Psychometric, Structural and Functional Correlates in Obsessive Compulsive Disorder


Abstract

We compared MRI and SPECT in patients with DSM IV obsessive-compulsive disorder and healthy controls as well as their performance on a battery of psychometric tests. Twenty patients with obsessive-compulsive disorder and ten healthy controls were assessed on WAIS, Bender Visual Motor Gestalt Test and Trail making Test; MRI; and semiquantitative analysis Tc 99m Hexamethyl propylene amine oxime (HMPAO) brain SPECT. Patients with OCD showed symmetrical decreased perfusion of caudate nuclei and bilateral increased perfusion of anterior frontal cortex. There were no differences between the patients and control group as regards MRI findings or psychometric tests. Our data implicate orbitofrontal cortex and caudate nuclei in the pathophysiology of OCD and mediation of its symptoms.

Introduction

Obsessive compulsive disorder (OCD) is a common disorder with an early age of onset and a poor response to treatment. The hallmark characteristics of this disorder are an inability to suppress repetitive, intrusive thoughts and performance of repetitive actions. These symptoms are distressful to the patient and result in interference with home, school and interpersonal functioning (Simpson and Baldwin, 1995). Recently epidemiological data suggest a life time prevalence of 2% to 3%. It is often disabling and associated with quite a high morbidity compared to other psychiatric conditions (Trivedi, 1996). Driven by the tragic waste of patients’ lives many clinicians and researchers were intrigued and challenged by OCD and its long misunderstood history (Rapoport, 1995). As with most psychiatric disorders and syndromes the earlier etiologic paradigms were mainly psychoanalytic (namely fixation due to excessive investment in anal eroticism and subsequent regression to an earlier anal sadistic developmental phase) (Simpson and Baldwin, 1995), but currently the main paradigm is a neurophysiological one especially in research. In case of OCD this mainly involved the basal ganglia as obsessive symptoms were observed in conditions in which they are involved as postencephalitic Parkinson’s disease, Huntington’s Chorea, Gilles de la Tourette and Sydenham Chorea (Insel, 1992). This together with the advent of precise structural morphometric MR imaging analytic techniques and high resolution functional imaging techniques as PET and SPECT opened new avenues for investigation enabling researchers to study the mediating neuroanatomy of OCD in an unprecedented way. The purpose of this work was to study the brains of OCD patients and compare them with those of normal healthy controls psychologically (using psychometry), morphologically (using MRI) and functionally using (SPECT). To our knowledge this is the first study to combine these three techniques in the evaluation of OCD patients.
Material and Methods

Subjects

20 male subjects who met DSM IV criteria for OCD without comorbid diagnoses on Axis I or II and rated as severe on the Yale-Brown Obsessive Compulsive Scale. Patients were referred to Outpatient Psychiatric Clinic of Cairo University Hospital.

10 male control subjects were recruited from the different faculties of Cairo University. They had no past history or current psychiatric disorders or psychotropic medication use and were medically healthy. All subjects were 19 years old or above. An informed consent was obtained from each of them.

Exclusion criteria included

1- subjects with cardiac pacemakers, metallic clips or implants or artifacts in their bodies.

2- subjects with significant medical illnesses: neurological (including head trauma and epilepsy), cardiac, pulmonary, renal, hepatic, endocrine or metabolic.

3- subjects with current or past DSM IV defined substance related disorders

4- subjects with current or past DSM IV axis I or II disorders other than OCD (to avoid confounding comorbidity).

5- DSM IV defined mental retardation.

Psychometric Assessments

All subjects were assessed by

Wechsler Adult Intelligence Scale (WAIS) for Intelligence Quotient

Yale-Brown Obsessive Compulsive Scale (Y-BOCS) to assess severity of obsessive compulsive disorder symptoms

Bender Visual Motor Gestalt Test for visuomotor coordination and

Trail making tests for visuomotor perception and motor speed.

Neuroimaging

MRI

MRI of the brain was performed for all patients using flex Art Toshiba Japan 0.5 Tesla Superconductive magnet. All patients were studied on both T1 and T2 weighted images using spin echo and fast spin echo pulse sequences.

Tc 99m Hexamethyl Propylene Amine Oxime (HMPAO) Brain SPECT

Tc 99m HMPAO was prepared by addition of freshly eluted Tc99m pertechnetate to a freeze dried kit of HMPAO at room temperature. 20 mCi were withdrawn and injected intravenously no more than 30 minutes from kit preparation. Injection was done in a quiet room with dimmed lights. Patients were allowed to relax for 10
minutes prior to injection, which was performed with eyes opened and ears unplugged. Subjects remained seated for the next 10 minutes post injection.

SPECT images were acquired 90 minutes postinjection by a single head gamma camera (Diacam-120 photomultiplier tubes) equipped with high resolution collimator interfaced to a dedicated computer.

Data were collected in a 64 x 64 matrix without zooming through a 360° rotation 6 angle interval for 40 seconds per arc interval. Approximately 6.5 million counts were acquired. Images were reconstructed and filtered using a butterworth filter (order 5, cut off frequency 5.5) and backprojection. The transaxial sections were reoriented parallel to the base of the brain to obtain sagittal and coronal reconstruction (Figure 1). No attempts were made to correct for partial volume or scatter effects. Regions of interest (ROIs) were placed on transverse (Figure 2) and sagittal (figure 3) slices using rounded and elliptical templates over the following regions on both hemispheres: cerebellum, caudate nuclei, supraorbital frontal cortex, anterior frontal cortex and high parietal cortex. These regions (except cerebellum) have hypothetical intervention in OCD (Lucey et al., 1995). Average counts/pixel expressing regional blood flow were calculated for each ROI and measured as a ratio to mean total cerebellar counts/pixel (right plus left cerebellar counts/pixel divided by two). The cerebellum was chosen as the reference region since it has not been directly associated with rCBF changes related to anxiety.

**Statistical Analysis** The statistical analysis was done using an IBM compatible computer and STATISTICA for MS Windows 97 statistical package. Statistical analysis was done according to Ingelfinger et al. (1994) and Knapp and Miller (1992).

**Statistical tests:**

Descriptive statistics was presented in frequency tables, means ± standard deviations, range and median whenever appropriate.

Analytical tests used included unpaired student t test (two sided) for comparing means of two groups. Correlation and regression analysis was also used.

**Significance level**

Significance level of 0.05 and 0.01 was used throughout all statistical tests within this study.

**Tabulation and graphical presentation,** was also done according to Knapp and Miller (1992).

**Results**

**I- Demographic data:** As table 1 shows patients with OCD and control subjects did not differ in mean ± SD age or years of education. All subjects were well educated and the majority were university students. All patients did not receive medication for their disorder.

**II- Psychometric measures**

A- WAIS: As table 2 shows there was no statistically significant difference between the patient and control group mean scores on the WAIS, its subscales nor the deterioration index.

B- Visuomotor testing: As table 3 shows there was no significant difference in the mean scores of the two groups as regards visuomotor coordination (Bender Visual Motor Gestalt) nor visuomotor perception and motor speed (Trail Making Tests).
III- Neuroimaging

A- MRI: We failed to identify any alteration of the normal MR signal pattern of the caudate and subfrontal cortex.

B- SPECT: As table 4 shows rCBF measurements showed significant reductions in right and left caudate of OCD patients (p= 0.0006 and 0.0001 respectively) and significant increments in the right and left anterior frontal (p= 0.0001). These results indicate a regional and not a generalized effect.

Table 1: Demographic Data of Patients and Healthy Controls

<table>
<thead>
<tr>
<th>Demographic Data</th>
<th>Patients (N= 20)</th>
<th>Control (N= 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Male 20 (100%)</td>
<td>10 (100%)</td>
</tr>
<tr>
<td></td>
<td>Female 0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Age</td>
<td>Mean ± SD 21.8 ± 2.3 y</td>
<td>21.9 ± 2.0 y</td>
</tr>
<tr>
<td>Marital Status</td>
<td>Single 20 (100%)</td>
<td>10 (100%)</td>
</tr>
<tr>
<td></td>
<td>Married 0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Divorced 0</td>
<td>0</td>
</tr>
<tr>
<td>Educational Years</td>
<td>Mean ± SD 12.5 ± 1.5 y</td>
<td>11.5 ± 2</td>
</tr>
<tr>
<td>Occupation</td>
<td>Students 18 (90%)</td>
<td>8 (80%)</td>
</tr>
<tr>
<td></td>
<td>Profession 2 (10%)</td>
<td>2 (20%)</td>
</tr>
</tbody>
</table>

Table 2: Mean Scores of Patient and Control Groups on WAIS Full Scale and Subscales

<table>
<thead>
<tr>
<th>WAIS</th>
<th>Case (Mean ± SD)</th>
<th>Control (Mean ± SD)</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full scale IQ</td>
<td>106 ± 3.64</td>
<td>109 ± 5.48</td>
<td>1.64</td>
<td>0.1112</td>
</tr>
<tr>
<td>Verbal IQ</td>
<td>106 ± 4.3</td>
<td>105 ± 4.54</td>
<td>0.24</td>
<td>0.8152</td>
</tr>
<tr>
<td>Performance IQ</td>
<td>104 ± 5.76</td>
<td>105 ± 3.63</td>
<td>0.80</td>
<td>0.4311</td>
</tr>
<tr>
<td>Deterioration Index</td>
<td>9.70 ± 7.66</td>
<td>5.30 ± 1.13</td>
<td>1.73</td>
<td>0.0942</td>
</tr>
</tbody>
</table>

Table 3: Mean Scores of Patient and Control Groups on Bender Gestalt and Trail Making Test

<table>
<thead>
<tr>
<th>Test</th>
<th>Patients (Mean ± SD)</th>
<th>Control (Mean ± SD)</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bender Gestalt</td>
<td>24.72 ± 11.38</td>
<td>20.30 ± 3.03</td>
<td>1.20</td>
<td>0.2407</td>
</tr>
<tr>
<td>Trail A</td>
<td>54.05 ± 13.39</td>
<td>56.20 ± 8.52</td>
<td>0.46</td>
<td>0.6483</td>
</tr>
<tr>
<td>Trail B</td>
<td>110 ± 39.75</td>
<td>118.5 ± 33.7</td>
<td>0.56</td>
<td>0.5787</td>
</tr>
</tbody>
</table>
Table 4: Comparison of Mean rCBF in Resting OCD Patients and Healthy Controls

<table>
<thead>
<tr>
<th>Region</th>
<th>Patients (Mean ± SD)</th>
<th>Control (Mean ± SD)</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rt Caudate</td>
<td>0.85 ± 0.04</td>
<td>0.91 ± 0.02</td>
<td>3.89</td>
<td>0.006*</td>
</tr>
<tr>
<td>Lt Caudate</td>
<td>0.85 ± 0.03</td>
<td>0.91 ± 0.02</td>
<td>6.28</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Rt Supraorbital Cortex</td>
<td>0.86 ± 0.06</td>
<td>0.87 ± 0.05</td>
<td>0.254</td>
<td>0.8015</td>
</tr>
<tr>
<td>Lt Supraorbital Cortex</td>
<td>0.86 ± 0.07</td>
<td>0.87 ± 0.05</td>
<td>0.304</td>
<td>0.7637</td>
</tr>
<tr>
<td>Rt Ant Frontal</td>
<td>0.93 ± 0.07</td>
<td>0.79 ± 0.07</td>
<td>5.239</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Lt Ant Frontal</td>
<td>0.93 ± 0.06</td>
<td>0.79 ± 0.05</td>
<td>6.143</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Rt H Parietal</td>
<td>0.88 ± 0.06</td>
<td>0.86 ± 0.05</td>
<td>0.671</td>
<td>0.5079</td>
</tr>
<tr>
<td>Lt H Parietal</td>
<td>0.88 ± 0.05</td>
<td>0.86 ± 0.06</td>
<td>1.12</td>
<td>0.2721</td>
</tr>
</tbody>
</table>

Fig. (1) shows Tc 99m HMPAO brain SPECT in sagittal plane

Fig(2): shows ROIs in axial plane
Discussion

To summarize our findings, psychometry for organicity and MRI failed to detect any differences between the OCD patients and normal controls, while SPECT showed bilateral significant differences between both groups, while in the resting state, in two regions namely the caudate and frontal cortex.

Our psychometric findings (tables 2 and 3) are similar to those of Schmidtke et al. (1988) who found OCD patients unimpaired at tests of abstraction, problem solving, active memory search and choice reaction speed when we applied the different subtests of the WAIS. However our results were different than those of Purcell et al. (1998a and b) who found OCD patients impaired on measures of executive and visual memory function as well as spatial working memory and motor initiation and execution.

Our MRI results as regard the caudate are similar to findings reported by Aylward et al. (1991 and 1996), and Kellner et al. (1996) who found no differences in caudate measures. However, several studies demonstrated differences between patients with OCD and control subjects. Scarone et al. (1992) reported a relatively increased right sided caudate volume in OCD patients while Robinson et al. (1995) observed a reduction in OCD patients' caudate volume when compared to controls. On the other hand, Calabrese et al. (1993) reported intensity asymmetries on MRI between caudate nuclei. Intensity asymmetry may reflect a disparity in grey matter density and hence possible cell loss or cellular water content and hence possibly a metabolic irregularity (Malizia and Nutt, 1997).

As regards the whole brain unlike our MRI results, Jenike et al. (1996) -who studied females- found evidence of globally reduced white matter and increased grey matter in women with OCD when compared to matched normal controls. Breiter et al. (1996) who used functional MRI found that 70% or more of OCD patients studied showed activation in medial orbitofrontal gyri, lateral frontal, anterior temporal, anterior cingulate and insular cortex as well as caudate, lenticulate
and amygdala. The results of the latter study were consistent with other studies using other functional modalities except for a more prominent activation of limbic and paralimbic regions.

Our SPECT results of increased rCBF to right and left anterior frontal cortex are similar to those reported by Baxter et al. (1988), Nordahl et al. (1989), Swedo et al. (1989) and Benkelfat et al. (1990) and Rubin et al. (1995) who reported increased blood flow and heightened glucose metabolism in frontal brain areas. Several suggestions have been offered to explain hyperfrontality. Hoehn-Saric et al. (1991) hypothesized that it could be related to patient's attempts to suppress compulsions during scanning and thus represent a nonspecific reversible compensatory effect for the illness; while McGuire et al. (1994) hypothesized that the increase in rCBF in the orbitofrontal cortex, neostriatum, globus pallidus and thalamus were related to urges to perform compulsive movements, while those in hippocampus and posterior cingulate corresponded to the anxiety that accompanied them. More recently Malizia and Nutt (1997) suggested that orbitofrontal cortex and anterior cingulate are involved in associated related to affective and attentive processes while the temporal and posterior structures in the associated anxiety.

Different to our findings and the above studies Mindus et al. (1986) and Martinot et al. (1990) have reported decrease in rCBF to the same anatomical locations i.e. orbitofrontal cortex, anterior cingulate and thalamus. This was attributed to the atypical selection of patients. Mindus' study involved treatment-resistant patients about to undergo capsulotomy while Martinot's patients were under treatment. this is in agreement with the report of Rubin et al. (1995) who stated that there is significant reduction of Tc 99m HMPAO uptake in these areas during treatment, which were overperfused in SPECT images prior to therapy.

Our SPECT results of reduced caudate uptake of Tc99m HMPAO are similar to those reported by Mindus et al. (1986), Martinot et al. (1990) Rubin et al. (1992), Edmonstone et al. (1994) and Lucey et al. (1995). Schwartz et al. also confirmed the finding that there is bilateral reduction in perfusion and glucose metabolism of caudate nuclei in patients with OCD. They stated that such reduction was significantly greater in responders to behaviour therapy than that seen in non responders to treatment.

Lucey et al. (1997) also reported a significant reduction in rCBF of right caudate in patients with OCD and post traumatic stress disorder (PTSD) but not those suffering from panic attacks nor healthy controls. On the other hand, Perani et al. (1995) reported non significant increase of glucose consumption of the caudate. Also, Alyward et al. (1990) denied any abnormality in perfusion of caudate nuclei in patients with OCD. In at trial to assess abnormality in rCBF during symptom provocation in patients with OCD Rauch et al. (1994) reported a significant increase in relative regional cerebral blood flow during the OCD symptomatic state versus the resting state in right caudate nucleus, left anterior cingulate cortex and bilateral orbitofrontal cortex. It seems that most of the positive correlation between symptom intensity and rCBF were unilateral with the majority lateralised to the right hemisphere with changes in association with treatment tending to be right sided. On the other hand, resting state
studies (as is the case in this work) have usually reported bilateral abnormalities (McGuire et al., 1994).

Neuroimaging studies, both structural and functional, have shown a variable degree of inconsistency yet have invariably implicated frontal (orbital, prefrontal, cingulate) cortex and basal ganglia particularly the caudate nucleus. Several factors have been enumerated to account for inconsistencies reported by the different studies. Among the most prominent are; heterogeneous nature of the disorder (Aylward et al., 1996); use of different scanning methods with different spatial resolution; subjects being sometimes studied with eyes opened while others with eyes closed, variation in the mental state of obsessive patients at the time of the scan including presence or absence of OCD symptoms; some studies have participants performing a sustained attention task; research designs studying patients before and after treatment have patients on and/or off treatment for variable periods of time, and presence and absence of comorbidity (Kotrla, 1997).

It has been suggested that inconsistent findings might be due to the subtle abnormalities of basal ganglia connectivity with other regions and hence does not need to be associated with abnormal caudate nucleus size, metabolic rate nor blood flow and hence not consistently visible to MRI, PET or SPECT (Aylward et al., 1996). Despite of these inconsistencies, most reports reproducibly demonstrated that patients with OCD have increased blood flow and glucose metabolism in frontal cortex and decrease in caudate nuclei in comparison to control group. Normalisation of perfusion or metabolism in these structures is associated with post treatment symptoms improvement. The frontal cortex an caudate nuclei are part of the circuit that also includes the thalamus that may be involved in the regulation of both consciously perceived emotional concerns and repetitive behaviour. There is inter-regional correlation between these structures, both before and after treatment, in patients with OCD which has not been seen in patients with unipolar depression or normal subjects. Therefore, taken together there is much evidence to support a role for this circuit in a neurobiologic model of OCD (Rauch et al., 1994).

Our study aimed at detecting any organic changes among OCD patients using psychometric tests (to detect global cognitive impairment), MRI (structural changes) and SPECT (functional changes). It seems that different methods used failed to detect consistent findings, with no abnormalities in both psychometry and MRI, but evident hypoperfusion in caudate nuclei and hyperperfusion in anterior frontal area in functional neuroimaging using brain SPECT.

So our data implicate orbitofrontal cortex and caudate nuclei in the pathophysiology of OCD and in mediating OCD symptoms.

It is recommended to perform further research on OCD patients from both sexes, using more specific and precise psychometric tests as Lauria Nebraska Battery; and to apply brain SPECT neuroimaging, while OCD patients are thinking about their OCD symptoms to compare it with studies carried on patients while in their resting state. Also follow-up studies, after using specific drugs, are needed to monitor the effect of applied therapy.
References


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