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Effort-Based Decision Making in Schizophrenia: Evaluation of Paradigms to Measure Motivational Deficits

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Effort-based decision making requires one to decide how much effort to expend for a certain amount of reward. As the amount of reward goes up most people are willing to exert more effort. This relationship between reward level and effort expenditure can be measured in specialized performance-based tasks that have only recently been applied to schizophrenia. Such tasks provide a way to measure objectively motivational deficits in schizophrenia, which now are only assessed with clinical interviews of negative symptoms. The articles in this theme provide reviews of the relevant animal and human literatures (first 2 articles), and then a psychometric evaluation of 5 effort-based decision making paradigms (last 2 articles). This theme section is intended to stimulate interest in this emerging area among basic scientists developing paradigms for preclinical studies, human experimentalists trying to disentangle factors that contribute to performance on effort-based tasks, and investigators looking for objective endpoints for clinical trials of negative symptoms in schizophrenia.

Key words: effort-based decision making/motivation/negative symptoms

It starts with a choice. It ends with a decision.

At its core, effort-based decision making involves deciding how much effort to expend for a certain amount of reward. As the amount of reward goes up the willingness to exert effort should go up as well. We confront such decisions repeatedly throughout our daily lives, but usually do not give them much thought. The reward can vary widely in type: money, food, professional status, social connections, etc. The time frame can vary from minutes to years. But at the core, it is a decision about matching one's effort to one's expectation of reward.

Why study effort-based decision making in schizophrenia, and why devote a theme in this journal to the topic? It was not an obvious area for exploration previously, as reflected by the fact that the first publication on effort-based decision making in schizophrenia appeared only 2 years ago (by Gold and colleagues[1]). One reason this area is applicable to schizophrenia is that effort-based decision making probably underlies some negative symptoms. The negative symptoms that we assess with clinical interviews reflect a combination of 2 separate factors.[2,3] One factor is expressive (blunted affect, alogia), and the other motivational or experiential (avolition, anhedonia, asociality). Notably, the motivational symptoms are more closely linked to daily functioning than the expressive symptoms.[4–6] If you want to improve one component of negative symptoms to enhance daily functioning, you should cast your lot with motivational negative symptoms.

But there is a problem. Currently, our only way to assess negative symptoms is with clinical interviews. These interviews are useful and have recently been refined, but they are chock full of potential threats to reliability and validity, including variability in the skills of the interviewers, the need for inter-rater reliability beyond test-retest reliability, and the ability of the participant to introspect and recall accurately their motivational levels over the past weeks. One way to circumvent these concerns would be to use an objective measure of motivation, both as an endpoint in clinical trials and to select participants for trials.

Aside from applications to human studies of motivation, effort-based decision-making tasks have deep roots in basic science. The neural systems involved in an animal's decisions about effort for reward are well identified and could be used as preclinical models for drug development. Indeed, some of the effort-based paradigms considered in this theme section are rather direct adaptations of animal paradigms.

This theme section consists of 2 introductory review articles that provide background and explain the value of this area, and 2 data-based articles. In the first review,

Table 1. Effort-Based Decision Making Paradigms: Overview and Comparison

	Effort Type	Calibration: Individual Titrated "Hard" Trials (Y/N)	Reward:Actual Earnings or Prefixed Amount	Probability (Y/N)	Time-Matched Hard/Easy Trials (Y/N)
Deck Choice Effort Task	Cognitive	No	Actual	No	Yes
Perceptual Effort Task	Perceptual	Yes	Actual	No	Yes
Grip Effort Task	Physical	Yes	Actual	No	Yes
Balloon Effort Task	Physical	No	Prefixed	No	No
EEfRT	Physical	Yes	Prefixed	Yes	No

Young and Markou[7] set the stage by providing an overview of preclinical models of effort-based decision making and related motivational constructs. They focus on rodent paradigms that show strong potential for cross-species extensions to humans, including tasks for physical and cognitive effort-based decision making, as well as probabilistic learning. Special attention is given to shared and unique neural mechanisms that underlie performance on these tasks. The second review by Green and colleagues[8] provides theoretical background on effort-based decision making paradigms in human studies and their clinical application to schizophrenia. In addition to reviewing existing studies of effort-based decision making in schizophrenia, they highlight some of the practical challenges in adapting and interpreting such measures in the context of clinical trials.

The last 2 articles evaluate the utility of 5 effort-based decision making paradigms for clinical trials in a large, diverse sample of outpatients with schizophrenia. As shown in table 1, the 5 paradigms span the domains of cognitive, perceptual, and physical effort. They also differ along several other dimensions, such as whether the difficulty levels are individually calibrated for "hard" vs "easy" trials, participants receive the actual monetary reward amount earned vs a prefixed amount, the probability is manipulated for receiving a reward after successful trials, and the time interval is equivalent for hard vs easy trials. Reddy and colleagues[9] evaluate the psychometric properties of the paradigms, including patient vs healthy control group differences, 4-week test-retest reliability, utility as a repeated measure, and tolerability. In the last article, Horan and colleagues[10] examine the external validity of the paradigms with respect to clinical interview-based negative symptoms ratings and clinically rated community role functioning and motivation, as well as other variables. They conclude with an integrative summary of findings across the 2 data-based articles and evaluate the suitability of the paradigms for use in clinical trials.

The findings presented in this theme section represent an excellent example of an academia-industry collaboration that was sponsored by Amgen. Data collection proceeded efficiently and was completed in less than 18 months. All statistical analyses were conducted by our research group in Los Angeles, and findings were made public through conference presentations and this theme section. We invited a renowned group of external consultants for the project (including Drs Barch, Buchanan, Gold, and Young) who voiced their perspectives, applied critical analysis, and prevented us from falling prey to insular thinking.

At this time, 8 articles have been published on effort-based decision making tasks in schizophrenia, and each article presented results from a single paradigm. The papers in this theme are the first attempts to integrate results across effort-based paradigms, in a study involving schizophrenia patients. These paradigms have been applied to schizophrenia only in the past 2 years; hence, this area is still in its infancy and basic questions remain unaddressed. But the level of interest is high and it has the practical significance of advancing the assessment of motivation in schizophrenia. We believe the articles in this theme will be useful to different researchers for different reasons: to basic scientists who are exploring ways to reverse translate paradigms for preclinical studies, to human experimentalists who are trying to disentangle the factors that contribute to performance on effort-based tasks, to clinical investigators who are studying other conditions in which motivation is a concern, and to clinical trialists who are seeking objective ways to measure endpoints associated with negative symptoms in schizophrenia.

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