Neural Basis of Anhedonia and Amotivation in Patients with Schizophrenia: The role of Reward System

Jung Suk Lee[1,2], Suwon Jung[3], Il Ho Park[4] and Jae-Jin Kim[2,5,*]

[1]*Department of Psychiatry, National Health Insurance Service Ilsan Hospital, Ilsan-ro 100, Ilsandong-gu, Goyang, Gyeonggi-do, Korea;* [2]*Institute of Behavioral Science in Medicine, Yonsei University College of Medicine, Seoul, Korea;* [3]*Columbia University, New York, NY, United States;* [4]*Department of Psychiatry and Behavioral Neurosciences, International St. Mary's Hospital, Catholic Kwandong University, Incheon, Korea;* [5]*Department of Psychiatry, Yonsei University College of Medicine, Seoul, Korea*

J.J. Kim

Abstract: Anhedonia, the inability to feel pleasure, and amotivation, the lack of motivation, are two prominent negative symptoms of schizophrenia, which contribute to the poor social and occupational behaviors in the patients. Recently growing evidence shows that anhedonia and amotivation are tied together, but have distinct neural correlates. It is important to note that both of these symptoms may derive from deficient functioning of the reward network. A further analysis into the neuroimaging findings of schizophrenia shows that the neural correlates overlap in the reward network including the ventral striatum, anterior cingulate cortex and orbitofrontal cortex. Other neuroimaging studies have demonstrated the involvement of the default mode network in anhedonia. The identification of a specific deficit in hedonic and motivational capacity may help to elucidate the mechanisms behind social functioning deficits in schizophrenia, and may also lead to more targeted treatment of negative symptoms.

Keywords: Amotivation, anhedonia, anterior cingulate cortex, orbitofrontal cortex, reward system, schizophrenia, ventral striatum.

INTRODUCTION

Schizophrenia is characterized by a variety of symptoms such as delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behaviors, and various negative symptoms [1]. Particularly, there has been a growing interest in negative symptoms due to their adverse impact on treatment responsiveness and long-term functional outcome. Traditional domains of negative symptoms in schizophrenia have been considered to be blunted affect, alogia, asociality, avolition, and anhedonia [2]. However, a review of factor analytic studies suggested that a two-factor model including diminished pleasure/motivation and affective flattening best described negative symptoms of schizophrenia [3]. In particular, diminished pleasure/motivation may be the most prominent or influential factor in causing the poor social, educational and vocational achievement in schizophrenia [4]. Another term for diminished pleasure/motivation is anhedonia and amotivation. In this review, we focus on these two symptoms, providing a brief overview of the neural correlates and the relationship with the reward system.

Anhedonia

Anhedonia, a diminished or lack of ability to experience pleasure, is an eminent characteristic of schizophrenia [5].

This symptom is attributed to a reduction in hedonic capacity, which is defined as one's ability to feel pleasure in positive encounter [5]. Hedonic capacity, in turn, is a kind of inherited trait that is naturally observed in the population, and anhedonia lies at the low end of the continuum for basic hedonic capacity [6]. Pleasure can be divided into two categories according to their temporal component – anticipatory and consummatory pleasure [7]. Anticipatory pleasure comes from anticipation of a particular positive stimulus and the capability to image the stimulus, and is best explained as "wanting". On the other hand, consummatory pleasure is "in-the-moment" or on-line experience of pleasantness in response to the stimulus, and is best explained as "liking". Anticipatory pleasure is commonly associated with motivation and goal-directed behavior, whereas consummatory pleasure refers to a liking that comes from fulfilling a desire [7].

Many researchers have reported that patients with schizophrenia experience a normal level of pleasure when participating in pleasurable activities, though they encounter positive events in their lives at lower frequency [8-10]. This finding suggests that patients with schizophrenia have an intact capacity in feeling consummatory pleasure and intact "in-the-moment" experience of emotion. However, they have an abnormality in anticipating hedonic experience that will happen in the future, which is a deficit in anticipatory pleasure [11]. In other words, patients with schizophrenia envision future daily life events to be less pleasurable in spite of intact on-line experience of pleasantness. Therefore,

*Address correspondence to this author at the Department of Psychiatry, Gangnam Severance Hospital, 211 Eonju-ro, Gangnam-gu, Seoul, Korea 135-720; Tel: 82-2-2019-3341; Fax: +82 2 3462 4304; E-mail: jaejkim@yonsei.ac.kr

anhedonia in schizophrenia may primarily come from the lack of anticipatory pleasure [12, 13].

Consummatory pleasure is defined by a sense of "current feelings", whereas anticipatory pleasure derives from "noncurrent feelings". Accordingly, reports of current feelings study how a person feels right now at this moment, whereas reports of noncurrent feelings use various response formats including prospective, retrospective, trait, and hypothetical self-reports [14]. Prospective self-reports require participants to predict their emotions in the future. Retrospective self-reports bring back past memories of feeling. Trait self-reports study how much participants generally feel a specific emotion. Hypothetical self-reports ask participants to report their idea of how they would feel in a certain hypothetical situation. The Chapman Physical and Social Anhedonia Scale [15] is a typical example of hypothetical self-reports. Patients with schizophrenia tend to express a normal level of positive emotion when reporting current feelings, but lower level of positive emotion when reporting noncurrent feelings. Strauss and Gold [14] argued that this discrepancy happens because patients with schizophrenia do not possess beliefs regarding whether specific situations lead to pleasure like healthy controls.

Amotivation

Amotivation, also known as avolition, is a psychological condition defined as "a reduction in the motivation to initiate or persist in goal-directed behavior" [4]. Motivation enables an individual to sustain rewarding value of an action into an uncertain future. Thus, amotivation affects the subjective and behavioral aspects of goal-directed activity [2]. Bluer described patients with schizophrenia to be neglectful and lazy without an impetus to do anything – whether it is for intrinsic or extrinsic reason [16]. Amotivation can arise from lack of competence to carry out an activity, lack of expectation that an action will result in desired outcome, and lack of any desire from the first place [17]. These deficiencies in patients with schizophrenia can affect various social aspects, including working toward goals that others may find pleasurable, engaging in productive occupational work, and even seeking help and treatment [18].

According to Self-Determination Theory, motivation, just like pleasure, can also be divided into two categories [17]. Extrinsic motivation is to do something for a separable, tangible reward. Intrinsic motivation, on the other hand, is to do something for the sake of itself or because of its inherent satisfaction. Intrinsic motivation is further classified into approach and avoidance motivations according to models of self-regulation. Approach motivation is the desire to obtain a positive outcome or achieve personal mastery and avoidance motivation is the desire to avoid a negative outcome or evaluation [18]. Intrinsic motivation is enhanced when approach motivation is manipulated, but is reduced when avoidance motivation is manipulated.

Both extrinsic and intrinsic motivations play a role in amotivation in patients with schizophrenia. For example, a study about the role of tokens as an extrinsic reward found that the token economy can effectively increase adaptive behaviors in patients with schizophrenia [19]. As a matter of fact, as extrinsic motivation is much easier to access than intrinsic motivation, most studies on amotivation in schizophrenia have focused on extrinsic motivation. However, a recent review has highlighted the role of intrinsic motivation reinforcement for treatment success in schizophrenia [20]. Although how much a person relies on extrinsic or intrinsic motivation can vary over time, it is highly likely that these two types of motivation work in conjunction [20]. For example, extrinsic motivation for various rewards is often utilized to develop a level of intrinsic motivation for successful cognitive remediation in patients with schizophrenia [21].

ASSESSMENT OF ANHEDONIA AND AMOTIVATION

There are three major approaches for assessing anhedonia and amotivation in schizophrenia: interview-based instruments, self-reports, and laboratory-based assessments. One of the widely used interview-based assessment tools is the Scale for the Assessment of Negative Symptoms (SANS) [22], which consists of five domains, such as (1) affective flattening or blunting (a characteristic impoverishment of expression), (2) alogia (impoverished thinking and cognition), (3) avolition/apathy (a characteristic lack of energy), (4) anhedonia/asociality (a difficulty in experiencing interest or pleasure), and (5) attention (a difficulty in focusing his attention). Each of these domains is measured in a five-point scale from 0 (being nonexistent) to 5 (being the most severe). Anhedonia and amotivation are assessed in the domains of anhedonia/asociality and avolition/apathy, respectively.

Another interview-based measure is the Schedule for the Deficit Syndrome (SDS) [23], which consists of six items, such as (1) restricted affect, (2) diminished emotional range, (3) poverty of speech, (4) curbing of interests, (5) diminished sense of purpose, and (6) diminished social drive. Of these items, diminished emotional range refers to reductions in the experience of both pleasant and unpleasant emotions, and thus assesses anhedonia. Curbing of interests, diminished sense of purpose, and diminished social drive are all related to amotivation. The Apathy Evaluation Scale (AES) has also been used to assess motivation in patients with schizophrenia, by reflecting on patients' behaviors and internal motives [24]. Although clinician-rated, informant-rated, and self-rated versions of the AES have been developed [24], the clinician-rated version was usually administered to patients with schizophrenia based on a semi-structured interview. This scale has been used in a number of studies for patients with schizophrenia, and seems to show superior psychometric properties over the SANS in assessing amotivation [25].

Recently, the Collaboration to Advance Negative Symptom Assessment in Schizophrenia (CANSAS) project has led to the development of the Clinical Assessment Interview for Negative Symptoms (CAINS), which employs a two-factor structure of expression (consisting of 4 items) and motivation/pleasure (consisting of 9 items) [26]. Through grouping motivation and pleasure together, the scale displays strong convergent validity and stronger relations to real-world settings than the SANS.

A typical example of the self-report questionnaires is the Physical Anhedonia Scale (PAS) and Social Anhedonia

Scale (SAS) [27], which are the most frequently used questionnaires of anhedonia by far. These scales consist of 61 and 48 true/false questions, respectively, with higher scores representing greater anhedonia. The PAS contains items regarding pleasures in response to taste, sight, touch, sex and smell, whereas the SAS includes items about pleasures during talking and socializing. Another self-report questionnaire is the Temporal Experience of Pleasure Scale (TEPS), an 18-item measure of pleasure in anticipation of future activities (10 items) and momentary pleasure (8 items) [7]. Another self-report assessment is the Motivation and Pleasure Scale – Self-Report (MAP-SR) was recently developed based on the CAINS [28]. This scale does not assess deficits in emotional expression due to poor reliability and validity, and instead exclusively focuses on deficits in motivation and pleasure.

Laboratory-based assessments typically instruct subjects to rate pleasant emotion when exposed to a variety of evocative stimuli, including complex pictures, faces, sounds, words, and food [8-10,12]. Patients with schizophrenia displayed consistently high levels of internal consistency in these laboratory-based assessments of pleasant emotions [29]. The effort-expenditure for rewards task involves making choices between easy and hard tasks that can bring different amount of potential rewards [30]. The effort-expenditure for rewards task objectively measures the reward motivation and effort-based decision-making in humans.

Similarities between Items of Anhedonia and Amotivation in Assessment Tools

Researches have outlined the similarities in assessing items between anhedonia and amotivation, and identified difficulties in separating the two as distinct symptoms. A previous review [29] has established that both the anhedonia and amotivation subscale ratings overlap in regards to their incorporation of the frequency of certain activities such as hygiene and work-related activities, as well as the surveying of subjective emotional and physical experiences. Both of these scales measure the level of interest and productive community functioning, thus demonstrating a need for a clearer distinction between the two terms. Treadway and Zald have argued that there are two aspects of anhedonia, the "motivational" and "consummatory" anhedonia, yet the current underspecified definition of anhedonia integrates these two aspects as one [31]. Further confusion arises considering the fact that patients with schizophrenia tend to show decreases in anticipatory pleasure rather than consummatory pleasure [13], implying that their diminished anticipatory pleasure arises not from deficiency in the pleasure functions themselves but in their undervaluing of future benefits. Based on this evidence, Foussias and Remington have claimed that patients with schizophrenia do not have a hedonic deficit in the strictest sense and instead experience amotivation rather than anhedonia [2].

Factor analytic studies [32, 33] have demonstrated that there are interrelationships between anhedonia and amotivation, demonstrating that SANS measures of avolition/apathy and anhedonia/asociality are closely related. Further studies have suggested the possibility of grouping these two factors together. Sayers *et al.* [33], in particular, grouped them as what he called "social amotivation."

REWARD PROCESSING MODEL

Model for the Normal Reward Processing

In order to understand anhedonia/amotivation in patients with schizophrenia, it is important to figure out the mechanism of reward processing in normal people. Suppose that a person encounters a pleasurable event, for instance, seeing a chocolate lying on a table, in which a person then decides to eat it. Upon taking the chocolate, he or she feels consummatory pleasure from its delicate taste, and this pleasurable memory will be stored and maintained until the next encounter of such event. When this person re-encounters a chocolate on a table, he or she will recall the memory from the past and will be able to feel anticipatory pleasure before even consuming the chocolate. This will induce motivation with the person to eat the chocolate, due to the aforementioned anticipation of the taste. This motivation will naturally lead to the goal-directed behavior (in this case, the consumption of the chocolate). Eventually, the cycle is formed; upon eating the chocolate, the person again feels consummatory pleasure, reinforcing the memories of such pleasurable experience. Each step in this cycle is essential in the reward processing, and a deficit in any step leads to breakdown of the whole cycle; for the cycle to function normally, each step has to be intact.

This cycle can be summarized as shown in Fig. **1**, which is based on the reward model suggested by Berridge and Robinson [34]. In this model, the reward processing is divided into three parts: emotion or affect which is associated with "liking", learning which is related to associative conditioning, and motivation which includes "wanting". While it might seem at first glance that "liking" is associated with anhedonia, this model links "liking" to consummatory pleasure. On the other hand, "wanting" is regarded as the motivational drive that comes from anticipatory pleasure. Again, anticipatory pleasure and motivation, instead of being distinct processes, are grouped as one [34].

Emotion or affect, a "liking" process that refers to consummatory pleasure, can be further broken down into the explicit hedonic feelings as conscious pleasure and the implicit hedonic feelings as core hedonic impact. The neurotransmitter systems including opioid, endocannabinoid and GABA play an important role in the "liking" process, which may particularly occur in the nucleus accumbens and ventral pallidum [35-37]. In the example above, the feeling of liking experienced upon consuming chocolate is relevant to this emotion or affect part of the reward.

Another component in this model, "learning", consists of identifying the relationship between stimuli and responses. Learning happens through two possible processes: associative conditioning and conscious memory. Associative conditioning is a process in which a person learns to make reward prediction through stimulus-stimulus conditioning, stimulus-response conditioning and response-contingent reinforcement. This process refers to Pavlovian conditioning or instrumental association. The amygdala, nucleus
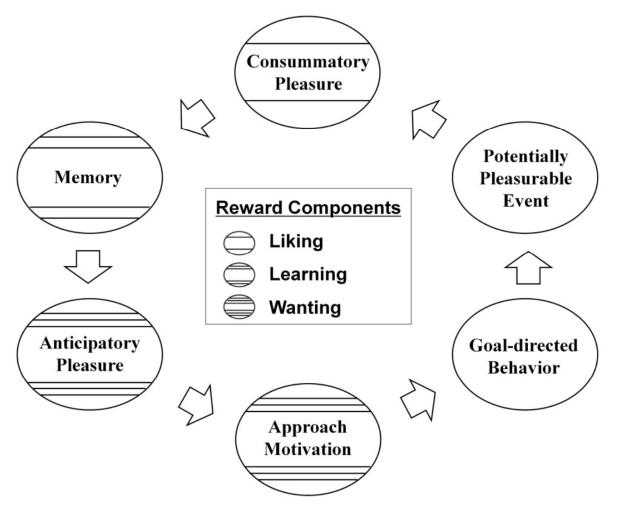
Fig. (1). Normal reward processing model.

accumbens and prefrontal cortex are involved in this type of learning [38]. The second type of learning is conscious memory that recalls temporal, spatial, predictive, and causal relationships, assisting a person in conducting the goal-directed action. This process involves reward expectancy and comprehension of act outcome causation. The orbitofrontal cortex, insula, and subcortical structures such as the amygdala, entorhinal cortex and hippocampus are engaged in this type of learning [39-41]. In the example above, learning in reward processing corresponds to forming the connection between eating chocolate (stimulus) and feeling the taste of liking (response).

The last part of reward, motivation, includes incentive salience and cognitive incentives. Incentive salience is a "wanting" process and promotes approach toward the rewards. Its attribution transforms sensory information or cues regarding the rewards into desired incentives. Unlike "liking", this process is mediated by mesolimbic dopamine neurotransmission. Cognitive incentives refer to instrumental cognitive representations of act-outcome, which rely on neocortical structures including the orbitofrontal cortex and insula. Feeling anticipatory pleasure from imagining the previously tasted chocolate and having the urge to pursue the chocolate is the motivation part of the reward system.

Model for Patients with Schizophrenia

We have seen earlier evidence that consummatory pleasure is intact in patients with schizophrenia. Therefore, a step that is impaired in schizophrenia is not the "liking" aspect, but rather the remaining two – "learning" and "wanting" [4]. The impairments in these two aspects show strong correlations to one another. In modifying the reward processing model for patients with schizophrenia, it is necessary to find out how these impairments interact, and the role that anhedonia and amotivation play in the model (Fig. **2**).

Contribution of Learning Impairment to Anhedonia and Amotivation

When cognitive incentives, a part of the learning process, are damaged, the cognitive expectation process is also damaged. Berridge and Robinson's model explains the consequences as impairments in incentive representation, hedonic expectation, cognitive desire (or "wanting"), and act-outcome causality [34]. The abnormal encoding of prediction errors that comes from impairments in learning in patients with schizophrenia leads to decreased attribution of salience to potentially rewarding occasions (either externally or internally), thus increasing anhedonia and amotivation [42]. For example, a study has demonstrated the possibility that amotivation in
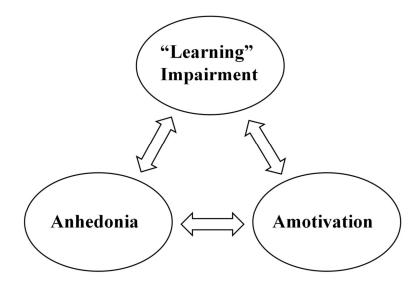
Fig. (2). Impaired reward processing model for patients with schizophrenia.

schizophrenia stems from difficulty representing the reward value of stimuli that is not currently present [18]. Additionally, since patients with schizophrenia have impairments in memory for emotional experience which is important for the learning process, emotional memory impairments may contribute to anhedonia and amotivation [43].

Functional neuroimaging studies also provide evidence of the involvement of learning impairments in anhedonia and amotivation. For example, a previous study found that patients with schizophrenia showed reduced activations in the ventral striatum and ventromedial prefrontal cortex during reinforcement learning and those activations correlated significantly with ratings for anhedonia and amotivation [44]. In addition, altered activation in the ventral striatum during emotional memory task has been related to more severe anhedonia in schizophrenia [45]. These results suggest that impairments in learning processes including reinforcement learning and emotional memory may contribute to anhedonia and amotivation in schizophrenia.

Interrelationship of Anhedonia and Amotivation

Numerous studies have demonstrated the correlation between anhedonia and amotivation. For example, a study investigating physical and social anhedonia found that there were significant correlations between the levels of anhedonia and amotivation [46]. A study using the effort-expenditure for rewards task showed that anhedonia was associated with decreased motivation [30]. Furthermore, an animal study found that inhibitions in hedonic capacity through administration of the dopamine receptor antagonist led to significant decrease in the frequency of entering a created niche to get food, whereas a feeding behavior seemed intact when food was directly offered to the rats [47], demonstrating that a decrease in the hedonic capacity may lead to decreased motivation. Based on these researches in humans and animals, Kring and colleagues have argued that anticipatory pleasure is essential for approach motivation and behavior [48]. Patients who have amotivation have been found to be deprived of the will to take themselves in activity that will give them pleasure. Since memory of

pleasurable moment is important for anticipatory pleasure, decreased participation in pleasurable activity will make patients become even more anhedonic [4]. Likewise, a recent study for depressed patients has claimed that anhedonia and amotivation are correlated and deficits in motivation are what lead to decreased anticipatory pleasure [49]. Taken together, these results demonstrate that learning impairments, anhedonia and amotivation are all connected and are bound together mutually. The ties between anhedonia and amotivation can be clearly seen in this new model (Fig. **2**). Both anhedonia and amotivation stem from impairment in the reward processing and work mostly in conjunction to one another.

NEUROIMAGING FINDINGS

Common Neural Correlates for Anhedonia and Amotivation

The cortico-ventral basal ganglia circuit is the main brain network associated with the reward processing. This circuit or the reward network includes the orbitofrontal cortex, anterior cingulate cortex, ventral striatum, ventral pallidum, and midbrain dopamine neurons (Fig. **3**). Out of these, the ventral striatum, considered to be the "reward center" of the brain, has been commonly linked to the negative symptoms of schizophrenia [50]. It is important to understand how these regions interact. The orbitofrontal cortex and ventral striatum receive inputs from the sensory cortices and calculate the reward values for each process. The information is then projected to the anterior cingulate cortex, in which the cost/benefit analysis is run to calculate the effort for the various actions. In turn, the anterior cingulate cortex sends projections to the anterior ventromedial prefrontal cortex and dorsolateral prefrontal cortex, which help in the ultimate decision-making process through reward value, effort, and reinforcement history information [51]. The following discussion reviews three of the regions in the reward network in greater detail, examining their functional roles in anhedonia and amotivation based on imaging data.
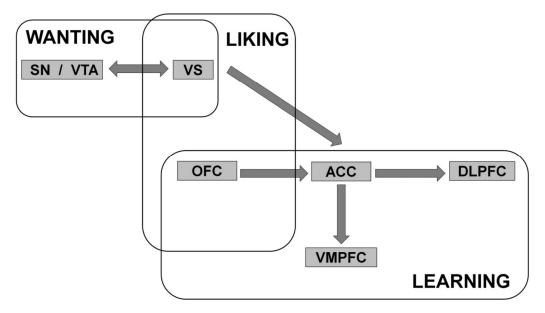
Fig. (3). Schematic illustration of the key structures and pathways of the reward system. SN: substantia nigra. VTA: ventral tegmental area. VS: ventral striatum. OFC: orbitofrontal cortex. ACC: anterior cingulate cortex. DLPFC: dorsolateral prefrontal cortex. VMPFC: ventromedial prefrontal cortex.

Ventral Striatum

The ventral striatum includes the nucleus accumbens, which is a central node within the limbic system [52]. The nucleus accumbens is divided into two subterritories: the core and shell. The core is linked to brain regions responsible for cognition and motor control, whereas the shell linked to primarily limbic structures [53]. The shell influences activity in the core through direct or indirect interactions, and thus the nucleus accumbens may serve as an limbic-motor interface, contributing to the translation of motivation to action [53].

Of the basal ganglia circuit, the ventral stratum is most commonly related to both anhedonia and amotivation. Its link to anhedonia has been proven in neuroimaging studies. For example, a study for patients with schizophrenia showed reduced ventral striatal activity during valence ratings for emotional pictures, which was correlated with the level of anhedonia [54]. The involvement of the ventral striatum in anhedonia has also been supported by other fMRI studies in schizophrenia [45, 55]. Recent studies have found that the anticipation of the reward – i.e. anticipatory pleasure – consistently activates the ventral striatum [56, 57]. Therefore, deficits in anticipatory pleasure in patients with schizophrenia may be reflected in the link between the severity of anhedonia and ventral striatal activity.

Furthermore, the ventral striatal involvement in the reward processing has been demonstrated more consistently in amotivation-related experiments than anhedonia-related experiments. The examples include reports that the ventral striatal control may be involved in reward-enforced learning [58], whereas the ventral stratum dysfunction may be associated with reduced motivation [59]. In a computerized study performing a progressive ratio task that measured the pursuit of monetary reward, lower motivation in schizophrenia was related to hypofunction in the ventral striatum [60].

Anterior Cingulate Cortex

Numerous studies have suggested that the anterior cingulate cortex is related to subjective ratings of pleasure [61]. The anticipation (prediction) of pleasure has been found to correlate with reduced activity in the rostral anterior cingulate cortex [62]. Within the anterior cingulate cortex, it appears that the rostral part, which has the highest density of opioid-binding receptors, is mainly responsible for happiness processing [63]. In patients with schizophrenia, reduced activation of the rostral anterior cingulate cortex was correlated with a deficit in the prediction of pleasure, signifying a failure in their capacity for feeling anticipatory pleasure [64].

In addition, the anterior cingulate cortex has recently been highlighted for its role in effort cost computation, which occurs while making an estimation of whether the benefits associated with an action outweigh the "costs" needed to obtain a reward [25]. A deficit in effort cost computation has been suggested to be one of possible mechanisms for reduced motivation in patients with schizophrenia [65]. In a study for 16 male patients with schizophrenia, a positive correlation was found between the volume of left anterior cingulate cortex and unconstrained motor activity reflecting avolition [66]. These reports propose that the anterior cingulate cortex may play a critical role in reduced motivation through impairments in effort computation.

Orbitofrontal Cortex

The orbitofrontal cortex and pleasure processing have been found to have significant correlations [67]. Studies have found that the orbitofrontal cortex is active during

emotional experience across a wide range of emotion elicitation studies. A previous study has identified the orbitofrontal cortex as playing a key role in determining the level of pleasantness [68]. In fact, the orbitofrontal cortex is thought to be primarily associated with the integration of information to update and maintain values and the establishment of the absolute value of threat or reward value of a stimulus [54].

Researches pertaining to the orbitofrontal cortex and its relationship with anhedonia and amotivation in schizophrenia have yielded consistent results. Orbitofrontal activity has been found to be negatively correlated with anhedonia in patients with schizophrenia [55]. High levels of motivation have been found to correlate with increased connectivity in the orbitofrontal cortex [69]. A study of self-fulfillment achievement motivation has also shown that motivation scores are negatively correlated with gray matter density of the orbitofrontal cortex [70]. These results suggest a possibility that orbitofrontal cortex could be a common neural correlate for anhedonia and amotivation in schizophrenia.

Distinct Neural Correlates for Anhedonia

Besides the reward network, other brain regions have also been considered to contribute to anhedonia. The default mode network (DMN) including the dorsomedial and ventromedial prefrontal cortices and posterior cingulate/ retrosplenial cortex may be an example. This network is an interconnected and anatomically defined brain system that is preferentially activated when individuals engage in internal tasks, and is suspended only during specific goal-directed behaviors [71]. A recent fMRI study demonstrated that reduced activation in the ventromedial prefrontal cortex during anticipation of reward was related to increased severity of physical anhedonia in patients with schizophrenia [72]. A PET study showed that in patients with schizophrenia, resting state metabolic activity was significantly reduced in the dorsomedial prefrontal cortex compared to healthy controls, and was correlated with the severity of physical anhedonia in the ventromedial prefrontal cortex and precuneus [73]. A recent study demonstrated that gray matter volumes of the precuneus and posterior cingulate cortex were also negatively correlated with the severity of physical anhedonia in patients with schizophrenia [74]. In addition, a study using diffusion weighted imaging demonstrated that fractional anisotropy value of the cingulum, which is known to connect the medial prefrontal cortex and posterior cingulate cortex, was correlated with the severity of physical anhedonia in patients with schizophrenia [75]. These findings suggest a possible involvement of the DMN in anhedonia.

Because one of the main functions of the DMN is self-referential processing [76], abnormalities of the DMN could lead to disrupted self-reflection and self-consciousness. The involvement of the DMN in anhedonia is consistent with a previous notion that abnormal self-consciousness is a possible cause of anhedonia in schizophrenia [77]. Given that anhedonia is most frequently assessed through the use of self-reports [29], the DMN may play a role in the self-

referential aspect of anhedonia. There is a suggestion that mental time travel - the mental reconstruction of personal events from the past and the mental construction of possible events in the future - is modulated by the DMN [78]. According to Strauss and Gold [14], retrospective and prospective self-reports of pleasure rely on mental time travel process. Therefore, dysfunctional DMN may contribute to an "Emotion Paradox" in schizophrenia, which refers to the fact that patients report less pleasure only when reporting noncurrent feelings.

Distinct Neural Correlates for Amotivation

Amotivation involves a deficit in distinct but interrelated neurobehavioral components of the dopaminergic reward system such as reinforcement learning and incentive motivation [34,79]. Reinforcement learning occurs when the midbrain dopaminergic neurons begin to respond to the preceding stimuli that predict unexpected or repeated rewards [34]. Incentive motivation has a drive-like effect of strengthening goal-directed behavior, and involves an attraction to conditioned stimuli or acceleration of the operant response [79]. The mesolimbic and nigrostriatal dopaminergic systems have been consistently demonstrated to be engaged in various aspects of motivation [80].

Phasic dopaminergic activity projects to the ventral and dorsal striatum, which play distinctive roles in reinforcement learning. The ventral striatum plays an important role in reward prediction, whereas the dorsal striatum is engaged in modulation of stimulus-response association according to rewarding outcomes of actions in instrumental conditioning [81,82]. In addition, increased midbrain dopaminergic firing has been observed when risky decisions are made with highly anticipated reward [83]. The anterior insula also takes part in loss or risk aversion and risk prediction [84].

In schizophrenia, a dysfunction of the dorsal striatum and anterior insula as well as the ventral striatum and anterior cingulate cortex has been associated with deficits in positive reinforcement learning, reversal learning, and classical conditioning [85-87]. Recently, the reinforcement learning-related network for the translation of dopaminergic signaling to voluntary goal-directed behavior has been studied in patients with schizophrenia using fMRI [88]. In this study, rostro-ventral anterior cingulate cortex activation during reinforcement learning was correlated with positive reinforcement-related responsiveness, which represents motivational drive, in controls and social amotivation subdomain scores in patients, underscoring the role of the cingulo-striatal network in amotivation in schizophrenia.

CONCLUSION

This review has demonstrated recently growing field of evidence that anhedonia and amotivation are tied together, and yet that distinct components of these symptoms exist. In particular, patients with schizophrenia tend to show diminished augmentation of hedonic enjoyment between the predictive and experiential stages of anticipatory pleasure, and this abnormal feature is related to reduced activity in the reward-related regions during the prediction of pleasure. Therefore, it is important to note that both anhedonia and

amotivation may derive from deficient functioning of the reward network. A further analysis into the neuroimaging findings of schizophrenia shows that the neural correlates overlap in the reward network including the ventral striatum, anterior cingulate cortex and orbitofrontal cortex. Additional anhedonia-related regions in schizophrenia include the DMN. The identification of a specific deficit in hedonic and motivational capacity may help to elucidate the mechanisms behind social functioning deficits in schizophrenia, and may also lead to more targeted treatment of negative symptoms.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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