

Abnormalities in motor adaptation to different types of perturbations in schizophrenia

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ABSTRACT

Schizophrenia is a mental health disorder that often includes psychomotor disturbances, impacting how individuals adjust their motor output based on the cause of motor errors. While previous motor adaptation studies on individuals with schizophrenia have largely focused on large and consistent perturbations induced by abrupt experimental manipulations, such as donning prism goggles, the adaptation process to random perturbations, either caused by intrinsic motor noise or external disturbances, has not been examined – despite its ecological relevance. Here, we used a unified behavioral task paradigm to examine motor adaptation to perturbations of three causal structures among individuals in the remission stage of schizophrenia, youth with ultra-high risk of psychosis, adults with active symptoms, and age-matched controls. Results showed that individuals with schizophrenia had reduced trial-by-trial adaptation and large error variance when adapting to their own motor noise. When adapting to random but salient perturbations, they showed intact adaptation and normal causal inference of errors. This contrasted with reduced adaptation to large yet consistent perturbations, which could reflect difficulties in forming cognitive strategies rather than the often-assumed impairments in procedural learning or sense of agency. Furthermore, the observed adaptation effects were correlated with the severity of positive symptoms across the diagnosis groups. Our findings suggest that individuals with schizophrenia face challenges in accommodating intrinsic perturbations when motor errors are ambiguous but adapt with intact causal attribution when errors are salient.

1. Introduction

Schizophrenia (SZ) is a chronic mental health disorder, and its prevalent positive symptoms include reality distortions such as hallucinations, delusions, and other bizarre beliefs (DiPiro et al., 2014; Gold and Harvey, 1993; Hyde et al., 1994; Morice and Delahunty, 1996; Silver et al., 2003). Individuals with SZ also show psychomotor disturbances that are intricately linked to the psychotic disorder with a shared neural basis (Bernard et al., 2017; Hirjak et al., 2015; Walther and Mittal, 2017). One common difficulty for them is to distinguish whether action consequences are generated by their own actions or others

(Averbeck et al., 2011; Frith and Friston, 2013).

In daily life, the motor system constantly performs causal inference computations as it needs to accommodate various perturbations according to their sources. From a normative perspective, a motor error caused by internal perturbations within the motor system, e.g., muscle fatigue or inappropriate motor commands, should be readily adapted by sensorimotor recalibration, while a movement error caused by external perturbations, e.g., a friction change of the supporting surface when people walking from a concrete-paved road to an icy surface, should be dismissed from recalibration (M. Berniker and Kording, 2008). The latter external perturbations have been recently further divided into two

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types: one is random perturbations, such as an unexpected gust of wind perturbing the basketball shot, and the other is consistent perturbations, such as persistent wind with a steady strength. Consistent perturbations are accommodated by forming an explicit compensation strategy (Taylor and Ivry, 2014), while random external perturbations only invoke fast temporal correction without a strategy (K. Wei et al., 2010). Inference of motor error is plagued by uncertainties in the sensorimotor system and the environment. However, normal individuals can flexibly adapt by probabilistically inferring the cause of the motor error, per the Bayesian principle (Max Berniker and Kording, 2008; Marko et al., 2012; Vyas et al., 2020; Wei and Kording, 2009).

Despite the prominent deficits in self-agency and causal inference among individuals with schizophrenia, previous studies have not examined motor adaptation with the recognition of the three causal structures of motor errors. Most, if not all, previous studies utilized consistent perturbations that are applied abruptly and then remain for a block of trials. For goal-directed hand movement, researchers typically distorted visual feedback, including shifted visual scenes with prism goggles (prism adaptation; Bartolomeo et al., 2020; Bigelow et al., 2006; Ninomiya et al., 1998), rotated (visuomotor rotation adaptation, Bansal et al., 2019; Cornelis et al., 2022; Synofzik et al., 2010) or amplified/reduced (visuomotor gain adaptation, Cornelis et al., 2022; Knoblich et al., 2004) visual motion of the hand representation on the screen display. For these consistent visual perturbations, individuals with schizophrenia have shown reduced adaptation rate, smaller adaptation extent, less aftereffect (reflecting implicit recalibration of the motor system), and less spatial generalization (Bansal et al., 2019; Bartolomeo et al., 2020; Bigelow et al., 2006; Coesmans et al., 2014; Cornelis et al., 2022; Ebner et al., 1971; Ninomiya et al., 1998; Pitblado et al., 1980). These adaptation deficits have been attributed to impairments in procedural learning (Bigelow et al., 2006; Ninomiya et al., 1998), overreliance on visual feedback and thus less recalibration of proprioception (Bartolomeo et al., 2020), impaired sense of agency (Bansal et al., 2019), or cerebellar dysfunction (Cornelis et al., 2022).

However, these large and consistent perturbations can be unambiguously inferred as an external environmental change and thus invite the formation of explicit strategy. For example, the participants experienced a sudden rotation of the hand presentation by 30° (Bansal et al., 2019) or donning prism goggles to shift the visual scene by 12° (Bartolomeo et al., 2020). These “environmental” changes prompt participants to use strategic learning (Oh and Schweighofer, 2019; Taylor and Ivry, 2014), which is essentially cognitive, relying on working memory and reaction time (Samuel D McDougle and Taylor, 2019) and drastically different from procedural learning or implicit visual-proprioceptive recalibration that was the subject of previous investigations in schizophrenia (Bartolomeo et al., 2020; Bigelow et al., 2006). Thus, the widely observed reduced adaptation among individuals with schizophrenia might reflect their abnormal strategic learning instead of impairment in sensorimotor learning of procedural nature.

How individuals with schizophrenia adapt to random, instead of consistent, motor errors, either from internal or external sources, has yet to be examined. Motor errors resulting from one's own motor noise (van Beers, 2009) or random external perturbations (Kunlin Wei and Kording, 2009) were corrected efficiently among individuals without SZ. Here, we hypothesized that individuals with SZ would show impaired adaptation to their own motor noise since motor errors are small and ambiguous and individuals with schizophrenia have reduced perceptual sensitivity to errors (Synofzik et al., 2010) or impaired self-monitoring of actions (van der Weiden et al., 2015). In contrast, large motor errors induced by random external perturbations should be adapted normally as the errors are perceptually salient. Using a Bayesian probabilistic model, we quantitatively estimate their causal inference about these large motor errors to examine the link between motor adaptation and causal attribution of errors (Kunlin Wei and Kording, 2009). For completeness, we included a condition with consistent perturbations to confirm the classical finding of reduced adaptation. Lastly,

to elucidate how the heterogeneity and severity of schizophrenia symptoms affect sensorimotor adaptation, we also included a group of youth with ultra-high risk of psychosis and a group of individuals with SZ at the remission stage, besides a group of age-matched healthy controls. One hypothesis is that the deficit in motor adaptation differs between the patients with different severity levels of SZ symptoms. Or, we could explore whether the deficit in motor adaptation resembles a trait marker or a state marker of schizophrenia. If it is a trait marker, it should not differ between the patients with active symptoms and the patients at the remission stage. Lastly, we are also interested in whether motor adaptation can serve as a sensitive behavioral marker to distinguish different diagnosis groups. For the practical purpose, including multiple diagnosis groups would also enable us to perform correlational analyses between motor adaptation measures and clinical symptoms.

2. Methods

2.1. Participants

Seventy individuals were enrolled in this study, including 57 patients and 13 age-matched healthy controls (Table 1). The patients were recruited from the outpatient department in Beijing Anding Hospital (Beijing China), including 15 ultrahigh-risk patients (*UHR* group), 25 SZ patients with active positive symptoms (*SZ-active* group), and 17 remitted patients with SZ (*SZ-remission* group).

The participants in the *UHR* group would be included in the study if they meet the criteria below: (a) diagnosed by two qualified psychiatrists via the Chinese version of Structured Interview for Prodromal Syndromes/Scale for the Assessment of Prodromal Symptoms (SIPS/SOPS, Miller et al., 2002); (b) aged from 13 to 40 years; (c) belonged to three subtypes based on the *UHR* criteria, including the attenuated positive symptoms (APS) syndrome, the brief limited intermittent psychotic symptoms (BLIPS), and the genetic risk and/or the deterioration (GRD) syndrome. The participants in *UHR* group would be excluded if they meet any criteria below: (a) with a history of serious or unstable somatic disorders; (b) unattended or unable to take medicine as directed by a doctor; (c) with severe suicidal tendencies and a history of neurobiological disorders or a family history of hereditary neurological diseases.

The participants in the *SZ-active* group would be included if they meet the criteria below: (a) diagnosed by two qualified psychiatrists based on DSM-IV criteria, (b) aged from 16 to 45 years, (c) predominantly characterized by positive symptoms such as hallucinations and delusions, (d) scored ≤ 3 on the Brief Psychiatric Rating Scale for items assessing ‘Conceptual Disorganization’, ‘Suspiciousness’, ‘Hallucinatory Behavior’, and ‘Unusual Thought Content’. The patients in the *SZ-remission* group were included if (a) they were diagnosed by two qualified psychiatrists based on DSM-IV criteria, (b) aged from 16 to 45 years, and (c) scored ≤ 3 points for the 8 items of the Positive and Negative Syndrome Scale (PANSS) for at least 6 months (Andreasen et al., 2005). The participants in the *SZ-active* group and *SZ-remission* groups were excluded if they (a) had a current comorbid substance-use disorder, (b) had a history of neurobiological disorders or a family history of hereditary neurological diseases, (c) scored ≥ 1 on the Extrapyramidal Symptom Rating Scale (ESRS). These patients were also assessed by the Global Assessment of Functioning Scale (GAF), the Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984) and PANSS.

We also recruited 13 healthy participants (*Control* group) who had no personal or family history of an Axis I disorder (Internal Neuropsychiatric Interview, MINI). The drug usage for each patient group was detailed in the supplemental material (Table S1), and their daily dose was converted to Chlorpromazine equivalents (Woods, 2003). All participants had normal or corrected vision. Written consent was obtained before the experiment. All procedures were approved by the Ethics Committee of Peking University and Beijing Anding Hospital.

Table 1
Participants characteristics.

	<i>UHR</i>	<i>Patient</i>	<i>Remission</i>	<i>Control</i>	$F/t/\chi^2$	<i>p</i>
N	15	25	17	13	–	–
Female (Male)	6 (9)	13 (12)	7 (10)	5 (8)	0.96	0.81
Age	18.7 ± 4.4	20.7 ± 5.6	23.7 ± 4.8	21.7 ± 3.3	4.0	0.024
GAF	65.00 ± 4.29	29.04 ± 9.26	77.59 ± 4.32	–	276.8	<0.001
Average daily dose, mg/day (Chlorpromazine equivalents)	66.67 ± 58.76	464.00 ± 90.74	458.82 ± 64.31	–	149.4	<0.001
PANSS score	36.53 ± 2.33	65.68 ± 8.92	35.35 ± 5.07	–	140.4	<0.001
Positive symptoms (SAPS)	–	22.56 ± 14.15	4.59 ± 0.80	–	27.1	<0.001
Hallucinations	–	6.44 ± 7.22	1.12 ± 0.33	–	9.1	0.004
Delusions	–	7.76 ± 5.60	1.41 ± 0.51	–	21.6	<0.001
Bizarre Behavior	–	7.88 ± 5.57	1.00 ± 0.00	–	25.7	<0.001
Positive Formal Thought Disorder	–	0.48 ± 1.66	1.06 ± 0.24	–	2.0	0.163
Sum of Hallucinations + Delusions	–	14.20 ± 11.32	2.53 ± 0.72	–	17.9	<0.001

2.2. Experimental setup and task

The seated participants performed repetitive hand-reaching movements on a tabletop in a virtual reality setting (Fig. 1A). They made quick and accurate movements from a starting position to a visual target 10 cm away on the straight right. The hand was concealed by a semi-transparent mirror, which reflected the visual stimuli that were displayed on an opaque projection screen. The visual stimuli were projected by a projector (refreshing rate 75 Hz; P1270, Acer) onto the projection screen. The starting position and the target were shown as a green and a yellow cross, respectively, extended 4 pixels both ways. The position of the right index finger was tracked by a motion track system (Codamotion, Charnwood Dynamics, UK; sampling rate ~ 200 Hz) and displayed as a solid green circle (hand cursor) with a radius of 7 pixels.

A trial started when the participant put their hand cursor at the starting position (Fig. 1B). After 100 ms, the starting cross and the hand cursor disappeared, and the target appeared to signal the reaching movement. The participants were required to make a fast movement toward the target, “slicing” the target as accurately as possible. A slow trial was repeated if the movement was not stopped in 3 s after target appearance, with a warning text “too slow” shown on the screen. Importantly, when the hand cursor traveled across the target, the hand cursor would appear briefly for 500 ms at the location aligned horizontally with the target (endpoint feedback). Thus, the visual error was only specified in the depth (vertical) direction. The depth position of the endpoint feedback was either veridical or spatially perturbed either toward or away from the body. This endpoint feedback, relative to the target vertically, served as a potent motor error for adaptation in the next trial.

2.3. Experimental procedure

The experiment was organized into four phases. In the familiarization phase, the participants practiced for 30 trials with veridical endpoint feedback to familiarize them with the task. In the subsequent perturbation-free phase, we aimed to evaluate how participants corrected their own motor errors. Thus, they were instructed to reach the target with veridical endpoint feedback for 50 trials. In the random-perturbation phase, the visual feedback was perturbed in the depth direction randomly by one of nine possible sizes: 0, ±1, ±2, ±4, and ±8 cm (Fig. 1B). There were 50 trials for each perturbation size, resulting in a total of 450 randomly-ordered trials. Even the smallest perturbations (i.e., ±1 cm) were perceptually discernable from normal motor noise. Participants were instructed to aim the hand straight at the target, thus, were discouraged from forming an explicit strategy (e.g., intentionally aiming away from the target) for these random perturbations. They were told that the cursor might deviate from their actual hand trajectory but their goal was still to “hit” the target with the hand. In the final consistent-perturbation phase, a fixed perturbation (+2 cm) was presented on each trial for 30 consecutive trials. In this phase, the participants were instructed to hit the target with the cursor despite possible deviations of the cursor. All participants finished all the experimental phases, but three participants from the *UHR* group and fourteen from the *SZ-active* group did not perform the consistent-perturbation phase due to our change of the experimental design after early data collection.

2.4. Data analysis

The endpoint cursor feedback was the sole visual feedback to drive adaptive responses. We defined motor error as the vertical deviation of the endpoint from the target. Correcting the motor error would cause a

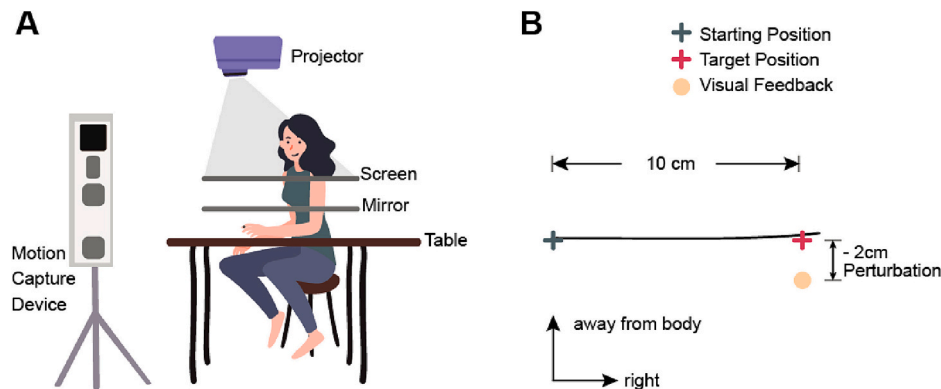


Fig. 1. The illustrations for the experimental setup and the task. (A) Experimental setup. The visual feedback was projected onto a mirror system, which occluded the direct vision of the hand whose motion was measured by a motion capture system. (B) A visual illustration of the movement task. The starting position was shown at the center of the workspace, and the target was shown 10 cm horizontally to the right. The hand trajectory was shown for illustration purposes; the hand cursor only appeared at the movement end, whose location was either veridical or perturbed. A 2 cm downward perturbation is shown.

change in the direction of hand movement, opposite to the original error. We computed the lag-1 autocorrelation (ACF1) of the error sequences from the 50 trials in the perturbation-free phase. As unperturbed trials produce errors following stationary random distributions, the ACF1 is indistinguishable from zero in neurotypical participants (van Beers, 2009). Reduced error correction would lead to positive ACF1 and large error bias (thus large average error) since motor errors are left inadequately corrected. We also computed the standard deviation of absolute errors as an indicator of motor variability or motor prediction error (Synofzik et al., 2010). We examined the response time (RT), the time difference between target appearance and movement onset when the hand speed exceeded 2 cm/s, and movement time (MT), the duration from the movement onset to its end when the hand speed dropped below 2 cm/s.

In the random-perturbation phase, the visual perturbation was fully randomized in size and direction, thus preventing the participants from forming explicit strategies to adapt. Our previous study on normal participants showed that people would adapt to the just-experienced motor error by moving in the opposite direction in the next trial (Kunlin Wei and Kording, 2009; K. Wei et al., 2010). The adaptation increases with increasing perturbation size but eventually saturates (for a preview, see Fig. 4). To quantitatively show this nonlinearity of adaptation, we computed the linear regression coefficient between adaptation and perturbation size separately for small perturbations (i.e., 0, ± 1 , and ± 2 cm) and all perturbations (i.e., 0, ± 1 , ± 2 , ± 4 , and ± 8 cm). A significantly larger slope for the small perturbations than for all the perturbations would indicate nonlinear learning.

Importantly, nonlinear learning has been attributed to the causal inference of motor errors. Small errors are more likely to be attributed to the intrinsic noise in the motor system and thus corrected more aggressively; large errors are more likely to be attributed to random environmental perturbation and thus be less likely to be corrected. Using the probabilistic model based on Bayesian inference, we could estimate people's beliefs about the relevance of error for adaptation (Kunlin Wei and Kording, 2009). The likelihood (abbrev. $P_{\text{relevance}}$) that an error is relevant can be computed for each perturbation size and for each participant, enabling us to compare causal inference of random motor errors between groups.

For the consistent-perturbation phase, we computed the adaptation rate for correcting the fixed perturbation (+2 cm) over 30 successive trials. We defined the initial learning as from the first trial to the trial when motor error stopped decreasing, as indicated by comparisons between adjacent trials via paired *t*-test (Yin and Wei, 2020). The window was from trial 1 to 7 based on data from the *Control* group. We calculated the average hand deviations within this window as a proxy of the learning rate. The larger the average deviation, the faster the learning. The learning extent was defined as the average hand deviation of the last three trials.

We also explored possible associations between motor adaptation and the severity of symptoms quantified by PANSS and SAPS scores. For SAPS, the four component scores (hallucination, delusion, bizarre behavior, and positive formal thought disorder), the total score, and the sum of hallucination and delusions scores were examined separately, thus Bonferroni correction was used for multiple tests (Synofzik et al., 2010). For PANSS, only its total score was used for correlational analysis; thus, no correction was needed. To minimize the confound from the extrapyramidal effect, we used the daily drug dose (Chlorpromazine equivalents) as a covariate when conducting partial correlation analyses. All the behavioral measures of motor adaptation mentioned above (e.g., RT, ACF-1, $P_{\text{relevance}}$) were tested. As shown in Table 1, SAPS were measured for all the three patient groups but PANSS was measured only for the *SZ-active* and *SZ-remission* groups. Our correlational analyses used all the data available accordingly.

All analyses were conducted using SPSS (24.0) and Matlab (2020b). For group comparisons, one-way independent-sample ANOVA or the Kruskal-Wallis test was used, depending on the normality of the data

examined by the Shapiro-Wilk test. Greenhouse–Geisser tests were used if the equal variance assumption for ANOVA was violated, and pairwise comparisons were conducted using Scheffe's tests. For testing ACF1 against 0, we used a one-sample *t*-test. The alpha level was set at 0.05.

3. Results

The deviation of the hand from the target position in the vertical direction changes over trials, either driven by internal motor noise or by adaption to perturbations (Fig. 2). The hand deviation hovered around zero in the perturbation-free phase with small fluctuations. In the random-perturbation phase, the “fluctuations” increased when the participant adapted to random visual perturbations. In the consistent-perturbation phase, the hand deviation asymptotically increased to adapt to the +2 cm perturbation.

3.1. Reduced adaptation to small and intrinsic motor errors

For the perturbation-free phase, the groups of individuals with SZ exhibited larger mean errors (error bias, $H(3) = 12.58$, $p = .006$; Fig. 3A), which amounted to 1.95 ± 0.61 , 2.39 ± 1.39 , 2.52 ± 1.58 , and 3.04 ± 2.38 cm (median and iqr across participants; same below) for the *Control*, *Remission*, *UHR*, and *SZ-active* group, respectively. Similarly, the groups also exhibited larger across-trial error variance ($H(3) = 15.10$, $p = .002$; Fig. 3B), which amounted to 2.20 ± 0.52 , 2.59 ± 1.27 , 2.97 ± 1.80 , and 3.31 ± 2.27 cm for the *Control*, *Remission*, *UHR*, and *SZ-active* group, respectively. The lag-1 correlation (ACF1) between successive movement errors also differed between groups ($F(3,66) = 3.67$, $p = .016$; Fig. 3C). ACF1 was 0.04 ± 0.06 , 0.23 ± 0.09 , 0.11 ± 0.10 , and 0.38 ± 0.06 for the *Control*, *Remission*, *UHR*, and *SZ-active* group, respectively. Importantly, we found that all but the *UHR* group had ACF1 significantly larger than 0, while the *Control* group, as expected, showed otherwise (paired *t*-tests: $t = 0.66$, $p = .52$; $t = 2.44$, $p = .027$; $t = 1.21$, $p = .25$; $t = 6.09$, $p < .001$ for the *Control*, *Remission*, *UHR*, and *SZ-active* group, respectively). Thus, individuals with SZ showed the sign of inadequate adaptation to their errors perceived in the previous trial. Furthermore, we found that the ACF1 was positively associated with error bias ($r = 0.547$, $p = .006$) but not with the error variance ($r = 0.137$, $p = .524$). Overall, individuals with schizophrenia showed reduced adaptation to their own motor errors, and this reduced adaptation was related to persistent motor errors.

The *SZ-active* group exhibited the slowest RT among all the groups ($F(3,66) = 6.86$, $p < .001$; Fig. 3D). The average RT was 283.95 ± 8.59 , 351.71 ± 27.49 , 310.70 ± 19.55 , and 414.05 ± 31.57 ms for the *Control*, *Remission*, *UHR*, and *SZ-active* group, respectively. However, we did not find any group difference in MT ($F(3,66) = 0.074$, $p = .97$), which was 453.86 ± 20.61 , 468.70 ± 29.06 , 461.00 ± 27.32 , and 471.04 ± 27.18 ms for the four groups.

3.2. Intact adaptation to large yet random perturbations

We did not find any group difference in adaptation to random perturbations (Fig. 4). The hand deviation in the next trial showed a typical nonlinear relationship with the perturbation size: the hand deviation increased approximately linearly for small perturbations, but the increase was dampened for large perturbations. We submitted average hand deviations to a two-way mixed ANOVA (5 perturbation sizes $\times$ 4 groups). We collapsed data from the perturbations of the same amplitude but in the opposite direction to reduce the number of conditions from 9 to 5. Neither the main effect of the group nor the interaction was significant ($F_{\text{group}}(3, 66) = 0.81$, $p = .49$; $F_{\text{interaction}}(12, 264) = 0.49$, $p = .92$). The main effect of perturbation size was significant ($F(4, 264) = 8.13$, $p < .001$), and posthoc comparisons indicated that the adaptation increased with perturbation size but was saturated at the 4 cm perturbation. This nonlinear learning was further revealed by linear regression analysis. The regression coefficient (slope) of the hand deviation against

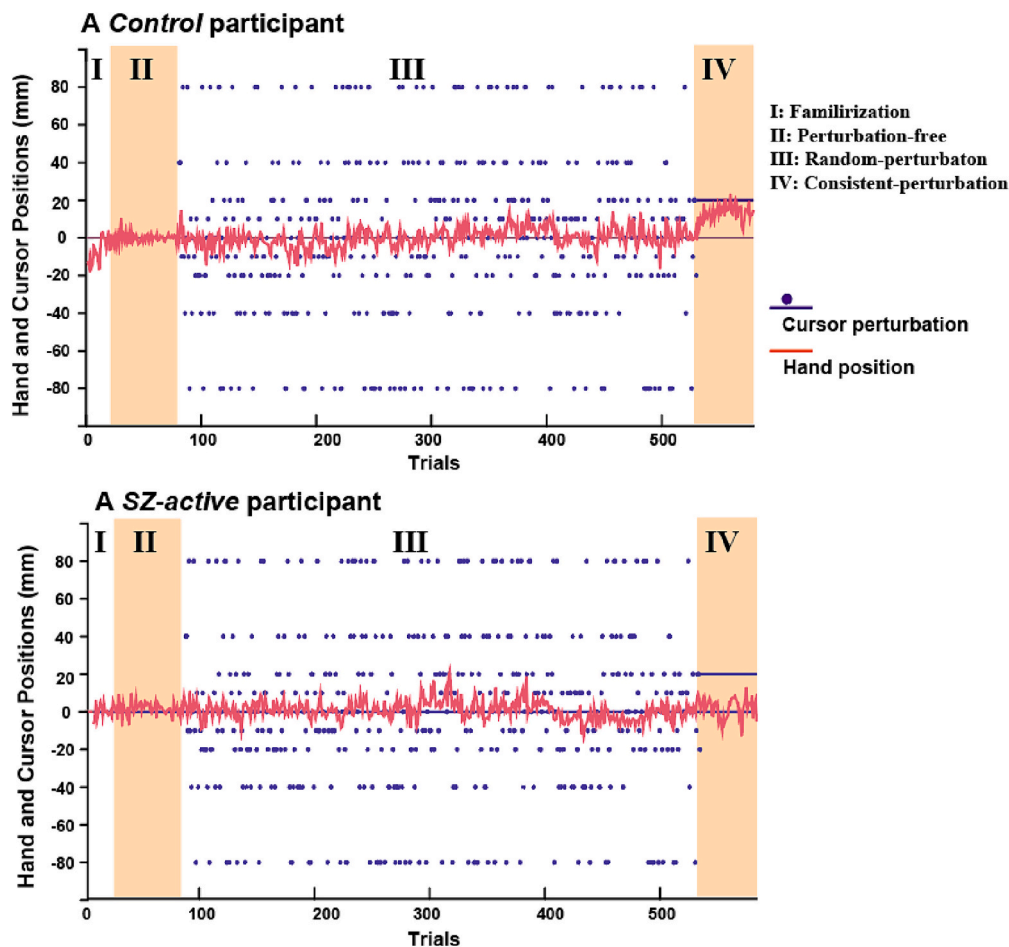


Fig. 2. The hand positions and the perturbations in all trials from a typical subject from the *Control* group (A) and one from the *SZ-active* group (B). The perturbation was applied in the vertical direction; the hand position was shown in the vertical direction only with respect to the target.

the size of small perturbations (0, ± 1 , and ± 2 cm) and against all perturbations (0, ± 1 , ± 2 , ± 4 , and ± 8 cm) were compared, and a steeper slope for the former case would be indicative of nonlinear learning. A paired *t*-test indicated that the slope was steeper for the small perturbations than for all perturbations for each group. One-way ANOVAs showed that the slope did not differ between groups (for small perturbations: $F(3, 64) = 0.35$, $p = .79$; for all perturbations, $F(3, 64) = 0.39$, $p = .76$).

Nonlinear learning enabled us to examine the subjective belief of the causality of different perturbation sizes with our Bayesian model. The model fit individual participants' nonlinear learning function with decent accuracy, yielding an average R^2 of 0.86 ± 0.15 (see an exemplary subject in Fig. 4B). We computed the likelihood of regarding an error as caused by the agent ($P_{relevance}$), thus relevant for adaptation as a function of perturbation size (Fig. 4C). There was an increasing tendency for the SZ groups to attribute the perturbation as self-made when compared to the control group. We submitted $P_{relevance}$ to a 4 perturbations (1, 2, 4, and 8 cm) $\times$ 4 groups mixed ANOVA. The main effect of visual perturbations was significant ($F(3, 183) = 346.87$, $p < .001$; Fig. 4C), suggesting that the larger the perturbation, the smaller the $P_{relevance}$. However, the effect of group and group-by-perturbation interaction was not significant ($F_{group}(3, 61) = 1.08$, $p = .37$; $F_{interaction}(9, 183) = 0.32$, $p = .97$), suggesting that all groups' learning behaviors are governed by similar causal inference.

3.3. Reduced adaptation to a large yet consistent perturbation

In the consistent-perturbation phase, all groups showed gradual

adaptation to counter the perturbation (Fig. 5A). However, their learning rate and learning extent appeared different. We found a significant group difference in learning rate (average hand deviation in initial trials; $F(3,52) = 3.18$, $p = .032$; Fig. 5B). This average learning rate was 9.31 ± 8.48 , 1.68 ± 6.54 , 6.36 ± 7.14 , and 4.79 ± 4.45 mm for the *Control*, *Remission*, *UHR*, and *SZ-active* group, respectively. Post-hoc tests found that the *SZ-remission* group adapted slower than the *Control* group ($p = .004$) and the *UHR* group (marginally significant with $p = .076$). The difference in learning rate was accompanied by a similar group difference in learning extent, though it was only marginally significant ($F(3,66) = 2.56$, $p = .07$; Fig. 5C). The learning extent was 15.03 ± 1.97 , 8.40 ± 2.17 , 15.66 ± 2.32 , and 11.39 ± 2.34 mm for the *Control*, *Remission*, *UHR*, and *SZ-active* group, respectively. The lack of group difference in learning extent might be related to the limited phase duration (only 30 trials).

3.4. Correlation with clinical scores

Consistent with the group comparisons above, we only found that the adaptation to one's own motor errors was correlated with the severity of clinical symptoms (Fig. 6). We used partial correlation with the dose of antipsychotics as a covariate since it correlated with RT in the perturbation-free trials (Spearman $r = 0.311$, $p = .018$). Error bias, error variance, and RT were specifically correlated with the hallucination sub-scale, less so with the delusion sub-scale and the sum of hallucination and delusion sub-scales, after Bonferroni correction. This means that the more severe the positive symptoms, the worse the performance in the unperturbed trials. Besides, RT and ACF1 were also significantly correlated

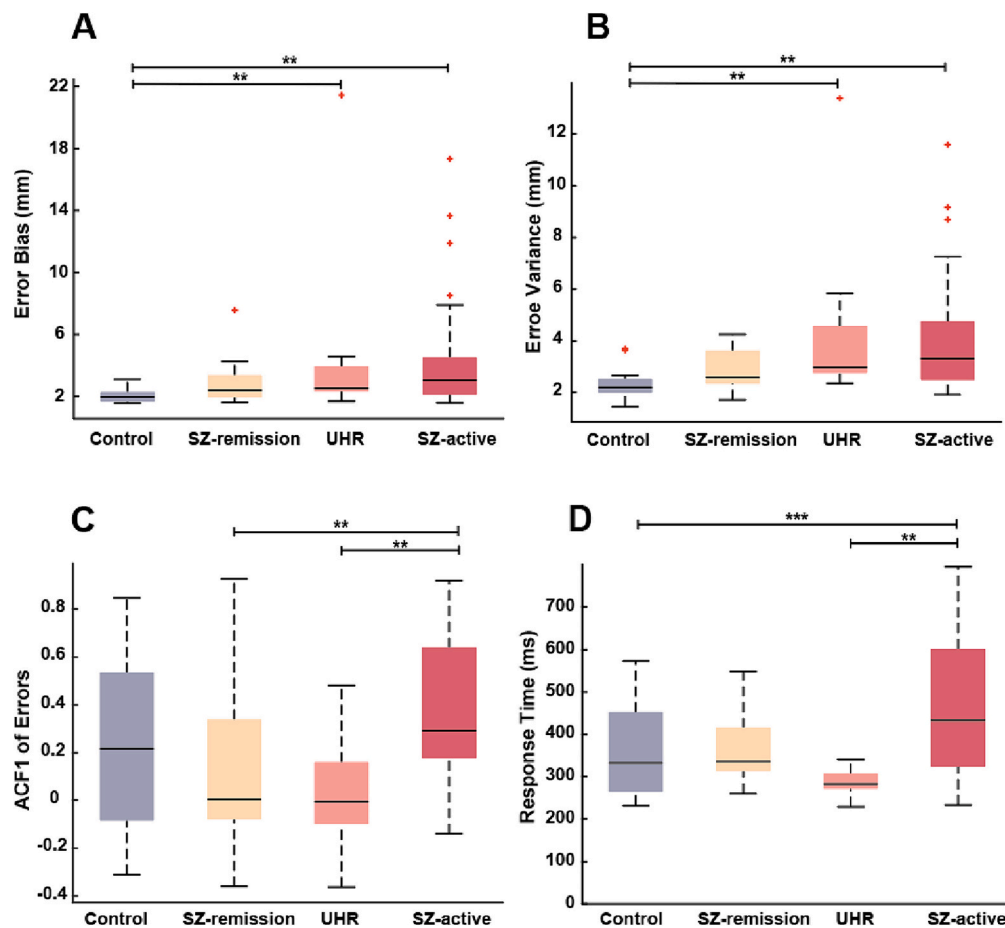


Fig. 3. Results of the perturbation-free phase. The bias (A) and variance (B) of absolute errors are shown with boxplots. ACF1 (C) and response time (D) are shown with error bars (mean and SEM). * $p < .05$. ** $p < .01$. *** $p < .001$.

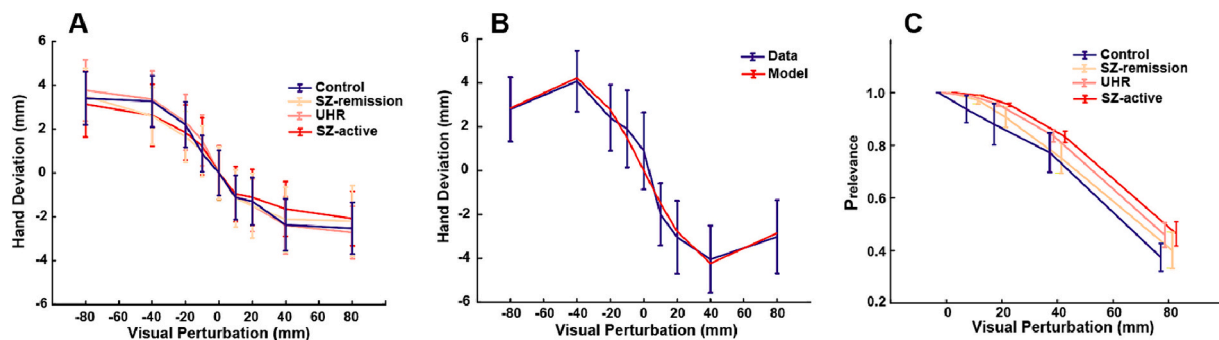


Fig. 4. Results of the random-perturbation phase. (A) Average hand deviations in the next trial following a perturbation plotted as a function of perturbation. (B) Exemplary model fitting for a typical participant from the SZ-active group. (C) The $P_{relevance}$ as a function of absolute perturbation size. Error bars denote mean and standard error across participants.

with PANSS ($r = 0.471$ and 0.301 , $p = .0001$ and 0.023 , respectively). No correlation was found for adaptation measures from the random perturbation and consistent perturbation phases.

4. Discussion

Previous studies have exclusively examined how individuals with schizophrenia adapt to large and persistent perturbations that invoke cognitive adaptation strategy. Contrary to previous reports of reduced adaptation, we found that individuals with SZ showed intact adaptation to random yet salient perturbations and intact causal attribution of

motor errors, as estimated by our Bayesian statistical inference model. However, individuals with SZ adapted less to their own motor errors than controls, as indicated by their positive lag-1 cross-correlation of motor errors, larger error bias and error variance. We also replicated the reduced adaptation to consistent perturbations. The reduced adaptation to self-made motor errors, but not that to externally-applied errors, were correlated with their clinical symptoms as indexed by SAPS scores, especially for hallucination and delusion of control. The schizophrenia-specific changes appeared to depend on diagnosis grouping, as individuals with active psychotic symptoms were affected most, while individuals in remission and the UHR youth were less affected.

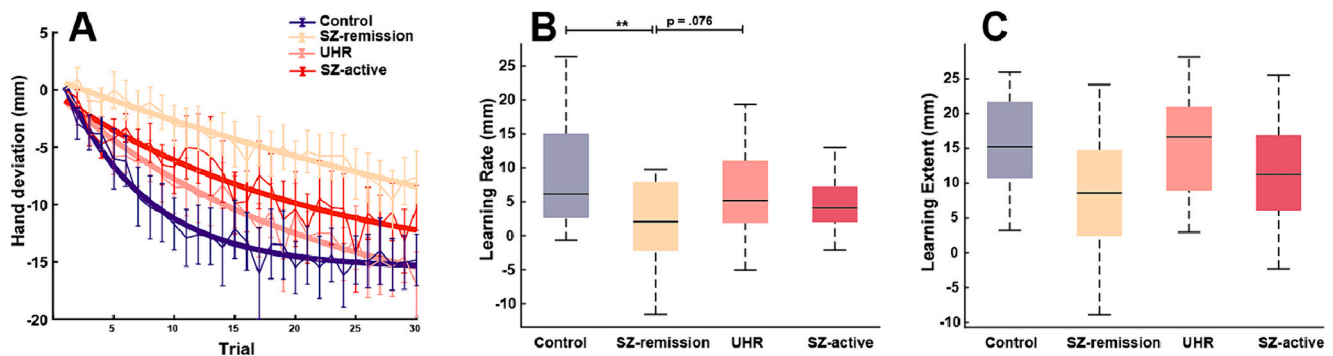


Fig. 5. Results of the consistent-perturbation phase. (A) The learning curves for the four groups. Learning rate (B) and learning extent (C) are plotted as a function of the group. Error bars denote SEM. ** $p < .01$.

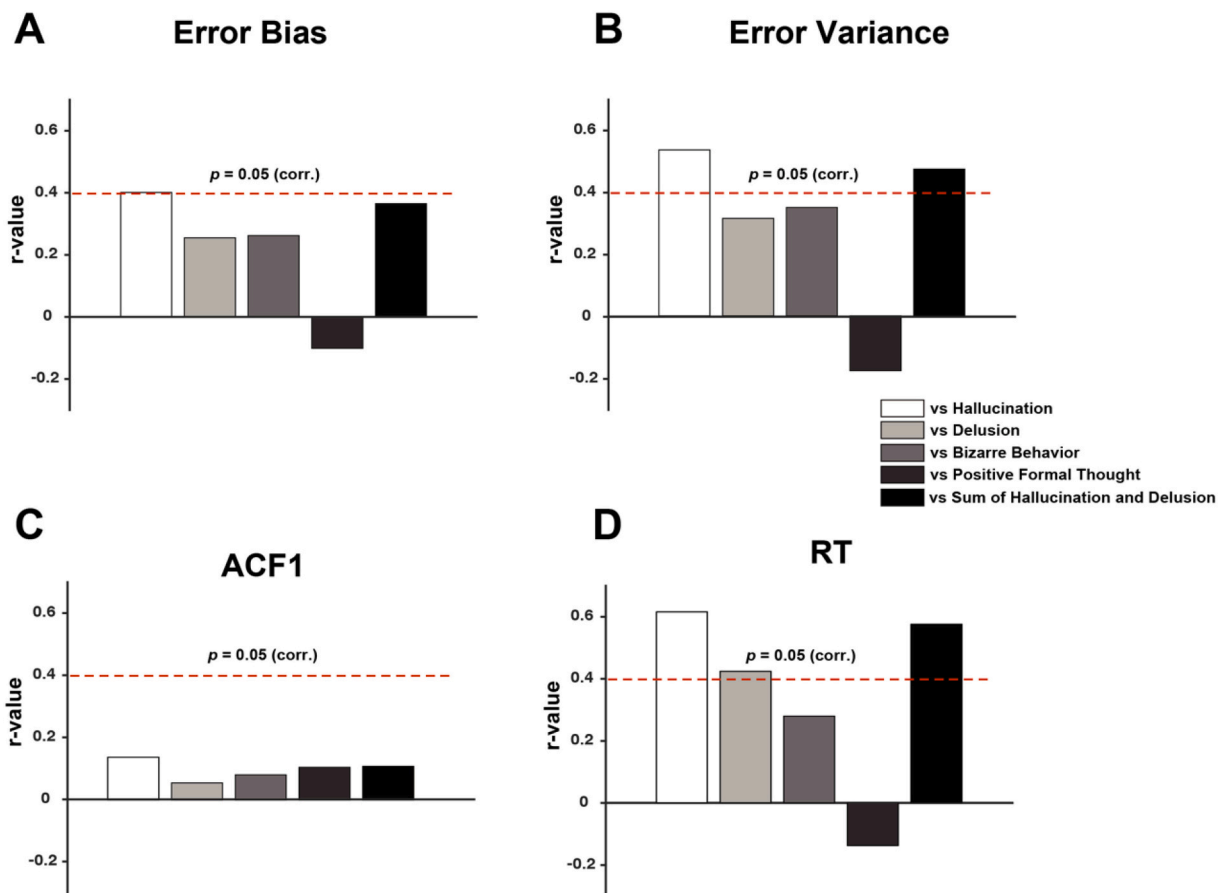


Fig. 6. The performance measures in the perturbation-free phase correlated with clinical scores. The mean error (A), error variance (B), and RT (D) positively correlated with hallucination, leading to a significant correlation with the sum of hallucination and delusion scores. The AFC1 (C) is not correlated. The red dash line denotes the critical r value, with experiment-wise type 1 error capped by Bonferroni correction for multiple tests. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

4.1. Reduced adaptation to intrinsic errors

Adaptation to intrinsic motor errors has not been investigated among individuals with schizophrenia. The increase in error bias indicates that motor error persists for an unusually long sequence of trials. Normal people's first few reaches to a visual target typically have large errors, which are quickly corrected in subsequent reaches (van Beers, 2009). The reduced adaptation to intrinsic errors, manifested by positive ACF1, might prevent quick error reduction and lead to persistent errors. This novel finding is ecologically important since the motor system constantly re-calibrates itself to accommodate small changes in daily

life. The reduced adaptation might be related to the impaired perception of small motor errors, which is at least a magnitude smaller than motor errors caused by external perturbations (Fig. 2). When action feedback is ambiguous, individuals with SZ are perceptually less sensitive to perturbed feedback (Hommes et al., 2012; Synofzik et al., 2010; Werner et al., 2014), or have poor self-monitoring of actions in general (van der Weiden et al., 2015).

We observed large error variance in perturbation-free trials, in line with previous reports of abnormally large motor variability (Nguyen et al., 2016; Synofzik et al., 2010). Researchers have associated increased motor variability with aberrant forward motor control and

impaired internal motor prediction in schizophrenia (Synofzik et al., 2010). Our data support this association by additionally showing prolonged RT in the perturbation-free trials and its significant association with the severity of positive symptoms. The deficit in forward motor control can lead to imprecise predictions of action consequences, possibly contributing to impaired perception of ambiguous errors and reduced adaptation (Synofzik et al., 2010).

The reduced adaptation to intrinsic motor errors is akin to the reduced perceptual attenuation among individuals with schizophrenia (Lindner et al., 2005; Shergill et al., 2005; Shergill et al., 2014), which has been linked to impaired predictions of action consequences as well (Shergill et al., 2005; Shergill et al., 2014). Motor adaptation relies on motor predictions of action consequences, especially for implicit motor adaptation for small errors (Krakauer et al., 2019). Thus, schizophrenia-specific abnormalities in perception and action might share the same underlying deficit, i.e., imprecise predictions about the sensory consequences of actions.

An alternative explanation for reduced adaptation here is that individuals with SZ are compromised in their motor capacity for error correction. However, this is unlikely since reaching a target is a simple action, and adaptive response to salient motor errors is intact among individuals with schizophrenia (Delevoeye-Turrell et al., 2002; Fournier et al., 2001; Knoblich et al., 2004). Furthermore, our participants also showed intact adaptation to large and salient errors in the random perturbation phase.

4.2. Intact adaptation to random yet large perturbations

Consistent with our hypothesis, people with schizophrenia adapted to random yet salient perturbations equally well as healthy controls. Random perturbation, differing in size and direction from trial to trial, does not invoke the formation of a re-aiming strategy (Tsay et al., 2022) but rather mostly involves implicit adaptation (Hutter and Taylor, 2018). It is widely used as a testbed for studying sensorimotor adaptation (Coltman et al., 2021; K. Wei and Körding, 2010; K. Wei et al., 2010). Our participants exhibited classical nonlinear learning patterns as healthy controls, with larger learning rates for small errors than for large errors (Fig. 4). Both their behavioral pattern and the model results indicate that causal inference of errors is intact. Recently, our group has shown that implicit adaptation is supported by multimodal cue combination according to Bayesian principles (Zhang et al., 2023). Thus, our findings here can also be interpreted as intact cue combination during action control.

Why did individuals with SZ show reduced adaptation to their motor noise, which is random, but not to these random external perturbations? The applied random perturbations were rather large, e.g., the smallest perturbation (± 1 cm) was 2.44 times larger than the standard deviation of the unperturbed motor errors for the *SZ-active* group. We postulate that when perceptual challenges are alleviated by sufficient error saliency individuals with SZ will exhibit normal behaviors. This is not the case for small random errors resulted from one's own motor variability. In a similar vein, delusion of control primarily involves deficits on the perceptual level but not on the motor level (Synofzik et al., 2008b). Interestingly, salience dysregulation among individuals with schizophrenia, impairing their ability to correctly identify and prioritize important stimuli, has been implicated in the domain of perception and cognition (Kapur, 2003). Our results can be viewed as a null effect of salience dysregulation in the motor domain: the random-perturbation condition provided task-irrelevant feedback (the participants were told and learned the visual perturbations were irrelevant to their task performance) to perturb people's actions, but the adaptive response to this irrelevant feedback was not exaggerated or damped, suggesting that the motor system's response to irrelevant feedback is intact in schizophrenia.

4.3. Reduced adaptation to a consistent perturbation

As shown in Fig. 5A, we replicated previous findings of a reduced adaptation to consistent perturbations (Bansal et al., 2019; Bartolomeo et al., 2020; Bigelow et al., 2006; Cornelis et al., 2022; Knoblich et al., 2004; Ninomiya et al., 1998; Synofzik et al., 2010). We note that the reported motor adaptation deficits in schizophrenia are mostly observed during the initial learning phase, which is dominated by explicit strategy learning (Krakauer et al., 2019; S.D. McDougle et al., 2015). A recent study also concluded an explicit learning deficit in schizophrenia based on the smaller learning in the first adaptation trials (Cornelis et al., 2022).

Our findings might reflect the prevalent cerebellar abnormalities among individuals with schizophrenia (Ding et al., 2019). A disrupted prefronto-thalamo-cerebellar circuit has been proposed to underlie the pathophysiology of schizophrenia (Andreasen et al., 1998), and received renewing support (Cao et al., 2018; Giraldo-Chica et al., 2018; Koshiyama et al., 2018). The cerebellum is crucial for motor adaptation, given its role in processing sensory prediction errors and action-related feedback (Houk et al., 1996; Synofzik et al., 2008a; Tseng et al., 2007). The abnormality in the cerebellum potentially affects motor predictions and the detection of ambiguous motor errors, leading to reduced adaptation to motor errors and increased motor variability (Becker and Person, 2019; Izawa et al., 2012). Importantly, recent studies also revealed that the cerebellum is essential for explicit strategic learning during motor adaptation: cerebellar patients had difficulty forming aiming strategies in visuomotor rotation adaptation (Butcher et al., 2017).

4.4. Motor adaptation and diagnosis grouping of schizophrenia

Though to a lesser degree, aberrant motor adaptation was also observed among individuals with SZ in remission and youth with ultra-high risk of psychosis. UHR youth have shown disturbances in thought, language, social, attention, perception, and motor aspects (Cornblatt et al., 2007; Klosterkötter et al., 2000; Lencz et al., 2006; Philippos et al., 2002). Relevant to our study, they also exhibited an attenuated form of the sense of self (Nelson et al., 2008). However, there is limited research investigating their motor behaviors. We found that the *UHR* group, but not the *SZ-remission* group, showed significantly larger error bias and variance than the *Control* group when their movement was unperturbed. However, the *SZ-remission* group, but not the *UHR* group, showed inadequate adaptation to their own motor errors (manifested by their positive ACF1) and significantly slower adaptation to consistent perturbations. Hence, both the *Remission* and *UHR* groups' abnormalities in adaptation were less pronounced when compared to the *SZ-active* group. These group differences were reflected in correlational analyses, which showed that the more severe the clinical symptoms, the more deviant the motor measures. Our findings suggest that impaired adaptation to intrinsic motor errors is a robust finding across diagnosis groups of schizophrenia and relates to the severity of psychopathological symptoms. As our task is simple to execute without high cognitive demands, the observed motor abnormalities for the *UHR* group might be promising for aiding early diagnosis of schizophrenia (Nelson et al., 2008).

4.5. Relation to agency and error monitoring

How can we reconcile the intact causal inference during motor adaptation and the prevalent self-agency problems among individuals with positive symptoms? Studies on agency with motor actions typically distorted the visual feedback of self-actions and asked the participants to judge whether the feedback was caused by themselves or by external changes (Daprati et al., 1997; Franck et al., 2001; Haggard et al., 2003; Hauser et al., 2011; Knoblich et al., 2004; Synofzik et al., 2010; Werner et al., 2014). Individuals with schizophrenia make poor judgments with higher tolerance to feedback distortion and a tendency to attribute the

distorted feedback to themselves, often referred to as hyperassociation or over-attribution of agency (Daprti et al., 1997; Haggard et al., 2003). Instead of demanding an explicit judgment about feedback attribution, we simply instructed our participants to reach the target and utilized their trial-by-trial motor responses to derive their implicit error attribution. The deduced causal inference thus reflects the implicit agency during motor adaptation. Thus, we postulate that explicit judgment and implicit adaptation of distorted feedback are dissociated in schizophrenia, akin to the distinction between the explicit and implicit sense of agency (Synofzik et al., 2008b).

4.6. Limitations of the study

The first limitation was the small sample size of our study, especially for the consistent-perturbation phase ($n = 11$ for the SZ-active group). Originally, we did not include a consistent-perturbation phase for the experiment since it has been shown in a few previous studies (e.g., Bansal et al., 2019). This caused 14 of our SZ-active participants missed for this particular experimental condition. Though the remaining eleven participants constituted a typical sample size for motor adaptation studies (Krakauer et al., 2005; Kunlin Wei and Kording, 2009), our results would be more solid if we could have included more participants, given the heterogeneity of the patient population. The second limitation was that we did not directly measure participants' explicit learning for the consistent-perturbation phase. We hypothesized that individuals with schizophrenia had difficulty in forming explicit strategy for motor adaptation, which leads to reduced adaptation for a consistent perturbation (Cornelis et al., 2022). Using the so-called aiming report paradigm or exclusion paradigm (Maresch et al., 2021) can provide direct evidence for this hypothesis.

5. Concluding remarks

Using a unified visuomotor adaptation setting, we showed that individuals with schizophrenia reduced adaptation to their own motor errors and to a consistently-presented perturbation, but remained intact for adaptation to random perturbations, when compared to the control group. Reduced correction to small intrinsic motor errors possibly reflects perceptual difficulty, poor action monitoring, and impaired sensory prediction of actions in schizophrenia. In contrast to implications from previous studies, the reduction in adaptation to consistent perturbations but not to random perturbations suggest that individuals with schizophrenia might have difficulty in forming adaptation strategies, which demands flexible cognitive solution, while remain intact in causal attribution of salient errors. The contrast in adaptation to these two perturbation schedules also suggests that the directly linking impaired motor adaptation to abnormal causal inference in schizophrenia should be cautioned. The effects observed here were also graded by the severity of clinic symptoms across diagnosis groups, corroborating the association between psychotic disorders and motor deficits and also highlighting the importance of taking the patient heterogeneity into consideration for future studies.

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CRediT authorship contribution statement

All authors contributed significantly to the conception, design, execution, and interpretation of the study. K.W. and H.J. contributed to the conception and design of the study. J.M. and Y.J. were responsible for data acquisition. J.M., H.D., K.W. contributed to data analysis and

statistical analysis. H.J. and K.W. contributed to interpretation of the data. K.W., H.D., and H.J. were responsible for drafting and finalizing the manuscript. All authors have approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Declaration of competing interest

All authors declare no conflicts of interest.

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