

Schizophrenia Symptomatology: Explaining the Role of Dopamine and its Etiological Significance

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ABSTRACT

A previously atypical symptom report of a hospitalized patient experiencing unusual visual broadcasting has been documented but has received minimal attention in the research and clinical field of psychiatry. A preliminary hypothesis is proposed of an implicit mechanism of motivation for action and emotional relief functional significance of elevated cortisol and dopamine correlation, that is loosely based on the concept of stress-induced psychosis and which could have led to a concurrent "visual and thought" psychotic episode. In addition, the implication of the effect of increased dopamine on intracranial pressure and indirectly on cerebral perfusion pressure is briefly discussed. A follow-up on the insight and comprehensive understanding of such atypical and novel symptom as an extension of schizophrenia is warranted.

ETIOLOGICAL SIGNIFICANCE

The concept of stress-induced psychosis could be considered to address a potential causality that links concurrent upsurge in dopamine release as an opposing response to high-intensity emotional and mental distress. The rare symptom of visual broadcasting in the patient above progressed from that of thought broadcasting and persecutory delusions of schizophrenia. Elevated level of cortisol has long been a typical outcome of stressful life experiences, which logically do not exclude severe delusional psychotic symptoms. Based on evidence of a positive correlational relationship between cortisol and dopamine release in human subjects, research should attempt to answer the question of a conceptual likelihood of whether the more cortisol is produced in the body during intense stress, the more dopamine would be released in excess as a functional and motivational response to act on countering the ill effects of cortisol [2,3]. On the other hand, the potential emotional relieving benefit of dopamine in response to stress-induced cortisol increase could be implied from a study by Hamidovic and colleagues who reported positive correlation between elevated cortisol following performance of a stressful task by healthy subjects and positive mood induced by administration of amphetamine [4]. As amphetamine has been known to increase dopamine concentrations in a number of studies, this correlation points to an intimate relationship between cortisol and dopamine that is both complementary and counteracting which could potentially affect vulnerable healthy human individuals [5-8]. Such correlational release may be functional in the manner that there is

an underlying purpose to oppose or deliberately reduce the negative valenced emotional outcome of increased cortisol through the promotion of action-oriented motivational response and positive mood induction by dopamine which could have unfortunately spiraled excessively to culminate in a psychotic episode.

Rothschild and colleagues [9] once reported in their study that the levels of plasma free dopamine in their unmedicated human subjects were considerably 3-4 times higher after two administrations of a small dose dexamethasone than immediately before administrations in the morning and evening, offering hints of support to their explanation that corticosteroids such as dexamethasone may increase dopamine and subsequently produce psychotic experiences in unmedicated individuals. Although the underlying association between increased plasma dopamine and its corresponding release in the brain is open to investigation, the finding of depressed individuals with higher cortisol levels being prone to psychosis warrants consideration of its significance in a deeper understanding of the etiology of schizophrenia. This conjecture de-emphasises geneticism as a sole reasoning basis for the causation and challenged stability of traditional prevalence rates of schizophrenia in current societies [10,11]. In addition, it also helps shed light on an alternative target of intervention for stress-induced psychosis, i.e. cortisol other than dopamine D2 receptors, through cognitive and emotional stress regulation channel. Perhaps, cortisol and dopamine have mutual functional significance which is intimately linked in the event of acute stress to provide emotional and physiological regulation outcomes for

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an individual. Therefore, studies show that antipsychotics affect both cortisol and dopamine levels in the body in that there was reduction in salivary and serum cortisol levels after treatment [12,13]. Such could suggest an answer to the question why psychosis tends to manifest its first episode during late teens and early twenties in the youth population. During this critical period of transition in a young individual's life, peer pressure, high school to university environmental and performance demands and complex relationship changes all combined to induce heavy stress on a highly constrained cerebral space of the brain which may still be developing onward to full maturity. It gives even more reason to say that this particularly sensitive age window during one's youth in life leaves wide open an individual's vulnerability to psychotic manifestation. Therefore, heavy educational and social demands placed on a sensitive brain over this burdensome transitional period in life have a significant role to play in the etiology and development of first psychotic episode in youth. The likelihood that cortisol functions as a "precursor" status leading to an upsurge of dopamine to produce psychotic episodes which are stress-induced cannot be ruled out. With respect to the latent motivational consequence(s) of dopamine upsurge during psychosis in response to stress induction, it should be noted that one of the negative effects on the health of increased levels of cortisol is tissue inflammation, and there have been indications that dopamine could potentially lower inflammation based on its varied immunomodulatory functions on a short-term basis [14]. Dopamine also has an anti-inflammatory role which is still under-explored. In one mice model study, the activation of dopamine D2 receptors by agonists suppressed neuroinflammation and ameliorated brain edema [15]. Although pro-inflammatory markers have been shown to be elevated in schizophrenic individuals, it is still questionable whether there is a direct causality link between excessive dopaminergic activity and inflammation in the brain, as opposed to be attributed to invasive pathogenic substances [16].

VISUAL SENSORY ASSOCIATION

The precedence of pre-existing paranoia and thought disturbances in the above mentioned patient [1], presumably induced by excessive dopaminergic activity, could potentially indicate a spreading of psychotic disturbances to the sensory and perceptual domains, based on consideration of the symptom of thought broadcasting concurrently experienced. Research has discovered the presence of specific population of D1/ D2 receptors in the retinal cells, which brings us to question the extent to which dopaminergic receptors beyond the mesolimbic reward pathways could present vulnerability to psychotic disturbances due to structural and functional similarities shared between same classes of receptors [21,22]. Reports of low cortical signal-to-noise ratio in schizophrenia simply indicates that there is extensive background noise neurotransmission occurring within cortical networks which lends to a form of activity-caused burden on intracerebral space [23]. Whether this might lead to a form of outward-directed "diffusion" of neurochemical activity in reality, as described by this patient who experienced visual broadcasting symptom, in order to ease the distressing burden on intracranial spatial limitation remains to be further investigated. On the other hand, there is also the question of how the retinal cells connect with the population of receptors in

the visual association cortex to affect one's perceptual and cognitive distortions, which should be considered for future research.

DISCUSSION

The above suggested mechanism of connective pathway(s) between visual sensory and perceptual cognition hints at a highly integrated and connected neural system consolidating both central and peripheral networks. In addition, there could be an underlying latent synchronization of dopaminergic activity at play on a global scale as opposed to concentrating on localised units, rendering a simultaneous manifestation of "visual and thought" psychotic episode, just like how increased plasma free dopamine is associated with frequent psychotic disturbances in subjects administered dexamethasone [9]. Intuitively, if such distinct symptom can be categorised as sensory/perceptual distortion, the neural processing involved could be undergoing a reversal in direction based on the patient's account that the real-life images he saw were "diffused and transmitted" outwardly in that the process of visual perception was being directed in a contra- or opposing pattern that has surpassed the boundary of normality. As long as dopaminergic receptors are present and distributed in a system, there exists the likelihood of "sensory psychotic" processing to be induced such observations should encourage the opportunity to reassess the potential sensory role of dopamine beyond reward, learning and memory. Although research on dopaminergic involvement is mostly concentrated on the inner brain's mesolimbic reward pathways, the actual mechanism of action of D2 type receptors, which primarily contribute to psychotic disturbances, cannot be ruled out on peripheral populations of D2 receptors elsewhere that bear similar neurochemical and structural makeup. It would certainly be beneficial if the authors could share further detail on the course of medication which has helped alleviate this symptom of the patient in the article, thus potentially offering positive hope for others who could have been affected but are suffering in silence and isolation to maintain privacy in symptom disclosure. In addition, an interactive process of comfort and assurance by the attending psychiatrist that is patient-centred and focused could potentially hasten recovery if utilised to a greater degree than currently in place in most institutions.

CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

AUTHOR CONTRIBUTIONS

RK contributed to the idea, concept, preparation, writing and editing of article content.

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