THE RELEVANCE OF MOTIVATION IN SCHIZOPHRENIA

Review Article

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Abstract: Lately there is a growing interest in the negative symptoms in schizophrenia and their mechanisms of action, with special focus on the motivation process. The lack of motivation is increasingly recognized to be a very important impediment to positive management in schizophrenic pathology. In this mini-review, we described the current understanding of the nature and causes of the specific motivational deficits in schizophrenia in order to find better management strategies for this heterogeneous disorder.

All the data and theories presented here clearly demonstrate that amotivation is a fundamental aspect of the negative symptomatology in schizophrenia and could represent a useful factor in understanding and improving the mechanisms and further management of schizophrenia.

Key words: motivation; schizophrenia; cognition

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INTRODUCTION

The relevance of motivation in the management of schizophrenia

As is well known, the pathological manifestations in schizophrenia can be expressed as positive symptoms, which are classically referred to as psychotic behaviors, hallucinations, delusions, disorganized speech or behavior, and negative symptoms such as reduced facial expressiveness, anhedonia (pathological lack of pleasure) and the loss of personal motivation (Antonova et al., 2004).

There is increased interest in the negative symptoms of schizophrenia and their neuronal and mechanistic bases, with special focus on the motivation process. This is because amotivation is increasingly recognized to be a fundamental impediment to good and positive management of patients with schizophrenia (Medalia and Brekke, 2010). As we will show in this mini-review, the motivation process in schizophrenia is modifiable, which makes it an important target for treatment and schizophrenic management application.

Motivation could represent a fundamental treatment and interventional avenue in schizophrenia, considering its adaptive nature in this disorder and its relevance in designing new management approaches, especially since these patients are often characterized by a decreased motivation in participating in treatment and learning activities, including forgetting to take medication or perform important assignments (Medalia et al., 2008; Choi et al., 2010).

Considering schizophrenia could be considered an impairment of wanting, with motivation being a fundamental negative symptom that is well correlated with the poor management of schizophrenia,
it is important to understand the nature and causes of this motivational impairment, which could result in better strategies to enhance management motivation and engage patients in the process of recovery (Medalia and Brekke, 2010; Barch and Dowd, 2010). However, although motivation deficits are important in schizophrenia, very little is known about the underlying mechanisms of motivational processes and the relevance of their mechanisms in this very complex disorder (Gard et al., 2014). In this review, we will try to describe the current understanding of the nature and causes of specific motivational deficits in schizophrenia in order to find better management strategies in this heterogeneous disorder.

Current knowledge and the main mechanisms of motivational processes in schizophrenia

As defined by Medina et al. (2010), motivation represents the processes where various activities are sustained and can be thought of as the product of a complex interaction between a variety of physiological and mechanistic processes, combined with other social aspects, which are not relevant for us in the present research context. Our interest is focused on the mechanisms implicated in the motivation process in schizophrenia and how understanding these mechanisms will result in its better management. Since motivation could be considered one of the most important triggers of the reactions of the main biological behaviors, lately there is an increased interest in the biomedical applications of studying motivational processes, with a multitude of recent studies referring to the relevance of the motivation in human behavior (Woody and Szechtmaman 2013; Van Dijk et al., 2013; Burris et al., 2013; Baeten et al., 2013).

The main mechanisms and physiological processes implicated in the motivational modifications in schizophrenia, and their anatomical support, are the main prefrontal and subcortical mesolimbic dopamine systems and their fundamental role in this area of research, which were described by Barch and Dowd in 2010 (they even suggested a prefrontal-striatal interaction modulating these aspects).

The main motivation deficiencies in schizophrenia are connected to dopaminergic neurotransmission, including several other areas, such as the midbrain dopamine system, orbitofrontal, anterior cingulate and dorsolateral prefrontal cortices (Barch and Dowd, 2010). It seems that the midbrain dopaminergic systems and their projections to the ventral and dorsal striatal regions of the basal ganglia are very important in motivational processes, especially the substantia nigra and the ventral tegmental area that are implicated in predicting reward processes (Schultz et al., 2007). We previously demonstrated in rats that lesions in both areas results in significant memory deficits, as seen in the performance of behavioral tasks included mazes based on food reward, an eight arm radial maze, while also demonstrating the relevance of oxidative stress status (Hritcu et al., 2008). Some reports state that not only the dopaminergic system is implicated in motivation responses in schizophrenia, since it was shown that a decrease in central dopamine concentrations does not automatically result in the reduction of motivation or enjoyment, as determined through specific facial expression measurements (Berridge et al., 2004).

It seems that GABAergic and opioid neurotransmission are also implicated in motivational aspects of schizophrenia. GABA transmission in the nucleus accumbens, which is a collection of neurons that form the main part of the ventral striatum, seems to be very important, as well as its projections into the ventral pallidum and the orbital-frontal cortex (Barch and Dowd, 2010; Collins et al., 2005). The importance of the nucleus accumbens in this context could be explained by its fundamental roles in the so-called decision-making behavior and its modulation of various reward, pleasure, laughter, addiction, aggression and fear manifestations (Reynolds et al., 2002). Our research group studied the effects of a 6-ODA-induced lesion in the nucleus accumbens, which is also known as an important dopaminergic structure, on a specific behavioral task involving both short-term and long-term spatial memory (the 8 arm radial maze task), as well as on the oxidative stress markers (two antioxidant enzymes: superoxide dismutase plus glutathione peroxidase and a lipid peroxidation marker
− malondialdehyde). Our results showed some significant effects of this lesion on reference memory errors and time necessary to finish the 8 arm radial maze task. Additionally, increased oxidative stress status was demonstrated in the temporal lobe of the lesioned rats, as demonstrated by the high levels of lipid peroxidation and decreased total antioxidant status. Significant correlations were reported here between the behavioral parameters that we studied in the 8 arm radial maze and the aforementioned oxidative stress markers (Lefter et al., 2013).

Regarding the relevance of the accumbens nucleus in schizophrenia and motivation, we have to mention the connections between this nucleus and the dorsal anterior cingulate cortex, which appears to be implicated in behavior related to the effort associated with rewards and outcomes, since its lesion in animal models will result in specific behavior manifestations, as defined by the choosing of an low efforts + low reward option vs. an higher reward + higher effort behavior (Barch and Dowd, 2010).

Since we also mentioned the relevance of the oxidative stress status in this context, which is an imbalance between the systemic reactive oxygen species concentration vs. the biological system’s antioxidants (Bild et al., 2013), it should be remembered that there are also several very recent reports describing an important correlation between the motivation process and oxidative stress status (Johnson et al., 2013). In addition, it is known that oxidative stress could be heavily implicated in the pathology of schizophrenia, as our research group also previously showed (Ciobica et al., 2011; Padurariu et al., 2010). It seems there could a very strong and relevant interaction between motivation, schizophrenia and oxidative stress status.

Another important mechanistic role in motivational deficiencies in schizophrenia could that of the striatum and its connection to reward prediction behavior (Medalia et al., 2010). A recent paper by Strauss et al. (2014) described reward processing and motivational impairments in schizophrenia as mainly due to the dopamine-mediated networks from the basal ganglia connected to reinforced memory and learning processes, the orbitofrontal cortex, implicated in reward and value engrams, the anterior cingulate cortex and midbrain dopaminergic-mediated areas, as well as prefrontal cortex areas that are known to be connected to motivational and exploratory behavior (Strauss et al, 2014).

**The interactions between motivation and cognitive processes in schizophrenia**

Lately there is an increased interest in understanding how cognitive impairments (which are quite well known in schizophrenia and will be described) interact with reward and motivation systems in schizophrenia (Barch et al., 2010; Choi et al., 2010). This could be quite important, as cognitive deficits in schizophrenia mainly refer to deficiencies in memory, attention, motor skills, executive function or intelligence, with cognitive impairment often preceding the illness and being related to the social and functional outcome of the patient (O’Carrol et al., 2000).

Interactions between motivation and cognition in schizophrenia seem quite important, since there are reports stating that motivation could actually modulate the relationship between cognition and general functioning (Nakagami et al., 2008; Medalia et al., 2010). It seems that the interaction between amotivation and poor cognitive processing in schizophrenia could be relevant to the management of this disorder, since, as previously mentioned, cognitive and memory deficits seem to have a very important role in the pathology of schizophrenia. The connection between these two aspects could be explained by the fact that it was previously shown that a limited working memory status results in a reduced capacity to mediate between multiple goals and has been linked to reduced motivation (Medalia et al., 2010).

This interaction between motivation and cognition in schizophrenics was studied by Choi et al. (2010), who, by using 57 patients with schizophrenia or schizoaffective disorder, showed that the use of various motivational techniques could actually increase learning and attention in these patients. It would appear that therapeutics targeting intrinsic
motivation for cognitive tasks could result in the better management of schizophrenia (Choi et al., 2010). In a study published in Schizophrenia Research, Nakagami et al. (2008) demonstrated on 120 schizophrenic patients an important interaction between intrinsic motivation and neurocognition by using specific psychosocial measurements (Nagakami et al., 2008). In addition, Silverstein et al. (2010) showed an important correlation between extrinsic motivation and cognitive remediation in schizophrenia. This connection between the decreased motivational processes in schizophrenia and the altered cognitive status of this disorder could be explained by the fact that the same mechanisms leading to cognitive deficits in schizophrenia also contribute to the lack of pleasure and motivation (Green et al., 2004). Thus, it seems reasonable that treatments designed to improve the cognitive manifestations in schizophrenia could also help the motivational processes, with an increased impact on future management of schizophrenic patients (Barch et al., 2010).

This could be also relevant in the aforementioned context, since the motivational processes were previously demonstrated to be modifiable in the management of schizophrenia, as for example Choi et al. (2010) reported that schizophrenia patients do respond to motivationally enhancing instructional techniques, while the incorporation of these techniques into training exercises significantly enhanced the further memory processes. Moreover, in a similar approach, other researchers showed that motivation in schizophrenia could suffer various and important modifications during an experiment that lasted for one year (Nakagami et al., 2008).

CONCLUSIONS

In conclusion, all these data and theories regarding the relevance of motivation in schizophrenia presented here clearly demonstrate that motivation is a fundamental aspect of the negative symptomatology in schizophrenia and could provide a very promising and useful factor for understanding and improving the mechanisms and further management of schizophrenic pathology. These aspects could be relevant also considering the various public health implications of schizophrenia, as it is known that a failure to engage in motivated goal-directed behavior can manifest as reduced educational, occupational and social achievement (Barch et al., 2010). That is why there is an urgent need to understand the mechanisms that may lead to deficits in motivation in schizophrenia.

Future management approaches could consider the use of some specific antipsychotic medications that interact with dopaminergic receptors and have the capability to affect both the cognitive and motivational systems. Thus, further follow-up studies regarding these aspects seem warranted and could have fundamental importance for the management of schizophrenia.

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REFERENCES


Motivation in Schizophrenia


