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Abnormal cognitive effort allocation and its association with amotivation in first-episode psychosis

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Abstract

Background. Abnormal effort-based decision-making represents a potential mechanism underlying motivational deficits (amotivation) in psychotic disorders. Previous research identified effort allocation impairment in chronic schizophrenia and focused mostly on physical effort modality. No study has investigated cognitive effort allocation in first-episode psychosis (FEP).

Method. Cognitive effort allocation was examined in 40 FEP patients and 44 demographically-matched healthy controls, using Cognitive Effort-Discounting (COGED) paradigm which quantified participants' willingness to expend cognitive effort in terms of explicit, continuous discounting of monetary rewards based on parametrically-varied cognitive demands (levels *N* of *N*-back task). Relationship between reward-discounting and amotivation was investigated. Group differences in reward-magnitude and effort-cost sensitivity, and differential associations of these sensitivity indices with amotivation were explored.

Results. Patients displayed significantly greater reward-discounting than controls. In particular, such discounting was most pronounced in patients with high levels of amotivation even when *N*-back performance and reward base amount were taken into consideration. Moreover, patients exhibited reduced reward-benefit sensitivity and effort-cost sensitivity relative to controls, and that decreased sensitivity to reward-benefit but not effort-cost was correlated with diminished motivation. Reward-discounting and sensitivity indices were generally unrelated to other symptom dimensions, antipsychotic dose and cognitive deficits.

Conclusion. This study provides the first evidence of cognitive effort-based decision-making impairment in FEP, and indicates that decreased effort expenditure is associated with amotivation. Our findings further suggest that abnormal effort allocation and amotivation might primarily be related to blunted reward valuation. Prospective research is required to clarify the utility of effort-based measures in predicting amotivation and functional outcome in FEP.

Introduction

Psychotic disorders are a group of severe mental disorders representing one of the leading causes of disability worldwide (Global Burden of Disease Study 2013 Collaborators, 2013). Reduced motivation and goal-directed behavior (amotivation) is a central feature of negative symptoms (Foussias and Remington, 2010) in psychotic disorders and is critically associated with functional impairment. In particular, recent studies showed that amotivation is already prevalent in patients with first-episode psychosis (FEP) (Fervaha *et al.*, 2015*a*; Norman *et al.*, 2015). Accumulating evidence further indicated that amotivation emerged in the early stage of illness significantly predicts both short-term (Faerden *et al.*, 2013; Fervaha *et al.*, 2015*a*; Chang *et al.*, 2016, 2017, 2018*a*; Lutgens *et al.*, 2019) and long-term (Ventura *et al.*, 2015; Chang *et al.*, 2018*b*) negative symptom and functional outcomes. Given that a significant proportion of FEP patients experience persistent functional impairment even after clinical stabilization (Chang *et al.*, 2012, 2018*c*; Verma *et al.*, 2012), amotivation thus constitutes an important therapeutic target for promoting early functional recovery as well as preventing the development of enduring negative symptoms.

There has been growing interest in clarifying neurobiological mechanisms underlying amotivation in psychotic disorders with an aim to facilitate the development of effective interventions. Effort-based decision-making has recently been proposed as a useful translational

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paradigm linking well-studied preclinical models of effort-cost computation with evaluation of motivational impairment in schizophrenia (Green *et al.*, 2015; Young and Markou, 2015). These paradigms offer quantitative, performance-based measurement of amotivation by examining participants' willingness to expend effort for rewards. Of note, effort-based decision-making can be classified on the basis of effort modalities, i.e. physical and cognitive effort, and recent data have suggested that these two effort modalities are mediated by similar neural systems (Schmidt *et al.*, 2012; Chong *et al.*, 2017). As dopamine neurotransmission and corticostriatal circuits, especially anterior cingulate cortex, are both crucially involved in effort-cost computation (Croxson *et al.*, 2009; Bailey *et al.*, 2016) and implicated in the pathophysiology of psychotic disorders (Minzenberg *et al.*, 2009; Howes *et al.*, 2012), it is thus suggested that effort-based decision-making would likely be impaired in patients with the disorder.

Recently, an increasing number of studies have been conducted to investigate effort-based decision-making in schizophrenia, with the vast majority focusing on physical effort allocation (Gold *et al.*, 2015*a*; Culbreth *et al.*, 2018; Hartmann-Riemer *et al.*, 2018). Most studies revealed evidence of the inflated estimated cost of physical effort in patients, who were less willing to select high-effort/high-reward options than healthy controls. Such reduced effort expenditure was also found to be associated with higher levels of amotivation in many (Gold *et al.*, 2013; Barch *et al.*, 2014; Fervaha *et al.*, 2015*b*; Hartmann *et al.*, 2015; Horan *et al.*, 2015; Wang *et al.*, 2015; Strauss *et al.*, 2016; Serper *et al.*, 2017), though not all (Docx *et al.*, 2015; Treadway *et al.*, 2015; McCarthy *et al.*, 2016; Bismark *et al.*, 2018) previous studies. Conversely, cognitive effort-based decision-making, which may arguably be even more important than physical effort-cost valuation for adequate everyday functioning in modern society, has been much less studied in psychotic disorders. Until now, there are only five published reports examining cognitive effort allocation in schizophrenia (Wolf *et al.*, 2014; Gold *et al.*, 2015*b*; Reddy *et al.*, 2015, 2018; Culbreth *et al.*, 2016), and the results are less consistent as compared to those of physical effort-based decision-making. Several past studies demonstrated decreased willingness to exert cognitive effort for rewards in patients relative to controls (Wolf *et al.*, 2014; Reddy *et al.*, 2015, 2018; Culbreth *et al.*, 2016) while others revealed a lack of significant group difference in cognitive effort avoidance (Gold *et al.*, 2015*b*). Mixed findings were also observed regarding relationship between diminished motivation and cognitive effort allocation, with some studies indicating that more severe amotivation was associated with an aversion to higher levels of cognitive effort in pursuit of rewards (Wolf *et al.*, 2014; Culbreth *et al.*, 2016) but not others (Gold *et al.*, 2015*b*; Reddy *et al.*, 2015, 2018).

It is noteworthy that despite clinical significance and prognostic implication of amotivation in early psychosis, previous research examining effort-based decision-making in psychotic disorders only focused on chronically-ill samples (Culbreth *et al.*, 2018; Hartmann-Riemer *et al.*, 2018) which are confounded by illness chronicity and prolonged exposure to antipsychotic treatment. Whether impairment in effort-cost computation has already taken place in the initial phase of illness remain to be clarified. In fact, our recent investigation (Chang *et al.*, 2019) was the first to provide evidence of abnormal physical effort allocation in FEP patients who displayed reduced willingness to expend effort for high-reward/high-probability options during a button-pressing effort-related experiment (Treadway *et al.*, 2009), with such impairment being most pronounced in patients with high levels of amotivation. In the current study, we sought to extend our work on physical effort expenditure by investigating cognitive effort-based decision-making in FEP patients. To assess cognitive effort, we adopted a recently developed Cognitive Effort-Discounting (COGED) paradigm (Westbrook *et al.*, 2013) which was based on the behavioral economic approach and has previously been studied in chronic schizophrenia (Culbreth *et al.*, 2016). In brief, COGED assesses participants' subjective willingness to expend cognitive effort for reward which was quantified in terms of explicit, continuous discounting of monetary rewards based on parametrically-varied cognitive loads (by levels *N* of *N*-back working memory task) (Westbrook *et al.*, 2013). Hence, this paradigm provides an objective, continuous measure of subjective cognitive effort costs and reward benefits, with more extensive discounting indicating more subjectively costly cognitive effort, reduced incentive motivation, or both. Based on prior literature, we hypothesized that FEP patients would exhibit impairment in cognitive effort-based decision-making by discounting reward value significantly more steeply as a function of effort than healthy controls, and that dysfunctional effort allocation would be associated with higher levels of amotivation. In addition, we conducted exploratory analyses clarifying potential differences between patients and controls in the sensitivity to reward magnitude and effort cost, as well as differential relationships between these sensitivity indices and amotivation in FEP patients.

Methods

Participants

Forty patients in their first psychotic episode, aged 15–40 years, were recruited from the outpatient unit of a specialized early intervention service for FEP in Hong Kong. Diagnosis was ascertained using the Chinese-bilingual Structured Clinical Interview for DSM-IV (APA, 2000; CB-SCID-I/P; So *et al.*, 2003) (27 received a DSM-IV diagnosis of schizophrenia, seven with schizophreniform disorder, one with schizoaffective disorder, three with brief psychotic disorder, one with delusional disorder, and one with psychotic disorder not otherwise specified). First-episode status was verified using the Interview for Retrospective Assessment of Onset of Schizophrenia (IRAOS; Häfner *et al.*, 1992). Study assessments were administered to patients within 6 months following antipsychotic initiation (mean: 131 days; S.D.: 44), at which point all patients had been on stable antipsychotic regimens for at least 4 weeks.

Forty-four healthy controls were recruited from the community via advertisements and word-of-mouth among recruited participants. Patients and controls were matched for age, gender, and educational level. Controls were screened to confirm that they had no current psychiatric diagnosis (by CB-SCID-I/P), family history of psychotic disorder, and were not taking any psychotropic medications.

The study was approved by the local institutional review boards, and all participants provided written informed consent. For those aged under 18 years, parental consent was also obtained. Any individual showing evidence of substance abuse (by Alcohol Use Scale and Drug Use Scale; Drake *et al.*, 1996), intellectual disability, or neurological disease was excluded from participation.

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Clinical and cognitive assessments

Positive and disorganization symptoms were assessed using the Positive and Negative Syndrome Scale (PANSS; Kay *et al.*, 1987). Negative symptoms were measured by the Brief Negative Symptom Scale (BNSS; Kirkpatrick *et al.*, 2011). As the negative symptom construct has consistently demonstrated two distinct subdomains of amotivation and diminished emotion-expressivity (DE) (Messinger *et al.*, 2011), we derived amotivation and DE scores based on the method applied by previous research (Strauss et al., 2012; Hartmann *et al.*, 2015): Amotivation consisted of items of Anhedonia, Avolition and Asociality subscales on the BNSS; and DE comprised items of Blunted affect, Alogia, and Lack of normal distress subscales. Depression was evaluated using the Calgary Depression Scale (CDS; Addington *et al.*, 1992). Antipsychotic-induced Parkinsonism was examined by the Simpson–Angus Scale (SAS; Simpson and Angus, 1970). Cognitive assessments included letter–number span (Gold *et al.*, 1997), digit symbol subtest from the Wechsler Adult Intelligence Scale-Revised (WAIS-R; Hong Kong Psychological Society, 1989*a*), letter cancellation test (Diller *et al.*, 1974), Trail making test (Reitan, 1955), and logical memory subtest from the Wechsler Memory Scale-Revised (WMS-R; Hong Kong Psychological Society, 1989*b*).

Cognitive effort assessment

The COGED paradigm (Westbrook *et al.*, 2013) was administered to measure the participant's subjective willingness to expend cognitive effort for monetary reward. Schematic illustration of the COGED task is shown in online Supplementary Fig. S1. Briefly, first, participants underwent an *N*-back practice by completing two runs of *N*-back (levels $N = 1$–5) for each level (64 items with 16 targets per run), in order of increasing difficulty. Inter-item intervals were 2 s regardless of *N*-back level, and duration of each run was 128 s. Next, in discounting procedure, participants made a series of two alternative choices between repeating a harder *N*-back level ($N > 1$, high-effort trial) for a larger monetary reward or an easier 1-back level (low-effort trial) for a smaller monetary reward. Specifically, after each choice, the 1-back reward offer (starting at $1) was titrated until participants were approximately indifferent between a fixed greater reward offer for each of the harder *N*-back levels ($N = 2$–5) and a lesser reward offer for the easiest 1-back level (i.e. reaching subjective equivalence of reward offers being equally preferred). For instance, on a given trial, if the larger reward offer was selected, the offer for the 1-back level was increased; and if the smaller reward offer was chosen, it was decreased. Each time a choice was made, adjustments of the reward offer were half as much as on the prior adjustment. In this study, two base reward offers ($2 and $4) were used for the harder *N*-back levels and each pair of *N*-back level–reward offer was titrated over a series of five decision-making trials, with the resulting amount following the final choice for each *N*-back level being taken as the participant's point of indifference. Thus, there were a total of 40 decision-making trials with eight indifference points for each participant. The point of indifference was critical as the indifference offer at each level quantified subjective effort costs in terms of discounted reward value (i.e. how much more subjectively costly the harder *N*-back level was relative to the easier 1-back level). For example, if a participant was indifferent between $1.70 for the 1-back and $4.00 for the 3-back, then the subjective cost of the 3- *v.* the 1-back was $2.30. Finally, one of the participant's choices was randomly selected for repetition (up to 10 more times) which determined what level of *N*-back trial they repeated and the amount of task bonus paid to them upon completion. Participants were instructed that payment was contingent on 'maintaining their effort', but not on performance. In actuality, all participants were paid the task bonuses, as well as the base-compensation of HK$100 (US$13), for completion of the study assessment.

Statistical analysis

The primary analysis aimed to examine whether the subjective value (SV) of cognitive effort-demanding rewards was lower for FEP patients than controls. Subjective willingness for cognitive effort expenditure (based on effort-cost/reward-benefit estimation) was quantified as the SV of discounted monetary rewards in COGED. The indifference point, namely the reward amount following a final choice of five-iterated decision-making trials, for a given pair of *N*-back level–reward offer was normalized by the base reward offer to derive an SV. To compare the degrees of effort discounting between patients and controls, multilevel models were employed which accounted for hierarchical nesting of SVs within participants. Following the method applied by previous research (Culbreth *et al.*, 2016), we fit diagnostic group membership (patients *v.* controls), *N*-back level *N* (task load), and group × level interaction as fixed factors in an initial model for predicting SVs, with subject-specific intercept and *N*-back level effects being allowed to vary by participants. Separate multilevel models were also constructed to test for potential effects of *N*-back performance and base reward amount on effort discounting. Likelihood-ratio test was then used for nested model comparison to determine the most parsimonious model for patient-control difference in effort discounting. Multilevel models were fit in R using the lme4 package (Bates *et al.*, 2015), version 3.4.4 (R Core Team, 2018).

To investigate the relationship between SV and negative symptoms, two approaches were adopted: First, as evidence suggested that amotivation subdomain of negative symptoms may be specifically linked to abnormal effort-cost computation, we employed a categorical approach by classifying patients into high (HIGH-AMO) and low (LOW-AMO) amotivation subgroups, based on a median split on BNSS amotivation score (split score = 15). Multilevel model analyses were conducted to examine the differences between HIGH-AMO, LOW-AMO, and control groups in effort discounting. Second, we calculated the area under the discounting curve (AUC) connecting SVs across all *N*-back levels ($N = 2$–5) as a summary measure of effort costliness for each participant (Westbrook *et al.*, 2013; Culbreth *et al.*, 2016). A smaller AUC corresponded to steeper effort discounting. We then examined correlations between AUC and negative symptom measures (BNSS amotivation and BNSS total scores). Evaluating the effects of negative symptoms both categorically and dimensionally is important because the construct is not purely continuous, but rather a hybrid categorical–dimensional nature (Ahmed *et al.*, 2015). Correlations of AUC with other symptom dimensions, antipsychotic dose, and cognitive functions were also assessed. Additionally, given that SV of discounted monetary rewards could be affected by subjective effort-cost estimation and/or reward-magnitude valuation, exploratory analyses were conducted to investigate group differences in the utilization of reward-magnitude and effort-cost information in effort-based

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decision-making, as well as their differential relationships with negative symptoms and amotivation. Taking reference to the methodology adopted by previous research on physical effort allocation (Treadway *et al.*, 2015), individual multiple regression analyses were performed for each participant with the base amount and task load as regressors predicting SV. The β weight (standardized regression coefficient) of base amount represented as an index for reward-benefit sensitivity, while β weight of task load was an index for effort-cost sensitivity. Group comparisons on sensitivity indices were conducted using independent-samples *t* tests (FEP *v.* controls) and analyses of variance (ANOVAs; HIGH-AMO, LOW-AMO, and controls) as appropriate. Correlations of sensitivity indices with other symptom dimensions, antipsychotic dose, and cognitive functions were examined.

Results

Characteristics of the sample

Demographics, cognitive functions, and clinical characteristics of the participants are summarized in Table 1. There were no significant differences among controls, HIGH-AMO, and LOW-AMO groups in age, gender, or educational levels. Controls had significantly better performance in all individual cognitive tests than the two patient groups. Among FEP patients, HIGH-AMO group had significantly higher BNSS total, amotivation, and DE scores than LOW-AMO group. No other significant differences were observed between the two patient groups in demographics, cognitive functions, clinical, and treatment characteristics.

Effort task performance in the FEP sample

In general, *N*-back performance declined with an increase in task load (*N*-back level *N*), and patients displayed significantly poorer performance than controls at all *N*-back levels (Table 2). Both patients and controls discounted reward offers for higher levels of *N*-back task, with a decrease in SV for every *N*-back level. This indicates that discounting for participants in both groups was sensitive to task demand, and subjective effort costs increased with objective load (Fig. 1*a*).

Multilevel model analysis was performed to test for group difference in SVs. As shown in Table 3, Model 1 demonstrated a significant effect of group membership on predicting SV, such that patients discounted rewards more steeply relative to controls. We fit *N*-back performance and base reward amount in two separate multilevel models to examine their potential effect on effort discounting. Our results showed that neither *N*-back performance ($\beta = 0.03$, S.E. = 0.01, $p = 0.06$) nor base amount ($\beta = 0.02$, S.E. = 0.01, $p = 0.07$) was a significant predictor of SV (albeit showing marginal level of significance). Larger model including either measure also did not explain sufficient additional variance to justify the added model complexity (*N*-back performance: $\chi^2 = 3.75$, $p = 0.07$; base amount: $\chi^2 = 3.34$, $p = 0.07$), as determined by a nested model comparison. Thus, Model 1 represented the most parsimonious model for patient-control difference in effort discounting. Of note, we also conducted supplementary analysis by including both measures in the same multilevel model which, however, revealed loss of significant main effect of group (online Supplementary Table S1).

Effort task performance in high and low amotivation patient groups

As shown in Table 2, overall, *N*-back performance worsened with an increase in task load in both HIGH-AMO and LOW-AMO patients. The two patient groups did not differ from each other in *N*-back performance across task levels. A multilevel model (Model 2) testing differences in effort discounting among three groups revealed a significant effect of HIGH-AMO group membership on predicting SV (Table 3). A significant task × HIGH-AMO group interaction was also observed. As seen in Fig. 1*b*, HIGH-AMO patients had significantly lower SVs than both controls and LOW-AMO patients at every *N*-back level except $N = 5$ (no group difference), while there were no significant differences between controls and LOW-AMO patients in SVs across all task levels. Thus, HIGH-AMO patients discounted rewards more steeply relative to controls and LOW-AMO patients. To determine whether HIGH-AMO group effect on effort discounting could be explained by group differences in *N*-back performance, Model 3 was constructed which included task performance as a potential predictor of SV. A significant effect of *N*-back performance ($\beta = 0.03$, S.E. = 0.01, $p = 0.04$) was observed. Importantly, the effects of HIGH-AMO group membership and task × HIGH-AMO group interaction remained significant even after task performance was fit into the multilevel model (Table 3). A model comparison showed that Model 3 explained sufficient additional variance in SV relative to Model 2 ($\chi^2 = 4.25$, $p = 0.04$), justifying the added model complexity. We fit base amount in a separate multilevel model which was only marginally significant in predicting SV ($\beta = 0.02$, S.E. = 0.01, $p = 0.07$), and the model complexity was increased unjustifiably as revealed by a nested model comparison ($\chi^2 = 3.34$, $p = 0.07$). Supplementary analysis was also conducted to include both *N*-back performance and base amount in the same multilevel model which still demonstrated significant effects of HIGH-AMO group membership and task × HIGH-AMO group interaction (online Supplementary Table S2).

Relationships of effort task measure with clinical and cognitive variables

Table 4 summarizes the correlations of AUC, a summary measure of subjective effort cost, with clinical and cognitive variables. AUC did not correlate with BNSS total score, amotivation score, or DE score. However, partial correlation analysis, controlling effect of antipsychotic dose, revealed a marginal level of significance ($p = 0.06$) in the association between amotivation and AUC (online Supplementary Fig. S2A). No significant correlations were observed between AUC and clinical ratings on positive symptoms, disorganization, depressive symptoms, and antipsychotic-induced Parkinsonism. AUC was not related to antipsychotic dose. There were also no significant correlations between AUC and any of the individual cognitive measures or cognitive composite score in both patients and controls.

Exploratory analyses on reward-benefit and effort-cost sensitivity indices

Patients had significantly lower reward-benefit sensitivity and effort-cost sensitivity than controls (online Supplementary Table S2). Three-group comparison analyses revealed a significant difference in reward-benefit sensitivity and marginal level of

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Table 1. Demographics, cognitive functions, and clinical characteristics of patients and controls

Variables[d]	Patients[a] (*N* = 40)	Controls (*N* = 44)	Statistic[b] (t/χ^2)	*p*	HIGH-AMO (*N* = 18)	LOW-AMO (*N* = 22)	Statistic[c] ($F/t/\chi^2$)	*p*
Demographics								
Age in years	24.2 (6.6)	25.1 (6.8)	−0.61	0.55	22.7 (4.7)	25.4 (7.8)	0.99	0.38
Male gender, *n* (%)	16 (40.0)	17 (38.6)	0.02	0.90	9 (50.0)	7 (31.8)	1.39	0.50
Years of education	13.4 (2.8)	13.6 (2.6)	−0.41	0.69	13.7 (2.9)	13.1 (2.7)	0.27	0.76
Cognitive function								
Digit symbol coding	10.8 (2.8)	14.4 (3.0)	5.66	<0.001	10.1 (2.7)	11.4 (2.8)	17.14	<0.001
Logical memory	7.5 (4.0)	11.7 (3.0)	5.54	<0.001	7.78 (4.1)	7.23 (3.9)	15.62	<0.001
Letter cancellation	122.2 (28.7)	107.1 (27.4)	2.46	<0.05	137.4 (32.8)	109.7 (17.4)	8.77	<0.001
Trail making A	30.0 (8.7)	22.7 (7.2)	4.13	<0.001	32.1 (7.9)	28.3 (9.2)	9.73	<0.001
Trail making B	64.3 (22.2)	48.1 (17.2)	3.68	<0.001	67.7 (23.4)	61.3 (21.2)	7.25	<0.01
Cognitive composite score[e]	−1.1 (0.98)	0.0 (0.6)	6.48	<0.001	−1.2 (1.1)	−1.1 (0.9)	20.96	<0.001
Clinical characteristics								
Age at onset, years	23.3 (6.6)	–	–	–	22.7 (4.7)	25.4 (7.8)	1.35	0.19
DUP, days (median)	95.0	–	–	–	95.5	95.0	–	–
Log DUP[f]	2.0 (0.6)	–	–	–	2.0 (0.7)	1.9 (0.5)	0.46	0.65
PANSS positive symptom score[g]	10.1 (4.2)	–	–	–	11.1 (5.1)	9.2 (3.1)	1.49	0.15
PANSS disorganization score[g]	8.0 (2.0)				8.4 (2.6)	7.6 (1.1)	1.22	0.24
BNSS total score	23.0 (14.6)	–	–	–	35.3 (11.0)	12.9 (8.0)	7.44	<0.001
BNSS amotivation score	15.5 (9.8)	–	–	–	24.6 (5.9)	8.1 (4.6)	9.87	<0.001
BNSS diminished expression score	7.0 (6.3)	–	–	–	10.0 (7.1)	4.5 (4.5)	2.99	0.01
CDS total score	1.7 (2.5)	–	–	–	1.9 (3.3)	1.3 (1.6)	0.72	0.51
SAS average score	0.1 (0.2)	–	–	–	0.1 (0.2)	0.1 (0.1)	0.75	0.46
Chlorpromazine equivalents[h], mg/day	314.2 (173.1)	–	–	–	272.9 (158.5)	347.9 (180.6)	1.38	0.18

AMO, amotivation; BNSS, Brief Negative Symptom Scale; CDS, Calgary Depression Scale; DUP, duration of untreated psychosis; PANSS, Positive and Negative Syndrome Scale; SAS, Simpson–Angus Scale.

[a]All patients were receiving antipsychotic medication: 30 on second-generation antipsychotic (SGA) monotherapy, three on first-generation antipsychotic (FGA) monotherapy, six on two SGAs, and one on combined FGA and SGA treatment.

[b]Potential group differences were examined using independent-samples *t* tests and χ^2 tests for continuous and categorical variables, respectively.

[c]Test statistic and *p* values reflect three-group analyses in demographic, cognitive, and self-report anhedonia data, conducted on HIGH-AMO (patients with high amotivation), LOW-AMO (patients with low amotivation), and control groups. Patient group comparisons on clinical characteristics were examined using independent-samples *t* tests and χ^2 tests for continuous and categorical variables, respectively.

[d]Data are presented in mean and standard deviations, except gender and DUP.

[e]Cognitive composite score for each participant was calculated by averaging the *z*-scores of individual cognitive tests. Standardized *z*-score of each of the cognitive tests were computed based on the performance of healthy controls.

[f]DUP was log-transformed for analysis due to its skewed distribution.

[g]PANSS positive symptom and disorganization scores were derived on the basis of a previous factor-analytic study on first-episode psychosis patients (Emsley *et al*., 2003).

[h]Chlorpromazine equivalents were computed according to Gardner *et al*. (2010).

significance ($p = 0.05$) in effort-cost sensitivity. Post-hoc analyses showed that HIGH-AMO group had significantly lower reward-benefit sensitivity than controls ($p = 0.01$). However, none of the post-hoc pairwise contrasts for effort-cost sensitivity was significant after Bonferroni correction. Reward-benefit sensitivity was negatively correlated with BNSS total and amotivation scores, even when the effect of antipsychotic dose was adjusted (online Supplementary Table S3, Figs S2B and S2C). Reward-benefit sensitivity was also correlated with digit symbol coding performance. Effort-cost sensitivity was not correlated with negative symptoms and amotivation. There were also no other significant correlations of two sensitivity indices with other symptom dimensions, antipsychotic dose, and cognitive functions (online Supplementary Tables S3 and S4).

Discussion

The aim of the current study was to examine cognitive effort-based decision-making in FEP patients using an effort discounting paradigm which quantified subjective cognitive motivation as the degrees of devaluation of monetary rewards by cognitive demands. We found that, in general, both patients and controls showed greater reward discounting with more demanding *N*-back levels. This indicates that participants from both groups

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Table 2. *N*-Back performance[a] of patients and controls

	N-Back level *N*				
Group	1	2	3	4	5
Controls	2.45 (0.96)	1.71 (0.74)	1.44 (0.81)	1.49 (0.96)	1.43 (0.82)
Patients	1.51 (1.19)	0.55 (1.10)	0.67 (0.98)	0.72 (1.01)	0.54 (0.93)
Wilcox *p*	<0.001	<0.001	<0.001	<0.001	<0.001
Cohen's *d*	0.39	0.51	0.37	0.40	0.43
LOW-AMO	1.41 (0.26)	0.67 (0.21)	0.81 (0.21)	0.71 (0.22)	0.50 (0.20)
HIGH-AMO	1.66 (0.29)	0.36 (0.32)	0.46 (0.25)	0.74 (0.24)	0.60 (0.22)
Wilcox *p*	0.51	0.62	0.25	0.92	0.77

HIGH-AMO, patients with high amotivation; LOW-AMO, patients with low amotivation.
[a]Mean (s.d.) *d'*, a signal-detection parameter *d*-prime which reflected the sensitivity of participants to discriminate items as previously presented (or not) *N* trials back, was used to quantify *N*-back performance and was presented. Raw *d'* values were log-linear transformed to address extreme false-alarm and hit proportions (Hautus, 1995; Culbreth *et al*., 2016).

were sensitive to task demand, with subjective effort cost increasing with objective cognitive load. Importantly, our results demonstrated that patients exhibited greater effort discounting than controls, thereby confirming our hypothesis of reduced cognitive motivation in FEP. To the best of our knowledge, this is the first study to provide direct evidence of aberrant cognitive effort allocation in FEP populations. This is consistent with a recent study which adopted the same COGED paradigm and revealed that chronic schizophrenia patients exhibited reduced willingness to expend cognitive effort for reward relative to controls (Culbreth *et al*., 2016). Our findings also concur with several previous reports showing greater avoidance of or decreased persistence with the cognitively effortful task in schizophrenia patients relative to healthy participants (Wolf *et al*., 2014; Reddy *et al*., 2015, 2018). Of note, the effort discounting paradigm we used has conferred several methodological advantages on the assessment of cognitive effort allocation as compared to other effort-related tasks applied by some prior research in schizophrenia patients. First, in COGED, time-on-task across load levels is held constant so confounding effect of differential task duration (i.e. temporal discounting) on effort-cost valuation could be avoided. Second, a continuous measure of subjective willingness for cognitive effort expenditure derived from COGED may provide a more sensitive evaluation of the presence and the extent of abnormal allocation of cognitive effort than binary choice of demand avoidance (Gold *et al*., 2015*b*; Reddy *et al*., 2015, 2018). Third, task demand and effort-based choices in COGED are fully explicit. This thus minimizes the influence of patients' reduced ability to detect difference in cognitive demand on effort-based decision-making as observed in one past study using implicit paradigms (Gold *et al*., 2015*b*).

In an attempt to investigate the relationship between amotivation and cognitive effort-based decision-making, we categorized patients into those with high *v.* low levels of amotivation for comparison. Critically, our results revealed that high-amotivation patients displayed significantly greater discounting of monetary rewards than both low-amotivation patients and controls, while the latter two groups showed comparable performance on reward devaluation across all *N*-back levels. Furthermore, this between-group difference remained statistically significant even when *N*-back task performance and base reward amount were taken into consideration. In fact, this accords with many previous reports, including our earlier study on first-episode sample (Chang *et al*., 2019), which found that schizophrenia patients with high levels of negative symptoms or amotivation displayed significantly decreased willingness to expend physical effort for high-value/high-probability reward (Gold *et al*., 2013; Fervaha *et al*., 2015*b*; Hartmann *et al*., 2015; Wang *et al*., 2015; Serper *et al*., 2017). Our findings thus suggest a critical role of amotivation on aberrant cognitive effort-based decision-making in the early course of psychotic disorders. Of note, we failed to demonstrate a significant association between effort discounting and amotivation (albeit marginally significant, Table 4, online Supplementary Fig. S2A) or negative symptoms using correlation analyses. However, negative symptoms are characterized by a hybrid dimensional–categorical structure (Ahmed *et al*., 2015) which distorts observations made using a purely dimensional correlational approach. Failure to examine negative symptoms from both a categorical and dimensional approaches may explain inconsistencies within the literature. In fact, several other studies have only found significant negative symptom effects via categorical, but not continuous correlational approaches (Gold *et al*., 2013; Fervaha *et al*., 2015*b*; Wang *et al*., 2015; Chang *et al*., 2019). Alternatively, the choice of symptom assessment might partly contribute to non-significant findings in our correlation analyses. Emerging evidence has indicated that multiple momentary symptom assessment in daily life using experience-sampling methodology (ESM) might represent a more sensitive measurement of amotivation than clinician-rated symptom scales, which are based primarily on retrospective evaluation that could be significantly affected by patients' cognitive impairment. One recent study has further demonstrated that amotivation assessed by ESM but not by clinician-administered symptom scale was correlated with effort-task performance in schizophrenia patients (Moran *et al*., 2017). More research is required to verify whether ESM-measured amotivation aligns consistently better than clinician-rated symptoms with effort allocation.

It is acknowledged that deficits in precisely representing expected value (i.e. reward magnitude in this study) and effort costs of actions both undermine cost/benefit estimation. In particular, either undervaluing reward magnitude or overestimating effort cost would result in decreased willingness to expend effort for reward. Our exploratory analyses revealed two intriguing findings in this respect. First, patients displayed a reduction in both reward-benefit sensitivity and effort-cost sensitivity (rather than heightened effort-cost estimation) relative to controls. Second,

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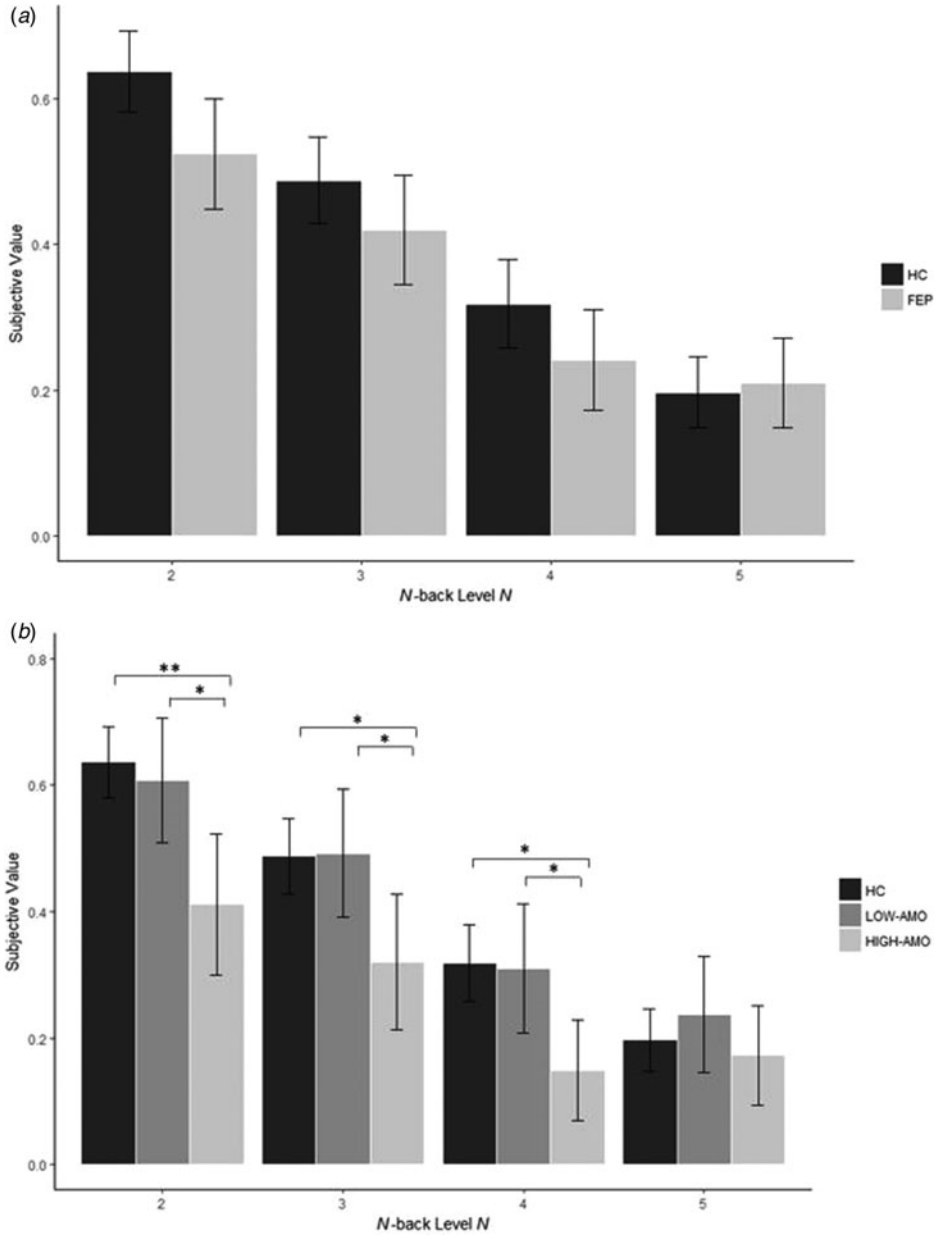

Fig. 1. Subjective value by *N*-back level. (a) Comparison between overall patient group and controls. (b) Comparison between high (HIGH-AMO) and low (LOW-AMO) amotivation patient groups, and controls. $^{*}p < 0.05$; $^{**}p < 0.01$.

reward-benefit sensitivity was consistently and more strongly related to amotivation than effort-cost sensitivity in both categorical and correlational analyses. Hence, our results suggest that reduced willingness for cognitive effort expenditure in FEP might mainly be attributable to degraded reward-value representation. Moreover, our findings further indicate that deficient reward valuation but not aberrant estimation of effort cost plays a critical role in motivational impairment in FEP. This is in fact consistent with the postulation of impaired reward-value representation as a major contributor to suboptimal effort allocation in psychotic disorders (Gold *et al.*, 2015*a*, Waltz and Gold, 2016). Our results are also in line with accumulating data demonstrating reduced ability to represent reward value in chronic schizophrenia patients, especially those with high levels of amotivation (Gold *et al.*, 2012; Hernaus *et al.*, 2018). Alternatively, our finding that FEP patients exhibited blunted effort-cost sensitivity agrees with recent data which found that chronic schizophrenia patients showed reduced ability to detect differences in cognitive effort demands associated with response alternatives (Gold *et al.*, 2015*b*). This is also in keeping with another study which adopted ESM approach and demonstrated that schizophrenia patients had decreased accuracy in estimating the levels of difficulty in relation to an effortful goal (Gard *et al.*, 2014). Given the exploratory nature of our additional analyses, however, our findings regarding reward-benefit sensitivity and effort-cost sensitivity should be treated with caution. Owing to the paucity of existing data, particularly in first-episode populations, further research is warranted to clarify potential differential roles of reward devaluation and altered effort-cost estimation on effort-based decision-making in FEP.

It is worth noting that although findings of cognitive effort-based decision-making largely converge with the literature on physical effort allocation in psychotic disorders showing that patients were significantly less willing to expend effort for rewards

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Table 3. Parameter estimates of tested models for group differences in effort discounting

Parameter	Estimate	s.e.	*t*	*p*
Model 1: patients *v.* controls				
Intercept	0.78	0.05	15.89	<0.001***
Task[a]	−0.15	0.02	−9.85	<0.001***
Group[b]	−0.15	0.07	−2.14	0.04*
Task × group	0.04	0.02	1.68	0.10
Model 2: HIGH-AMO *v.* LOW-AMO *v.* controls				
Intercept	0.78	0.05	16.51	<0.001***
Task[a]	−0.15	0.01	−10.02	<0.001***
LOW-AMO group	−0.04	0.08	−0.45	0.66
HIGH-AMO group	−0.29	0.09	−3.35	<0.01**
Task × LOW-AMO group	0.01	0.03	0.50	0.62
Task × HIGH-AMO group	0.07	0.03	2.39	0.02*
Model 3: HIGH-AMO *v.* LOW-AMO *v.* controls adjusting for *N*-back performance				
Intercept	0.73	0.05	13.68	<0.001***
Task[a]	−0.15	0.02	−9.72	<0.001***
LOW-AMO group	−0.00	0.08	−0.01	0.99
HIGH-AMO group	−0.27	0.09	−2.99	<0.01**
Task performance	0.03	0.01	2.07	0.04*
Task × LOW-AMO group	0.01	0.03	0.39	0.69
Task × HIGH-AMO group	0.06	0.03	2.28	0.02*

HIGH-AMO, patients with high amotivation; LOW-AMO, patients with low amotivation.
[a]Task refers to the main effect of *N*-back task level in predicting subjective value.
[b]Group refers to the main effect of diagnostic group (patients *v.* controls) in predicting subjective value.
*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

Table 4. Correlations of AUC for effort discounting with clinical and cognitive variables[a]

	Patients		Controls	
Variables	*R*	*p*	*r*	*p*
Clinical characteristics				
BNSS total score	−0.19[b]	0.25	–	–
BNSS amotivation score	−0.23[b]	0.15	–	–
BNSS diminished expression score	0.04	0.79	–	–
PANSS positive symptom score	−0.12	0.44	–	–
PANSS disorganization score	−0.12	0.47	–	–
CDS total score	−0.25	0.13	–	–
SAS average score	0.02	0.90	–	–
Chlorpromazine equivalents	−0.20	0.23	–	–
Cognitive function				
Digit symbol coding	0.14	0.39	−0.08	0.59
Logical memory	−0.29	0.08	0.07	0.67
Letter cancellation	0.16	0.32	−0.16	0.32
Trail making A	−0.08	0.65	0.13	0.41
Trail making B	0.11	0.50	0.05	0.75
Cognitive composite score	0.11	0.49	0.16	0.31

BNSS, Brief Negative Symptom Scale; CDS, Calgary Depression Scale; PANSS, Positive and Negative Syndrome Scale; SAS, Simpson–Angus Scale.
[a]Pearson product-mean correlation analyses were performed.
[b]We also performed partial correlation analyses between AUC and BNSS total and amotivation scores, controlling for the effect of chlorpromazine equivalents, as antipsychotic treatment may cause secondary negative symptoms and modulates effort-based decision-making processing. Results showed that AUC was uncorrelated with BNSS total score ($r = -0.26$, $p = 0.11$). There was a marginally significant association ($r = -0.31$, $p = 0.06$) between AUC and BNSS amotivation score.

than controls (Culbreth *et al.*, 2018), this does not necessarily indicate that cognitive and physical effort modalities are subsumed under a unitary construct, underpinned by similar neurobiological processes. In fact, there is increasing evidence demonstrating that cognitive and physical effort-cost valuations are subserved by overlapping, yet distinct, neural circuitry (Hosking *et al.*, 2014; Westbrook and Braver, 2015). Additionally, recent preclinical research revealed that dopamine antagonism significantly decreased preferences for physical, but not cognitive, effort for rewards in rats (Hosking *et al.*, 2015). Cognitive and physical effort may thus represent related but dissociable domains in effort-based decision-making, and may differentially impact on motivational impairment. This further implies that effort modality-specific interventions may be required to address dysfunction in cognitive *v.* physical effort allocation, and hence highlights the importance in studying cognitive effort as a distinct form of effort-based decision-making in psychotic disorders.

Several methodological limitations warrant consideration in interpreting the study results. First, our lack of assessment on social and role functioning precludes us from examining the relationship between cognitive effort allocation and real-world functional outcome. Second, we did not assess dysfunctional attitudes, for instance, defeatist performance beliefs which were found to significantly moderate the association between amotivation and cognitive effort avoidance in schizophrenia patients (Reddy *et al.*, 2018). Finally, all patients in the current study were receiving antipsychotics at the time of assessment. Although our analyses revealed no significant correlations between antipsychotic dose and effort-task performance, we cannot rule out an effect of dopamine D2-receptor antagonist on effort allocation (Wardle *et al.*, 2011; Salamone *et al.*, 2012). Prospective investigation of effort allocation prior to and following antipsychotic treatment in FEP patients is warranted to differentiate the impacts of illness and medication on cognitive effort-based decision-making.

In conclusion, the current study extends previous research on cognitive effort-based decision-making in chronic schizophrenia to FEP, and provides the first evidence showing abnormal cognitive effort allocation in first-episode patients who exhibited reduced willingness to expend cognitive effort for reward relative to healthy participants. Moreover, such diminished effort expenditure was most pronounced in patients with high levels of amotivation. Our exploratory analysis further suggested that suboptimal

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effort allocation and motivational impairment in FEP might primarily be driven by impaired representation of reward magnitude rather than altered effort-cost sensitivity. Future research clarifying the determinants as well as neural underpinnings of impaired cognitive effort-based decision-making would facilitate the development of effective therapeutic strategies to alleviate diminished motivation, and hence to promote early functional recovery in FEP patients.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0033291719002769

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Conflict of interest. Author E.Y.H.C. has participated in the paid advisory board for Otsuka, has received educational grant support from Janssen-Cilag, and has received research funding from Astra-Zeneca, Janssen-Cilag, Eli Lilly, Sanofi-Aventis, and Otsuka. E.H.M.L has been a member of the paid advisory boards for Eli Lilly and AstraZeneca. The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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