

Appendix 1 to Faivre N, Roger M, Pereira M, et al. Confidence in visual motion discrimination is preserved in individuals with schizophrenia. *J Psychiatry Neurosci* 2020.

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Participants

Exclusion criteria for both groups of participants were a moderate-to-severe substance use disorder (DSM-5 criteria) within the 12 months preceding the study, and a current or prior untreated medical illness, including neurologic illness, an IQ < 70 based on three subtests of the Wechsler Adult Intelligence Scale (see SI), and an age > 60 years. Schizophrenia and schizoaffective disorders were diagnosed by M.R. based on the Structured Clinical Interview for assessing the DSM-5 criteria ¹. Another licensed psychiatrist (patient's treating psychiatrist) confirmed the diagnosis for each patient according to the DSM-5 criteria. The control group was screened for current or past psychiatric illness, and individuals were excluded if they met the criteria for a severe and persistent mental disorder.

Procedure

Among multiple perceptual paradigms, coherent motion discrimination was chosen because it had been recommended as a promising perception paradigm for translation for use in clinical trials due to good psychometric validity ². All stimuli were prepared and presented using the psychophysics toolbox under Matlab ³⁻⁵, based on a previous study ⁶. Participants started each trial by clicking on a 1.2° x 3.6° box placed at the bottom of the screen (Figure 1). The mouse click triggered the display of a 0.1° fixation dot presented in the middle of a circular frame (3° radius) for 250 ms over a gray background, followed by the display of a random dot kinetogram (RDK). The RDK consisted of 100 dots (radius 0.1°) moving pseudo randomly at a constant speed of 3°/s. The motion direction of each dot was drawn every 16 ms from a von Mises distribution that determined both the mean ($\pm 45^\circ$ relative to the vertical) and variance of the motion direction. Visual transients at stimulus onset were smoothed using a linear ramp in contrast. On each trial, participants were asked to indicate the mean motion direction by clicking within a circular frame (radius 1.35°) located on the top, to the right or to the left of the RDK. Responses slower than 6 s were discouraged by playing a loud alarm sound. The task difficulty was adjusted by a one-up two-down staircase procedure to make the first-order performance rate converge to 71 % ⁷. Perceptual evidence was defined as the inverse of variance in motion direction, increasing after one incorrect response and decreasing after two consecutive correct responses. After providing their first-order response, a visual analog scale appeared, and participants were asked to report how confident they were about it by moving a slider vertically using the mouse. The scale was presented until a response was provided, with marks between 0 % (certainty that the first-order response was erroneous) and 100 % (certainty that the first-order response was correct) with 5% steps. The initial position of the cursor was always 50 %. The experiment was divided into 10 blocks of 30 trials and lasted about 1 hour. The perceptual difficulty was pre-tuned to individual perceptual abilities by performing 80 trials without confidence ratings prior to the main experiment.

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Statistical models

Bayesian models were created in Stan computational framework (<http://mc-stan.org/>) accessed with the brms package ⁸, based on four chains of 10000 iterations including 2000 warmup samples. A normal prior with mean = 2 and SD = 5 was used for the main effect of confidence. A normal prior with mean = 0 and SD = 5 was used for the main effect of group. A normal prior with mean = -1 and SD = 5 was used for the difference in effect of confidence between schizophrenia and control groups. Other priors were by default according to the brms package in R ⁸. We report the highest density probability for all estimates, which specifies the range covering the 95% most credible values of the posterior estimates. Mixed-effects models included random intercepts by participants and full random effects structure. Robust Bayesian correlations were computed using Stan with 10000 iterations including 2000 warmup samples and non-informative priors, assuming that pairs of psychometric and behavioral outcomes followed a bivariate Student's t-distribution. We used the same hierarchical meta-d' model as defined in Fleming, 2017⁹.

First-order performance

At the first-order level, individuals with schizophrenia had a tendency to judge the RDK as moving rightward more often (criterion schizophrenia: -0.32 ± 0.15 , criterion controls: 0.00 ± 0.21 , $t(37.7) = 2.50$, $p = 0.02$, $BF = 3.24$). However, the two groups had similar discrimination performance (d' schizophrenia: 1.29 ± 0.08 , d' controls: 1.38 ± 0.11 , $t(36.7) = 0.85$, $p = 0.40$, $BF = 0.41$). The variance in motion direction corresponding to such performance as titrated with an adaptive procedure (see methods) was higher in controls (2.01 ± 0.20) than in patients (1.59 ± 0.17 , $t(38.9) = 3.09$, $p = 0.004$, $BF = 10.60$), indicating that patients had reduced perceptual abilities. The difference in the variance of stimulus intensity during the main experiment did not differ between groups (Wilcoxon rank sum test on the variation of intensity with respect to the first trial: $W = 268$, p -value = 0.13). Trials in which reaction times were above 6 s or below 200 ms were excluded (first-order responses: 2.2 ± 0.9 % of total trials; second-order response 1.5 ± 0.7 %).

Evidence accumulation model

To compare the underlying decision mechanisms between groups, we fitted an evidence accumulation model ¹⁰⁻¹³ to movement onset timings and the accuracy of the initial direction of the mouse trajectories. The decision process was modeled using two anticorrelated race accumulators (one accumulating evidence for left choices and one for right choices). Confidence ratings were simulated by extending the evidence accumulation process after the initial decision ¹³. The model comprised five free parameters. The *non-decision time* was the sum of the time needed before visual information started being integrated by the evidence accumulation process and the delay between the decision and the actual movement initiation. The *decision bound* corresponded to the amount of evidence needed to initiate a movement and the *drift rate* to the average slope of the evidence accumulation process. Finally, two *confidence criteria* were used to define three confidence quantiles as used above.

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To reduce the degrees of freedom of the model, we fixed the standard deviation of the non-decision time to 60 ms, the standard deviation of the within-trial noise to 1 and the correlation of the two accumulators to $-\sqrt{0.5}$ as in previous works¹³. The accumulation process was bounded negatively to zero. We used Euler's method to simulate 1000 trials of the evidence accumulation process and the corresponding response times (i.e. movement onsets) and choice accuracies (i.e. accuracy of the movement direction at the onset), which were fitted to the observed data for every participant. For this, we maximized the log-likelihood using a Nelder-Mead simplex method. The log-likelihood was computed using a two-sample Kolmogorov-Smirnov test on the simulated and observed movement onset times, inverting their sign when the direction was incorrect. We repeated this procedure with a wide range of initial parameters to avoid local minima. We fitted confidence ratings in a second stage; we simulated 1000 paths of the evidence accumulation process and discretized the winning accumulator (at a fixed readout time after the decision) into three confidence levels using two criteria. The values of the two criteria were initialized to approximate the proportion of high and low confidence ratings and then fitted to the data using a Nelder-Mead simplex method. For this, we computed the log-likelihood using a Bernoulli probability distribution for each confidence level and choice accuracy. We repeated this procedure using readout timings going from 0 s after the initial decision to 1 s after the initial decision by steps of 100 ms and used the model with the best likelihood. Of note, our results still held when using fixed readout times across participants or when fitting confidence ratings to the state of the losing accumulator¹² or to the difference between the winning and losing accumulator (*balance-of-evidence*^{9,15}).

Similar levels of goodness of fit were obtained between groups, both regarding first-order (log-likelihood patients: -0.41 ± 0.13 ; log-likelihood controls: -0.59 ± 0.13) and second-order outcomes (log-likelihood patients: -29.50 ± 1.72 ; log-likelihood controls: -25.80 ± 1.14). No differences across groups were found for the five parameters (non-decision time: $t(35.7) = 0.46$, $p = 0.75$, $BF = 0.39$; decision bound: $t(37.5) = 0.05$, $p = 0.96$, $BF = 0.31$; drift rate: $t(35.1) = 0.01$, $p = 0.99$, $BF = 0.31$; confidence criterion 1: $t(37.6) = -0.04$, $p = 0.97$, $BF = 0.31$; confidence criterion 2: $t(36.2) = -0.29$, $p = 0.77$, $BF = 0.32$, see Figure 4). This is at odds with the first study employing this technique in schizophrenia, showing that patients had an increased non-decisional time, higher boundary separation and lower drift rate in a punishment learning task¹⁶. Longer non-decisional time and lower drift rate were also recently found for speeded judgments among individuals with schizophrenia and their siblings compared to healthy controls¹⁷. In addition, metacognitive efficiency resulting from these simulated data was equivalent in individuals with schizophrenia (mean estimate = 0.52, highest posterior density interval = [0.40 0.65]) and healthy controls (mean estimate = 0.58, highest posterior density interval = [0.40 0.88]), mimicking our behavioral results.

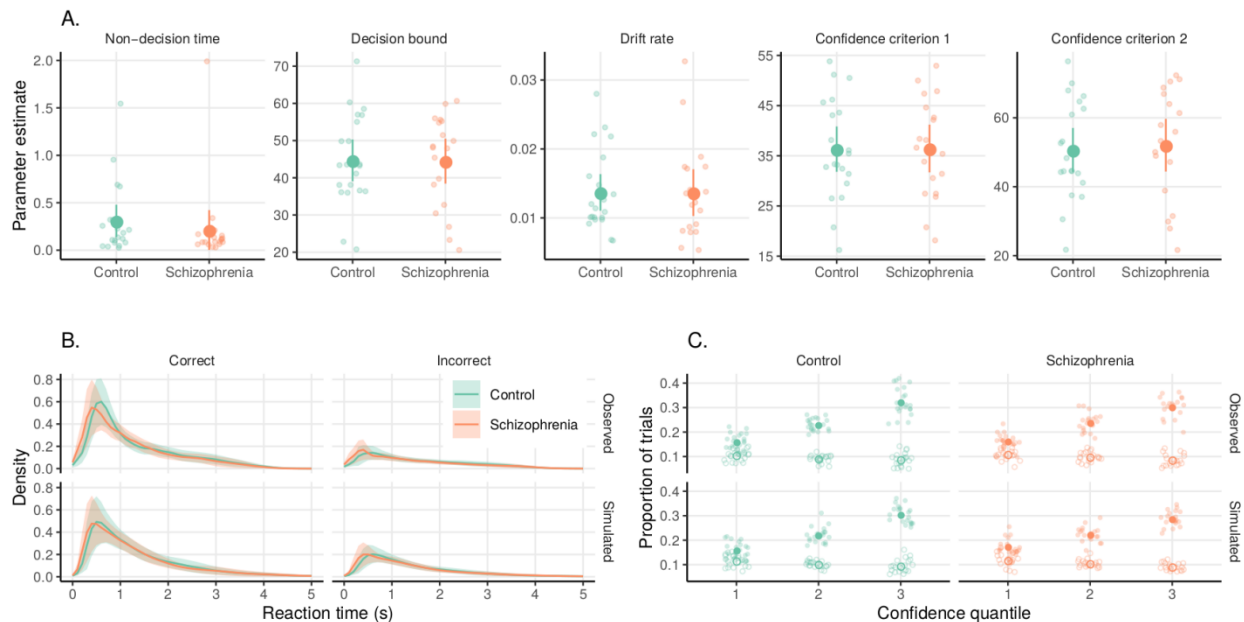


Figure S1: Evidence accumulation model of first and second-order behavior in the control (green) and schizophrenia group (orange). A. Parameter estimates. B. Distributions of observed simulated first-order reaction times for correct and error responses. C. Proportion of trials across confidence quantiles for correct (full dots) and incorrect responses (empty dots). Large dots represent average estimates, error bars represent the 95 % confidence intervals. Small dots represent individual estimates. Shaded areas represent the 95 % confidence intervals.

Second-order reaction times

Interestingly, a similar pattern to what we found for first-order reaction times was found for standardized second-order reaction times: a linear mixed-effects regressions revealed a main effect of confidence (estimate = -0.02 [-0.03 -0.01], evidence ratio = 71.73) which was stronger in the control vs. schizophrenia group (interaction group * second-order reaction times: estimate = 0.02 [0.00 0.04], evidence ratio = 12.51). Of note, raw first and second-order reaction times per se did not differ between groups ($t(39.0) = 1.07$, $p = 0.29$, $BF = 0.49$ and $t(36.0) = 1.41$, $p = 0.17$, $BF = 0.66$, respectively).

Trajectory tracking

Kinematics (instantaneous velocity and acceleration) associated with first-order responses were smoothed using a Savitzky-Golay filter of order 2 and length 5. Trajectories were temporally realigned with respect to movement onset, defined as the time when velocity reached 20% of the maximal velocity in a given trial. Trajectories were spatially realigned with respect to the spatial coordinate at movement onset (i.e., starting point). Changes of mind were defined as

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trials in which the sign of the trajectory angle at movement onset was opposite to that of the landing point (i.e, when participants started moving towards one side of the screen but ended responding on the other side). Only initial angles with an absolute value between 10 and 80 degrees were considered to exclude trials with vertical or horizontal trajectories at movement onset. Of note, the relationships between confidence, first-order accuracy and standardized reaction times reported in the main text were similar to the ones mentioned above when excluding trials with changes of mind.

Neuropsychological evaluations

Both individuals with schizophrenia spectrum disorders and healthy controls were evaluated on several neuropsychological domains:

- perceptual reasoning with the standardized score on the matrices subtest of the Wechsler Adult Intelligence Scale 4th version (WAIS-IV ¹⁸)
- verbal reasoning with the standardized score on the vocabulary subtest of WAIS-IV
- working memory with the standardized score on the letter-number sequencing subtest of WAIS-IV
- executive functions with the raw total and error scores on the Modified Six Elements Test ¹⁹
- depressive symptoms with the Calgary Depression Scale (CDS) ²⁰
- cognitive insight with the composite index on the Beck Cognitive Insight Scale (BCIS) ²¹. The composite index of the BCIS reflects the cognitive insight and is calculated by subtracting the score for the self-certainty scale from that of the self-reflectiveness scale.
- the National Adult Reading Test (NART) provided an estimate of premorbid IQ ²²

The following clinical evaluations were run for patients only:

- the intensity of schizophrenia symptoms with the Positive And Negative Syndrome Scale ²³
- social functioning using the Personal and Social Performance Scale (PSP) ²⁴
- clinical insight using the Birchwood insight scale ²⁵

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Supplementary tables

Covariates		Correlation coefficient	HPD		Posterior probability	Bayes Factor
Confidence	Age (years)	0.19	-0.14	0.48	0.123	0.33
	Beck Cognitive Insight Scale	-0.29	-0.58	0.04	0.046	0.75
	Calgary Depression Scale	-0.19	-0.48	0.14	0.137	0.33
	Education level (years)	-0.08	-0.40	0.25	0.315	0.20
	Premorbid IQ	0.19	-0.12	0.50	0.129	0.31
	Six Elements Test (errors)	0.29	-0.01	0.57	0.036	0.83
	Six Elements Test (points)	-0.06	-0.39	0.26	0.356	0.19
	WAIS matrix subtest	-0.37	-0.63	-0.07	0.014	2.42
	WAIS mequence subtest	0.04	-0.30	0.36	0.402	0.18
	WAIS vocabulary subtest	0.13	-0.20	0.44	0.228	0.23
M-Ratio	Age (years)	-0.25	-0.54	0.06	0.064	0.54
	Beck Cognitive Insight Scale	0.17	-0.15	0.48	0.159	0.29
	Calgary Depression Scale	0.18	-0.16	0.47	0.140	0.31

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	Education level (years)	0.20	-0.12	0.50	0.122	0.34
	Premorbid IQ	0.25	-0.05	0.54	0.061	0.55
	Six Elements Test (errors)	-0.22	-0.53	0.08	0.088	0.46
	Six Elements Test (points)	0.28	-0.03	0.55	0.046	0.71
	WAIS matrix subtest	0.46	0.20	0.70	0.002	13.88
	WAIS mequence subtest	0.33	0.02	0.59	0.022	1.45
	WAIS vocabulary subtest	0.32	0.02	0.58	0.024	1.13

Table S1: Correlations between behavioral results and neuropsychological characteristics of individuals with schizophrenia spectrum disorders and controls.

Covariates		Correlation coefficient	HPD		Posterior probability	Bayes Factor
Confidence	Birchwood Insight Scale	0.12	-0.33	0.57	0.315	0.29
	Chlorpromazine equivalent	0.17	-0.30	0.57	0.233	0.32
	Illness duration	0.27	-0.17	0.66	0.118	0.51
	PANSS Negative symptoms score	0.05	-0.38	0.52	0.416	0.25
	PANSS Positive symptoms score	0.36	-0.06	0.73	0.065	0.84

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	PANSS General psychopathology score	-0.22	-0.62	0.25	0.183	0.37
	PANSS total score	0.01	-0.44	0.46	0.486	0.25
	Personal and Social Performance Scale	-0.22	-0.63	0.22	0.175	0.39
M-Ratio	Birchwood Insight Scale	0.13	-0.34	0.54	0.299	0.29
	Chlorpromazine equivalent	-0.15	-0.56	0.32	0.266	0.30
	Illness duration	-0.54	-0.83	-0.18	0.006	5.22
	PANSS Negative symptoms score	-0.31	-0.67	0.15	0.095	0.55
	PANSS Positive symptoms score	-0.19	-0.60	0.28	0.223	0.34
	PANSS General psychopathology score	0.03	-0.43	0.47	0.450	0.24
	PANSS total score	-0.13	-0.54	0.32	0.295	0.28
	Personal and Social Performance Scale	0.31	-0.13	0.69	0.090	0.61

Table S2: Correlations between behavioral results and clinical characteristics of individuals with schizophrenia spectrum disorders.

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