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Low time resolution in schizophrenia Lengthened windows of simultaneity for visual, auditory and bimodal stimuli

J.R. Foucher [a,*], M. Lacambre [a], B.-T. Pham [a], A. Giersch [a], M.A. Elliott [b]

[a] *Clinique Psychiatrique — INSERM U666, Hôpitaux Universitaires — BP 406 - 67091 Strasbourg Cedex — France*
[b] *Department of Psychology National University of Ireland, Galway, Republic of Ireland*

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Abstract

The guarantee of perceptual coherence for events through everyday life situations depends upon the capacity to correctly integrate series of multi-sensory experiences. Patients with schizophrenia have been shown to reveal a deficit in integrating, i.e., "binding", perceptual information together. However, results in the literature have also suggested the reverse effect. Indeed, in certain paradigms patients have revealed more binding phenomenon than healthy controls and reported experiencing two distinct events as occurring "together". This finding suggests that patients may require longer time intervals between two distinct events before being able to perceive them as "one-after-the-other". The question here was to test whether this perceptual binding abnormality in schizophrenia is confined to events within the same modality or whether it is also present across sensory modalities.

Thirty patients with schizophrenia were compared with 33 normal controls using a simultaneity judgement paradigm. There were two uni-modal conditions in which stimuli were presented in the same modality (visual or auditory) and one bimodal condition (audio-visual). Participants were presented with stimuli varying across a range of inter-stimulus intervals (ISI). They were required to judge whether they experienced two stimuli as occurring "together" or "one-after-the-other".

Compared to controls and in all conditions, patients needed larger ISI to experience two stimuli as "one-after-the-other" (all ISI × Group interactions $p < 5 \cdot 10^{-5}$). These abnormalities correlated with the disorganization dimension but not with the dosage of chlorpromazine equivalent.

The increase of the time interval needed to perceive two stimuli as "one-after-the-other", reflect an abnormally low time resolution in patients with schizophrenia. We discuss the possible involvement of anatomical disconnectivity in schizophrenia which would specifically affect the time integration properties of neural assemblies.

Keywords: Schizophrenia; Integration; Time; Synchrony; Multi-modality; Disconnectivity

1. Introduction

Humans evolve in a multi-sensory context, which confers a general information-processing advantage. Indeed, through this mechanism, information from one sense can complete missing information from another

* Corresponding author. Tel.: +33 3 88 11 62 34; fax: +33 3 88 11 54 22.
E-mail addresses: jf@evc.net, foucher@alsace.u-strasbg.fr (J.R. Foucher).

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(Stein et al., 2004). As such, multi-sensory integration should not be conceived as a mere juxtaposition of two or more representations, but rather as the integration or "binding" of sensory data to form a completely new percept. A classical example of this is the "McGurk effect" for which a subject hearing /*ba*/ while looking at a face articulating /*ga*/, will actually perceive /*da*/ (McGurk and MacDonald, 1976). In this case, integration of visual and auditory information provides the means to construct a coherent representation, i.e. a parametric fusion of each contributive sense.

Because our perceptual field comprises a number of independent sources of information, one pre-requisite of such a fusion ability is that only those stimuli belonging to a given event are integrated together. Perception operates in real time and thus, it must be dynamic in nature. Perhaps because of this, our brain tends to integrate events that co-occur within short intervals of time. This phenomenon has often been referred to in the literature as the "windows of simultaneity", i.e. the time window within which two stimuli are perceived as occurring together (see, e.g., Bertelson and de Gelder, 2004; Elliott et al., 2006; Exner, 1875; Poppel, 2004). This form of temporal integration has been shown to be automatic, unconscious and unmodified by attention (Bertelson and de Gelder, 2004).

Schizophrenia is generally held to include a problem of cognitive integration (Tononi and Edelman, 2000). Evidence has been found by examining the patients' susceptibility to the McGurk effect. For example, using synchronized audio and visual cues, de Gelder et al., 2003, 2005) found in patients with schizophrenia a reduction in the bias induced by the visual cues leading to less frequent perception of the multimodal (and illusory) phoneme /*da*/. This was interpreted as being caused by a deficit in integrating visual and auditory stimuli, maybe because of faulty synchronization mechanism of simultaneous cues. Conversely, studies exploring an "ownership illusion" based on the integration of proprioceptive and visual cues reported a reversed pattern of effects in patients when the two sources of information were presented slightly asynchronously, i.e. one after the other. In this case, patients made abnormal over-attribution of a hand to themselves when this hand was viewed though a mock TV screen and when it more or less imitated their true movements (Daprati et al., 1997, Franck et al., 2001). Interpreted in the framework of multimodal integration, the perception of visual and proprioceptive information as occurring together bring about an incorrect integration of invalid cues within a single, coherent perceptual event. Similarly a feeling of ownership for an artificial rubber hand was shown to appear when the hand was stimulated together with the subjects true hand (Botvinick and Cohen, 1998). Here, the "rubber hand" illusion was shown to be stronger and to occur more rapidly in patients than in controls (Peled et al., 2000, 2003).

We propose that the seemingly contradiction in the literature for evidence of abnormal multi-sensory integration in schizophrenia results from a combination of two factors. First, the integration process itself may be faulty and prone to non-systematic errors (Tononi and Edelman, 2000; de Gelder et al., 2003, 2005). Second, windows of simultaneity may be lengthened in patients. If this latter possibility were true, in spite of relatively long intervals between two stimulus events, patients would continue to bind those events and thus, should perceive two stimuli as occurring together. In contrast, at similarly time intervals control participants should no longer perceive the simultaneity but should judge stimuli as appearing one after the other.

The problem of time has already been raised as a key issue in studies conducted in patients with schizophrenia. But this has especially been the focus of the action literature interested for gaining a better understanding of the fluency deficits in schizophrenia, e.g. for the coordination of movement and thought (Andreasen, 1999). When considering sensory processing, timing abnormalities have been described for example using either "span of apprehension" or "backward masking" paradigms (Nuechterlein and Dawson, 1984; Saccuzzo and Schubert, 1981). In these tasks, subjects are asked to locate, detect or identify a first stimulus, which is followed after a varying delay by a second meaningless stimulus — the mask. Patients with schizophrenia were shown to need typically a longer time interval than controls between target and mask in order to perform the task successfully (Braff, 1981; Butler et al., 1996; Rund et al., 1993). This could be due to the fusion of the first stimulus with the mask when both fall within the same (lengthened) window of simultaneity.

The study described here was designed to answer two related questions. First, we wanted to assess whether simultaneity thresholds are larger in patients with schizophrenia when stimuli are presented in two different modalities. The simultaneity threshold is defined as the time interval separating two stimuli, below which the subject perceive the stimuli as occurring together in more than half of the trials. If this was the case, the threshold's increase could account for the results of increased binding in multi-sensory integration experiments. To test this idea we used a temporal discrimination paradigm, i.e. asking subjects to judge whether they perceive two stimuli as occurring

Table1
Presents the group demographics

	Patients	Controls
N	30	33
Sex (*n* female)	9/30 (30%)	11/33 (33%)
Age	33±9 Y	32±11 Y
Academic Y	12±3 Y	14±3 Y
Smoker	19/30 (63%)	12/33 (36%)
Left-handed	1/30	1/33
PANSS	54±18	
Eq Cpz	223±200 mg (2 without)	

PANSS and neuroleptic dosage in clozapine equivalent are given for the patient group only.
Number of participants (*N*), sex distribution (number of females per group), mean age in years (Y), mean academic years, proportion of smokers, and proportion of left-handed participants are provided for each experimental group.

"together" or "one-after-the-other". This approach is different from the standard duration discrimination task in that it offers an assessment of basic phenomenological time and does not rely on working memory, which is known to be impaired in patients with schizophrenia (Pouthas and Perbal, 2004; Salame et al., 1998). For the multi-sensory condition we used a combination of auditory and visual stimuli. The second question concerned the origin of low temporal resolution. More specifically, we asked whether the increase of the simultaneity threshold in the audio-visual modality is a generalized problem of integration of events across time. We will present evidence that suggests that the increase of the simultaneity threshold is also altered in patients with schizophrenia for unimodal conditions and at a similar degree. More specifically, by showing that the deficits for unimodal and bimodal windows of simultaneity are correlated and of similar extent in auditory, visual and audio-visual conditions, a strong case will exist for a generalized low time resolution in schizophrenia. This may relate to a common core defect and its relation with clinical symptoms will be discussed.

2. Materials and methods

2.1. Subjects

Thirty patients participated in the study (10 women, 1 left-handed). All met the DSM IV-R criteria for schizophrenia (18) or schizo-affective disorders (12). Patients were excluded if they had a past history of neurological disorder, dyslexia (associated with increased simultaneity thresholds — Fischer and Hartnegg, 2004) or current treatment with benzodiazepines. Indeed, it has been shown that the latter affects retrograde masking and thus, could induce problems in temporal discrimination (Giersch and Herzog, 2004). All patients but two were under neuroleptic treatment (6 typical, 22 atypical), 5 patients were taking SSRI, and 3 patients were taking antiepileptic drugs as mood stabilizers. All patients were more than two months from the end of their last acute phase. The control group consisted in 33 participants (11 women, 1 left-handed). None had undergone psychotropic treatment, had personal or familial history of neuropsychiatric disorder or dyslexia. Table 1 summarizes the group characteristics. There were no significant differences except for the number of years of education, which

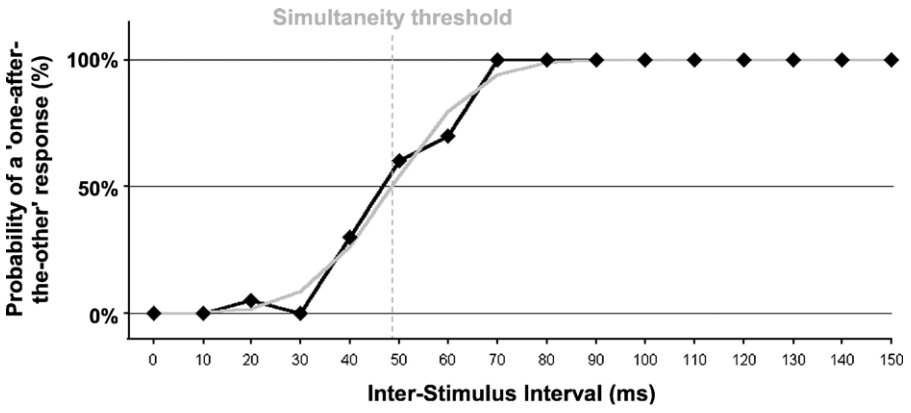

Fig. 1. Illustrates the fit between the error function and the probability to respond "one-after-the-other". The probability of one patient in the auditory condition is plotted against the ISIs (black curve). The error function (grey curve) is fitted to the observed values by optimising two parameters: the centre of the curve that corresponds to the threshold of simultaneity, and its width that defines the slope. The averaged absolute differences between observed and predicted values are 2% (visual and auditory) and 3% (bimodal) without significant differences between patients and controls.

Table 2
Group comparisons under each condition

	n	Group	ISI	Order	
Visual	29/33	$F_{1,60}=11.3$, $p=0.001$	$F_{12,720}=420$, $p<10^{-15}$	$F_{1,60}=9.7$, $p=0.003$	
Auditory	30/33	$F_{1,61}=10.7$, $p=0.002$	$F_{15,915}=314$, $p<10^{-15}$	$F_{1,61}=22.2$, $p=1.4\ 10^{-5}$	
Bimodal	29/33	$F_{1,60}=10.6$, $p=0.002$	$F_{14,840}=205$, $p<10^{-15}$	$F_{1,60}=1.7$, ns	
		Group × ISI	Order × ISI	Group × Order	Group × Order × ISI
Visual		$F_{12,720}=3.5$, $p=4.2\cdot10^{-5}$	$F_{12,720}=7.4$, $p=7.3\cdot10^{-13}$	$F_{1,60}=0.1$	$F_{12,720}=1.4$
Auditory		$F_{15,915}=4.5$, $p=2.1\cdot10^{-8}$	$F_{15,915}=5.3$, $p=1.8\cdot10^{-10}$	$F_{1,61}=0.1$	$F_{15,915}=0.6$
Bimodal		$F_{14,840}=4.4$, $p=1.3\cdot10^{-7}$	$F_{14,840}=3.4$, $p=2.5\cdot10^{-5}$	$F_{1,60}=0.7$	$F_{12,720}=0.9$

As expected, the ISI effect was very large, representing the slope of the sigmoidal PF, itself arising as a consequence of the increasing tendency to judge the stimuli as "one-after-the-other" rather than "together" with increasing ISIs. The group × ISI interaction was always significant and was due to the patients requiring longer ISIs before judging the stimuli as "one-after-the-other". However, patients were similar to controls at extreme ISIs demonstrating that they understood and performed the task correctly (see Fig. 2 and Supplementary material no. 1). Of some surprise was the order effect which arose under the visual and auditory conditions because "one-after-the-other" was more frequently chosen when the first stimulus appeared on the right. Moreover, the order × ISI interaction was significant under all conditions. Under the unimodal conditions, subjects revealed shorter window of simultaneity when the first stimulus appeared on the right (Supplementary material no. 1). Under the bimodal condition, our results reflected an increased tendency to answer "one-after-the-other" between 40 and 150 ms when the visual stimuli was presented first, while the tendency to answer "one-after-the-other" was increased between 270 and 470 ms (Supplementary material no. 1). However, since neither the group × order nor the group × order × ISI interactions were significant, this bias appears to affect both groups equally.
Under all conditions, the group effect was found to be significant because patients judged the two events to occur "together" more often than did the controls.

was 1.5 years higher for control participants ($p<0.01$). All participants gave written informed consent before taking part in the study.

2.2. Task

The experiment was run in a quiet and comfortably illuminated room with participants seated 1 m in front of a CRT monitor screen (17 in.–43 cm, 80 Hz). Responses were recorded using a computer mouse in such a way that the thumb of each hand was above the buttons of its respective side. Subjects were required to perform the same task whatever the stimuli, pressing the left button when judging two stimuli as occurring "together" and the right button when perceiving them as occurring "one-after-the-other". The button order was not randomised and participants were given no feedback. The experiment consisted in three 5-minute sessions, which were always administered in the same order: visual, auditory and visuo-auditory conditions. Before each session, the subject was trained until his performance demonstrated a clear understanding of the task.

In the visual modality, the subjects were asked to focus on a white cross in the middle of a black screen (drawing of 1 pixel width, 11 pixels long at 320×240 pixel resolution). Two white circles (∅ ~4 cm, ~2.2°) were then presented one on each side of the cross. Each circle was presented for a unique 12.5 ms frame. The two circles were presented either together (simultaneously) or with an inter-stimulus interval (ISI) that varied across the range of −150 to +150 ms in 12.5 ms steps (negative timing defining that the left circle was presented before the right one). The experimental conditions were presented in pseudo-random order and for each ISI there were 13 repetitions except for the 0 ms lag (simultaneous presentation) which was presented 26 times.

In the auditory modality, the subjects were presented with multi-frequency clicks at a comfortable volume (~60 dB SPL) via two speakers positioned at angles of approximately 26° to viewing angle and at the same distance from the participant's head. Each sound was of 10 ms duration and the waveform of one track was the backward inversion of the other. In spite of this, the two sounds were very similar to one another. ISI ranged between −150 and +150 ms in 10 ms steps (negative timing defines that the left stimulus was presented before the right one). Each condition was presented 10 times except for the simultaneous presentation which was presented 20 times.

In the visuo-auditory condition, the subjects were asked to focus on the centre of the monitor screen and were presented with one sound corresponding to the previously described clicks and one circle as described above. The circle was displayed in the centre of the screen at the same location as the fixation cross. ISIs ranged from −470 to 470 ms in 30 ms steps (negative timing indicating that the sound was presented before the image). Each condition was presented 10 times.

All the tasks were programmed in e-basic (e-prime, Psychology Software Tools, Pittsburgh — USA).

2.3. Data analysis

2.3.1. Single condition group comparisons

This first analysis aimed at evaluating between group differences in simultaneity thresholds in each of the three conditions: visual, auditory and audio-visual. For each ISI, we initially computed the proportion of "one-after-the-other" judgements — the simultaneous responses being their complement: p(one-after-the-other)+p(together)=1. The data were then analysed by means of a repeated-measures analysis of variance (ANOVA) with the factors: Group (patients and controls), Order and ISI, with the later two being repeated factors.

2.3.2. Comparative and correlation analyses

We calculated simultaneity thresholds in each condition and for each participant. The threshold was determined as the ISI at which there was an equal

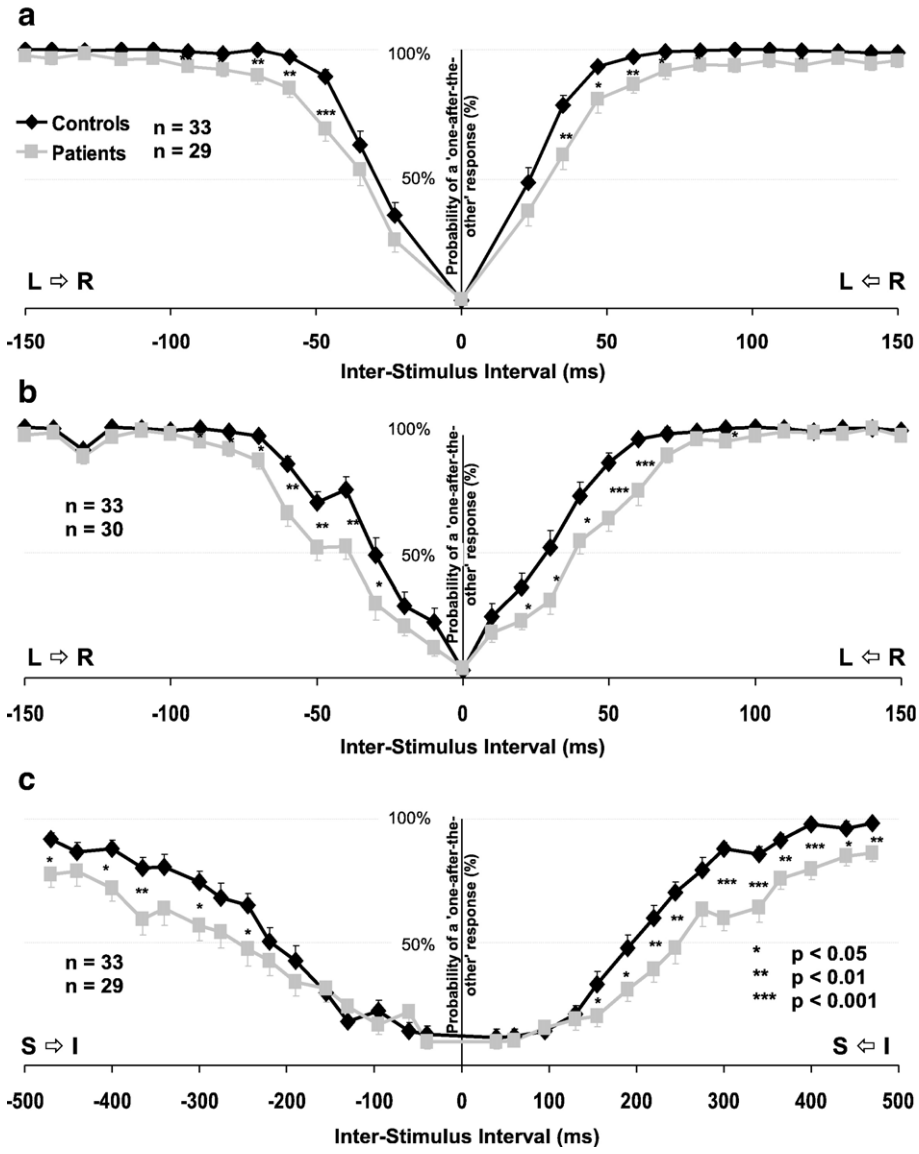

Fig. 2. Presents the simultaneity thresholds under the visual (a), auditory (b) and bimodal (c) conditions. The mean probability to respond "one-after-the-other" is plotted against the ISIs, for the control group (black diamonds) and the patient group (grey squares) with corresponding standard errors. For the visual (a) and auditory (b) graphs, negative ISIs correspond to the situation where the left stimulus is presented before the right one. For the bimodal plot, negative ISIs correspond to the situation where the sound is presented before the image. The stars specify the t-test values when running a comparison between the two experimental groups under one condition only (two-sided, no correction for multiple testing).

Table 3
Average size of the window of simultaneity for each group under all conditions

	Patients	Controls
Visual	37±15 ms	27.5±8 ms
Auditory	42.7±16 ms	30.5±17 ms
Bimodal	265±86 ms	203±51 ms

probability of responding "together" and "one-after-the-other".

In an initial step, the probability values were averaged for each ISI between the two judgements. Then, a response function was fitted with an error function, erf, to derive the psychometric function, PF (see Fig. 1, Cody, 1969).

$$\mathrm{erf}(x) = 2/\sqrt{\pi}\int_{0\to\times} e^{-t^2}\mathrm{d}t.$$

Fitting was calculated using a gradient descending algorithm to minimize the absolute value of the difference between the measured and estimated curves. This was preferred over the classical least-squares method as it is relatively uninfluenced by outliers and thus, provides the means to determine a more robust estimator. The estimated curve was then defined by two values optimised through this procedure: its centre, which was the simultaneity threshold, and its width.

We then tested for variations in thresholds between conditions. We expressed simultaneity thresholds as relative differences, i.e. percentage of the means measured in the control participants, and this was done for each condition. For example, a 10% increase suggested a similar relative lengthening whether the main window was 10 or 100 ms, although the absolute differences would be in fact 1 and 10 ms, respectively. We looked once more for group × condition interaction using these relative values. To give an idea of effect size, i.e. the magnitude of the difference between the two populations, we computed Cohen's "*d*" for all conditions (differences between mean values of patients and controls divided by the pooled standard deviation — Cohen, 1988). Correlations between the condition thresholds were then calculated after correcting for overall group effect.

Finally, we looked at the correlations between visual, auditory and the bimodal thresholds as well as those correlations with symptomatic dimension, chlorpromazine equivalent, age, years of education and response time. For the symptoms dimension, we used the positive and negative symptoms from the PANSS to determine 3 factors using a PCA with Varimax rotation. The first 3 components explained 68% of the variance. The first dimension was disorganization (conceptual disorganization, excitation, difficulties in abstraction and stereotyped thinking). The second corresponded to negative symptoms (blunted affect, emotional withdrawal and

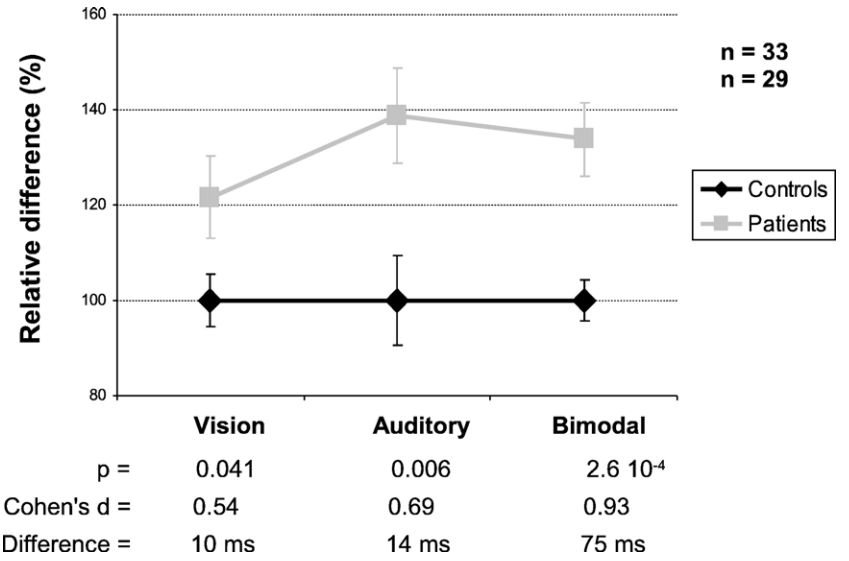

Fig. 3. Comparison of the relative difference and effect size between conditions. The curve in the control group is flat and is taken as the reference (100% — black diamonds). Bars denote standard errors. Whereas patients (grey squares) tend to reveal a larger impairment under the auditory and bimodal conditions relative to the visual one, the interaction is non-significant.

poor rapport), whereas the third matched with reality distortion (delusion and hallucination). For gender and smoking, effects were tested using an ANOVA. Statistics were computed after correcting for the overall group effect when appropriate. All statistics were performed with Statistica v5.1 (StatSoft — Tulsa, USA).

3. Results

3.1. Single condition group comparisons

Table 2 summarizes the effect of each factor. In all conditions, the Group effect was significant. Indeed, patients judged the two events as occurring "together" over a longer range of ISIs than controls. This was corroborated statistically in the Group × ISI interaction, which was significant with patients requiring longer ISIs before judging the stimuli as being "one-after-the-other" than controls. At extreme ISIs, patients showed similar performance patterns than controls, indicating that they had understood and performed the task correctly (see Fig. 2 and Supplementary material no. 1). The mean and standard errors of the simultaneity thresholds for both groups and in the three conditions are given in Table 3 (see also Supplementary material no. 1 page 4).

3.2. Group × condition interaction and correlation analysis

Even when using values relative to that measured in the control group, a main effect of Group was revealed ($F_{1,60}=14.3$, $p=3.6\cdot10^{-4}$), which indicated a larger simultaneity thresholds in patients irrespective to condition (Fig. 3). However, the group × condition interaction was none significant ($F_{2,120}=0.37$, ns), which suggest that the groups were affected in a similar way by the different conditions. The effect size, as assessed by Cohen's d, decreased progressively in the bimodal condition (0.93), the auditory condition (0.69), and the visual condition (0.54).

The results obtained in the three conditions were highly correlated: visual–auditory ($r=0.51$, $n=62$, $p=5.3\cdot10^{-6}$), visual-bimodal ($r=0.28$, $n=61$, $p=0.026$) and auditory-bimodal ($r=0.41$, $n=62$, $p=5.5\cdot10^{-4}$). The correlation between symptom dimensions and simultaneity thresholds were none significant for the negative dimension ($r\subset[0.02, 0.18]$). On the other hand, disorganization was found to be significantly correlated with the bimodal threshold ($r=0.37$, $n=28$, $p=0.046$) although not significantly correlated with either of the two unimodal thresholds ($r=0.25$, $n=28$, $p=$ns). The positive dimension exhibited a trend towards correlation with auditory simultaneity thresholds ($r=0.32$, $n=28$, $p=0.091$) but the correlations for both the visual and the bimodal thresholds were none significant ($r\subset[0.21, 0.27]$, $n=28$, $p=$ns).

Finally, all other correlations were non-significant whether it be with age ($r\subset[0.03, 0.21]$), with chlorpromazine equivalent ($r\subset[-0.29,-0.18]$, see Supplementary material no. 2 for the results for the individual medications) or with the number of years of education ($r\subset[-0.13, 0.18]$). Finally, gender ($F_{1,59}=0.9$, ns) and smoking quantity ($F_{1,59}=0$, ns) were not correlated with the simultaneity thresholds.

4. Discussion

The hypothesis of lengthened windows of simultaneity in patients suffering from schizophrenia was here confirmed by revealing in our patient group greater simultaneity thresholds in visual, auditory and also for bimodal stimuli, i.e. patients needed larger ISI to judge two stimuli as occurring "one-after-the-other". Highly significant correlations between simultaneity thresholds for visual, auditory and bimodal stimuli is of importance as it suggests that simultaneity thresholds refer to a unique and basic timing property of brain functioning, which would be impaired in patients with schizophrenia whatever the sensory modality.

When comparing across conditions, the percentage of threshold increase was found to within a similar range in both the patient and the control groups. Again this observation favours the hypothesis that the additional 75 ms under the bimodal condition builds upon the same causes as the more modest increase that was observed under the unimodal conditions (10 and 14 ms, for vision and audition, respectively). We also reported a slight but significant correlation between the bimodal thresholds and the disorganization dimension, on the one hand, and a trend for a correlation between the auditory threshold and the reality distortion dimension, on the other hand.

A limitation of our study is the usual covariance of the group effect with the treatment effect. For this point, it is important to consider those patient groups who have a natural significant decrease in dopamine levels, e.g., patients with Parkinson's disease, because they have been shown to be characterised by an increased threshold. This observation would lead us here to expect that when giving medication that blocs dopamine transmission one should be able to induce similar effects than that observed in patients with schizophrenia. To note that patients with Parkinson's disease also possess increased simultaneity thresholds than that

observed in healthy controls when off medication, and this effect is partly corrected by L-Dopa (Artieda et al., 1992; Lee et al., 2005). But for the patients who participated in the present study, chlorpromazine equivalents were not only non-significantly correlated with the thresholds, but all correlation coefficients revealed to be negative, even when taking into account the different types of medication. Moreover, the two untreated patients revealed threshold increases under the auditory and the bimodal conditions. Overall, these findings suggest that the impairments reported here for extended windows of simultaneity in patients suffering from schizophrenia is not due to treatment.

Our results clearly demonstrate that patients with schizophrenia do not judge the timing of events with the same temporal resolution as healthy controls. Because the perception of two stimuli as being simultaneous encourages their integration, it is possible to infer that patients will continue to bind stimuli that are separated by a time window (ISI) for which controls would perceive two stimuli as being two separate events. This may explain the results observed in different "ownership illusions", for instance in the rubber hand illusion. Indeed, slight discrepancies in the time arising as a consequence of manual stimulation concurrent with viewing the artificial limb could have discouraged the tendency in the controls to integrate the two sources of information. In the patients' case, an inability to use small asynchronies to judge correctly that proprioceptive and visual stimuli are not occurring in the same time, could lead to the illusion that the artificial hand was in fact their own hand (Peled et al., 2000; Peled et al., 2003). It would be interesting to know whether the same result would have been observed when comparing internal and external events, or even when comparing two internal events, e.g. emotions and saliencies (Kapur, 2003). This very fundamental disorder ("lathomenologic" — Andreasen, 1999) might also explain other symptoms, such as some loosening of associations or "knight move thinking" and other aspects of disorganization. Our results provide a significant argument to this later theory as we report a significant correlation between extended windows of simultaneity and the symptomatic dimension of disorganization. Such an idea of a "cognitive disynchronia" comes directly from the concepts of "intrapsychic ataxia" proposed by Stranski (1904), in Stranski (1987) and further developed into the "cognitive dysmetria" hypothesis" by Andreasen (1999).

We assume that because all simultaneity thresholds were correlated they might refer to a common underlying process. As patients are no more deficient in one condition relative to another, we suggest that schizophrenia may affect the basic brain processing for time phenomenology. But what could this processing be and what may its properties be? It has generally been suggested that time could be processed by a dedicated brain system. Andreasen hypothesized that schizophrenia might present timing problems because the cerebellum shows disordered activation (Andreasen, 1999). Indeed, one of the many functions associated with the cerebellum is the time clock concept that is central for motor timing and duration discrimination, but not as yet in perceptual timing (Ivry, 1996; Jueptner et al., 1995). Others, on the basis of similar increase of simultaneity thresholds in Parkinson's disease (Artieda et al., 1992; Lee et al., 2005; Pastor et al., 1992) and dystonia (Bara-Jimenez et al., 2000; Tinazzi et al., 2004), have argued that the basal ganglia play a central role in timing but at the perceptual level (Perbal et al., 2005; Pouthas et al., 2005). Finally, patients with brain lesions in the left temporo-parietal region also show increased thresholds in temporal order judgements (Lacruz et al., 1991; Wittmann et al., 2004; von Steinbuchel et al., 1999).

Our hypothesis is that there is no dedicated network for time perception, but that it is an embedded property of each neural net. Because time resolution is lower in all conditions, the dysfunction affects many (perhaps even all) brain systems. Indeed, schizophrenia has been proposed to be a disorder of anatomical connectivity (Foucher and Luck, 2006; Weinberger et al., 1994) which brings about abnormal functional integration (Foucher et al., 2005). Myelin alterations in schizophrenia (Mitelman et al., 2006) are believed to lengthen conduction times. Consequently, action potentials may be delayed and may not arrive in synchrony (Foucher and Luck, 2006). This might well challenge the time resolution of neural assemblies. By impeding time resolution, these alterations may induce a difficulty in discriminating between simultaneous and asynchronous events, thus leading to longer windows of simultaneity and extended intervals within which events will be integrated or bound together. On the other hand, fast oscillatory activity in neural systems in the gamma band is believed to bring about perceptual binding (Singer, 2001), which appears deficient in schizophrenia (see a review in Uhlhaas and Singer, 2006). This may emerge due to an underlying anatomical disconnectivity, which impacts on the neural system's capacity to oscillate and synchronize at particular frequencies (Foucher and Luck, 2006). Thus we suggest that basic deficit in connectivity could account for both the decrease and increase of binding function depending on task specificity and its timing properties.

5. Conclusion

Increased simultaneity thresholds in bimodal conditions could well account for the apparent increase of integration of sensory information demonstrated in patients with schizophrenia. Interestingly, these extensions build upon a general problem with timing which is also observed at the mono-sensory processing stage. Although the way the brain perceives time remains to be elucidated, the anatomical disconnectivity hypothesis may account for the results reporting in schizophrenia both hypo and hyper integration capacities depending on the inter-stimulus interval. Future studies would take great advantage of close collaborative work between neurophysiology and time perception in the field of experimental psychology.

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Contributors

Author JRF designed the study, wrote the protocol, collected data, performed their analysis and wrote the first draft of the manuscript. Authors ML and BTP collected data and contributed to the analysis. Author AG managed the literature. Author MAE managed the literature and provided major revisions to the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of interest

All authors declare that they have no conflicts of interest.

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Appendix A. Supplementary data

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