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The Use of the Emotional Stroop Test to Establish the Onset and Efficacy of Antipsychotic Activity

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Twenty-eight subjects who met criteria for delusional disorder, of whom 16 were on neuroleptic treatment and 12 were not, were tested using an Emotional Stroop Test to measure aspects of their deployment of attentional resources in response to emotionally valent material. Interference indices were calculated to assess their level of accommodation to depressive, anxiety-related and threat-related words. Those who were on neuroleptics demonstrated significantly less interference from anxiety and threat-related words, raising the possibility that this test might provide a sensitive measure of the onset and efficacy of antipsychotic activity. The differential effects on anxiety and threat-related words also suggest that the antipsychotic activity of current neuroleptics is non-specifically tranquillizing rather than specifically psychotolytic in nature.

KEY WORDS — neuroleptic; Emotional Stroop Test; antipsychotic activity

INTRODUCTION

There have been difficulties in determining the optimal dose of neuroleptic or antipsychotic drugs. As a result, there are problems in knowing whether a treatment regime is active, particularly in individuals who are apparently treatment non-responsive. There are in addition difficulties in knowing whether a regime is working during the first few weeks of treatment — other than when a patient, who needs immobilization or sedation, is appropriately immobilized or sedated. There are furthermore difficulties in knowing when a medication regime could be reduced or halted following what may be months or even years of treatment and an apparently satisfactory clinical course.

Common to these difficulties is a lack of appropriate intermediate-term treatment targets. Clearly discharge from hospital is one such target in the case of antipsychotic effects (as opposed to the immobilisation or sedation needed for behavioural control) but equally clearly, in the past individuals have been discharged from hospital on immobilizing doses of neuroleptic drugs rather than doses in what is now considered to be the optimally therapeutic range. Less than a decade ago doses 10-fold greater than those currently recommended were in common use (Baldessarini *et al.*, 1988; Van Putten *et al.*, 1990; Rifkind *et al.*, 1991). A further possible target is to aim at self-reports from subjects as to whether the regime they are on is helpful (May *et al.*, 1976). While highly desirable in many respects, there are ambiguities with this latter target in that subjects may clearly respond in a deceptive fashion and in addition at present there is no consensus among prescribers as to what statements from subjects would qualify as indicating potential responsiveness.

The advent of neuroimaging has thrown up the possibility that the central receptor occupancy of antipsychotic drugs might be determined by this means (Farde *et al.*, 1988). Such technology, however, is some years away from routine use and in addition it is not clear at present whether imaging technology could be expected to distinguish between therapeutic responders and non-responders on the basis of receptor occupancy.

A further possibility is to establish a surrogate endpoint that does not depend on either the 'objective' observations of ward staff or others or the 'subjective' views of patients. The possibilities here lie in biological, psychophysiological or cognitive-neuropsychological markers. Each of these has their respective merits. This study explores the possibility of using a cognitive-neuropsychological measure, the Emotional Stroop Test (EST) for this purpose.

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METHOD

As part of a study to investigate cognitive processes in Delusional Disorders (DD), 28 subjects who satisfied DSM-IIIR criteria for this disorder (APA, 1987) were recruited (Fear, 1995; Fear *et al.*, 1996). These could be divided into two age-sex-and IQ-matched groups, one of which contained 16 currently neuroleptic medicated (treated) subjects and the other 12 neuroleptic-free (untreated) subjects. Premorbid intelligence was measured using the National Adult Reading Test (NART) (Nelson, 1982).

Subjects' delusions were rated for characteristics such as preoccupation, conviction, affect, idiosyncracy of ideation, liability to action, maintaining factors, systematization and insight using the Maudsley Assessment of Delusions Schedule (MADS) (Wessely *et al.*, 1993). This is a standardized interview in which the principle delusional belief is identified and rated to give individual scores for the above dimensions and a composite total score which corresponds to the overall severity of the delusional phenomena. Subjects also completed the Beck Depression Inventory (BDI) (Beck and Beamesderfer, 1974), the Magical Ideation scale as a measure of schizotypy (Eckblad and Chapman 1983) and the 40-item Dysfunctional Attitudes Scale (DAS) (Weissman, 1979).

Finally, subjects were also tested using an emotional Stroop task, developed to measure preconscious processing of information and consequent covert attention bias. The original Stroop task (Stroop, 1935) is a test of attention in which subjects are presented with a card with the names of colours written in the corresponding ink colour and another where the printed names of colours and the actual colour in which they are printed do not match, creating inputs which are antagonistic. When asked to name the ink colours as quickly and accurately as possible, the antagonistic inputs cause subjects to take longer over the latter card. This gives rise to a characteristic interference effect. The EST is a modified version of this in which colour names are replaced by neutral or affect-laden words (Williams *et al.*, 1988).

Five word cards were used in this study, comprising random strings of OOs (non-words), neutral-, depressive-, threat-, and anxiety-valenced words. The word cards were A4 in size, constructed with words selected for equivalent length and frequency in the English language (Bentall and Kaney, 1989). Each had 10 rows of five words presented in random order and randomly in black, blue, green, red and yellow ink on a white background, so that each colour appeared 10 times. The first card had strings of Os three, five, six, seven or nine characters long. Subsequent cards had five neutral (BUD, RECIPE, NUMBER, DIAMOND, COLLECTOR), depressive (SADLY, DEFEAT, AFRAID, REJECT, HOPELESSLY), threat (SPY, THREAT, FOLLOW, WHISPER, PERSECUTE) or anxious words (DIE, PANIC, TERROR, FEARFUL, COLLAPSE).

Subjects were told to say the colours on the cards as quickly and accurately as possible and were timed with a stopwatch. The time to completion of each of the word cards was measured in seconds. The cards were presented in a random order to avoid practice effects differentially enhancing performance on any one set of words. To standardize the results, interference indices were calculated for the depressive, threat and anxiety word cards by subtracting the time taken on the neutral word card from the time taken on each of these (see Fear *et al.*, 1996).

Statistical analyses were performed using one-way analyses of variance (ANOVA) for parametric data, a chi-squared test for non-parametric data and, in the case of EST data which is subject to large variances, the Kruskal–Wallis non-parametric ANOVA (KW). Correlations were calculated using the Spearman's rank correlation coefficient.

RESULTS

Demographic data for the treated ($n = 16$) and untreated ($n = 12$) subjects are presented in Table 1. No statistically significant differences were found for age, sex ratio, age at onset or duration of illness. Treated subjects were receiving a mean daily dose of neuroleptic medication equivalent to 306·9 mg of chlorpromazine (SD 272·9; range 30–857 mg daily).

The characteristics of delusions in the treated and untreated groups as measured by the MADS did not differ. While no significant differences between the groups were found for depression, measured by the BDI, or schizotypy, measured using the MIS, neuroleptic-treated subjects had significantly higher scores on the DAS than did their untreated counterparts ($F[1,26] = 5·003$, $p = 0·035$).

On the EST, treated subjects showed a tendency towards taking longer to complete the non-word

Table 1. Demographic data and results from BDI, DAS and MIS

	Treated ($n = 16$)	Untreated ($n = 12$)
Age (years)	51·4 (15·8)	51.6 (14·9)
Sex		
Male	12	6
Female	4	6
Premorbid I.Q.	111·1 (9·0	108·1 (7·7)
Age at onset (years)	35·4 (17·4)	39·4 (13·3)
Duration of illness (years)	16·0 (13·1	12·3 (11·1)
Neuroleptic dose (mg chlorpromazine equivalents)	306·9 (272·9)	0
MADS total	39·8 (8·6)	40·3 (5·5)
BDI	7·6 (5·2)	5·9 (8·6)
DAS*	158·4 (25·2)	130·6 (39·5)

*$p = 0{\cdot}035$.

Table 2. Emotional Stroop task data

	Treated ($n = 16$)	Untreated ($n = 12$)
OOOO (time taken in seconds)	48·15 (24·83)	36·67 (11·08)
Neutral words (time taken in seconds)	54·33 (26·27)	43·46 (13·59)
Depressive interference index	0·18 (5·32)	3·26 (0·90)
Threat interference index*	2·81 (4.62)	6·05 (3·84)
Anxiety interference index†	0·12 (3·02)	6·70 (6·66)

*$p = 0{\cdot}016$.
†$p = 0{\cdot}002$.

and neutral word cards than did neuroleptic-free subjects, but these differences were not statistically significant, possibly due to the large variances (Table 2). These times were considerably longer than those reported by Fear *et al.*, (1996) for an age- and sex-matched group of normal subjects ($27{\cdot}13 \pm 3{\cdot}96$ for non-words and $33{\cdot}32 \pm 4{\cdot}63$ for neutral words).

There was interference from depressive-, threat- and anxiety-related words in both groups in contrast to normals where such emotionally valent material may, for reasons that are not clearly understood, speed up performance (Fear *et al.*, 1996). When treated and untreated groups were compared, the interference from depressive-valenced words was greater in the untreated group although not significantly so. There were, however, highly significant differences between the treated and untreated groups on the interference indices for threat (Kruskal–Wallis $\chi^2 = 5{\cdot}828$, $df = 1$, $p = 0{\cdot}016$) and anxiety-valenced (Kruskal–Wallis $\chi^2 = 12{\cdot}376$, $df = 1$, $p = 0{\cdot}002$) words, with greater interference in the untreated subjects compared to those in the treated group.

Correlating interference indices against neuroleptic doses gave negative correlations for threat-related words ($r = -0{\cdot}45$, $p = 0{\cdot}016$) and for anxiety words ($r = -0{\cdot}54$, $p = 0{\cdot}003$).

DISCUSSION

The findings for this group of subjects with delusional disorder suggest that the Emotional Stroop Test may pick up clinically meaningful effects of neuroleptic drugs in addition to the non-specific retarding effects that these drugs also appear to have produced in the test. The results, however, call for a number of comments.

First there is the finding that even on non-words and neutral words subjects with DD perform considerably slower than controls. This finding has been noted before but in general attributed to the retardant effects of antipsychotic medication (Bentall and Kaney, 1989; Fear *et al.*, 1996). The results from untreated subjects, however, indicate that there is in addition something about the psychopathology of delusional disorders that contributes to a slowing of performance. We have found a similar slowing in obsessive–compulsive disorder; this is a finding for which at present there is no satisfactory explanation (Fear *et al.*, submitted).

Second, in subjects with DD emotionally-valent words produced a clear interference effect. This is not found in controls, whose performance is in the main facilitated by words with an emotional content (Fear *et al.*, 1996). There is no clear specificity as regards emotional content, although there was a tendency for words with both threat-related and anxiety-related content to produce the greater interference, which was borne out by the significant correlations between neuroleptic dose and EST responses for these words. The direction of effects was such that the higher the treatment dose, the greater the suppression of disruptive responses. A larger subject panel and perhaps tests with words tailored to match the contents of individual delusional systems would be needed to establish whether the genesis and/or maintenance

of particular delusions correlates with a sensitivity to particular emotional contents.

The findings also raise the possibility that assessment of the Emotional Stroop Test before commencing and subsequently while on drug treatment could be used to see whether treatment is having a significant effect on variables that would seem to have a certain face validity in terms of the genesis and/or maintenance of delusional systems. Performance on this test would, at the very least, not seem to be quite as open to deception as simple interrogation of the patient.

In this case it appeared that there was response in those who were taking neuroleptic treatment that was consistent theoretically with their deriving a benefit from treatment. At present our understanding of either delusional processes or the profile of effects produced on the Stroop test in psychotic and other disorders is not sufficiently advanced to allow us to determine whether effects such as these produced by neuroleptics would reliably translate into clinical benefits. Intuitively, however, it would seem probable that the effects are of some clinical utility. In support of this argument is the fact that while at the time of the study the overall score on the MADS was similar for both groups one might expect that the treated group would have initially been the more severely disabled of the two groups. This hunch is supported by the higher scores on the BDI scale and the DAS scales in the treated as opposed to the untreated group.

There are difficulties in developing this paradigm. There would seem to be little point in giving neuroleptics to healthy volunteers and testing them before and after as the characteristic interference on the Stroop Test following emotionally-valent words found in deluded subjects should not be present in such subjects. The optimal experimental procedure would be to track naturalistically over time a large cohort of subjects who were admitted to hospital, some of whom were drug free on admission, and to observe over time changes in their EST performance in order to determine whether such changes correlate with clinical benefits.

Such a programme might reveal whether a point is reached, where the underlying sensitivity to delusion formation has been extinguished as opposed to simply suppressed so that treatment could be discontinued. If such outcomes are found, the method might provide a measure to assist clinical judgments on the question of discontinuing treatment. In those cases in which treatment is stopped further ESTs might be used to forewarn of relapse, on the basis of re-emergence of detectable sensitivity prior to frank relapse. A further possible benefit is that the test could be used to establish the appropriate dose of neuroleptic in individual cases.

These data shed light on a further issue. This has to do with the locus of action of neuroleptic drugs. It would appear that these drugs are not specific to the disturbances in processing provoked by ideas with threat/paranoid content. Words taken from the classical anxiety domain appear to provoke comparable disturbances in our group of subjects and neuroleptics if anything proved more potent at ameliorating the disturbances caused by such themes. Such findings suggest a relatively non-specific tranquillizing effect of these compounds rather than a specific psychotolytic effect. Further exploration of this issue would seem called for and could perhaps be undertaken by constructing Stroop Tests with words targeted specifically to the primary delusional system of the individuals being investigated.

If the effects of current antipsychotic medication are shown to be relatively non-specific, a further clinical benefit of use of the EST could be envisaged. Its use might enable a demonstration of reduced sensitivity to emotionally-valent material in a proportion of individuals who display ongoing delusional systems or other psychopathological features; for patients with this profile, the implication would be that neuroleptic tranquillization as an antipsychotic principle would need to be supplemented by other therapeutic manoeuvres. All too often it seems as though a failure of the clinical state to resolve is taken as an indication to increase the level of medication on the basis that it appears not to be working; this reflex might be tempered in some cases by a demonstration that treatment is working in so far as this type of treatment could be expected to work, clinical appearances notwithstanding.

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