

Received: 2015.07.29
Accepted: 2015.09.17
Published: 2015.09.30

Depression: Evolutionary New Neural Circuitries Are Still Adjusting for Cognition

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Source of support: Self financing

Depression can be both normal and abnormal, and the balance of its expression determines the behavioral outcome/diagnosis. It is a complex pathophysiology based on a heterogeneous syndrome whose etiology is diverse as well. Within the context of a central nervous system, the nervous system blueprint can be found in single cells (sensory, motor, and integrative processes). These consolidated functions provide for novel coping strategies for survival. The maintenance and evolution of this system into a central nervous system is based on conserving these functions, including chemical messengers and functionality in having specific cells mediate these primordial functions. Additionally, this neural coping strategy provides advantages for DNA. Thus, with different neural cells at work, pathways/networks would evolve, producing more complex behaviors and become a very critical phenomenon for future advances. This evolution has taken over 1 billion years to develop. In so doing, as with any new programming (e.g., cognition), errors will occur. Given the widespread qualities of depression, it is surmised that this abnormality, and other psychiatric disorders, may emerge due to inherent neural weaknesses related to cognition being a recent evolutionary development.

MeSH Keywords: **Depression • Evolution, Molecular • Molecular Biology • Repetitive Sequences, Nucleic Acid • Serotonin**

Full-text PDF: <http://www.basic.medscimonit.com/abstract/index/idArt/895991>

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Background

Depression is a mental disorder that is characterized by persistent feelings of sadness and loss of interest [1,2]. It is associated with significant life-long consequences. It affects how you feel, think, and behave and it can lead to disturbances of daily habits (e.g., work). Interestingly, women are more susceptible to depression. The complexity of depression is demonstrated by the existence of a variety of factors involved in this disorder, such as biological (e.g., genetic) [3,4] differences and brain chemistry (i.e., neurotransmitters, hormones, decreased serotonin levels in the blood, and last, but not least, a person's genes) [2,5]. There are many factors that seem to increase the risk of triggering depression as well, including low self-esteem, traumatic/stressful events, drugs, alcohol, and other mental health disorders [2].

Untreated depression can lead to eating problems, such as obesity, which in turn can lead to consequences such as heart disease and type 2 diabetes, social isolation, suicide attempts, and alcohol abuse [2,6]. Also, with this condition, there are elements of an inflammatory response, as noted by an increased level of pro-inflammatory cytokines such as interleukin-1 α , tumor necrosis factor- α , and interleukin-6 [2,5].

There are, as can now be expected, different types of depression: major depressive disorder (also known as unipolar depression), bipolar disorder, psychotic depression, postpartum depression, and seasonal affective disorder. The major pathophysiological basis for depression appears to be a depletion of the neurotransmitters serotonin, norepinephrine, or dopamine in the central nervous system [2]. In this regard, serotonin emerges as the main neurotransmitter in depression, where it is significantly reduced. Levels of dopamine metabolites are consistently reduced in depression, suggesting decreased dopamine turnover.

Finally, genetic factors play a major role in depression, with 30–40% of these patients exhibiting genetic symptoms [3,4]. The studies revealed a 40–50% prevalence of depression in monozygotic twins and 25% in dizygotic twins. The risk of having depression between first-degree relatives is 10–25%. There is a correlation between greater family burden and the earlier onset of a disease [3,6]. There are tens of genes involved in predisposition to depression, interacting with one another and with the environment. Thus, a pattern of specific gene expression appears to be responsible for depression. Clearly, the factors noted earlier support a multiple gene expression pattern in this disorder, given all of its variations and associations.

Discussion

Multicellular animals, in general, require a nervous system to mediate reproduction and food acquisition, which are major

survival strategies for hunters. The fundamental characteristics of the human central nervous system can be found in single cells, such that they have sensory and motor mechanisms that are appropriate (integrated) [7,8]. Clearly, even at the single-cell level, a nervous system blueprint, as just noted, provides for novel coping strategies for surviving. Indeed, multicellular organisms evolved in such a manner that their cells could differentiate a common functional morphology into specialized cells (e.g., nervous tissues). Here too, allowing the system to further evolve, was its chemical communication system and impulse generator, which operates by way of conformational matching, retaining chemical signaling, once evolved, and thus further developing the blueprint [9]. Importantly, given the magnitude of the cellular chemical messenger presence, it is unlikely that evolution will generate another chemical messenger system [10].

Cellular chemical communication was so effective that the next stage of evolutionary change in the nervous system involved generating intra-nervous system networking/pathways, which further advanced the coping strategy of endowed animals by providing a mechanism that was ever more sophisticated, rapid, and efficient in its performance. Additionally, by its very nature, further novel development of behaviors is possible. This sophistication allowed animals to remain in complex and difficult environments, exhibiting different behavioral attributes for specific coping strategies. This level of sophistication is so intricate that it can mask the basic original life objectives: reproduction (e.g., DNA) and food acquisition for survival of the species. Clearly, given its commonality, the origin of the “signal” must be in DNA [11].

It is important to note, we surmise, that novel networking is an ongoing phenomenon. Additionally, at the cutting-edge of this novel networking is the newly created (comparatively speaking) function of cognition in humans. This enables a whole series of other behaviors to emerge that can now be incorporated into a single phenomenon – the mind – all within the realm of an organism's control. Just unto itself, this was truly an amazing outcome; however, with its newly evolved internal constructs, there may be major problems (e.g., depression) given its newly created state in the long process of evolution [12–16].

One may also argue that if cognition is such a powerful evolutionary, revolutionizing tool, why have there not been other species exhibiting this phenomenon? The answer may lie in the first emergence of this phenomenon, in that it actively prohibited cognition from emerging in other species by eliminating them as a perceived threat. The elimination of cognitive competitors can be ascertained from our preference for having basically docile domestic and commercialized animals. Outliers from this behavioral characteristic are not tolerated

and in actuality may be difficult to deal with. In achieving dominance in our evolution, the competitors of *Homo sapiens* were eliminated. We speculate that the need for the emergence of a single high-level cognitive species is similar to that for having a single mind in brain evolution, which can organize the functions of a single organism without impairing survival. This is opposed to having multiple “minds”, which is regarded as pathological since a dysfunctional person exhibiting this phenomenon could not function in our environment.

We further surmise that a singularity of mind must be one constructed on the foundation of superiority. That is, in an individual there is a “force” that demands that one is always right and others are wrong. This deception can be a driving force in evolution because it is powerfully motivating [17–19]. Hence, the phenomenon of humans killing humans, despite creating sophisticated technologies, is hard to diminish because it is part of the cognitive evolutionary story. In the end, DNA, the selfish gene, wins, regardless of who has it and their desires to advance [11]. This critical phenomenon of superiority obviously has been retained in evolution and resides at the DNA level, insuring its success.

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Conclusions

Depression can be both normal and abnormal and the balance of its expression determines the behavioral outcome/diagnosis. It is a complex pathophysiology based on a heterogeneous syndrome whose etiology is also complex. In keeping with the focus of this mini-review, recent state-of-the-art technologies have revealed this condition may arise from poorly adapted neural circuitries. In part, these circuits are also implicated in coping with stress, sharing commonalities as noted by the co-morbidities. Given the many triggers of depression, behavioral process associations, and definitions, it becomes apparent that the pathophysiological problem is one of malfunction of both chemical neuro-signaling and pathway dynamics. We speculate that this abnormality, as well as other disorders (e.g., schizophrenia), might be occurring because of the “newness” of cognition in humans. The pathways that have been developed in this regard are complex, having errors in their expression due to their newness, which suggests they are still evolving.

Acknowledgments

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