

Cognitive Binding in Schizophrenia: Weakened Integration of Temporal Intersensory Information

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Cognitive functioning is based on binding processes, by which different features and elements of neurocognition are integrated and coordinated. Binding is an essential ingredient of, for instance, Gestalt perception. We have implemented a paradigm of causality perception based on the work of Albert Michotte, in which 2 identical discs move from opposite sides of a monitor, steadily toward, and then past one another. Their coincidence generates an ambiguous percept of either “streaming” or “bouncing,” which the subjects (34 schizophrenia spectrum patients and 34 controls with mean age 27.9 y) were instructed to report. The latter perception is a marker of the binding processes underlying perceived causality (type I binding). In addition to this visual task, acoustic stimuli were presented at different times during the task (150 ms before and after visual coincidence), which can modulate perceived causality. This modulation by intersensory and temporally delayed stimuli is viewed as a different type of binding (type II). We show here, using a mixed-effects hierarchical analysis, that type II binding distinguishes schizophrenia spectrum patients from healthy controls, whereas type I binding does not. Type I binding may even be excessive in some patients, especially those with positive symptoms; Type II binding, however, was generally attenuated in patients. The present findings point to ways in which the disconnection (or Gestalt) hypothesis of schizophrenia can be refined, suggesting more specific markers of neurocognitive functioning and potential targets of treatment.

Key words: cognitive coordination/perceived causality/Gestalt dysfunction/intersensory integration/temporal perception/disconnection hypothesis

Introduction

A growing number of studies has pointed to dysfunctions in the coordination of cognitive processing as one fundamental disturbance in schizophrenia spectrum disorder.^{1,2}

Particularly, the capacity to integrate contextual information has been shown to be impaired in individuals with schizophrenia.³ “Spatial and temporal context fail to activate appropriate stored regularities.”^{4(p977)} The impaired capacity to make use of contextual information may be at the basis of the well-established finding that perceptual coordination (ie, the feature binding needed in perception of Gestalt-like patterns) and, more generally, cognitive coordination are impaired in schizophrenia patients. In their extensive review, Uhlhaas and Silverstein² suggested that perceptual coordination dysfunctions were related to the degree by which tasks required top-down feedback to sensory processes. In contrast, the use of bottom-up cues appeared to be relatively unimpaired. Interestingly, while thought disorder and other disorganization symptoms are associated with a weakening of perceptual coordination, some studies indicated that positive and prodromal symptoms may be related to enhanced perceptual coordination. This was operationalized by various Gestalt perception paradigms.^{5–7}

Disturbances in perceptual and cognitive coordination have their biological correlates in abnormal neural integration (disconnection hypothesis⁸; cognitive dysmetria⁹). Several studies suggested that the mechanism underlying integration impairments in schizophrenia may lie in neural synchrony, ie, long-range temporal coordination across spatially distributed cortical areas.^{1,10} Such abnormalities in long-range synchronization of neural activity were found to be associated with deficits in Gestalt perception and disordered neurocognitive binding.^{11,12}

Disturbances in cognitive coordination, ie, the “binding-together” of information processes, may provide an explanation for the dysfunctions in time perception and temporal processing that have been consistently observed in schizophrenia patients. Studies showed that these patients are less accurate in the estimation of time durations and that they tend to overestimate time intervals.^{13–15}

Impairments in time estimation affect durations ranging from milliseconds through several seconds to minutes^{15,16} and relate to both visual and auditory stimuli.¹⁷ Schizophrenia patients were found¹⁸ to display a significantly longer threshold for order discrimination of visual stimuli (normally in the 20–40 ms range), pointing to abnormalities in the perception of temporal sequences. These findings indicate a fundamental timing deficit in schizophrenia that is independent of sensory modality and length of duration.

Abnormalities in cognitive binding may also be responsible for disturbances in causal inferences such as in the phenomenon of “jumping to conclusions,” a cognitive property commonly associated with delusions.^{19,20} In the 1940s, Michotte²¹ developed an experimental task for the study of the perception of causality: some geometric object A moves toward object B, which is stationary. After collision, object A is stationary and B moves away from A evoking an immediate perception that the first motion caused the second—“A pushed B”. Michotte proposed that phenomenal causality is a spontaneous perceptual Gestalt with “ampliation” as its essence. With ampliation, he referred to the idea that motion is transferred from one object to the other and that “for a brief time just after impact (approximately 200 ms), the motion is phenomenologically duplicitous: It “belongs” to the first object while the second object *has* it.”^{22(p441)} This interpretation suggests that the involvement of perceptual binding in perceived causality, as the feature of movement, is shared and transferred from one object to another.

In their study, Tschacher and Kupper²³ found that perceptual binding in a Michotte-like task was associated with psychopathology of schizophrenia patients. In fact, positive symptoms were associated with heightened perceived causality and cognitive disorganization symptoms with reduced perceived causality. They interpreted this as supportive of the notion that perceptual binding is related to the formation of symptoms in schizophrenia. Patients however did not significantly differ from healthy controls in the total amount of perceived causality.

A variant of the Michotte paradigm includes the presentation of short sounds with a sharp onset (usually “clicks”) given at varying temporal lags. Several studies could show that such sounds induce a higher probability of bouncing perception when presented during a time window in the range of –300 to +200 ms around the onset of the visual stimulus.^{24–26} A 2-component explanation has been advanced to account for this result.²⁷ First, the sound may influence visual motion perception as it mimics a real-world situation in which an impact sound occurs when 2 objects collide.^{28,29} Second, the sound may cause a diminished allocation of attention to vision which would in turn inhibit the integration of the visual stimuli and lead to a diminished streaming perception.^{30,31} The audiovisual integration underlying

the effects of this variant of the Michotte task addresses a different type of binding compared with the original task. In this case, acoustic information is instrumental in modulating visual binding.

Schizophrenia patients typically show reduced audiovisual integration^{32–34} and, in particular, a reduction of the effect of auditory stimuli on visual perception.³⁵ Thus, in the present study, based on the dataset of Tschacher and Kupper,²³ we hypothesized that the integration of acoustic contextual information, given at different temporal lags, should distinguish between the schizophrenia and healthy groups as well as between subgroups. We distinguished perceptual binding in the perceived causality task (binding type I) from binding on the basis of additional contextual information (intersensory feature binding; binding type II). Type II binding in this paradigm required both using information provided in a different sensory modality and information given with different temporal lags.

Our primary hypothesis was that schizophrenia patients showed less type II binding in the context of perceived causality. In a secondary, exploratory analysis, we investigated covariates of binding processes in this paradigm in an endeavor to define and test subgroups of the sample. We hypothesized that perceived causality is associated with cognitive traits of healthy subjects such as external control beliefs and personality traits.

Methods

Participants

The study sample consisted of 34 patients (27 men and 7 women) with mean age 27.9 years (SD 7.1) and 34 healthy control subjects (26 men and 8 women; mean age 27.9 y, SD 8.0). Here, we analyze data on the integration of contextual information not considered in the earlier analysis of 62 matched patients and control subjects.²³ All patients were recruited on units of the University Hospital of Psychiatry in Bern, Switzerland. Thirteen inpatients had been admitted to a community-based acute unit (Soteria Bern) and 19 patients were undergoing psychiatric outpatient treatment in two day-hospitals. All patients had been diagnosed as suffering from schizophrenia spectrum disorder according to the International Classification of Diseases, ICD-10 (F20 schizophrenia, 27; F21 schizotypal disorder, 1; F23 acute psychotic disorder, 2; F25 schizoaffective disorder, 4). The mean Chlorpromazine equivalent (CPE) prescribed on the day of testing was 267 mg (SD 220 mg). Twenty-six patients were receiving atypical neuroleptics, 2 Haloperidol Decanoate, and 6 were unmedicated. All participants took part in the study based on prior written informed consent. The study was approved by the Cantonal Ethics Committee.

Thirty-one of the patients participated in standardized clinical interviews (positive and negative syndrome scale, PANSS³⁶) to assess the level of symptoms at the time of

Table 1. Characteristics of Subgroups of $N = 68$ Subjects, Values Listed as Mean (SD)

	Groups		Patient Subgroups	
	Control Group ($N = 34$)	Patient Group ($N = 34$)	High pos/cog ($N = 17$)	Low pos/cog ($N = 14$)
Age	27.94 (7.97)	27.88 (7.07)	25.13 (5.01)	30.47* (5.48)
Female (%)	23.53	20.59	18.75	26.67
Patients (%)				
Age at first hospitalization		23.84 (5.09)	22.51 (4.26)	25.39 (5.45)
Number of hospitalizations		3.32 (4.50)	2.63 (3.01)	2.93 (4.42)
PANSS positive		1.96 (0.87)	2.35 (0.86)	1.55** (0.69)
PANSS negative		1.95 (0.93)	1.85 (0.55)	2.04 (1.23)
PANSS excitement		1.50 (0.44)	1.53 (0.43)	1.47 (0.47)
PANSS depression		1.90 (0.60)	2.08 (0.65)	1.72 (0.49)
PANSS cognitive		1.63 (0.74)	1.46 (0.55)	1.80 (0.89)

Note: PANSS, Positive and Negative Syndrome Scale (Available in 31 Patients); High pos/cog, high ratios of positive by cognitive symptoms; Low pos/cog, low ratios of positive by cognitive symptoms.

* $P < .05$; ** $P < .01$; 2-tailed t test and Pearson Chi-square tests. Asterisks refer to differences between Groups and Patient subgroups.

testing. Trained psychologists not linked with the project performed the interviews. The model of Lindenmayer et al.³⁷ was used to cluster PANSS psychopathology into 5 factors: positive symptoms, negative symptoms, excitement, depression, and cognitive symptoms of schizophrenia. The average symptom level of study patients was moderate to low (table 1). As a measure of psychosocial functioning, the Global Assessment of Functioning Scale (GAF, after *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*) was rated. Patients' age at the time of first psychiatric hospitalization and number of hospitalizations were retrieved from case histories. In the healthy participants, PANSS and GAF were not administered; the five-factor personality inventory (NEO-FFI)³⁸ and a questionnaire of internal and external control beliefs (FKK)³⁹ were used.

We defined the following variables to identify potential predictors of neurocognitive binding. In all subjects, we tested age at time of testing and gender. In patients, we computed the 5 PANSS factors, GAF, CPE, and age at first hospitalization. In control subjects, we used the following predictors: the 5 NEO factors "Neuroticism," "Extraversion," "Openness to experience," "Agreeableness," and "Conscientiousness." Control beliefs of subjects were represented by the 3 FKK factors "Internality" of control beliefs, control attributed to "Powerful others," and "Externality" of control beliefs.

Materials and Procedures

The perceived causality paradigm was presented on a 17-inch computer screen at a viewing distance of 50 cm (shown schematically in figure 1). The test was carried out on working days between 10.00 and 12.00 o'clock at the hospital's research department. Subjects were instructed to fixate a cross 2.5 cm (visual angle, 2.9°) be-

low the center of the display. In each participant, up to 60 runs of the paradigm were evaluated. Participants were informed about the bistable character of the stimulus, ie, that 2 alternative events could be seen, either bouncing or streaming of the discs. If undecided or "in-between," a third response (unclear) was allowed. All data were used for ensuing statistical analysis.

Each run lasted approximately 2.5 s, with an interval of random duration (range, 1–3 s) between runs. Two white discs (diameter 0.5 cm, visual angle 0.6°) appeared on both sides above the fixation cross against a black background. Discs were initially separated by 12 cm (13.7°). Immediately after onset, the discs moved horizontally toward each other with a constant speed of 10 cm/s (11.4°/s), coincided in the screen center, and continued moving until

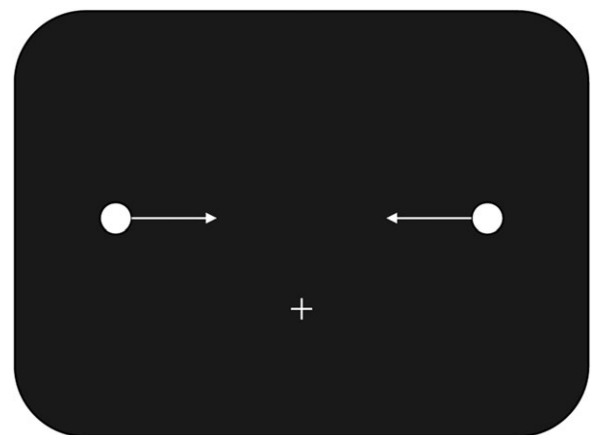


Fig. 1. Screen display (schematic) for the perceived causality paradigm. Two discs move horizontally toward each other with constant speed, coincide in the screen center, and continue moving until they are again separated by their initial distance. The auditory stimulus is presented relative to the time of coincidence.

they were again separated by 12 cm; discs then disappeared. At around the time of coincidence, a click sound of 40 ms duration was presented from 2 speakers next to the monitor; the click sound “clickup.wav” integrated in the computer operating system Microsoft Windows 98 was used. The timing of the sound defined the following 5 conditions, which were slightly distributed due to internal irregularities of the operating system: condition 1, 157 ms (SD 12.3 ms) before coincidence; condition 2, 70 ms (SD 9.7 ms) before coincidence; condition 3, 17 ms (SD 12.0 ms) simultaneous with or minimally after coincidence; condition 4, 104 ms (SD 11.8 ms) after coincidence; and condition 5, 190 ms (SD 19.1 ms) after coincidence. In statistical analyses, we used the exact timing of the independent variable “timing condition.” Each condition occurred with equal probability in random sequence throughout the 60 runs. After each run, an identical written text was shown which contained the instruction to press the left (right; middle) button of the computer mouse when a bouncing (streaming; unclear) perception had resulted in the run just observed. In the complete sample, 3834 runs were recorded (median number of runs per subject, 59; range 16–60). The responses after each run served as the dependent variable in this analysis. For mixed-effects hierarchical analysis, this dependent variable “Perceived causality” was given the values 2 (bouncing), 1 (unclear), or 0 (streaming).

The variable “perceived causality” was expected to depend on the timing of the acoustic stimulus^{24,40} and on properties of the subject, such as his or her psychopathology. On the basis of theory and empirical studies, this measure allows one to distinguish between the 2 kinds of perceptual binding. First, the presence or absence of perceived causality (ie, the bouncing perception) indicates that Michotte-like binding has occurred or not (binding type I). Second, the degree of modulation of perceived causality resulting from the 5 timing conditions indicates the degree of intersensory feature binding (binding type II).

Statistical Treatment

The complete dataset of all runs of $N = 68$ subjects comprised $n = 3,834$ observations. This dataset contains statistically dependent data because the paradigm was repeatedly presented to each subject. We used a hierarchical modeling procedure in which we considered different explanatory variables as predictors of perceptual binding. To do this we used a step-up procedure, considering each explanatory variable in turn to explore different combinations of predictors (ie, models). We evaluated the models in terms of the Akaike information criterion (AIC)⁴¹ to select the best model. Our main analysis included all subjects (patients and controls) looking specifically for group differences in type I or type II binding. We then performed a series of group specific analyses to see if there were any within-group parametric variables that could explain between-subject differences

in binding. We applied mixed-effects analysis to explain the variance of the dependent variable “perceived causality” by the following fixed effects (ie, predictors): “timing condition,” “group,” “timing condition \times group,” “age,” and “gender.” The software package used was JMP8 (SAS Institute Inc, Cary, NC). In all models, “Subject” was entered as a random effect, which defined the dependency structure inherent to this hierarchical dataset.⁴² In this statistical approach, binding type I is represented by the degree of the dependent variable “Perceived causality.” Any group difference (schizophrenia patients vs healthy controls) would be marked by a significant fixed effect “group.” Binding type II is represented by the fixed effect timing condition; any group differences of this type of binding would result in a significant interaction timing condition \times group.

The main statistical approach (approach a) implemented mixed-effects hierarchical analysis of perceived causality in the whole sample. Modeling details were computed separately for each independent variable. The best-fitting and most parsimonious model was selected with the following procedure: we incrementally entered the predictors (fixed effects) in the sequence of the list above. Statistical significance ($P < .05$) of the entered predictor was applied as a criterion to either keep the current predictor and add the following predictor or skip the current predictor and enter the following predictor. In this manner, 6 models (models a.1–a.6) were computed for the dependent variable perceived causality. Finally, AIC was used, a common approximation to model evidence. The AIC includes both an accuracy and complexity term, in other words, it identifies the most accurate model that can also provide a parsimonious explanation for observed data. Smaller AIC indicates the better model. The respective AIC-optimal models are printed bold in the resulting tables below.

Analogous procedures were applied in approaches b, c, and d. In approach b, perceived causality in the patient sample was modeled by psychopathology (PANSS, GAF) and medications. In approach c, perceived causality in the healthy control sample was modeled by the personality factors (NEO-FFI) and control beliefs (FKK). Approach d was performed to wrap up the findings of the previous approaches in the complete sample: perceived causality was modeled with respect to subgroups. Clustering was based on the finding that positive and cognitive symptoms influenced perceived causality.²³ We therefore defined a variable that divided the sample into 3 clusters: those patients who had high ratios of positive by cognitive symptoms (high pos/cog), those with low ratios (low pos/cog), and the control subjects. Table 1 displays descriptive statistics of these subgroups. Patients in the low pos/cog subgroup showed higher average age and lower PANSS positive symptoms than the high pos/cog subgroup. The 2 groups were not significantly different with respect to the PANSS cognitive factor.

Table 2. Mixed-Effects Models (Complete Sample with $n = 3834$ Runs Observed in $N = 68$ Subjects) of Associations Between Binding (Dependent Variable ‘Perceived Causality’) and Predictors

	Model a.1 ($n = 3834$)	Model a.2 ($n = 3834$)	Model a.3 ($n = 3834$)	Model a.4 ($n = 3834$)	Model a.5 ($n = 3834$)	Model a.6 ($n = 3834$)	
Fixed effects	Parameter estimate, t value	1.036, $t = 13.43^{****}$	1.023, $t = 13.26^{****}$	1.023, $t = 13.34^{****}$	1.023, $t = 13.26^{****}$	1.526, $t = 5.16^{****}$	0.884, $t = 9.95^{****}$
	Timing condition		0.001, $t = 8.70^{****}$	0.001, $t = 8.70^{****}$	0.001, $t = 8.68^{****}$	0.001, $t = 8.69^{****}$	0.001, $t = 8.68^{****}$
	Group (2 = healthy subjects; 1 = patients)			-0.103, $t = -1.34$			
	Timing condition \times group				-0.0003, $t = -2.59^{**}$	-0.0003, $t = -2.59^{**}$	-0.0003, $t = -2.59^{**}$
	Age					-0.018, $t = -1.76$	
	Gender (2 = female; 1 = male)						0.24, $t = 2.79^{**}$
Random effect	Subject (% of total variance)	40.74	41.16	40.87	41.21	40.44	38.80
	R ² of model (% of total variance)	41.6	42.8	42.8	42.9	42.9	42.89
	AIC	-2131.56	-2205.64	-2204.68	-2210.52	-2209.49	-2209.38

Note: AIC, Akaike’s Information Criterion. AIC minimum printed bold.

* $P < .05$; ** $P < .01$; *** $P < .001$; **** $P < .0001$

Results

Tables 2–5 report the results of our hierarchical model optimization. The parameter estimates (and associated t or F statistics) in each column show which predictors were included in each model. The quality of the model is reported by the AIC in the lower row. The top row provides the parameter estimate and significance of a model with just a constant term and no predictors entered. The top row also gives the number n of observations, which may vary between models because PANSS predictors were available of 31 patients only.

The mixed-effects analysis supported the presence of binding type II throughout: the independent variable timing condition was a significant predictor in the complete sample (table 2, model a.2) as well as in the patient sample (table 3, model b.2) and the sample of healthy subjects (table 4, model c.2). This indicated that all groups were able to integrate acoustic information into a visual task; it also showed that subjects distinguished between stimuli presented at differing temporal lags (relative to the visual task), spread across a period of about 350 ms.

At the same time, the timing condition \times group interaction was significant. This points to a marked difference between patients and control subjects in how they implemented binding type II (table 2, model a.4), whereas binding type I did not differentiate between the groups (model a.3). The schizophrenia patients group used the contextual information of the acoustic stimuli less than the control group, as indicated by the flatter curve for patients in figure

2. This finding, which also generated the best model a.4 of table 2, was consistent with the primary hypothesis.

Model a.6 showed that gender is a significant predictor of perceived causality such that female subjects had attenuated causality perceptions. Other secondary analyses followed approaches b, c, and d (tables 3–5). Approach b integrated a number of psychopathology predictors in the patients group, showing that positive symptoms enhanced perceived causality perception, whereas cognitive symptoms reduced it (table 3, model b.7). GAF, psychotropic dosage (CPE), and age at first hospitalization were not statistically related to the dependent variable. Approach c (table 4) addressed the control group only. Contrary to expectations, we found that neither personality nor control beliefs helped explain the variance of perceived causality. The best model is c.2, which manifests the presence of binding type II in healthy subjects.

In approach d (table 5), clustering formulations were tested competitively to explore the subgroup that differentiated best between degrees of binding. As expected, binding type I did not differentiate between patients and controls (insignificant group effect in table 5, model d.1), whereas binding type II differentiated between the groups (significant interaction effect in model d.1). The subgroups that were defined by psychopathology (high ratio pos/cog, low ratio pos/cog, and control subjects) differed with respect to binding type I as well as binding type II (model d.2). As may be seen in figure 2, the patients with high ratios of positive/cognitive symptoms had the highest levels of type I binding, patients with low

Table 3. Mixed-Effects Models (Patient Sample with $n = 1894$ Runs Observed in $N = 34$ Subjects) of Associations Between Binding (Dependent Variable ‘Perceived Causality’) and Predictors

	Model b.1 ($n = 1894$)	Model b.2 ($n = 1894$)	Model b.3 ($n = 1723$)	Model b.4 ($n = 1723$)	Model b.5 ($n = 1723$)	Model b.6 ($n = 1723$)	Model b.7 ($n = 1723$)	Model b.8 ($n = 1723$)	Model b.9 ($n = 1723$)	Model b.10 ($n = 1723$)
Parameter estimate, t value	0.933, $t = 7.70****$	0.923, $t = 7.63****$	0.206, $t = 0.73$	0.522, $t = 1.37$	-0.031, $t = -0.07$	0.243, $t = 0.58$	0.513, $t = 1.84$	-0.158, $t = -0.21$	0.617, $t = 2.01$	1.464, $t = 2.63*$
Fixed effects		0.001, $t = 4.65****$	0.001, $t = 4.25****$	0.001, $t = 4.25****$	0.001, $t = 4.25****$	0.001, $t = 4.25****$	0.001, $t = 8.68****$	0.001, $t = 4.25****$	0.001, $t = 4.25****$	0.001, $t = 4.26****$
Timing condition										
PANSS positive symptoms			0.367, $t = 2.78**$	0.355, $t = 2.71*$	0.333, $t = 2.36*$	0.370, $t = 2.71*$	0.608, $t = 4.12***$	0.725, $t = 3.76***$	0.633, $t = 4.17***$	0.536, $t = 3.67***$
PANSS negative symptoms				-0.151, $t = -1.23$						
PANSS excitement					0.202, $t = 0.73$					
PANSS depression						-0.029, $-t = 0.14$				
PANSS cognitive symptoms							-0.481, $t = -2.76*$	-0.489, $t = -2.80**$	-0.510, $t = -2.85**$	-0.510, $t = -2.21*$
GAF								0.010, $t = 0.94$		
CPE									-0.000, $t = -0.82$	
Age at first hospitalization										-0.040, $t = -1.94$
Random effect										37.20
Subject (% of total variance)	50.43	50.63	44.62	44.19	45.04	45.49	39.47	39.56	39.79	
R ² of model (% of total variance)	50.7	51.2	50.3	50.3	50.3	50.3	50.3	50.3	50.3	50.3
AIC	-1385.07	-1404.90	-1249.54	-1248.56	-1248.54	-1248.54	-1248.53	-1247.53	-1247.56	-1247.58

Note: PANSS, Positive and Negative Syndrome Scale (available in 31 patients); GAF, Global Assessment of Functioning Scale; CPE, Chlorpromazine equivalents; AIC, Akaike’s Information Criterion. AIC minimum printed bold.

* $P < .05$; ** $P < .01$; *** $P < .001$; **** $P < .0001$

Table 4. Mixed-Effects Models (Healthy Control Subjects with $n = 1940$ Runs Observed in $N = 34$ Subjects) of Associations between Binding (Dependent Variable ‘Perceived Causality’) and Predictors

	Model c.1 ($n = 1940$)	Model c.2 ($n = 1940$)	Model c.3 ($n = 1820$)	Model c.4 ($n = 1820$)	Model c.5 ($n = 1820$)	Model c.6 ($n = 1820$)	Model c.7 ($n = 1820$)	Model c.8 ($n = 1820$)	Model c.9 ($n = 1820$)	Model c.10 ($n = 1820$)
Parameter estimate, t value	1.139, $t = 12.06^{****}$	1.121, $t = 11.87^{****}$	1.163, $t = 4.24^{***}$	1.094, $t = 1.77$	0.882, $t = 2.04$	0.643, $t = 0.81$	1.014, $t = 2.03$	1.264, $t = 1.80$	1.006, $t = 2.02$	1.629, $t = 3.26^{***}$
Fixed effects		0.001, $t = 7.47^{****}$	0.001, $t = 7.97^{****}$	0.001, $t = 7.97^{****}$	0.001, $t = 7.97^{****}$	0.001, $t = 7.97^{***}$	0.001, $t = 7.97^{****}$	0.001, $t = 7.97^{****}$	0.001, $t = 7.97^{****}$	0.001, $t = 7.97^{****}$
NEO neuroticism			-0.004, $t = -0.28$							
NEO extraversion				-0.000, $t = -0.00$						
NEO openness to experience					0.007, $t = 0.50$					
NEO agreeableness						0.001, $t = 0.57$				
NEO conscientiousness							0.002, $t = 0.16$			
FKK internality								-0.006, $t = -0.25$		
FKK powerful others									0.004, $t = 0.18$	
FKK externality										-0.024, $t = -1.31$
Random effect										
Subject (% of total variance)	30.47	31.08	31.31	31.37	31.19	31.13	31.35	31.32	31.34	30.13
R ² of model (% of total variance)	31.8	33.7	33.6	33.6	33.6	33.6	33.6	33.6	33.6	33.6
AIC	-795.00	-848.97	-779.85	-779.85	-779.85	-779.85	-779.85	-779.84	-779.85	-779.85

Note: NEO, five-factor inventory of personality; FKK, questionnaire of control beliefs (NEO and FKK available in 32 subjects); AIC, Akaike’s Information Criterion. AIC minimum printed bold.

* $P < .05$; ** $P < .01$; *** $P < .001$; **** $P < .0001$.

Table 5. Mixed-Effects Models (Complete Sample with $n = 3834$ runs Observed in $N = 68$ Subjects) of Associations Between Binding (Dependent Variable ‘Perceived Causality’) and Predictors

		Model d.1 ($n = 3834$)	Model d.2 ($n = 3663$)
Fixed effects	Intercept	1.023 $t = 13.33^{****}$	0.980 $t = 13.27^{****}$
	Timing condition	$F = 75.4^{****}$	$F = 47.2^{****}$
	Group (healthy vs patients)	$F = 1.80$	
	Timing condition \times Group	$F = 6.73^{**}$	
	Subgroup PANSS ratio pos/cog		$F = 9.98^{***}$
	Timing condition \times subgroup PANSS ratio pos/cog		$F = 3.51^*$
Random effect	Subject (% of total variance)	40.93	34.38
	R^2 of model (% of total variance)	42.9	42.0
	AIC	-2209.55	-2059.03

Note: PANSS, Positive and Negative Syndrome Scale (available in 31 patients); High pos/cog, high ratios of positive by cognitive symptoms; Low pos/cog, low ratios of positive by cognitive symptoms; AIC, Akaike’s Information Criterion. AIC minimum printed bold.

* $P < .05$; ** $P < .01$; *** $P < .001$; **** $P < .0001$.

ratios had the lowest binding levels, and healthy subjects were between these upper and lower bounds. A descriptive observation is that in all (sub)groups timing conditions 4 and 5, ie, acoustic sounds given more than 100 ms after the visual coincidence, generated the highest perceived causality.

Discussion

Neurocognitive binding is an essential feature of cognitive functioning. Unfortunately, research on this feature has used a puzzling range of different nomenclature—cognitive (perceptual) coordination, cognitive (perceptual) organization, temporal integration, contextual integration, Gestalt perception—which may obfuscate the common denominator. The different theoretical approaches, and the different biological or neuropsychological methods by which they are operationalized, may not be as heterogeneous as the terminology

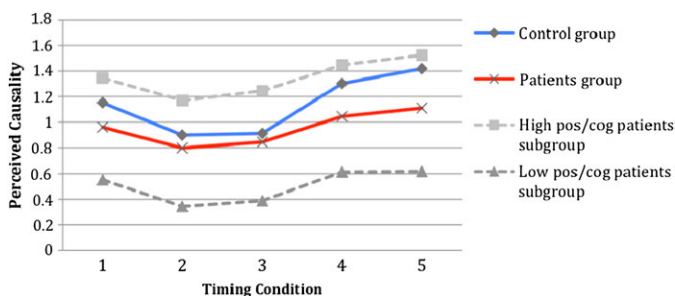


Fig. 2. Mean perceived causality by timing conditions of subgroups of the sample. Control group ($N = 34$), Patients group ($N = 34$), high ratios of positive by cognitive symptoms (high pos/cog) patients subgroup ($N = 17$), low ratios of positive by cognitive symptoms (low pos/cog) patients subgroup ($N = 14$). Abscissa, timing conditions: acoustic stimulus prior to (1 and 2), during (3), and after (4 and 5) coincidence of discs in the Michotte paradigm.

that is being used. There is growing evidence that binding problems may underlie schizophrenia, substantiating a disconnection hypothesis of this disease.⁸ The disconnection hypothesis is more than a phenomenological description of action and perception in schizophrenia; it rests on a failure to optimally modulate synaptic efficacy or gain. This is perfectly consistent with our findings and the Gestalt perspective in the following sense: modern theories of perception appeal to the idea that the brain makes inferences about the causes of its sensations. This inference depends in a sensitive way on the appropriate balance of bottom-up sensory information and top-down expectations.⁴³ This balance is thought to reply upon the precision of information that is encoded by synaptic gain. In other words, optimal inferences about the causes of sensory input (ie, binding) may be impaired in schizophrenia by a failure to optimally modulate synaptic gain, resulting in the abnormal intersensory binding reported in this study.

This study used a paradigm of causality perception that goes back to ideas of the Gestalt psychologist Albert Michotte. We observed (at least) 2 facets of binding. The first, type I, consisted of the observers’ attributions of causal relations (bouncing) to visual objects that may as well be perceived moving independently of each other (streaming). Type I binding in this paradigm is measured by the overall degree of perceived causality. The second type of binding (type II) is realized when further information is processed and is becoming instrumental in modulating the perception of causality. In the present study, this further information had 2 stimulus properties: as acoustic information, it comprised stimuli of a different sensory modality; as distributed across a time span, the stimuli additionally afforded temporal integration. Timing conditions 4 and 5, with presentations of the “click” sound after the visual contact of the discs, resulted in higher perceived causality—this may appear unexpected

since simultaneous visual and acoustic stimulation is realized by condition 3. We may observe here a bias “built into” intersensory neurocognitive binding⁴⁴: sound travels much slower than light, therefore a certain delay of an acoustic stimulus would generally result from a causing event that occurs in some spatial distance from the observer. This interpretation however is speculative.

In this study, we find that type II binding distinguished between schizophrenia patients and healthy controls (see model a.4), whereas type I binding did not (model a.3). Model a.4 rests on the significant contributions of 2 fixed effects, timing condition and the interaction timing condition x group, for the explanation of perceived causality. We interpret this as pointing to a schizophrenia-related dysfunction not so much at the type I level because causality attributions (type I binding) of patients may even be enhanced. Enhanced attribution is related to increased positive and decreased cognitive symptoms (the high pos/cog patients subgroup). Phenomenologically, high pos/cog patients often show a jumping to conclusions style of cognition, which would be in line with enhanced causality perception: paranoia in the shape of excessive causality attributions. Accordingly, patients overall were not impaired with respect to type I binding—at a time when patients have increased positive and decreased cognitive symptoms they even experience more cognitive type I binding than control subjects. Rather, we found that type II binding was generally attenuated in the patients, as a tendency even in those patients who had excessive type I binding. It may be mentioned here that anti-psychotic medication per se was not predictive of feature binding, so that medication may not explain the binding abnormalities described.

It is noteworthy that an interaction effect analogous to model a.4 had failed to reach significance in a previous analysis using MANOVA.²³ The present application of mixed-effects models is methodologically superior in that it avoids averaging over the single records of the dataset to not lose degrees of freedom. Mixed-effects methods thus have greater statistical power and sensitivity. As hierarchical datasets with dependent and repeated measurements are common in the field of schizophrenia research, it appears desirable to consider such analyses more frequently.

The present paradigm did not allow disentangling the 2 different sources of type II binding, intersensory context and temporal differentiation. Confounding of these 2 sources of binding is a shortcoming of this paradigm. It is therefore necessary and feasible to estimate their relative contributions in more refined and specific tasks. In conclusion, one may have to look at specific aspects of feature binding in a search for better phenotypic markers of cognitive dysfunction in schizophrenia. Our study suggests that such markers may lie in the processing of contextual information of a different modality and/or the processing of information given at different points in

time. Identification of these specific markers could lead to the development of diagnostic tools, which may prove applicable also as early prognostic measures. A further step of investigation is to assess the modifiability of type II binding processes that may then serve as targets of cognitive remediation therapy.

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