, especially the DLPFC, and the other brain areas it communicates with most, to better understand disorders marked by deficits in executive function. These include many of the most common and devastating neuropsychological illnesses, from the dementia seen in Alzheimer's patients, disorientation and loss of function in some patients who suffer physical trauma to the head (traumatic brain injury, abbreviated as TBI), and schizophrenia, to various mood disorders, such as bipolar disease and major depression.

AGING AND DEMENTIA

It seems natural to assume that executive function declines along with the rest of human functioning as people age. However, it appears to be so critical that while various contributing neurological functions may decline, one study suggests that the brain adjusts accordingly to maintain at least some healthy executive function. A 2016 study by Dulas and Duarte argues that while older adult humans show a level of dysfunction

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in their DLPFC, they can recruit VLPFC in order to perform similarly to younger adults on tests of executive function, in this case testing their working memory.[3] Dementia is therefore a distinctive phenomenon, rather than purely age-related.

As the researchers Manning and Ducharme describe in their 2010 review, dementia is defined as a "decline in memory and a decline in at least one additional area of cognition including aphasia [inability to cognitively produce or comprehend speech], apraxia [inability to physically produce speech], agnosia [inability to recognize sensory experiences], or a decline in executive functioning."[9] They note that deficits in EF have important consequences for everyday functioning, from planning to self-care.[9] They also argue that more severe cases of Alzheimer's often involve executive dysfunction, meaning it is much harder for patients to take care of themselves when executive dysfunction is present.[9] While it is tempting to think of dementia as a natural part of aging, it is in fact no less a disruption in health and function than other life-threatening diseases, because of the central role of executive function in our lives.

The most common form of dementia is the one that accompanies many cases of Alzheimer's disease. Though the specific mechanisms are not well-understood, this dementia somehow relates to the distinctive neurological characteristics of Alzheimer's. These are primarily various protein aggregates.[9] Tellingly, one of these diagnostic markers is also called senile plaque.[12] Another common manifestation of dementia is vascular dementia (VD), which is as-

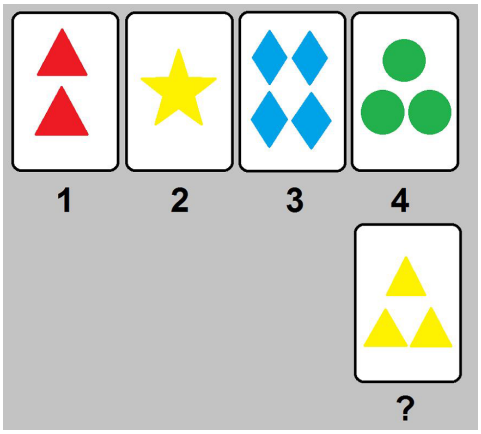

Figure 2. Wisconsin Card Sorting Test.
The card can be matched by shape (1), color (2), or number (4). The subject is told to sort by one rule in the first section, then another in the second. Results from the test are generally used as a proxy for executive function in humans. Variants are also used to test EF in humans and monkeys.

sociated with health events that affect blood flow to parts of the brain, such as stroke. When executive dysfunction appears in VD, it tends to affect patients' capacities for focus and and problem-solving.[9]

TRAUMATIC BRAIN INJURY

Traumatic brain injury (TBI) - injury to the brain resulting from physical trauma - is also associated with executive dysfunction in some cases. Recently, a study showed that TBI patients with at least moderate levels of injury - severe enough to necessitate a caregiver at the time of the study - are worse at comprehending subtleties in spoken language.[1] Specifically, the researchers found it hard to distinguish between direct, indirect, deceitful, and ironic verbal communication. Meanwhile, they do not show a notable difference compared to controls on comprehension of direct verbal communication, where there is little need for cognitive flexibility and applying previous experiences of extralinguistic cues (e.g. sarcasm). The researchers developed the distinction between extralinguistic and direct communication after running a battery of tests on the TBI patients and matched controls, then using a statistical model to evaluate which explanatory variables correlate with the various communicative deficits observed. The model only showed statistically significant correlations between executive function and extralinguistic deficits.[1] They concluded the difference between TBI patients and controls on extralinguistic comprehension is best explained by the state of executive functions in the subject (working memory, planning, and cognitive flexibility), as opposed to lower-level, less conscious forms of cognition, like attention, long-term memory, and theory of mind.[1] One notable scientist, Muriel Lezak, argues that deficits in executive function form the basis for "the most crippling and often the most intractable disorders associated with severe TBI."[8] This is because they tend to affect our self-awareness, which can significantly reduce our abilities to direct and control ourselves, and properly understand and interact with others.[8] It also affects our ability to properly access and apply perceptions and memories to new contexts, which is the basis for correctly responding to new situations. This is demonstrated by the fact that among patients with physical traumas to the nervous system, those with worse executive function after their injuries tended to be less independent in their daily lives a few months after injury.[8]

SCHIZOPHRENIA

Executive function deficits are also characteristic of schizophrenia, which has a strong genetic component and typically takes hold relatively early in life. Some researchers argue that the degree of patients' various deficits in everyday functioning directly correlate to executive dysfunction, such being productive at work, effectively socializing, etc.[7] EF deficits strongly correlate to the "disordered" aspects of schizophrenia.[7] Notably, schizophrenia also tends to be accompanied by altered functioning of the DLPFC and ACC.

Some people are at a higher genetic risk for schizophrenia, meaning they carry some version of at least one gene (an allele) that is correlated with higher risk, and are therefore considered "risk allele" carriers. Risk allele carriers, in addition to people with schizophrenia themselves, show unusual patterns of activation in the ACC and DLPFC, among other areas in the PFC.[14] Interestingly, risk allele carriers also show increased connectivity of the ACC and DLPFC, which authors of a review (Sutcliffe et al.) suggest to be the result of "context-inappropriate hyperfunction" which disrupts regular executive function - for example, paying excessive attention to one situation you should respond to automatically affects your ability to appropriately respond to another, newer one.[14] First-degree non-affected relatives of patients with schizophrenia, although they may or may not carry risk alleles, are statistically more likely to develop schizophrenia than the general population; they have also been found to have similar, but much less severe, cognitive deficits as patients with schizophrenia relative to members of the general population.[6]

While executive dysfunction makes it fairly impossible for patients with schizophrenia to lead normal lives, EF may soon be targeted by drugs that would magnify the effect of two very common and important neurotransmitters, glutamate and dopamine.[2] A study by Desai et al. showed that set-shifting ability was impaired when glutamate and dopamine were inhibited from binding to the NMDA and D1 receptors respectively, using drugs that would compete with the neurotransmitters.[2] Neurotransmitters are small chemicals, produced by neurons, which elicit some response in target neurons through binding. Glutamate and dopamine are both excitatory neurotransmitters for the receptors targeted by these drugs, which means they amplify the function of their target neurons. The researchers believe that defects in both receptors' functions led to the mice being unable to adapt to behavioral conflict, although individual dosages of drugs targeting either function still allowed for adaptation.[2]

Without EF, leading an independent modern life is nearly impossible. However, this makes EF a good target for treatment in many psychological diseases. In humans, a large review of existing research suggests that psychological treatments to restore EF, such as cognitive rehabilitation, can treat some symptoms of schizophrenia.[7] Recent studies in animal models suggest possible pharmaceutical treatment directions as well, especially in

"Set-shifting ability was reduced by the inhibition of glutamate and dopamine binding to the NMDA and D1 receptors."

schizophrenia. Treatment of executive dysfunction is currently a promising and important area of growth in of psychiatry.

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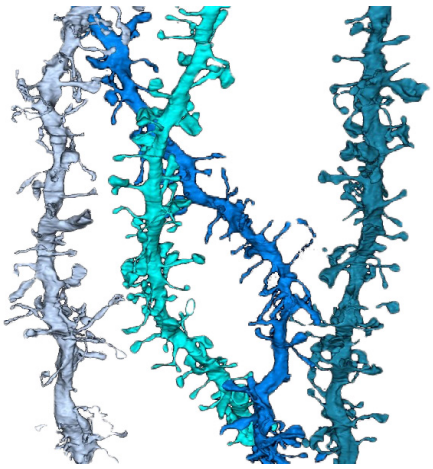

Figure 3. A rendition of dendritic spines, which are points of informational input for neurons. Each protrusion represents one possible synapse, or connection, with another neuron.

IMAGES

Cover. https://i0.wp.com/neurosciencenews.com/files/2016/06/prefrontal-cortex-mood-neurosciencenews.jpg
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