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BRAIN EXECUTIVE FUNCTIONS: UNDERSTANDING NEUROLOGICAL AND BIOCHEMICAL RESPONSES TO PROLONGED STRESS AND ANXIETY

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ABSTRACT

Comprehending the mechanisms underpinning neurological and biochemical neuropsychiatric disorders opening new avenues to treatment. Neurochemistry is an essential and practical science within the core of the multi-disciplinary field of neuroscience, who become the foundation for understanding all the mechanisms of brain functions, the biological processes and it explains how neurochemicals influence the operation of neurons. Neuroscience encompasses both a life science and a chemical science. While, neurochemistry is relevant to the scientific basis of neurology and synergy of both discipline, broaden our understanding of the complex interactions of multiple neuronal systems that depend on the fundamental principle that neurons communicate chemically by the activity-dependent secretion of neurotransmitters, that underlie the emergence and rich diversity of cognitive function, regulation and expression of all the biological basis for behavior. Nevertheless, we are looking to understand the impact of stress and anxiety upon executive functions through the lens of the interaction between neurology and biochemistry. What is happening neurologically, biochemically and how we can exert influence or control over how we react psychologically? The mental abilities that converge into the executive functions are vital for formulating tasks, designing strategies, forward planning and implementing the objectives successfully to distinguish the achievements from failures. Rational executive functions require appropriate mental health free from outside pressures, which may compromise rational decisions and may precipitate decision biases especially in fateful issues, resulting in negative outcomes, and "Brain Blindness." Neuropsychological evidence suggests that executive functions are intimately dependent on

intact function of the frontal cortices and surrounding brain processes, acting as a system of independent components, interrelated, but having distinct composition components. Executive dysfunction refers to structural or functional frontal pathology of brain networks comprising the prefrontal cortex (PFC) and its correlations with other brain regions, alteration in the Hypothalamic-Pituitary-Adrenal (HPA) axis and disequilibrium of neurotransmitters in the brain. Hence, decision-making and risk-taking is predicated on normal brain executive function. However, when we are under chronic stress, automatized, leisurely, and quick reactions, minimal cognitive efforts are required to perform unpredictable or uncertain decisions that may predominate over prudence forethought in decision-making processes. In this case the command is under our emotional intuitions in the subcortical emotion regions, triggered by our gain, reward, motivation and prior accumulated information, in contrast to our analytic system located in cortical regions – cognitive abilities –which is suspended. This down-top change in tasks leads to dysfunction of the cortical executive function and leads to decision-making biases. Herein, we are looking to illuminate the neurocircuitry underlying these inconveniences in a hope to understand the mechanisms underpinning these perturbations that provoke changes in our behavioral and exacerbate decision making biases. Neural mechanisms for chronic stress and anxiety and their impact on our executive function, cognitive performance, and our decision-making necessitate intensive researches. Understanding the brain circuits, the neurotransmitters activities under stress and anxiety may increase our knowledge and clarify the paths that we should select, and they may draw lessons for possible medical interventions.

KEYWORDS: Executive functions, cognitive abilities, prefrontal cortex, stress, anxiety, decision making.

INTRODUCTION

Usually humans carry two objectives important for daily life activities: The “Wrist watch” for timing -time management- and the “pen” for writing. These two things are useful for our service, daily regulation, but are also extremely dangerous in terms of uncalculated decisions. When we use pen quickly to sign important documents without taking considerations to the reactions emanating from them and when we ignore the reference to “timing” represented in our wrist watch to draw premeditation decisions promptly, without self-organization across time. Adequate decision-making is in the realm of mature mental abilities located in the prefrontal cortex (PFC).

One of the cardinal functions of the PFC is the elucidation of our daily events, by modulation and mitigation of our reaction to stressful events by managing our stress thereby creating adequate solutions to stressful situations.[1] PFC is the headquarter of executive function, and stress and anxiety are an underlying risk factor for many physical and mental diseases.[2] Our resiliency to stress, or our cognitive resiliency, is our ability to conquer the negative consequences of stress and it is in direct proportion to our strong executive function capabilities.[3] Conversely, our susceptibility to stress is a result of inadequate executive functioning. Additionally, executive function is a neuropsychological Phrase where intellectual capacities converge with previously acquired and learned experiences.[4] Integrity and maturation of executive function areas implicated in executive activity in frontal lobes, especially in the prefrontal areas, are critical for adequate tasks of the executive functions away from illnesses and external stressors.[5]

Executive functions are composed of four distinguished components: fluency, inhibition of potent responses including behavioral control, working memory, and mental set shifting including cognitive and mental flexibility which are tightly linked to creativity.[6] From these high components, executive-cognitive functions emerge and are built. It is worth mentioning, that executive functions encompass a vast array of brain functions that converge in harmony to monitor behaviors indispensable for safeguarding focus and realizing outcomes which are essential for physical and mental health.[7]

A plethora of descriptions were given in the literature to this neuropsychological phrase. Roughly 35 dimensions of executive functions were explored and many theories were canvassed.[8] The mental abilities converging into the executive-cognitive functions are vital for formulating tasks, designing strategies, drawing paths and realizing them, and implementing the objectives successfully.[9]

Rational executive functions require appropriate mental health free from impulsiveness, uncalculated reactions, and external stress, which may compromise rational decisions and may potentiate decision biases especially in issues leading to negative adverse results. Disturbances in executive function brain circuit, leading to accelerated heuristic, temerarious and distorts decisions difficult to fix in post factum. In 2015, Graybiel, Friedman,[10] described the brain circuit underlying normal decision-making. He illustrated that the connection between the PFC and striatum has a crucial role in the creation of normal decision-making under normal circumstances without stress. In the beginning of this

mechanism, high-firing of the interneurons of the PFC are observed, followed by suppression of the striatum neurons. Under stressful events this circuit (PFC - Striatum) works inappropriately, leading to inadequate decision-making.

In this case, one desideratum is to settle and restore the normal behavior and decision-making affected from stressful events which requires decreasing the external stress and restoring the collaboration and enhancing the activity of PFC interneurons. The connections of the brain circuit and brain microcircuit involved in decision-making in the PFC and the normalization of the communication between PFC and striatum by suppressing the overexcited neurons of the striatum are necessary to restore normal brain functioning.[10,11]

Indeed, stress, impulsiveness, disordered thought processes, agitation and tension lead to lack of discipline and a crippling of executive function and accelerated decisions hardly to recover. The interaction between the brain's internal cognitive network processing and behavior, accompanied by the external negative/positive environmental factors, influence negatively or positively the human judgment, proper thinking, and decision-making to achieve a particular goal. Thus, the interplay between peace of mind, psychological comfort and the supportive environment, produces faithful and consonantal cognitive function.[12]

In fact, neuropsychological evidence suggests that intact executive functions are intimately dependent on intact function of the frontal cortices and surrounding brain processes acting as a network of independent components, interrelated, but with distinct composition components. Controversially, executive dysfunction generally refers to structural or functional frontal pathology of brain networks comprising proper functioning of the PFC and its correlations with other brain regions such as the orbitofrontal cortex, amygdala and limbic system.[13] Indeed, the PFC, anatomically located ventrally to the motor and premotor areas, consists of three main regions: Orbitofrontal cortex (OFC), Lateral prefrontal cortex, and basomedial prefrontal cortex that contains the anterior cingulated cortex.[14]

The PFC by its various cortical and subcortical ramifications and connections including thalamic nucleus, ventral striatum and amygdala, by its functional heterogeneity, by its structure complexity make it a center of interest for many researchers as an area that accommodates higher cognitive functions that are superior in humans than in other species.[15] Hence, cognitive abilities including decision-making processes and risk taking is governed by intact brain executive function. In fact, executive functions are an umbrella for a

constellation of cognitive capacities that act in harmony to regulate thoughts, emotions, attention, behaviour, and are responsible for higher-level action monitoring and controlling. These are critical for maintaining a target and achieving the outcomes in adverse circumstances. The efficacy measure of any victorious executive function or high mental skill is a function, or collection, of occurring or context-dependent in terms of intellectual integrity and mental capabilities.

The outcomes of our behaviour depend on the ability of our brain to extort control of its processing from reflexive reactions to the environment in order to direct it toward hidden goals. Nevertheless, executive-function features distinguish the sane human from other creatures, because humans have a highly developed brain, comprised of more than 100 billion neurons and roughly 100 trillion of synapses, divided in left dominant and right non-dominant hemispheres.[16] The unique structural and functional lateralization of the human brain gives it the capability to integrate the functions of both hemispheres in order to enable us to focus our efforts to perform sophisticated complex sequences of behavior, judgment, language production, and problem-solving. These advantages distinguish the human brain from that of other species.[17] Surely, chronic stress is perceived in sensory organs characterized by two main types: A physical stressors which work mainly on the brainstem, and the psychological stressors which disturb the limbic system (Figure 1). Additionally, stress activates two biological systems: the Hypothalamic-Pituitary-Adrenal gland Axis (HPA) and the Autonomic Nervous System (ANS),[18] (Figure 2).

The Hypothalamus releases the peptide hormone [(Corticotrophin-releasing hormone (CRH)], which stimulates the pituitary gland to release Adrenocorticotropic (ACTH) hormone and in turn activates the adrenal medulla to release Catecholamine (Norepinephrine, Epinephrine and Dopamine) and cortisol from the adrenal cortex. Excess production of the catechol-amines negatively influence different brain structures involved in executive function, especially decision-making (Dorsal prefrontal cortex, ventromedial prefrontal cortex, anterior cingulate cortex, striatum, hippocampus and amygdala)[19,20] (Figure 2). In the same context, the high production and long activity of cortisol leads to decreased activity of the orbitofrontal cortex, medial prefrontal cortex, anterior cingulate cortex, and ventrolateral prefrontal cortex (Figure 3). Cortisol, also causes shrinkage in the hippocampus and in the medial prefrontal cortex, and its impact is not limited to the above

structures but also causes hypertrophy and over-activity of the amygdala and orbit-prefrontal cortex.[21-23]

Indeed, stress inverts executive brain functions by bolstering the activity of the subcortical structures on account of the cortical activity (Bottom-top brain circuit instead of top-down brain circuit). These changes, together as a result of stress and anxiety, intervene to compromise our cognitive abilities causing impairment of prefrontal regulation, altering the functions of executive function network and the neural-cycle involved in decision-making in the PFC,[24-27] (Figures 1, 2, 3).

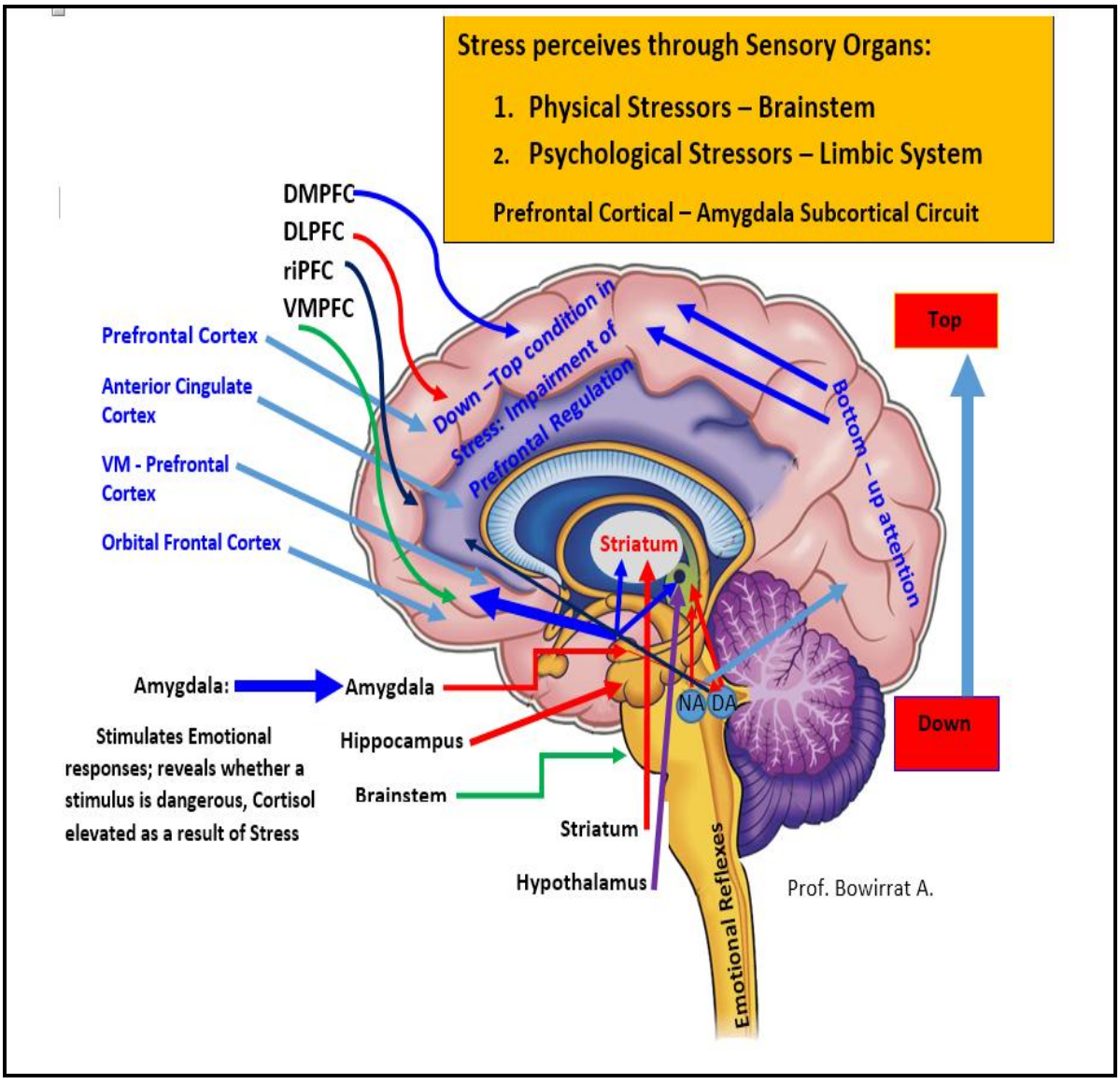

Figure 1: A physical stressors and the psychological stressors which disturb Brainstem and the limbic system respectively. The Cortical and subcortical structures involved in stress and anxiety and their impact on the brain (Bottom-up regulation).

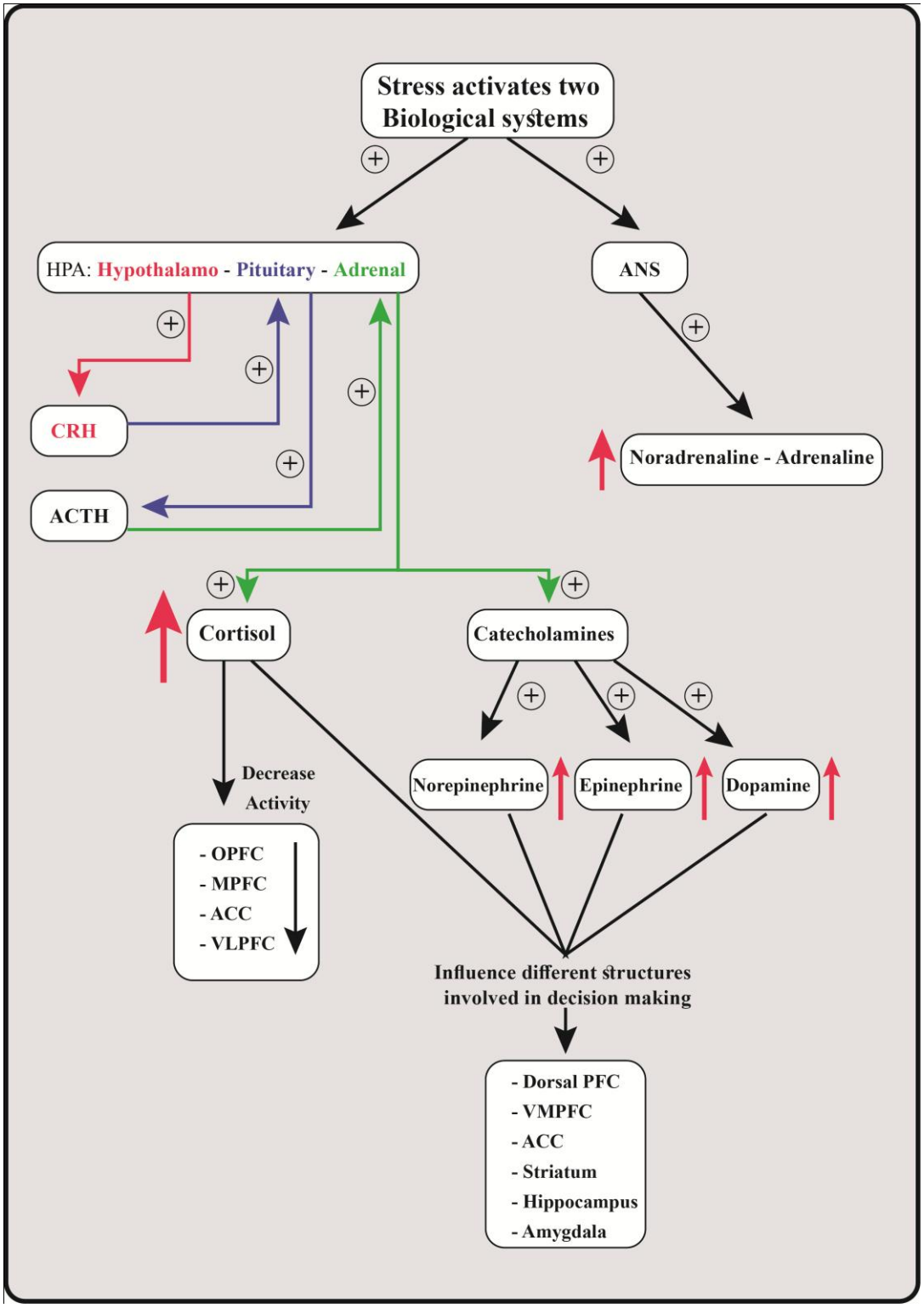

Figure 2: Stress activates two biological systems HPA and ANS. The effect of Catecholamine's and cortisol on different brain structures involved in decision-making.

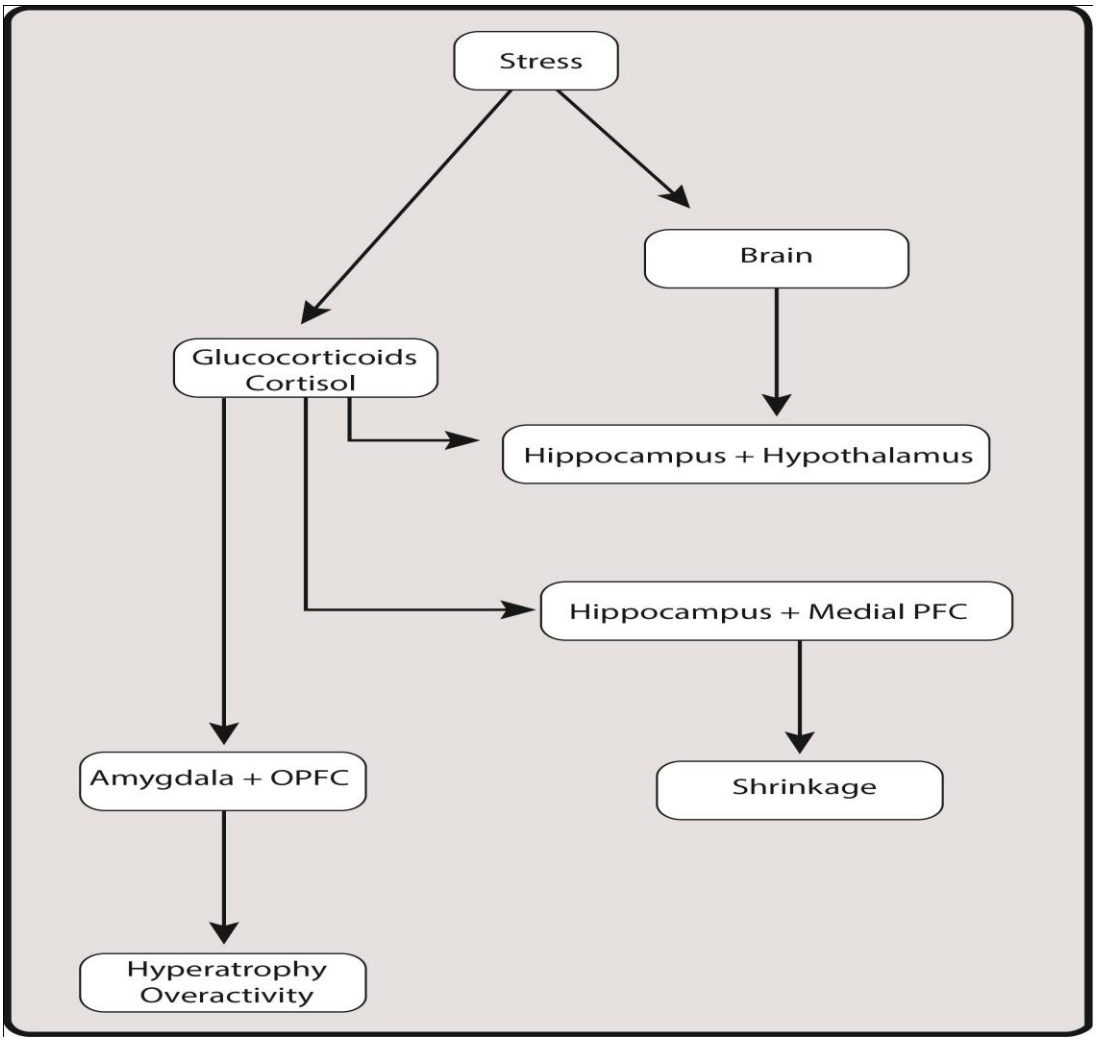

Figure 3: Stress impact on hippocampus, hypothalamus, amygdala and Orbital-prefrontal cortex.

CONCLUSION

‘‘Executive function’’ is a powerful neurocognitive mental capacity that encompasses a vast array of brain functions that work together in converge to monitor behaviors indispensable for safeguarding focus and realizing outcomes. The mental abilities that converge into the executive functions are vital for formulating tasks, designing strategies, forward planning and implementing the objectives successfully to distinguish the achievements from failures.

The link and integration between the brain’s internal cognitive network processing and behavior, accompanied with the external negative/positive environmental factors, influence human judgment, wisdom and decision-making. The cohesion between the brain and the surrounding environment is required for faithful and consonantal cognitive function.

Additionally, the term executive dysfunction generally refers to structural or functional frontal pathology of brain networks comprising the prefrontal cortex (PFC) and its correlations with other brain regions, alteration in the adrenal hormones production and disequilibrium of neurotransmitters in the brain. Hence, decision-making and risk-taking is predicated on normal brain executive function. It is clear that environmental factors influence our decision-making ability.

Here I explore the impact of chronic stress and anxiety upon higher-order cognitive and emotional behaviors. We realize that executive functions demand completeness of a complex neural system and stable internal and external mental environment away from emotional and external stressful events to provide impulsive decisions.

We believe that chronic stress and anxiety potentiate precocious decision-making, impaired cognitive flexibility, and facilitate spontaneous and inappropriate calculations especially in complex tasks. When we are under chronic stress, automatized, leisurely, and quick reactions, minimal cognitive efforts are required to perform unpredictable or uncertain decisions that may predominate over prudence forethought in making decision-making processes. In this case the command is under our emotional intuitions (our innate sensation) in the subcortical emotion regions, triggered by our gain, reward, motivation and prior accumulated information, in contrast to our analytic system located in cortical regions – cognitive abilities –which is suspended. This down-top change in tasks leads to dysfunction of the cortical executive function and leads to decision-making biases.

Stress and anxiety induce an array of psychological, behavioral and physical disturbances originating from internal (mental) or external environment, causing physical, biological and psychological pressure, all of which trigger physiological and behavioral reactions.[28,29]

When stress becomes chronic, its adverse consequences on the body and immune system are accompanied without fail by brain disturbances. Thus, executive malfunctioning as a result of stress will be catastrophically evident, leading to concerned brain structures (Prefrontal cortex, amygdala, and hippocampus regions) to succumb to structural remodeling.[30,32]

As a result of stress, cognitive impairment negatively impacts performance, and decision-making tasks will be impaired due to the continuous release of cortisol from the adrenal cortex into the blood stream.[33,34]

The high concentration of cortisol into the prefrontal cortex leads to its impairment. Indeed, it is a condition of dissonance or a threat to homeostasis.[35]

In this context, other potential player, who conducts disturbances too to the PFC is anxiety. Anxiety occurs without direct physical danger and may be a normal response to fear, its impact on executive function depending on its strength, and its destructive ability is proportional to its magnitude.[36]

In fact, anxiety switches to unpredictable severe phenomenon, thus, out of our control when it becomes a disorder.[37,38] In this stage, individuals with anxiety disorder may already carry overload irrelevant information (sometimes unjustified worries with unknown etiology) and sustained fear that interdict their flexibility to accept new real information or opinions. The loss of concentration, attentional control and intrusive reflections in addition to enhanced distractibility observed among anxious individuals are considered the main features of anxiety disorders.[39]

Intolerable stress and excess anxiety lead in the end to an impairment in cognitive performance, cognitive processes, and emotional processes and decreased executive control to varying degrees.[40]

It is well known that excessive stress (hyper-arousal) and anxiety disorders make their mark and influence on brain functioning in different manners and lead to disturbances in the different anatomical brain structures, neurotransmitters, hormonal changes and finally a change in whole brain circuit. In our time we believe that stressful and anxious events interfere with our capacity to adapt to everyday tasks especially in response to the stresses and demands of the modern word, era of speed and strained life where we are facing a tidal wave of missions. Recently, it dawned on me the importance to illuminate the impact of internal and external factors such as neural circuits, neurochemical and chronic stress and anxiety on higher-order cognitive and emotional behaviors.

Our perspectives are that chronic stress and anxiety precipitate inadequate decision-making and impulsivity via different pathways. We realized that executive functions demands completeness of complex neural systems and calm mental environments to provide necessitate fateful decisions. Protection of our thoughts and behaviors requires moral support, hard ground, and joint work far from the rumblings.

Herein, we illuminate these inconveniences and we designate the neurocircuitry of stress and anxiety and their impact on our mental abilities in the hope to extend the understanding of the mechanisms underpinning these perturbations that provoke changes in our behavioral and exacerbate decision-making biases. This information may increase our knowledge and specifically the path that we should select to restore brain circuitry to its normal way, potentially opening avenues to possible medical interventions.

Conflict of Interest Information

The author have no conflicts of interest to disclose.

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