INVESTIGATING THE PERCEPTION OF SIMULTANEITY IN PSYCHOSIS: A COMPARISON OF FIRST-EPISODE PSYCHOSIS AND TREATMENT-RESISTANT SCHIZOPHRENIA PATIENTS WITH HEALTHY CONTROLS

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Abstract

In order to investigate whether difficulties with temporal event-coding, previously reported in patients with schizophrenia, are already present during first-episode psychosis (FEP) or if they develop gradually over time, the subjective judgments of the simultaneity of visually presented stimuli were compared between 46 healthy controls, 29 treatment-resistant schizophrenia (TRSZ) patients with schizophrenia and 29 FEP patients. Participants underwent two experiments, where they were asked to indicate whether two vertical bars appeared simultaneously or at different times on the screen. The results of both experiments suggest that particularly TRSZ patients required longer intervals between stimulus onsets than did controls to detect the asynchrony. Both patient groups showed much higher elevated thresholds when the range of SOAs used were increased, which might reflect differences in symptomology. Particularly TRSZ patients appear to experience difficulties with judging simultaneity. FEP patients also appear to have slight impairments but the extent of these impairments is less pronounced than in the TRSZ sample.

The ability to experience time is fundamental to consciousness as all cognitive experiences require temporal continuity in itself (Vogeley & Kupke, 2007). Husserl (1928) originally proposed that consciousness is made up of three parts, the past (retentional), the present (presentational) and the future (protentional) and that all three need to be integrated appropriately to experience time appropriately. Adapting Husserl's framework of time phenomenology might help to understand the nature of deficits observed in schizophrenia as it emphasises the subjectivity of human experiences and how this is disturbed in mental disorders. Temporal constraints and intact functioning of timing are crucial for cognitive functioning (Szymaszek, Sereda, Pöppel & Szelag, 2009) and many of the problems observed in schizophrenia patients, e.g. cognitive impairments, hallucinations and delusions, could be due to an impaired sense of timing. According to Pöppel (1985), the experience of time is hierarchical so in order to be able to structure which events come first, one needs to experience simultaneity as compared to asynchrony. Brecher (1932) experimentally showed that in healthy adults, simultaneity thresholds (i.e. the SOAs at which there is an equal probability of responding either simultaneous or asynchronous) are located at SOAs of around 55 ms: findings corroborated more recently by Elliott et al. (2007) and Giersch et al. (2009). Foucher et al. (2007) and Giersch et al. (2009) both showed that patients with schizophrenia require extended SOAs to judge stimuli onsets to have been presented in succession, accompanied by increased simultaneity thresholds. However, to our knowledge, most relevant research on the perception of simultaneity has focused only on chronic schizophrenia. Therefore, the aim of the present study was to compare visual simultaneity thresholds of patients with treatment-resistant schizophrenia (TRSZ) to those of FEP patients, i.e. at illness

onset, and healthy controls. We hypothesised that FEP patients would show elevated thresholds compared to healthy controls but not to the same extent as TRSZ patients.

Method

Participants

In total, 29 FEP patients (20 males), 29 TRSZ patients (20 males) and 46 group-matched healthy controls (32 males), recruited from the in-and outpatient units in the University College Hospital Galway (UCHG) and the Regional Hospital in Ennis, Republic of Ireland, participated in this study. Groups did not differ significantly with regard to gender (χ^2 (2, N = 104) = 0.004, p = 0.998), age (χ^2,(54, N = 104) = 57.33, p = .322) or IQ (χ^2 (44, N = 80) = 40.29, p = .632) as measured by the NART (National Adult Reading Test, Nelson, 1991) using a statistical significance level of 0.05. All patients were diagnosed by psychiatrists from UCHG using the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (SCID-P, First, Spitzer, Gibbon & Williams, 1995, DSM-IV, APA, 1994). In order to provide information about symptom predominance and severity, PANSS scores (Positive and Negative Syndrome Scale, Kay, Fiszbein & Opler, 1987) were also collected for each patient. The FEP sample comprised different disorders; 5 patients with paranoid schizophrenia, 10 with schizophreniform disorder, 5 with bipolar disorder with psychotic features, 4 with depressive disorder with severe psychotic features, 2 not-otherwise specified psychosis patients, 1 with delusional disorder persecutory type, 1 with a brief psychotic episode and 1 with substance-induced psychosis. All but 11 of the TRSZ sample were treated with clozapine (mean dose = 869 mg/day of chlorpromazine equivalents, *SD* = 794) and all but two (who were medication free) of the FEP sample were receiving atypical neuroleptic treatment for less than 6 weeks at the time of testing (mean dose = 273 mg/day of chlorpromazine equivalents, *SD* = 294). The mean duration of untreated psychosis for the FEP sample was 14.10 months (*SD* = 17.23). The mean duration of illness for the TRSZ sample was 144.88 months (*SD* = 60.24). 18 FEP, 17 TRSZ patients and 34 healthy controls participated in experiment 1, 11 FEP, 12 TRSZ patients and 11 healthy controls participated in experiment 2.

Apparatus and Stimuli:

Stimuli were presented on a Pentium 4 PC running Windows XP equipped with a Cambridge Research Systems (Rochester, Kent, UK) visual stimulus generator (ViSaGe), which was programmed in C language using the VSG software library. The visual stimuli were presented using a Mitsubishi Diamond Pro 2070SB monitor with the refresh rate set to 120 Hz.

The target stimuli consisted of two vertical gray bars separated by 13° of visual angle at a viewing distance of 100 cm at which each bar subtended 3° x 10° of visual angle. Target bars increased luminance twice: The first change (from a background of 0.06 cd/m^2 – gradually and nonlinearly - to a peak luminance of 14.4 cd/m^2) occurred within a premask comprising the onset, presentation for 75 ms, and then offset in series of 6 flanker bars, rendering the first change in target luminance below detection thresholds. The second change in luminance (gradually and nonlinearly from14.4 cd/m^2 to 29.8 cd/m^2) occurred in the absence of flankers. It was to this change that observers made their judgement of the simultaneity or asynchrony change. Stimulus presentation occurred in an environment of low intensity, ambient light (0.1 cd/m^2) to reduce the impact of onscreen persistence. The premask took the form of 6 flanker bars of identical dimensions to the target bars but the flankers were oriented pseudo-randomly 45° to the left or right of the vertical meridian. The masking bars

onset in pseudo-random order and temporally interleaved with the first change in target-bar luminance. The first change in target bar luminance occurred in two conditions; synchronously (SB_S) or asynchronously (SB_A). In $SB_{S,}$ the two bars started to change luminance at the same time, while in $SB_{A,}$ the two bars proceeded to change luminance at SOAs no lower than a previously determined simultaneity threshold for two bars presented in isolation and no higher than a previously determined simultaneity threshold in the presence of flankers. This ensured that, for SB_A conditions, the first change in target luminance occurred at SOAs, which did not descend below the SOAs, at which targets would ordinarily be perceived as simultaneous (without flankers) and at the same time maintained at an upper level that ensured that the change was masked and remained below detection threshold.

Procedure:

The method of constant stimuli was employed to determine visual simultaneity thresholds. Two experiments were run, the first using target SOAs of 0-110ms, the second one extending these target SOAs from 0-330ms. Each consisted of three parts, two staircase procedures to determine the lower and upper simultaneity thresholds, and the main experiment.

Staircase Procedures: Two staircase procedures determined lower and upper simultaneity thresholds. In the lower threshold procedure, participants judged the simultaneity or asynchrony of luminance changes between two target bars without presentation of flankers, whereas in the upper threshold procedure, changes in target luminance were embedded in a sequence of flankers. The two thresholds were used to determine the range over which prime SOAs were varied, which was derived from the median value between lower and upper thresholds, measured in terms of the delay between the onset of the first and the second bar (i.e. the bar-bar SOA). Staircases used the stochastic approximation procedure developed by Treutwein (1995), in which the 2 bars were initially presented with an SOA above threshold and were then gradually reduced on a trial-by-trial basis until the subject responded 'synchronous'. An initial threshold of 80 ms began the adaptive procedure. Both lower and upper threshold were estimated separately and at least twice in order to ensure more reliable stable parameterisation of SB_A in the main experiment. In both staircase procedures, stimulus presentations were preceded by the 500ms presentation of a fixation frame (four corner junctions), comprising a 13° x 13° square region, within which the stimuli were presented.

Main experiment: The premask bars were presented within a pseudo-randomised sequence of flankers, rapidly switched on and off at locations flanking the premasks. In contrast to the procedure used to determine the upper threshold, a second change in (target) luminance occurred at the location of the premask bars after the flankers had been switched off and was fully visible. Participants had to report whether this change in target luminance was synchronous or asynchronous. The SOAs between premask bars were set at 0 ms for synchronous premasks and within the range of SOAs circumscribed by the lower and upper thresholds for asynchronous premasks. The second change in target luminance occurred 150 ms after the change in premask luminance with no flankers present. There were 12 target SOAs (each level presented 40 times). Subthreshold SOAs were pseudo-randomly varied between the lower and upper thresholds established by the staircase procedures. The order of the target bars was randomised across trials with an equal amount of trials presenting the first bar on the left and right. The targets retained their luminance level for 2 seconds before the next trial commenced. The main experiment consisted of one session of 10 blocks comprising 48 trials per block and participants were advised to take breaks. The keyboard was used to respond by pressing the letters 'F' for synchronous and 'J' for asynchronous bars. The space bar was pressed to start a trial block.

Results and Discussion

Group Differences in Simultaneity Thresholds

Psychometric functions (PFs) were calculated individually. Preliminary inspection of the data revealed a high guess rate, which recommended correction. On this basis, the individual data were submitted to the following probability-based correction:

$$P_{adj}(x) = \frac{P(x)}{P(0)} \quad (1)$$

where P (0) is percentage of 'synchronous response' for 'subthreshold simultaneity (i.e. subthreshold SOA = 0) to eliminate the problem of a bias towards asynchronous responses. Individual thresholds were calculated as the SOAs corresponding to a rate of 50 % simultaneity responses for synchronous and asynchronous premasks separately using the Curvefit toolbox on Matlab 7.0. The overall threshold was defined as the mean of thresholds of synchronous and asynchronous premasks. Data were then analysed using SPSS version 15 and Statistica Version 8.

Experiment 1: SOAs of 0-110ms

A one-way ANOVA revealed significant group differences in the overall simultaneity thresholds between FEP, treatment-resistant schizophrenia patients and healthy controls (F (2, 52) = 8.59, p = 0.001, see figure 2). Planned contrasts revealed that patients had significantly higher thresholds compared to controls (t (52) = 3.46, p = 0.001) and significant differences also existed between FEP and TRSZ patients (t (52) = 2.65, p = 0.011). Healthy controls showed thresholds of 50ms, compared to 58ms for FEP patients and 80ms for TRSZ patients. The premask was also found to influence thresholds (F (1, 51) = 21.68, p = .000) with thresholds being significantly higher when the premask bars changed luminance simultaneously (healthy controls: 54ms, FEP patients: 59ms, TRSZ: 87ms) as compared to asynchronously (healthy controls: 47ms, FEP patients: 50ms, TRSZ patients: 74 ms). Comparing the psychometric curves of each group for both experiments (see figure 1), we found that the slopes for responses to synchronous and asynchronous premasks widened for patients, particularly for TRSZ patients. The psychometric functions for patients never approached complete certainty of asynchronies, possibly due to an uncertainty of knowing what true asynchronies of luminance looked like as their thresholds might lie outside a frame of 110 ms. Since we could not establish thresholds within the 110 ms SOAs for 14 patients (6 FEP, 8 TRSZ), we explored the possibility that patients' thresholds were located beyond the maximum SOA of 110 ms tested in experiment 1. Therefore, we increased the range of SOAs from 0- 330 ms in experiment 2 and where possible retested some of these patients and also new patients and controls with extended SOAs ranging from 0 to 330 ms and with 30 ms intervals.

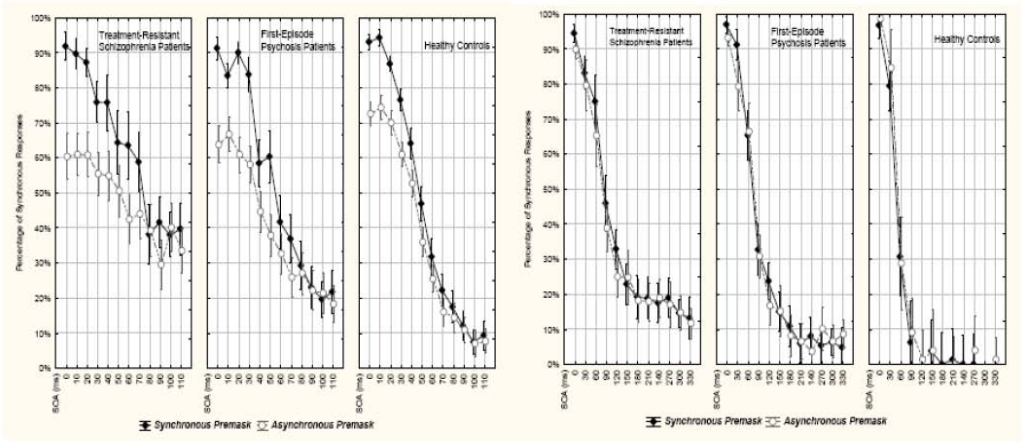

Figure 1: Mean psychometric functions for each individual group showing the percentage of responding synchronous for various target SOAs (in ms) ranging from none (left) to max (right). On the left are the psychometric functions for Experiment 1, on the right for Experiment 2.

Experiment 2: SOAs of 0-330ms

A one-way ANOVA showed similar results as experiment 1 with significant group differences in the overall simultaneity thresholds between FEP, TRSZ patients and healthy controls (F (2, 16.21) = 12.31, p = 0.001, see figure 2). Planned contrasts revealed that patients had significantly higher thresholds compared to controls (t (19.011) = 5.00, p = 0.000) and that FEP and TRSZ patients also differed significantly with regard to overall thresholds (t (15.70) = 2.345, p = 0.033). Healthy controls (HC) showed identical thresholds to those of experiment 1 (53ms) but both patient groups showed elevated thresholds (FEP: 87ms, TRSZ: 147ms). As in experiment 1, the premask influencing thresholds (F (1, 31) = 6.00, p = 0.020) with thresholds higher for synchronous premasks (HC: 54ms, FEP: 93ms, TRSZ: 150ms) compared to asynchronous ones (HC: 46ms, FEP: 81ms, TRSZ: 143ms). However, compared to experiment 1, the curves of the psychometric functions are similar in shape as those of controls for experiment 2 (see right part of figure 1). This suggests that indeed uncertainty might have influenced simultaneity judgements in patients at SOAs below 110ms and that this uncertainty disappeared given longer target SOAs or that indeed their thresholds were situated close to the max of 110 ms and experiment 1 simply insufficient in locating their threshold due to this.

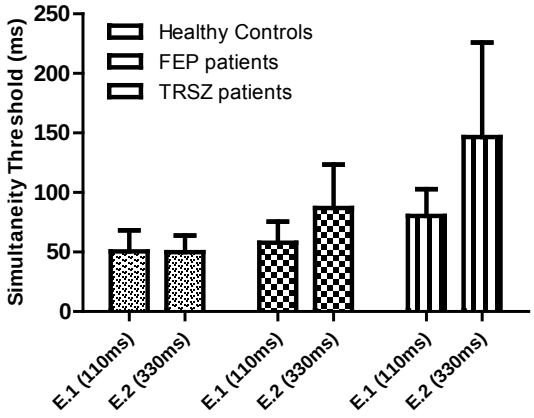

Figure 2: Overall simultaneity thresholds for healthy controls, First-Episode Psychosis and Treatment-Resistant Schizophrenia patients for Experiments 1 and 2.

The fact that both patient groups showed higher thresholds in experiment 2 than 1 but not controls (see figure 2) could have several explanations. Patients that completed the second

experiment or repeated the experiment with longer SOAs might simply have been more severely impaired and thus reflect true elevated simultaneity thresholds. This claim is supported by the fact that we found significant positive correlations between duration of untreated psychosis (DUP) and simultaneity thresholds, with elevated thresholds being more prominent in patients with longer DUPs for both experiments 1 (ρ = .425, $p < 0.01$) and 2 (ρ = .763, $p < 0.01$). Higher thresholds were significantly correlated with negative symptoms, as assessed by the PANSS, in experiment 2 only (ρ = .587, $p < 0.01$). This is in line with the general finding that a predominance of negative symptoms is associated with a poorer outcome, potentially due to the inefficacy of most antipsychotics in eliminating negative symptoms. We cannot exclude that medication might have played a role although this seems unlikely given that the average medication dosages for TRSZ patients were actually lower in experiment 2 (684 mg) than in experiment 1 (684mg) and only marginally bigger in experiment 2 for FEP patients (295mg compared to 261mg). Since medication dosages were not found to be significantly different between the two experiments for either FEP or TRSZ patients, this explanation seems unlikely.

The results of this study are in line with previous findings (Foucher et al., 2007, Giersch et al., 2009) of elevated windows of simultaneity in patients suffering from schizophrenia. The thresholds of controls in this study are identical to the ones originally reported by Brecher (1932) and Elliott et al. (2006). Our findings that FEP patients showed slightly elevated thresholds, especially in experiment 2, though not as pronounced as in the TRSZ group, suggest that brain changes might already be present at the onset of the illness. The fact that FEP patients showed higher thresholds in experiment 2 than in experiment 1 could be due to subclusters of FEP, a possibility that needs to be explored further.

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