NEUROBIOLOGY OF PSYCHOSIS. CLINICAL AND PSYCHOSOCIAL IMPLICATIONS

This is a new Section of *Epidemiologia e Psichiatria Sociale*, called *Neurobiology of Psychosis, Clinical and Psychosocial Implications*, that will regularly appear in each issue of this Journal to describe relevant neuroscience topics. In particular, studies investigating the relationship between neurobiology and psychosocial psychiatry in major psychoses will be debated. The aim of these articles is to provide a better understanding of the neural basis of psychopathology and clinical features of these disorders in order to raise new perspectives in every-day clinical practice.

Paolo Brambilla, *Section Editor* and Michele Tansella, *Editor* EPS

The use and meaning of the continuous performance test in schizophrenia

MARCELLA BELLANI[1,3] and PAOLO BRAMBILLA[2, 3]

[1]*Department of Medicine and Public Health, Section of Psychiatry and Clinical Psychology, University of Verona, Verona (Italy)*
[2]*Section of Psychiatry, Department of Pathology and Experimental & Clinical Medicine, University of Udine, Udine (Italy)*
[3]*Inter-University Centre for Behavioural Neurosciences (ICBN), University of Verona and University of Udine*

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The continuous performance test (CPT) is a behavioural assessment of attentional modulation of the motor system (Rosvold *et al.*, 1956). It has firstly been used in patients with brain injuries and then applied to assess sustained attention and vigilance in epilepsy, brain tumor, dementia, schizophrenia and other psychiatric diseases, such as attention-deficit hyperactivity disorder (ADHD) and anxiety disorders (Rosvold *et al.*, 1956; Honey *et al.*, 2005; Kanaka *et al.*, 2008). There are several versions of the test. For instance, the X-CPT version presents randomly different stimuli and subjects are asked to push a button only on presentation of the target stimuli (X). In the AX-CPT version, the subjects are required to push the button only when a cue stimulus is presented before the target one (A before X). The following items are measured for the X and AX tasks: omission errors (number of times subjects fail to respond to target stimulation), commission errors (number of times subjects respond to non target stimulation), average reaction time and coefficient of variance for both correct reactions and commission errors (Suwa *et al.*, 2004). There are other versions, such as the CPT-not X version where the subjects are asked not to push a button when the target stimulus (X) is presented; the Degraded Stimuli (DS)-CPT (Nuechterlein, 1983); the CPT playing card version (Rutschmann *et al.*, 1977); and the CPT Identical Pairs version (Cornblatt *et al.*, 1988), which is a more difficult task prepared to assess high risk population. Interestingly, the Identical Pairs version has been included in the Matrics neurocognitive assessment, a consensus cognitive battery for clinical trials of cognition in schizophrenia (Nuechterlein *et al.*, 2008).

In general, the CPT can detect deficit in vigilance, selective attention, as well as sustained attention. In this regard, sustained attention (and vigilance) was one of the earliest impaired cognitive dimension described in patients with schizophrenia (Orzack & Kornetsky, 1966; Wohlberg & Kornetsky, 1973) and also in their relatives (Erlenmeyer-Kimling & Cornblatt, 1978; Rutschmann *et al.*, 1977; Keshavan *et al.*, 2005). In this perspective, it has been suggested that altered sustained attention is an index of severity and chronicity as well as of vulnerabil-

Address for correspondence: Dr. M. Bellani, Department of Medicine and Public Health, Section of Psychiatry and Clinical Psychology, University of Verona, Piazzale L.A. Scuro 10, 37134 Verona (Italy).
Fax: +39-045-585.871
E-mail: marcella.bellani@univr.it

ity for the disorder (Asarnow & MacCrimmon, 1978; Grunebaum *et al.*, 1974; Cremasco & Cappa, 2002). Nonetheless, in patients with schizophrenia all aspects of attention have been reported to be abnormal, especially the ability to select and shift attention (Heinrichs & Zakzanis, 1998). Indeed, CPT performance is considered moderately heritable in humans (Chen *et al.*, 1998; Cornblatt & Malhotra, 2001), and performance impairment is shown to be a stable trait in individuals with schizophrenia (Wood *et al.*, 2004; Liu *et al.*, 2002), being observed in both acute and remitted patients (Asarnow & MacCrimmon, 1978; Cornblatt & Keilp, 1994; Neuchterlein *et al.*, 1991). Altered attention has been shown to be also associated with schizotypal personality (Gooding *et al.*, 2006). However, two studies failed to find the presence of vigilance and sustained attention deficits in the very early phase of schizophrenia (Erickson *et al.*, 1984; Rund *et al.*, 1998).

In addition, CPT is also useful to analyze context processing, defined as "*the adaptive control of current behaviour through the use of prior context information*" (Mac Donald *et al.*, 2000). Context processing provides information on prefrontal cortex function (Barch *et al.*, 2001; MacDonald & Carter, 2003; MacDonald *et al.*, 2005) being therefore a useful dimension to be studied in schizophrenia and major psychoses. It is composed by representation, which involves the construct and use of the context information, and maintenance, which refers to the storage of context representation. It subsumes independent dimensions of cognitive functions such as working memory, cognitive control, and response inhibition (Miller, 2000; MacDonald *et al.*, 2000). Context processing deficits have been described in first episode and chronic patients with schizophrenia (Cohen *et al.*, 1999; Javitt *et al.*, 2000; Barch *et al.*, 2003), in high risk subjects (MacDonald *et al.*, 2003) and in bipolar disorder individuals as well (Brambilla *et al.*, 2007). Moreover, several functional magnetic resonance imaging (fMRI) studies suggested that impairment of context processing in schizophrenia, as investigated with the CPT, correlates with hypoactivation of prefrontal cortex, specifically the dorsolateral prefrontal cortex (Volz *et al.*, 1999; Barch *et al.*, 2001; Perlstein *et al.*, 2003; Mac Donald & Carter, 2003) (Table I). Consistently, PET reports found hypometabolism in midfrontal areas and in basal ganglia of individuals with schizophrenia while executing the CPT (Buchsbaum *et al.*, 1992; Siegel *et al.*, 1993; Schroeder *et al.*, 1994). Furthermore, in a recent magnetic resonance spectroscopy (MRS) study, Purdon *et al.* (2008) found a significantly better CPT performance in siblings of patients with schizophrenia with low levels of glutamate in medial frontal cortex compared to those with high concentrations, which was not shown in healthy comparisons. This suggests a potential pathogenic role of glutamate in executive function deficits on the CPT in schizophrenia.

In conclusion, CPT is a very important and helpful task in elucidating the cognition of schizophrenia (Jablensky, 2005; Birkett *et al.*, 2007). Based on the literature, there is some evidence that deficits in sustained attention, as detected by the CPT, might be considered as an intermediate endophenotype of schizophrenia, potentially sustained by abnormal activation and biochemistry of prefrontal cortex (Gottesman & Gould, 2003; Danese, 2006; Sponheim *et al.*, 2006; Killackey *et al.*, 2007).

Table I – *Functional magnetic resonance imaging (fMRI) studies exploring the neural basis of attention and vigilance in schizophrenia with the continuous performance.*

Study	Subjects	Age (years)	Lengh of illness	CPT Test versions	Findings
Volz *et al.*, 1999	14 patients 20 healthy controls	34.1±12.3 28.2±5.7	Chronic illness	CPT-double-T-version	Hypoactivation in right PFC, right cingulate and left thalamus in schizophrenia
Barch *et al.*, 2001	14 patients 12 healthy controls	23.6±8.0 24.5±5.6	First episode medication naïve	AX-CPT	Hypoactivation of DLPFC in schizophrenia
MacDonald *et al.*, 2003	17 patients 17 healthy controls	34.2±7.7 33.5±5.8	Chronic illness	AX-CPT	Increased left DLPF activity in healthy controls, but not in patients with schizophrenia
Perlstein *et al.*, 2003	16 patients 15 healthy controls	36.8±1.9 36.4±1.8	Chronic illness	AX-CPT	Hypoactivation of PFC in schizophrenia

CPT = continuous performance test; DLPFC = dorsolateral prefrontal cortex; PFC = prefrontal cortex.

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