Anhedonia, avolition, and anticipatory deficits: Assessments in animals with relevance to the negative symptoms of schizophrenia

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Abstract
Schizophrenia represents a complex, heterogeneous disorder characterized by several symptomatic domains that include positive and negative symptoms and cognitive deficits. Negative symptoms reflect a cluster of symptoms that remains therapeutically unresponsive to currently available medications. Therefore, the development of animal models that may contribute to the discovery of novel and efficacious treatment strategies is essential. An animal model consists of both an inducing condition or manipulation (i.e., independent variable) and an observable measure(s) (i.e., dependent variables) that are used to assess the construct(s) under investigation. The objective of this review is to describe currently available experimental procedures that can be used to characterize constructs relevant to the negative symptoms of schizophrenia in experimental animals. While negative symptoms can encompass aspects of social withdrawal and emotional blunting, this review focuses on the assessment of reward deficits that result in anhedonia, avolition, and abnormal reward anticipation. The development and utilization of animal procedures that accurately assess reward-based constructs related to negative symptomatology in schizophrenia will provide an improved understanding of the neural substrates involved in these processes.

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1. Introduction

In recent years, research has advanced our understanding of the neural substrates that contribute to the neuropathology of schizophrenia. However, there is a distinct lack in our ability to effectively manage the domain of negative symptoms evident in many schizophrenia patients. The negative
symptoms domain includes deficit symptoms that reflect a 
reduction of emotions or behaviors usually present in the 
healthy population, such as anhedonia, avolition, flat affect 
or emotional blunting, reductions of verbal fluency or 
poverty of speech, and defects in social behavior. This cluster 
of symptoms is largely unresponsive to current antipsychotic 
medications. The severity of negative symptoms has been 
suggested to impact and predict the functional and occupa-
tional outcome of schizophrenia patients (Ho et al., 1998; 
Kirkpatrick et al., 2006). Because of the detrimental effects 
of negative symptoms, coupled with the unmet therapeutic 
need in addressing this symptomatic domain, much research 
in recent years has focused on improving the understanding 
and treatment of negative symptoms associated with schizo-
phrenia (Kirkpatrick et al., 2006).

The purpose of the present review is to describe experi-
mental animal procedures that allow investigators to eval-
uate constructs thought to be central to the negative 
symptomatology of schizophrenia. Various experimental 
manipulations used to induce deficits in reward processes 
will be discussed briefly, but the focus will be primarily on 
describing the specific behavioral tasks used to characterize 
these deficits. Anhedonia, avolition, emotional blunting, 
alogia, and social withdrawal all fall under the umbrella 
that encompasses negative symptoms. Some of these fea-
tures may not be mutually exclusive (e.g., avolition may 
(a) promote social withdrawal), and some are difficult to assess 
in animals (e.g., emotional blunting and alogia). Procedures 
that model social withdrawal in experimental animals are 
reviewed elsewhere in this Special Issue (Koenig et al., in 
this issue).

2. Reward deficits and anhedonia 
in schizophrenia patients

Anhedonia refers to the inability or diminished capacity to 
experience pleasure and is thought to reflect deficits in brain 
reward system function. Anhedonia has long been 
suggested to be a core symptom of schizophrenia, falling 
within the cluster of features that encapsulates the nega-
tive symptomatology associated with schizophrenia. Anhe-
 donia was originally described by Kraepelin in his first 
descriptions of dementia praecox (later come to be known 
as schizophrenia) as a central component of the disorder 
(Kraepelin, 1921; Bleuer, 1924; Strauss and Gold, 2012), and 
it is included as a symptom in the Diagnostic and Statistical 
Manual of Mental Disorders (DSM-V) (American Psychiatric 
Association, 2013). The definition of anhedonia is sometimes 
extended incorrectly to encompass additional deficits in 
reward-related processes, such as the pursuit of pleasure. 
This extension of the definition of anhedonia should be 
avoided because the ability to experience pleasure and the 
desire to engage in pleasurable activities are subserved by 
distinct neural pathways (Berridge and Robinson, 2003; Der-
Avakian and Markou, 2012) and should be treated as separate 
constructs. Interview-based measures or self-report style 
questionnaires are often used to assess anhedonia in schizo-
phrenia patients. However, it has been suggested recently 
that schizophrenia is not associated with diminished capacity 
to experience pleasure per se (Horan et al., 2006), but rather 
may reflect deficits in other components of the reward 
system. Deficits in brain reward function are multifaceted 
and can include other features in addition to hedonic 
capacity, such as altered reward prediction, anticipation or 
valuation. Deficits in any one of these processes may lead to a 
reduction in the engagement of pleasurable activities, even 
when the individual still has the capacity to experience 
pleasure. Given the dissociation between anhedonia and 
other deficits of brain reward systems, anhedonia may not 
be as central to schizophrenia as it was once thought to be. 
Schizophrenia patients have been reported to indeed have 
the ability to experience affective consummatory pleasure 
(Gard et al., 2007; Heerey and Gold, 2007), indicating that 
 schizophrenia patients are not necessarily anhedonic. Rather , 
these patients may have a dissociation of hedonic capacity 
from motivated behavior (Heerey and Gold, 2007), deficits in 
reward anticipation (Dowd and Barch, 2012; Gard et al., 
2007), and/or a reduced ability to draw upon memories of 
previous pleasurable activities (Simpson et al., 2012). Deficits 
in accurately recalling previously pleasurable activities or 
predicting pleasure from future events likely gives the 
impression of a global reduction of the capacity to experience 
pleasure. As a result, these deficits may elicit the false 
impression of anhedonia, reflected in interview-based ques-
tionnaires, while not necessarily being attributable to deficits 
in the pleasure systems of the brain that mediate hedonic 
reactions.

3. Motivational deficits and avolition 
in schizophrenia patients

Like anhedonia, a deficit in motivational capabilities, or 
avolition, is also a symptom included in the original descrip-
tions of schizophrenia (Kraepelin, 1921; Foussias and Remi-
ington, 2010). Deficits in a patient’s ability to become moti-
vated and engage in a given task has been suggested to 
considerably affect their quality of life, leading to a reduced 
drive to initiate or persist in goal-directed behavior (Barch and 
Dowd, 2010). Moreover, the severity of these deficits is 
believed to be closely correlated with the functional outcome 
of schizophrenia patients (Simpson et al., 2012). In fact, 
reductions of volition or impairments in the patient’s motiva-
tional capabilities have been suggested to be not only one of 
the most disabling facets of schizophrenia but is also likely to 
underpin some of the accompanying negative symptoms, such 
as social withdrawal, and cognitive impairments associated 
with schizophrenia (Brebion et al., 2009).

To address this fundamental aspect of negative sympto-
matology and understand the process of avolition, one must 
explore the factors that drive an organism to become 
motivated. Reward processing has many facets, including 
aspects of learning, reward valuation, emotional or affective 
factors, and purely motivational components (Berridge and 
Robinson, 2003; Gold et al., 2008). Two of these elements 
may be particularly important to motivated behavior. First is 
the affective component. If an organism derives pleasure 
from something, then it is more likely to expend energy to 
orient towards it (Salamone, 2009). Thus, consummatory pleasure is 
conducive to motivation because it provides the hedonic 
component that drives motivated behavior. However, as 
described above, evidence suggests that the hedonic reac-
tions to evoked stimuli are unimpaired in schizophrenia, and
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