

Volatility Estimates Increase Choice Switching and Relate to Prefrontal Activity in Schizophrenia

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ABSTRACT

BACKGROUND: Reward-based decision making is impaired in patients with schizophrenia (PSZ), as reflected by increased choice switching. The underlying cognitive and motivational processes as well as associated neural signatures remain unknown. Reinforcement learning and hierarchical Bayesian learning account for choice switching in different ways. We hypothesized that enhanced choice switching, as seen in PSZ during reward-based decision making, relates to higher-order beliefs about environmental volatility, and we examined the associated neural activity.

METHODS: In total, 46 medicated PSZ and 43 healthy control subjects performed a reward-based decision-making task requiring flexible responses to changing action–outcome contingencies during functional magnetic resonance imaging. Detailed computational modeling of choice data was performed, including reinforcement learning and the hierarchical Gaussian filter. Trajectories of learning from computational modeling informed the analysis of functional magnetic resonance imaging data.

RESULTS: A 3-level hierarchical Gaussian filter accounted best for the observed choice data. This model revealed a heightened initial belief about environmental volatility and a stronger influence of volatility on lower-level learning of action–outcome contingencies in PSZ as compared with healthy control subjects. This was replicated in an independent sample of nonmedicated PSZ. Beliefs about environmental volatility were reflected by higher activity in dorsolateral prefrontal cortex of PSZ as compared with healthy control subjects.

CONCLUSIONS: Our study suggests that PSZ inferred the environment as overly volatile, which may explain increased choice switching. In PSZ, activity in dorsolateral prefrontal cortex was more strongly related to beliefs about environmental volatility. Our computational phenotyping approach may provide useful information to dissect clinical heterogeneity and could improve prediction of outcome.

Keywords: Bayesian learning, Computational psychiatry, Neuroimaging, Psychosis, Reinforcement learning, Schizophrenia

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Cognitive and motivational deficits are important characteristics of patients with schizophrenia (PSZ) associated with clinical and social outcomes (1–5). Reward-based learning and decision making require the integration of cognition and motivation and are impaired in PSZ (6,7). These impairments are present at the onset of the disorder, are independent of lower general IQ, remain stable over time (8,9), and have been proposed as neurocognitive markers with potential clinical utility (10). However, the mechanisms and associated neural signatures remain to be identified.

Flexible reward-based learning and decision making can be probed via variants of reversal learning [e.g., (11)]. In such tasks, PSZ show increased switching between choice options (8,12–17). The mechanisms of this unstable behavior remain unknown but can be targeted by computational modeling (18). In reinforcement learning (RL) (19), choices are selected based on expected values, which are learned by weighting reward prediction errors (RPEs) with a learning rate. RPEs closely align

with phasic dopamine (20,21). Considering enhanced presynaptic dopamine synthesis capacity in striatum of PSZ (22,23), this could translate into enhanced phasic dopamine in PSZ, which in turn might result in increased learning rates (24). This could theoretically account for unstable behavior in PSZ, but increased learning rates were not found [for reviews, see (18,24,25)].

Theories of predictive coding (26) and hierarchical Bayesian inference hypothesize that symptoms of PSZ (27–29) are a consequence of false inference about the world due to altered precision attributed to beliefs at different hierarchical levels. Dysfunction at higher levels, which are thought to extract and represent general and stable features of the environment, might lead to experiencing the world as being more or less volatile. With regard to positive symptoms (30), this is supported by empirical evidence [e.g., (31)]. When applying this framework to reward-based decision making, beliefs about the probability of rewards are formed at lower levels but are also

determined by learning about the volatility of reward probabilities (32). This environmental volatility is related to learning from lower-level RPEs in that it scales the belief update. Thus, a belief in high environmental volatility can induce rapid updates of lower-level beliefs about reward probabilities and promote enhanced choice switching in PSZ.

Striatal and prefrontal activity is reduced during reward anticipation and receipt in PSZ (33–35). Reduced striatal RPE activity was observed in nonmedicated PSZ (17) but not in medicated PSZ (15,36). Neural correlates of hierarchical Bayesian learning were demonstrated in functional magnetic resonance imaging (fMRI) studies in healthy individuals (37,38), linking volatility and uncertainty to activity in frontostriatal circuits (32,39). While neural correlates of hierarchical Bayesian learning were successfully used to distinguish between individuals with and without hallucinations and PSZ with and without psychosis (31), this has not yet facilitated an understanding of the cognitive and motivational processes underlying impairments in flexible reward-based decision making.

Here, we used a reward-based reversal learning task during fMRI in PSZ and healthy control subjects (HCs). Computational modeling was applied to the behavioral data by comparing RL and a hierarchical Bayesian learning model, the hierarchical Gaussian filter (HGF) (40,41). We hypothesized that enhanced choice switching in PSZ relates to higher-order beliefs about the volatility of the environment and examined the associated neural activity as measured by fMRI.

METHODS AND MATERIALS

Participants and Instruments

In total, 46 medicated PSZ and 43 HCs were included (see Supplemental Table S1). Measures used to characterize participants are summarized in Supplemental Table S1 and the Supplement. Written informed consent was obtained from all participants. The study was performed in accordance with the Declaration of Helsinki and was approved by the local ethics committee of Charité Universitätsmedizin.

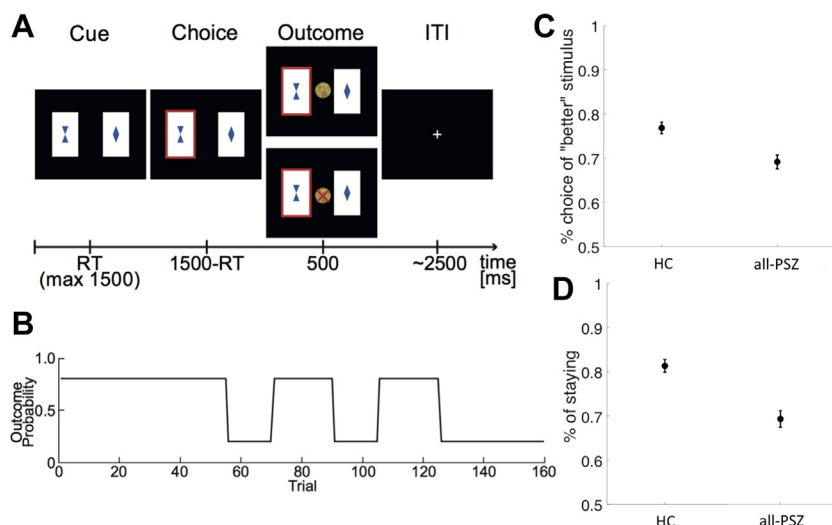


Figure 1. (A) Trial sequence from the decision-making task. (B) Reward probabilities of both choice options were perfectly anticorrelated and were stable for the first 55 trials (pre-reversal); changed 4 times, after 15 or 20 trials, during the reversal phase; and remained stable for the last 35 trials (post-reversal). (C) Percentage choices of the stimulus with 80% reward probability were significantly lower in the patients with schizophrenia (PSZ) group (main effect of group, $F = 14.52$, $p < .001$). (D) PSZ were less likely to repeat the previous action independent of feedback received in the previous trial (main effect of group, $F = 27.77$, $p < .001$; feedback $\times$ group interaction, $F = 0.02$, $p = .89$). HCs, healthy control subjects; ITI, intertrial interval; RT, reaction time.

Task

Participants performed a task requiring flexible decision making during fMRI (42–44). The task had 160 trials, each with a choice between two cards (Figure 1A). The selected card resulted in a monetary win or a monetary loss of 10 Eurocents. One card was initially assigned with a reward probability of 80% and a loss probability of 20% (vice versa for the other card). The task had a simple higher-order structure (Figure 1B): an anticorrelation between the reward probabilities; whenever one card was associated with a probability of 80%, the other card would be associated with a probability of 20%. Reward contingencies were stable for the first 55 trials (pre-reversal) and for the last 35 trials (post-reversal). During the reversal phase, contingencies changed four times after 15 or 20 trials. For more details, see Supplement.

Analysis of Choice Behavior

Performance was quantified by correct choices of the stimuli with high (80%) reward probability and was analyzed using repeated-measures analysis of variance (ANOVA) with the between-subject factor group and the within-subject factor phase (pre-reversal, reversal, or post-reversal). Repeated-measures ANOVA was used to test the effect of feedback on subsequent choices (win-stay and lose-stay).

Computational Models of Learning

In RL, the difference between received rewards and expectations, the RPE, is used to update expectations for the chosen stimulus (weighted by the learning rate α). For comparison with previous work (17,42–44), we included RL with separate learning rates for reward and loss trials (RL1 and RL2).

The HGF describes learning as a process of inductive inference under uncertainty. It considers hierarchically organized states in which learning at a higher-level state determines learning at a lower-level state by dynamically adjusting the lower level's learning rate. In our case, the top level represents environmental volatility (how likely a change in

action–outcome contingencies is to occur). This top-level estimate is dynamically coupled with learning at the lower level (see Figure 2). Trial-by-trial updates of posterior means at each level are proportional to the prediction error (PE) from the level below weighted by a precision ratio. See Supplement for equations. We were particularly interested in environmental volatility (μ_3) and its coupling with the lower level (κ) and thus inferred subject-specific parameters. We included a 2-level variant (HGF2) to test whether the representation of volatility in the 3-level HGF3 made it superior in explaining behavior.

HGF and RL provide different ways to learn expectations about rewards, and both update expectations of the chosen card only (single update [SU]). Based on the anticorrelated task structure, we implemented a variant of each model updating values (RL) or posterior means (HGF) of the unchosen card simultaneously; that is, an increase of the chosen card implies a decrease of the unchosen card (double update [DU]). For equations, see Supplement. SU and DU variants of each model (RL1, RL2, HGF2, and HGF3) were fit to the choice data (Table 1).

Decision Models

Values (RL) or posterior means (HGF) were transformed to choice probabilities by using the softmax (logistic sigmoid) function (see Supplement). In binary choice tasks with anticorrelated reward probabilities such as ours, there is choice perseveration independent of learning or inference that differs

between win and loss trials. We captured this by estimating parameters for win and loss trials that reflect this difference in choice perseveration (ρ_{win} and ρ_{loss}). Models that included inverse decision noise β as a free parameter had lower evidence (see Supplement) than models where this was fixed to unity ($\beta = 1$). We also tested the possibility that volatility is directly linked to choice probabilities by letting third-level trial-by-trial volatility (HGF3) serve as the inverse decision noise (see Supplement). Because this introduced a volatility scale anchored in observed behavior (switching or staying), it allowed for estimating the mean of the subjective a priori belief about initial volatility at the third level, $\mu_3^{(0)}$, as a parameter of HGF3. This cannot be applied to RL and HGF2 because they do not feature inference on volatility. This led to 2 additional models (HGF3-SU-V and HGF3-DU-V), resulting in a total of 10 models. For model fitting, see Supplement.

Model Selection

The negative variational free energy (an approximation to the log model evidence) was used for random-effects Bayesian model selection (45). The protected exceedance probability (PXP) governed our model selection, which protects against the null possibility that there are no differences in the likelihood of models across the population (46). We also examined whether the models explained the data better than chance (17,47). A subject was classified as not fit better than chance if the log likelihood of the data relative to the number of trials did not significantly differ from chance (see Supplemental Methods). Simulations of the task were run using the inferred parameters to reproduce the observed data.

Model Parameters

Parameters of the winning model were compared between groups using *t* test or the nonparametric Mann-Whitney *U* test if assumptions of normality were violated (Kolmogorov-Smirnov test). Bonferroni correction was applied according to the number of parameters.

Statistical Analysis of fMRI Data

Using the general linear model approach in SPM8, an event-related analysis was applied. On the first level, 1 regressor spanned the entire trial from cue to outcome as in a previous study (38). We added the following 5 modeling-based trajectories as parametric modulators (not orthogonalized) to best capture different aspects of the hierarchical inference process: second- and third-level precision-weighted PEs (ϵ_2 and ϵ_3), which were time locked to the outcome, precision weights (ψ_2 and ψ_3), and the third-level volatility (μ_3). All regressors spanned the entire trial and changed at outcome accordingly to PE updates identical to Iglesias *et al.* (38). Regressors were convolved with the canonical hemodynamic response function in SPM8 and its temporal derivative (see Supplemental Methods). For second-level analysis, a random-effects ANOVA model, including contrast images of the 5 modeling-based trajectories (precision-weighted PEs [ϵ_2 and ϵ_3], precision weights [ψ_2 and ψ_3], and the third-level volatility [μ_3] and the factor group, was estimated.

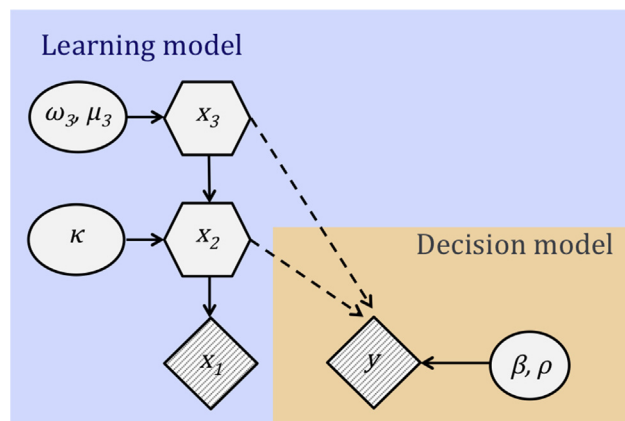


Figure 2. Model graph. The hierarchical Gaussian filter deploys hierarchically organized states in which learning about environmental volatility at a higher-level state x_3 determines lower-level learning about reward probabilities x_2 . The lowest level, x_1 , is binary and corresponds to a choice being rewarded ($x_1 = 1$) or not ($x_1 = 0$) at a given trial. The probability of a choice being rewarded is a logistic sigmoid function of x_2 : $p(x_1 = 1) = s(x_2)$. y represents the response of the subject. Shaded quantities are observed. Solid lines indicate dependence in the generative model. Dashed lines indicate dependence on inferred quantity (the generative model for y depends on μ_2 and μ_3 , the inferred values of x_2 and x_3 , respectively). The constant step size ω_3 is the evolution rate of environmental volatility. κ reflects the coupling between the levels. The best-fitting model was a three-level implementation (HGF3-DU-V) with double updating (not illustrated) together with a decision model capturing choice repetition separately after rewards and losses (ρ), third-level environmental volatility determining decision noise, and the initial belief about environmental volatility μ_3 as an additional parameter inferred from the data. DU, double update; HGF, hierarchical Gaussian filter; V, environmental volatility.

Table 1. Bayesian Model Selection

		RL1-SU	RL1-DU	RL2-SU	RL2-DU	HGF2-SU	HGF2-DU	HGF3-SU	HGF3-DU	HGF3-SU-V	HGF3-DU-V
HCs + PSZ All (<i>n</i> = 89)	PP	9.4	5.1	7.4	3.0	3.1	7.0	3.3	7.7	5.3	48.8
	XP	0	0	0	0	0	0	0	0	0	100
	PXP	0	0	0	0	0	0	0	0	0	99.9
HCs All (<i>n</i> = 43)	PP	4.4	4.7	4.4	3.8	2.7	5.1	2.7	5.3	5.8	61.1
	XP	0	0	0	0	0	0	0	0	0	100
	PXP	0	0	0	0	0	0	0	0	0	100
PSZ All (<i>n</i> = 46)	PP	11.8	7.1	11.6	4.75	8.3	10.0	9.3	10.9	4.9	21.4
	XP	6.9	0.7	6.21	0.1	1.4	3.4	2.5	4.6	0.2	74.0
	PXP	10.0	10.0	10.0	10.0	10.0	10.0	10.0	10.0	10.0	10.1
HCs + PSZ Fit (<i>n</i> = 73)	PP	9.4	5.1	7.4	3.0	3.2	6.9	3.3	7.7	5.3	48.8
	XP	0	0	0	0	0	0	0	0	0	100
	PXP	0	0	0	0	0	0	0	0	0	100
HCs Fit (<i>n</i> = 42)	PP	4.5	4.5	4.5	3.8	2.8	5.3	2.8	5.5	5.8	60.5
	XP	0	0	0	0	0	0	0	0	0	100
	PXP			0	0	0	0	0	0	0	100
PSZ Fit (<i>n</i> = 31)	PP	11.6	8.2	11.3	4.9	7.9	9.7	8.9	10.4	4.9	22.3
	XP	5.5	1.1	4.8	0.1	1.0	2.5	1.7	3.3	0.1	80.0
	PXP	10.0	10.0	10.0	10.0	10.0	10.0	10.0	10.0	10.0	10.1

Bayesian model selection was governed by protected exceedance probabilities (PXPs) to protect against the risk that differences in model evidence occur by chance. In this table, we also report exceedance probabilities (XPs) and expected posterior probabilities (PPs); also see the [Supplement](#). XP describes the probability of a model exceeding all other models in the comparison set, the probability that expected PPs differ.

DU, double update; HCs, healthy control subjects; HGF, hierarchical Gaussian filter with 2 or 3 levels; HGF3--V, 3-level HGF with environmental volatility linked to decision noise with either SU or DU; PSZ, patients with schizophrenia; RL, reinforcement learning with one learning rate (RL1) or separate learning rates for rewards and losses (RL2); SU, single update.

RESULTS

Behavioral Data

Repeated-measures ANOVA on correct choices showed that performance differed between phases, dropping during the reversal phase (main effect of phase, $F = 23.74$, $p < .001$). PSZ chose the better card less frequently irrespective of task phases (main effect of group, $F = 14.52$, $p < .001$, and phase $\times$ group interaction, $F = 1.87$, $p = .16$) ([Figure 1C](#)). The factor phase was dropped from further analyses.

Repeated-measures ANOVA on the probability of choice repetition showed that all participants stayed more with the previous action after rewards compared with losses (main effect of feedback, $F = 369.80$, $p < .001$) and that PSZ switched more independent of feedback from the previous trial (main effect of group, $F = 27.77$, $p < .001$, and feedback $\times$ group interaction, $F = 0.02$, $p = .89$) ([Figure 1D](#)).

Computational Modeling: Model Selection

Random-effects Bayesian model selection revealed a 3-level HGF with double updating and third-level environmental volatility linked to decision noise ([Figure 2](#)) as the most plausible model (HGF3-DU-V, PXP = 99.5%; for PXPs of all models, see [Table 1](#)). This model (HGF3-DU-V) was superior in HCs (PXP = 100%, Bayes omnibus risk = 0) and remained first ranking in PSZ (posterior probabilities = 21.4%, PXP = 74.0%). In PSZ, there was no convincing evidence that models performed differently from each other (Bayes omnibus risk = 1, all PXPs = 10.0%).

In total, 15 PSZ and 1 HCs were not fit better than chance by any model ([Figure 3A](#)). Neither when considering all PSZ (PSZ-fit + PSZ-nofit) nor when considering PSZ-fit alone did Bayesian model selection reveal a clearly superior model (both times Bayes omnibus risk = 1) ([Table 1](#)). However, the identification of PSZ-fit ensures that individuals included in further modeling-based analyses are fit better than chance by every model (i.e., equally good models instead of equally poor models).

Revisiting Behavioral Data

Based on this heterogeneity in PSZ regarding absolute model fit, we revisited choice data with respect to 3 groups (HCs, PSZ-fit, and PSZ-nofit). There was a main effect of group on correct choices ($F = 32.63$, $p < .001$) ([Figure 3B](#)). PSZ-nofit showed performance around chance levels (HCs vs. PSZ-nofit, $t = 7.04$, $p < .001$; PSZ-fit vs. PSZ-nofit, $t = 6.90$, $p < .001$) ([Figure 3B](#)), while PSZ-fit had performance comparable to HCs ($t = 1.51$, $p = .14$) ([Figure 3B](#)). The analysis of win-stay and lose-stay behavior revealed a group $\times$ feedback interaction ($F = 20.68$, $p < .001$). This resulted from a pronounced reduction of win-stay behavior in PSZ-nofit only (PSZ-fit vs. PSZ-nofit, $t = 10.74$, $p < .001$) ([Figure 3C](#)), while reduced lose-stay was not significantly different between PSZ-fit and PSZ-nofit ($t = 0.01$, $p = .99$) ([Figure 3D](#)). A group $\times$ feedback interaction was also significant when comparing only HCs and PSZ-fit ($F = 6.79$, $p = .01$) as well as significant main effects of feedback ($F = 636.30$, $p < .001$) and group ($F = 10.22$, $p = .01$). This difference between HCs and PSZ-fit was driven by switching after loss ([Figure 3C, D](#)).

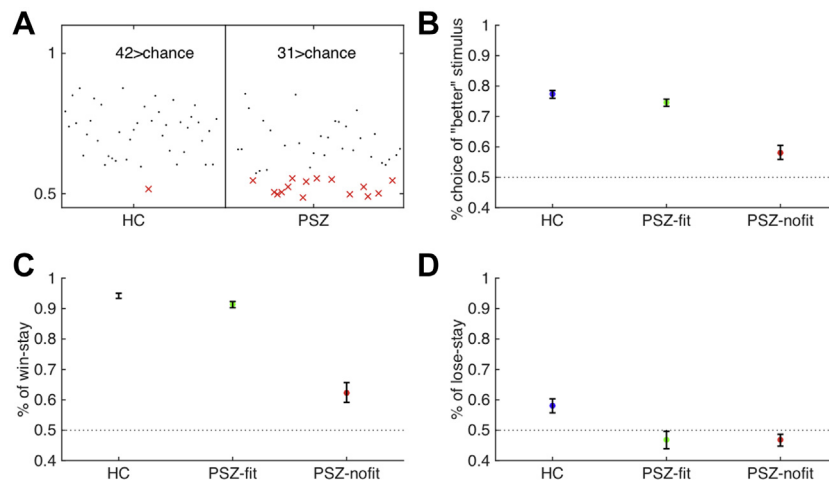


Figure 3. (A, B) Classification above (black dots) and below (red crosses) chance (A) and its influence on overall choice performance (B). There was a main effect of group ($F = 32.63$, $p < .001$). Patients with schizophrenia (PSZ)-nofit (red) showed overall poor performance (healthy control subjects [HCs] vs. PSZ-nofit, $t = 7.04$, $p < .001$; PSZ-fit vs. PSZ-nofit, $t = 6.90$, $p < .001$), while PSZ-fit (green) performed comparably to HCs (blue) ($t = 1.51$, $p < .14$) (B). (C, D) Analysis of win-stay (C) and lose-stay (D) behavior showed a group $\times$ feedback interaction ($F = 20.68$, $p < .001$). There was a pronounced reduction of win-stay behavior in PSZ-nofit only (PSZ-fit vs. PSZ-nofit, $t = 10.74$, $p < .001$) (C), while reduced lose-stay behavior characterized both groups of PSZ (PSZ-fit vs. PSZ-nofit, $t = 0.01$, $p = .99$) (D). This group $\times$ feedback interaction was also significant when comparing only HCs and PSZ-fit.

In an exploratory analysis of 6 cognitive tests, only measures of verbal memory and working memory differed between the 2 groups of PSZ, that is, were more impaired in PSZ-nofit compared with PSZ-fit (see [Supplemental Results](#)). This suggests that PSZ-fit and PSZ-nofit mapped on distinct cognitive profiles. Because poor fit hinders the interpretation of modeling-based behavioral and neuroimaging analyses in the PSZ-nofit subgroup, all subsequent modeling-based results are reported based on HCs ($n = 42$) and PSZ-fit ($n = 31$) only.

Computational Modeling: Parameters

Comparison of parameters of HGF3-DU-V ([Table 2](#) and [Figure 4](#)) revealed that the estimated mean of the a priori belief about initial environmental volatility $\mu_3^{(0)}$ was higher in PSZ ($z = 3.15$, $p < .01$) ([Figure 4A](#)). Trial-by-trial environmental volatility was more strongly coupled with lower-level updating, as demonstrated by higher κ in PSZ ($z = 2.51$, $p < .01$) ([Figure 4B](#)). The evolution rate of environmental volatility ω_3 did not differ significantly between groups ($z = 0.73$, $p = .47$). To illustrate the effects of differences in parameters on behavior after losses (when PSZ-fit showed increased switching), we analyzed the trajectory of μ_3 in a mixed-effects regression model with group and feedback as predictors. This revealed higher μ_3 in PSZ-fit overall. Across groups, μ_3 was higher after losses compared with rewards, which was more pronounced in PSZ (resulting from enhanced coupling between higher and lower levels of κ). For statistics, see [Supplemental Results](#) and [Supplemental Figure S2](#).

Computational Modeling: Reproducing Observed Behavior

Simulating data based on the inferred parameters of HGF3-DU-V (42 HCs, 31 PSZ-fit, 10 simulations per subject) showed that PSZ-fit switched more than HCs (main effect of group, $F = 11.17$, $p < .001$) and showed a pronounced tendency to switch after losses (group $\times$ feedback, $F = 7.68$, $p = .01$). Between-group findings on behavioral data were fully reproduced, which yields an important validation of the model's ability to capture the observed data.

Computational Modeling: Replication in Nonmedicated PSZ

We tested our model (HGF3-DU-V) in an independent sample of nonmedicated PSZ ($n = 24$) and HCs ($n = 24$), who performed another reversal-learning task (17). For statistics, see [Table 2](#). This replicated between-group findings and remained significant when excluding participants not fit better than chance (23 HCs, 13 PSZ; not reported).

Relation to Symptoms

We explored the relation between the 2 parameters that differed between groups with different measures of cognition ($n = 6$) and clinical measures ($n = 7$) within PSZ ([Supplemental Table S1](#)) applying Bonferroni correction ($p < .0083$). In PSZ, a higher initial belief about volatility $\mu_3^{(0)}$ was associated with reduced executive functioning and cognitive speed (Trail Making Test B: $r = -.56$, $p < .001$; Digit Symbol Substitution Test: $r = -.56$, $p < .001$) ([Supplemental Table S3](#) and [Supplemental Figure S3](#)). These correlations were not present in the HC group. For all explorative correlations, see [Supplemental Table S3](#).

fMRI Task Effects (Pooled Across Groups)

Activity related to ε_2 (a precision-weighted RPE) peaked in bilateral ventral striatum and ventromedial prefrontal cortex (PFC) among other regions ($p\text{-FWE}_{\text{wholebrain}} < .05$, where FWE is familywise error) ([Figure 5A](#) and [Supplemental Table S4](#)), including the midbrain ($p\text{-FWE}_{\text{midbrain-voi}} < .05$, where voi is volume of interest) ([Supplemental Table S9](#)), a well-known network associated with RPEs. In contrast, third-level precision-weighted PE (ε_3) was associated with activity in prefrontal, parietal, and left insular regions ([Figure 5A](#) and [Supplemental Table S5](#)). Environmental volatility (μ_3) covaried with activation in bilateral insula, cingulate cortex, parietal cortex, middle temporal gyrus, globus pallidus, and thalamus as well as superior, middle, and inferior frontal gyrus ([Figure 6A](#), [Supplemental Figure S5](#), and [Supplemental Table S8](#)). For more details on group-level fMRI effects, including activity

Table 2. Between-Group Comparisons of Model Parameters Using *t* Tests or the Nonparametric Mann-Whitney *U* Test If Assumptions of Normality Were Violated

Models	HCS (<i>n</i> = 42)	PSZ (<i>n</i> = 31)	Test Statistic
Learning Model			
μ_3	-0.84 ± 0.49	-0.47 ± 0.48	$z = 3.15, p < .01$
κ	0.87 ± 0.60	1.35 ± 1.12	$z = 2.51, p < .01$
ω_3	-6.00 ± 0.02	-5.99 ± 0.05	$z = 0.73, p = .47$
Decision Model			
ρ_{win}	0.97 ± 0.57	1.08 ± 0.49	$z = 0.88, p = .38$
ρ_{loss}	0.08 ± 0.31	-0.12 ± 0.44	$z = 2.37, p = .02$
Replication Sample ^a			
	HCS (<i>n</i> = 24)	Nonmedicated PSZ (<i>n</i> = 24)	Test Statistic
Learning Model			
μ_3	-1.17 ± 0.61	-0.43 ± 0.70	$z = 3.88, p < .01$
κ	0.61 ± 0.58	1.56 ± 1.21	$z = 3.46, p < .01$
ω_3	-6.09 ± 0.02	-5.99 ± 0.06	$z = 1.35, p = .18$
Decision Model			
ρ_{win}	0.70 ± 0.74	0.43 ± 0.66	$z = 1.35, p = .18$
ρ_{loss}	-0.07 ± 0.59	-0.28 ± 0.77	$z = 1.05, p = .30$

Bonferroni correction was applied according to the number of parameters (5) ($p < .01$).

HCS, healthy control subjects; PSZ, patients with schizophrenia.

^aSchlagenhauf *et al.* (17).

specific for each group outside the effect of each regressor combined for HCs and PSZ, see [Supplemental Results](#).

fMRI Between-Group Effects

We conducted between-group comparison of the covariance between the modeling regressors derived from the best-fitting model and blood oxygen level-dependent response within SPM. For the regressor of environmental volatility μ_3 , a group difference between HCs and PSZ was found in right dorso-lateral PFC (DLPFC) (*F* contrast, using a mask representing the average effect of μ_3 over all participants for correction of multiple comparison [$x = 34, y = 44, z = 24$], $F = 19.89, z = 4.24, p_{FWE} = .04$) (Figure 6B). Post hoc analysis revealed stronger activity related to volatility in DLPFC of PSZ compared with HCs ($t = 4.46, z = 4.4, p_{FWE} = .02$) (Figure 6C). There was no significant difference between groups for any other regressor.

DISCUSSION

To the best of our knowledge, this is the first study to apply hierarchical Bayesian learning to choice and fMRI data of PSZ

during reward-based decision making. We present two main findings. First, our modeling suggests that medicated PSZ acted under an a priori enhanced higher-level belief about initial environmental volatility and increased coupling between higher and lower levels of learning, which leads to enhanced lower-level belief updating about action–outcome contingencies. This provides a computational account of choice switching, as was previously observed in PSZ (8,12–17). Using parameters of the winning model to simulate new data, we fully reproduced observed patterns in the behavioral data, and we replicated our findings on parameters in an independent cohort of non-medicated PSZ. Second, medicated PSZ displayed higher DLPFC activity related to environmental volatility, which points toward a prominent role of this region in promoting unstable behavior in PSZ.

PSZ show enhanced choice switching (8,12–17), and we demonstrate a possible underlying mechanism: an enhanced initial belief about the environmental volatility and a stronger coupling of volatility and lower-level learning of action–outcome contingencies. This has two consequences. First, PSZ had an overall stronger tendency to switch (enhanced initial belief about volatility). Second, lower-level beliefs fluctuated more strongly and

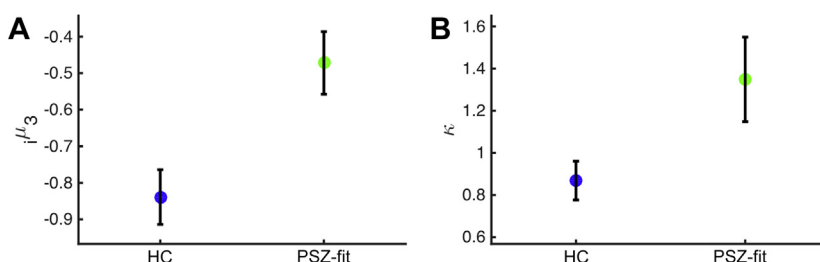


Figure 4. (A) The initial estimate of environmental volatility is significantly higher in patients with schizophrenia (PSZ)-fit ($n = 31$) as compared with healthy control subjects (HCs). (B) The coupling between the third level (environmental volatility) and the second level is significantly stronger in PSZ-fit ($n = 31$) compared with HCs.

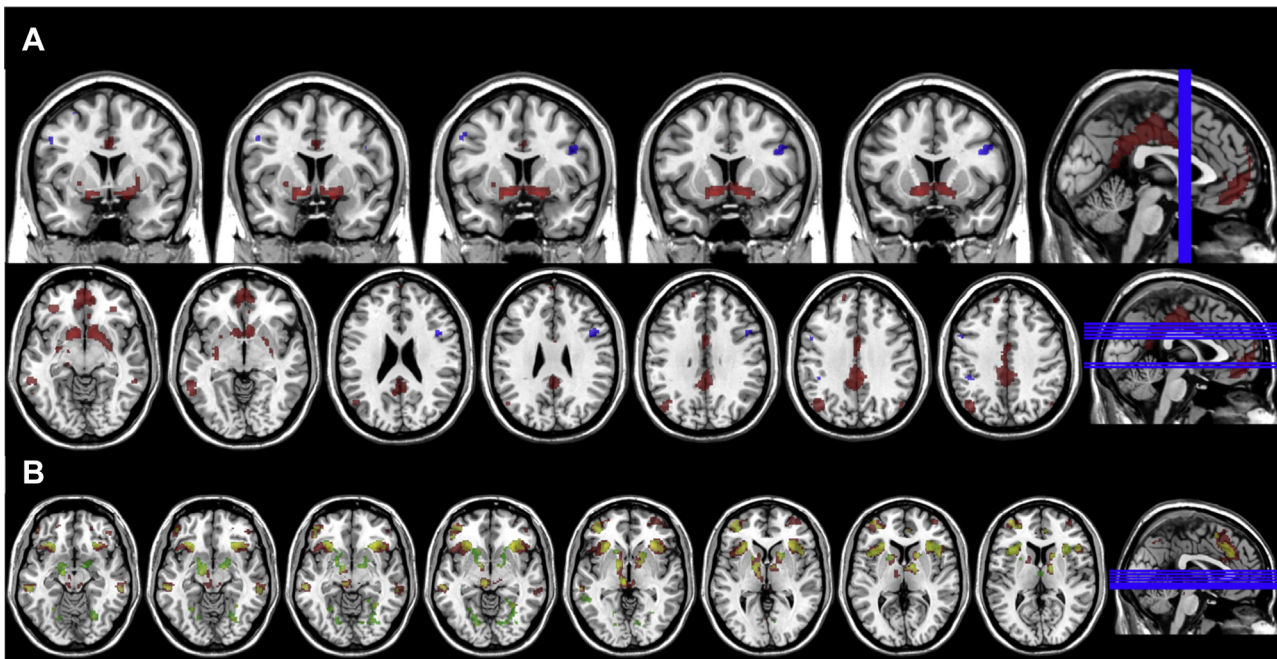


Figure 5. Blood oxygen level–dependent signal across all participants related to precision-weighted prediction errors from the second (red) and third (blue) levels (**A**) and precision weight from the second (red) and third (green) levels (**B**), with overlap in yellow (both at $p\text{-FWE}_{\text{wholebrain}} < .05$, $k = 10$). FWE, familywise error.

led to increased choice switching, particularly after (irrelevant) losses. Thus, PSZ inferred more contingency changes in this dynamic task environment that are putatively signaled through losses. Enhanced estimates of changes in context probabilities were also found in PSZ in the nonreward domain (48). In contrast to our finding of enhanced initial belief about volatility, Powers *et al.* (31) probed conditioned hallucinations and reported stronger lower-level priors about perceptual inputs combined with reduced evolution of volatility in hallucinating participants. A possible explanation may be that alterations of volatility estimates differ with regard to the investigated functional domain, potentially related to different symptom dimensions. As suggested by our finding, cognitive beliefs about the structure of the environment appear to be more unstable, while perceptual beliefs about sensory inputs appear to be overly stable and not appropriately adjusted following changes in the environment (31).

Because our model revealed consistent results in medicated and nonmedicated PSZ, elevated beliefs about environmental volatility may represent an important mechanism of impaired flexible decision making. In a similar vein, an inability to stabilize behavior according to an internal model of action–outcome contingencies was found after administration of ketamine in healthy control subjects (49), in line with the assumption that reduced (prefrontal) NMDA receptor functioning (27,50) may lead to aberrant cortical information processing (51). In line with this idea, we found a stronger association in PSZ than in HCs of beliefs about volatility with blood oxygen level–dependent activity in DLPFC. However, in our fMRI study, we cannot infer about involved neurochemical systems. On the behavioral level, beliefs about higher volatility, in our model directly linked to decision noise, can lead to more stochastic behavior (in our task overall more choice switching). We therefore suggest that

heightened neural representation of volatility may generate more stochastic behavior, although in our correlational and cross-sectional study we cannot ascertain a causal link. We found a negative correlation of the initial belief about volatility with independent neuropsychological measures of executive functioning and cognitive speed in PSZ, thereby emphasizing its dysfunctional character, while these associations were not observed in the HC group.

PSZ's heightened belief about volatility may render a system (hyper)sensitive to any new input (51,52), thereby impeding the detection of regularities in probabilistic environments and leading to (hyper)flexible updating in response to (irrelevant) information. Meta-analyses showed reduced prefrontal activity in PSZ compared with HCs for (relevant) task versus (irrelevant) conditions across multiple cognitive measures (53,54). On the one hand, prefrontal dysfunction in PSZ may contribute to an enhanced higher-level belief about volatility (e.g., by impairing the detection of higher-level regularities), and such beliefs about volatility might be assigned with enhanced precision (potentially in a compensatory manner). On the other hand, lower-level beliefs may be more unstable and presumably assigned with lower precision, leading to distinct aberrant experiences and behaviors depending on the tested domain, with most evidence so far coming from perceptual processing (55).

Aberrant cortical processing was theorized, at least in nonmedicated PSZ, to increase striatal dopamine turnover (27,50), which might interfere with striatal and midbrain RPE signals. Indeed, in nonmedicated PSZ, striatal RPE activity was found to be reduced (17,56). In RL accounts (24), enhanced spontaneous phasic dopamine transients could highlight irrelevant stimuli and disturb the signaling of (relevant) RPEs. In our medicated sample of PSZ, no significant differences in striatal activations to RPEs

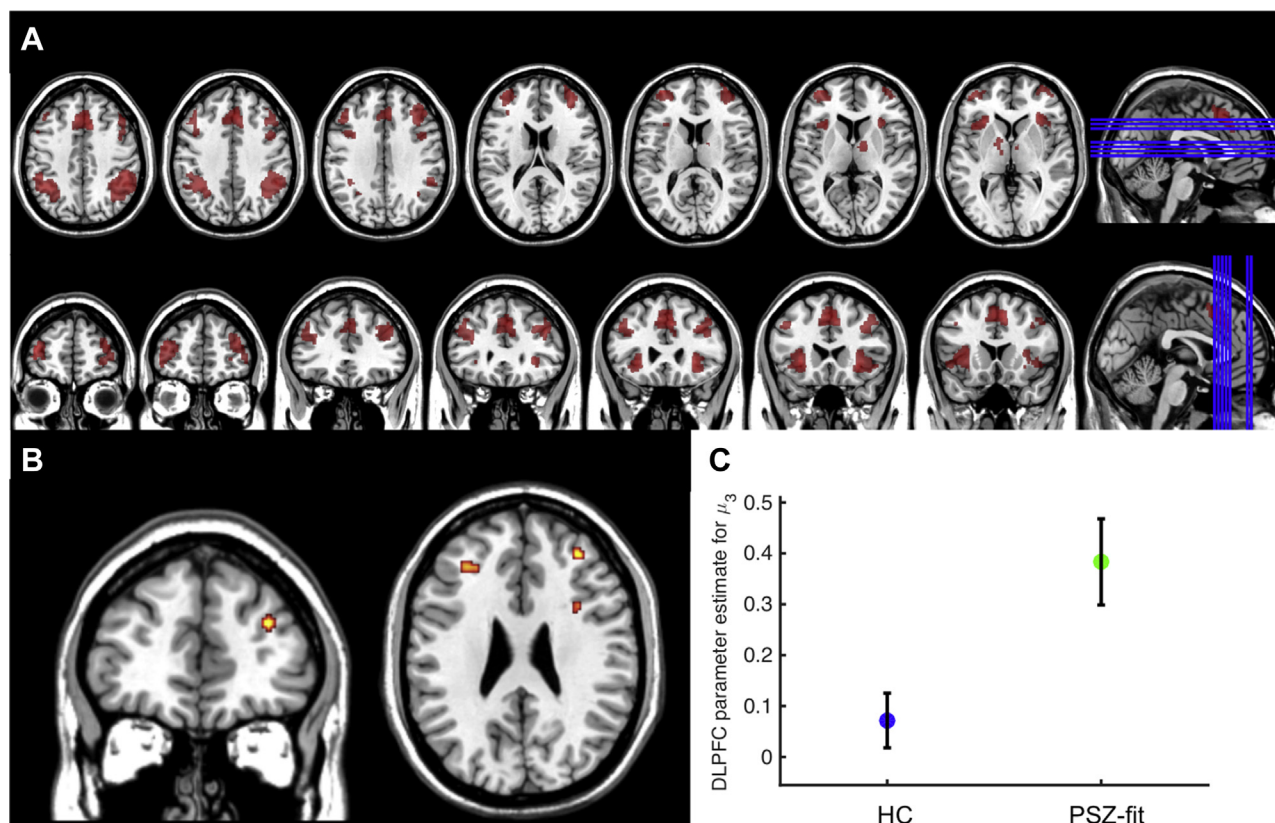


Figure 6. (A) Across all participants, blood oxygen level–dependent signal related to volatility estimate from the third level at p -FWE $< .05$ for the whole brain, $k = 10$. (B) μ_3 -related blood oxygen level–dependent signal in the dorsolateral prefrontal cortex (DLPFC) differs between patients with schizophrenia (PSZ)-fit ($n = 31$) and healthy control subjects (HCs) (F contrast displayed at $p < .001$ uncorrected; corrected for main effect of μ_3 over all participants [$x = 34$, $y = 44$, $z = 24$], $F = 19.89$, $z = 4.24$, $p = .038$). (C) A post hoc analysis of regression parameter estimates at the peak of the group difference ($x = 34$, $y = 44$, $z = 24$) showed that this was driven by heightened activation related to environmental volatility in DLPFC of PSZ-fit ($n = 31$) compared with HCs ($t = 4.46$, $z = 4.4$, $p = .019$). FWE, familywise error.

were observed, in line with reports of absent differences in striatal RPEs in medicated PSZ (14,15). This suggests medication status as an important factor relating to striatal RPE signaling similar to medication effects on striatal reward anticipation in PSZ (35,57,58). In hierarchical Bayesian learning, representation of lower-level PEs may be similar in patients and control subjects, but potentially reduced precision of lower-level beliefs might highlight irrelevant inputs (e.g., resulting in choice switching). This could, at least in theory, result from a common aberrant prefrontal process, as discussed above, but also from an effect of antipsychotic D_2 receptor antagonists in the striatum (29). However, we did not observe group differences in midbrain and striatum for precision weights and precision-weighted PEs. While our data indicate a disrupted higher-level process with evidence from behavioral modeling and fMRI, disturbed lower-level processes are supported by our behavioral modeling but not by the presented fMRI data.

Limitations

First, the lack of clear superiority of any model for the data from PSZ, as well as the substantial number of PSZ in which no model fitted better than chance, needs to be considered. Excluding these patients from further modeling-based analyses can be considered restrictive and may reduce the

generalization of results. However, 2 subgroups were identified with (task-independent) different cognitive profiles, which contributes to disentangling heterogeneity across PSZ—a fundamental challenge for psychiatric research (59). By controlling whether subjects' performance can actually be interpreted as assumed by the theories, we eliminated a potential key confound. Nevertheless, it remains problematic if clinical groups differ in how well they are described by models of interest, as observed in our study because parameters are conditional on the model. This impedes the interpretation of differences in parameters across groups [for a discussion of this problem, see (60)]. In principle, Bayesian model averaging (61) can help, but this is not established for non-nested models as used here. Future studies might implement tasks with adaptive difficulty to reduce the number of patients whose behavior cannot be explained by any model, which may potentially be a result of excessive cognitive demands. Furthermore, the relation between different Bayesian modeling approaches such as the HGF and active inference models should be explored (62).

Second, we suggest that overestimating volatility is one possible explanation for choice switching. However, in our model, volatility partly determines decision noise. This limits the differentiation between the concepts of volatility and

exploration and limits interpretability of volatility estimates to some extent. The finding that this model performs best is an indication that our data do not fully support a strong distinction between volatility and exploration. Additional task-based manipulations would be required to overcome this (37), which would most likely involve longer tasks than our patient-friendly fMRI task (<15 minutes, 160 trials). The formulation of our response model suggests that results are still informative. We control for overall differences in stickiness with 2 parameters that change the shape of the decision function differently for wins and losses and exert a bias toward repeating or switching responses irrespective of learned expectations (see Supplement). Therefore, decision noise is determined not only by trialwise volatility but also by subject-specific traits that are expressed in a condition-specific fashion. This disentangles volatility and decision noise to some degree.

Third, this is a case-control study that fundamentally limits the inferences that can be drawn from the results, for example, the development of inappropriately high initial beliefs about volatility over the course of illness, its stability over time, and its relation to broader cognitive deficits consistently found in PSZ.

In summary, we present a computational mechanism putatively underlying unstable behavior in PSZ: a stronger coupling of heightened beliefs about environmental volatility with lower-level learning, which was present in medicated and nonmedicated PSZ. In medicated PSZ, this was accompanied by enhanced activity related to environmental volatility in DLPFC. Future studies should aim to test specificity of the presented results for PSZ and overcome the limitation of the lack of longitudinal clinical data. Computational modeling may aid in the identification of subgroups of PSZ (63) and potentially inform the prediction of treatment response to antipsychotic drugs by aiming to dissect the important biological heterogeneity and interindividual differences among patients (64). These steps toward clinically useful procedures will require carefully designed prospective studies in the framework of computational psychiatry (29,65–67).

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LD, CM, KES, and FS designed the study. LD, RB, TK, and JK performed research. LD and RB analyzed the data. CM and FS supervised data analysis. LD and RB wrote the initial version of the manuscript. LD, RB, TK, JK, CM, KES, AH, and FS read and corrected versions of the manuscript.

Data from this study were presented at the following conferences: 71st annual meeting of the Society for Biological Psychiatry, May 12–14, 2016, Atlanta, Georgia; 6th biennial Schizophrenia International Research Society Conference, April 4–8, 2018, Florence, Italy; and 11th Forum of Neuroscience, July 7–11, 2018, Berlin, Germany.

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