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Treating Executive Dysfunction to Improve Insight in Psychiatric Disorders

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Abstract

Executive dysfunction is not a primary psychiatric diagnosis in DSM 5, but it plays an important role in insight. This in turn determines treatment adherence, relapse prevention and functional improvement. This article shades light into importance of addressing executive dysfunction in treating acute mental illness, in order to improve overall outcome.

INTRODUCTION

Executive Function (EF) is an umbrella term that encompasses a cluster of very important cognitive functions needed for an individual to survive in today's critical world. The expression "Executive Function" became a favored title to describe those functions, because of the complexity and their roles in a person's life e.g. to guide him /her in making everyday decisions, to have goal directed activities, planning & organizing, to be able to adapt to the changes of environment, inhibit impulses and to be socially appropriate (1,4). Executive dysfunction is often used synonymously with frontal lobe deficits, prefrontal syndrome or frontal network syndrome.

The study of the functions of the brain , specially the frontal lobes, attained more attention after the famous railroad accident case of Phineas Gage in 1848, where, Mr. Gage, a young 25 year old healthy male had a penetrating brain injury from a blast. An iron road entered through his left cheek, frontal lobe and exited through his skull. He completely recovered physically following his injuries but was left with serious behavioral changes. Lauria in 1966, used the term "Frontal lobe syndrome" to describe similar symptom executive dysfunction, that was caused by frontal lobe deficit. The term "Executive" was first used by Baddeley in 1986, to describe this array of functions (4). There is no consensus definition of executive functioning and many researchers have described these complex functions in their own definitions but overall, included similar functions.

COMPONENTS OF EXECUTIVE FUNCTION

Several components of EF have been identified by various researchers which include:

- Working Memory
- Response Inhibition
- Set shifting
- Initiation
- Anticipation
- Attention
- Planning & organizing
- Fluency
- Monitoring self or metacognition
- Goal directed activities

Working Memory

Is short term memory, where an individual uses cognitive function to retain information for a short period of time in order to prepare for the next step of decision making, planning and organizing. People with working memory problems have difficulty with attention, decision making, planning and organizing.

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Response Inhibition

Is the ability to hold back on responding in appropriately or impulsively based on previously learned responses, which may not be appropriate at the present scenario. People with difficulty with response inhibition have difficulty ignoring unnecessary external stimuli and become easily distracted and impulsive. Patients may exhibit utilization behaviors (picking up objects with no clear intent), echolalia and echopraxia. (4)

Set Shifting or Flexibility

Is the ability to change one's action and behavior depending on the changes of the environment or circumstances. Deficit in this cognitive function would result in rigidity and perseveration. People with problem with flexibility find difficulty in relationships and socialization.

Initiation

Is an important cognitive function for an individual to thrive in his or her life. Persons with initiation deficits lack motivation to start a planned task. It is often found to be associated with traumatic brain injury.

Anticipation

Is the ability to predict an outcome based on previous experience and the circumstances. Humans have some innate abilities to predict time, place, space, comparability, causality and based on those abilities they are able to anticipate a probability. This is an important cognitive function for decision making and impairment of this ability would cause impaired decision making.

Attention

is the ability to ignore the unwanted external and internal stimuli and to covert unwanted thoughts. It is integral to working memory functioning.

Planning & Organizing

are the higher order cognitive functions where an individual has to have good working memory, anticipation and initiation to put the gathered information into a blueprint to act on. So, we can actually call it a secondary or tertiary level of executive functioning.

Fluency

Is the ability to maximize the production of responses within a specific time period.

Monitoring Self or Metacognition

Is the ability to monitor one's own action or behavior, ability to compare and judge whether or not it is appropriate to the situation or the circumstances.

Goal Directed Activities

The ability to initiate and sustain one's activities as planned and organized. Again this too needs intact other functions like working memory, attention, response inhibition, planning, organizing etc.

PSYCHIATRIC DISORDERS AND EXECUTIVE DYSFUNCTION

Executive dysfunction is found in many psychiatric disorders. The neurodevelopmental disorders like Autism, ADHD, Schizophrenia, Mood disorders, both depression and Bipolar disorder, neurocognitive disorders, Personality disorders like borderline and antisocial personality disorders are associated with executive dysfunction (3).

NEUROBIOLOGY OF EXECUTIVE FUNCTION

Executive functions are delivered like a highly synchronized orchestra with their conductor prefrontal cortex along with areas through their highly developed network system. The brain areas responsible for EF are the prefrontal cortex, parietal cortex, basal ganglia, thalamus and cerebellum and the networks between these areas are crucial for proper EF. (1,5). In order for the executive functions to be delivered properly, the prefrontal cortex continuously monitors and controls other cortical and subcortical areas (6). The controlling of the other areas is done by "Top down mechanism" by which the PFC sends inhibitory signals to the subcortical areas to control their activities. These Top down mechanism of functioning of PFC has been demonstrated by various studies including Trans cranial magnetic imaging studies and fMRI studies (6). By top down action PFC is able to down regulate the overactive limbic system, so called emotional brain, and by this it controls an individual's emotional overreaction.

The executive functions develop parallel to the myelination and synapse formation in the frontal lobes. Executive functions are vulnerable to white matter injury and disturbances in cholinergic, noradrenergic, serotonergic and dopaminergic neurotransmitter systems in the brain (4).

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Dr. Arnsten and colleagues at Yale University have been researching the role of PFC in various cognitive functions and it's molecular biology. The dorsal and lateral PFC networks regulates the attention, thought and action whereas, the ventral and medial PFC networks are associated with emotion regulation and regulation of the physiological state. The abstract thinking is operated by more rostral part of the PFC. The PFC which is a part of the neocortex is composed of six layers of neurons, which are minutely interconnected to form complex neural networks (2). Dr. Patricia Goldman-Rekic from Yale University, a pioneer of PFC research found that the layer III of the PFC expands most during primate evolution and is associated with neuropil loss in schizophrenia. Another important discovery was that Dopamine (DA) inputs in PFC have modulatory effects on dorsolateral PFC and working memory which can be impaired in schizophrenia as a result of impaired DA secretion (7).

Besides DA, Norepinephrine (NE) is also found to be equally important for PFC functioning. NE works via postsynaptic \propto 2A adrenoceptor stimulation (7).

INSIGHT

Insight is a multidimensional construct which is associated with treatment adherence, global functioning and work performance, prognosis and treatment outcome in mental or physical illness. According to the theories of insight, Osatuke and colleagues (2008) stated that lack of insight is associated with the symptoms of illness, impaired theory of mind and neuropsychological deficiencies. There is a significant interest towards lack of insight and neurocognitive deficit in schizophrenia (8). The dimensions of insight was described by Mintz and colleagues in 2003 which are:

- Awareness of having a mental illness
- Awareness of symptoms
- Attribution of the illness
- Awareness of social consequences of having this illness
- Awareness of need for treatment.

In 1991, Amador and colleagues suggested similarities between lack of insight in schizophrenia and neurological condition anosognosia, where an individual is unaware of their own body parts as a result of stroke and is associated with frontal lobe lesion. Amador argued that lack of insight causes inability to self-monitor and self-correct leading to deficit in awareness (Lack of metacognition). People with schizophrenia have poor insight as well as cognitive difficulties. Several studies were done to find relationship of insight and EF, but results have been inconsistent.

NEUROBIOLOGY OF INSIGHT

Studies of neurobiology of insight using fMRI studies have found specific common areas involved in both lack of insight and executive dysfunction, which are PFC, basal ganglia, parietal cortex and limbic areas (9).

IMPROVING EXECUTIVE FUNCTION TO IMPROVE INSIGHT IN ACUTELY ILL PSYCHIATRIC PATIENTS

If we consider insight as a cognitive process and that it shares commonalities with executive function e.g. metacognition, then hypothetically, if we improve executive functioning by improving the PFC functioning, we will also be able to improve insight. Although it may not be as simple as it sounds. Referring to studies done by imminent researchers like Dr. Goldman- Rekik and Dr. Arnsten, who emphasized on importance of postsynaptic \propto 2A adrenoceptors stimulation to improve executive function would be important to consider. Long acting Postsynaptic <2A adrenoceptor agonist Guanfacine has been approved for ADHD in children, which is also used off label for Tourette's syndrome, Traumatic brain injuries with frontal lobe deficits, PTSD and Substance use disorders to improve cognition. This could be a novel way to improve insight.

MEDICATIONS

Medications which are found to help with ADHD also improves executive functions.

Both stimulant and non-stimulant medications are found to improve executive function by improving PFC function. The stimulant medications are mostly amphetamine based and long acting versions of these drugs are used to treat ADHD. Out of the non-stimulant medications Clonidine and Guanfacine are identified to have significant improvement of PFC functions (7).

Clonidine is a $\propto 2$ receptor agonist and reduces the firing of noradrenergic receptors of the Locus coeruleus of the brain stem. This is used to treat hyperactive behaviors related to opiate withdrawal, ADHD, Tourette's syndrome and is found to improve

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the PFC function. Its potential side effect of sedation and lowering of blood pressure can be a hindrance at times and needs frequent monitoring. Guanfacine is a specific agonist of \propto 2A adrenoceptor and was found to improve working memory, attention regulation, and behavioral inhibition. It is more powerful than clonidine in increasing working memory and is weaker than clonidine in producing hypotension. Guanfacine was found to have enhancing effect at the cellular level in the dorsolateral prefrontal cortex, an important area for executive functioning (7).

CONCLUSION

As we are advancing our knowledge of neurobiology of various psychiatric disorders, a neurobiological approach to treat mental illness with evidence based approach is much desired like any other branch of medicine. More research into this area is needed to establish concrete evidence of such hypothesis. Other factors like treating Nutritional deficiency especially low iron and ferritin, psychotherapies e.g. cognitive and mindfulness based therapies alongside medication management will be important to improve executive functioning and possibly insight.

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