The relationships between cognition, motivation and emotion in schizophrenia: How much and how little we know.

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Abstract

This article summarizes a workshop discussion focused on the current state of our understanding of the ways in which cognitive dysfunction in schizophrenia is related to, influenced by, or even leads to disturbances in areas such as emotion, motivation and stress, as well as areas in need of further research. A major emphasis in the workshop discussion was the critical importance of motivation and its potential influence on cognitive function and learning in schizophrenia. As such, the members of the workshop suggested a number of questions regarding motivation that need further research, including: 1) the definition and measurement of different components of motivation; 2) the relationship between intrinsic motivation and incentive drive and hedonic processing; 3) the integrity of motivational processes, incentive drive, and hedonic processing in schizophrenia; 4) the influence of cognitive deficits on motivational disturbances in schizophrenia; 5) the influence of antipsychotic medication on incentive drive and hedonic processing in schizophrenia; and 6) the relationships between cognitive function, stress, and the processing of aversive stimuli.
The focus of the MATRICS process has been on understanding the nature and breadth of cognitive dysfunction in schizophrenia in order to facilitate the development of treatments that will hopefully ameliorate this debilitating aspect of schizophrenia. In doing so, the work conducted as part of MATRICS has drawn from the large body of research focused on understanding the neural bases of specific cognitive functions in both animal and human models, as well as the research on the nature and neurobiology of cognitive dysfunction in individuals with schizophrenia. The goal of the workshop reported upon in this article was to begin to discuss the ways in which cognitive dysfunction in schizophrenia is related to, influenced by, or even leads to disturbances in areas such as emotion, motivation and stress. Any individual who has worked extensively with individuals who have schizophrenia knows that, although cognitive dysfunction is prominent, these individuals can also display a host of emotional and motivational deficits. These deficits can include blunted affect or inappropriate affect, lack of achievement motivation, social withdrawal and reports of reduced ability to experience pleasure. Historically, work on cognitive and emotional/affective function in schizophrenia has tended to proceed in parallel, with researchers focused on either one domain or the other. However, more recent work has begun to explore the critical interactions between emotion and cognition in schizophrenia, work which helped to inform the content and suggestions of the workshop members.

If one were to identify the strongest theme running through the discussion of in this workshop, it would be the emphasis on the importance of understanding the integrity of motivational processes in schizophrenia. One of the reasons for the emphasis was the possibility or concern that some aspects of cognitive dysfunction in schizophrenia might be secondary to either a general lack of motivation that spans all aspects of an individual’s life, or to more specific motivational deficits associated with intrinsic motivation to do well on abstract cognitive
tasks. In other words, studies of cognition function in healthy individuals often rely on the assumption that people are motivated in some way to do well on the cognitive task, either because of some intrinsic drive to do well or because of the external reinforcement provided by praise or even money. However, such assumptions may not necessarily hold true for individuals with schizophrenia, if the illness itself may impair either intrinsic motivational drives or responsivity to extrinsic reinforcers (a topic which will be returned to below). If so, then it could be that poor performance on cognitive tasks reflects a lack of engagement or motivation to do well rather than an inherent difficulty with the cognitive process tapped by the task. Consistent with this hypothesis, several studies have shown that performance on cognitive tasks such as the Wisconsin Card Sorting Task, the Span of Apprehension, and facial affect perception can be improved via the use of monetary incentives. However, a number of other studies have not shown that monetary reinforcement significantly improves cognitive task performance among patients with schizophrenia, and even those studies showing improvements due to monetary reinforcement do not necessarily show a complete amelioration of cognitive dysfunction. Thus, the role that motivation plays in impaired cognitive task performance in schizophrenia is still unclear. Further, even if additional research should unequivocally demonstrate that some proportion of cognitive impairment in schizophrenia is due to motivational factors, we would need to understand how this might interact with the influence of cognition on social and occupational function in this illness. It is intuitively easy to understand how a lack of “motivation” could lead to poor performance on experimental cognitive tasks in a laboratory setting that may have no inherent salience or relationship to life function. However, it is somewhat less intuitive to explain how motivational issues could be influence a relationship between cognitive function and social/occupational function. One possibility is that motivational
deficits are a “third” variable factor that leads to a spurious relationship between cognitive and life function, without there being a direct causal relationship between the two. In other words, motivational deficits among individuals with schizophrenia may lead to poor performance on cognitive tasks in the laboratory and to a failure to engage in or perform life functions necessarily to live and work independently.

A second reason for the emphasis on understanding motivation among the workshop members was the way that learning may be influenced by motivation or reinforcement in schizophrenia. Individuals presumably learn from errors made either during cognitive task performance or in real life situations because of intrinsic motivations to do well or because they are motivated to obtain some more concrete reinforcer contingent upon successful performance. As such, motivational deficits could lead individuals with schizophrenia to respond to errors differently, or to fail to learn from feedback, problems with could lead to significant impairment in both the laboratory and in real life function. In fact, there is research to suggest that individuals with schizophrenia show impaired behavioral (e.g., post-error or conflict slowing) or neurophysiological responses to errors, though there are also a number of other studies suggesting intact error processing in schizophrenia. Again, more work is clearly needed to understand the influence of motivational factors on learning in schizophrenia, both in the laboratory and in real-life settings.

**Basic Research On Motivation**

In order to better understand motivational function in schizophrenia, the workshop members identified a number of unanswered questions that need to be addressed and areas in which further research is needed. A first major question is how to define what we mean by motivation, and how to distinguish it from other related constructs such as effort. There is a long
history of research on various aspects of motivation in both psychology and behavioral neuroscience, which have emphasized the importance of motivational factors as a source of variability in behavior, a reason why behavior can appear flexible and adaptable in different situations, and as a reason why putatively species specific behavior can be modified. Much of the research on motivation in the behavioral neuroscience literature has focused on the concept of homeostatic drives, or the idea that organisms may be driven to maintain a stable internal state in regards to variables such as thirst, hunger, or other injective behaviors (see 23 for a review). This view of motivation focuses on the fact that a deficit or error signal in such systems (e.g., lack of water, hunger, low blood glucose, etc) triggers behaviors designed to return to the system to a set point or stable state (though see Berridge for a discussion of alternative settling point views). Related discussions of the construct of motivation also often involve discussion of the properties of motivation. For example, it is has been suggested that motivation involves both appetitive and consummatory phases, with the appetitive phase referring to the signal that indicate the potential availability of a “desired” stimulus as well as the means or instrumental behaviors used to move toward the goal.

Conceptualizations of motivation that rely on homeostatic mechanisms have powerful explanatory force in many domains. However, many researchers have argued that other types of mechanisms that do not rely on explicit error signals are needed to explain the full range of “motivated” behaviors seen in animals and humans. Animals and humans may be motivated to seek stimuli that are reinforcing in some sense, even if these stimuli do not necessarily serve to remediate some internal deficit state. This view of motivation focuses on the appetitive approach, or incentive drive concepts of motivation 23. In many ways, such views of motivation may be easier to apply to understanding motivation influences on cognitive function and social
function than homeostatic views. Some of the drives that govern our daily behaviors relate to basic needs such as food and water. However, many of the domains in which we think motivation is important are those that are much more abstract and removed from basic needs, such as achievement motivations, interpersonal needs or desires.

The function of appetitive or incentive motivation systems has received much attention in the animal behavioral literature, and some aspects of the ways these systems work in animals have been relatively well worked out (though this is an active and evolving area of research). For example, work by Schultz and Berridge as well as others has highlighted the important role that the dopamine system plays in approach related behaviors. Schultz’s work has demonstrated that the dopamine system is involved in predicting rewards associated with upcoming stimuli. More specifically, Schultz’s work has shown dopamine bursts to unpredicted rewards help the system learn about temporally preceding cues that may predict those rewards, particularly if appropriate actions are taken in response the cues. Over time, the dopamine response occurs to the earliest predictive cue, instead of to the reward itself. Further, animals exhibit a phasic depression in the dopamine response when a predicted reward does not occur, which can serve as an indicator that inappropriate actions have been taken or the reward contingencies have changed. Such results are consistent with computational theories of reinforcement learning which postulate that organisms modulate their behavior in response to errors of reward prediction that serve as learning or teaching cues.

On a related note, Berridge has suggested that the dopamine system is specifically involved in wanting (working towards desirable goals) as compared to liking (hedonic responses to obtained goals). Thus, in Berridge’s framework, deficits in dopamine function might lead to disturbance in incentive drives or approach behavior that would lead to the obtainment of a
rewarding stimulus, even if the hedonic response to that stimulus is intact. Further, the work on incentive motivation provides a way to understand how motivating properties can be transferred from primary reinforcers such as food and water to more abstract reinforcers that predict these primary motivators. Specifically, this work suggests that in addition to an association being learned between the cue and a reinforcer, a motivational transformation occurs in which the predictive cue (the conditioned stimulus) take on at least some of the motivation properties of the unconditioned stimulus \(^{27-29}\). The critical role of dopamine in incentive motivation is particularly relevant to understanding motivation deficits in schizophrenia, given longstanding hypotheses regarding the role of dopaminergic disturbances in the pathophysiology of schizophrenia.

Despite the wealth of research on animals, there are several areas in which much more basic work is needed to understand how these systems operate even in healthy humans let alone how they may be impaired among individuals with schizophrenia. First, much of the work in animals has used stimuli that are primary reinforcers, such as food, water and juice. Recent work suggests that these systems may operate similarly in humans responding to the same types of reinforcers, or even more abstract monetary reinforcers \(^{30-33}\). However, the ways in which systems that have developed to predict primary reinforcers become adapted to predict or modulate behaviors related to secondary reinforcers is humans is not yet clear. As described above, incentive motivation theories provide mechanisms by which a predictive cue can take on the motivation properties of an intrinsically rewarding stimulus. However, it is not clear over what temporal distance such associative chains can work. In fact, it is not at all clear whether the same systems that respond to the prediction of reward in terms of primary reinforcers, or even money, play a role in governing incentive motivation in humans related to very abstract goals such as achievement, safety, or interpersonal relatedness. Further, very little is known about the
neural or psychological mechanisms that give rise to what is often referred to as intrinsic motivation, defined here as the positive feelings associated with an activity or action in absence of any tangible reward, or actions that are taken for their own sake that do not require external supports or reinforcements to be initiated or sustained. In addition, relatively little is known about the role that this incentive systems may play in learning related behaviors on the types of cognitive tasks studied in the laboratory, or on learning related behaviors necessary for successful social, occupational and educational function. Many of these questions are ones that are being actively pursued in the basic science literature on motivation and approach/withdrawal behavior. Nonetheless, these questions are highlighted here to emphasize that an understanding of the basic mechanisms will help us to understand how these mechanisms may go awry in disorders such as schizophrenia.

It is also important to note that there is a very rich basic behavioral science literature on motivation that also has much to offer in our attempts to understand the interrelationship between motivation and cognitive function in schizophrenia. This work comes out of a different tradition that the animal studies on motivation, and some theories are less clearly tied to specific neural systems. However, the work coming for this tradition is likely to be highly informative regarding the ways in which expectations about outcomes influences the choices and decisions that individuals with schizophrenia make regarding potentially affectively laden outcomes, as well as the types of individual difference variables that may be important to consider in understand motivational function in schizophrenia.

Motivation in Schizophrenia

Even if we fully understand the neural and psychological mechanisms that supported all types of motivational and incentive drives in healthy humans, the workshop members suggested
that much remains to be learned about the function of these systems in individuals who have schizophrenia. At the most basic level, much more work is needed on responses to reward and punishment in schizophrenia, both in behavioral and neurophysiological terms. As noted above, many theories postulate a role for dopamine in mediating either responses to rewards themselves or in learning to predict reward or learn from error feedback. If some aspect of the dopamine system is dysfunctional in schizophrenia, then there is good reason to believe that responses to rewards and/or error feedback are disturbed in this illness. As alluded to above, there is data to suggest abnormal responses to errors in schizophrenia, both behaviorally and neurophysiologically. However, the source of such deficits is not clear, nor are many aspects of basic reward or appetitive drive processing in schizophrenia. Many different types of abnormalities could influence such deficits in reward or error processing, and different mechanisms may point to different directions for treatment. For example, it is not clear whether individuals with schizophrenia have intact responses to basic or primary reinforcers such as food, water, or smells, either in terms of behavior or brain function. Anhedonia, or the inability to experience pleasure, has long been considered a key symptom of schizophrenia \cite{41}. One might think of anhedonia as evidence for a reduced response to rewarding or pleasurable stimuli. However, the assessment of anhedonia symptoms is often done based on clinical interview or responses to questionnaires, which may or may not reflect how individuals respond when presented with specific stimuli. Many studies have examined self-reports of either valence or arousal to stimuli such as words, pictures, films, or faces, many of which suggest relatively intact pleasure responses \cite{42-46}. Many fewer studies have examined responses to stimuli that might be more analogous to primary reinforcers (e.g., smells, sucrose), and these studies have evidence for both impaired \cite{47} and intact responses \cite{48}. Further, most of these studies have relied just on self-
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reports of responding, and more research is needed that examine other response channels, such as functional brain activation or peripheral physiology.

Second, it is not clear whether responses to secondary reinforcers than can also serve to predict primary rewards (i.e., money) are intact in schizophrenia. As with a number of other areas, there is conflicting evidence in this regard, with at least one study suggesting intact responses to monetary rewards and punishment in a gambling task \(^4^9\) and another showing impaired performance \(^5^0\). Again, should further research indicate a reliability deficits in responding to monetary rewards, a number of different factors could lead to such a deficit, including: 1) deficits in the link between monetary reinforcers and more primary reinforcers; 2) deficits in detecting the occurrence of reward in relationship to the behavioral predictors; 3) deficits in the ability to use previous experiences to guide future responding. At an even more complicated level, we know almost nothing about even more abstract aspects of motivation in schizophrenia, such as the development of intrinsic motivation.

**Measurement Issues**

In addition to work focused on understanding basic mechanisms of motivation, reward processing, and incentive drives, in both healthy individuals and individuals, the workshop members felt that more work was also needed on measurement issues. If motivational factors are having a critical influence on cognition in schizophrenia, then it would be important to have reliable, valid and practical measures of motivation. One can measure motivation behaviorally, in the sense of examining when an organism works towards some putatively desirable goals (i.e., lever pushing in rats, speed of responding in humans). However, such an approach to measuring motivation could be time consuming and potentially confounded by cognitive deficits themselves. **There are questionnaires based approaches available for measuring constructs such**
as: 1) behavioral activation and behavioral inhibition, which assesses individual differences in reactivity to reward and threat cues; 2) promotion (drive towards obtaining positive outcomes and avoiding the absence of such positive outcomes) and prevention (drive towards avoiding negative outcomes); and 3) intrinsic versus extrinsic motivation, such as the Motivational Trait Questionnaire. However, we need more information on the ability of these measures to predict behavioral outcomes of interest in schizophrenia and their validity in individuals with schizophrenia remains to be demonstrated. A subpoint to this focus on measurement issues was the suggestion that we need to develop or use what was termed more "ecologically valid" tests of cognition. More specifically, the tasks that we use in the laboratory tend to be very cold tasks that use stimuli that have no particular personal salience for the individual or motivational relevance. We may increase our ability to predict life function from cognitive performance by creating tasks that use stimuli that more clearly tap into the kinds of salient information that people have to manipulate in their everyday lives. There is a growing body of work on the use of such task in the social cognitive neuroscience literature, and schizophrenia researchers may wish to adapt such paradigms for work in clinical populations.

*Cognitive Influences on Motivation*

The workshop members also suggested that it is important to examine the possibility of a different type of relationship between cognition and motivation, namely the possibility that cognitive deficits in schizophrenia could be contributing to motivational deficits in schizophrenia, as well as or instead of motivational deficits leading to the appearance of cognitive deficits. As an example, one important component in appetitive drives towards potentially rewarding stimuli could be the ability to represent and/or maintain cognitive representations of either the stimuli themselves or the reward value of these stimuli. Tomarken
and Keener (1998) have put forth a similar argument in trying to explain the functional importance of frontal asymmetries in understanding vulnerability to depression. Numerous studies have demonstrated that individuals with schizophrenia have deficits in working memory, or the ability to actively maintain information over time. In addition, many studies have associated altered dorsolateral prefrontal cortex activity (a region important for the active maintenance of information) with working memory impairments in schizophrenia (Barch, 2005). It is possible that deficits in the ability to actively maintain information in working memory in schizophrenia, potentially related to altered prefrontal function, may lead to deficits in ability to represent goal or reward related information. If motivation depends in part on the ability to actively represent and maintain information about anticipated rewards, then deficits in the ability to maintain such representations could contribute to motivational or anticipatory pleasure deficits. Such a hypothesis is consistent with recent work on the neural systems supporting emotional regulation.

**Potential Medication Influences**

Another major theme in the discussion of this workshop was that more research was needed to understand the potential negative effects that treatments for schizophrenia may have on motivation, incentive drive, and responses to rewards. As noted above, many theories posit a central role for the dopamine system in these functions. All of the medications used as primary treatments for schizophrenia have an influence on the dopamine system, with many of them serving to block one or more dopamine receptor types. As such, it is possible that the medications used to ameliorate some symptoms of schizophrenia may actually be contributing to motivational disturbances or reductions in responses to pleasurable stimuli. It seems unlikely that all components of reduced motivation or even anhedonic symptoms in schizophrenia can be
attributed to medications, as the clinical literature contains reports of such symptoms in this illness long before medications were available to treat schizophrenia. Nonetheless, it may be that antipsychotic medications are exacerbating preexisting disturbances in motivation or other aspects of incentive drive or hedonic processing.

Stress and Other Aspects of Emotional Processing

The majority of this article has been focused on additional research needed to understand the relationships between motivation, incentive drives and cognitive function in schizophrenia. However, the workshop members also highlighted the need for further research on other related domains, such as the relationship between stress and cognitive function in schizophrenia, as well as other aspects of emotional processing, such as the processing of aversive stimuli. In regards to stress, additional research is needed to understand the degree to which responses to either acute or chronic stressors are intact versus impaired in schizophrenia, as the current literature provides mixed and somewhat sparse data. In addition, the workshop members suggested that more research was needed to determine the degree to which cognitive function in schizophrenia was modulated by stress, as assessed either by objective stress measurements or perceived or subjective stress measurements. As with the discussion of motivation, it will also be important to determine the ways in which cognitive deficits among individuals with schizophrenia may also alter responses to stress.

Summary

In summary, the outcome of the results of this discussion in this workshop provided suggestions for several areas in need of further attention and research, both in regards to basic and clinical science. First, we suggested that more work is needed to understand the psychological and neural mechanisms that support motivation drives for goals or stimuli that are
not necessarily primary reinforcers and to understand that mechanisms that support intrinsic motivational processes. Second, we suggested that much more work needs to be devoted to understanding the function of a range of incentive, motivation, and hedonic processes in schizophrenia. Third, we suggested that additional attention is needed to measurement issues, so that we can utilize tools that will allow for reliable, valid and practical assessments of motivation as well as ecological valid assessments of cognitive function. Fourth, we suggested that more research is needed on the ways in which pharmacological treatments for schizophrenia may be interacting with or even contributing to deficits in motivation or other aspects of incentive or hedonic processing. Lastly, we suggested that similar research is needed on understand the potential influences of related constructs such as stress or the processing of aversive stimuli.
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