Single Photon Emission Computerized Tomography in Obsessive Compulsive Disorder: A Preliminary Study

Beverly L. Adams, M.D.[1], Lorne B. Warneke, M.D.[2], Alexander J. B. McEwan, M.B.[3], Barbara A. Fraser, M.Ed.[4]

[1]Department of Psychiatry, University of Alberta, Edmonton, Alberta, [2] Grey Nuns Hospital, Edmonton, Alberta, [3]Department of Nuclear Medicine, Cross Cancer Institute, Edmonton, Alberta, [4]Department of Psychology, Grey Nuns Hospital, Edmonton, Alberta

Patterns of cerebral perfusion in patients with obsessive compulsive disorder were evaluated using single photon emission computerized tomography. Eleven patients, who satisfied the DSM-III-R criteria and Research Diagnostic Criteria for the disorder, were evaluated using the distribution of 99m-Tc-HMPAO as a radiotracer. The Yale-Brown Obsessive Compulsive Scale was administered to each patient to assess the severity of their symptoms. The images obtained were evaluated qualitatively and semi-quantitatively by a physician in nuclear medicine who was blind to the patients' diagnoses. Eight of the 11 patients demonstrated asymmetric perfusion of the basal ganglia; the left side showed impaired perfusion in six patients.

Key Words: SPECT, OCD, Y-BOCS, basal ganglia, hypoperfusion

INTRODUCTION

Obsessive compulsive disorder (OCD) is one of the psychiatric illnesses most resistant to treatment. It can be an incapacitating illness and has an estimated lifetime prevalence of two percent to three percent of the general population in the United States (Robins et al 1984). These figures were confirmed in a Canadian city by Bland and colleagues (1988), who studied 3,258 randomly selected community residents and found a lifetime prevalence of three percent.

Some lines of evidence suggest that the illness has a neurophysiological basis. Evidence dates back to the early 1900s, when Von Economo reported a somnolent-like state with parkinsonian features after an outbreak of "viral encephalitis lethargica" in Europe (Schilder 1938). He reported that this infectious neurotoxic lesion involved the basal ganglia and was associated with a sense of compulsion experienced by the patients in addition to peculiar motor tics.

Address reprint requests to: Dr. Beverly L. Adams, Department of Psychiatry, 1E1.01 Walter Mackenzie Health Sciences Centre, University of Alberta, 8440–112 Street, Edmonton, Alberta, Canada T6G 2B7.

Laplane et al (1984) reported a case of a wasp sting which resulted in a 24-hour coma, which was followed by choreic movements and later by stereotyped activities. The patient's compulsions included frequent mental counting and switching a light on and off for one hour or more. A CT scan revealed an abnormality in the internal part of the lentiform and caudate nuclei. There are similar reports of basal ganglia lesions occurring after carbon monoxide poisoning and leading to an obsessional illness.

An association between obsessive compulsive disorder and Sydenham's chorea was noted by Chapman et al in 1958 (Swedo et al 1989). In this study, four of eight children with Sydenham's chorea had obsessive symptoms, which included sequencing and washing compulsions. Husby et al (1976) examined antibodies in the sera of children with acute rheumatic fever. They found that a higher proportion of sera (46.6%) were positive for antibodies to the caudate and subthalamic nuclei in the children with chorea than in those with active carditis (14.0%).

Other movement disorders have also been associated with obsessive compulsive disorder. The association of Tourette's syndrome and multiple motor tics with OCD suggests basal ganglia dysfunction. Nee et al (1980) found that 68% of

patients with Tourette's syndrome had obsessive compulsive symptoms which met the DSM-III criteria for OCD. The patients with Tourette's syndrome and OCD were those most likely to have a family history of tics.

Wise and Rapoport (1989) have postulated that selective basal ganglia dysfunction are involved in OCD. They suggest that the basal ganglia may be a repository of innate motor programs and may have an inborn releasing mechanism. The recognition of key stimuli causes a release of a fixed-action pattern. Modell and his group (1989) have also postulated neurophysiological dysfunction in the basal ganglia/limbic striatal and thalamocortical circuits as a pathogenetic mechanism in obsessive compulsive disorder. They propose that obsessive compulsive symptoms occur when an aberrant positive feedback loop develops in the excitatory frontothalamic neuronal interchange, which is inadequately integrated or inhibited by the ventromedial (limbic) portions of the striatum.

Luxenberg et al (1988) studied CT scans of patients with OCD and found smaller volumes of the caudate nuclei bilaterally than in the control subjects. Studies using positron emission tomography (PET) have found higher than expected glucose metabolic rates in the head of the caudate nucleus and orbital frontal cortex of OCD patients (Baxter et al 1988; 1987).

In this study, patterns of cerebral perfusion in OCD were evaluated using single photon emission computerized tomography (SPECT). With the use of a short-lived radiotracer, SPECT imaging allows for the three-dimensional measurement of regional cerebral blood flow. SPECT now rivals PET technology in resolution and sensitivity (Devous 1989) and is more economical and more widely available than PET.

METHOD

The patients were selected consecutively from a major general hospital in a city with a population of approximately 750,000, as well as from out-patient private practices. All patients satisfied the DSM-III-R criteria and Research Diagnostic Criteria (Spitzer et al 1975) for OCD, as determined by a member of the research team (B.A.). The exclusion criteria were as follows: having any other Axis I diagnosis (DSM-III-R), including a major depression; being under age 13 or over age 50; and having epilepsy or having experienced any major head injury. The study was approved by the ethics committees of the two hospitals involved. Appropriate informed consent was obtained before the patients were admitted to the study and before the SPECT scan was conducted.

All the patients were markedly symptomatic at the time the imaging was completed even though pharmacotherapy had been started. Nine of 11 patients were being treated with oral or intravenous clomipramine, and two were receiving fluoxetine. Treatment was initiated before the SPECT scans were conducted to alleviate disabling symptomatology and because it is well established that between eight and 12 weeks are required before any response is seen. Active symptoms suggested that brain pathology had not been altered.

The Yale-Brown Obsessive Compulsive Scale (Y-BOCS) was administered to each patient. This clinician-rated, ten-item scale was designed to assess the severity of the patients' obsessive compulsive symptoms and their response to treatment. Five items on the scale deal with obsessions and five items deal with compulsions; each item is rated from 0 (asymptomatic or aproblematic) to 4 (extreme symptomatology). The Y-BOCS is reported to have high internal consistency and interrater reliability, moderate convergent and divergent validity and acceptable criterion-related validity (Goodman et al 1988).

The Beck Depression Inventory (BDI) is a 21-item, self-rated inventory of symptom severity, measuring attitudes and symptoms commonly associated with depression (Shaw et al 1985). This test was administered to assess whether or not a significant degree of depression was present even though none of the patients met the DSM-III-R criteria for major depression.

SPECT scans were conducted according to a standard protocol. The radiopharmaceutical used in the imaging procedure was 99m-Tc-HMPAO (99m-Tc-hexamethyl propylene-amine oxime). This is a neutral and lipid soluble complex which crosses the blood-brain barrier and is distributed in proportion to regional cerebral blood flow (Sharp et al 1986). First pass extraction is high (85%), and the compound is retained in the brain for four hours. This allows sufficient time for imaging with a gamma camera (Hooper et al 1990).

A rotating gamma camera was used (General Electric, 400 AC/T, Milwaukee, WI), equipped with a low-energy, general purpose parallel-beam collimator and linked to a commercial nuclear medicine computer system (Picker PCS-512, Solon, OH). The resolution obtained with this system was 12 mm.

The standardized imaging protocol was completed for each patient. The imaging was performed with the patient's eyes open to provide a baseline stimulus. A butterfly cannula was inserted into the forearm vein, and the patient rested in a quiet, darkened room for 20 minutes before the injection. The radiotracer was then injected intravenously and the patient rested for another five minutes. SPECT imaging was performed within one hour of the injection. The images were analyzed by a specialist in nuclear medicine who was unaware of the patient's diagnosis. The scans of the subjects were then compared with those of age-matched controls. Normative data for the control group had been obtained from a separate study by Hooper et al (1990). In their study, normal ranges for cerebral perfusion in a healthy population were defined.

Sagittal, axial and coronal sections of the images were assessed qualitatively and semi-quantitatively. The semi-quantitative analysis technique was developed by Hooper et al (1990). This three-dimensional region-of-interest (ROI) model subdivides the brain into 14 discrete regions (frontal, superior and inferior, parietal, temporal, basal ganglia, occip-

ital and cerebellum). This model is interactively aligned to a SPECT brain study using a computer program developed specifically for this purpose. Once an operator is satisfied with the ROI fit to a particular SPECT study, the program calculates the total number of counts and volume (in voxels) in each region defined by the model. Counts from the 15 ROIs were standardized in two ways: by dividing by the total brain count, and by dividing by the total cerebellar count. Regional counts were expressed as a fraction of total brain counts and as a fraction of total cerebellar counts. The counts of the different groups were then compared and with the pre-determined regional means for cerebral perfusion in the control group. The number of standard deviations that a value was above or below the pre-defined mean for a particular region were quantified and compared with age-matched controls. The only values considered significant were those that fell 2.5 standard deviations from the mean. In order to minimize partial volume effects, voxels lying on ROI boundaries were subdivided among the nearest ROIs, using a three-dimensional linear interpolative weighting. This entire process was accomplished with the aid of computerized software designed specifically for this purpose (Hooper et al 1990).

RESULTS

The sample consisted of 11 patients: six of the patients were male, and five were female; eight were inpatients and three were outpatients. The age range was 17 to 40 years, with a mean age of 28 years (SD = 6.8). Ten of the patients were right-handed and one was left-handed. Five of the 11 patients had suffered traumatic deliveries at birth (including mid-forceps deliveries and uterine hemorrhages). Unfortunately, Apgar scores were not available.

The patients' mean score on the Y-BOCS was 28.1, with a standard deviation of 7.4 and a range of 14 to 37. This placed most patients in the moderately severe category for obsessive compulsive symptoms. The mean score on the Beck Depression Inventory was 14.1, with a standard deviation of 12.2 and a range of 0 to 39. The scores of two patients were high, although there was no clinical evidence of a major depression. However, the BDI is a self-rated scale and is influenced by the patient's affect at a particular time.

Eight of the 11 scans completed revealed asymmetric perfusion of the basal ganglia. Six of the eight displayed left basal ganglia hypoperfusion, and two displayed right hypoperfusion. Three of the scans were normal. Of the patients with normal scans, one was 17 years of age, the youngest of the group, and was in the early stages of his illness; another patient, although having met the criteria for OCD, experienced very little disturbance in social or occupational functioning.

In addition to the common finding of basal ganglia hypoperfusion, there was left frontal underperfusion in one scan and bilateral parietal hypoperfusion in another.

DISCUSSION

Althought the number of patients in this pilot study is small, the results are intriguing. Basal ganglia hypoperfusion in eight of the 11 scans is in keeping with the hypothesis of dysfunction in this area in OCD.

The results correlate with the findings of Baxter et al (1987) using positron emission tomography. They reported elevated glucose metabolic rates in the head of the caudate nucleus and orbital frontal cortex. Although these areas have high levels of glucose utilization, they may be dysfunctional. Haier's group (1988) reported higher glucose metabolic rates in the PET scans with poorer performance on tests of abstract reasoning (Raven's Advanced Progressive Matrices) among normal subjects. These dysfunctional areas could account for the decrease in cerebral perfusion seen in the basal ganglia in this study.

As Wise and Rapoport (1989) have postulated, the basal ganglia may be a repository of innate motor programs that are released when there is a dysfunction in this area. Luxenberg's evidence of smaller volumes of caudate nuclei, as mentioned previously, supports the neuroanatomical evidence of basal ganglia dysfunction (Luxenberg et al 1988). Psychosurgery in this dysfunctional area for treatment-resistant patients with OCD has had favorable results. Bilateral anterior cingulate lesions or anterior capsulotony have resulted in dramatic amelioration of the symptoms of OCD (Mindus et al 1988).

A number of well controlled studies have confirmed that clomipramine is superior to placebo in the treatment of OCD (Ananth et al 1979; Insel et al 1983; Jenike et al 1989). Clomipramine has a relative specific potency for blocking the reuptake of serotonin. Recent studies have indicated a higher concentration of serotonin receptors and serotonin itself in the basal ganglia than had been recognized previously (Pazos and Palacios 1985). Thus, the serotonergic hypothesis also fits in with the neuroanatomical explanation of basal ganglia dysfunction.

The high percentage of patients with basal ganglia hypoperfusion seen in this preliminary study warrants further investigation. Pre- and post-treatment studies with serotonin reuptake blocking agents are needed. Comparison of those who do and do not respond, before and after treatment, would help to determine whether basal ganglia hypoperfusion is reversible or is "state" versus "trait".

SPECT imaging presents exciting possibilities for the understanding of the pathophysiology of obsessive compulsive disorder. SPECT is a feasible and economical imaging procedure that is available in smaller clinical centres.

These preliminary results suggest the possibility that SPECT may be developed as a diagnostic test for the disorder. The results also emphasize the importance of neuroimaging in psychiatry.

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