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# Duration judgements in patients with schizophrenia

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## ABSTRACT

**Background.** The ability to encode time cues underlies many cognitive processes. In the light of schizophrenic patients' compromised cognitive abilities in a variety of domains, it is noteworthy that there are numerous reports of these patients displaying impaired timing abilities. However, the timing intervals that patients have been evaluated on in prior studies vary considerably in magnitude (e.g. 1 s, 1 min, 1 h etc.).

**Method.** In order to obviate differences in abilities in chronometric counting and place minimal demands on cognitive processing, we chose tasks that involve making judgements about brief durations of time (<1 s).

**Results.** On a temporal generalization task, patients were less accurate than controls at recognizing a standard duration. The performance of patients was also significantly different from controls on a temporal bisection task, in which participants categorized durations as short or long. Although time estimation may be closely intertwined with working memory, patients' working memory as measured by the digit span task did not correlate significantly with their performance on the duration judgement tasks. Moreover, lowered intelligence scores could not completely account for the findings.

**Conclusions.** We take these results to suggest that patients with schizophrenia are less accurate at estimating brief time periods. These deficits may reflect dysfunction of biopsychological timing processes.

## INTRODUCTION

Distortions in the sense of time have featured prominently in psychoanalytical accounts of psychopathology in general (Hartocollis, 1975) and schizophrenia specifically (Seeman, 1976). Indeed, research on time estimation in schizophrenia has a long history (Clausen, 1950; Lhamon & Goldstone, 1956; Webster *et al.* 1962; Lhamon *et al.* 1965; Orme, 1966; Carlson & Feinberg, 1968), and there have been numerous reports of impaired temporal comprehension in these patients (Dilling & Rabin, 1967; Johnson & Peztel, 1971; Lhamon & Goldstone,

1973; Densen, 1977; Wahl & Sieg, 1980; Tysk, 1983*a, b*, 1984, 1990; Rammsayer, 1990; Tracy *et al.* 1998; though see Webster *et al.* 1962; Goldstone *et al.* 1979; Crain *et al.* 1975). Studies have indicated that schizophrenic patients are not simply less accurate in time estimation tasks, but show a particular kind of distortion in timing, in that they tend to overestimate time intervals (Tracy *et al.* 1998; Tysk, 1983*a, b*, 1984, 1990). In an unpublished study, we had participants tap in synchrony with an auditory beat (a metronome at 30 or 60 beats per minute (bpm)) for 5 min. The metronome was then switched off and participants were to continue as before for 5 min, but now were required to generate the rhythm internally. Not surprisingly, when asked to tap without the metronome,

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controls were better able to generate a constant tempo with minimal fluctuations than were patients with schizophrenia. Interestingly, in the 30-bpm task patients disproportionately speeded up their responses over time. Somewhat similar findings have been observed in Parkinson's disease patients who showed shorter inter-response intervals with greater variance (O'Boyle *et al.* 1996).

On the basis of such studies, a timing deficit in schizophrenia would appear to be well established. These findings of timing disturbances may provide important clues concerning the core cognitive deficits in schizophrenia (Andreasen *et al.* 1999). However, it is important to consider whether such findings reflect general impairments in cognitive processes rather than a specific difficulty with temporal processing (Rammsayer, 1990, 1999). For example, memory for temporal order has been shown in amnesic patients with Korsakoff's syndrome to be dissociable from item memory (Shimamura *et al.* 1990). However, we found that, although memory for temporal order was compromised in patients with schizophrenia, this deficit was highly correlated with generally poorer item memory (i.e. recall; Elvevåg *et al.* 2000). This difficulty of dissociating problems in time estimation from those in memory dysfunction is found also in the neurological literature (e.g. Williams *et al.* 1989; Mimura *et al.* 2000).

Moreover, a number of studies of human timing (Fortin *et al.* 1993; Zakay & Block, 1996, 1997; Fortin, 1999) have indicated that accurate estimation of intervals in the order of several seconds requires sustained focusing of attention, and furthermore strategies such as counting can be recruited in making such judgements. The involvement of attentional and strategic processes in these tasks is also potentially problematical, given the well-documented attentional impairments in patients with schizophrenia (e.g. Nuechterlein & Dawson, 1984; Cornblatt *et al.* 1989; Cornblatt & Keilp, 1994), along with working memory deficits (e.g. Elliot *et al.* 1995, 1998; Park *et al.* 1995; Fleming *et al.* 1997; Stone *et al.* 1998). Researchers who have conducted studies of time estimation in schizophrenia are well aware of the role of counting strategies in performing such tasks: Tysk (1983a) has interpreted his results as indicating that patients with schizophrenia 'tend to count seconds too

fast' (p. 913; see also Lhamon & Goldstone, 1956), although we contend that this interpretation is rather unlikely since patients' rate of articulation is likely to be somewhat slower, in the context of general slowing on tests of speed and reaction time (King, 1976). Although it is sometimes explicitly assumed that the rate of counting directly reflects the operation of an internal clock (see Pastor *et al.* 1992), it seems highly likely that the rate of counting will be affected by other factors. Thus, while Tysk may be correct that patients with schizophrenia differ from controls in the nature of their counting, and are impaired on some time estimation tasks, it is difficult to conclude that this impairment reflects deficits in basic timing mechanisms.

Although many of the reported deficits in timing in schizophrenia may be explicable in terms of impairments in other cognitive processes, there are nevertheless reasons to believe that primitive timing mechanisms are also impaired in this population. Rammsayer (1990) has shown that patients with schizophrenia perform worse than controls on a task that requires discrimination of very brief durations (in the order of 50–100 ms), a task that is perceptual in nature and places minimal demands on non-temporal processes. In addition, extensive research on animal and human timing has suggested that timing mechanisms are affected by the functioning of dopamine (Maricq *et al.* 1981; Maricq & Church, 1983; Church, 1984; Meck, 1986, 1996; Rammsayer, 1989, 1993, 1997, 1999; Rammsayer & Gallhofer, 1995; Harrington & Haaland, 1998), a neurochemical system that is implicated in schizophrenia (for a review see Carlsson *et al.* 1999). Moreover, there is considerable debate regarding the role of the cerebellum in representing temporal information (for a review see Ivry, 1997). The dysfunction of timing mechanisms in schizophrenia is therefore further complicated by the fact that these patients have been shown to have cerebellar pathology (for a review see Martin & Albers, 1995) and 'cognitive dysmetria' due to postulated dysfunctional prefrontal-thalamic-cerebellar circuitry (Andreasen *et al.* 1996).

In the current study we sought to examine the timing problem in schizophrenia while attempting to minimize the role of confounding cognitive processes and focus more directly on

timing mechanisms by employing brief stimuli so that the use of certain strategies, such as counting, would be reduced or eliminated. The current research focuses on examination of what processes may be impaired in time estimation over short time scales. This information may then shed light on how these faulty processes give rise to the cognitive deficits at the level assessed in standard psychological assessments. The aim of the current study was to examine whether timing was impaired in schizophrenia by examining performance on two tasks that are generally agreed to measure the functioning of certain timing mechanisms directly, and which place a limited demand on other cognitive processes. These tasks are temporal generalization (Wearden, 1992; Wearden & Towse, 1994; Wearden *et al.* 1997a) and temporal bisection (Allan & Gibbon, 1991; Wearden, 1991b; Wearden & Ferrara, 1995, 1996; Nichelli *et al.* 1996; Penney *et al.* 1998) which are analogues of animal timing tasks (Church & Deluty, 1977; Church & Gibbon, 1982). Although, these tasks only measure certain aspects of timing behaviour, they offer a number of advantages for comparing clinical populations with controls. The tasks involve simple comparative judgements about durations and thus are easy to explain to participants. The stimulus durations that are employed are short enough (typically less than 1 s) to prevent chronometric counting (although longer durations can be used if counting is suppressed; Wearden *et al.* 1997a). Furthermore, the bisection task has been used successfully to demonstrate deficits in timing of short intervals in patients with cerebellar degeneration or frontal damage (Nichelli *et al.* 1995, 1996). A further advantage of these tasks is that mathematical models that assume that performance is based directly on internal clock processes provide extremely good accounts of the data generated from them under a wide variety of experimental conditions (Allan & Gibbon, 1991; Wearden, 1991; Wearden & Ferrara, 1995, 1996; Wearden *et al.* 1997b; Penney *et al.* 1998) in healthy individuals. Most of these formal models fall within the general framework of Scalar Expectancy Theory (Gibbon, 1977; Gibbon *et al.* 1984), which is a successful and widely applied theory of timing, accounting for a broad range of animal and human data.

Table 1. *Background scores for the control participants and patients*

Measure	Controls		Patients	
	Mean	(s.d.)	Mean	(s.d.)
Age (years)	29.43	(11.50)	32.80	(8.39)
WRAT-R IQ**	112.48	(9.32)	102.63	(13.28)
WAIS-R IQ**	118.23	(20.81)	91.24	(18.87)
Cattell IQ**	109.39	(12.56)	88.59	(13.06)

\*\*  $P < 0.01$ .

## METHOD

### Participants

Nineteen in- or out-patients (15 male and four female) from the National Institute of Mental Health participated in this study. All patients fulfilled DSM-IV criteria for schizophrenia, as determined by the Structured Clinical Interview for DSM-IV (SCID) with three psychiatrists reaching a consensus diagnosis. Patients generally had multiple hospital admissions due to incomplete responses to conventional treatments. All of the patients were receiving atypical neuroleptic medication at the time of the study (11 on clozapine or olanzapine, seven on risperidone and one on quetiapine) and two were also receiving typical neuroleptic medication (fluphenazine). Four patients also received anticholinergic medication, and 16 were on adjunctive medication. Twenty-three normal healthy control volunteers (six males and 17 females) were recruited through the National Institutes of Health volunteer panel. Out-patients and control volunteers were paid for their participation.

No participant (control or patient) had a history of traumatic brain injury, epilepsy, developmental disorder, diagnosable current substance dependence, or known neurological condition. All participants had normal or normal corrected vision. The internal review board at the National Institute of Mental Health approved this study and informed consent was obtained from all participants prior to testing.

Table 1 shows the mean ages and background test scores of the patients and controls. Three baseline tests were used to index intellectual function. The first was a test of reading proficiency – the Wide Range Achievement Test-Reading (WRAT-R) (Jastak & Wilkinson, 1984), which is widely used as a putative

measure of pre-morbid intellectual functioning (Wiens *et al.* 1993; Goldberg *et al.* 1995; Kremen *et al.* 1996). The second was a standard test of current non-verbal or fluid intelligence: Cattell's Culture Fair Intelligence Test (Cattell, 1971; Institute for Personality and Ability Testing, 1973), Scale 2, Form A. The test involves timed non-verbal problem-solving. Participants were also evaluated on a short version of the Wechsler Adult Intelligence Scale (WAIS-R) (Wechsler, 1981; see also Kaufman, 1990; Missar *et al.* 1994). The substantial drop in intelligence from estimated pre-morbid function is often reported in schizophrenia (Weickert *et al.* 2000). Significant differences were revealed by *t* tests (in all cases,  $P < 0.01$ ) between the groups in terms of scores on the WRAT-R, Cattell Culture Fair Intelligence Test and WAIS-R. There was no significant group difference in age ( $P > 0.1$ ). Patients' digit span (forwards and backwards) was also assessed (Wechsler Memory Scale-Revised, Wechsler, 1987), and their average raw combined span was 13.8 (out of 24; s.d. = 4.1).

#### Apparatus and stimuli

An Apple Macintosh computer running Cedrus Superlab software controlled stimulus generation for Experiments 1 and 2. The auditory stimuli were 500 Hz tones produced by the computer's speaker, and the visual displays were presented on a black-and-white screen. All participants were tested individually, and gave verbal responses.

### EXPERIMENT 1: TEMPORAL GENERALIZATION

In the temporal generalization task, participants were initially presented with a standard duration tone (500 ms), and at the test phase they judged whether presented stimuli of various durations (125, 250, 375, 625, 750 and 875 ms) were or were not the standard. Plots of the proportions of positive responses to standard and non-standard test stimuli yield characteristic generalization gradients, with the probability of giving an erroneous positive response to a non-standard stimulus declining with its 'distance' from the standard (Wearden, 1992; Wearden *et al.* 1997*a, b*). The index of accuracy of time estimation on this task is the steepness of such generalization gradients, with previous

studies showing that young children and elderly adults will produce relatively flat gradients (i.e. greater numbers of erroneous positive responses to non-standard stimuli relative to the number of correct positive responses to standard stimuli; McCormack *et al.* 1999; Wearden *et al.* 1997*b*).

When plotted on a linear scale, such gradients are normally asymmetrical, with positive responses more likely to stimuli that are longer than the standard than to those shorter than the standard but of equal distance away (Wearden, 1992; although this is not always true for animal performance on temporal generalization tasks, Church & Gibbon, 1982). For example, if the standard were 500 ms, more erroneous positive responses are normally given to a 625 ms stimulus than a 375 ms stimulus. This asymmetry reflects a basic property of human timing (Wearden, 1993). However, the extent to which gradients are asymmetrical in this way in any given study also reflects the veridicality of long-term memory of the standard. Previous research suggests that the representation of the time intervals may become distorted in long-term memory (Meck & Church, 1987*a*; Meck *et al.* 1987; Shurtleff *et al.* 1992), with the standard being systematically mis-remembered as being either shorter (McCormack *et al.* 1999) or longer (Wearden *et al.* 1999; McCormack *et al.* 2002) than it actually was. Since responses are made by comparing the memory representation of the standard with the representation of the current test stimulus, such distortion will affect the probability that erroneous positive responses are given to stimuli shorter or longer than the standard. Thus, the degree of asymmetry of the generalization gradient will in part depend on the extent to which such distortion occurs.

The present study compared performance of schizophrenic patients and controls on such a task. In particular, we were interested in whether the patients would produce flatter gradients than controls, indicating less accurate interval timing, and whether the degree of asymmetry of their gradients would differ, indicating impaired or distorted memory for durations.

#### Procedure

Participants were seated in a quiet room in front of a computer monitor. A version of the generalization task was used that had been designed for participants who may find it difficult to

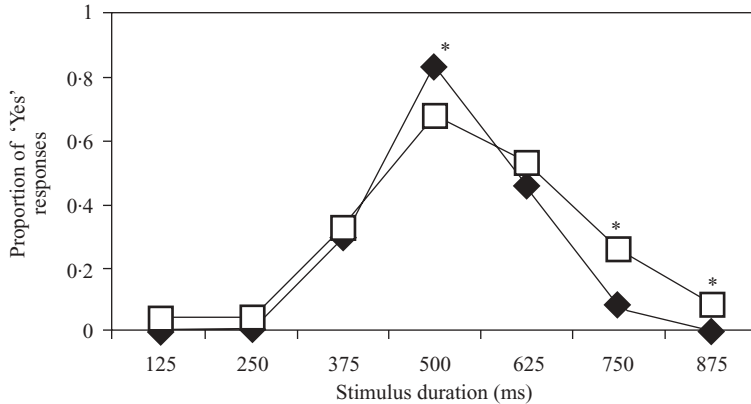


FIG. 1. Proportion of 'Yes' responses as a function of stimulus duration for schizophrenic patients ( $\square$ ) and control participants ( $\blacklozenge$ ) in the temporal generalization task (Experiment 1). (\*Group difference significant in *post hoc t* tests.)

understand abstract computerized tasks (such as children or very elderly adults; McCormack *et al.* 1999). Rather than instructing participants to identify a standard, the stimulus identification task was set in an easily comprehensible context. Participants heard a tone 500 ms in length while viewing a picture of an owl on a computer screen, and they were told it was 'the sound made by the owl'. Participants were told that the owl's sound was always the same pitch and was always of the same duration, and then were presented with the owl's sound four more times. Participants then had four demonstration trials in which they heard tones of length 500, 750, 500 and 250 ms. After each tone was played, they were told whether the tone was or was not the owl's sound, and it was then explained to participants that their task was to judge whether other sounds were or were not the owl's sound. Participants then had five practice trials: one of the practice trials was the 500 ms tone and one each of the other test stimuli that had not been previously played (125, 375, 625 and 875 ms). Participants were given feedback as to whether their responses were correct or not. Testing immediately followed the last practice trial, with test stimuli presented in eight blocks of eight trials (64 trials in total). Each block included one presentation of each nonstandard tone (e.g. 125, 250, 375, 625, 750 and 875 ms) and two presentations of the standard 'owl' tone of 500 ms. Participants were assigned to one of two versions of the task, with the order in which the stimuli were presented in each block

reversed between versions. Responses were given verbally, and were recorded by the experimenter. As in the practice trials, feedback was given after each response.

## Results

Accuracy was first examined as overall 'yes' responses across tone length. An analysis of variance (ANOVA) was conducted on these data with diagnostic group (controls and patients) as a between-subjects factor and tone-length as the within-subjects factor (125, 250, 375, 500, 625, 750 and 875 ms). The main effect of group failed to reach significance though a trend was present,  $F(1, 40) = 3.57$ , mean s.e. = 0.038,  $P = 0.07$ , but there was a significant effect of tone-length,  $F(6, 240) = 134.64$ , mean s.e. = 0.024,  $P < 0.01$ , and, importantly, there was a significant interaction between group and tone-length,  $F(6, 240) = 4.293$ , mean s.e. = 0.024,  $P = 0.01$  (see Fig. 1).

*Post hoc t* tests were calculated to compare the groups at the different stimulus durations, correcting for multiple tests of comparison using a modified Bonferroni method (Holm's (1979) sequentially rejective procedure). These revealed that the patients made significantly more erroneous positive responses to the 750 and 875 ms stimuli, and significantly fewer correct positive responses to the 500 ms stimulus than did controls.

In order to ascertain whether these results might be attributable to a decay of the standard in general, we compared performance on the

first half of the experiment with the second half by calculating ANOVAs separately for patients and controls. Although such an analysis cannot totally eliminate the possibility of memory decay operating during the task, the fact that there was not a significant effect of time in either group (in both cases,  $P > 0.1$ ) thus does not provide support for the idea of a general mnemonic failure (i.e. forgetting) over time.

Further analyses examined the shape of the generalization gradients in more detail. Inspection of the gradients (see Fig. 1) suggests that both groups showed the usual asymmetry, with more positive responses to stimuli longer than the standard than to those shorter than the standard but of equal distance from it. This asymmetry appears to be more marked in the gradient of the group of patients. Asymmetry was tested by separate comparisons of the proportions of positive responses to each of the three pairs of durations of equal distance from the standard. There was insufficient variance in the data to compare the 125 and the 875 ms stimuli. However, both groups produced significantly more positive responses to the 750 than the 250 ms stimulus ( $F(1, 22) = 9.16$ , mean s.e. = 0.006,  $P < 0.01$  for controls;  $F(1, 18) = 17.3$ , mean s.e. = 0.026,  $P < 0.01$  for the group of patients), with the patients, but not the controls, also producing significantly more positive responses to the 625 than the 375 ms stimulus ( $F(1, 18) = 4.47$ , mean s.e. = 0.083,  $P < 0.05$ ). Thus, asymmetry was significant to some extent for both groups, and extended to more stimulus pairs for patients than the controls.

Since the groups differed significantly on all three measures of IQ, subsequent analyses addressed the possibility that the significant interaction between group and tone length might be a result of such differences. An analysis of covariance (ANCOVA) with a between-subjects factor of group, a within-subjects factor of tone length, and three covariates of WAIS-R, WRAT-R and Cattell scores was carried out, with four participants excluded from the analysis for whom scores on one or more of the IQ measures were not available. Inspection of the epsilon values, to check the assumption of homogeneity of variance, showed that there was a high degree of departure from the sphericity assumption (Greenhouse-Geisser  $\epsilon = 0.39$ ); we therefore report the results of the corresponding

multivariate analysis. When WAIS-R, WRAT-R, and Cattell scores were covaried in this way, the interaction between group and tone length was near significance ( $F(6, 28) = 2.33$ ,  $P = 0.06$ ). This suggests that group differences in IQ contributed to group differences in performance to some degree, although the fact that the interaction remained marginally significant when all three IQ measures were taken into account indicates that the results cannot be completely explained in this way. Moreover, correlating patients' forwards and backwards digit span with a single measure of the proportion correct (the number of 'yes' responses to the 500 ms stimulus divided by the total number of 'yes' responses) did not reveal a significant correlation ( $r(19) = -0.161$ ,  $P > 0.5$  for forward digit span;  $r(19) = 0.241$ ,  $P > 0.1$  for backward span), a finding we take to suggest that working memory alone (as measured by the digit span task) cannot sufficiently explain the results from Experiment 1.

## EXPERIMENT 2: TEMPORAL BISECTION

In the temporal bisection task, there were two standards, one long and one short, and participants judged whether test stimuli were more similar to the long or to the short standard. Like the generalization task, the bisection task is based on a paradigm originally used to study animal timing (Church & Deluty, 1977; Maricq *et al.* 1981), which has been successfully adapted for use with humans (Allan & Gibbon, 1991; Wearden, 1991; Nichelli *et al.* 1995, 1996; Wearden & Ferrara, 1995, 1996; McCormack *et al.* 1999; Droit-Volet & Wearden, 2003). Data from this task are normally plotted as S-shaped bisection curves, in which the proportion of 'long' responses is plotted as a function of stimulus duration. Performance is indicated by the steepness of this function, with the bisection curves of patients with frontal damage (Nichelli *et al.* 1995), and patients with cerebellar degeneration (Nichelli *et al.* 1996) being less steep than those of healthy adults (at least over some ranges of intervals).

Another aspect of this function that is usually analysed is the bisection point. This is the hypothetical duration at which responses would be equally divided between long and short. In human timing, this point is normally located

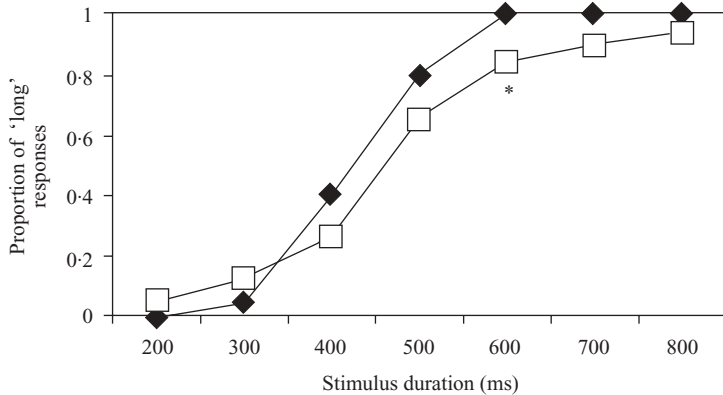


FIG. 2. Proportion of 'long' responses as a function of stimulus duration for schizophrenic patients (□) and control participants (◆) in the temporal bisection task (Experiment 2). (\*Group difference significant in *post hoc* *t* tests.)

between the arithmetic and the geometric means of the two standard durations, although it is often closer to the arithmetic mean when the ratio of the short to long standards is large (see Allan & Gibbon, 1991).<sup>†</sup> The formal measure of steepness of the bisection gradients is the Weber ratio. This is calculated using the bisection point and difference limen. The bisection point is the hypothetical duration at which 50% of responses are classified as 'long', and the difference limen is half the difference between the hypothetical durations at which 25% and 75% of responses are long. Thus, the Weber ratio is calculated by dividing the difference limen by the bisection point. The Weber ratio provides a measure of a participant's precision and ability to discriminate specific stimuli that is independent of the actual values of the physical stimuli.

We compared performance of schizophrenic patients and controls on this temporal bisection task. On the basis of the findings of Experiment 1, we predicted that patients would produce flatter gradients than controls, indicating less accurate interval timing.

### Procedure

Participants were seated in a quiet room in front of a computer monitor. As in Experiment 1, the task was set in a context designed to make it easy for participants to understand. A computer

monitor displayed two birds, a big one and a small one. Participants were told that the two birds made sounds of different lengths and that the big bird made a long sound and the small bird made a short sound. Participants then heard examples of the short (200 ms) and long (800 ms) sound while the appropriate picture was shown on the screen. There were five alternating presentations of each of the sounds. Participants then had seven practice trials (one example of each of the stimuli: 200, 300, 400, 500, 600, 700 and 800 ms) during which they heard a tone and had to state whether it was more like the big bird's or the small bird's sound. No feedback was given as to participants' accuracy. After the practice trials, participants completed five blocks of seven trials, with each block containing one presentation of each stimulus (35 trials in total). The experimenter recorded the responses given ('small bird' or 'big bird'). As in Experiment 1, participants were assigned to one of two versions of the task, with the order of stimulus presentations within each block reversed between versions.

### Results

Fig. 2 shows the bisection curves for the two groups. Performance was first examined as the overall proportion of 'long' responses across tone length. An analysis of variance was conducted on these data with diagnostic group (controls and patients) as a between-subjects

<sup>†</sup> The notes will be found on page 1259.



factor and tone-length as the within-subjects factor (200, 300, 400, 500, 600, 700 and 800 ms). There was a main effect of group,  $F(1, 40) = 5.10$ , mean s.e. = 0.066,  $P < 0.03$ , with the control group producing more 'long' responses than the patient group, and a significant effect of tone-length,  $F(6, 240) = 239.63$ , mean s.e. = 0.030,  $P < 0.01$ , and importantly there was a significant interaction between group and tone-length,  $F(6, 240) = 3.34$ , mean s.e. = 0.030,  $P < 0.01$ .

*Post hoc t* tests, corrected as before for multiple tests of comparison (Holm's (1979) sequentially rejective procedure), which compared the groups at the different stimulus durations revealed a significant group difference on the 600 ms stimulus only.

As in the analysis of the data from Experiment 1, we examined whether the significant interaction between group and tone length might be a result of group differences in IQ. An analysis of covariance (ANCOVA) with a between-subjects factor of group, a within-subjects factor of tone length, and three covariates of WAIS-R, WRAT-R, and Cattell scores was carried out, with four participants excluded from the analysis for whom scores on one or more of the IQ measures were not available. However, checking the assumption of homogeneity of variance by inspecting the epsilon values showed that there was a high degree of departure from the sphericity assumption (Greenhouse-Geisser  $\epsilon = 0.47$ ); therefore, we report the results of the corresponding multivariate analysis. When WAIS-R, WRAT-R, and Cattell scores were covaried out in this way, the interaction between group and tone length remained significant ( $F(6, 28) = 2.53$ ,  $P < 0.05$ ). Thus, group differences in IQ cannot explain the effect of group on performance. Moreover, correlating patients' forwards and backwards digit span separately with the Weber ratio (see below) did not reveal significant correlations ( $r(17) = -0.247$ ,  $P > 0.1$  for forward digit span;  $r(17) = -0.037$ ,  $P > 0.1$  for backward digit span) a finding we take to suggest that working memory alone (as measured by the digit span task) cannot sufficiently explain the results from the temporal bisection task.

In order to calculate the values of the difference limen and bisection point every participant's bisection curve was modelled using the

following equation:

$$P(\text{long}|D_i) = \frac{1}{1 + e^{-s \cdot (D_i - \text{mean})}}$$

where  $P(\text{long}|D_i)$  is the probability of responding 'long' to a given test stimulus  $D_i$ ,  $s$  is the slope of the S-shaped curve and *mean* is the Bisection Point. For each participant  $s$  and *mean* were estimated separately. The median  $R^2$  value obtained was 0.99 for the controls, and 0.98 for the 17 patients we included.

The mean difference limen of the group of patients was 27.28, and that of the control group was 57.17.<sup>2</sup> An ANOVA found that there was a significant difference between the groups in the size of the difference limen,  $F(1, 38) = 6.17$ , mean s.e. = 1416.00,  $P < 0.02$ . Inspection of the bisection gradients (Fig. 2) suggests that the bisection points for the two groups are somewhere between the arithmetic (500 ms) and the geometric (400 ms) mean. The mean bisection point was 431.74 ms for the control group and 481.59 ms for the patients. An ANOVA found a significant difference between the groups in the value of the bisection point,  $F(1, 38) = 7.04$ , mean s.e. = 3450.70,  $P < 0.02$ .

The difference limen and the bisection point were used to calculate the Weber ratio. The mean Weber ratio of the control group was found to be 0.064, and that of the patient group was 0.12. An ANOVA found a marginally significant difference between the groups,  $F(1, 38) = 4.04$ , mean s.e. = 0.007,  $P = 0.052$  in the value of the Weber ratio. Although the steepness of the curves is different between the groups, as shown by the significant group effect on the difference limen, the difference between them is only marginally significant when steepness is adjusted to take into account the bisection point.

## DISCUSSION

In both Experiments 1 and 2, the performance of patients with schizophrenia differed from that of healthy adults on tasks that involved making judgements about the durations of brief auditory stimuli. Our results indicate that timing is impaired in patients even when the tasks involve judgements about very short durations (see also Rammsayer, 1990). Importantly, these

impairments could not be explained fully in terms of group differences in estimated pre-morbid or current intelligence or patients' poor working memory ability (as measured by digit span<sup>3</sup>). In Experiment 1, patients' generalization gradient was less steep than that of controls. Although there were significant group differences in performance on the temporal bisection task, the difference in the Weber ratio between groups was only marginally significant. The fact that group differences were more pronounced on the generalization task, notwithstanding the provision of feedback in Experiment 1 but not 2, is consistent with findings of previous studies that have indicated that the generalization task is a more sensitive task than the bisection task (Wearden *et al.* 1997*a, b*).

In addition to group differences in overall levels of performance, some features of the data suggested that there may be qualitative differences between timing in patients and controls. In Experiment 1, the generalization gradient was more markedly asymmetrical in patients than in controls. Furthermore, in Experiment 2, the bisection point was larger for patients than for controls. These effects can be addressed within the framework of Scalar Expectancy Theory. Formal models of timing assume two separate mnemonic components are involved in the tasks in Experiments 1 and 2. Long-term memory holds the standard, and working memory is used to compare the test durations with the retrieved representation of the standard from long-term memory. If the representation of a standard duration in long-term memory is systematically distorted (e.g. remembered as longer than it really is) effects akin to those observed here may be obtained. For example, McCormack *et al.* (1999) attributed qualitative differences in children's temporal generalization to memory distortion. If the standards are remembered by patients as longer than they truly are, the two key effects reported above may be explained. Greater asymmetric generalization (Experiment 1) could result because a given test duration that is longer than the true standard will be closer to the distorted memory of the standard. In the bisection experiment, a proportional distortion (e.g. a 10% increase) of memory of both the short and the long standards will lead to a mid-range stimulus becoming relatively closer to the remembered short

standard than to the remembered long standard. However, it should be noted that alternative explanations may be possible. For example, greater asymmetry in temporal generalization tasks is often associated with lower overall levels of performance (Wearden *et al.* 1997*a, b*; McCormack *et al.* 1999), and rightward shifts in bisection point could result from a simple bias against responding long.

We note that not all timing deficits in schizophrenia can be explained by reference to distorted standards. Indeed, Rammsayer's (1990) findings would suggest that patients with schizophrenia are impaired on tasks that do not have a long-term memory component, implicating clock processes. Further research explicitly addressed at partitioning variability in performance to perceptual *versus* memory processes is necessary to resolve this issue.

Unlike Rammsayer's (1990) study of timing of brief intervals in schizophrenia, the current tasks have a long-term memory component (since the standard is assumed to be held in long-term or reference memory), a component that appears not to be involved in temporal discrimination of extremely brief intervals (Rammsayer, 1999). It is not clear to what extent either of the memory components in formal models derived from Scalar Expectancy theory can be identified with the types of memory measured by standard memory tasks (but see Fortin, 1999 for an alternative view). However, in the light of the absence of a general mnemonic failure over time or a significant correlation with a working memory measure such as digit span, we suggest that simply explaining the findings in terms of working memory would be insufficient. Indeed, the type of memory distortion that might underlie our findings is generally considered to be a long-term memory factor rather than a working memory one (although we acknowledge the current major research effort to develop a variety of techniques with which to disentangle working memory from long-term memory, from short-term memory and from controlled attentional processes – see Engle *et al.* 1999).

Attempting to separate differences between specific deficits and generalized deficits (as in the current study) is a major issue in cognitive research in patients with schizophrenia, especially those with chronic courses. Indeed, it

is important to establish whether patients' performance reflects the illness itself or whether it is attributable to the difficulty level of the tasks (Chapman & Chapman, 1978). We have preliminary evidence for patients demonstrating an impairment in stimulus identification when the stimuli are tones of varying durations, but not when the stimuli are lines of varying lengths. Importantly, task difficulty issues alone could not account for these new data since the line length judgement task did not seem to be an easier task given the large number of errors made by both groups. We regard this as evidence that patients do not have a global problem with stimulus identification, and thus take our findings to support the notion of a specific impairment in timing abilities in patients with schizophrenia.

On the basis of the current findings and those of numerous previous studies, schizophrenic patients appear to have deficits in timing in a very wide range of time intervals from <100 ms (Rammsayer, 1990), <1 s (the current study) through to intervals in the order of seconds (Tracy *et al.* 1998) and many minutes (Tysk, 1983*a*). An unresolved, but important, issue in timing research is whether there are separable clock systems for these different interval ranges. A considerable body of research links clock processes with the basal ganglia (Meck, 1986; Artieda *et al.* 1992; Pastor *et al.* 1992; Harrington & Haaland, 1998; Harrington *et al.* 1998*a*), although Ivry and colleagues (Ivry & Keele, 1989; Ivry, 1993; Clarke *et al.* 1996) have argued that the cerebellum is heavily implicated not only in motor timing but in at least some kinds of temporal duration judgements. Other neuroanatomical areas are associated with the memory and decision processes in the timing system (Nichelli *et al.* 1993, 1995; Shaw & Aggleton, 1994). Given that time perception relies on a variety of hierarchically organized structures and processes it is not surprising that the underlying cortical networks are vast (e.g. right hemisphere prefrontal-inferior parietal network; Harrington *et al.* 1998*b*). Moreover, it seems likely that attention and working memory contribute to temporal perception. Thus, given that schizophrenia may be considered to be a disorder of connectivity (Weinberger *et al.* 1992; Fletcher *et al.* 1999; Tononi & Edelman, 2000), including problems in attention and working

memory, the challenge to fractionate the way in which the dynamic network of cortical and subcortical activation contributes to the function and dysfunction of the different components of time perception is clearly important (see Volz *et al.* 2001).

This issue is further complicated by the involvement of the dopaminergic and cholinergic systems in timing, suggested by reports of deficits in both motor timing and time estimation or perception in Parkinson's disease (for reviews, see Gibbon *et al.* 1997; Harrington & Haaland, 1998; but see Ivry & Keele, 1989), and from research with animals and humans who have been administered dopamine antagonists (Meck, 1986, 1996; Rammsayer, 1993, 1999) or agonists (Stubbs & Thomas, 1974; Rapp & Robbins, 1976; Rammsayer, 1990; Rammsayer & Vogel, 1992), or choline modulators (Meck & Church, 1987*b*; for a review see Meck, 1996). Regarding the issue of whether the observed impairments in duration judgements of the patients with schizophrenia are side-effects of neuroleptic medication, evidence from previous studies is mixed (Lhamon & Goldstone, 1956; Goldstone *et al.* 1979; Tysk, 1983*a*; Tracy *et al.* 1998) with different neuroleptics exerting different effects on timing tasks (Meck, 1986; Rammsayer, 1990, 1997; Rammsayer & Gallhofer, 1995). It is possible that the use of a psychiatric control group (especially unmedicated) could have helped clarify the particular relevance of time judgement deviations in schizophrenia. The patients in the current study were on neuroleptics and the effects on timing of many of the specific drugs that the patients were taking have not been explored. Specifically, the consequences of patients with schizophrenia who are on drugs that manipulate dopaminergic and cholinergic systems warrants examination, in a patient sample in which this is possible, and in which there is the statistical power to evaluate the effect of cholinergic modulation on the time-keeper in patients with schizophrenia. Clearly, further research is necessary to establish if such medication does contribute to the timing deficit in schizophrenia.

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## NOTES

- <sup>1</sup> The geometric mean is the square root of the product of the standards.
- <sup>2</sup> Data from two participants (both patients) were excluded from analysis. There was one participant for whom no clear bisection point could be determined, and there was a further participant who had a bisection point which was more than two standard deviations away from the group mean.
- <sup>3</sup> We note that digit span is only one of many measures of working memory, and that other measures are likely to be important as well.

## REFERENCES

- Allan, G. A. & Gibbon, J. (1991). Human bisection at the geometric mean. *Learning and Motivation* **22**, 39–58.
- Andreasen, N. C., O'Leary, D. S., Cizadlo, T., Arndt, S., Rezai, K., Boles Ponto, L. L., Watkins, G. L. & Hichwa, R. D. (1996). Schizophrenia and cognitive dysmetria: a positron-emission tomography study of dysfunctional prefrontal-thalamic-cerebellar circuitry. *Proceedings of the National Academy of Science, USA* **93**, 9985–9990.
- Andreasen, N. C., Nopoulos, P., O'Leary, D. S., Miller, D. D., Wassink, T. & Flaum, M. (1999). Defining the phenotype of schizophrenia: cognitive dysmetria and its neural mechanisms. *Biological Psychiatry* **46**, 908–920.
- Artieda, J., Pastor, M. A., Lacruz, F. & Obeso, J. A. (1992). Temporal discrimination is abnormal in Parkinson's disease. *Brain* **115**, 199–210.
- Carlson, V. R. & Feinberg, I. (1968). Individual variations in time judgement and the concept of an internal clock. *Journal of Experimental Psychology* **77**, 631–640.
- Carlsson, A., Waters, N. & Carlsson, M. L. (1999). Neurotransmitter interactions in schizophrenia-therapeutic implications. *Biological Psychiatry* **46**, 1388–1395.
- Cattell, R. B. (1971). *Abilities: Their Structure, Growth and Action*. Houghton-Mifflin: Boston.
- Chapman, L. J. & Chapman, J. P. (1978). The measurement of differential deficit. *Journal of Psychiatry Research* **14**, 303–311.
- Church, R. M. (1984). Properties of the internal clock. In *Timing and Time Perception* (ed. J. Gibbon and L. G. Allan), pp. 566–582. New York Academy of Sciences: New York.
- Church, R. M. & Deluty, M. Z. (1977). Bisection of temporal intervals. *Journal of Experimental Psychology: Animal Behavioral Processes* **3**, 216–228.
- Church, R. M. & Gibbon, J. (1982). Temporal generalization. *Journal of Experimental Psychology: Animal Behavior Processes* **8**, 165–185.
- Clarke, S., Ivry, R., Grinband, J., Roberts, S. & Shimizu, N. (1996). Exploring the domain of cerebellar timing systems. In *Time, Internal Clocks, and Movement* (ed. M. A. Pastor and J. Artieda), pp. 257–280. Elsevier Science: Amsterdam.
- Clausen, J. (1950). An evaluation of experimental methods of time judgment. *Journal of Experimental Psychology* **40**, 756–761.
- Cornblatt, B. A. & Keilp, J. G. (1994). Impaired attention, genetics, and the pathophysiology of schizophrenia. *Schizophrenia Bulletin* **20**, 31–46.
- Cornblatt, B. A., Lenzenweger, M. F. & Erlenmeyer-Kimling, L. (1989). The Continuous Performance Test, Identical Pairs Version: II. Contrasting attentional profile in schizophrenic and depressed patients. *Psychiatry Research* **29**, 65–85.
- Crain, P., Goldstone, S. & Lhamon, W. T. (1975). Temporal information processing and psychopathology. *Perceptual and Motor Skills* **41**, 219–224.
- Densen, M. E. (1977). Time perception and schizophrenia. *Perceptual and Motor Skills* **44**, 436–438.
- Dilling, C. A. & Rabin, A. I. (1967). Temporal experience in depressive states and schizophrenia. *Journal of Consulting Psychology* **31**, 604–608.
- Droit-Volet, S. & Wearden, J. H. (2003). Temporal bisection in children. *Journal of Experimental Child Psychology*.
- Elliot, R., McKenna, P. J., Robbins, T. W. & Sahakian, B. J. (1995). Neuropsychological evidence for fronto-striatal dysfunction in schizophrenia. *Psychological Medicine* **25**, 619–630.
- Elliot, R., McKenna, P. J., Robbins, T. W. & Sahakian, B. J. (1998). Specific neuropsychological deficits in schizophrenic patients with preserved intellectual function. *Cognitive Neuropsychology* **3**, 45–70.
- Elvevåg, B., Egan, M. F. & Goldberg, T. E. (2000). Memory for temporal order in patients with schizophrenia. *Schizophrenia Research* **46**, 187–193.
- Engle, R. W., Kane, M. J. & Tuholski, S. W. (1999). Individual differences in working memory capacity and what they tell us about controlled attention, general fluid intelligence, and functions of the prefrontal cortex. In *Models of Working Memory: Mechanisms of Active Maintenance and Executive Control* (ed. A. Miyake and P. Shah), pp. 102–134. Cambridge University Press: Cambridge.
- Fleming, K., Goldberg, T. E., Binks, S., Randolph, C., Gold, J. M. & Weinberger, D. R. (1997). Visuospatial working memory in patients with schizophrenia. *Biological Psychiatry* **41**, 43–49.
- Fletcher, P., McKenna, P. J., Friston, K. J., Frith, C. D. & Dolan, R. J. (1999). Abnormal cingulate modulation of fronto-temporal connectivity in schizophrenia. *Neuroimage* **9**, 337–342.
- Fortin, C. (1999). Short-term memory in time interval production. *International Journal of Psychology* **34**, 308–316.
- Fortin, C., Rousseau, R., Bourque, P. & Kirouac, E. (1993). Time estimation and concurrent nontemporal processing: specific interference from short-term-memory demands. *Perceptual Psychophysiology* **53**, 536–548.
- Gibbon, J. (1977). Scalar expectancy theory and Weber's law in animal timing. *Psychological Review* **84**, 278–325.
- Gibbon, J., Church, R. M. & Meck, W. H. (1984). Scalar timing in memory. In *Timing and Time Perception. Annals of New York Academy of Sciences* 423 (ed. J. Gibbon and L. Allan), pp. 52–77. New York Academy of Sciences: New York.
- Gibbon, J., Malapani, C., Dale, C. L. & Gallistel, C. R. (1997). Towards a neurobiology of temporal cognition: advances and challenges. *Current Opinion in Neurobiology* **7**, 170–184.
- Goldberg, T. E., Torrey, E. F., Gold, J. M., Bigelow, L. B., Ragland, R. D., Taylor, E. & Weinberger, D. R. (1995). Genetic risk for neuropsychological impairment in schizophrenia: a study of monozygotic twins discordant and concordant for the disorder. *Schizophrenia Research* **17**, 77–84.
- Goldstone, S., Nurnberg, H. G. & Lhamon, W. T. (1979). Effects of trifluoperazine, chlorpromazine, and haloperidol upon temporal information processing by schizophrenic patients. *Psychopharmacology (Berlin)* **65**, 119–124.
- Harrington, D. L. & Haaland, K. Y. (1998). Sequencing and timing operations of the basal ganglia. In *Timing of Behavior: Neural, Psychological, and Computational Perspectives* (ed. D. A. Rosenbaum and C. E. Collyer), pp. 35–61. MIT Press: Cambridge, MA.
- Harrington, D. L., Haaland, K. L. & Hermanowicz, N. (1998a). Temporal processing in the basal ganglia. *Neuropsychology* **12**, 3–12.
- Harrington, D. L., Haaland, K. Y. & Knight, R. T. (1998b). Cortical networks underlying mechanisms of time perception. *Journal of Neuroscience* **18**, 1085–1095.
- Hartocollis, P. (1975). Time and affect in psychopathology. *Journal of the American Psychoanalysis Association* **23**, 383–395.
- Holm, S. (1979). A simple sequentially rejective multiple test procedure. *Scandinavian Journal of Statistics* **6**, 65–70.

- Institute for Personality and Ability Testing (1973). *Measuring Intelligence with the Culture Fair Test*. The Institute for Personality and Ability Testing: Champaign, IL.
- Ivry, R. (1993). Cerebellar involvement in the explicit representation of temporal information. In *Temporal Information Processing in the Nervous System: Special Reference to Dyslexia and Dysphasia*. *Annals of the New York Academy of Sciences* 682 (ed. P. Tallal, A. M. Galburda, R. R. Llinás and C. Von Euler), pp. 214–230. New York Academy of Sciences: New York.
- Ivry, R. (1997). Cerebellar timing systems. *International Review of Neurobiology* 41, 555–573.
- Ivry, R. L. & Keele, S. W. (1989). Timing functions of the cerebellum. *Journal of Cognitive Neurosciences* 1, 136–152.
- Jastak, S. & Wilkinson, G. S. (1984). *The Wide Range Achievement Test – Revised Administration Manual (Revised Edition)*. Jastak Assoc. Inc.: Wilmington, DE.
- Johnson, J. E. & Peztel, T. P. (1971) Temporal orientation and time estimation in chronic schizophrenics. *Journal of Clinical Psychology* 27, 194–196.
- Kaufman, A. (1990). *Assessing Adolescent and Adult Intelligence*. Allyn & Bacon: Boston.
- King, H. E. (1976). Psychomotor correlates of behavior disorder. In *Experimental Approaches to Psychopathology* (ed. M. L. Kietzman, S. Sutton and J. Zubin), pp. 421–450. Academic Press: New York.
- Kremen, W. S., Seidman, L. J., Faraone, S. V., Pepple, J. R., Lyons, M. J. & Tsuang, M. T. (1996). The '3 Rs' and neuropsychological function in schizophrenia: an empirical test of the matching fallacy. *Neuropsychology* 10, 22–31.
- Lhamon, W. T. & Goldstone, S. (1956). The time sense: estimation of one second duration by schizophrenic patients. *Archives of Neurology and Psychiatry* 76, 625–629.
- Lhamon, W. T. & Goldstone, S. (1973). Temporal information processing in schizophrenia. *Archives of General Psychiatry* 28, 44–51.
- Lhamon, W. T., Goldstone, S. & Goldfarb, J. L. (1965). The psychopathology of time judgment. In *The Psychopathology of Perception* (ed. P. H. Hoch and J. Zubin), pp. 164–188. Grune & Stratton: New York.
- McCormack, T., Brown, G. D. A., Maylor, E. A., Darby, R. J. & Green, D. (1999). Developmental changes in time estimation: comparing childhood and old age. *Developmental Psychology* 35, 1143–1155.
- McCormack, T., Brown, G. D. A., Maylor, E. A., Richardson, L. B. & Darby, R. J. (2002). Effects of aging on absolute identification of duration. *Psychology and Aging* 17, 363–378.
- Maricq, A. V. & Church, R. M. (1983). The differential effects of haloperidol and methamphetamine on time estimation in the rat. *Psychopharmacology (Berlin)* 79, 10–15.
- Maricq, A. V., Roberts, S. & Church, R. M. (1981). Methamphetamine and time estimation. *Journal of Experimental Psychology: Animal Behavior Processes* 7, 18–30.
- Martin, P. & Albers, M. (1995). Cerebellum and schizophrenia: a selective review. *Schizophrenia Bulletin* 21, 241–250.
- Meck, W. H. (1986). Affinity for the dopamine D2 receptor predicts neuroleptic potency in decreasing the speed of an internal clock. *Pharmacology, Biochemistry and Behavior* 25, 1185–1189.
- Meck, W. H. (1996). Neuropharmacology of timing and time perception. *Cognitive Brain Research* 3, 227–242.
- Meck, W. H. & Church, R. M. (1987a). Nutrients that modify the speed of the internal clock and memory storage processes. *Behavioral Neuroscience* 101, 457–464.
- Meck, W. H. & Church, R. M. (1987b). Cholinergic modulation of the content of temporal memory. *Behavioral Neuroscience* 101, 457–464.
- Meck, W. H., Church, R. M., Wenk, G. L. & Olton, D. C. (1987). Nucleus basalis magnocellularis and medial septal area lesions differentially impair temporal memory. *Journal of Neuroscience* 7, 3505–3511.
- Mimura, M., Kinsbourne, M. & O'Connor (2000). Time estimation by patients with frontal lesions and by Korsakoff amnesics. *Journal of the International Neuropsychological Society* 6, 517–528.
- Missar, C. D., Gold, J. M. & Goldberg, T. E. (1994). WAIS-R short forms in chronic schizophrenia. *Schizophrenia Research* 12, 247–250.
- Nichelli, P., Venneri, A., Molinari, M. & Grafman, J. (1993). Time estimation in different memory disorders. *Cognitive Brain Research* 1, 87–93.
- Nichelli, P., Clark, K., Hollnagel, C. & Grafman, J. (1995). Duration processing after frontal lobe lesions. *Annals of the New York Academy of Sciences* 769, 183–190.
- Nichelli, P., Alway, D. & Grafman, J. (1996). Perceptual timing in cerebellar degeneration. *Neuropsychologia* 34, 863–871.
- Nuechterlein, K. H. & Dawson, M. E. (1984). Information processing and attentional functioning in the development course of schizophrenic disorders. *Schizophrenia Bulletin* 10, 160–203.
- O'Boyle, D. J., Freeman, J. S. & Cody, F. W. (1996). The accuracy and precision of timing of self-paced, repetitive movements in subjects with Parkinson's disease. *Brain* 119, 51–70.
- Orme, J. E. (1966). Time estimation and the nosology of schizophrenia. *British Journal of Psychiatry* 112, 37–39.
- Park, S., Holzman, P. S. & Goldman-Rakic, P. S. (1995). Spatial working memory deficits in the relatives of schizophrenic patients. *Archives of General Psychiatry* 52, 821–828.
- Pastor, M. A., Artieda, J., Jahanshahi, M. & Obeso, J. A. (1992). Performance of repetitive wrist movements in Parkinson's disease. *Brain* 115, 875–891.
- Penney, T. B., Allan, L. G., Meck, W. H. & Gibbon, J. (1998). In *Timing of Behavior: Neural, Psychological and Computational Perspectives* (ed. D. A. Rosenbaum and C. E. Collyer), pp. 165–193. MIT Press: Cambridge, MA.
- Rammesayer, T. (1989). Is there a common dopaminergic basis of time perception and reaction time? *Neuropsychobiology* 21, 37–42.
- Rammesayer, T. (1990). Temporal discrimination in schizophrenic and affective disorders: evidence for a dopamine-dependent internal clock. *International Journal of Neuroscience* 53, 111–120.
- Rammesayer, T. H. (1993). On dopaminergic modulation of temporal information processing. *Biological Psychology* 36, 209–222.
- Rammesayer, T. H. (1997). Are there dissociable roles of the mesostriatal and mesolimbocortical dopamine systems on temporal information processing in humans? *Neuropsychobiology* 35, 36–45.
- Rammesayer, T. H. (1999). Neuropharmacological evidence for different timing mechanisms in humans. *Quarterly Journal of Experimental Psychology: Comparative and Physiological Psychology* 52B, 273–286.
- Rammesayer, T. & Gallhofer, B. (1995). Remoxipride versus haloperidol in healthy volunteers: psychometric performance and subjective tolerance profiles. *International Clinical Psychopharmacology* 10, 31–37.
- Rammesayer, T. H. & Vogel, W. H. (1992). Pharmacologic properties of the internal clock underlying time perception in humans. *Neuropsychobiology* 26, 71–80.
- Rapp, D. L. & Robbins, T. W. (1976). The effects of d-amphetamine on temporal discrimination in the rat. *Psychopharmacology (Berlin)* 51, 91–100.
- Seeman, M. V. (1976). Time and schizophrenia. *Psychiatry* 39, 189–195.
- Shaw, C. & Aggleton, J. P. (1994). The ability of amnesic subjects to estimate time intervals. *Neuropsychologia* 32, 857–873.
- Shimamura, A. P., Janowsky, J. S. & Squire, L. R. (1990). Memory for the temporal order of events in patients with frontal lesions and amnesic patients. *Neuropsychologia* 28, 803–813.
- Shurtleff, D., Raslear, T. G., Genovese, R. F. & Simmons, L. (1992). Perceptual bisection in rats: the effects of physostigmine, scopolamine and pirenzepine. *Physiology and Behavior* 51, 381–390.
- Stone, M., Gabrieli, J. D., Stebbins, G. T. & Sullivan, E. V. (1998). Working and strategic memory deficits in schizophrenia. *Neuropsychology* 12, 278–288.
- Stubbs, D. A. & Thomas, J. R. (1974). Discrimination of stimulus duration and d-amphetamine: a psychophysical analysis. *Psychopharmacologia* 36, 313–322.

- Tononi, G. & Edelman, G. M. (2000). Schizophrenia and the mechanisms of conscious integration. *Brain Research and Brain Research Reviews* **31**, 391–400.
- Tracy, J. I., Monaco, C., McMichael, H., Tyson, K., Chambliss, C., Christensen, H. L. & Celenz, M. A. (1998). Information-processing characteristics of explicit time estimation by patients with schizophrenia and normal controls. *Perceptual and Motor Skills* **86**, 515–526.
- Tysk, L. (1983a). Time estimation by healthy subjects and schizophrenic patients: a methodological study. *Perceptual and Motor Skills* **56**, 983–988.
- Tysk, L. (1983b). Estimation of time and the subclassification of schizophrenic disorders. *Perceptual and Motor Skills* **57**, 911–918.
- Tysk, L. (1984). A longitudinal study of time estimation in psychotic disorders. *Perceptual and Motor Skills* **59**, 779–789.
- Tysk, L. (1990). Estimation of time by patients with positive and negative schizophrenia. *Perceptual and Motor Skills* **71**, 826.
- Volz, H. P., Nenadic, I., Gaser, C., Rammsayer, T., Häger, F. & Sauer, H. (2001). Time estimation in schizophrenia: an fMRI study at adjusted levels of difficulty. *NeuroReport* **12**, 313–316.
- Wahl, O. F. & Sieg, D. (1980). Time estimation among schizophrenics. *Perceptual and Motor Skills* **50**, 535–541.
- Wearden, J. H. (1991). Human performance on an analogue of an interval bisection task. *Quarterly Journal of Experimental Psychology* **43B**, 59–81.
- Wearden, J. H. (1992). Temporal generalization in humans. *Journal of Experimental Psychology: Animal Behavior Processes* **18**, 134–144.
- Wearden, J. H. (1993). Decisions and memories in human timing. *Psychologica Belgica* **33**, 241–253.
- Wearden, J. H. & Ferrara, A. (1995). Stimulus spacing effects in temporal bisection in humans. *Quarterly Journal of Experimental Psychology: Comparative and Physiological Psychology* **48B**, 289–310.
- Wearden, J. H. & Ferrara, A. (1996). Stimulus range effects in temporal bisection by humans. *Quarterly Journal of Experimental Psychology: Comparative and Physiological Psychology* **49B**, 24–44.
- Wearden, J. H. & Towse, J. N. (1994). Temporal generalization in humans: three further studies. *Behavioural Processes* **32**, 247–264.
- Wearden, J. H., Denovan, L., Fakhri, M. & Haworth, R. (1997a). Scalar timing in temporal generalization in humans with longer stimulus durations. *Journal of Experimental Psychology and Animal Behavioral Processes* **23**, 502–511.
- Wearden, J. H., Wearden, A. J. & Rabbitt, P. M. A. (1997b). Age and IQ effects on stimulus and response timing. *Journal of Experimental Psychology: Human Perception and Performance* **23**, 962–979.
- Wearden, J. H., Pilkington, R. & Carter, E. (1999). Subjective lengthening during repeated testing of a simple temporal discrimination. *Behavioural Processes* **46**, 25–38.
- Webster, F. R., Goldstone, S. & Webb, W. W. (1962). Time judgement and schizophrenia: psychophysical method as a relevant contextual factor. *Journal of Psychology* **54**, 159–164.
- Wechsler, D. (1981). *Wechsler Adult Intelligence Scale – Revised*. Psychological Corporation: San Antonio, TX.
- Wechsler, D. (1987). *Wechsler Memory Scale – Revised*. Psychological Corporation: San Antonio, TX.
- Weickert, T. W., Goldberg, T. E., Gold, J. M., Bigelow, L. B., Egan, M. F. & Weinberger, D. R. (2000). Cognitive impairments in patients with schizophrenia displaying preserved and compromised intellect. *Archives in General Psychiatry* **57**, 907–913.
- Weinberger, D. R., Berman, K. F. & Torrey, E. F. (1992). Evidence of dysfunction of a prefrontal-limbic network in schizophrenia: a magnetic resonance imaging and regional cerebral blood flow study of discordant monozygotic twins. *American Journal of Psychiatry* **149**, 890–897.
- Wiens, A., Bryan, J. & Crossen, J. (1993). Estimating WAIS-R FSIQ from the National Adult Reading Test-Revised in normal subjects. *Clinical Neuropsychologist* **7**, 70–84.
- Williams, J. M., Medwedeff, C. H. & Haban, G. (1989). Memory disorders and subjective time estimation. *Journal of Clinical and Experimental Neuropsychology* **11**, 713–723.
- Zakay, D. & Block, R. A. (1996). The role of attention in time estimation processes. In *Time, Internal Clocks and Movement* (ed. M. A. Pastor and J. Arnted). pp. 143–164. Elsevier: Amsterdam.
- Zakay, D. & Block, R. A. (1997). Temporal cognition. *Current Directions in Psychological Science* **6**, 12–16.