Wisconsin Card Sorting Test Synchronizes the Prefrontal, Temporal and Posterior Association Cortex in Different Frequency Ranges and Extensions

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Abstract: Current findings show some brain regions consistently related to performance of the Wisconsin Card Sorting Test (WCST). An increase of local cerebral blood flow or metabolic demands has been detected in those regions. Functional integration of the neuronal circuits that subserve the task performance, based upon the identification of the oscillations and their distributed cerebral sources, has not been accomplished previously. The event-related tonic oscillations within a period of 2,000 msec after the stimulus onset and the probable neural substrate were evaluated in healthy volunteers by variable-resolution brain electrical tomography (VARETA). The WCST induced a significant increase of δ , θ , β -2, and γ oscillations, but decrease of α . Areas such as the frontal subregions, temporal, cingulate, parahippocampal, parietal, occipitotemporal cortex, and occipital poles showed modified activity during the task, with EEG spectral band selectivity as well as some overlapping among them. Frontal and temporal regions generated the δ/θ oscillations. Additionally, the occipitotemporal and parietal regions were the source of the δ activity, lacking θ activation. The parietal region also showed tonic α , β -2 and γ changes. These data imply that different processes have been simultaneously mediated during task performance. Relationships among the individual bands, the neural substrata and the specific cognitive process that support the task were established. The selectively distributed δ , θ , α , β -2 and γ oscillations reflect communication networks through variable populations of neurons, with functional relations to the working memory functions and the information processing that subserve the WCST performance. *Hum. Brain Mapping* 17:37–47, 2002. © 2002 Wiley-Liss, Inc.

Key words: VARETA; oscillations; neural networks; cognitive task

INTRODUCTION

The Wisconsin Card Sorting Test (WCST) is a neuropsychological test that has been associated with the integrity of the dorsolateral prefrontal cortex (DLPFC). Many clinical studies suggest that patients with frontal lobe lesions, especially in the DLPFC, show greater impairment on the WCST than patients with lesions in other areas [Arnett et al., 1994]. In normal subjects, functional imaging techniques, such

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as single photon emission tomography (SPECT), positron emission tomography (PET), functional magnetic resonance (fMRI) and near infrared spectroscopy (NIRS), show an increase in the local cerebral blood flow (CBF) or metabolic demands in the DLPFC, mostly in both hemispheres [Fallgater and Strik, 1998; Nahagama et al., 1996; Parellada et al., 1994].

Accordingly, the WCST has become a common clinical method to assess changes in the cognitive function of individuals with frontal and non-frontal pathologies, particularly in such neuropsychiatric patients as schizophrenics. In this visual task, subjects need to match a target card to reference stimuli on the basis of one of three pre-established categories. The subjects have to determine which category is correct, using only the feedback that indicate whether each response is right or wrong. The correct sorting principle change in a predetermined pattern of which the subjects are not informed. The complex higher-level cognitive processes mediating this task have been approached variously as a whole or by contrasts between them (e.g., set shifting, reason) leading to some apparent differences in interpretation of the results [Konishi et al., 1998]. In a uniquely designed study, however, Dumbiar and Sussman [1995] showed that accurate performance of the WCST requires functional integrity of the working memory system. They concluded that the higher-level cognitive process observed during the WCST performance involves the maintenance of a temporary representation in working memory (WM). Thus, we are addressing here only short term memory aspect of WCST. Indeed, WM provides the basic ability to keep track of and update information at every moment, and is one of the emergent properties of the interaction of the prefrontal cortex with other brain areas in domain-specific cortical networks [Goldman-Rakic, 1995; McIntosh, 1999].

Current knowledge provides strong support for the assumption that oscillations reflect a basic form of communication between cortical cells assemblies and during mental task activity in humans [Klimesch, 1996a]. Synchronization between different cortical networks may mediate top-down effects. During task performance, several simultaneously active neuronal assemblies may occupy different cortical areas, producing an EEG activity with complex spatiotemporal patterns [Fernandez et al., 1998].

Generally, the oscillations assessed have concentrated on the conventional clinical frequency ranges, with the classical distinction between the δ , θ , α , beta, β -2 and γ bands. This has permitted the establishment of some relationships between a particular range of oscillations and a specific cognitive process. A well-

documented interaction is the δ - θ activity induced during short-term memory or working memory [Harmony et al., 1996; Klimesch et al., 1996b; Sarnthein et al., 1998]. Further, α activity reflects a dynamic change of the attentional demand during information processing, whereas β -2/ γ oscillations have been related to sensory perceptual processes and subsequent information processing, e.g., short-term memory in humans [Tallon-Baudry et al., 1998; von Stein and Sarnthein, 2000; Wei et al., 1998].

Although these results are well-known, none of these studies has analyzed the functional integration among the neuronal circuits mediating the WCST performance, accomplishing the identification of the independent oscillations and their distributed cortical sources. Thus far, the majority of the spatial analyses carried out in humans have been restricted to the measurement of local cerebral blood flow or metabolic rates with little temporal resolution.

Classical electroencephalographic studies have established an association between the EEG frequency and regional cerebral blood flow, as well as regional glucose metabolism and oxygen uptake by cortical gray matter [Ingvar et al., 1976]. Cognitive activity induces both electrical and metabolic changes in the cerebral tissue that reflect neuronal activation, with higher temporal resolution afforded by electrophysiological measures. Time-locked tonic oscillations have a high degree of dynamic variability and a rapid onset and offset of synchrony among interacting populations of neurons, lasting from around 100 msec to a second [Gray et al., 1992]. Therefore, it seems reasonable to expect that electrophysiological assessments can be correlated with the previous functional studies, but will provide higher temporal resolution analysis that may give some new insights into the elements comprising this distributed system.

We attempt to identify the principal EEG induced changes within the 0.5–30 Hz frequency range in a time window of 2 sec from the stimulus onset. The spatially distributed neural substrates will be identified that generate specific oscillations. These presumably bind the distributed networks supporting a specific state of activation, mediating performance of the WCST. A recently developed technique, the variable resolution brain electrical tomography (VARETA) [Valdés et al., 1996] was employed to reach this goal.

In view of the complexity of the WCST, we expect to uncover more than one network that share some functional areas and fire sequentially or simultaneously within a short interval of time, but oscillate in different frequency ranges. This method may allow us to distinguish among the several cognitive processes in-

Figure 1.

The WCST, as presented on the computer monitor. Top row: the reference card including the three categories; bottom row: the target card.

volved, by drawing inferences from the pattern of the distributed networks presumably bound by the oscillations.

Additionally, to clarify some discrepancies in the literature usually attributed to the use of different controls, we devised an intra-individual assay that compared three frequently described baseline states to each other before opting for one of them.

MATERIALS AND METHODS

Twelve healthy, right-handed adult candidates took part in the experiment. Five of the subjects were males, mean age 28.5 years (SD 3.12). All of them had at least 13 years of education. None of the subjects reported a personal or family history (first degree) of psychiatric or neurological disorders, alcohol consumption, and none were on any medication. Once the experiment was fully explained, an informed consent was obtained from each subject.

The WCST was presented on a computerized version (DIANA, Neurocognitive Assessment, Neuronics SA, Havana, Cuba) (Fig. 1). Subjects were instructed to match target card to reference stimuli on the basis of one of the three possible categories: number, color, or shape. The correct sorting principle changed in a predetermined pattern of which the subjects were not informed. The subjects had to determine which category was correct, using only the feedback displayed on the monitor that indicated whether each response

was right or wrong. When the subject maintained a correct progression through ten trials that utilized a specific category, the principle was changed without warning, and the subject then had to search for the new correct category. Stimuli were presented on a computer screen and the subjects used the arrow key to select the target card. Once the task was started, it continued until a maximum of six categories had been achieved or 128 cards had been sorted. Subjects were encouraged to work as efficiently and rapidly as possible, but otherwise were allowed to proceed at their own pace. The WCST performance was automatically scored using the criteria provided by Heaton et al. [1993]: categories, total errors, perseverative errors, nonperseverative errors, % perseverative errors, trials to first category, and failure to maintain a set.

Each subject was seated in a comfortable chair in an air-conditioned room under dimmed room light, followed by the electrode placement and instrument calibration. They were instructed to keep their eyes open and fixed on a point in the center of the screen placed in front of them (100 cm) and to avoid unnecessary eye movement. The procedure was explained shortly before the experiment started. Baseline condition was recorded by having the subjects at rest looking at the computer screen with the target and reference cards, but without response. The data acquisition started simultaneously with the cognitive task and continued until the task ended. Before choosing the above baseline state, five candidates were tested during three different state by simply looking at the monitor: 1) without any stimulus (in black); 2) similar task background without any cards; and 3) with target and reference cards without any response.

Nineteen Ag/AgCl electrodes were bilaterally placed on each subject's scalp using electrode cream and the 10/20 system electrode placement at Fp1, Fp2, F3, F4, C3, C4, P3, P4, O1, O2, F7, F8, T3, T4, T5, T6, Fz, Cz, and Pz. The electrooculogram (EOG) to control the eye movements was recorded from two electrodes, one placed on the inferior lateral canthus of the right orbit and the other on its superior ridge. Each recording session took about 12 min. Electrode impedance was kept at 5 k Ω . Raw EEG signals were recorded using the Medicid-4 (Neuronics SA, Havana, Cuba) digital data acquisition system, with a monopolar montage referred to linked earlobes and filtered at 0.5–30 Hz. The data from all the trials were stored for a subsequent off-line analysis. To avoid any performance that might introduce undesirable sources of variance into the data, only nine individuals that achieved at least five categories were included. Thus, the possibility to obtain frequency changes involving

an active region not closely related to correct task performance was minimized.

After visual editing to exclude artifacts, an average of 24 trials/subject was selected. Each trial consisted of an EEG epoch triggered by onset of stimulus presentation and lasting 2,000 msec. Similar 'baseline' epochs were selected from the EEG during the resting state. No epochs with a response shorter than this period were included. For each monopolar lead, the fast Fourier transform was computed and the power spectra was calculated at 0.5 Hz intervals, from 0.5–30 Hz.

To obtain the inverse solution, the crossspectral matrix was computed using the quantitative-EEG Tomography workstation (Neuronic SA, Havana, Cuba) to estimate the current source generators of EEG from the crossspectral matrix. This program is based on the method of variable resolution electromagnetic brain tomography, or VARETA [Bosch-Bayard et al., 2001; Valdés et al., 1996]. This technique enabled us to calculate the distributed sources for each frequency.

In VARETA, the current sources are restricted to the gray matter by using an anatomical mask derived from a probabilistic brain atlas (PBA) developed at the Montreal Neurological Institute [Evans et al., 1993]. The PBA provides a priori information on where gray matter can be expected to be present in a subject with no abnormalities of brain morphology. This estimate is scaled in Talairach space.

The statistical significance of the inverse solution data was assessed on a voxel-by-voxel basis, comparing the values across the conditions (baseline vs. WCST), by using a multivariate non-parametric permutation test [Galán et al., 1997]. The global null hypothesis tested was the equality between the power spectra recorded in two different conditions in all derivations and all frequencies. The marginal null hypothesis was the equality of the power at a particular frequency in different locations. The permutation methodology offers the following advantages: the tests are distribution free, no assumptions of an underlying correlation structure are required, and they provide exact *P*-values for any number of subjects, frequencies and recording sites.

The spectral curves in all the electrode sites obtained for each subject in the baseline state were compared across all subjects by a test of correlation.

RESULTS

The subjects generally performed well on the WCST (Table I), and were selected for this analysis based on their task results. Only those with at least five cate-

TABLE I. The WCST performance in the definitive candidates

Subjects (n = 9)	Scores
Categories	5.7 (0.06)
Nonperseverative errors	16.4 (8.9)
Perseverative errors	2.3 (1.9)
Total errors	18.8 (10.4)
% Perseverative errors	14.0 (6.8)
Failure to maintain set	2.1 (1.6)
Trial to first category	15.5 (1.4)

Values are mean (SD).

ries achieved were included (n = 9, mean = 5.7 categories, SD = 0.06).

The intra-individual baseline state comparisons showed no differences. On the contrary, they had a high correlation index, ~0.98, among the corresponding induced spectral curves.

The modifications of the brain electrical activity induced by the WCST were concentrated in the δ , θ , and α frequencies. Statistically significant changes relative to the baseline state were consecutively from 0.5–6.50 Hz, involving each individual frequency in δ and some in the θ range. Significant deviations of α activity were found in all the individual frequencies (from 8–12 Hz), but the remarkable feature was an inhibition of all frequencies within this band. Beta-2 and γ bands also showed a modified pattern, with activation within 20–30 Hz.

The brain electrical tomography method (VARETA) identified the distributed sources of the EEG spectral perturbation recorded on the scalp. Table II shows each individual band, within the 0.5–12 Hz and 20–30 Hz frequency range, that changed as a consequence of WCST performance. The entire δ band was sensitive to the task and the sources of these frequencies (0.5–4.0 Hz) were located bilaterally, in the prefrontal region (medial, lateral), orbitofrontal region, anterior cingulate cortex, subregions of temporal cortex (including the inferior, middle and superior areas), parahippocampal zone, ventral occipitotemporal region and parietal lobe, but with an asymmetry favoring the left hemisphere. In the θ range, some frequencies (4.0–6.5 Hz) were modified significantly relative to the control condition. Most of the peaks were located in the bilateral prefrontal regions (medial, lateral), the orbitofrontal and cingulate cortex and the temporal lobe, with left and anterior dominance. The source distributions of α frequencies (8.0–12.0 Hz) showed peaks of task effects in the right occipitotemporal regions as well as the bilateral parietal areas (Table II). The fast oscilla-

TABLE II. Induced oscillations during the WCST performance in normal subjects[†]

Oscillations ($P < 0.05$)	Left hemisphere (Brodmann area)	Right hemisphere
Delta range 0.5–4.00 Hz (increase)	Orbitofrontal (11/47), dorsolateral frontal (10/46), superior frontal (9/8), inferior temporal (20/21), middle temporal (22/37), superior temporal (40/39), parietal (7/40/19), parahippocampal, occipitotemporal (37), cinguli cortex (32/24), medial frontal (32)	Orbitofrontal, dorsolateral frontal, inferior temporal, middle temporal, superior temporal, occipitotemporal, cinguli cortex, medial frontal
Theta range 4.0–6.5 Hz (increase)	Orbitofrontal (11/47), dorsolateral frontal (10/46), inferior temporal (20/21), middle temporal (22/37), cinguli cortex (32/24), medial frontal (32)	Orbitofrontal, dorsolateral frontal, middle temporal, cinguli cortex, medial frontal
Alpha range 8.0–12.0 Hz (decrease)	Parietal (7/40/19), occipital pole (19/18/17)	Parietal, occipito temporal (BA 37/39), occipital pole
β -2 range 20– 25.5 Hz (increase)	Superior temporal (40/39), parietal (3/7/39/40)	
γ -range (27– 30 Hz) (increase)		Parietal (BA 3/7/39/40)

[†] Note the left/right difference in each individual band.

tions, β -2/ γ , showed a distribution confined to the parietal regions, but opposite: 20–25 Hz (β -2) on the left side and 27–30 Hz (γ) on the right. The β -2 also engaged the left superior temporal region.

When the tomography was examined as a function of the frequency bands, it appeared that the functional areas in the frontal, temporal, parietal, and occipito-temporal regions were involved in different ways. They displayed EEG spectral band selectivity with some overlapping across the different spectral bands. The frontal and temporal areas generated the δ / θ oscillation, but with a left dominance more pronounced in the θ frequencies. Areas such as the parahippocampal gyrus, the occipitotemporal region, and the parietal lobe were the source of the δ activity, while lacking θ activation. The parietal lobe was also the source of the α / β 2– γ changes with an inverse pattern of the two ranges, desynchronization vs. synchronization.

Table III shows the numerical value of the maximum (greatest peak at each narrow frequency) concentrated in specific functional areas involved in the task performance. We arbitrarily denoted this as the “participation index.” Most of the regions (14) had about four peaks of oscillation, whereas the remaining regions (7) contain approximately three times the previous number of peaks (~ 13). Regions such as the superior temporal, dorsolateral prefrontal, the orbito-

frontal, the inferotemporal, the middle temporal, in this order, were the most involved (higher participation index) within the δ - θ activation, but with a significant left dominance. Posterior areas such as the right occipitotemporal and the parietal regions were involved as well. These posterior areas were related to the α inhibitory patterns, as well as to the β -2/ γ activation. Those areas with the highest indexes may be the most implicated in the cognitive processing required by the task.

The brain electrical tomographic images obtained during the performance of the WCST display the cortical sources of the most significant level of activation/inhibition in each band during the task performance. Figure 2 shows the peak of activation distributed within the brain, with a clear EEG-narrow spectral band selectivity presumably binding different neural networks. δ oscillation occurred in different regions that are functionally and anatomically interconnected and build up a virtual network involved in the WCST solution. The other activated networks (θ) supporting the test solution are more circumscribed than the δ networks, into frontotemporal areas with a slight left and frontal dominance. At some frequencies, the asymmetry was remarkable (Fig. 3).

The α inhibition during the test solution is shown in Figure 4. The pattern of α inhibition may be observed over wide areas of the scalp in the right hemisphere,

TABLE III. Numerical value of the maximum (greatest peak at each narrow frequency) concentrated in specific functional areas involved in the task performance[†]

Cortical region	Δ/θ	α	β -2	γ	Total
<i>Left orbito frontal</i>	13				13
Right orbito frontal	4				4
<i>Left dorsolateral frontal</i>	13				13
Right dorsolateral frontal	5				5
Left superior frontal	3				3
Left medial frontal	4				4
Right medial frontal	4				4
<i>Left inferior temporal</i>	11				11
Right inferior temporal	4				4
<i>Left middle temporal</i>	9				9
Right middle temporal	3				3
<i>Left superior temporal</i>	6		8		14
Left cinguli cortex	1				1
Right cinguli cortex	4				4
Left parahippocampal	4				4
Right parahippocampal	5				5
<i>Left parietal</i>	2	3	7		12
<i>Right parietal</i>		8		8	16
Left occipito temporal	2				2
<i>Right occipito temporal</i>	2	8			10
Left occipital pole		2			2
Right occipital pole		2			2

[†] The principal nodes related to the task are italicized.

such as the occipitotemporal region and the parietal region. Additionally, the inferior parietal region participates in the network activated by the fast oscillations. Figure 5 shows the distributed sources of β -2 oscillation restricted to a small region in the left hemisphere, while the γ oscillation presents a similar picture but in the contralateral hemisphere.

DISCUSSION

During the solution of the WCST, the cerebral electrical activity was modified, inducing oscillations within the δ , θ , β -2, and γ ranges, as well as producing α desynchronization. The topographies of the maximum peaks of activation were quite similar in most of the frequencies within each wide band, although different among them. The cortical sources generating the δ activity were located in the frontal regions, such as the dorsolateral (Brodmann areas 9, 46), the orbito-frontal, the medial frontal, the inferior, the middle and the superior temporal regions, as well as the parahippocampal area, the anterior cingulate cortex, the parietal lobe and the ventro-occipitotemporal region of both cerebral hemispheres, with a slight left dominance. The θ activity was located on the bilateral pre-

frontal cortex, the lateral and the medial, the orbito-frontal cortex and the bilateral inferior and the middle temporal lobe, with a left and frontal dominance. Alpha inhibition was found at right occipitotemporal region, and on the bilateral parietal regions and the occipital pole as well. The β -2 activity increased at left superior temporal and parietal regions, whereas the γ activation evolved at right parietal lobe. The time-locked transient activation of several regions in the same range of frequency was interpreted to indicate the synchronization of neuronal assemblies forming a functional network related to the task.

The δ and θ bands each have their cerebral areas well defined although they share some of them. The α oscillation differs from the previous one that appears in a posterior inhibitory system that co-exists in the left parietal region with the δ oscillations. At this site, β -2 oscillations also appear, while the contralateral region develops both α inhibition and γ activity. Beta-2 and δ oscillations coexist in the left superior temporal region as well. Different time-locked transient oscillations within the same region imply that different processes have been locally served simultaneously during task performance.

Figure 2.

Brain electrical tomography (VARETA) in the frequency domain. The cortical sources of maximum to δ oscillations during the WCST on the average brain from the PBA are shown. The images show different activated region in the δ range resulting in functional interconnected areas, that sustain the test performance. In the top row the picture corresponds to the activation of the frontotemporal regions (a) and the ventro-occipitotemporal area

(b). The row at the bottom shows a coronal section of the activated temporal areas (inferotemporal, parahippocampal). Plane of sections are in Talairach space: (a, b) sagittal $x = 21$, (c) coronal $y = -18$. R, right; L, left; A, anterior; P, posterior. Scale refers to P -values. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

EEG rhythms must be understood in the context of the interconnected brain networks mediating synchronized activities of the neuronal ensembles. Each rhythm should be placed within the context of a distinct behavioral state [Steriade et al., 1990]. In this study, rather than adopting a unique condition as a stable baseline state, different resting situations with

presumable different visual attentional level were explored as possible explanations of some discrepancies reported in literature [Nagahama et al., 1996]. One of the above referenced states required attention to WCST targets and reference cards on the computer screen but with no behavioral response. Using this condition, any significant effect among these states

Figure 3.

VARETA. Regions with a maximal peak for the θ oscillations with different patterns of activation are shown. The bilateral fronto-temporal activation (right) in a particular frequency, in contrast to the interhemispheric asymmetry for another θ frequency (left),

can be observed. There are areas that participate in more than one network. Plane of axial section: $Z = 0$. (Talairach space). Scale refers to P -values. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

Figure 4.

VARETA. The maximum of inhibition of the α range during the WCST solution. α desynchronization occurs over wide areas of the scalp, such as the right occipitotemporal region (**A**) or restricted to the right parietal area (**B**). R, right; L, left; A, anterior; P, posterior. Scale refers to *P*-values. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

could be found. The observed task-induced EEG variations appear to be a direct consequence of the cognitive activity that underlies solution of the WCST and can not be attributed to general non-specific attentional demands.

The relation of the δ and θ frequencies to such an internal process as memorization and the flow of information between the neuronal circuits that link the target cortical areas with the hippocampal complex and working memory, has been postulated [Harmony

Figure 5.

VARETA. Right: the sources of β -2 oscillation restricted to a small region in the left hemisphere, while the contralateral region (left) develops γ oscillation. Note the selective laterality to the oscillations. Scale refers to *P*-values. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

et al., 1996; Klimesch et al., 1996b; Sarnthein et al., 1998]. We propose that the short-term memory function, specifically the working memory system, may be the principal process inducing these oscillations in our study. Some features, however, may be distinguished regarding the cognitive components that are utilized. Processes such as maintenance and shifting of category set may overlap in the major areas activated within frontal regions, and may extend differently into other regions.

In good performers, set shifting is infrequent. The maintenance of sets becomes the main function sustained throughout the task and is independent of the particular category set. The induced δ oscillations evolve as the most consistent change involving the prefrontal regions, temporal region including the parahippocampal areas, and the parietal and occipitotemporal regions. These regions subserve different functions necessitated by the transient memory load in the working memory system that resides in prefrontal structures [Monchi et al., 2001]. Regions related to set shifting are restricted to the prefrontal areas in which the function of response inhibition may be located [Konishi et al., 1998]. It seems that the induced θ oscillations reproduce this pattern, extending partially to the left temporal regions that may also be related to the working memory update. The α oscillations demonstrate relatively widespread inhibition in memory tasks and seem to reflect general task demands and attentional processes, which probably develop during the processing of sensory semantic information [Klimesch, 1996a; Pfurtscheller and Lopes da Silva, 1999]. Selective attention to different categories during the WCST may induce inhibition of α oscillations in posterior associative areas of both hemispheres because categories are processed at both sites but with marked lateralization [Nagahama et al., 1996]. The information maintained in the working memory system is closely related to the attended category, and the decrease of α oscillations contributes to this process.

The design of the WCST requires visual information processing of the specific stimulus attributes (color, shape, number), a process related to the posterior regions. Fast oscillations, β -2 and γ , have been related to visual perception, subsequent information processing, and the function of working memory [Tallon-Baudry et al., 1998]. The activity in these regions induced by the WCST suggests a relationship between the category sets and the range of the oscillations. β -2 oscillations are restricted to the left side and γ oscillations to the right side. Individual hemispheric engagement by processing requirements of the different categories may account for the lateralized oscillations.

Although the activation of the posterior areas may also be attributed to global visual stimulation, it is unlikely that such a general demand would induce a selective distribution of different ranges of oscillations. The WCST-induced changes in posterior regions seem more likely to be related to higher-level information processes at supramodal areas.

The identification of the target sources of the activity in the frontal, temporal, and parietal regions during the WCST is not unexpected. Most neuropsychological studies demonstrate a relationship between the dorsolateral frontal cortex and the WCST. Although the activation observed in the DLPFC during the WCST is consistent with the results of previous neuroimaging studies [Berman et al., 1995; Fallgater and Strik, 1998; Parellada et al., 1994; Monchi et al., 2001], the present study also shows that not only the DLPFC but also other areas, such as the orbito- and medial-frontal cortex, the anterior cingulate cortex, the inferior, middle and superior temporal gyri, the occipitotemporal gyrus, the parahippocampal gyrus, and the occipital poles are involved in cognitive processing during the WCST. The results of this study incorporate several principal areas described previously and separately in different experiments by different research groups. Diverse peaks of different oscillation ranges were identified within the 2,000 msec intervals after visualization of the cards. Because normal people take about 2 sec to classify a card, this analysis epoch contains information about all the tonic transient processes involved, with the exception of the subsequent sensory-motor response. Incorrect responses were not evaluated in this study because their occurrence was insufficient to obtain reliable results. Various reports [Berman et al., 1995; Nagahama et al., 1996] have shown that the inclusion of incorrect feedback stimulus simply enhances the activation of the detected areas related to set shifting.

If we analyze the "participation index," considering the distinct functional behavior (activation vs. inhibition), the regions saliently related to the WCST are: the left dorsolateral prefrontal, orbitofrontal, inferotemporal, middle temporal, superior temporal, parietal (bilaterally) and the right occipitotemporal regions. These results agree with those [Berman et al., 1995; Nagahama et al., 1998] mentioned in previous studies. This study provides evidence that the synchronized networks overlap and interact profusely with one another, and indicate that a particular region can participate in more than one network. The VARETA method unquestionably facilitates separation of these simultaneous events by their inherent oscillations and quantification of the distinctive frequencies characterizing

the local involvement with specific cognitive task demands.

The "participation index" also offers a measure of the hemispheric dominance, which was significantly higher in left regions, with the exception of the ventral and medial areas (cingulate cortex and ventral occipitotemporal area) where it was bilateral, and the occipitotemporal region with right dominance. The laterality is closely related to the particular range of oscillations under study and should be regarded therefore as a functional feature belonging to each separate cognitive component of the task that induced the oscillations and not interpreted as a unitary phenomenon.

The activation of the prefrontal cortex, the temporal structures, and the parietal lobe suggests a functional connection among these areas involving the solution of WCST. Prefrontal areas are involved in the active maintenance of problem-related information in the working memory and may be involved in maintaining a specific cognitive strategy. The temporal regions contribute to this information, updating the working memory system throughout the visual encoding processes. In addition, the parietal lobes guide the attentional process to the different category sets, gating the inhibitory system that in turn favors visual information processing and object recognition.

This study proposes that the selectively distributed δ , θ , α , β -2, and γ oscillatory systems act as resonant communication networks engaging large populations of neurons, with functional relations to the working memory and integrative functions that subserve the WCST solutions. The knowledge of the organization of the functional neuroanatomical systems that sustain the WCST can improve its usefulness in interpreting the results of behavioral studies in clinical practice as well as in research. To our knowledge, this is the first demonstration of relationships between performance of the WCST and induced EEG oscillations in brain regions belonging to specific neuroanatomical networks.

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