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The Continuous Performance Test, Identical Pairs: norms, reliability and performance in healthy controls and patients with schizophrenia in Singapore

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ABSTRACT

Aim: To provide normative values for the healthy ethnic Chinese Singaporean population and a large sample of patients with schizophrenia for the Continuous Performance Task-Identical Pairs (CPT-IP). **Participants** Data were collected on 1011 healthy ethnic Chinese and 654 patients diagnosed with schizophrenia, all between 21 and 55 years of age.

Methods: Data were stratified by age and gender. The effects of age, gender and education were explored in patients and controls. Performance indices were assessed in their ability to predict group inclusion. Controls' performance was compared with that reported in a US sample.

Results: Performance was affected by age, sex, and education, with youth, male sex and higher education providing a performance advantage. Patients' performance was lower than controls' by more than 1 standard deviation, with the 3-digit *d'* score most significantly discriminating between controls and patients. The effects of socio-demographic factors on performance were in line with those conducted in the US and previously reported in the literature.

Conclusions: This is the largest norming study ever conducted on the CPT-IP. It will enable investigators and clinicians to select appropriate indices to assess severity of cognitive decline and/or evaluate cognitive remediation therapy outcomes after taking into account age, gender and education factors.

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1. Introduction

The measurement of attention has been repeatedly identified as one of the key methodologies for assessing cognitive impairment in psychological studies of schizophrenia (Green et al., 1997; Freedman et al., 1997; Chen and Faraone, 2000). Continuous Performance Tests (CPTs) are a family of neuropsychological measures originally developed to assess sustained attention and vigilance following traumatic brain injury (Rosvold et al., 1956). All CPTs share (1) the rapid presentation of series of stimuli, and (2) requirement that participants respond whenever a designated target occurs in the series.

They can be grouped into three main categories: "Target-Only", "Signal-Target" and "Identical-Pairs" (Borgaro et al., 2003). The CPT-X and CPT-AX versions, the first to be developed, are examples of the first and second category: they require participants to respond whenever an 'X' appeared, or when an 'A' was presented immediately preceding an 'X', during presentation of letters in rapid succession.

Although "Target-Only" and "Signal-Target" paradigms are able to discriminate between healthy individuals and patients diagnosed with schizophrenia (Cornblatt et al., 1989a; Obiols et al., 1992), attention deficit with hyperactivity disorder (Rosenthal and Allen, 1978; O'Dougherty et al., 1984), conduct disorder (Shapiro and Garfinkel, 1986), and learning disabilities (Beale et al., 1987), they were found to be too easy to detect the subtle deficits seen in non-diagnosed participants who may be at risk for psychopathology.

Identical-Pairs (CPT-IP) tasks were developed over the course of the New York High-Risk Project (Cornblatt and Erlenmeyer-Kimling, 1985;

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Erlenmeyer-Kimling and Cornblatt, 1992) to increase the information-processing load in participants at risk for schizophrenia. Attentional deficits in such participants were expected to be qualitatively similar to, but quantitatively subtler than, the dysfunctions characterizing patients (Cornblatt and Keilp, 1994).

The CPT-IP requires subjects to respond when the same stimulus appears twice in a row (an 'identical pair'), so that subjects need to decode each stimulus carefully and keep it in working memory until it can be compared with the one immediately following (Cornblatt et al., 1988; Franke et al., 1994; Keilp et al., 1997; Laurent et al., 1999).

The ability to sustain attention is essential to performance with all CPT versions. However, as opposed to other CPT paradigms, the CPT-IP does not only measure vigilance and sustained attention but also working memory (Nuechterlein, 1983; Nuechterlein and Dawson, 1984; Cornblatt and Erlenmeyer-Kimling, 1985; B.A. Cornblatt et al., 1989a, b), which, unlike sustained attention, has been found to be a critical component of the profile of cognitive impairment in schizophrenia (Cornblatt et al., 1989a; Cornblatt et al., 1997; Cornblatt and Malhotra, 2001).

Significantly low CPT-IP performance in schizophrenia patients is not an epiphenomenon of chronicity, illness severity or hospitalization status (Nuechterlein, 1991; Cornblatt and Malhotra, 2001), does not normalize with medication (Cornblatt and Keilp, 1994; Bergman et al., 1995; Cornblatt et al., 1997; Liu et al., 2000), can be detected in at-risk samples before clinical symptoms emerge (Erlenmeyer-Kimling and Cornblatt, 1987a, 1987b, 1992; Ingraham et al., 1995), remain stable throughout development (Cornblatt et al., 1989a; Cornblatt et al., 1999), are specific to those at-risk individuals who later develop psychotic spectrum disorders (Cornblatt and Malhotra, 2001), seem associated to genetic-risk factors (Chen and Faraone, 2000; Egan et al., 2000) and functional/structural brain abnormalities (Herrera et al., 1991; Cornblatt and Keilp, 1994; Keilp et al., 1997; Salgado-Pineda et al., 2003, 2004). Moreover, CPT-IP performance is poorer in schizophrenia patients compared to depression patients and adolescents at-risk for affective disorders (Cornblatt et al., 1989a; Van Den Bosch et al., 1996; Cornblatt et al., 1997, 1999).

We selected the CPT-IP in our large schizophrenia cognition study due to its value as a standard measure of attention in patients with schizophrenia as well as its inclusion in the Measure and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Consensus Cognitive Battery (MCCB) as a measure of vigilance/attention in clinical trials (Kern et al., 2008; Nuechterlein et al., 2008).

In this study, we (1) report the effect of age, gender and education on performance, (2) assess performance in an ethnic Chinese Singaporean sample while adopting a Western norming sample as a benchmark (3) report norms collected on both healthy and clinical samples (4) assess the discriminant validity of the CPT for group inclusion.

2. Methods

2.1. Study sample

A total of 1011 healthy participants (HC) - 529 males and 482 females - and 654 patients diagnosed with schizophrenia (SZ) - 351 males and 303 females - were recruited as part of the Singapore Translational and Clinical Research in Psychosis ("Elucidating the Genetic Architecture of Neurocognitive Endophenotypes in Schizophrenia, Grant: NMRC/TCR/003/2008). HC were recruited from the general public by advertisement. SZ patients were recruited from community rehabilitation and care centers, outpatient clinics and inpatient wards. Data collection was completed in approximately three years. Inclusion criteria required all participants to be of Chinese ethnicity, aged between 21 and 55 years, and able to converse in English. Participants were required to have completed the Primary School Leaving Examination (PSLE), which is the standardized national examination of academic ability, administered after 6 years of compulsory education. All participants were

required to have no history of substance abuse, neurological disorders or traumatic brain injury.

All patients were interviewed with the Structured Clinical Interview for DSM-IV-TR Axis 1 Disorders, SCID-I Patient version (First et al., 2002) and met DSM-IV diagnostic criteria for schizophrenia. Almost all patients were being pharmacologically treated with atypical (37% of the patients' sample) typical (38%) or both typical and atypical antipsychotics (19%) at the time of assessment. Healthy participants were excluded if they had a current or past psychiatric condition or a first-degree biological relative diagnosed with any psychotic disorder.

HC and SZ samples were stratified by gender and within seven "age-brackets": 21–24, 25–29, 30–34, 35–39, 40–44, 45–49 and 50–55 (Table 1). An adjusted years of education index (AYE) was computed for each participant by weighing years of education in accordance to the specific educational pathway attended. AYE has been shown to have a higher correlation with cognitive performance than the simple sum of schooling years (Lam et al., 2013), and reflects the Singaporean system of streaming pupils into different schools early in their educational progress.

The study was approved by the National Health Group (Domain Specific Review Board). All participants provided written informed consent for this study.

2.2. Assessments

Neuropsychological testing and clinical assessments were conducted in English, by trained psychometricians and via standard laptop computers equipped with the Continuous Performance Test, Identical Pairs version (CPT-IP). Visual stimuli in the form of digits were displayed in white on a black background, at a constant rate of 1 per second and 50 ms onset interval. The whole task was composed of three (two-digit, three-digit and four-digit) conditions, each lasting approximately 3 minutes. Two-, three- and four-digit numbers were adopted as stimuli in the two-, three- and four-digit conditions respectively. Participants were instructed to click the left button on a mouse held in the dominant hand, as fast as possible, whenever two identical stimuli appeared one after the other. Each condition comprised of 150 trials: 20% of these (30) were target trials (e.g. "5421" followed by "5421"). Each condition also included 30 "catch trials": numbers similar - but not identical - to the one that preceded (e.g. "5421" followed by "5423"). Each participant was guided through at least one practice session, comprising of 10 trials, during which a perfect score was required before starting the task.

2.3. Performance indices

Responses to catch-trials were considered "false alarms". Responses to targets were "hits". Responses to non-targets were considered "random errors". The theoretical range for "hits" in each of the three conditions is 0 to 30. The primary composite measure that is derived from the CPT-IP is the signal detection index (d' statistic) (Green and Swets, 1966; Rutschmann et al., 1977), which is calculated as the ratio between number of 'hits' (responses to, e.g., '5421' followed by '5421') and number of 'false alarms' (responses after presentation of 'catch-trials': e.g. '5421' followed by '5423'). Higher d' values indicate better performance (Cornblatt and Keilp, 1994). The theoretical range for d' is -4.24 to 4.24, but scores below -1.00 were considered to be significantly worse than chance, and were excluded from analysis. The d' index is independent from differences in response rates (Bergman et al., 1995; Thaden et al., 2006) and has shown a high sensitivity and specificity in discriminating healthy controls from patients with schizophrenia (Cornblatt et al., 1988, 1992, 1997; Cornblatt et al., 1989b; Egan et al., 2000; Cosway et al., 2002; Rhinewine et al., 2005; Thaden et al., 2006).

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