Putative Tests of Frontal Lobe Function: A PET-Study of Brain Activation During Stroop’s Test and Verbal Fluency?

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ABSTRACT

Stroop’s test and the Verbal Fluency test are commonly argued to be measures of the integrity of the prefrontal cortex. This assumption has only to some degree been confirmed by lesion studies. In the present study, Positron Emission Tomography (PET) with H₂¹⁵O was used to further validate Stroop’s test and the Verbal Fluency as measures of frontal lobe function; both tests were implemented as activation paradigms during scanning of normal middleaged individuals. Stroop interference was found to activate the left anterior cingulate cortex, the supplementary motor cortex, thalamus, and the cerebellum. Although the prominent anterior cingulate activation is in the frontal lobe, it is not prefrontal. Verbal Fluency activated the left inferior frontal cortex and the left dorsolateral prefrontal cortex, the supplementary motor cortex, the anterior cingulate cortex and the cerebellum. These results bring this latter test closer to being a specific test of prefrontal function.

Stroop’s test (Stroop, 1935) and the Verbal Fluency test (Borkowski, Benton, & Spreen, 1967) are classic experimental paradigms used in both clinical neuropsychological and research settings. Both tests are commonly assumed to be measures of the integrity of the prefrontal cortex. Theoretically, the Stroop test has been linked to effortful processing (Cohen, Dunbar, & McClelland, 1990), attention, and response selection or inhibition. Fluency tasks have been linked with response initiation, access to semantics, strategy and attention (Frith, Friston, Liddle, & Frackowiak, 1991; Ruff, Light, Parker, & Levin, 1997). These functions are arguably dependent on prefrontal cortex integrity.

Several studies have attempted to validate these assumptions in neurological patients with and without prefrontal lesions. Generally, it has been confirmed that the two tests, especially Verbal Fluency, have some degree of sensitivity to prefrontal lesions, but results on specificity have been conflicting (Reitan & Wolfson, 1994; Stuss, Floden, Alexander, Levine, & Katz, 2001).

Use of the Stroop test as a sensitive and specific test of frontal lobe function is mainly based on the study by Perret (1974) on presurgical tumor patients. Patients with tumors in the left frontal lobe were much slower in naming incongruent colors than any of the right hemisphere groups and patients with posterior left hemisphere lesions. Vendrell et al. (1995), however, found an increased error rate only in patients with right prefrontal lesions, and naming time in the incongruent part of the test did not differ significantly in any of the

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patient groups compared with controls. Vendrell et al. also noted that 71% of the patients with prefrontal lesions performed entirely normally on the Stroop test. Other studies have also failed to find differences between patients with prefrontal lesions and controls (Ahola, Vilkki, & Servo, 1996; Stuss et al., 1998).

Early studies on the Verbal Fluency test indicated that the critical lesion for impaired performance was in the left frontal lobe (Milner, 1964; Perret, 1974; Ramier & Hecaen, 1970) or bilaterally in the frontal lobes (Benton, 1968; Borkowski et al., 1967). Using a written version Pendleton, Heaton, Lehman, and Hulihan (1982) confirmed this, but also indicated a sensitivity to focal lesions with other localizations, especially diffuse lesions. The Verbal Fluency test did not differentiate between patients with frontal lobe dementia and Alzheimer patients (Pasquier, Lebert, Lavenu, & Petit, 1998), probably due to the deficits in semantic memory associated with temporal lobe pathology in Alzheimer patients. Verbal Fluency may also be sensitive to left focal temporal lobe lesions (Jokeit, Heger, Ebner, & Markowitsch, 1998; Martin, Loring, Meador, & Lee, 1990). In spite of the lack of specificity to lesions of the prefrontal cortex, direct comparisons have usually indicated a maximal sensitivity to prefrontal lesions.

Neuroimaging offers the opportunity to supplement previous clinical validations of neuropsychological tests with the mapping of the functional anatomy (regional cerebral blood flow/rCBF or metabolism/rgluCMB) underlying test performance. The purpose of the present study was to validate the use of Stroop’s test and the Verbal Fluency test as measures of frontal lobe function by implementing both tests as activation paradigms during Positron Emission Tomography (PET) scanning of normal individuals.

Specifications of this assessment is described in the following together with findings from previous activation studies.

**Stroop’s Test**

The basic principle of the test is to create interference between word reading and color naming (Mitrushina, Boone, & D’Elia, 1999; Shum, McFarland, & Bain, 1990). We chose to include the congruent condition in this version of Stroop’s test which is a color naming task of matching colors and color words (e.g., the word red printed in red) and the incongruent condition in which the colors of mismatching words and colors have to be named (e.g., the word red printed in green).

Reading is a highly automatized process. Color naming is a less automatic process which is vulnerable to interference from the more automatic process. This interference is observed as an increase in reaction time and errors from congruent to incongruent tasks. The Stroop paradigm is suitable as an activation paradigm of effortful processing as it consists of identical tasks, except for the critical component of effort to counteract the interference in the incongruent version. Previous studies of primarily young healthy subjects have tried to localize the particular areas involved in the processes of selective attention. The most consistent findings have been increased rCBF in the anterior cingulate gyrus and prefrontal cortex during the performance of Stroop’s test (Audenaert et al., 2001; Bench et al., 1993; Carter, Mintun, Nichols, & Cohen, 1997; George et al., 1997; Larrue, Celsis, Bes, & Marc Vergnes, 1994; Pardo, Pardo, Janer, & Raichle, 1990; Peterson et al., 1999; Taylor, Kornblum, Lauber, Minoshima, & Koepp, 1997).

**The Verbal Fluency Test**

In this study we used the phonological Verbal Fluency test (outlined by Lezak, 1995) asking the subjects to produce as many words as possible beginning with the letter ‘T’ during the scan. Contrary to Stroop’s test this test does in itself not hold different operations which can be subtracted from one another to isolate one specific component in functional imaging. Therefore, comparisons have typically been made with either a resting condition or fairly low-level control tasks such as word repetition, word reading, or an extrinsic word monitoring task, for example deciding whether a word is meaningful or not (Frith et al., 1991). In this study we compared the Verbal Fluency task of generating ‘T-words’ with a simple reading task, the reading of neutrally colored color words. This reading task should not hold the intrinsic (self-generating) aspect since
the ability to read is highly automatized and does not require the need to inhibit competing words. Yet, the reading task shares most other cognitive components with the Verbal Fluency task, namely the identification and pronunciation of words, visual stimulation (the subject was also given visual stimulus while generating words), and the auditory attendance to the subject’s own voice.

In previous neuroimaging studies word generation has mainly activated areas in the frontal cortex (Audenaert et al., 2000), specifically in the dorsolateral left prefrontal cortex (Frith et al., 1991; Petersen, Fox, Posner, Mintun, & Raichle, 1988; Phelps, Hyder, Blamire, & Shulman, 1997; Warkentin & Passant, 1997; Warkentin, Risberg, Nilsson, Karlson, & Graae, 1991). Two of these studies also found activation in the anterior cingulate gyrus. In addition to the prefrontal activation, Schlösser et al. (1998) reported a right cerebellar activation. Parks et al. (1988) and Philpot, Banerjee, Needham Bennett, Costa, and Ell (1993) showed activations in the frontal cortex in both hemispheres.

Age Effects
In the majority of the above neuroimaging studies the subjects were young adults. However, there are some indications that activation patterns may change with age. For instance, the frontal activation seen in memory tasks may be more heterogeneous in elderly subjects than in younger subjects (Madden et al., 1999). Nielson, Garavan, Ross, Rao, and Stein (1999) reported a more diffuse frontal activation in a ‘go–no go’ task in elderly subjects compared with young.

The subjects selected for the present study were middle-aged. Results from this age group may also be more relevant for the neuropsychological applicability of these tests.

METHODS

Subjects
Forty-six normal volunteers, mean age 41 ± 11.6 years (range 21–65 years, 16 males/30 females), participated in the study as part of a larger study dealing with affective disorders (Ravnkilde et al., 2001; Videbech et al., 2001a, 2001b, 2001c). The subjects were recruited by newspaper advertisement and had an average of 12.4 ± 2.4 years of education. Exclusion criteria were known organic brain disease, known drug or alcohol dependence, or ongoing abuse (according to ICD-10 and DSM-III-R). According to the Oldfield scale of handedness (Oldfield, 1971) only 3 were left-handers. All subjects underwent an extensive examination program consisting of both a physical examination and a neurological examination. Subjects were screened by blood tests and urine samples for significant medical diseases or hidden abuse of psychoactive substances. Subjects were also excluded if the MRI scans showed any cerebral focal abnormality or generalized brain disease except so called white matter lesions (Fazekas et al., 1993). Both the Hamilton Depression Scale (Hamilton, 1967) and a structured psychiatric interview (SCID for DSM-III–R; Spitzer, Williams, Gibbon, & First, 1992) were administered. None of the subjects or their first degree relatives had any history of psychiatric disorders. All subjects gave written informed consent. The project was approved by the Scientific Ethical Committee for Aarhus County and by the Danish Data Protection Agency.

Imaging Procedures
All subjects underwent measurement of cerebral blood flow during a total of five scans using radioactive water (H_2^15O) in a Siemens Ecat Exact HR47 Positron Emission Tomograph with a frame of 40 s for each scan. All scans were performed between 9 and 12 a.m. to account for diurnal variation in blood flow.

The subjects were supine with their heads fixed in a vacuum pillow to reduce head movement. Earplugs were used to dampen background noise, and room lights were dimmed. Five studies, one at rest and four activation tasks, were completed once for each subject. All instructions and injections were given by the same two persons. Further details of imaging and statistical methods are described elsewhere (Videbech et al., 2001b).

T1-weighted magnetic resonance images of the subjects’ brains were coregistered to the coordinate system by Talairach and Tournoux (1988) using an automatic algorithm with a linear 12 parameters fit. Furthermore, each subject’s MR image was coregistered to the PET images from the resting state using the MINC-TRACC algorithm, with a linear 6 parameters fit. The other PET images were then coregistered to this same PET image. This procedure is described in detail by Videbech et al. (2001b) and was done to correct for movement artifacts in the subtractions and to allow for precise anatomical localization of the activations. The radioactivity in every voxel was normalized to the average activity of all
intracranial voxels to minimize effects of intersubject variation of the global cerebral blood flow.

**Statistical Analysis**

Statistical analysis of the images was performed using the Montreal method (Worsley, Evans, Marrett, & Neelin, 1992) as implemented in the DOT software program. A within-subject subtraction of the congruent version of Stroop’s test from the incongruent version, and a subtraction of a simple reading task from the Verbal Fluency task (as described below) were performed. This procedure was followed by a computation of voxel-by-voxel multiple regression statistic of the regional cerebral blood flow (rCBF) differences controlling for age and gender. A voxel-specific standard deviation was used for the calculations. Correcting for multiple comparisons a t value of 5.63 was set as the threshold for statistical significance (p < .05 – corresponding to a whole brain volume of 1400 ml with df = 45; Videbech et al., 2001b).

**Experimental Tasks**

Four out of the five scans were accompanied by activation tasks. The order of the tasks was fixed. To isolate and visualize the active neural systems particularly involved in processing the Stroop interference task and the Verbal Fluency test, single words and visual stimuli were presented individually on a video monitor placed 50 cm in front of the subject’s face outside the scanner.

*The activation tasks were presented as follows:*

- A resting state in which the subject had to focus on a small white cross as a fixation point on the monitor screen.
- Reading color words printed in white.
- Naming the color of matching color words (e.g., the word red displayed in red color), the congruent version of Stroop’s test.
- Naming the color of incongruent color words (e.g., the word red displayed in green color), the incongruent Stroop’s test.
- Naming as many words as possible beginning with the letter ‘T’ while focusing eyes on a flashing big white cross on the screen, the Verbal Fluency test.

The color word stimulus consisted of a randomly ordered presentation of the four colors, red, green, yellow, and blue. No colors or color words were repeated consecutively. The words were approximately 150 mm × 50 mm presented in capital letters against a black background. A small white cross was placed 5 mm above the word stimuli as a fixation mark. The stimuli were displayed for 1 s with an interstimulus interval of 1 s. In all tasks the subjects were given instructions to react as quickly as possible to each presented stimulus, and in the incongruent condition of the Stroop task they were asked explicitly not to *read* the color words. Practice of a few stimuli from each condition was given once, prior to the actual five scans. In some subjects reaction times were measured for the four activation tasks during each scan using a microphone placed on the subject’s chest and connected to a computer.

**RESULTS**

**Reaction Time and Word Generation**

The mean reaction time recorded for the congruent Stroop was 398 ± 88.8 ms and 690.7 ± 125.2 ms.
for the incongruent Stroop \((N = 39)\). The difference in reaction time between the two tasks was statistically significant \((t\text{-test}, p < .001)\). In the congruent situation the subjects produced an average of 0.68 errors, whereas the error rate was an average of 1.6 in the incongruent situation.

During the Verbal Fluency test the subjects produced an average of 16.6 (range 5.5–29.2) words/min \((N = 41)\).

The PET activations in Tables 1 and 2 are reported as local maxima. Stroop activations are shown in Figure 1, Verbal Fluency activations in Figure 2.

**Stroop**

When subtracting the congruent Stroop task from the incongruent task (Table 1), the left anterior cingulate gyrus \((p < .01)\) as well as the left

### Table 2. Local Maxima (Verbal Fluency Minus Reading Task).

<table>
<thead>
<tr>
<th>Localization</th>
<th>Brodmann area no.</th>
<th>No. of max</th>
<th>X</th>
<th>Y</th>
<th>Z</th>
<th>min (t) – max (t)</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left cingulate gyrus</td>
<td>32, 24</td>
<td>2, 1</td>
<td>-5.4</td>
<td>25.3</td>
<td>34.5</td>
<td>10.53 – 16.43</td>
<td>.000</td>
</tr>
<tr>
<td>Right cingulate gyrus</td>
<td>32, 24</td>
<td>1, 1</td>
<td>9.4</td>
<td>35.6</td>
<td>18.0</td>
<td>10.50</td>
<td>.000</td>
</tr>
<tr>
<td>Left supplementary motor cortex</td>
<td>6, 7</td>
<td>1, 1</td>
<td>-40.2</td>
<td>8.1</td>
<td>28.5</td>
<td>10.89</td>
<td>.000</td>
</tr>
<tr>
<td>Left inf. frontal gyrus</td>
<td>47, 47</td>
<td>3, 1</td>
<td>-46.9</td>
<td>18.4</td>
<td>1.5</td>
<td>8.78 – 10.79</td>
<td>.000</td>
</tr>
<tr>
<td>Right inf. frontal gyrus</td>
<td>47, 47</td>
<td>1, 1</td>
<td>57.6</td>
<td>30.4</td>
<td>-1.5</td>
<td>7.45</td>
<td>.000</td>
</tr>
<tr>
<td>Left dorsolateral pre-frONTAL cortex</td>
<td>45, 9</td>
<td>1, 1</td>
<td>-45.6</td>
<td>23.6</td>
<td>16.5</td>
<td>10.62</td>
<td>.000</td>
</tr>
<tr>
<td>Left fronto-orbital gyrus</td>
<td>11, 25</td>
<td>1, 1</td>
<td>-28.1</td>
<td>44.2</td>
<td>-16.5</td>
<td>7.11</td>
<td>.001</td>
</tr>
<tr>
<td>Left thalamus</td>
<td>4</td>
<td>1, 1</td>
<td>-13.4</td>
<td>8.1</td>
<td>-16.5</td>
<td>7.08</td>
<td></td>
</tr>
<tr>
<td>Right thalamus</td>
<td>3</td>
<td>1, 1</td>
<td>-5.4</td>
<td>-22.9</td>
<td>6.0</td>
<td>6.31 – 8.36</td>
<td>.007</td>
</tr>
<tr>
<td>Left cerebellum</td>
<td>9</td>
<td>1, 1</td>
<td>-5.4</td>
<td>-59.0</td>
<td>-12.0</td>
<td>5.85 – 12.42</td>
<td>.028</td>
</tr>
<tr>
<td>Right cerebellum</td>
<td>14</td>
<td>1, 1</td>
<td>42.9</td>
<td>-77.9</td>
<td>-34.5</td>
<td>6.83 – 10.55</td>
<td>.003</td>
</tr>
<tr>
<td>Left inferior/superior temporal gyrus</td>
<td>21, 38</td>
<td>1, 1</td>
<td>-54.9</td>
<td>-41.8</td>
<td>-13.5</td>
<td>7.20</td>
<td>.001</td>
</tr>
<tr>
<td>Left superior occipital gyrus</td>
<td>19, 16</td>
<td>1, 1</td>
<td>-12.1</td>
<td>-84.8</td>
<td>39.0</td>
<td>7.62</td>
<td>.000</td>
</tr>
<tr>
<td>Right cuneus</td>
<td>1</td>
<td>1, 1</td>
<td>17.4</td>
<td>-67.6</td>
<td>15.0</td>
<td>7.17</td>
<td>.001</td>
</tr>
<tr>
<td>Left superior parietal lobe</td>
<td>7</td>
<td>1, 1</td>
<td>-10.7</td>
<td>-76.2</td>
<td>52.5</td>
<td>5.99</td>
<td>.018</td>
</tr>
<tr>
<td>Right insula</td>
<td>1</td>
<td>1, 1</td>
<td>37.5</td>
<td>18.4</td>
<td>-3.0</td>
<td>9.61</td>
<td>.000</td>
</tr>
<tr>
<td>Left insula</td>
<td>3</td>
<td>1, 1</td>
<td>-32.2</td>
<td>21.8</td>
<td>1.5</td>
<td>9.28 – 10.85</td>
<td>.000</td>
</tr>
<tr>
<td>Left anterior internal capsule</td>
<td>1</td>
<td>1, 1</td>
<td>-13.4</td>
<td>-4.0</td>
<td>-3.0</td>
<td>7.39</td>
<td>.000</td>
</tr>
<tr>
<td>Right globus pallidus</td>
<td>1</td>
<td>1, 1</td>
<td>14.7</td>
<td>-0.5</td>
<td>-7.5</td>
<td>6.74</td>
<td>.002</td>
</tr>
<tr>
<td>Brainstem</td>
<td>1</td>
<td>1, 1</td>
<td>2.7</td>
<td>-2.2</td>
<td>-10.5</td>
<td>7.71</td>
<td>.000</td>
</tr>
<tr>
<td>Left frontal lobe (WM)</td>
<td>7</td>
<td>1, 1</td>
<td>-33.5</td>
<td>47.6</td>
<td>10.5</td>
<td>8.36 – 13.12</td>
<td>.000</td>
</tr>
<tr>
<td>Right frontal lobe (WM)</td>
<td>2</td>
<td>1, 1</td>
<td>24.1</td>
<td>51.1</td>
<td>-6.0</td>
<td>5.87 – 5.92</td>
<td>.025</td>
</tr>
<tr>
<td>Left temporal (WM)</td>
<td>1</td>
<td>1, 1</td>
<td>-25.5</td>
<td>-24.6</td>
<td>-3.0</td>
<td>6.55</td>
<td>.003</td>
</tr>
</tbody>
</table>

*Note.* Localization of significant activations. Brodmann area number. Number of local maxima in specific area. Talairach coordinates \((x, y, z)\) for highest activation. Range of \(t\)-values. \(P\)-value. When local maxima are multiple, \(p\)-value equals least significant activation.
supplementary motor cortex ($p < .05$) showed significant activations. The cerebellum reached significant levels bilaterally ($p < .05$). The right thalamus, the left insula ($p < .01$), and white matter in the right frontal lobe ($p < .05$) were also activated. The left prefrontal cortex was not significantly activated. The highest activation within the prefrontal cortex was $t = 4.27, p > .2$.

In the subtraction of the Stroop test a single significant deactivation (local minima) was found in the right temporal gyrus ($p < .05$).

**Verbal Fluency**

In the Verbal Fluency test the reading of neutral color words was subtracted from the Verbal Fluency task of naming words beginning with the...
letter ‘T.’ This subtraction gave significant activations in several brain regions (Table 2). The primary activations were seen in the left supplementary motor cortex, the dorsolateral prefrontal cortex, the left and right inferior frontal cortex, and in the left fronto-orbital cortex. The left fronto-orbital cortex was also activated ($p < .001$). The thalamus was activated bilaterally ($p < .001$) as was the insula ($p < .001$). Many significant activation sites were detected in the cerebellum mainly in the right side ($p < .01$). A few maxima were located in the left temporal cortex ($p < .001$), the left occipital cortex ($p < .001$), and the left parietal cortex ($p < .05$).

Local minima were detected in both occipital lobes ($p < .001$) and in the right temporal cortex ($p < .01$) when making this subtraction.

Correcting for gender and age did not alter the results significantly for either Stroop’s test or the Verbal Fluency test.

Fig. 2. The coregistered PET and MR images demonstrating the subtracted Verbal Fluency activations in the left anterior cingulate gyrus, left supplementary motor cortex, left dorsolateral prefrontal cortex, and left inferior-, and orbito-frontal cortex. Activations are also seen in the temporal cortex.

The cerebellum mainly in the right side ($p < .01$).
DISCUSSION

Stroop’s Test
In this study the subtraction of two tasks only diverging in one aspect has resulted in significantly increased anterior cingulate activity. The divergent aspect is hypothesized to be the attentional demands of the selection process between competing cognitive processes, reading and color naming.

Several previous studies using this single-trial Stroop procedure for cognitive activation have also found increased rCBF of the anterior cingulate gyrus although only one study (George et al., 1997) reported activation limited to the left side of this structure as in our study. However, a left hemisphere predominance is in accordance with most studies using lateralized stimuli (MacLeod, 1991) and at least one lesion study (Perret, 1974).

The area our study has illuminated as a core structure in selective attention is well in accordance with the tripartite attentional system described by Posner (Posner & Dehaene, 1994; Posner & Raichle, 1995). According to this network theory of the attentional system, the anterior cingulate gyrus is active whenever a conflict is present between simultaneous processes (Posner & DiGirolamo, 1998). The conflict is evident from the difference in reaction time between the incongruent and the congruent Stroop task. Some component has been added in the incongruent condition making the time to respond longer than in the corresponding congruent task.

This conflict requires some sort of control mechanism or a selective attentional function of response selection. Presumably, the anterior cingulate inhibits the automatic response to the word name in order to facilitate or selectively attend to the execution of the less automatic process – that of ink-color naming in Stroop’s test. Recent studies confirm that the anterior cingulate gyrus is indeed involved in detecting and monitoring the occurrence of conflicts in information processing, although it may not exert the attentional control mechanism in selecting particular stimuli for action (Botvinick, Nystrom, Fissell, Carter, & Cohen, 1999; MacDonald, Cohen, Stenger, & Carter, 2000).

The inconsistent findings as to whether selective attention tasks involve the right or the left half of the cingulate structure may not be as important a discussion as the question of which different processes are actually entailed within this relatively large brain structure. The hemispheric differences of these specific processes may well be decided by particular features of the task stimuli such as patterns, symbols, or colors.

Although the anterior cingulate gyrus forms a component of a higher level system for response selection or conflict monitoring it may be implicated in other functions as well. Activation of this structure has also been reported in studies of divided attention (Corbetta, Miezin, Dobmeyer, Shulman, & Petersen, 1991), pain (Coghill et al., 1994), motor action (Paus, Petrides, Evans, & Meyer, 1993), and expectation (Murtha, Chertkow, Beauregard, Dixon, & Evans, 1996). It has also been assigned a role in emotion (Devinsky, Morrell, & Vogt, 1995).

These apparently conflicting results may relate to different parts of the anterior cingulate gyrus. Devinsky et al. (1995) have proposed a subdivision of the anterior cingulate cortex into areas related to either emotional or cognitive functions. The cognitive divisions include Brodmann’s areas 32 and 24 (caudal) whereas the emotional divisions involve areas 25, 33, and 24 (rostral). Bush et al. (1998) provided a map of anterior cingulate activation points from many different paradigms. Activations from cognitive/motor tasks (including attention) were clearly clustered in the caudal division of the anterior cingulate gyrus, providing solid support for the proposed subdivision. We note that the activation in our study is close to the center of this ‘cognitive cluster.’

According to this subdivision the activation seen in Stroop’s test, which was localized to Brodmann’s area 32 in our study, cannot be ascribed to mere motivation to respond or, for instance, to anticipatory anxiety caused by procedural factors. Another finding supporting the role of the anterior cingulate gyrus in attention was reported by Raichle et al. (1994). In this study the anterior cingulate activation in a verb generation task was eliminated after practice (i.e., automatization) and reinstated with novel stimuli.

Contrary to some other studies we did not find activations in either prefrontal cortices when making the subtraction of the two tasks. Clinically...
Stroop’s test has been used as an estimate of prefrontal damage, but our result is at variance with this. Our findings, thus, suggest that the prefrontal activation may not be as essential a component of selective attention as the cingulate activation.

Instead the supplementary motor cortex was activated. The lateral and mesial premotor cortices (BA 6) have been associated with the neural systems underlying visuospatial attention (Nobre et al., 1997) and with the temporal orienting of attention, for example in the ability to focus resources in order to optimize behavior at a particular moment in time (Coull, Frith, Buchel, & Nobre, 2000). The visuospatial and temporal aspects are part of the performance on Stroop’s test when the test is presented on a computer monitor at a paced speed. The activation of this particular brain area has also been noticed in previous studies (Pardo et al., 1990; Peterson et al., 1999; Taylor, Kornblum, Lauber, Minoshima, & Koeppe, 1997).

The significant cerebellar activation may also be of some interest. It is now recognized that the cerebellum not only participates in motor activities, but is in fact active during many different and also purely mental activities (Desmond & Fiez, 1998; Jenkins & Frackowiak, 1993; Jernigan et al., 1998; Thach, 1996). Hence, the activity seen in this study should not necessarily be ascribed to the motor aspect of producing speech, which was also assumed to be identical in the two Stroop tasks. Recent PET-studies have shown a cerebellar activation in connection with language tasks that merely involve inner speech production, without the actual vocalization of words (Gabrieli, Poldrack, & Desmond, 1998; Schlosser et al., 1998). So it seems that the cerebellum is somehow a partaker when we are composing words without being a true center of speech or language. The fact that subjects are unavoidably aware of two words at a time in Stroop’s test, the color name and the printed word, may be one explanation why the cerebellum seems so active during the task.

The Verbal Fluency Test

The fact that the subtraction task for the Verbal Fluency test is not as suitable in terms of sharing common features as the congruent Stroop test when compared to the incongruent Stroop, may partly explain why this subtraction results in several significantly activated brain areas. On the other hand, it may be an illustration of how a relatively simple cognitive task actually may involve several different cognitive components served by a cortical network (Friston, Frith, Liddle, & Frackowiak, 1993). Details have varied between studies, probably mainly due to the use of different subtraction tasks. However, our results are generally consistent with other studies of Verbal Fluency activation particularly in showing a left prefrontal and inferior frontal lobe activation.

The role of the left dorsolateral prefrontal cortex in the performance of Verbal Fluency can be seen both as a semantic role and as an initiating and modulating role. Based on a number of PET-studies, the hypothesis has been suggested that the left prefrontal cortex is involved in retrieval of information from semantic memory (Peterson et al., 1988), although recent fMRI studies have added to the complexity of the exact relationship between retrieval and this brain area (Mitchell, Johnson, Raye, & D’Esposito, 2000).

This memory function is concerned with people’s general knowledge of the world and also in the encoding process into episodic memory which is the conscious recollection of personally experienced events (Nyberg, Cabeza, & Tulving, 1996). The Verbal Fluency test does entail both these functions concurrently. In order to generate different words the subject has to retrieve these from semantic memory, but at the same time the subject has to store the event of generating the specific words (the occurrence) into episodic memory in order to avoid repetitions.

The activations seen in the left inferior frontal gyrus tend to be related to semantic search or access (Baker, Frith, & Dolan, 1997; Buckner & Koutstaal, 1998). Gabrieli et al. (1998) hypothesized that activation in the inferior prefrontal area occurs during semantic, relative to non-semantic, tasks for the generation of words. Furthermore it was hypothesized that it reflects a domain-specific semantic working memory capacity invoked particularly when a response must be selected among many alternatives, as is the case when generating words with a fixed letter.

According to Frith et al. (1991) the activation of the left dorsolateral prefrontal cortex in word
generation, however, reflects intrinsic, or selfinitiated, generation, whether the material is semantic or not. If so, this area could be activated by nonsemantic or nonverbal tasks as well. This has been supported by PET-scans of tasks in which the generated response was strictly motoric (Pardo, Fox, & Raichle, 1991). The left dorsolateral prefrontal cortex has popularly been named the ‘center of initiative’ as the activity here seems to precede the actual execution of the activity (Pedersen et al., 1998). So the left prefrontal cortex may be related to the initiating component of the Verbal Fluency test whereas the activation of the temporal cortex may represent the semantic component. Listening to words activates the temporal cortex (Wise, Hadar, Howard, & Patterson, 1991) which is also the case when hearing one’s own voice. The identification of words and the spreading activity of word associations when producing words are therefore plausible accounts of activity within the temporal area. Frith, Friston, Liddle, and Frackowiak (1991) also found a deactivation in the left superior temporal gyrus and suggested that the relationship between the dorsolateral prefrontal cortex and the temporal cortex is reciprocal in nature with the prefrontal cortex being an inhibitor of the activation in the temporal lobe. We did not observe this deactivation in the left hemisphere, but found an activation in corroboration with several previous studies (Boivin et al., 1992; Parks et al., 1988; Philpot et al., 1993).

We also found activation of the anterior cingulate gyrus, similar to that in Stroop’s test, and we therefore suggest that the cingulate gyrus is responsible for the selection of the words in question, that is, which associations in the temporal cortex should be attended to and which should be suppressed and ignored. The volitional preference of one set of stimuli over another seemed exactly to be the role of this area in Stroop’s test. In this view, the prefrontal cortex is involved in initiations of the Verbal Fluency performance task and possibly in the retrieval of the words that are freely associated in the temporal cortex, whereas the process of being selectively attentive to a specifically requested group of words is being performed by the anterior cingulate gyrus.

The activations registered in the right cerebellum have also been reported in previous studies (e.g., Schlosser et al., 1998; or review by Desmond & Fiez, 1998). Cerebellar activation may be explained in general terms as above in the discussion of Stroop’s test, but is not really understood. There is some indication that mild deficits in language production may occur following cerebellar lesions (Leiner, Leiner, & Dow, 1993), and patients with Broca’s aphasia show a crossed cerebellar diaschisis (Abe, Ukita, Yorifuji, & Yanagihara, 1997).

Concluding Discussion

With qualifications, Stroop’s test and the Verbal Fluency test can be considered tests of frontal lobe functions. One of the qualifications, applying to both tests, is related to the heterogeneous nature of the frontal lobes. Obviously tests of circumscribed cognitive functions cannot be expected to activate all areas of this large part of the brain, and likewise, circumscribed lesions outside the areas subserving these functions cannot be expected to compromise them.

Stroop’s test as used in this study, that is, Stroop interference, is specifically related to the caudal division of the anterior cingulate cortex. While this is in the frontal lobe, it is not in the prefrontal cortex. The Stroop test is commonly regarded as a test of prefrontal function, but this study as well as several previous imaging studies questions this assumption which seems to have been based on a single influential lesion study (i.e., Perret, 1974). On the positive side, the anterior cingulate activation is obviously very robust, and the test seems to be very suitable as a measure of the attentional demands in effortful processing regarded as a core function of the caudal part of the anterior cingulate gyrus (Devinsky et al., 1995).

The Verbal Fluency test has been shown to activate large parts of the left dorsolateral prefrontal cortex in many imaging studies. This together with equally solid evidence from lesion studies bring this test closer to what is commonly understood by a ‘frontal lobe test,’ that is, a test of prefrontal function. It is less specific than Stroop’s test, however, as it also activates a temporal lobe area in imaging studies and is affected by lesions.
in the left temporal lobe. Other areas of activation in our study (e.g., cerebellum, supplementary motor area, cingulate gyrus) may be less robust in imaging studies, and the sensitivity of the test to lesions in these areas is, we believe, not known.

The specific purpose of the present study was to establish the validity and applicability of the two tests for studies of frontal lobe activation in imaging of attention and related functions in depression. The anterior cingulate gyrus and dorsolateral prefrontal cortex are both believed to be involved in major depression and their successful and robust activation in middle-aged normal subjects indicates that the two tests may be useful in clinical studies.

REFERENCES


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