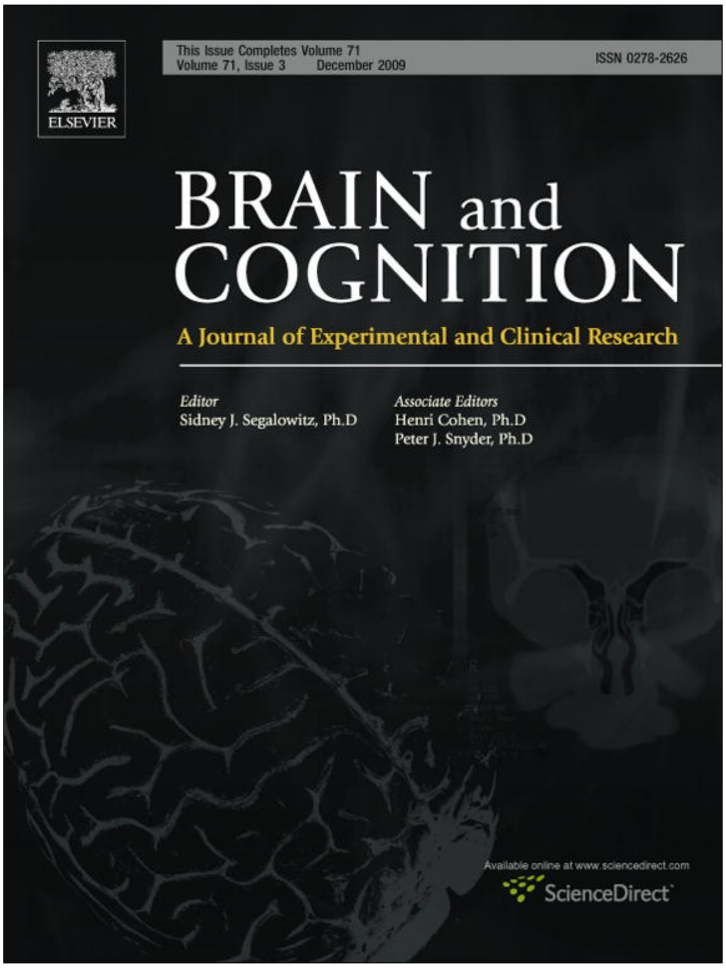
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The Wisconsin Card Sorting Test and the cognitive assessment of prefrontal executive functions: A critical update

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ABSTRACT

For over four decades the Wisconsin Card Sorting Test (WCST) has been one of the most distinctive tests of prefrontal function. Clinical research and recent brain imaging have brought into question the validity and specificity of this test as a marker of frontal dysfunction. Clinical studies with neurological patients have confirmed that, in its traditional form, the WCST fails to discriminate between frontal and non-frontal lesions. In addition, functional brain imaging studies show rapid and widespread activation across frontal and non-frontal brain regions during WCST performance. These studies suggest that the concept of an anatomically *pure* test of prefrontal function is not only empirically unattainable, but also theoretically inaccurate. The aim of the present review is to examine the causes of these criticisms and to resolve them by incorporating new methodological and conceptual advances in order to improve the construct validity of WCST scores and their relationship to prefrontal executive functions. We conclude that these objectives can be achieved by drawing on theory-guided experimental design, and on precise spatial and temporal sampling of brain activity, and then exemplify this using an integrative model of prefrontal function [i.e., Miller, E. K. (2000). The prefrontal cortex and cognitive control. *Nature Reviews Neuroscience*, *1*, 59–65.] combined with the formal information theoretical approach to cognitive control [Koechlin, E., & Summerfield, C. (2007). An information theoretical approach to prefrontal executive function. *Trends in Cognitive Sciences*, *11*, 229–235.].

1. Introduction

In the tradition of testing thinking processes or mental set, in 1900, Ach developed the sorting task in which subjects had to sort cards with non-sense words based on common features shared by the objects the words represented. Later, in 1920, Goldstein reported the use of sorting tasks to test concrete and abstract attitudes in brain-damaged patients. Following Ach and Goldstein, the Wisconsin Card Sorting Test (WCST) was devised in 1948 by Grant and Berg as an index of abstract reasoning, concept formation, and response strategies to changing contextual contingencies (Eling, Derckx, & Maes, 2008). Years later, Milner, a neuropsychologist at the Neurological Institute of Montreal, introduced the WCST to assess prefrontal lobe dysfunction in patients with brain lesions (Milner, 1963). Currently, there are at least two different systems of administration and scoring of the WCST; the standard version by Grant and Berg (1948) with Milnefs (1963) correction criteria and the shortened version by Heaton (Heaton, 1981; Heaton, Chelune, Talley, Kay, & Curtis, 1993). Furthermore, the test has been administered in modified versions by Nelson (1976), Delis, Squire, Bihrle, and Massman (1992), and Barceló (1999, 2003).

In its conventional form (Heaton, 1981; Heaton et al., 1993), the WCST consists of four key cards and 128 response cards with geometric figures that vary according to three perceptual dimensions (color, form, or number). The task requires subjects to find the correct classification principle by trial and error and examiner feedback. Once the subject chooses the correct rule they must maintain this sorting principle (or *set*) across changing stimulus conditions while ignoring the other – now irrelevant – stimulus dimensions. After ten consecutive correct matches, the classification principle changes without warning, demanding a flexible shift in set. The WCST is not timed and sorting continues until all cards are sorted or a maximum of six correct sorting criteria have been reached. Despite the fact that Heaton's correction norms offer sixteen different scores, due to the internal structure of the test, many authors normally rely on no more than two or three scores as an index of subject's performance, including: number of categories completed, number of perseverative errors, and number of non-perseverative errors (Barceló & Knight, 2002; Bowden et al., 1998; Greve, 1993; Greve, Bianchini, Hartley, & Adams, 1999; Greve et al., 2002).

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Several classic studies reported the sensitivity of the WCST to frontal lobe lesions (Drewe, 1974; Milner, 1963; Nelson, 1976; Robinson, Heaton, Lehman, & Stilson, 1980; Teuber, Battersby, & Bender, 1951). Many authors have later questioned the sensitivity and specificity of the WCST to frontal lobe lesion or dysfunction in neurological or psychiatric patients, respectively. Consequently, some handbooks of neuropsychological assessment advise about the risk of using WCST scores as a direct marker of frontal lobe damage without other converging evidence (Lezak, Howieson, & Loring, 2004; Strauss, Sherman, & Spreen, 2006). For example, the American Standardization warns about the use of the test as an anatomical marker of brain dysfunction (Axelrod et al., 1996).

In the following two sections we review two sources of evidence that have led to the present state of affairs. The first source is research with brain-damaged patients. Many studies have shown that damage in areas other than the frontal cortex significantly affects WCST performance. Table 1 provides details of the lesion location, paradigm, results, and conclusions for the results from the studies of brain-damaged patients reviewed below. The second source is functional neuroimaging of healthy subjects during WCST performance. These studies reveal activation in a widespread neural network of prefrontal, frontal, temporal, parieto-temporal, and parieto-occipital cortical regions during various stages of WCST performance. Table 2 provides details of the experimental design, brain imaging methods, results, and conclusions from the functional neuroimaging studies reviewed below. Although these results suggest that the WCST is not specific to frontal lobe function new experimental designs and methodologies, together with modern formal models of prefrontal executive functions (Koechlin & Summerfield, 2007; Miller, 2000) have provided new tools for understanding the cognitive processes and brain locations involved in the various component operations involved in WCST performance. For instance, it has recently been proposed that the WCST comprises task-switching demands associated with the reception of disconfirming feedback (Barceló, Escera, Corral, & Periañez, 2006; Barceló & Knight, 2002) which could be considered a component operation specific to prefrontal lobe function and can be measured more precisely using simplified task-switching paradigms (cf. Rubinstein, Meyer, & Evans, 2001; Shallice, Stuss, Picton, Alexander, & Gillingham, 2008).

2. Review of clinical studies

Milner's study, reported in the *Archives of Neurology* (1963), found that eighteen patients with epileptogenic foci in the dorsolateral prefrontal cortex (dPFC) committed more perseverative errors than patients with orbitofrontal cortex (oPFC), temporal, or parietal foci. The non-perseverative error score did not yield significant differences across clinical groups. Milner linked the fewer number of achieved categories in dPFC patients to their perseverative tendencies rather than to their tendency to being distracted (i.e., to non-perseverative errors). For years to come, these seminal findings and interpretations established the expected pattern of neuropsychological performance for patients with prefrontal lesions and, in particular, for patients with dPFC lesions. More than 40 years after Milner's original report (1963) we can verify the enormous impact her conclusions had for research and theorizing on prefrontal functions. Her conclusions influenced the interpretation of earlier and later studies. For example, the results by Teuber et al. (1951) were largely overlooked due to their poor correlation to Milner's interpretation. In addition, later studies adopted Milner's conclusions to interpret new results according to her seminal work. However, in many cases the correlation between studies is not complete. A group of prefrontal patients examined by Drewe (1974) achieved fewer categories and scored more perseverative errors than a group of patients with non-frontal lesions. However, it was the subgroup of patients with lesions in medial prefrontal cortex (mPFC), not dPFC patients, that showed the worst impairment in the number of categories achieved. In addition, there was large variability in the behavioral measures, making it difficult to classify individual cases into well-defined clinical groups. Debate over the location of WCST function has not only focused on specific areas of the frontal lobes. Teuber et al. (1951) carried out one of the first studies whose data argued against the specificity of the WCST as a test of frontal lobe function. These authors observed a larger number of total errors in subjects with lesions in posterior rather than frontal areas.

Recently, many clinical studies of WCST performance report impairment on the WCST with frontal cortex damage (Demakis, 2003; Freedman, Black, Ebert, & Binns, 1998; Giovagnoli, 2001; Goldstein, Obrzut, John, Ledakis, & Armstrong, 2004; Igarashi et al., 2002; Leskela et al., 1999; Mukhopadhyay et al., 2008; Nelson, 1976; Robinson et al., 1980; Stuss et al., 2000). Although there have been reports of left frontal damage affecting WCST performance more than right frontal damage (Goldstein et al., 2004), others report no difference in laterality of damage in the frontal cortex (Demakis, 2003; Giovagnoli, 2001). Moreover, many clinical studies show that damage in non-frontal (Leskela et al., 1999; van den Broek, Bradshaw, & Szabadi, 1993) or diffuse damage in frontal and non-frontal regions (Anderson, Damasio, Jones, & Tranel, 1991; Axelrod et al., 1996) both affect WCST performance. More specifically, many authors have reported that damage to temporal (Corcoran & Upton, 1993; Giovagnoli, 2001; Hermann, Wyler, & Richey, 1988; Horner, Flashman, Freides, Epstein, & Bakay, 1996; Strauss, Hunter, & Wada, 1993), subcortical (Mukhopadhyay et al., 2008), hippocampal (Corcoran & Upton, 1993; Giovagnoli, 2001; Igarashi et al., 2002), and even cerebellar regions (Mukhopadhyay et al., 2008) cause similar impairments on WCST performance as those subsequent to frontal lobe lesions.

3. Review of neuroimaging studies

Modern functional neuroimaging techniques have been used in many studies to describe changes in brain activation during WCST performance. Most of these studies have focused on groups of psychiatric patients and normal controls. Here we will focus on the results from normal controls. In principle, normal subjects show a more homogeneous level of behavioral performance than clinical samples and, consequently, their functional brain imaging results are expected to show better anatomical consistency and specificity than lesion studies.

Most neuroimaging studies on WCST performance report a significant increase in metabolic or neural activity within frontal or prefrontal cortical regions (Barceló & Knight, 2002; Barceló et al., 2006; Berman et al., 1995; Catafau et al., 1994, 1998; Cicek & Nalcaci, 2001; Gonzalez-Hernandez et al., 2002, 2003; Kawasaki et al., 1993; Konishi, Jimura, Asari, & Miyashita, 2003; Konishi et al., 1998, 2002; Lie, Specht, Marshall, & Fink, 2006; Lombardi et al., 1999; Marenco, Coppola, Daniel, Zigun, & Weinberger, 1993; Mentzel et al., 1998; Monchi, Petrides, Petre, Worsley, & Dagher, 2001; Nagahama et al., 1996, 1997, 1998; Parellada et al., 1998; Ragland et al., 1998; Rogers, Andrews, Grasby, Brooks, & Robbins, 2000; Tien, Schlaepfer, Orr, & Pearlson, 1998; Volz et al., 1997; Wang, Kakigi, & Hoshiyama, 2001). In a majority of the reviewed studies the increase in activation was found in dPFC (Berman et al., 1995; Gonzalez-Hernandez et al., 2002; Kawasaki et al., 1993; Lie et al., 2006; Lombardi et al., 1999; Marenco et al., 1993; Mentzel et al., 1998; Monchi et al., 2001; Nagahama et al., 1996, 1997; Nagahama et al., 1998; Ragland et al., 1998; Rogers et al., 2000; Volz et al., 1997; Wang et al., 2001) and some studies also revealed

Table 1
Clinical studies which used WCST scores to assess frontal or non-fontal localization of brain injury.

Authors and year	Type, lesion location, and sample size (*N*)	Task and brain imaging	Results	Conclusions
Teuber, Battersby, and Bender (1951)	War lesion Anterior (20), central (20), posterior (20) Healthy controls (40)	Surgeon and neurological report and X ray	Cat_N: less with posterior lesion Tot_Er: more with posterior lesion Pers_Er: not reported Npers_Er: not reported Failures_Set: not reported	Patients with parieto-occipital lesions made more errors than the frontal ones These errors were not due to visual deficits
Milner (1963)	Epilepsy (before and after surgery) dPFC (25), orbitotemporal (8), parietal (14), temporal (46) Healthy controls (0)	WCST Surgeon report	Cat_N: less with dPFC damage Tot_Er: more with dPFC damage Pers_Er: more with dPFC damage Npers_Er: no differences Failures_Set: not reported	dPFC patients achieved less categories and made more errors, mainly perseverative ones
Drewe (1974)	Tumor, epilepsy, CVD, TBI, surgery, atrophy Frontal (43), non-frontal (48) Healthy controls (0)	WCST Surgeon report	Tot_Er: more with left frontal damage Pers_Er: more with frontal damage NPers_Er: more with left frontal damage Failures_Set: not reported	The author affirms that his results replicate Milner's ones (1963): frontal patients achieve less categories and made more perseverative errors. Enormous variability
Nelson (1976)	Tumor Frontal (25), non-frontal (28) Healthy controls (46)	WCST[a] Not reported	Cat_N: less with frontal damage Tot_Er: more with frontal damage Pers_Er: more with frontal damage Npers_Er: not reported Failures_Set: not reported	The WCST[a] is proposed as a useful measure for detecting frontal lobe damage
Robinson, Heaton, Lehman, and Stilson (1980)	Tumor, hydrocephaly, dementia, meningitis, CVD, TBI, intoxication Frontal (46), non-frontal (23), diffuse damage (38) Healthy controls (123)	WCST Neurological report Angiography, EEG, CT	Cat_N: no differences Tot_Er: not reported Pers_Er: more with frontal damage Npers_Er: not reported Failures_Set: not reported	Perseverative responses were more frequent in frontal than non-frontal patients but without diffuse damage. The authors recommend caution in drawing anatomical inferences with WCST
Hermann, Wyler, and Richey (1988)	Epilepsy Left temporal (16), right temporal (19), widespread damage (6) Healthy controls (0)	WCST EEG	Cat_N: no differences Tot_Er: more with right temporal damage Pers_Er: more with right temporal damage Npers_Er: more with right temporal damage Failures_Set: not reported	WCST performance errors, especially perseverative responding, can occur in patients with primarily non-frontal lesions
Anderson, Damasio, Jones, and Tranel (1991)	Tumor, epilepsy, CVD Frontal (49), frontal and other areas (18), non-frontal (24) Healthy controls (0)	WCST CT and MRI	Cat_N: no differences Tot_Er: no differences Pers_Er: no differences Npers_Er: no differences Failures_Set: no differences	The WCST classifies successfully only 62% of the patients and, therefore, is not useful for localizing frontal lobe damage. The test can be useful to identify perseverative tendencies
Strauss, Hunter, and Wada (1993)	Epilepsy Left temporal early onset (14), left temporal late onset (21), right temporal early onset (12), right temporal late onset (30) Healthy controls (0)	WCST EEG, CT, and MRI	Cat_N: no differences Tot_Er: not reported Pers_Er: more with early than late onset left temporal and right temporal Npers_Er: more with early than late onset left temporal and right temporal Failures_Set: not reported	Non-frontal damage causes dysfunction that depends on laterality of temporal lobe damage and age of onset
Corcoran and Upton (1993)	Epilepsy Frontal (18), temporal (13), hippocampal (16) Healthy controls (0)	WCST[a] EEG and MRI	Cat_N: less with temporal damage Tot_Er: not reported Pers_Er: more with hippocampal damage Npers_Er: not reported Failures_Set: not reported	Hippocampal patients made more perseverative errors than frontal ones
van den Broek, Bradshaw, and Szabadi (1993)	Tumor, CVD, degenerative Frontal (29), non-frontal (14), mixed (34), diffuse (25) Healthy controls (77)	WCST[a] CT	Cat_N: no differences Tot_Er: no differences Pers_Er: no differences Npers_Er: no differences Failures_Set: no differences	The WCST[a] does not distinguish between frontal and non-frontal damage nor its laterality. Despite being sensitive to brain damage, it is not useful in identifying PFC damage
Axelrod et al. (1996)	Structural lesion Frontal (59), non-frontal (54), mixed (53), diffuse (177) Healthy controls (356)	WCST Angiography, CT, and MRI	Cat_N: no differences Tot_Er: not reported Pers_Er: no differences Npers_Er: more with mixed and diffuse lesions Failures_Set: not reported	The WCST does not discern between patient groups. The test performance implies frontal function, but it should not be considered as a pure indicator of frontal dysfunction
Horner, Flashman, Freides, Epstein, and Bakay (1996)	Epilepsy Frontal (6), left temporal (18), right temporal (20), non-localized (9) Healthy controls (0)	WCST EEG	Cat_N: no differences Tot_Er: more with temporal damage Pers_Er: more with temporal damage Npers_Er: not reported Failures_Set: not reported	Epilepsy in temporal lobe causes impairment on the WCST
Freedman, Black, Ebert, and Binns (1998)	Tumor, CVD, trauma, psychosurgery Frontal bilateral (6) Healthy controls (15)	WCST CT and MRI	Cat_N: less with frontal damage Tot_Er: not reported Pers_Er: more with frontal damage Npers_Er: not reported Failures_Set: not reported	Variable results depending on perseveration correcting criteria. There are not enough cases to make inferences

(continued on next page)

Table 1 (*continued*)

Authors and year	Type, lesion location, and sample size (*N*)	Task and brain imaging	Results	Conclusions
Leskela et al. (1999)	Ischemic Stroke Frontal (62), non-frontal (188) Healthy controls (39)	WCST[a] Neurological report and MRI	Cat_N: less with frontal and non-frontal damage Tot_Er: not reported Pers_Er: more with frontal and non-frontal damage Npers_Er: not reported Failures_Set: not reported	Frontal stroke was related to a slowing of mental processing but not executive functioning. Tests of executive functioning (WCST[a]) were sensitive to damage but did not differentiate between frontal and non-frontal damage
Stuss et al. (2000)	Stroke, trauma, tumor, hemorrhage, infarct, lobectomy Right dPFC (6), left dPFC (6), superior medial frontal (13), inferior medial frontal (10), right non-frontal (5), left non-frontal (6) Healthy controls (16)	WCST CT and MRI	Cat_N: less with all frontal damage except for inferior medial frontal damage Tot_Er: not reported Pers_Er: more with all frontal damage except for inferior medial frontal damage Npers_Er: not reported Failures_Set: no differences	The WCST is a multifactorial test that requires the integrity of a distributed neural network. Performance can be impaired for various reasons, not all of these related to the functions of the frontal lobes. Results also reveal a functional dissociation between superior and inferior frontal mesial regions
Giovagnoli (2001)	Epilepsy (Hippocampal sclerosis, lesion) Right frontal (23), left frontal (30), right temporal (47), left temporal (65) Healthy controls (36)	WCST[a] EEG and MRI	Cat_N: less with right and left frontal damage and with left hippocampal damage Tot_Er: not reported Pers_Er: more with right and left frontal damage and with left hippocampal damage Npers_Er: not reported Failures_Set: not reported	WCST[a] impairment in frontal and temporal lobe epileptic patients with left hippocampal lesion suggest the involvement of these regions in different cognitive processes required for card sorting
Igarashi et al. (2002)	Epilepsy Frontal (15), temporal with hippocampal atrophy (12), temporal without structural lesion (7) Healthy controls (30)	WCST[a] EEG, MRI, and SPECT	Cat_N: less with frontal damage, less with hippocampal damage Tot_Er: not reported Pers_Er: more with frontal damage, more with hippocampal damage Npers_Er: not reported Failures_Set: no differences	Frontal lobe function is disturbed in patients with mesial temporal lobe epilepsy although the underlying mechanism remains undetermined
Demakis (2003)	Meta-Analysis (42 studies) Frontal (644), right frontal (186), left frontal (194), non-frontal (705) Healthy controls (0)	Meta-Analysis	Cat_N: less with frontal damage, no differences between right and left frontal Tot_Er: not reported Pers_Er: more with frontal damage, no differences between right and left frontal Npers_Er: not reported Failures_Set: not reported	Frontal lobes are important for task performance on the WCST
Goldstein, Obrzut, John, Ledakis, and Armstrong (2004)	Low grade tumor Right frontal (15), left frontal (10), non-frontal (20) Healthy controls (63)	WCST[a] Surgeon report and MRI	Cat_N: less with left frontal damage Tot_Er: not reported Pers_Er: more with left frontal damage Npers_Er: not reported Failures_Set: not reported	Data derived from the WCST[a] on patients with low-grade tumors appear to support the use of this test as a valid indicator of executive functioning, although the impact of laterality remains inconclusive
Mukhopadhyay et al. (2008)	Tumor, stroke Frontal (30), subcortical (14), cerebellar (10) Healthy controls (54)	WCST[a] CT and MRI	Cat_N: less with frontal, subcortical, and cerebellar damage Tot_Er: not reported Pers_Er: more with left frontal, right thalamic, left temporo-parietal, and left cerebellar damage Npers_Er: not reported Failures_Set: not reported	Frontal lobes along with other cortical, subcortical, and cerebellar regions are important for completing complex tasks like the WCST[a]

Cat_N, number of achieved categories; CT, computerized tomography; CVD, cerebrovascular disease; dPFC, dorsolateral prefrontal cortex; EEG, electroencephalogram; Failures_Set, failures to maintain set; MRI, magnetic resonance imaging; Npers_Er, number of non-perseverative errors; Pers_Er, number of perseverative errors; PFC, prefrontal cortex; SPECT, single photon emission computed tomography; TBI, traumatic brain injury; Tot_Er, number of total errors.

[a] WCST, Modified Wisconsin Card Sorting Test.

activation in ventrolateral prefrontal cortex (vPFC) (Lie et al., 2006; Monchi et al., 2001). The laterality of this increase in activation of prefrontal cortex either in the left (Catafau et al., 1994, 1998; Cicek & Nalcaci, 2001; Kawasaki et al., 1993; Konishi et al., 2003; Monchi et al., 2001; Nagahama et al., 1997; Rogers et al., 2000; Tien et al., 1998), or in the right hemisphere (Konishi et al., 2002; Lie et al., 2006; Lombardi et al., 1999; Marenco et al., 1993; Mentzel et al., 1998; Nagahama et al., 1998; Rogers et al., 2000; Volz et al., 1997) continues to be the focus of current research.

The vast majority of functional neuroimaging studies demonstrate activation in a distributed network of brain regions associated with various aspects of WCST performance. Efficient performance on the WCST has consistently been related to an increase (or decrease) in neural activity in a widespread network of anatomical regions, which apart from prefrontal cortices also includes areas of the inferior parietal lobes (Berman et al., 1995; Cicek & Nalcaci, 2001; Gonzalez-Hernandez et al., 2002, 2003; Lie et al., 2006; Monchi et al., 2001; Nagahama et al., 1996, 1997; Tien et al., 1998), temporo-parietal association cortex (Barceló & Rubia, 1998; Barceló, Sanz, Molina, & Rubia, 1997; Barceló et al., 2006; Konishi et al., 2002; Ragland et al., 1998), as well as in primary and secondary association visual cortices (Berman et al., 1995; Gonzalez-Hernandez et al., 2002; Marenco et al., 1993; Nagahama et al., 1996, 1997, 1998; Ragland et al., 1998; Rogers et al., 2000). Somewhat less agreement exists on the implication of other structures such as the mid-thalamus (Mentzel et al., 1998; Monchi et al.,

Table 2
Functional neuroimaging studies that assessed the activation of frontal and non-frontal brain regions during performance of the WCST in healthy controls.

Authors and year	Experimental design	Sample size (N)	Brain imaging and regions of interest (ROI)	Results	Conclusions
Kawasaki et al. (1993)	Manual WCST Total recordings: 2 (26 min) Epoch: 630/930 sec Design: laterality, test–retest Basal: resting	Patients (10) and controls (10)	SPECT 44 areas	Activation in left dPFC in patients and normal controls. Patients show less activation in mPFC, no difference in test–retest	Schizophrenia is not only associated with dPFC deficit but also some other deficient components of the system involved in carrying out the WCST
Marenco, Coppola, Daniel, Zigun, and Weinberger (1993)	Computerized WCST Total recordings: 4 (4.5 min) Epoch: 60 sec Design: perseverative errors, attained categories, failure to maintain set Basal: simple matching-to-sample sensoriomotor task	(17)	SPECT 14 areas	Increased activation in right anterior dPFC and left OCC, and decreased activation at central (prerolandic) cortices in WCST compared to the Simple matching-to-sample sensoriomotor task	Right anterior dPFC becomes active during WCST performance, but there is also changes at other regions, including central and OCC.
Catafau et al. (1994)	Manual WCST Total recordings: 60 (30 min) Epoch: 30 sec Design: patients (schizophrenia) and controls Basal: resting condition	Patients (10) and controls (8)	SPECT 28 areas	Patients show hyperfrontality and hypotemporality at rest. During WCST controls showed increases in PFC (mainly in the left and including ACC) activation whereas patients did not	Activation during rest and during the WCST in patients and controls indicates a PFC (including ACC) and temporal lobe dysfunction in schizophrenia.
Berman et al. (1995)	Computerized WCST[a] Total recordings: 16 (4 min) Epoch: 10/30 sec Design: test–retest Basal: sensorimotor control task	Exp. 1 (40) and exp. 2 (9)	PET O^{15} MRI 2-T 32 areas	ROI analysis showed activation in the dPFC, right inferior MFG, inferior parietal lobule, and left OCC. SPM analysis showed additional activation in portions of the oPFC, mPFC, pPFC, inferior temporal cortex, and cerebellum. Similar results found when testing and retesting subjects	A number of brain regions cooperate to produce the complex sensory and cognitive processing and behavioral output required to perform the WCST.
Nagahama et al. (1996)	Computerized WCST[a] Total recordings: 6 (12 min) Epoch: 120 sec Design: three categories Basal: visuomotor control and resting	(18)	PET O^{15} 13 areas	Increased activation of dPFC, inferior parietal, striate cortex, left occipital cortex and cerebellum. Different areas are active during attention to color, form, and number	The involvement of the dPFC and other related areas such as the inferior parietal cortex in the execution of the WCST explains why a variety of brain lesions can result in impaired performance.
Barceló, Sanz, Molina, and Rubia (1997)	Computerized WCST[a] Total recordings: 264 (30 min) Epoch: 1.5 sec Design: early, late trials Basal: −0.2 sec prestimulus	(24)	Evoked potentials 15 areas	Increased bilateral activation in frontal (P2), temporo-parietal (P3b), and occipital (P1) regions. The target P3b response is larger in the late than in the early trials within each WCST series	In half a second, a wide neural network comprising frontal and posterior association areas becomes active during the WCST.
Nagahama et al. (1997)	Computerized WCST[a] Total recordings: 6 (12 min) Epoch: 120 sec Design: age Basal: WCST[a] only numbers	Young (6) and elderly (6)	PET O^{15} MRI 1.5-T 24 areas	Increased activation in left dPFC, rostral MFG, left inferior parietal, right intraparietal sulcus and angular gyrus, OCC, left striate, right parahippocampal gyrus, and left cerebellum. Less activation and poorer performance in elderly participants	WCST utilizes a network involving specific cortical areas including the dPFC and parahippocampal cortices. Impairment in set-shifting ability in elderly people is associated with dysfunction of this network.
Volz et al. (1997)	Computerized WCST Total recordings: 41 (21 min) Epoch: 31 sec Design: patients (schizophrenia) and controls Basal: finger tapping	Patients (13) and controls (31)	fMRI 1.5-T 24 areas	Controls show increased activation in right mesial and dPFC and medial thalamic nuclei. Compared to controls, patients show less activation in right PFC and increased activation in left temporal	Schizophrenics show a reduced ability to coordinate cerebral function.
Barceló and Rubia (1998)	Computerized WCST[a] Total recordings: 264 (30 min) Epoch: 1.5 sec Design: early, late trials Basal: −0.2 s prestimulus	(10)	Evoked potentials 29 areas	Increased bilateral activation in frontal (P2), temporo-parietal (P3b), and occipital (P1) regions. Maximal target P3b amplitudes in the late trials of each WCST series	In half a second, a wide neural network of frontal and non-frontal areas becomes active during WCST. Part of this activity seems generated in temporo-parietal and mesial temporal association cortices.

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Table 2 *(continued)*

Authors and year	Experimental design	Sample size (N)	Brain imaging and regions of interest (ROI)	Results	Conclusions
Catafau et al. (1998)	Manual WCST Total recordings: 60 (30 min) Epoch: 30 sec Design: WCST Basal: resting	(13)	SPECT 3 areas	Increased activation in left posterior frontal regions and left inferior cingulate. No significant differences in other frontal regions, or when testing for interhemispheric asymmetries	Findings suggest the importance of independently studying the contribution of the PFC and cingulate gyrus in cognitive tests used to assess frontal function.
Nagahama et al. (1998)	Computerized WCST[a] Total recordings: 10 (10 min) Epoch: 60 sec Design: 1–16 shifts in set Basal: WCST same card	(6)	PET O^{15} 35 areas	Activation in right dPFC, MFG, IFG, right parieto-occipital cortex, and left inferior occipital gyrus. Additional activation in right ACC gyrus, at lower number of shifts and in right inferior occipital gyrus and left cerebellum at higher number of shifts	Several regions in the PFC and related brain areas may participate in information processing during attentional set-shifting in different ways.
Parellada et al. (1998)	Manual WCST Total recordings: Not reported Epoch: Not reported Design: Patients (schizophrenia) and controls Basal: Resting	Patients (25) and controls (15)	SPECT 5 areas	No differences in activation during rest. Increased metabolic activation in inferior and superior PFC during WCST performance in controls but not in patients	There is no resting hypofrontality but a cognitive-dependent hypofrontality in schizophrenic patients.
Ragland et al. (1998)	Manual WCST[a] Total recordings: 4 (66 min) Epoch: 600 sec Design: patients (schizophrenia) and controls Basal: resting and number matching task	Patients (15) and controls (15)	PET O^{15} MRI 36 Areas	Increased activation in dPFC and inferior prefrontal, and occipito-temporal cortices in controls compared to patients	Executive and declarative memory tasks involve an integration of a widely distributed frontotemporal network.
Tien, Schlaepfer, Orr, and Pearlson (1998)	Computerized WCST Total recordings: not reported Epoch: not reported Design: learned WCST and long infusion Basal: match to sample card task	(5)	SPECT	Activation in left inferior frontal gyrus, right medial, inferior frontal, and inferior parietal cortex. Inactivation in anterior cingulate gyrus, right medial temporal gyrus, right caudate, left insula, and bilateral hipocampus	Learned WCST activates distinct areas in a distributed network involving association neocortex, other cortical regions, and basal ganglia.
Mentzel et al. (1998)	Computerized WCST Total recordings: 41 (21 min) Epoch: 31 sec Design: WCST Basal: resting	(31)	fMRI 1.5-T 24 areas	Activation in mesial and dPFC (mainly right) and also areas of the thalamic nuclei and basal ganglia	fMRI illustrates that WCST performance increases brain activity mostly in the right PFC, but including other post-rolandic areas as well.
Konishi et al. (1998)	Computerized WCST[a] Total recordings: not reported Epoch: 4 sec Design: 1, 2, or 3 dimensions Basal: −5 sec previous series	(7)	fMRI 1.5-T	Increased bilateral activation of inferior frontal, supramarginal gyrus, and ACC. Activity increased as the number of dimensions were increased	Inferior frontal cortex plays an important role in the flexible shifting of cognitive sets.
Konishi et al. (1999)	Computerized WCST[a] Total recordings: not reported Epoch: 4 sec Design: original and instruction condition Basal: N-back working memory task	(7)	fMRI 1.5-T	Transient activation in the posterior part of the inferior frontal sulci, greater in the original condition than in the instruction condition	The same areas in the PFC implement both working memory and cognitive set-shifting mechanisms of the WCST.
Lombardi et al. (1999)	Manual WCST auditory continuous performance task Total recordings: 4 (30 min) Epoch: 450 sec Design: perseverative errors (WCST) and regions of activity (ACPT with PET) Basal: not reported	(8)	PET MRI 1.5-T 10 areas	Inverse relationship between the number of perseverative errors (WCST) and PET activation (ACPT) in the right dPFC and caudate nucleus	It is more accurate to consider the entire dorsolateral frontal-subcortical circuit, rather than the dPFC alone, in contributing to WCST performance.

Rogers, Andrews, Grasby, Brooks, and Robbins (2000)	Computerized WCST[a] Total recordings: 12 Epoch: 90 sec Design: reversal, intradimensional (ID), and extradimensional (ED) shifts Basal: already learned discriminations	(12)	PET O^{15}	ED shift learning compared to ID shift learning produced activations in the left anterior PFC and right dPFC. Reversal learning, relative to ID shift learning, produced activations in the left caudate nucleus. Compared to reversal and ID shift learning, ED shift learning was also associated with relative deactivations in occipito-temporal pathways	Visual discrimination learning over multidimensional stimuli, like those underlying the WCST, requires different cognitive mechanisms that activate distinct cortical and subcortical neural networks.
Cicek and Nalcaci (2001)	Computerized WCST[a] Total recordings: 8 ± 1.3 Epoch: 1.28 sec Design: laterality Basal: two resting tasks and a visuomotor task	(16)	EEG spectral power analysis	Greater alpha during rest correlated with higher performance. Lower left frontal alpha power during WCST correlated with higher task performance. Greater bilateral parietal alpha power during WCST also correlated with higher task performance. Alpha during WCST was restricted to lower alpha power (8.6–10.2 Hz)	Laterality is important to look at in WCST task performance adding to data only taking into account task related changes in cortical activity.
Monchi, Petrides, Petre, Worsley, and Dagher (2001)	Computerized WCST Total recordings: 79–113 Epoch: 3.5 sec Design: receiving positive and negative feedback; card matching after positive and negative feedback cues Basal: card matching control task	(11)	fMRI 1.5-T	Activity of the mid-dPFC while subjects received either positive or negative feedback, mid-vPFC, caudate nucleus, and mid-dorsal thalamus increased activity specifically during the reception of negative feedback. Activity during matching after positive feedback included lateral premotor cortex and the left posterior parietal cortex. Additional activation found in the left posterior PFC, left putamen, and prestriate cortex while card matching after negative feedback	WCST activates a wide neural network. Each area seems to play different roles during different stages along task performance (e.g., monitoring and matching representations in working memory, set-shifting, and monitoring response selection).
Wang, Kakigi, and Hoshiyama (2001)	Computerized WCST[a] Total recordings: 120 (40 min) Epoch: 0.8 sec for feedback and 0.6 sec for card matching Design: receiving positive and negative feedback; card matching after positive and negative feedback Basal: not reported	(8)	MEG	Greater activation in negative feedback at dPFC and middle frontal cortex (460–640 ms). dPFC, supramarginal, middle and inferior frontal gyrus show greater activation during negative than during positive card matching (190–220 and 300–440 ms)	WCST activates a broad frontal area and the frontal-parietal network where both the shift of attention and enhanced visual working memory show effects at different time points, within the same neural network.
Gonzalez-Hernandez et al. (2002)	Computerized WCST[a] Total recordings: 24 (12 min) Epoch: 2 sec Design: oscillations in different regions Basal: resting	(9)	EEG spectral power analysis	Theta and delta found in dPFC, oPFC, medial frontal, inferior temporal, middle temporal, and cingulate regions. Additional delta activity in superior frontal, parietal, superior temporal, occipito-temporal, and parahippocampal. Alpha in parietal, occipito-temporal, and occipital pole. Beta-2 in parietal and superior temporal. Gamma in parietal	The selective distribution of oscillations reflect communicating networks that subserve WCST performance.
Konishi et al. (2002)	Computerized WCST[a] Total recordings: 68 Epoch: 4 sec Design: negative feedback and updating of behavior Basal: null task	(16)	fMRI 1.5-T	Multiple right lateral frontal regions (medial frontal cortex, anterior insula, precuneus, and temporo-parietal junction) were active during negative feedback. Multiple left lateral frontal regions and superior parietal lobule active during updating of behavior	Hemispheric asymmetries across bilateral frontal regions suggest that interhemispheric interactions during cognitive processing are necessary for efficient control of behavior.
Gonzalez-Hernandez et al. (2003)	Computerized WCST[a] Total recordings: 20 (12–20 min) Epoch: 2 sec Design: patients (schizophrenia) and controls Basal: 0.1 sec prestimulus	Patients (12) and controls (12)	EEG spectral power analysis	ERPs differed between groups in frontal (medial fronto-orbital and ACC), central (lateral inferior frontal), and parietal (precuneus) regions, primarily in the theta and delta frequency ranges at different time points following stimulus onset	Differential activations in patients suggest an input deficit more widespread than a local frontal hypofunction during WCST performance.
Konishi, Jimura, Asari, and Miyashita (2003)	Computerized WCST[a] Total recordings: 544 Epoch: 4 sec Design: dual match and exposure to interference Basal: informed exposure to interference task	Exp. 1 (36) and exp. 2 (16)	fMRI 1.5-T	Activation in the left MFG (superior frontal sulcus) during dual-match stimuli. Activation in the left posterior inferior frontal sulcus in control experiment in which subjects were informed of exposure to interference from previous sets	Inhibitory mechanisms in the superior PFC and the inferior PFC contribute differently to flexible behavior depending on task strategy.

(*continued on next page*)

Table 2 (*continued*)

Authors and year	Experimental design	Sample size (N)	Brain imaging and regions of interest (ROI)	Results	Conclusions
Periañez et al. (2004)	Computerized WCST[a] Total recordings: >250 trials Epoch: 0.7 sec Design: shift compared to non-shift trials Basal: not reported	(13)	MEG	Greater foci of activation during shift trials in inferior frontal gyrus (100–300 ms), anterior cingulate cortex (200–300 ms and 400–500 ms), and supramarginal gyrus (300–400 ms and 500–600 ms)	These results reveal activation in frontal and posterior areas involved with shifting and updating of information in working memory at different time points.
Nagahama, Okina, Suzuki, Nabatame, and Matsuda (2005)	Computerized WCST[a] Total recordings: 80 (20 min) Epoch: 15 sec Design: learned WCST and long infusion Basal: resting	Patients (72)	SPECT 4 areas	Less activation in mPFC for more stuck in set errors and less activation in left parietal for more recurrent perseverative errors	Multiple brain regions are involved in the WCST. Frontal lobes are important for set-shifting whereas parietal areas are important for the inhibition of irrelevant responding.
Lie, Specht, Marshall, and Fink (2006)	Computerized WCST[a] Total recordings: 362 (18 min) Epoch: 3 sec Design: comparison of original, instruction, instruction on each trial conditions Basal: WCST same card	(12)	fMRI 1.5-T	Activation right dPFC for executive function operations, right vPFC and superior parietal cortex for working memory, ACC and temporo-parietal for error detection, and cerebellum for instructions	WCST involves different neural correlates, including the right dPFC, vPFC, ACC, and parietal cortices, for various components involved in the task.
Barceló, Escera, Corral, and Periañez (2006)	Computerized WCST[a] Total recordings: 280 (18 min) Epoch: 0.7 sec Design: novel sounds, two-task & three-task switching Basal: −0.1 sec prestimulus	(16)	Evoked potentials 28 areas	Similar P3 response latency and topography to novel sound distractors and familiar task-switch auditory cues. P3 responses modulated by the amount of information conveyed by the sound stimulus	Novelty P3 responses reflect transient activation in a fronto-posterior neural network for updating task-set information for goal-directed behavior.
Periañez and Barceló (2009)	Computerized WCST[a] Total recordings: >200 trials Epoch: 0.9 sec Design: sensory *versus* task updating (switch vs. repeat) Basal: −0.1 sec prestimulus	(41)	Evoked potentials 28 areas	Both sensory- and task-updating evoked distinct cue- and target-locked ERPs. Task-switches enhanced cue-locked early P3 activity, whereas both cue- and task-switches enhanced cue-locked late P3 (*novelty P3*) activity	Behavioral switch costs and brain responses in a WCST analog reflect the accrual of various time-dependent control operations during response preparation and execution.

ACC, anterior cingulate cortex; CT, computerized tomography; EEG, electroencephalogram; fMRI, functional magnetic resonance imaging; IFG, inferior frontal gyrus; MEG, magnetoencephalogram; MFG, medial frontal gyrus; MRI, magnetic resonance imaging; OCC, occipital cortex; PET, Positron Emission Tomography; PFC, prefrontal cortex; dPFC, dorsolateral prefrontal cortex; vPFC, ventrolateral prefrontal cortex; oPFC, orbital prefrontal cortex; mPFC, medial prefrontal cortex; pPFC, fronto-polar prefrontal cortex; SPECT, single photon emission computed tomography; SPM, statistical parametric mapping.

[a] WCST, Modified Wisconsin Card Sorting Test.

2001; Volz et al., 1997), the basal ganglia (Lombardi et al., 1999; Mentzel et al., 1998; Monchi et al., 2001; Rogers et al., 2000; Tien et al., 1998), the parahippocampal gyri (Gonzalez-Hernandez et al., 2002; Nagahama et al., 1997), and the hippocampus proper (Periañez et al., 2004; Tien et al., 1998). These activations are in agreement with previous lesion studies and suggest the engagement of a widespread neural network involved in efficient WCST performance, which includes not only prefrontal and posterior multimodal association cortices but also subcortical structures like the basal ganglia (Monchi et al., 2001; Rogers et al., 2000).

4. Discussion

Current models of central executive function recognize that cognitive control involves a network of brain structures that are not exclusively localized to the frontal lobes (Baddeley, 2002). In addition, it has been shown that patients with frontal damage often do not show executive deficits, whereas patients without frontal damage often present executive deficits (Andres, 2003; Baddeley & Wilson, 1988). In agreement with current models of central executive function, the present review shows that WCST scores may not be considered as either valid or specific markers of prefrontal executive function. Research indicates that WCST performance does not engage one specific brain area, but involves a distributed neural network of both cortical and subcortical brain structures each carrying out distinct and specific operations that are dynamically integrated at a millisecond time scale (Barceló, 2003; Fernandez-Duque & Posner, 2001; Posner & Petersen, 1990). Among other component processes thought to underlie WCST performance, set-shifting seems to be a central cognitive mechanism (Barceló, 2001; Rubinstein et al., 2001) that seems to be specific to prefrontal function (Braver, Reynolds, & Donaldson, 2003; Shallice et al., 2008). Hence, an intact dPFC may be necessary to perform set-shifting operations, but may not be enough for accomplishing set-shifting and other cognitive operations utilized in the WCST.

In its original format as a paper-and-pencil test, the traditional WCST seems ill-suited to offer an accurate description of the type and severity of cognitive deficits or the anatomical location of the lesions ultimately responsible for those deficits (Bowden et al., 1998; Mountain & Snow, 1993; Reitan & Wolfson, 1994). On the positive side, these criticisms about the construct validity and anatomical specificity of traditional WCST scores reflect the great progress from neuropsychological research in the methodology and theory of frontal and executive functions over the last two decades (Rabbitt, 1997; Stuss & Knight, 2002). These new methodological and conceptual advances draw on theory-guided experimental designs, precise spatial and temporal sampling of brain activations, and the formulation of new integrative formal models of prefrontal executive functions (Koechlin & Summerfield, 2007; Miller, 2000), and could be eventually incorporated into the original WCST protocol and scoring system, or into newer versions capable of better delineating unitary cognitive operations, and pinpoint where those operations are implemented in the brain.

4.1. Construct validity of traditional WCST scores

The construct validity of the traditional WCST scoring system depends on the cognitive significance of perseverative and non-perseverative error scores. A combination of experimental design and electrophysiological measures has offered useful insights that could help improve the construct validity of future WCST scoring systems. The detailed analysis of non-perseverative WCST errors shows that they do not reflect one underlying process (Barceló, 1999, 2001). For example, studies have shown that the non-perseverative error score is actually an aggregate of at least two types of errors of a very different nature, which have been defined as *efficient errors* and *distraction errors*, respectively (Barceló & Knight, 2002). Efficient errors reflect the trial-and-error process of hypothesis testing necessary to successfully execute the task. An efficient error indicates an intentional shift to the 'wrong' one of the two remaining perceptual categories after receiving disconfirming feedback and is normally followed by correct sorting of the remaining cards in the series (Barceló, 1999; Barceló & Knight, 2002). In contrast, distraction errors are related to the 'set loss' score in Heaton et al.'s (1993) correction norms and suggest a genuine disruption in task-set maintenance when the subject selects an incorrect category after having acquired the correct one earlier in the series. The separate scoring of efficient errors and distraction errors would improve the construct validity of the test, as these two errors have distinct incidences in frontal patients and healthy controls (Barceló & Knight, 2002) and also elicit different patterns of brain activation (Barceló, 1999). Moreover, in the traditional WCST 'set loss' errors are scored after five or more correct responses to the new criterion in order to compensate for ambiguous sorts early in the series (Heaton et al., 1993; Stuss et al., 2000). This greatly reduces the sensitivity of WCST scores to the frequent set losses observed following a switch in classification criterion, an effect that is consistently found even in healthy young adults (Barceló & Knight, 2002; Barceló, Periañez, & Knight, 2002).

4.2. Anatomical specificity of traditional WCST scores

Over the last 20 years cognitive neuroscientists have come to realize that the purported lack of anatomical specificity in research on the WCST, as well as other neuropsychological assessment tools, derives from the theoretically ill-posed problem of trying to localize the brain region ultimately responsible for correct WCST performance. A more realistic objective would be to delineate the network of brain regions involved in accomplishing specific cognitive operations necessary for WCST completion (i.e., set-shifting). Current neural network models of cognition postulate that different divisions of the prefrontal cortex compute different cognitive operations (Koechlin & Summerfield, 2007; Robbins, 2007; Shallice et al., 2008). Cognitive control is implemented rapidly in our brains, and hence, the analysis of the neurophysiological correlates of the cognitive operations posits a considerable technical challenge (Posner & Dehaene, 1994). While a person may classify a target card stimulus in less than one second (Barceló, 2001), and critical cognitive operations underlying task-set switching may occur even before the onset of the stimulus card (Barceló et al., 2002, 2006), metabolic brain imaging techniques average these rapidly occurring cognitive processes over seconds or even minutes. To better delineate the neural network dynamics subserving specific cognitive operations requires both solid theory-based experimental designs and an appropriate temporal and spatial sampling of concurrent, rapidly changing, and widely distributed neural activations associated with cognition (Fernandez-Duque & Posner, 2001; Posner & Dehaene, 1994; Posner & Petersen, 1990). Although few studies listed in Table 2 meet all these requirements, some studies provide useful insights by capitalizing on recent advances in both experimental task design and in the spatiotemporal sampling of brain activity. Next we comment on some of this evidence and then use an integrative model of prefrontal function (Miller, 2000) together with formal information theoretical estimations (Koechlin & Summerfield, 2007), to describe and interpret some paradoxical results within a general framework of cognitive control and information processing.

4.3. Advances in experimental task design

Two WCST analogs combine knowledge from the fields of human and animal neuropsychology, experimental psychology, and cognitive electrophysiology, thus incorporating recent theoretical and methodological advancements into the assessment procedures. One of these WCST analogs is the Extra-Dimensional Intra-Dimensional Shift test of the CANTAB battery (Robbins, 1996; Robbins, Owen, Sahakian, McInnes, & Rabbitt, 1997; Roberts et al., 1994; Rogers et al., 1998). The other WCST analog has been referred to as the Madrid Card Sorting Test (MCST), and has been developed in our own laboratory (see Fig. 1; Barceló, 2001, 2003; Periañez & Barceló, 2009). These two WCST analogs provide more valid and reliable indices of the component processes underlying the WCST. In the following sections, we describe how research with our MCST adaptation could help improve the construct validity of WCST scores and map these more precisely onto specific cognitive operations and distinct neural network dynamics.

One way to improve the construct validity and anatomical specificity of WCST scores has been to try and separate out different stages of WCST performance through experimental design. For instance, Monchi et al. (2001) used a task design that allowed them to look separately at the brain activations associated with the feedback and card matching stages. Functional magnetic imaging results showed activity in the mid-dPFC associated with either positive or negative feedback, which was attributed to monitoring of information in working memory. In addition, the mid-vPFC, caudate nucleus, and mid-dorsal thalamus increased activity specifically in response to the negative feedback, prompting a change in the current task. Matching after positive and negative feedback yielded activation in left posterior parietal, prestriate, lateral premotor cortices, putamen, and posterior cingulate regions. Likewise, Lie et al. (2006) used a task design in which they had subjects perform four variants of the WCST differing in task complexity. The most complex was the standard WCST, the second was the WCST with warning of a dimensional change, the third was the WCST with explicit instruction of the correct dimension prior to each trial, and the fourth was a baseline condition where subjects merely matched identical cards. After subtracting the less complex tasks from the more complex tasks, functional magnetic resonance imaging results showed activity in right dPFC during more complex executive control operations, in anterior cingulate and temporal-parietal areas during error detection, in right vPFC and superior parietal cortex for attentional set-shifting, and in the cerebellum during instructed set-shifting. However, like in other neuroimaging studies, the limited temporal resolution of the BOLD signal could not discern brain activations to target cards from those to contextually relevant feedback signals (see also Konishi et al., 1998, 1999; Nagahama, Okina, Suzuki, Nabatame, & Matsuda, 2005; Rogers et al., 2000). This dilemma can be partly solved through the use of brain imaging techniques with higher temporal resolution.

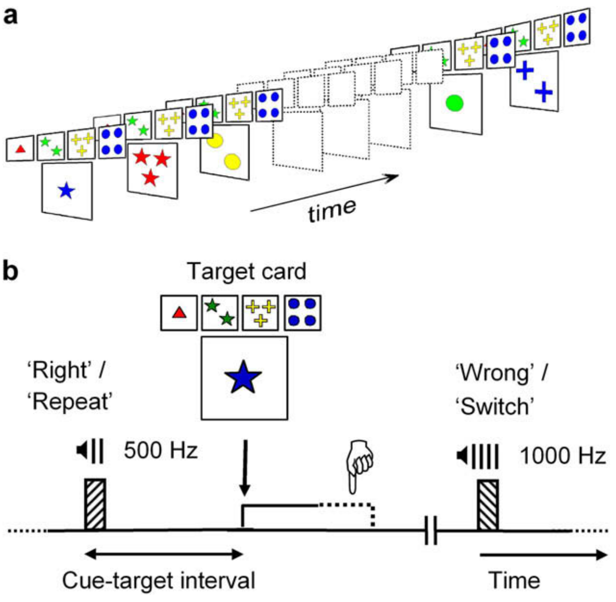

Fig. 1. Card sorting protocol adapted for the recording of event-related potentials. (a) Schematic of one series of the Madrid Card Sorting Test (MCST; Barceló, 2003), with choice-cards that can be unambiguously matched with each key-card based on only one perceptual dimension. (b) Schematic of one MCST trial converted into a task-switching protocol, where tonal 'switch' and 'repeat' cues signal unpredictable changes or repetitions in the previous sorting rule, respectively. The same tonal cues can also be instructed to signal 'wrong' and 'right' perceptual classifications, with similar effects on the pattern of observed ERP activations.

4.4. Advances in fast imaging of neural network dynamics

The foregoing discussion suggests that when exploring the validity and specificity of WCST scores, it is beneficial to combine theory-based task design with fast brain imaging. The magnetoencephalogram (MEG) provides good spatial resolution together with good temporal resolution down to the millisecond. Using MEG, Wang et al. (2001) compared the brain responses to both positive and negative feedback signals, as well as to the following target cards. These authors reported larger number of MEG dipole sources of activation during negative than positive feedback at dPFC and middle frontal cortex (460–640 ms). Likewise, greater MEG activation was found in dPFC, supramarginal, middle and inferior frontal gyrus during incorrect than during correct card matching (190–220 ms and 300–440 ms). These results are consistent with another MEG study by Periañez et al. (2004), who found greater MEG activation for switch compared to repeat task cueing events in inferior frontal gyrus (100–300 ms), anterior cingulate cortex (200–300 ms and 400–500 ms), and supramarginal gyrus (300–400 ms and 500–600 ms). Overall, these results reveal a widely distributed fronto-posterior network for switching and updating task-set information in working memory. The activation of this network seems to be maximal about 300–500 ms following the negative feedback cue (the task-switch cue) and, importantly, it occurs well before the next target card is displayed (Barceló et al., 2002, 2006).

In spite of its limited spatial resolution, the excellent temporal resolution of event related potentials (ERPs) offer important clues about the rapid neurocognitive processes that occur from stimulus onset to the motor response of the subject. Our research has contributed to the functional description of the scalp topography and amplitude changes in ERPs during WCST performance (Barceló, 1999, 2001; Barceló et al., 1997, 2002, 2006; Periañez & Barceló, 2009). The scalp distribution and intensity of ERP activations to various events in the MCST protocol show distinct changes within a millisecond time-scale across fronto-polar, frontal, central, temporal, parieto-temporal, and occipital areas (Barceló et al., 1997, 2006). By probing each peak of the ERP it has been possible to explore their underlying cognitive processes, and how they relate to various behavioral indices in the MCST adaptation. For instance, the scalp distribution and intensity of several ERP peaks vary from the early to late cards in a series (Barceló, Munoz-Cespedes, Pozo, & Rubia, 2000; Barceló et al., 2002), which is consistent with the change from extradimensional set-shifting during the early trials to intradimensional set-shifting in the late trials of each WCST series (see Dias, Robbins, & Roberts, 1997; Robbins, 1996). The activation of a category representation in working memory together with the concurrent inhibition of the previous category are some of the component operations thought to occur during set-shifting (Barceló et al., 2006; Robbins, 2007; Rogers et al., 2000).

Short-term phasic ERPs (P1 and N1) are overlapped with longer latency slow brain potentials, indicating both serial and parallel processing of information (Barceló et al., 2006; Periañez & Barceló, 2009). Some ERP components are modulated by processes distinct from the actual shift in set and may appear before and after it, such as task-set maintenance over trials and task-set implementation at card onset (Nicholson, Karayanidis, Poboka, Heathcote, & Michie, 2005). Some ERP components elicited to the target cards show an analogous mid-parietal scalp topography as the ERP signature of the shift in set at cue onset, and these components need to be segregated through experimental or statistical design to avoid potential confounds (Barceló et al., 2006; Periañez & Barceló, 2009). Current models of task-switching offer a number of plausible explanations for these accessory processes to set-shifting, including the encoding of cueing events, inhibition of (or interference from) irrelevant stimulus features or discarded categories, visual scanning, and decision making processes (Barceló, 2003; Monsell, 2005; Robbins, 2007; Rubinstein et al., 2001).

4.5. Advances in integrative theories of prefrontal function

Task-set switching has long been assumed to be a critical component process underlying WCST performance (Monsell, 2005; Rubinstein et al., 2001) and lateral prefrontal lesions are related to deficits in task-set switching ability (Rogers et al., 1998; Shallice et al., 2008). Task-switching protocols include a sequence of trials where each stimulus can be responded to in two or more possible ways (see Fig. 1). The subjects' task is to select the new correct rule of action after certain transition points and adjust their response set accordingly (Miller, 2000). However, it may be difficult to establish a direct comparison between WCST scores and the behavioral measures obtained in a variety of different task-switching protocols. The pattern of scalp-recorded ERPs provides a comparison of the neural dynamics underlying the WCST and task-switching paradigms. In a series of ERP studies, we compared the brain responses to WCST and task-switching stimuli. First, similar ERPs were elicited in response to negative feedback cues and task-switch cues, indicating that the brain responses to the feedback cues partly reflect anticipatory preparation of future actions (Barceló et al., 2002, 2006). Second, there were distinct ERPs to contextual cues and target cards, which suggest a functional dissociation between task preparation and task execution mechanisms (Barceló et al., 2002; Periañez & Barceló, 2009). This has been a consistent result across different task-switching procedures and stimulus materials (Barceló, Periañez, & Nyhus, 2008; Kieffaber & Hetrick, 2005; Nicholson et al., 2005; Rushworth, Passingham, & Nobre, 2002). Third, the most 'frontal' ERP activations were typically observed in response to the contextual switch cues, particularly when those cues conveyed relevant information about the next target response, which suggests that some critical task-set switching operations occur in anticipation of target onset (Monsell, 2005; Periañez & Barceló, 2009). Fourth, when card sorting proceeds in long runs of repetition trials with a few unexpected switch cues interspersed in between, as in the conventional WCST protocol, this 'frontal' ERP signature putatively related to set-shifting operations attenuates rapidly after the first repetition trial (Barceló et al., 2002). Finally, the ERPs to the negative feedback (or task-switch) cues is reminiscent of a brain *novelty P3* response to contextually novel and surprising distractors (Friedman, Cycowicz, & Gaeta, 2001) and they both seem to recruit activity from a common fronto-posteriorly distributed neural network responsible for processing contextual novelty (Barceló et al., 2006; Ranganath & Rainer, 2003).

The finding that 'task-irrelevant' novel distractors and 'task-relevant' task-switch cues elicit similar brain responses was quite surprising (Barceló et al., 2006), but has ultimately provided important insights on clinical studies showing that prefrontal lesions cause both perseverative and non-perseverative ('set loss') errors. In order to interpret these paradoxical results, we relied on an integrative model of prefrontal function (Miller, 2000) combined with the formal information theoretical approach to cognitive control (Koechlin & Summerfield, 2007). In the model depicted in Fig. 3, the neural representations of sensory stimulus features {$\boldsymbol{S}$} and motor responses {$\boldsymbol{R}$} are connected through hierarchically ordered levels of intervening sensorimotor processes (see Miller, 2000). The onset of a task-repeat tonal cue updates its associated sensory (*s2*) and sensorimotor (*sr*) units, without modifying the higher-order task-set unit for the ongoing task (the *color rule*). The corresponding sensorimotor (or stimulus-response) mapping for this color rule then determines that the 'one blue star' card stimulus, *s3,* is correctly responded to using the fourth response button, *r4*. The sustained maintenance of this higher-order *color* unit in working memory holds other subordinate sensorimotor units in an active state, thus keeping intervening pathways between sensory and motor units for efficient color sorting of the ensuing target cards. The lateral prefrontal cortex has been proposed as a candidate structure to hold these higher-order task-set units on-line in working memory (Miller, 2000). Conversely, the onset of a task-switch cue (*s1*) would trigger updating to a different higher-order task-set unit (i.e., when the *form* unit becomes active, the *color* unit is inhibited; see Fig. 3). The new task-set unit then reconfigures the sensorimotor mappings so that the same 'one blue star' card would now be responded to using the second response button, *r2*. Early in the new MCST series, the newly established *form rule* competes for resources with the old *color rule*, thus causing transient conflict and behavioral costs mostly during the early trials of the new classification series.

Up to this point, the description of task processes from our MCST closely follows Miller's (2000) integrative model of prefrontal function. Further insights could be gained from the combination of this model with formal information estimations of executive control processes (Koechlin & Summerfield, 2007). According to formal estimations of information transmission between stimuli and responses in Figs. 1 and 3, the amount of information $H(r_j)$ necessary for selecting the correct response *r2* to the 'one blue star', *s3,* is the sum of two terms (Eq. (1)): (i) the 'sensorimotor control' information conveyed by stimulus *s3* about response *r2* (Eq. (2)), which normally depends on the pools of all contextually related task stimuli {$\boldsymbol{S}$} and responses {$\boldsymbol{R}$} and their probabilistic association (Eq. (3)); and (ii) the remaining 'cognitive control' processes (Eq. (4)) that need to be called upon when the original sensorimotor control, or active stimulus-response mappings, does not suffice to produce an adaptive behavior (see Koechlin & Summerfield, 2007). Here we adopt a conservative view that cognitive control in this situation involves only the *contextual control* induced by task-switch and repeat cues (Eq. (4)). In other words, we assume that some extra control is required to process those contextual signals, *c* (i.e., negative feedback or task-switch cues) that prompt a change to new higher-order task-set units, *ts* (Eq. (4)).

$$H(r_j) = I(s_i, r_j) + Q(r_j|s_i) \tag{1}$$

$$I(s_j, r_i) = \log \frac{p(s_j, r_i)}{p(r_i)p(s_j)} \tag{2}$$

$$I(S;R) = \sum_i \sum_j p(s_j, r_i) \log \frac{p(s_j, r_i)}{p(r_i)p(s_j)} \tag{3}$$

$$Q(r|s) = I(c, r|s) \equiv I(c, ts) \tag{4}$$

From these theoretical premises, there are several interesting insights to be gained about the nature of the brain activations observed in response to contextual cues in our WCST analog (see Fig. 2). One intriguing corollary is that the working memory load associated with negative and positive feedback cues (or switch and repeat cues), and their corresponding brain responses, do not seem to depend on lower-level sensorimotor processes alone. In

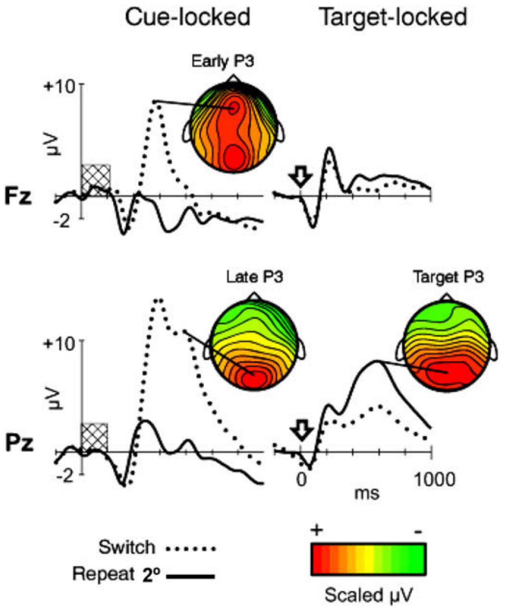

Fig. 2. Grand-average ERPs time-locked to the onset of auditory cues (shaded rectangle) and target cards (wide arrow) are displayed for task-switch and repeat trials (similar to 'wrong' and 'right' feedback cues) at the mid-frontal (Fz) and mid-parietal (Pz) sites. Voltages are in microvolts (μV). Scalp potential maps are shown for mean cue-locked early and late P3 potentials evoked by task-switch cues and for mean target-locked P3 activity evoked by the second task-repeat trial in a MCST series (adapted from Barceló et al., 2002).

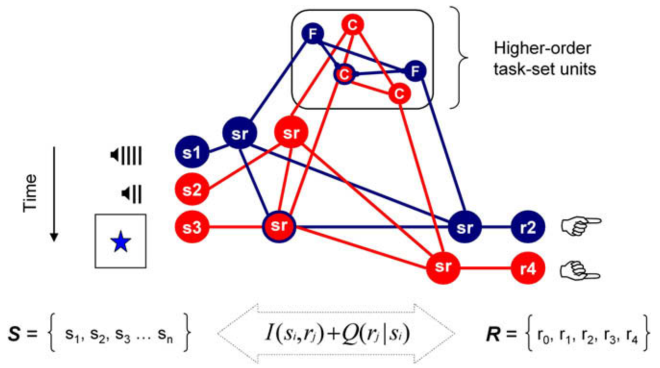

Fig. 3. Integrative model of prefrontal function (adapted from Miller, 2000) that accounts for the paradoxically similar ERPs to both novel sensory distractors and familiar task-switch cues in the MCST protocol. Red indicates active task-set units or pathways. Small circles represent conflict between two antagonistic higher-order task-set units. For simplicity, only the color and form rules are represented, together with only three stimulus features and two motor responses from the pool of all available stimuli and responses. Following Koechlin and Summerfield (2007), we employed information theoretic estimations of sensorimotor $[I(r_j, s_i)]$ and cognitive control $[Q(r_j|s_i)]$ to describe the processing demands associated with target cards and contextual information (task cues and feedback signals), and to guide our interpretation of brain responses (see the main text for an explanation).

spite of their very different probability of occurrence, it can be shown that these switch and repeat cues convey similar amounts of sensorimotor information for selecting their associated 'nogo' response (also transmitted information, cf. Miller, 1956). This is illustrated in the left panel of Fig. 4, where an infrequent switch cue ($p = 0.06$) conveys the same information as a frequent repeat cue ($p = 0.44$) for selecting their shared 'nogo' response. These mean probabilities are estimated for an ideal subject committing only eight errors while sorting the 64 WCST cards following the color rule (Fig. 4, left panel). These estimations for low-level sensorimotor control stay the same when either two rules (Fig. 4, middle) or three rules are involved (Fig. 4, right panel).

More interestingly, the information processing demands associated with the same task-switch cue increase as a function of the number of higher-order task-set units being held in working memory (Fig. 4, Eq. (4)). This higher information content is consistent with the larger behavioral costs and enhanced novelty P3 responses to task-switch cues observed under three task-set conditions relative to only two, or single task-set conditions (Barceló et al., 2006, 2008). This approach may help us formalize the intuitive idea that stimulus processing depends on the *task context*, and suggests that the amount of information conveyed by unexpected 'wrong' feedback signals (or by task-switch cues) partly depends on *task uncertainty*, i.e., the total number of stimuli, responses, and task rules being concurrently handled in working memory (Fig. 3). The larger the amount of task-set information (task uncertainty) conveyed by the contextual signals, the larger the amplitude of endogenous novelty P3 potentials elicited them (Barceló et al., 2006, 2008).

This information theoretical approach could aid interpretation of the behavioral results obtained from different WCST variants and comparison across different task-switching procedures. This approach provides common interpretative grounds for the type of cognitive control processes required by novel distractors during simple perceptual classifications, by task-switch cues in dual-task conditions, or by disconfirming negative feedback signals in the conventional WCST procedure. All these situations require a transient change in the higher-ordered representations responsible for goal-directed behavior. This set-shifting mechanism is fast and short-lived and depends on an intact lateral prefrontal cortex (Miller, 2000; Milner, 1963; Shallice et al., 2008), but also on a distributed network of cortical and subcortical structures necessary for processing novelty at the highest level of neural representation (Barceló & Knight, 2007; Ranganath & Rainer, 2003). Moreover, even if this set-shifting mechanism develops within a few milliseconds, it is most likely accompanied by parallel accessory processes, as revealed by lesion studies (Barceló & Knight, 2007; Shallice et al., 2008) and as indexed by overlapping slow ERP negativities (Barceló et al., 2006; Nicholson et al., 2005).

These recent findings help us put into perspective the original questions about the validity and anatomical specificity of WCST scores for assessing prefrontal function. The concept of an anatomically 'pure' test of prefrontal function does not seem only empirically unattainable, but also theoretically inaccurate. The information conveyed by a set-shifting stimulus depends not only on its physical parameters or mean probability of occurrence, but also on its probabilistic association with other contextually related low-level (sensory, motor) and high-level (sensorimotor) task-set representations, as can be formalized through Eqs. (1)–(4) (Koechlin & Summerfield, 2007), and is illustrated in Figs. 3 and 4 (cf. Miller, 1956). Therefore, it seems reasonable to infer that the brain responses elicited by those set-shifting events engage a widely distributed neural network of cortical and subcortical structures, reflecting the complex and dynamic interplay between the cerebral representations of the eliciting stimulus and its associated task context along several time scales. From these premises, a more realistic objective for neuropsychological tests of executive function would be to characterize and fractionate prefrontal cortex as a critical processing node within various distinct and overlapping neural networks subserving cognitive control (Koechlin & Summerfield, 2007; Miller, 2000).

5. Conclusions

The present interest in prefrontal cortex function has renewed the use of the WCST in clinical and experimental settings. However, much criticism has questioned the utility of this test as a marker of prefrontal function. A critical review of clinical studies

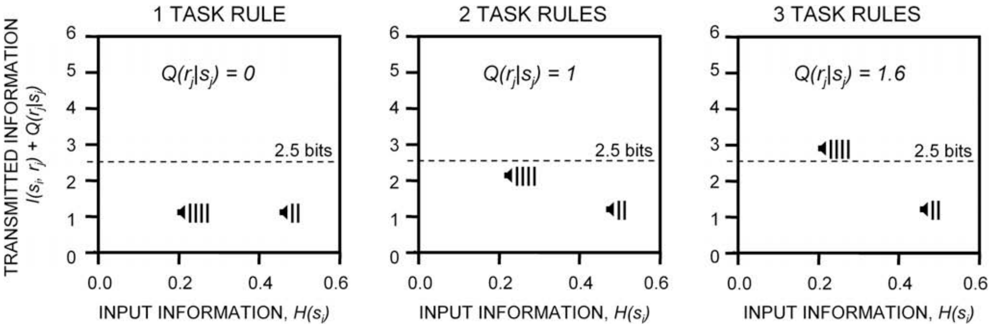

Fig. 4. A priori estimations of transmitted information between two tonal cues and their associated 'nogo' responses as a function of the sensory entropy ($H(s_1)$ = 0.25 and $H(s_2)$ = 0.50 bits for 'wrong' and 'right' feedback cues, respectively), and the number of task rules being handled in working memory (Koechlin and Summerfield, 2007; Miller, 1956). Estimations are made for an ideal subject committing only eight errors while sorting the 64 WCST cards. It can be shown that the amount of information conveyed by infrequent 'wrong' feedback cues (or by task-switch cues) depends on task uncertainty, that is, on the number of task rules being handled in working memory. The larger the amount of task uncertainty associated with auditory signals, the larger the amplitude of the novelty P3 potentials elicited by them (Barceló, Escera, Corral, & Periañez, 2006; Barceló, Periañez, & Nyhus, 2008; see the main text for an explanation).

suggests that the original WCST does not distinguish between frontal and non-frontal lesions. Likewise, functional neuroimaging studies confirm that delivery of negative feedback during WCST rule transitions activates a widespread network of frontal and non-frontal regions within a split-second time scale. New methodological and conceptual advances from theory-guided experimental designs, precise spatial and temporal sampling of brain activity, and modern integrative models of prefrontal function (Miller, 2000) combined with a formal information theoretical approach to cognitive control (Koechlin & Summerfield, 2007) can improve our understanding of the WCST and its relationship to prefrontal executive functions. These advances suggest that simple modifications of the original version of the WCST may offer more valid and reliable measures of key component operations, such as the maintenance, shifting, and updating of task-set information over trials. Fast brain imaging techniques help us put into perspective the specificity of the test as a marker of prefrontal function as a key node within the widely distributed and tightly interconnected neural networks subserving human cognition.

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