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The motivation and pleasure dimension of negative symptoms: Neural substrates and behavioral outputs

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Abstract

A range of emotional and motivation impairments have long been clinically documented in people with schizophrenia, and there has been a resurgence of interest in understanding the psychological and neural mechanisms of the so-called "negative symptoms" in schizophrenia, given their lack of treatment responsiveness and their role in constraining function and life satisfaction in this illness. Negative symptoms comprise two domains, with the first covering diminished motivation and pleasure across a range of life domains and the second covering diminished verbal and non-verbal expression and communicative output. In this review, we focus on four aspects of the motivation/ pleasure domain, providing a brief review of the behavioral and neural underpinnings of this domain. First, we cover liking or in-the-moment pleasure: immediate responses to pleasurable stimuli. Second, we cover anticipatory pleasure or wanting, which involves prediction of a forthcoming enjoyable outcome (reward) and feeling pleasure in anticipation of that outcome. Third, we address motivation, which comprises effort computation, which involves figuring out how much effort is needed to achieve a desired outcome, planning, and behavioral response. Finally, we cover the maintenance emotional states and behavioral responses. Throughout, we consider the behavioral manifestations and brain representations of these four aspects of motivation/pleasure deficits in schizophrenia. We conclude with directions for future research as well as implications for treatment.

Keywords

Schizophrenia; Motivation; Pleasure; Neural substrates; Effort; Anticipation

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1. Introduction

A range of emotional and motivation impairments have long been clinically documented in people with schizophrenia, and there has been a resurgence of interest in understanding the psychological and neural mechanisms of the negative symptoms in schizophrenia, given their lack of treatment responsiveness and their role in constraining function and life satisfaction in this illness. Negative symptoms comprise five consensus-based domains: anhedonia, asociality, avolition, alogia, and blunted affect (Kirkpatrick et al., 2006). However, conceptual and empirical reviews of newer (e.g., CAINS; (Kring et al., 2013) or BNSS (Strauss et al., 2012)) and older (e.g., SANS; (Andreasen, 1982)) interview-based measures of negative symptoms indicate that a two-factor model more parsimoniously describes the negative symptoms (Blanchard and Cohen, 2006; Kimhy et al., 2006; Messinger et al., 2011). The first factor reflects diminished motivation and pleasure across a range of life domains; the second factor reflects diminished verbal and non-verbal expression and communicative output. Newer measurement techniques for these two domains–motivation/pleasure and expression–may better capture the underlying mechanisms giving rise to negative symptoms (Blanchard and Cohen, 2006; Kring et al., 2013) and help in developing more effective treatments. In this review, we focus on the motivation/ pleasure domain, providing a brief review of the behavioral and neural underpinnings of this domain.

We have argued elsewhere that adopting a translational approach to research on negative symptoms has and will continue to give us the greatest purchase toward more clearly identifying mechanisms of negative symptoms and developing more effective and targeted treatments (Barch and Dowd, 2010; Kring and Elis, 2013). Indeed, adopting the methods, theories, and measures of affective science, as well as translating from the animal and human affective and cognitive neuroscience, has propelled us ever closer to identifying core deficits that give rise to motivation/pleasure deficits in schizophrenia and other disorders. Independently, we have developed theoretical frameworks to guide our research on the emotional and motivational underpinnings of negative symptoms, highlighting how these deficits necessarily also involve behavior and brain regions that are crucial for cognitive control. Both of us have translated animal and human cognitive and affective neuroscience research to our models of motivation/pleasure deficits in schizophrenia. Kring and colleagues have argued for the importance of characterizing the time course of emotion to distinguish among anticipatory, consummatory ("in-the-moment"), and maintenance of emotion responding (see Fig. 1). Relatedly, Barch and colleagues have argued for the importance of representations about motivationally salient incentives necessary to develop and actively maintain behavioral plans that are necessary to achieve desired pleasurable outcomes (see Fig. 2).

In this review, we integrate our approaches to highlight the latest advances in our understanding of behavioral and brain systems that contribute to diminished motivation and pleasure in schizophrenia (see Fig. 3). Specifically, we focus on four common aspects of our models. First, we cover liking or in-the-moment pleasure, which involves immediate responses to pleasurable stimuli. Second, we cover anticipatory pleasure or wanting, which involves a prediction about a future enjoyable outcome (reward) and/or a feeling of pleasure

in anticipation of that outcome. Third, we address motivation, which includes a calculation of how much effort is needed to achieve a desired outcome (reward), a plan of how to obtain that outcome, and the actual behavioral response to get the reward. Finally, we cover the maintenance of emotional states and behavioral responses. Throughout, we consider the behavioral manifestations and brain representations of these four aspects of motivation/pleasure deficits in schizophrenia.

2. In-the-moment emotional experience in schizophrenia

In-the-moment experience in our models refers to the responses people provide when presented with putatively positive things. That is, how do people report feeling when presented with funny pictures, tasty foods, or reward of $5? This in-the-moment experience is called consummatory pleasure or "liking" in some human and animal models (see Table 1). In this section, we review the evidence on the behavioral and brain responses people with schizophrenia exhibit when presented with positive stimuli.

Although people with schizophrenia often report limited experiences of positive emotion during interview based clinical assessments (Horan et al., 2006), behavioral research tells a different story. Specifically, one of the most well-replicated findings in schizophrenia research is that people with schizophrenia report experiencing similar (or slightly less) amounts of positive emotion compared to those without schizophrenia in the presence of emotionally evocative stimuli (Cohen and Minor, 2010; Kring and Moran, 2008; Llerena et al., 2012) and in daily life (Gard et al., 2007; Myin-Germeys et al., 2000; Oorschot et al., 2009, 2012), regardless of changes in medication status (Kring et al., 1999a, 1999b). Interestingly, a number of studies have found that people with schizophrenia report experiencing more *negative* emotion to putatively positive stimuli or events in daily life compared to people without schizophrenia (Kring and Elis, 2013; Strauss and Gold, 2012; Tremeau et al., 2009; Ursu et al., 2011) (see Cohen and Minor (2010) for meta-analysis). In short, people with schizophrenia generally report liking or enjoying positive things as much as do people without schizophrenia even as they may also report disliking them a bit more.

At least some aspects of liking or in-the-moment experience appears also appear to be intact at the level of the brain, though the findings are more variable and complicated by methodological differences across studies. Brain imaging studies examining striatal responses to the receipt of expected monetary rewards in schizophrenia have shown a consistent pattern of intact responses, regardless of typical or atypical antipsychotic medication status (Dowd and Barch, 2012; Kirsch et al., 2007; Simon et al., 2009; Walter et al., 2009). However, some studies have found abnormal cortical responses to reward receipt (Schlagenhauf et al., 2009; Walter et al., 2010; Waltz et al., 2010), particularly when the reward is unexpected (see also section on prediction error responses in the striatum). Further, a more mixed picture has arisen in non-monetary studies in schizophrenia (Crespo-Facorro et al., 2001; Paradiso et al., 2003), with some evidence for reduced activation of the insula (Plailly et al., 2006; Schneider et al., 2007), orbital frontal cortex (OFC) (Plailly et al., 2006) and striatum (Dowd and Barch, 2010; Grimm et al., 2012; Waltz et al., 2009).

Two recent meta-analyses that focused on responses to emotional stimuli (Anticevic et al., 2010; Taylor et al., 2012) reported consistent findings in regards to brain responses to emotion in schizophrenia, despite using different meta-analytic techniques. Both meta-analyses included studies that had the following characteristics: assessed in-the-moment responses to evocative stimuli; included contrasts between conditions (emotion condition–neutral condition as well emotion condition–baseline); included between group comparisons, and used standardized coordinates. Anticevic et al. focused primarily on the amygdala, whereas Taylor et al. examined whole brain activation. With respect to amygdala activation, an interesting and consistent result was found across the two meta-analyses. People without schizophrenia showed greater amygdala activation compared to people with schizophrenia, but only for contrasts that subtracted activation during a neutral condition from activation during a negative condition (Anticevic et al., 2010; Taylor et al., 2012). In contrast, when examining direct emotion contrasts (i.e. positive condition–baseline), Anticevic et al. found no between group differences in amygdala activation. Results from both meta-analyses suggest (but cannot fully demonstrate) that under-activation of amygdala in people with schizophrenia in response to evocative stimuli may reflect over-activation to the neutral stimuli, and suggest that responses to negative stimuli themselves are relatively intact. It remains important to examine responses to positive stimuli given that most studies included in the meta-analyses to date have included only negative and neutral stimuli.

Taylor et al. (2012) revealed other regions of activation that distinguished people with and without schizophrenia, including less activation in people with schizophrenia in dorsal medial and dorsolateral PFC, regions activated during emotion and cognitive tasks. Less activation was also observed in more posterior brain regions (occipital pole, fusiform gyrus) among people with schizophrenia, but this may reflect neural correlates of processing complex facial stimuli more than emotion per se. Taylor et al. also examined the potential moderating effects of task type on observed brain activation differences. As such, they compared implicit tasks (e.g., rate the gender of face) versus explicit tasks (e.g., rate your emotional experience), and found that the reduced activation among people without schizophrenia in amygdala and medial prefrontal cortex (PFC) was found primarily in implicit tasks. This raises the question as to whether these non-emotion focused aspects of the task may have contributed to the different patterns of activation.

To summarize, brain imaging studies suggest that people with and without schizophrenia show comparable brain activation in striatum to expected reward and amygdala (more so for negative stimuli relative to baseline) to people without schizophrenia. Despite these similarities, there is also evidence for differences in the insula, orbital frontal cortex (OFC) and striatum to positive non-reward stimuli, though these results are quite mixed with an equal number of studies finding intact responses to positive stimuli in these regions. There also appear to be differences in activation of regions that are also associated with cognitive control, including anterior cingulate cortex (ACC) and the dorsolateral prefrontal cortex (DLPFC).

If in-the-moment pleasure or liking at the level of self-report and the brain are relatively intact in schizophrenia, at least to expected stimuli, where might things go awry? Research from both of our groups as well as other laboratories suggests that more pronounced deficits

emerge at the intersection of emotion, cognition, and behavior. In the next sections, we review the fairly consistent behavioral and neural evidence for deficits in anticipation, maintenance, and motivated behavior in schizophrenia.

3. Anticipatory pleasure

Much of what is enjoyable or pleasurable about life is derived from thinking about the future. Will I enjoy having sushi for lunch? Will I be happy with my new job? Will I enjoy the family reunion? Thinking about pleasure or enjoyment in the future is broadly referred to as anticipatory pleasure or "wanting." Anticipatory pleasure involves a prediction component (how much will I enjoy dinner with my family?) as well as a feeling of pleasuring knowing that something positive is going to happen in the future (I am so excited, I can't wait to start my new job next week). It is in the domain of anticipatory pleasure that people with schizophrenia appear to have particular trouble.

Indeed, we have argued for and demonstrated anticipatory pleasure deficits in schizophrenia (Barch and Dowd, 2010; Dowd and Barch, 2010, 2012; Gard et al., 2007; Kring and Caponigro, 2010; Wynn et al., 2010). In the animal literature, anticipatory pleasure has been characterized as "wanting" and distinguished from "liking" or in-the-moment pleasure experience (Berridge, 2004; Berridge and Robinson, 1998). Compared to controls, people with schizophrenia are less likely to anticipate or predict that future events will be pleasurable, are less likely to experience pleasure *in anticipation* of things to come, and thus may be less motivated to seek out pleasurable experiences (see Fig. 3).

Neuroscience research on how animals and people translate these predictions and feelings about possible future rewards or enjoyable things into behavioral responses (Berridge, 2004; Schultz, 2004, 2007; Schultz et al., 1997; Wallis, 2007) has informed our work in schizophrenia. Specifically, animal work has demonstrated that the mid-brain dopamine (DA) system, particularly the projections to ventral and dorsal striatum mediates reward prediction and wanting (Berridge, 2004; Schultz, 2007). Many DA neurons in the substantia nigra and ventral tegmental area respond to stimuli that *predict* reward, as well as to the rewarding stimuli themselves, with the degree of response depending on reward predictability. If the reward was not predicted, then DA neurons fire strongly (positive prediction error); if a predicted reward does not occur, then there is a transient depression in DA neuron firing (negative prediction error) (Schultz, 1992, 2004, 2007, 1993, 1997). When neutral cues are repeatedly associated with rewards, over time DA neurons begin to fire to the predictive cues rather than to rewards themselves (Schultz, 2007). Human fMRI studies have found activation of ventral and dorsal striatum, major targets of midbrain dopaminergic neurons, in response to cues that predict expected reward (Knutson et al., 2001, 2000) as well as both positive and negative prediction error responses (Abler et al., 2006; McClure et al., 2003). A prominent, though slightly different theory, emphasizes the role of the DA-learning process in transferring incentive salience (i.e., the positive feelings in human terms) from the reward itself (e.g., tasty dinner) to the reward-predicting cues (restaurant review in the paper), thus imbuing these cues with motivational properties themselves (e.g., a "wanting" response (Berridge, 2004)).

fMRI studies of the prediction part of anticipatory pleasure in schizophrenia have reported reduced ventral striatum activity to cues predicting reward in unmedicated people with schizophrenia (Esslinger et al., 2012; Juckel et al., 2006b; Kirsch et al., 2007; Nielsen et al., 2012; Schlagenhauf et al., 2009), as well as in people taking typical, but not atypical antipsychotics (Juckel et al., 2006a; Schlagenhauf et al., 2008; Simon et al., 2009; Walter et al., 2009). Importantly, a number of these studies also showed a relationship between negative symptom severity and deficits in ventral striatal activity to cues predicting reward (Dowd and Barch, 2012; Juckel et al., 2006b; Waltz et al., 2010).

Prediction errors

A number of studies have also examined the role of the striatum in reward prediction by looking at prediction error responses–an *increase* in striatal (presumably dopaminergic) responses to unexpected rewards and a *decrease* in striatal responses when predicted rewards do not occur. Some studies have found reduced prediction error responses in the striatum to rewards among people with schizophrenia spectrum disorders (Jeon and Polich, 2003; Morris et al., 2012; Murray et al., 2008), coupled with enhanced prediction error responses to neutral stimuli (Murray et al., 2008) or to unsurprising rewarding stimuli not expected to elicit prediction errors (Morris et al., 2012). By contrast, Gradin found reduced prediction error responses in the caudate, but increased activation associated with expected reward value in the ventral striatum (Gradin et al., 2011). Waltz et al. (2009) found evidence for reduced positive prediction error responses in a range of regions that included the striatum (dorsal and ventral) as well as insula, but relatively intact negative prediction errors in these same regions. Dowd and Barch (2012) found intact prediction error responses in schizophrenia, but in cortical regions rather than striatal regions during a Pavlovian task (neither the controls nor the people with schizophrenia showed prediction error responses in the striatum). Taken together, these findings suggest evidence for reduced prediction error responses to unexpected outcomes in some striatal regions. It is not clear whether these abnormal responses reflect altered computations of the likelihood that stimuli will lead to reward (e.g., more of a problem anticipating the likelihood that a stimulus will lead to a reward) or a problem in updating the values associated with a stimulus at the time that the reward occurs. Further work will be needed to tease these apart and to clarify the reasons for abnormal prediction error responses in schizophrenia.

In summary, the literature on anticipatory pleasure in schizophrenia suggests more evidence for impairment than the literature on in-the-moment "liking" responses. People with schizophrenia self-report a reduction in the anticipation of pleasure in future events. Further, they show reduced responses in the striatum to cues that predict the future occurrence of reward, as well as abnormal responses to the receipt of rewards that are unexpected. A key question is then how this might influence the selection of behaviors that may or may not lead to future rewards.

4. Approach motivation and behavior: computing value, computing effort, and goal-directed behavior

Why are people motivated to seek out some rewards or positive outcomes but not others? Barch and Dowd (2010) have argued for the importance of distinguishing two key components of motivation. First, people compute the value of a reward or desirable outcome (value computation: do I really enjoy or desire that cup of tea?), and second, people compute how much effort or "work" it will take to get that reward or outcome (is it worth walking the two blocks to get the tea?). These two components of motivation then support goal-directed behavior–that is, the action or behavior need to achieve a desired goal or outcome/reward. In this section, we review the behavioral and neuroscience evidence for deficits in value computation, effort computation, and goal-directed behavior. First, we describe the current animal and human neuroscience findings on brain regions supporting theses motivation processes.

Neuroscience research has found that value computation is mediated in part by orbitofrontal cortex (OFC) (Padoa-Schioppa and Cai, 2011; Rudebeck and Murray, 2011). In animal work, value computation includes the positive/ rewarding properties of an outcome as well as the internal state of the organism (e.g., value of juice when thirsty versus not) (Rolls et al., 1989), which is akin to the human work on feeling pleasure in anticipation of a desired outcome (Gilbert and Wilson, 2007). Value computation also includes the delay before an outcome occurs (Roesch and Olson, 2005; Rudebeck et al., 2006b), the available outcomes (e.g., tea versus wine after a hard day) (Padoa-Schioppa, 2007; Padoa-Schioppa and Assad, 2006), and the changing contingencies associated with a stimulus (a previously rewarded response is now punished, such as when the rules change in a game you are playing) (Cools et al., 2002; Dias et al., 1996). Some researchers have described the OFC as being involved in "working memory for value", or the ability to maintain, update, and integrate different sources of information about value over a short period of time (Frank and Claus, 2006; Wallis, 2007).

Effort computation (i.e., determining the cost of engaging in whatever actions it will take to obtain an outcome) involves the dorsal anterior cingulate cortex (ACC) with contributions from DA input from nucleus accumbens and related forebrain circuitry (Botvinick et al., 2009; Croxson et al., 2009; Salamone, 2007; Salamone et al., 2007). For example, research has shown that ACC lesions, as well as depletions of accumbens DA, lead animals to choose low effort but low reward options over higher reward, but higher effort options (Rudebeck et al., 2006a, 2007, 2006b; Rushworth et al., 2007; Salamone, 2007; Salamone et al., 2007; Walton et al., 2007).

Integrating these computations alongside anticipatory pleasure propels the ability to generate and execute action plans necessary to achieve the valued outcome. A number of researchers have discussed the role of the lateral PFC (Braver and Cohen, 1999; Miller and Cohen, 2001; Wallis, 2007) in relation to goal-directed behavior (i.e., behavior that is enacted in the service or obtaining a goal or reward, such as walking the two blocks for an afternoon coffee). Indeed, other research and theory on DLPFC function has indicated that the DLPFC plays a role in top-down control of cognitive processing and provides a bias signal that helps

to facilitate goal-directed behavior (Miller and Cohen, 2001). In addition, people who have lateral prefrontal lesions show impairments in developing an "action plan" for enacting goal-directed behavior (Manes et al., 2002; Zalla et al., 2001). Finally, other studies show that increases in DLFPC activity mediate "motivated" cognitive control enhancements that occur with the provision of incentives in both animals (Kobayashi et al., 2006; Krawczyk et al., 2007; Sakagami and Watanabe, 2007; Watanabe, 1996), and humans (Beck et al., 2010; Jimura et al., 2010; Savine and Braver, 2010; Tsujimoto and Sawaguchi, 2005). In short, intact DLPFC function may be necessary to translate information about value into goal representations and to maintain such information so that is can be implemented as goal-directed behavior to achieve the desired outcome.

In schizophrenia, behavioral studies indicate that people with schizophrenia have deficits in value computation (Brown et al., 2013; Gold et al., 2012, 2008; Heerey et al., 2008). In addition, indirect evidence for deficits in value computation comes from studies showing deficits on two tasks that rely upon the OFC: (1) reversal learning (Ceaser et al., 2008; Elliott et al., 1995; Oades, 1997; Pantelis et al., 1999; Turnbull et al., 2006; Tyson et al., 2004; Waltz and Gold, 2007) but see (Hutton et al., 1998; Jazbec et al., 2007; Joyce et al., 2002) for exceptions; and (2) the Iowa Gambling task (Kester et al., 2006; Kim et al., 2009; Lee et al., 2007; Martino et al., 2007; Premkumar et al., 2008; Sevy et al., 2007; Shurman et al., 2005; Yip et al., 2009), but some exceptions (Evans et al., 2005; Rodriguez-Sanchez et al., 2005; Turnbull et al., 2006; Wilder et al., 1998). Both tasks require the integration of information about rewards and punishments across trials to then update value representations appropriately. There is also evidence for structural and functional changes in OFC in schizophrenia (Baare et al., 1999; Bertollo et al., 1996; Gur et al., 2000; Pantelis et al., 2003; Plailly et al., 2006), some of which are related to negative symptoms (Baare et al., 1999; Gur et al., 2000). In sum, there is growing evidence from the behavioral literature on schizophrenia for deficits in value computation in schizophrenia, as well as good evidence from the behavioral literature for deficits in tasks thought to reflect OFC function in schizophrenia, and at least some data suggesting that OFC changes may be related to negative symptoms.

Research in schizophrenia is just beginning to examine effort computation. For example, Gold et al. (2013) presented people with and without schizophrenia a computer task that allowed participants to choose between a more effortful response for a bigger monetary reward or a less effortful response for a smaller monetary reward while also varying the likelihood of receiving a reward (50% versus 100%). Interestingly, people with schizophrenia who had more negative symptoms were less likely than controls to expend more effort when the reward was *certain* (i.e., 100%). The authors speculated that the certainty of reward may have also made the effort expenditure more salient. In short, people with schizophrenia may have computed that the effort was not worth it when it was most salient. Barch et al. (in preparation) used a similar task developed by Treadway et al. (2009) to study effort computation as well. They also found that people with schizophrenia were less likely to exert greater effort as reward magnitude increased and as rewards became more likely. Further, they found that a reduction in the willingness to exert effort was associated with poor community and work function among people with schizophrenia.

Goal-directed behavior has been studied more frequently in schizophrenia, alongside deficits in DLPFC function. As noted earlier, an experience sampling study found that people with schizophrenia anticipated that goal-directed activities would be less enjoyable than did people without schizophrenia and they subsequently engaged in these types of activities less often (Gard et al., 2007). Thus some of the motivational impairments observed in schizophrenia may reflect, at least in part, problems in translating computations of value and effort into goal representations that can be used and maintained in DLPFC to guide goal-directed behavior. One way of examining this question is to determine how motivational incentives impact cognitive performance, potentially via modulation of DLPFC activity. Several studies suggest that people with schizophrenia are not able to improve their performance on cognitive tasks when offered monetary incentives (Green et al., 1992; Hellman et al., 1998; Roiser et al., 2009; Vollema et al., 1995); while an equal number suggest at least some evidence for improvement with reward (Kern et al., 1995; Penn and Combs, 2000; Rassovsky et al., 2005). There is also older clinical work on the use of token economies in schizophrenia that suggests functioning can be improved through an explicit reward system, though token economies provide a number of "external" supports for maintaining reward related information that could compensate for deficits in the ability to translate reward information into action plans. Further, there is strong evidence from a variety of sources for impairments in DLPFC function in schizophrenia (Glahn et al., 2005; Minzenberg et al., 2009; Van Snellenberg et al., 2006). However, to date, there are no fMRI studies examining whether or not anticipated reward or incentives modulate DLPFC activity during cognitive control or working memory tasks in schizophrenia.

5. Maintenance, integration, and updating

Not only is maintenance crucial for enacting goal-directed behavior, but also it is important for later encoding of pleasurable experiences. Indeed, human neuroscience findings in healthy people suggest that our ability to anticipate the future relies upon our ability to remember the past (Schacter et al., 2007, 2008), with a core network of brain regions, including areas of the medial prefrontal and medial temporal cortex, supporting both abilities. Thus, when we predict whether or not we will enjoy the latest novel by a favorite author, we likely draw upon our past experiences with the authors' novels to guide our predictions. Maintaining emotional experiences as they occur likely facilitates the development of memories for these experiences (Kring and Caponigro, 2010). There is a very robust literature suggesting that people with schizophrenia have deficits in active maintenance of non-emotional information in working memory, with a number of meta-analyses summarizing this evidence (Forbes et al., 2009b; Lee and Park, 2005). As such, it is should not be surprising that there is also evidence from psychophysiological and fMRI studies suggesting that people with schizophrenia have difficulty holding on to prior emotional experiences. For example, people with and without schizophrenia showed comparable and differentiated eyeblink responses to a startle probe during picture viewing (i.e., larger blinks to negative pictures, smaller blinks to positive pictures), yet just 2.5 s after the picture was removed from view, the schizophrenia group no longer showed this differentiated pattern of blink responses, though the control group did (Kring et al., 2011). Similarly, in an fMRI study, people with and without schizophrenia exhibited comparable

activation of visual, amygdala, and prefrontal cortical regions, consistent with intact in-the-moment emotional experience. However, during the 12.5 s period after pictures were removed from view, there were marked differences between groups across prefrontal and limbic regions, and reduced activity in the DLPFC was positively correlated with anhedonia (Ursu et al., 2011). Such findings are consistent with the hypothesis that people with schizophrenia may have difficulties actively maintaining emotional experiences. Further, an event related potential study found that people with schizophrenia exhibited comparable responses early and mid-way during picture viewing but the schizophrenia group differed late in the picture viewing window, suggesting that maintenance deficits may begin even before stimuli are removed from view (Horan et al., 2010). An important unanswered issue for future research is whether deficits in the maintenance of emotional or rewarding experiences are simply another manifestation of deficits in working memory more broadly.

6. Conclusions and unanswered questions, and future directions

Taken together, results from our review are consistent with the notion that "in-the-moment" experience of pleasure is relatively intact in schizophrenia. That is, people with schizophrenia report experiencing as much pleasure as do people without schizophrenia in the presence of putatively positive stimuli, and they show comparable brain activation, at least in response to expected positive stimuli or outcomes. Nevertheless, people with schizophrenia also report experiencing more negative emotion in response to positive stimuli and they also show different versus activation in response to unexpected outcomes suggesting that all is not completely intact when it comes to in-the moment responding or the liking aspect of our model. In addition, there is evidence that value computation is impaired in schizophrenia. Further, there is growing and consistent evidence that people with schizophrenia have deficits in both behavior and neural responses associated with the anticipation of future rewarding or pleasurable experiences, as well as with responses to unexpected rewards. In addition, they have impairments in value and effort computation and goal-directed behavior that are related to functioning in the world. There is suggestive evidence that the active maintenance of emotional information and the ability to use prior emotional experience to guide current behavior is also impaired, though the linkages between this and other cognitive deficits (i.e., working memory) have yet to be worked out.

To illustrate the ways in which breakdowns in the interplay among generation and anticipation of goals, value and effort computations, and maintenance may contribute to impairments in goal-directed behavior in schizophrenia, consider the following scenario. A person with schizophrenia may report enjoying brownies and show both behavioral and neural evidence of consummatory pleasure while eating brownies. However, she may not be able to engage in the behaviors necessary to obtain or make more brownies (Barch and Dowd, 2010; Kring and Moran, 2008). Planning, purchasing, preparing or baking the brownies requires ongoing maintenance or retrieval of the prior emotional experience of pleasure while consuming a brownie, as well as maintenance of contextual or cue information that should trigger associations about the food's rewarding properties. Such anticipation and maintenance of emotional information should guide the volitional pursuits and actions over time that may lead to such a reward (in this case intake of delicious food). An intact reward valuation and prediction system is necessary for this set of behaviors to

take place, and deficits in these functions in schizophrenia may reduce the ability of appetitive or pleasure cues to drive behavior. However, these functions also depend on the intact ability to maintain pleasure cues, experiences or context over time–a process that may be reliant on working memory and cognitive control, which are compromised in schizophrenia (Barch and Dowd, 2010; Ursu et al., 2011). Thus, deficits in reward prediction may be made worse by deficits in the ability actively maintain information about rewards or pleasure, which may extend beyond simple appetitive stimuli to more abstract rewards.

What is needed next is research that directly tests the ability to use and maintain internal representations of emotional experience and reward information to modulate behavior and brain function in schizophrenia, along with work that characterizes links between deficits in these abilities and everyday function in this illness. Further, more work is needed to understand the role that effort computations may also play in motivation impairments in schizophrenia. It may be that even when people with schizophrenia are able to generate or maintain representations of emotion or motivation, alternations in computing effort to reward valuation may inhibit the development of goal directed action plans that people need in order to pursue and obtain desired outcomes. Of course, these mechanisms may interact– difficulties in the anticipation of pleasurable outcomes may reduce the "reward" part of the value or effort computation, skewing such computations towards less willingness to exert effort if there is less perception of rewards due to representation and maintenance impairment. Further, much work is still needed to understand how these various deficits interact with medications and the course of illness. There is good evidence that negative symptoms are present in currently unmedicated people and in people who have never taken medication. However, it has been more difficult to conduct the experimental studies parsing mechanisms in unmedicated people, and thus future research is needed to disentangle the effects of the disease versus the effects of medication on these different mechanisms.

Another direction for future research is to examine how the components of the model we articulate here are or are not deficient in depression. The temporal course of reward processing impairments in schizophrenia and depression may be different, with more evidence that abnormal reward processing may be more trait-like in schizophrenia and more state-like in depression (Blanchard et al., 2001). Further, there is a growing evidence that the nature of reward processing abnormalities in depression may be different that those found in schizophrenia. For example, there is much more evidence for abnormal responses to the receipts of rewards in depression (Epstein et al., 2006; Eshel and Roiser, 2010; Forbes and Dahl, 2012; Forbes et al., 2009a; Pizzagalli et al., 2008). However, there is also evidence for some similar abnormalities, such as reduced effort computation (Treadway et al., 2012). Unfortunately, very few studies have directly compared different aspects of reward processing in schizophrenia and depression (though see Gradin et al. (2011)), and this will be a critical path for future research that will help us understand the structure of motivational impairments in relationship to varying manifestations of psychopathology.

Nonetheless, the intriguing research coming from the work on the mechanisms driving negative symptoms in schizophrenia is beginning to point towards specific processing and neural systems that could be ripe targets for interventions, both at a pharmacological and a

psychological level. It is interesting to speculate as to possible interventions that may help to remediate such impairments in reward prediction, effort allocation, and maintenance of information about emotional and/or reward information, with the hope of potentially improving quality of life and work and community function. There may be a range of pharmacological interventions that could manipulate the dopamine system in ways that could enhance reward processing, though the challenge is to ensure that such pharmacological approaches do not also increase positive symptoms, given the role of dopamine in the pathophysiology of the disorder. Further, there may be behavioral interventions that could be effective as well. Indeed, Grant et al. (2012) modified cognitive therapy for schizophrenia to emphasize goals, including changing beliefs that are associated with negative symptoms (Grant and Beck, 2009) and interfere with goal attainment as well as practice in action planning to achieve long- and short-term goals. Results from a randomized trial indicated that people with schizophrenia who received cognitive therapy had lower avolition at the end of treatment as well as better overall functioning. Other behavioral interventions have shown promise in increasing anticipatory pleasure (Favrod et al., 2010) and maintenance (Johnson et al., 2011), but these studies were very small, open trials that are in need of replication with larger samples and in randomized trials.

Additional treatment development work is needed, however, to more fully translate the findings we have reviewed here into behavioral interventions. For example, as described above, the work of Kring and colleagues suggests that emotional responses in schizophrenia may not be sustained when stimuli are not present in the immediate environment (Kring et al., 2011; Ursu et al., 2011) and other work suggests that people with schizophrenia have difficulties understanding which cues predict future rewards when stimuli. In other words, people with schizophrenia seem to have problems bridging the gap between the occurrence of stimuli that predict reward and the future obtainment that reward through the use of internal representations that can support temporally extended goal directed activities, suggesting a common mechanism that may be contributing to a range of impairments in motivation in this disorder. If so, then environmental supports or cues that remind people with this illness about rewarding outcomes over time may increase the likelihood of increased effort allocation to engage in the behaviors necessary to eventually achieve such goals. While speculative, such hypotheses help translate these experimental findings into interventions for motivational impairments in schizophrenia.

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None.

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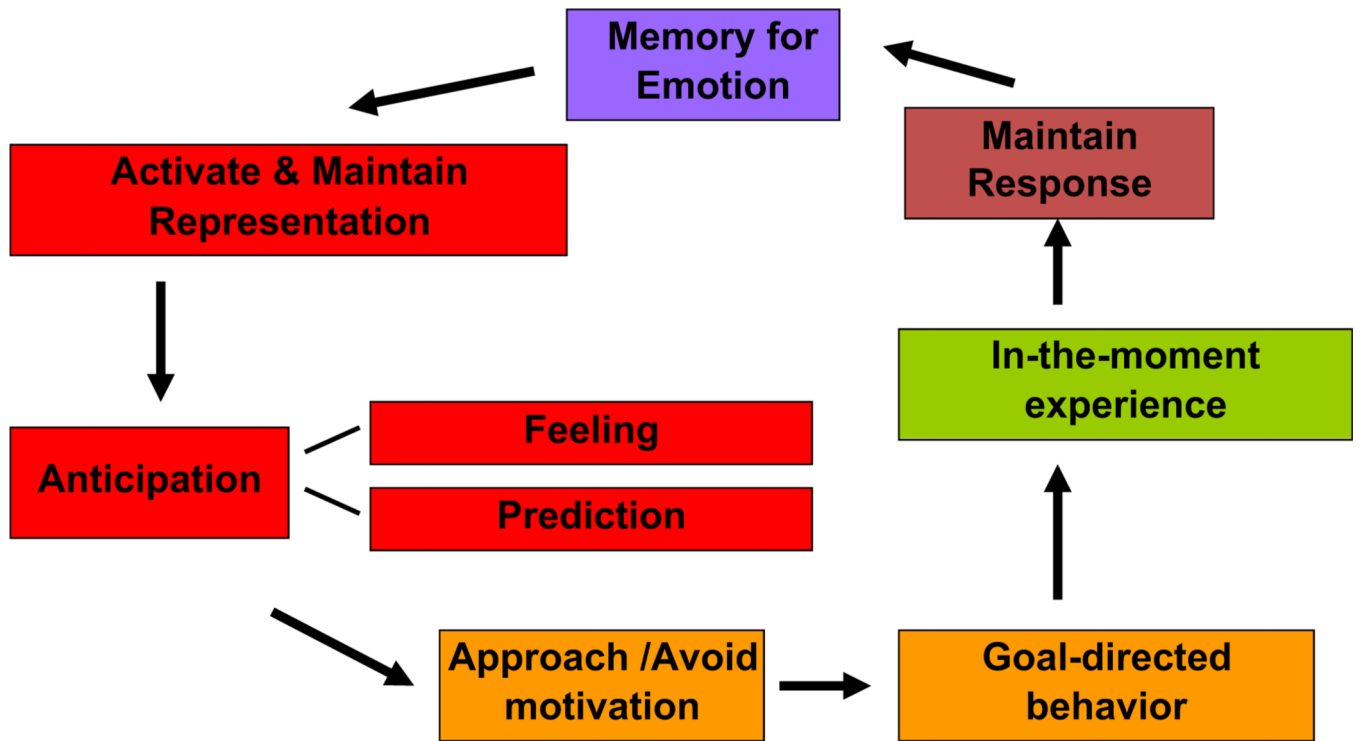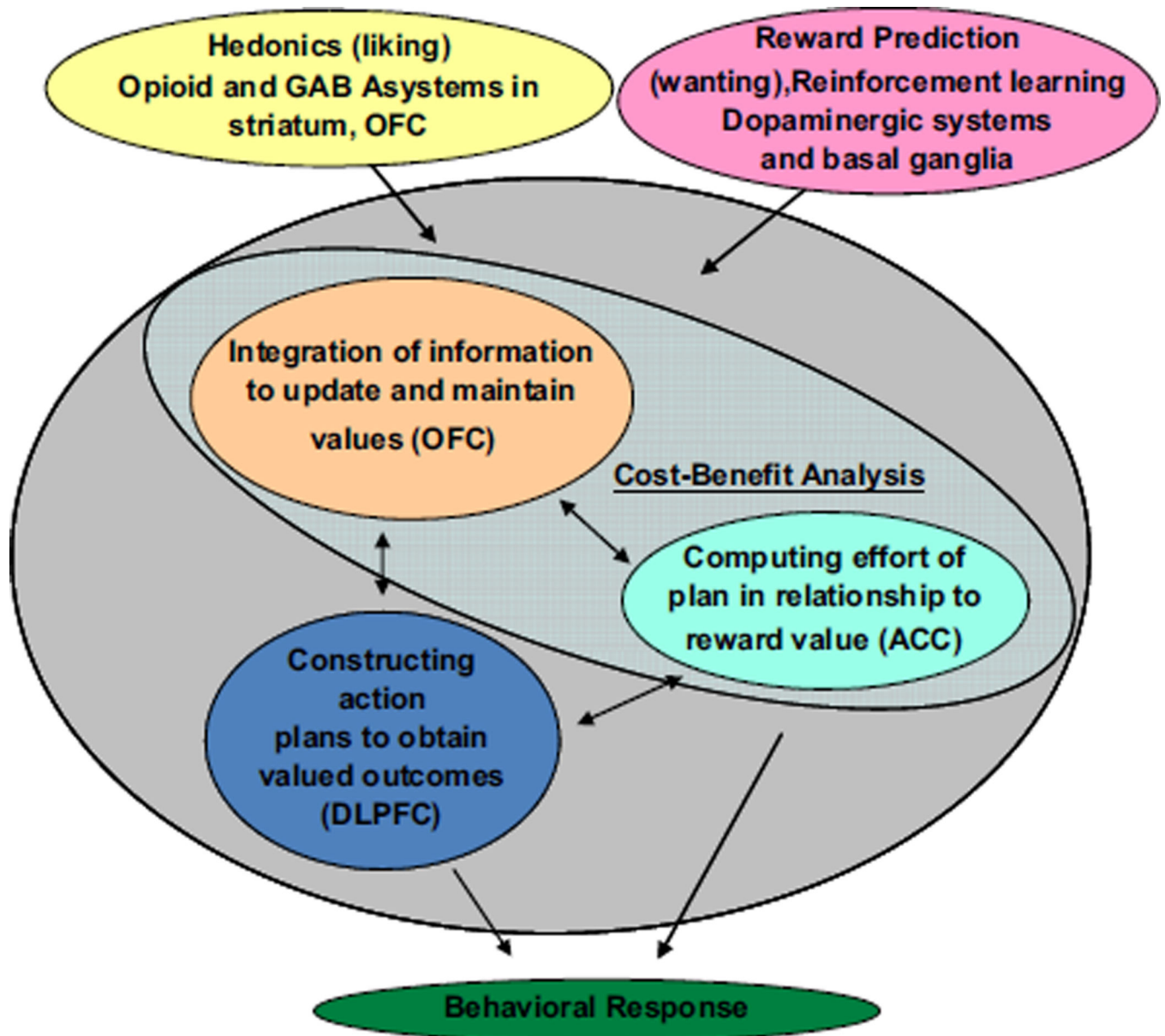
Fig. 1.
Temporal experience of emotion.

Components of Reward to Outcome Translation
Note: After Wallis (2007)

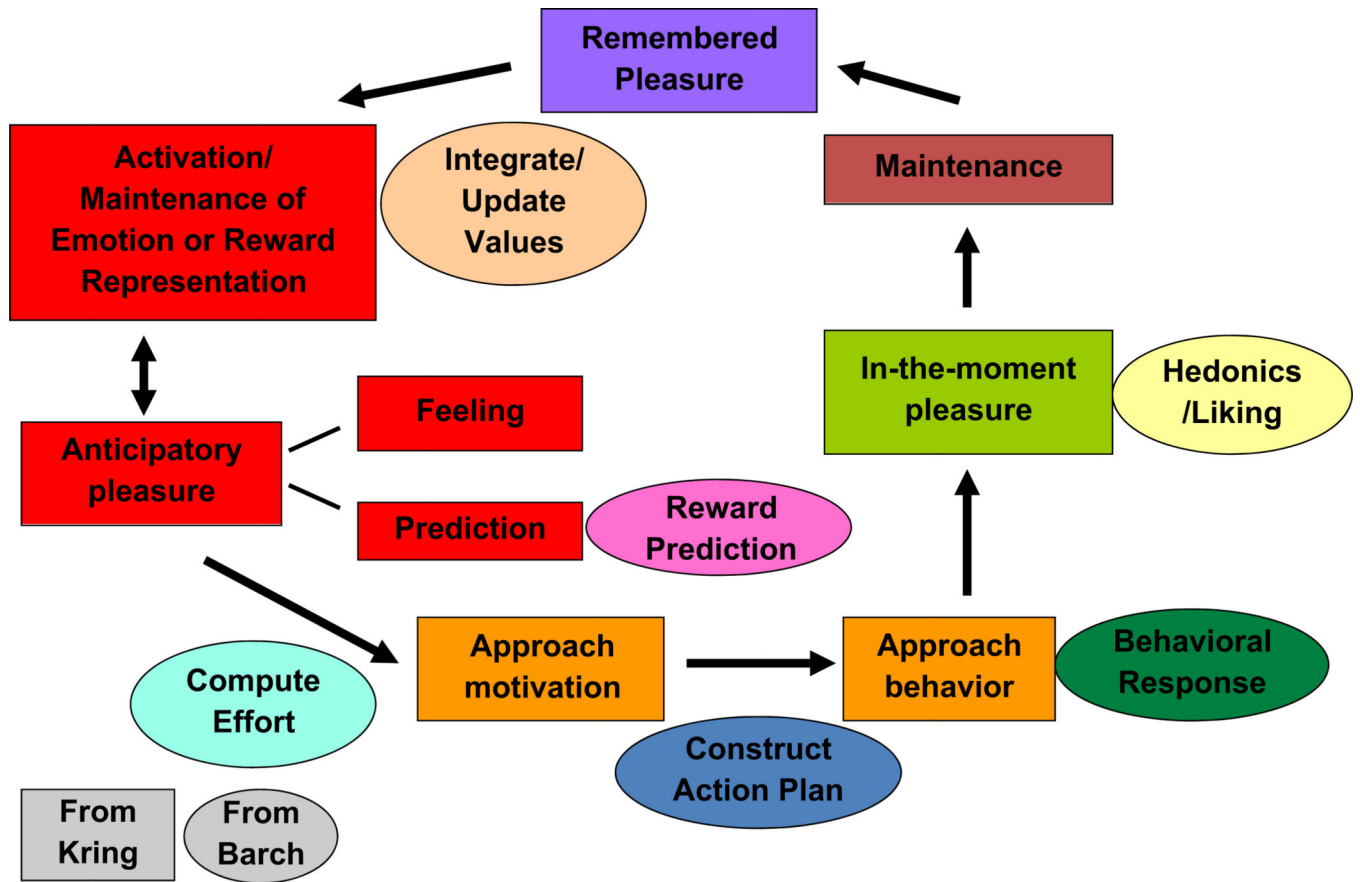**Fig. 2.**
Reward to outcome translation.

Fig. 3.
Integrating the temporal experience of emotion with reward to outcome translation (Kring & Barch).

Table 1

Key terms and concepts.

Term	Definition
In-the-moment pleasure experience ("liking" or "consummatory pleasure")	The responses people provide when presented with putatively positive things, such as how they people report feeling when presented with funny pictures, tasty foods, or reward of $5, or how their brain responds when presented with such stimuli
Anticipatory pleasure ("wanting")	A prediction about a future enjoyable outcome (reward) and/or a feeling of pleasure in anticipation of that outcome
Prediction error	An *increase* in striatal (presumably dopaminergic) responses to unexpected rewards and a *decrease* in striatal responses when predicted rewards do not occur
Effort computation	How much effort is needed to achieve a desired outcome (reward)
Value computation	How valuable a potential reward or desired outcome is, given the current state of the person (e.g., how valuable is a bottle of spring water when I am very thirsty versus when I just drank a bottle of water)
Reversal learning	When presented with a choice between two stimuli (e.g., door 1 or door 2), learning that a previously rewarded stimulus (e.g., door 1) is no longer associated with reward, and that the other stimulus is now associated with reward (e.g., door 2)
Goal-directed behavior	Selection and execution of actions necessary to obtain potentially desirable or rewarding outcomes that fulfill a goal (e.g., the experience of pleasure, or a special outcome)
DLPFC	Dorsolateral prefrontal cortex
OFC	Orbital frontal cortex
DA	Dopamine
ACC	Anterior cingulate cortex