Slow binocular rivalry in bipolar disorder

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ABSTRACT

Background. The rate of binocular rivalry has been reported to be slower in subjects with bipolar disorder than in controls when tested with drifting, vertical and horizontal gratings of high spatial frequency.

Method. Here we assess the rate of binocular rivalry with stationary, vertical and horizontal gratings of low spatial frequency in 30 subjects with bipolar disorder, 30 age- and sex-matched controls, 18 subjects with schizophrenia and 18 subjects with major depression. Along with rivalry rate, the predominance of each of the rivaling images was assessed, as was the distribution of normalized rivalry intervals.

Results. The bipolar group demonstrated significantly slower rivalry than the control, schizophrenia and major depression groups. The schizophrenia and major depression groups did not differ significantly from the control group. Predominance values did not differ according to diagnosis and the distribution of normalized rivalry intervals was well described by a gamma function in all groups.

Conclusions. The results provide further evidence that binocular rivalry is slow in bipolar disorder and demonstrate that rivalry predominance and the distribution of normalized rivalry intervals are not abnormal in bipolar disorder. It is also shown by comparison with previous work, that high strength stimuli more effectively distinguish bipolar from control subjects than low strength stimuli. The data on schizophrenia and major depression suggest the need for large-scale specificity trials. Further study is also required to assess genetic and pathophysiological factors as well as the potential effects of state, medication, and clinical and biological subtypes.

INTRODUCTION

Pettigrew & Miller (1998) recently reported that slow binocular rivalry is a novel candidate biomarker for bipolar disorder (BD). Binocular rivalry is a well-studied visual phenomenon characterized by perceptual alternations between two different images that are presented simultaneously, one to each eye (Blake, 1989; Fox, 1991; Howard & Rogers, 1995; Logothetis, 1998; Lumer *et al.* 1998; Tong *et al.* 1998; Ooi & He, 1999; Miller *et al.* 2000; see special issue *Brain and Mind*, 2001, vol. **2**, issue 1). Presenting vertical lines to one eye for example, and horizontal lines to the other, results in perception of the vertical lines for a few seconds, followed by perception of the horizontal lines for a few seconds, and so on. The study by Pettigrew & Miller (1998) found that the rate of this perceptual alternation was significantly slower in euthymic BD subjects than in controls, when viewing 'high strength' rivalry stimuli consisting of drifting vertical and horizontal gratings of high spatial frequency (8 cycles/°).

In the present study, we aimed to assess whether the finding of slow binocular rivalry in BD could also be demonstrated with lower

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strength ('low strength') stimuli and whether the use of such stimuli would alter the separation between BD and control groups. We used stationary vertical and horizontal gratings of low spatial frequency (4 cycles/°) and obtained rivalry rates for 30 subjects with BD and 30 age- and sex-matched controls. We also extended the earlier study by assessing the rivalry rates of 18 subjects with schizophrenia and 18 subjects with major depression. Along with rivalry rate, the predominance of rivaling images (the amount of time spent perceiving one image relative to the other) and the distribution of normalized rivalry intervals were assessed according to diagnostic group.

METHOD

Patients

Clinical subjects were recruited from out-patient clinics, hospital wards and patient databases in two Australian sites, one in Brisbane and the other in Sydney. Brisbane-based subjects comprised 19 of the 30 BD subjects, all 18 schizophrenia subjects and all 18 major depression subjects. These subjects had their diagnosis confirmed by DSM-III-R criteria, determined by detailed OPCRIT interview (McGuffin et al. 1991) and review of hospital records. Eleven BD subjects were Sydney-based and had previously participated in a genetic linkage study (Adams et al. 1998). They had been diagnosed according to DSM-III-R criteria with the Diagnostic Instrument for Genetic Studies (DIGS) (Nurnberger et al. 1994), which fully incorporates the OPCRIT system (Williams et al. 1996). Control subjects were recruited from hospital and university staff in Brisbane.

On clinical assessment, all of the 11 DIGSdiagnosed BD subjects were euthymic at the time of testing. Formal state ratings were obtained for the 19 OPCRIT-diagnosed BD subjects using the Clinician-Administered Rating Scale for Mania (CARS-M) (Altman *et al.* 1994) and the self-rated Beck Depression Inventory (BDI) (Beck *et al.* 1988). BDI state ratings were obtained for all subjects with major depression while the Positive and Negative Syndrome Scale (PANSS) (Kay *et al.* 1987) was used to assess state in all subjects with schizophrenia. There were not sufficiently high state ratings on the PANSS however, to classify subjects with schizophrenia as either predominantly positive or negative syndrome-type according to the method of Kay *et al.* (1987).

General exclusion criteria were: (i) a history of brain injury or other relevant medical conditions; (*ii*) strabismus and/or amblyopia; and (*iii*) visual acuity (corrected or uncorrected) worse than 6/9 in either eve. Reduced visual acuity can decrease an individual's rivalry rate by reducing the perceived contrast and spatial frequency of the stimuli (Fahle, 1982). There were approximately equal numbers of subjects with 6/9 acuity (in one or both eyes) in each of the groups and analysis of only those subjects with normal (6/6) acuity did not change the results. Subjects with a diagnosis of schizophrenia or major depression who had a first-degree relative with BD were excluded. Control subjects were included only if they had no personal or family history of psychiatric illness (determined by clinical interview).

None of the subjects in the present study had participated in the previous study by Pettigrew & Miller (1998). BD subjects comprised 19 females and 11 males, ranging in age from 22 to 77 years (mean age, 42.3 years); 21 (70%) had normal visual acuity. Control subjects comprised 18 females and 12 males, ranging in age from 27 to 63 years (mean age, 45.4 years); 23 (77%) had normal visual acuity. Subjects with schizophrenia comprised nine females and nine males, ranging in age from 21 to 69 years (mean age, 37.7 years); 12 (78%) had normal visual acuity. Major depressive subjects comprised 12 females and six males, ranging in age from 20 to 61 years (mean age, 32.8 years); 12 (78%) had normal visual acuity.

Of the 30 BD subjects, three were unmedicated, 14 were on lithium, seven were on valproate (including one subject also on carbamazepine), and four were on both lithium and valproate. One of the remaining two BD subjects was on fluoxetine only, the other on dothiepin only. Of the 25 BD subjects receiving lithium and/or valproate, eight were also receiving an antidepressant, 10 were also receiving a typical or atypical antipsychotic and five were also receiving a benzodiazepine. All 18 subjects with schizophrenia were receiving an atypical antipsychotic, three were also on a typical antipsychotic, and one was also on lithium. Of the 18 subjects with major depression, six were unmedicated and eight were on selective serotonin reuptake inhibitor (SSRI) antidepressants. Two of the remaining four major depression subjects were on venlafaxine, one was on dothiepin, and one was on moclobemide.

Procedure

Written, informed consent was obtained from all subjects according to a protocol approved by the University of Queensland's Medical Research Ethics Committee, and the relevant institutional ethics committees. All procedures were in accordance with the Helsinki declaration of 1975. Subjects were given a small participation payment and were asked to abstain from ingesting tea, coffee, cola and alcohol for 4 h prior to testing because caffeine may increase (George, 1936), and alcohol may decrease (McDougall & Smith, 1920), a subject's rivalry rate.

The rivaling stimuli were generated with ChasmTM stereographics software and were viewed through NuVisionTM liquid-crystal shutter goggles. This enabled each eye's image to be superimposed in the same retinal location so no special training in fixation was required. The stimuli were presented on a monochrome (green) computer monitor that was situated 300 cm from the subject. Stationary horizontal (right eye) and vertical (left eye) gratings, with a spatial frequency of 4 cycles/°, were presented in a circular patch subtending 1.5° of visual angle. The contrast of the gratings was 0.9. The subjects reported their perceptual alternations using two keys and the space bar on a standard keyboard. One key signalled the perception of vertical lines and the other key signalled horizontal lines. The space bar indicated fused percepts ('checkerboard'), mixed percepts ('mosaic'), or unusual percepts (e.g. filled green circle). The space bar was also used to indicate indecision, or having previously pressed the wrong response key. The periods immediately prior to and following a space bar response were excluded before analysis. Subjects were instructed to view the stimuli passively rather than attempting to influence the perceptual alternations. Each session was supervised throughout to ensure task compliance.

On-line rivalry data collection and off-line rivalry data analysis employed software developed specifically for this purpose (BiReme Systems[®]). After familiarizing the subject with the

task, each testing session ran for approximately 30 min and consisted of three blocks, each of 10 min. The blocks were separated by a rest period of 2 min. Each block consisted of four trials, each lasting 100 s. The trials were separated by a rest period of 30 s. The first block was considered training and was excluded before analysis.

The rivalry rate for each subject was calculated by dividing the number of perceptual alternations by the total time of rivalry (for blocks two and three only). Predominance was calculated by dividing the total time spent perceiving the vertical lines, by the total time spent perceiving the horizontal lines. The resulting value was then log-transformed. Correlation analyses were performed between block two and block three rate values and between block two and block three predominance values, to assess the within-session reliability of these parameters. These correlation analyses excluded two schizophrenia subjects who failed to complete the task. The rivalry rates of these two subjects were based on block two data only, while their predominance values were excluded from analysis. All predominance analyses were performed only on those subjects with the same visual acuity (6/6 or 6/9) in both eves.

Because the perceptual alternations of binocular rivalry are well described by a gamma function (Levelt, 1965; Fox & Herrmann, 1967; Walker, 1975; Logothetis *et al.* 1996), we performed gamma analyses on the rivalry data for each group. This enabled an assessment of groupspecific variation in the distribution of rivalry intervals, independent of rate and predominance parameters. The equation for the gamma distribution is:

$$f(x) = \lambda^{r} / \Gamma(r) x^{r-1} \exp(-\lambda x)$$

where $\Gamma(r) = (r-1)!$.

RESULTS

Fig. 1 presents the rivalry rates for all subjects in the present (and previous) study. A two-way ANOVA with rivalry rate as the dependent variable, and group and gender the independent variables, demonstrated a significant main effect for group only (F(3, 87) = 4.754, P < 0.01). There was no significant interaction between group and gender. Subsequent planned-comparison *t* tests

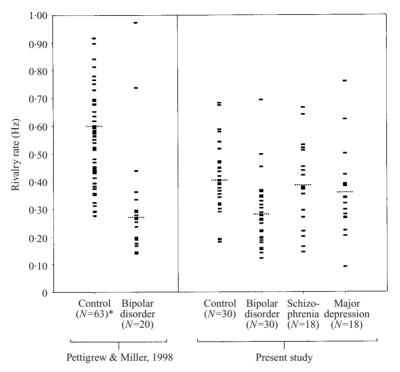


FIG. 1. Binocular rivalry rates for all subjects viewing stationary, vertical and horizontal gratings of low spatial frequency as used in the present study (right), and viewing drifting vertical and horizontal gratings of high spatial frequency (left; see Pettigrew & Miller, 1998). *Four control outliers not shown (rates = $1\cdot11$ Hz, $1\cdot11$ Hz, $1\cdot19$ Hz and $1\cdot48$ Hz).

of control rivalry rates (N=30, mean rate=0.40 Hz, s.d. = 0.13) versus BD rivalry rates (N=30, mean rate=0.28 Hz, s.d.=0.12) demonstrated significantly slower rates in the BD group (t=3.85, df=58, P<0.001). Plannedcomparisons between the schizophrenia (N = 18, mean rate = 0.39 Hz, s.D. = 0.15) and control groups, and between the major depression (N=18, mean rate=0.36 Hz, s.p.=0.15) and control groups, were not significant (t=0.47, df = 46, P > 0.05; t = 1.09, df = 46, P > 0.05, respectively), while those between the BD and schizophrenia groups (data not normally distributed; Mann-Whitney Rank Sum test, P < 0.05), and between the BD and major depression groups (data not normally distributed; Mann–Whitney Rank Sum test, P < 0.05), were significant.

Predominance values for each group are presented in Fig. 2. The apparent trend in the data that controls tend to see more of the horizontal (right eye) grating while BD subjects tend to see more of the vertical (left eye) grating was not statistically significant ($\chi^2 = 4.34$, df = 4, P > 0.05). There also did not appear to be any association of particular state ratings or medications with predominance values (Fig. 2), though these data were not sufficient to be statistically analysed.

Table 1 shows the correlation coefficients for the within-session reliability of rate and predominance values. Block 2 versus block 3 rate correlation coefficients were high in all groups, while predominance correlation coefficients were lower. Furthermore, rate and predominance values were unrelated in all groups as indicated by low correlation coefficients. Age versus rate correlation coefficients were also low in all groups, despite a report that increasing age is associated with slower rates of rivalry (Jalavisto, 1964; however that study assessed subjects aged 40 to 93 years). In the present study, three subjects with schizophrenia and four subjects with major depression were re-tested on a second occasion and demonstrated a similarly high between-session rate reliability (r=0.97) to that obtained by Pettigrew & Miller (1998) for BD and control subjects (r=0.83). High betweensession rate reliability has also been documented



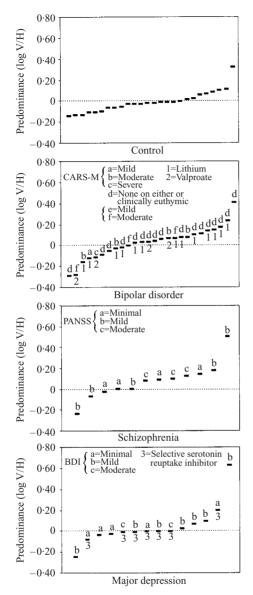


FIG. 2. Binocular rivalry predominance values for all groups. Points above the zero line represent greater time spent perceiving the vertical grating while points below the zero line reflect greater horizontal predominance. State-ratings are indicated with letters above the data points, while major medication groups are indicated with numbers below the data points.

for other types of perceptual rivalry (reviewed in Vickers, 1972) and for binocular rivalry (e.g. Enoksson, 1963).

The results of the gamma function analyses are presented in Fig. 3. It can be seen that the distribution of normalized rivalry intervals is

Blk 2 rate Blk 2 Predom. Rate Age v. v. v. Blk 3 rate Blk 3 Predom. Group Rate Predom. Control 0.380.970.83-0.15Bipolar disorder 0.32 0.96 0.70-0.01Schizophrenia 0.200.970.86-0.14Major depression 0.120.98 0.87-0.21

Correlation coefficients

Blk, Block; Predom., predominance.

Table 1.

well described by a gamma function in all groups. The schizophrenia group demonstrated the lowest R^2 value (0.92) while the BD, control and major depression groups all demonstrated R^2 values greater than or equal to 0.96. This suggests that despite the finding of slow rivalry rate in the BD group, there are no group differences in the distribution of interval durations when interval duration has been normalized. Finally, the data on medication and state effects with respect to rivalry rate were not considered sufficient to perform statistical analyses, but are presented in Fig. 4.

DISCUSSION

Slow binocular rivalry in bipolar disorder

The results of the present study are in accordance with those of Pettigrew & Miller (1998) in that the rate of binocular rivalry was significantly slower in the BD group than in the control group. Fig. 1 shows the rivalry rates of BD and control subjects obtained with low strength stimuli as used in the present study, and data obtained using high strength stimuli (Pettigrew & Miller, 1998). It can be seen that the distinction between BD and control subjects is greater for high compared with low strength stimuli. Fig. 1 also demonstrates that this difference in separation is due to control rivalry rate differences between the two types of stimuli. This is expected from the psychophysical literature (Breese, 1899; Walker & Powell, 1979; Fahle, 1982; Wade et al. 1984; Blake et al. 1985, 1998; Norman et al. 2000). The fact that the rivalry rates in the two BD groups did not differ suggests that BD subjects may have robustly slow rivalry, relatively insensitive to stimulus characteristics. This can be assessed by obtaining rivalry rate measurements with each type of stimulus within individual subjects. As well as providing

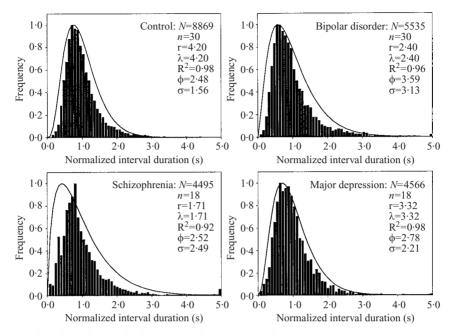


FIG. 3. Normalized rivalry interval distributions according to group. Following Logothetis *et al.* (1996): *N*, total number of intervals; *n*, number of subjects; \mathbb{R}^2 , coefficient of determination; ϕ , mean interval duration (s) for all subjects; σ , standard deviation of all intervals; *r*, calculated by squaring mean interval duration and dividing by variance of intervals; λ , calculated by dividing mean interval duration by variance of intervals.

greater separation between control and bipolar groups, the use of drifting rather than stationary gratings offers the possibility of objectively measuring an individual's rivalry rate by tracking alternating directions of optokinetic nystagmus (Enoksson, 1963; Fox *et al.* 1975; Wei & Sun, 1998). The present study also demonstrates that rivalry parameters other than rate, such as predominance (Fig. 2) and the distribution of normalized rivalry intervals (Fig. 3), are not abnormal in the BD group.

Our results for BD subjects are consistent with the early study of Hunt & Guilford (1933), which measured the rates of perceptual rivalry during viewing of the Necker cube in subjects with BD, schizophrenia (see below) and controls. The Necker cube is a two-dimensional line drawing with alternating depth perspectives that elicits a wide range of rivalry rates across individuals but relatively stable rates within individuals (reviewed in Vickers, 1972). Hunt & Guilford (1933) found that Necker cube rivalry rates in a BD group were four times as slow as those of controls during passive viewing trials and six times as slow during trials where subjects were instructed to voluntarily inhibit reversals. The concordance between our data and Hunt & Guilford's (1933) data can be explained by evidence that binocular rivalry and Necker cube rivalry share a similar neural mechanism (Walker, 1975; Logothetis, 1998; Leopold & Logothetis, 1999; Miller *et al.* 2000; Miller, 2001). Eysenck (1952) also demonstrated slower rivalry in BD compared with control subjects viewing the Necker cube, while Philip (1953) reported the same finding using a four-loop Lissajou figure (which appears to alternate its direction of rotation).

However, despite similar results for Necker cube and binocular rivalry, there are differences between these types of perceptual rivalry. For example, the influence of voluntary attention is more pronounced during Necker cube rivalry than during binocular rivalry (Washburn & Gillette, 1932; George, 1936). George (1936) also found a similar differential effect of drugs such as caffeine on the two types of perceptual rivalry. It is possible therefore, that state effects in BD subjects exert a similar differential effect. Indeed this may be pertinent to interpreting the recent report by Hoffman *et al.* (2001) that Necker cube rivalry in a sample of acutely manic

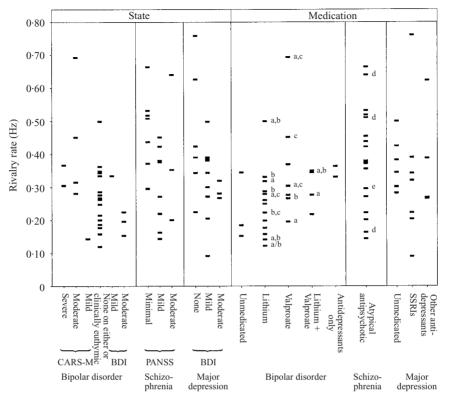


FIG. 4. Binocular rivalry rates according to state and medication ratings (a, also on a typical or an atypical antipsychotic; b, also on an antidepressant; c, also on a benzodiazepine; d, also on a typical antipsychotic; e, also on lithium; a/b, concomitant medication of two subjects with overlapping data points; SSRIs, selective serotonin reuptake inhibitor antidepressants).

BD subjects was significantly faster than normal. In the present study, although the data on state effects are inconclusive, there is a suggestion in Fig. 4 that manic states may be associated with faster binocular rivalry rates, though not faster than normal rates (see also Philip, 1953). Thus the apparent discrepancy between the data of Hoffman et al. (2001) and those of the present study, Pettigrew & Miller (1998), Hunt & Guilford (1933) and Eysenck (1952) may be explained if the effect of state, like the effect of voluntary attention and drugs, is more pronounced with Necker cube rivalry than with binocular rivalry. However, to accurately assess the effect of state on the rate of perceptual rivalry, it is necessary to perform withinsubject studies that measure rivalry rates before and after state changes (in individuals whose medication remains unchanged).

Possible effects of mood-stabilizing medication on rivalry rate should also be assessed within subjects, before and after medication onset and/or change (though if state effects exist, they may confound such assessments). Despite the suggestion of an association between lithium therapy and slower rivalry rates (see Fig. 4 and Abe *et al.* 2000), lithium is unlikely to be the cause of the slow rivalry trait given the presence of slow rivalry in unmedicated subjects (Fig. 4 and Pettigrew & Miller, 1998) and a similar finding of slow perceptual rivalry in BD demonstrated prior to the advent of lithium therapy (Hunt & Guilford, 1933). We cannot, however, exclude a confounding effect of medication at this stage. This will need to be clarified in future studies. Future studies can also assess genetic contributions to an individual's rivalry rate by studying first-degree well relatives of bipolar probands and rivalry rates in twin pairs (already underway), and can investigate the underlying neurobiology of the slow rivalry trait (e.g. Pettigrew & Miller, 1998).

Rivalry rates in other psychiatric disorders

The available data with respect to rivalry rates in psychiatric disorders other than BD are less clear. The present study demonstrates that rivalry rates in the schizophrenia group did not differ significantly from those of the control group. These results are consistent with Hunt & Guilford's (1933) data on Necker cube rivalry where subjects with schizophrenia ('dementia praecox') were not significantly different from those of controls. Hoffman et al. (2001) showed the same result with the Necker cube, as did Keil et al. (1998) and Calvert et al. (1988) with the Schröder's staircase (a reversible figure similar to the Necker cube). Keil et al. (1998) went on to show that when perceptual rivalry was elicited with the Rubin's face/vase reversible figure, the schizophrenia group actually had significantly faster rates of rivalry than the control group, while Calvert et al. (1988) showed a trend towards faster Schröder's staircase rivalry in subjects with schizophrenia compared with controls. Both Calvert et al. (1988) and Keil et al. (1988) reported that subjects with schizophrenia spent significantly less time viewing the stairs from above.

On the other hand, some early studies have reported slow binocular rivalry rates (Sappenfield & Ripke, 1961; Fox, 1965) and slow Necker cube rivalry rates (Eysenck, 1952; Nemor, 1953; D'Agata & Gaffuri, 1968) in subjects with schizophrenia compared with controls. However, all of these studies were limited by short total observation periods for each subject $(\leq 2 \text{ min for all studies except Nemor (1953)})$ which involved a 4-min observation period) compared with the present study of 14 min of rivalry following a 7-min practice period. The observation times in other cited studies are worth detailing as well, and include 27 min in the study by Hunt & Guilford (1933), 10 min in Philip (1953), but only 3 min in Keil et al. (1998) and 1 min in Hoffman et al. (2001) and Calvert et al. (1988). Longer total observation periods diminish the effects of erroneous perceptual reports and allow rivalry rates to stabilize. Rate increases within individuals have been shown to occur in the first few minutes of viewing both ambiguous figures (Brown, 1955; Price, 1969*a*, *b*; Toppino & Long, 1987; Li et al. 2000; see also Vickers, 1972) and binocular rivalry (Hodges & Fox, 1965; Aafjes, 1966; Goldstein, 1968; Hollins, 1980). The reliability of longer observation periods (with interspersed rest intervals however, see Bruner *et al.* 1950; Torii, 1960; Vickers, 1972), as used in the present study, is supported by the high correlation between block 2 and block 3 rivalry rates demonstrated for all groups (Table 1). This high correlation further suggests that comparison of block 2 and block 3 rivalry rates can provide a simple measure of an individual's task compliance.

The only available data on binocular rivalry rates of major depressive subjects compared with controls, to our knowledge, are those of the present study. The major depression group did not have significantly different rivalry rates compared with the control group, but was significantly different from the BD group. However, as with the data on schizophrenia, further investigation is required and two factors in the study of major depressives could confound results. First, some subjects thought to have major depression may actually have BD, having not yet experienced a manic episode. Secondly, comorbid anxiety disorders (also pertinent to BD) may be relevant given that Li et al. (2000) recently reported that subjects with generalized anxiety disorder have faster rates of perceptual rivalry than controls when viewing the Schröder's staircase, though the differences were not statistically significant. Although Meldman (1965) reported that Necker cube rivalry in subjects with anxiety disorders increased with increasingly anxious states and returned to normal with effective treatment, this effect was not found by Li et al. (2000). It is also interesting to note reports that attention deficit hyperactivity disorder (ADHD) is associated with fast rivalry rates during viewing of the Necker cube (Gorenstein et al. 1989), as is obsessivecompulsive disorder during viewing of the Schröder's staircase (Li et al. 2000).

As for subjects with BD, the potential effects of state and medication on rivalry rates in subjects with major depression or schizophrenia should be assessed by repeated measures within individuals. There have been reports of a nonsignificant reduction in rivalry rate of the Schröder's staircase in normal subjects administered chlorpromazine (Harris & Phillipson, 1981; Phillipson & Harris, 1984). Calvert *et al.* (1988) however, did not find significant effects of antipsychotic medication on rivalry rate in subjects with schizophrenia. In relation to the potential state effects of depression, a small study reported slowing of Schröder's staircase rivalry with increasing depressive states within individuals (Cameron, 1936; no comparison with control rivalry rates was made in that study), while Meldman (1965) reported that Necker cube rivalry is slower than normal in acute depressive states (with psychomotor retardation), normalizing with a return to euthymia.

The presence of a few BD subjects with fast rivalry rates in both the present study and the study by Pettigrew & Miller (1998), along with the wide scatter of rivalry rates in the schizophrenia and major depression groups shown in the present study (and in other studies of schizophrenia), suggests that future studies might attempt to correlate rivalry rates with biological, phenomenological or other subtypical aspects of BD, schizophrenia and major depression. For example, both Hunt & Guilford (1933) and Philip (1953) report that subjects with paranoid schizophrenia have rivalry rates between those of BD subjects and non-paranoid schizophrenics, though this is not consistent with the data of Keil et al. (1998) in which nearly all subjects studied had paranoid schizophrenia and rivalry rates were not significantly different from controls.

The results of the present study with respect to BD, schizophrenia and major depression, suggest that large-scale sensitivity and specificity assessments of rivalry rate should be performed in individuals with established diagnoses, as well as prospectively in acute presentations of psychosis and depression.

Conclusions

In this study we have replicated, in a new sample and using different stimulus characteristics, the finding by Pettigrew & Miller (1998) that binocular rivalry is significantly slower in subjects with bipolar disorder than in controls. We have also shown that predominance and the distribution of normalized rivalry intervals are not abnormal in BD. Moreover, we have provided preliminary data on binocular rivalry rates in schizophrenia and major depression, though further study of these groups, the subtypes of all groups, state and medication issues, and genetic factors is required. Comparison with previous data suggests that drifting gratings of high spatial frequency more effectively distinguish BD from control subjects than stationary gratings of low spatial frequency, and because of this, high strength stimuli should be used in large-scale sensitivity and specificity assessments. Perceptual rivalry represents an exciting approach to the study of psychiatric illnesses.

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REFERENCES

- Aafjes, M., Heuting, J. E. & Visser, P. (1966). Individual and interindividual differences in binocular retinal rivalry in man. *Psychophysiology* 3, 18–22.
- Abe, M., Herzog, E. D. & Block, G. D. (2000). Lithium lengthens the circadian period of individual suprachiasmatic nucleus neurons. *Neuroreport* 11, 3261–3264.
- Adams, L. J., Mitchell, P. B., Fielder, S. L., Rosso, A., Donald, J. A. & Schofield, P. R. (1998). A susceptibility locus for bipolar affective disorder on chromosome 4q35. *American Journal of Human Genetics* 62, 1084–1091.
- Altman, E. G., Hedeker, D. R., Janicak, P. G., Peterson, J. L. & Davis, J. M. (1994). The clinician-administered rating scale for mania (CARS-M): development, reliability, and validity. *Biologi*cal Psychiatry 36, 124–134.
- Beck, A. T., Steer, R. A. & Garbin, M. G. (1988). Psychometric properties of the Beck Depression Inventory: twenty-five years of evaluation. *Clinical Psychology Review* 8, 77–100.
- Blake, R. (1989). A neural theory of binocular rivalry. *Psychological Review* 96, 145–167.
- Blake, R., Zimba, L., Williams, D. (1985). Visual motion, binocular correspondence, and binocular rivalry. *Biological Cybernetics* 52, 391–397.
- Blake, R., Yu, K. & Lokey, M. (1998). Binocular rivalry and motion perception. *Journal of Cognitive Neuroscience* 10, 46–60.
- Breese, B. B. (1899). On inhibition. *Psychological Monographs* 3, 1–65.
- Brown, K. T. (1955). Rate of apparent change in a dynamic ambiguous figure as a function of observation time. *American Journal* of *Psychology* 68, 358–371.
- Bruner, J. S., Postman, L. & Mosteller, F. (1950). A note on the measurement of reversals of perspective. *Psychometrika* 15, 63–72.
- Calvert, J. E., Harris, J. P., Phillipson, O. T., Babiker, I. E., Ford, M. F. & Anteb, D. L. (1988). The perception of visual ambiguous figures in schizophrenia and Parkinson's disease. *International Clinical Psychopharmacology* 3, 131–150.
- Cameron, D. E. (1936). Studies in depression. Journal of Mental Science 82, 148–161.
- D'Agata, G. & Gaffuri, G. (1968). La percezione del cambiamento di prospettiva di una figura ambigua nella schizophrenia. *Neuropsichiatrica* 2, 357–363.
- Enoksson, P. (1963). Binocular rivalry and monocular dominance studied with optokinetic nystagmus. *Acta Ophthalmologica* 41, 544–563.

- Eysenck, H. J. (1952). Cyclothymia and schizothymia as a dimension of personality. *Experimental Journal of Personality* 20, 345–384.
- Fahle, M. (1982). Binocular rivalry: suppression depends on orientation and spatial frequency. *Vision Research* 22, 787–800.
- Fox, R. (1965). Rate of binocular rivalry alternation in psychotic and nonpsychotic patients. *Journal of Abnormal Psychology* 70, 34–37.
- Fox, R. (1991). Binocular rivalry. In Vision and Visual Dysfunction (ed. J. R. Cronly-Dillon), pp. 93–110. Macmillan: London.
- Fox, R. & Herrmann, J. (1967). Stochastic properties of binocular rivalry alternations. *Perceptual Psychophysiology* 2, 432–436.
- Fox, R., Todd, S. & Bettinger, L. A. (1975). Optokinetic nystagmus as an objective indicator of binocular rivalry. *Vision Research* 15, 849–853.
- George, R. W. (1936). The significance of the fluctuations experienced in observing ambiguous figures and in binocular rivalry. *Journal of General Psychology* 15, 39–66.
- Goldstein, A. G. (1968). Retinal rivalry and Troxler's effect: a correlation. *Perception and Psychophysics* 4, 261–263.
- Gorenstein, E. E., Mammato, C. A. & Sandy, J. M. (1989). Performance of inattentive-overactive children on selected measures of prefrontal-type function. *Journal of Clinical Psychology* 45, 619–632.
- Harris, J. P. & Phillipson, O. T. (1981). Chlorpromazine reduces the perceptual ambiguity of a reversible visual figure. *Neuropharma*cology 20, 1337–1338.
- Hodges, W. F. & Fox, R. (1965). Effect of arousal and intelligence on binocular rivalry rate. *Perceptual and Motor Skills* 20, 71–75.
- Hoffman, R. E., Quinlan, D. M., Mazure, C. M. & McGlashan, T. M. (2001). Cortical instability and the mechanism of mania: a neural network simulation and perceptual test. *Biological Psychiatry* 49, 500–509.
- Hollins, M. (1980). The effect of contrast on the completeness of binocular rivalry suppression. *Perception and Psychophysics* 27, 550–556.
- Howard, I. P. & Rogers, B. J. (1995). *Binocular Vision and Stereopsis*. Oxford University Press: New York.
- Hunt, J. & Guilford, J. P. (1933). Fluctuation of an ambiguous figure in dementia praecox and in manic-depressive patients. *Journal of Abnormal and Social Psychology* 27, 443–452.
- Jalavisto, E. (1964). The phenomenon of retinal rivalry in the aged. *Gerontologia* 9, 1–8.
- Kay, S. R., Abraham, F. & Opler, L. A. (1987). The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizo-phrenia Bulletin* 13, 262–276.
- Keil, A., Elbert, T., Rockstroh, B. & Ray, W. J. (1998). Dynamical aspects of motor and perceptual processes in schizophrenic patients and healthy controls. *Schizophrenia Research* 33, 169–178.
- Leopold, D. A. & Logothetis, N. K. (1999). Multistable phenomena: changing views in perception. *Trends in Cognitive Science* 3, 254–264.
- Levelt, W. (1965). *On Binocular Rivalry*. Royal VanGorcum: Assen, The Netherlands.
- Li, C.-S. R., Chen, M.-C., Yang, Y.-Y., Chang, H.-L., Liu, C.-Y., Shen, S. & Chen, C.-Y. (2000). Perceptual alternation in obsessive compulsive disorder – implications for a role of the cortico-striatal circuitry in mediating awareness. *Behavioral Brain Research* 111, 61–69.
- Logothetis, N. K. (1998). Single units and conscious vision. *Philosophical Transactions of the Royal Society of London B Biological Sciences* 353, 1801–1818.
- Logothetis, N. K., Leopold, D. A. & Sheinberg, D. L. (1996). What is rivalling during binocular rivalry? *Nature* 380, 621–624.
- Lumer, E.D., Friston, K.J. & Rees, G. (1998). Neural correlates of perceptual rivalry in the human brain. *Science* 280, 1930–1934.
- McDougall, W. & Smith, M. (1920). The Effects of Alcohol and Some other Drugs during Normal and Fatigued Conditions. HMS Office: London.

- McGuffin, P., Farmer, A. & Harvey, I. (1991). A polydiagnostic application of operational criteria in studies of psychotic illness. Development and reliability of the OPCRIT system. *Archives of General Psychiatry* 48, 764–770.
- Meldman, M. J. (1965). The quantitative analysis of anxiety and depression. *Psychosomatics* 6, 8–15.
- Miller, S. M. (2001). Binocular rivalry and the cerebral hemispheres: with a note on the correlates and constitution of visual consciousness. *Brain and Mind* 2, 119–149.
- Miller, S. M., Liu, G. B., Ngo, T. T., Hooper, G., Riek, S., Carson, R. G. & Pettigrew, J. D. (2000). Interhemispheric switching mediates perceptual rivalry. *Current Biology* 10, 383–392.
- Nemor, N. (1953). The alternation of an ambiguous figure in paretics and schizophrenics. *Journal of Abnormal and Social Psychology* 48, 445–447.
- Norman, H. F., Norman, J. F. & Bilotta, J. (2000). The temporal course of suppression during binocular rivalry. *Perception* 29, 831–841.
- Nurnberger, J. I. Jr, Blehar, M. C., Kaufmann, C. A., York-Cooler, C., Simpson, S. G., Harkavy-Friedman, J., Severe, J. B., Malaspina, D. & Reich, T. (1994). Diagnostic interview for genetic studies: rationale, unique features, and training. NIMH genetics initiative. Archives of General Psychiatry 51, 849–859.
- Ooi, T. L. & He, Z. J. (1999). Binocular rivalry and visual awareness: the role of attention. *Perception* 28, 551–574.
- Pettigrew, J. D. & Miller, S. M. (1998). A 'sticky' interhemispheric switch in bipolar disorder? *Proceedings of the Royal Society of London B Biological Sciences* 265, 2141–2148.
- Philip, B. R. (1953). Reversals in the perception of lissajou figures by psychotics. *Canadian Journal of Psychology* 7, 115–126.
- Phillipson, O. T. & Harris, J. P. (1984). Effects of chlorpromazine and promazine on the perception of some multi-stable visual figures. *Quarterly Journal of Experimental Psychology* 36A, 291–308.
- Price, J. R. (1969*a*). Studies of reversible perspective: a methodological review. *Behaviour Research Methods and Instrumentation* 1, 102–106.
- Price, J. R. (1969b). Effect of extended observation of reversible perspective duration. *Psychonomic Science* 16, 75–76.
- Sappenfield, B. R. & Ripke, R. J. (1961). Validities of three visual tests for differentiating organics from schizophrenics and normals. *Journal of Clinical Psychology* 17, 276–278.
- Tong, F., Nakayama, K., Vaughan, J. T. & Kanwisher, N. (1998). Binocular rivalry and visual awareness in human extrastriate cortex. *Neuron* 21, 753–759.
- Toppino, T. C., Long, G. M. 1987. Selective adaptation with reversible figures: don't change that channel. *Perception and Psychophysics* 42, 37–48.
- Torii, S. (1960). Figure–ground reversals under successively repeated observations. *Japanese Psychological Research* 9, 25–37.
- Vickers, D. (1972). A cyclic decision model of perceptual alternation. *Perception* 1, 31–48.
- Wade, N. J., de Weert, C. M. M. & Swanston, M. T. (1984). Binocular rivalry with moving patterns. *Perception and Psychophysics* 35, 111–122.
- Walker, P. (1975). Stochastic properties of binocular rivalry alternations. *Perception and Psychophysics* 18, 467–473.
- Walker, P. & Powell, D. J. (1979). The sensitivity of binocular rivalry to changes in the nondominant stimulus. *Vision Research* 19, 247–249.
- Washburn, M. F. & Gillette, A. (1932). Motor factors in voluntary control of cube perspective fluctuations and retinal rivalry fluctuations. *American Journal of Psychology* 45, 315–319.
- Wei, M. & Sun, F. (1998). The alternation of optokinetic responses driven by moving stimuli in humans. *Brain Research* 813, 406–410.
- Williams, J., Farmer, A. E., Ackenheil, M., Kaufmann, C. A., McGuffin, P. & Opcrit Reliability Research Group (1966). A multicentre inter-rater reliability study using the OPCRIT computerized diagnostic system. *Psychological Medicine* 26, 775–783.