Oculomotor Performance in Obsessive-Compulsive Disorder

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**Objective:** Neuroimaging studies have shown abnormalities of the frontal cortex and basal ganglia in persons with obsessive-compulsive disorder. Since lesions in the frontal cortex and basal ganglia areas affect performance on goal-guided saccadic eye movements, this study investigated the relation between the diagnosis of obsessive-compulsive disorder and oculomotor performance. **Method:** Eleven patients with the clinical diagnosis of obsessive-compulsive disorder and 14 normal subjects were assessed with respect to their performance on both visual-guided and goal-guided oculomotor tasks. Fixation performance was also measured. **Results:** The group with obsessive-compulsive disorder had a very significantly greater error rate and a significantly greater rate of inaccurate saccades on the goal-guided antisaccade task, whereas they were not different from the normal group in reaction time, saccadic velocity, and accuracy on the visual-guided saccade task. The distribution of error rates for the patients with obsessive-compulsive disorder was broad, with more than one-half outside the range of the normal group. Most of the abnormal findings were among male patients. **Conclusions:** The results support the hypothesis of a relationship between impaired performance on goal-guided saccadic eye movement tasks and the diagnosis of obsessive-compulsive disorder, but they also suggest a gender-related subgroup within the group with obsessive-compulsive disorder.


The frontal cortex and basal ganglia appear to be involved in obsessive-compulsive disorder (1). Static imaging in research on persons with obsessive-compulsive disorder has demonstrated structural abnormalities in the basal ganglia (2), and positron emission tomography (PET) and single photon emission computed tomography (SPECT) imaging studies of brain metabolism and blood flow have observed abnormalities in the orbital-frontal cortical and/or basal ganglia regions (3-6). Pharmacotherapeutic normalization of clinical symptoms of obsessive-compulsive disorder has been associated with normalization of cerebral blood flow and glucose metabolism in both the frontal cortex and the caudate nucleus (7, 8).

Brain circuits involving the frontal cortex and basal ganglia appear to be essential for executing behaviors that are based on internal representations (9). These behaviors may include certain kinds of eye movements, one major class of which is saccadic (from the French *saccade*, meaning “jerk”). Saccadic eye movements can be consciously controlled, directing the line of sight to discrete points in the visual field. Enough is known about the functional neuroanatomy of saccadic oculomotor control to allow investigators to relate saccades with differing degrees of conscious control to certain brain areas. There appear to be two major pathways, anterior and posterior, by which the cerebral cortex can generate saccades.

The anterior pathway projects from the frontal eye fields both directly to the brainstem and indirectly to the brainstem through the superior colliculus (10). This projection is also indirect through the basal ganglia and is involved in generating saccades that are directed by internal models or representations (“goal-guided” saccades) (11). Saccades to remembered targets and saccades to imagined targets are of this type and are under a high degree of conscious control. Performance of goal-guided saccades is vulnerable to lesions involving the frontal eye fields and basal ganglia (12). Lesions in the prefrontal cortex, which projects to the frontal eye fields, also impair goal-guided saccades (12). Frontal lobe lesions and degenerative disorders involving the basal ganglia result in saccadic intrusions and inappropriate reflexive saccades in response to extraneous visual stimuli (13, 14). (In a similar way, apparently “frontal” neuropsychological syndromes can be produced by...
TABLE 1. Oculomotor Performance of 14 Normal Subjects and 11 Patients With Obsessive-Compulsive Disorder

<table>
<thead>
<tr>
<th>Task</th>
<th>Normal Subjects</th>
<th>Patients With Obsessive-Compulsive Disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean SD</td>
<td>Mean SD</td>
</tr>
<tr>
<td>Fixation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saccadic intrusions</td>
<td>2.2 3.3</td>
<td>4.4 3.8</td>
</tr>
<tr>
<td>Blinks</td>
<td>3.7 3.6</td>
<td>6.7 7.9</td>
</tr>
<tr>
<td>Temporally random</td>
<td></td>
<td></td>
</tr>
<tr>
<td>saccades</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reaction time</td>
<td>201 24</td>
<td>206 28</td>
</tr>
<tr>
<td>(milliseconds)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right velocity</td>
<td>675 251</td>
<td>738 86</td>
</tr>
<tr>
<td>(degrees per second)</td>
<td>0.93 0.05</td>
<td>0.93 0.05</td>
</tr>
<tr>
<td>Left accuracy (gain⁴)</td>
<td>699 262</td>
<td>682 78</td>
</tr>
<tr>
<td>(degrees per second)</td>
<td>0.93 0.06</td>
<td>0.93 0.06</td>
</tr>
<tr>
<td>Left accuracy (gain⁴)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antisaccades</td>
<td>0.12 0.11</td>
<td>0.39 0.23</td>
</tr>
<tr>
<td>Errors (proportion)ᵇ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inaccurate saccades</td>
<td>0.33 0.13</td>
<td>0.49 0.22</td>
</tr>
<tr>
<td>(proportion)⁴</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

³Ratio of eye movement to target movement.
ᵇSignificant difference between groups (t=−3.61, df=23, p=0.003).
⁴Significant difference between groups (t=−2.10, df=23, p=0.05).

damage to basal ganglia areas connected to prefrontal areas [15]).

The posterior pathway projects from the posterior parietal cortex and neighboring regions to the superior colliculus and then to the brainstem and is involved in generating “visual-guided” and “reflexive” saccades (12). Such saccades can be considered to be under a lower degree of conscious control than goal-guided saccades. “Spontaneous” saccades do not appear to depend on the cerebral cortex at all and are presumably generated entirely by subcortical structures (16).

On the basis of reports showing frontal lobe and basal ganglia abnormalities in subjects with obsessive-compulsive disorder and the functional neuroanatomy of control of saccadic eye movements, an impairment in goal-guided (but not visual-guided) saccadic performance related to obsessive-compulsive disorder seemed likely. This article reports an experiment to test this hypothesis.

METHOD

The psychiatric subjects were drawn from a highly selected clinical group. Eleven individuals (five male) with the DSM-III-R clinical diagnosis of obsessive-compulsive disorder were recruited from the anxiety disorders clinic at Johns Hopkins Hospital (all diagnoses were made by R.H.S.). Fourteen normal comparison subjects (seven male) were recruited from the hospital staff. All subjects were screened with the Structured Clinical Interview for DSM-III-R (17). Exclusion criteria were any major psychiatric disorder, substance abuse or dependence, and history of injury to the central nervous system. No subjects had schizotypal personality disorder. The mean age of the group with obsessive-compulsive disorder was 39 years (SD=7, range=27–54 years); the mean age of the normal group was 38 years (SD=10, range=22–56 years). All of the subjects with obsessive-compulsive disorder had at least a high school education, and four of the five male subjects had at least a college education. The normal subjects were similarly educated. The family histories of all subjects were negative for obsessive-compulsive disorder and tics, and no subjects reported a family history of schizophrenia.

For the patients with obsessive-compulsive disorder, the mean total score on the Yale-Brown Obsessive Compulsive Scale (18) at the time of diagnostic evaluation was 24.4 (SD=4.5, range=17–30). Their mean score was 12.4 (SD=3.2, range=5–15) on the Yale-Brown obsessions subscale and 12.2 (SD=3.1, range=6–15) on the compulsions subscale. Their mean score on the National Institute of Mental Health Global Obsessive Compulsive Scale (19) was 9.1 (SD=1.1, range=7–11). Only one patient had a history of a tic, but it was not present during oculomotor testing. At the time of oculomotor assessment, one patient was taking clomipramine, one was taking no medication, and the other nine were taking fluoxetine. All 23 subjects had clinically normal magnetic resonance imaging (MRI) brain scans.

Saccadic eye movements were assessed by means of a computerized target presentation/data acquisition system. Targets were presented on an AT-type personal computer with a VGA (640x480 pixels) graphics adapter and monitor. Saccades were recorded with infrared reflection. A chin rest and head restraint minimized head movement. Data acquisition routines sampled horizontal eye movement at 1,000 samples per second.

Two tasks were used to assess saccadic performance, and a fixation task was also given. Each task was recorded for 45 seconds. For each, the subjects practiced until they understood the task, in order to reduce the impact of potential generalized learning deficits. The order of tasks was as follows.

Fixation. The task consists of fixing the gaze on a small central target and maintaining fixation as well as possible. Square wave jerks (saccadic intrusions) were identified and counted. Square wave jerks are conjugate saccades that move the eyes away from fixation and then, after 100–300 msec, back to the fixation point. The number of blinks was also counted.

Temporally random saccades. This task uses spatially regular 20° displacements between left and right targets, with a random time interval ranging from 1 to 3 seconds. Reaction time, saccadic velocity (degree of eye movement per second), and gain (ratio of eye movement to target movement) were measured. The task tests performance on visual-guided saccades.

Antisaccades. After fixation of a central target, a peripheral target appears simultaneously with the offset of the fixation target. Subjects were instructed to make a saccade to the mirror location opposite that of the target. Subjects were allowed to practice until at least four correct trials were observed. The number of trials
RESULTS

On the fixation task there were more blinks and more square wave jerks in the group with obsessive-compulsive disorder than in the normal group (table 1), but these differences were not significantly different at the p<0.05 level (independent-sample t tests with separate variance) because of relatively large variance in both groups. Table 1 also shows measures of performance on the temporally random visual-guided saccade task. Mean reaction times were not significantly different between groups, and variance in reaction time also was not significantly different (F=1.42, df=12, 8, p=0.56). Left and right saccadic velocity were not significantly different, but there was more variance in velocity performance in the normal group (for right velocity variance, F=8.48, df=12, 8, p=0.009; for left velocity variance, F=11.13, df=12, 8, p=0.004). Visual-guided saccadic gain or accuracy was identical, within rounding error, for the two groups.

There was a significant difference between the groups in performance on the antisaccade task. Examples of antisaccade performance are shown in figure 1 and figure 2. Figure 1 shows that a normal subject made a very inaccurate saccade on the first trial but subsequently improved in accuracy, with relatively small hypometric or hypermetric inacuracies. This subject made no errors (saccades toward the antitarget stimuli). Figure 2 shows performance by a patient with obsessive-compulsive disorder. This subject made four errors and also performed poorly in controlling the amplitude of saccades, even when successfully inhibiting reflexive glancing at the antitargets. Performance over the last five tri-

\[ \text{FIGURE 1. Antisaccade Performance of a Normal Subject}\]

\[ \text{FIGURE 2. Antisaccade Performance of a Patient With Obsessive-Compulsive Disorder}\]

\[ ^{a}\text{Dashed squares enclose inaccurate antisaccades.}\]

\[ ^{b}\text{Dashed circles enclose saccadic errors; dashed squares enclose inaccurate antisaccades.}\]
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Figure 3. Antisaccade Error Rate of 14 Normal Subjects and 11 Patients With Obsessive-Compulsive Disorder

Figure 4. Antisaccade Accuracy of 14 Normal Subjects and 11 Patients With Obsessive-Compulsive Disorder

Black symbols are male subjects; white symbols are female subjects. Horizontal bars are statistical means; vertical bars are 95% confidence intervals for the means.

As improved, but all subjects had demonstrated understanding and ability to do the task during practice before assessment.

On the antisaccade task, the mean proportion of errors was more than three times higher in the group with obsessive-compulsive disorder than in the comparison group (table 1). To analyze gender effects in more detail, the proportion of errors was examined as a dependent variable in a multivariable regression model using diagnosis, gender, and the interaction between diagnosis and gender. The beta for diagnosis was 1.7 (t=3.95, df=1, p=0.001), the beta for gender was 0.05 (t=0.27, df=1, p=0.79), and the beta for the interaction was -1.2 (t=-2.71, df=1, p=0.01) (model F=11.05, df=3, 21, p=0.0001). Thus, although there was a large effect for male subjects with obsessive-compulsive disorder (figure 3), there was still a gender-independent difference in performance between the group with obsessive-compulsive disorder and the normal group.

The proportion of inaccurate saccades in the antisaccade task was analyzed in the same way. The beta for diagnosis was 0.4 (t=0.73, df=1, p=0.48), the beta for gender was -0.1 (t=-0.56, df=1, p=0.58), and the beta for the interaction was -0.1 (t=-0.08, df=1, p=0.94) (model F=1.80, df=3, 21, p=0.18). Diagnosis modeled alone had a beta of 0.4 (t=2.23, df=1, p=0.04) (model F=15.23, df=1, 21, p=0.0007). Thus, there did not appear to be a gender-related difference in antisaccade accuracy, but there was a difference between diagnostic groups (figure 4).

Discussion

The results support the hypothesis of a deficit in goal-guided saccadic performance related to the diagnosis of obsessive-compulsive disorder. The fact that the visually-guided but not the goal-guided saccadic performance of the patients with obsessive-compulsive disorder appeared to be normal supports an inference of frontal cortical and/or basal ganglia functional abnormality underlying this performance deficit. This does not necessarily imply a structural deficit in these areas. It is possible that anxiety alone could account for poorer performance. Although the subjects were rated with the Hamilton Scale for Anxiety at the time of diagnostic interview (and there was no correlation of these ratings with oculomotor performance), a quantitative rating of anxiety at the time of oculomotor testing was not obtained, so this question cannot be answered here.
The gender difference in antisaccade error rate among the subjects with obsessive-compulsive disorder was an unexpected finding. There were no other apparent factors (including age at onset, duration of the disorder, other concurrent diagnoses, family history, and medication) that might have accounted for this difference. Another gender difference has been reported for obsessive-compulsive disorder: a trend for earlier age at onset among males (20). How these findings might be related is unclear, but the two together suggest further study of possible gender differences in obsessive-compulsive disorder.

As in research on eye movements in schizophrenia, although there were significant differences between group means, there was overlap between individuals in each group. Several factors may account for the variability in the group with obsessive-compulsive disorder. The categorical decision on the clinical diagnosis may have been in error. Although it seems unlikely that there were false negative diagnoses in the normal group, there may have been false positive diagnoses in the group with obsessive-compulsive disorder. There may be etiologic heterogeneity for developing obsessive-compulsive disorder, so that only some patients have functional brain pathology. There may be a normal distribution of oculomotor performance, so that even if relative impairment of oculomotor control is invariably associated with obsessive-compulsive disorder, absolute differences from normal are not always observed because a given individual's hypothetical baseline performance was better. In addition, clinical state at the time of testing, medication levels in blood or brain, and perhaps the nature of specific obsessions and compulsions might have effects.

Variability in the normal group could also have been due to a number of factors. For example, there is evidence that poor smooth pursuit eye movement is a manifestation of a latent trait related to schizophrenia (21). Although no subjects reported a family history of schizophrenia, this is probably not a reliable method for determining family history. Furthermore, schizophrenia spectrum conditions such as schizotypal personality disorder were not systematically assessed in the subjects' relatives. These conditions have been associated with poor smooth pursuit eye movement (22) and could possibly be associated with poor antisaccade performance.

Sampling bias might have confounded our findings. Berkson (23) suggested that when any single medical condition is apt to result in treatment with less than perfect certainty, individuals with more than one condition (including unmeasured conditions) are more likely to be in treatment than those with only one. The logic of Berkson's bias implies that individuals in treatment-based samples are more likely to reveal overlap of conditions than those in the general population who have the same conditions. Being in psychiatric treatment may be related to more general deficits in goal-guided or "executive" functioning and thus deficits in goal-guided saccadic eye movements.

CONCLUSIONS

This is the first report of a deficit in oculomotor control among subjects with the diagnosis of obsessive-compulsive disorder. The results are consistent with evidence from other research suggesting frontal lobe and basal ganglia abnormalities in obsessive-compulsive disorder. However, replication in an independent group is needed. Although no cross-sectional associations were apparent, longitudinal study of relationships between clinical status, medication, and oculomotor performance is indicated. Study of unaffected relatives of patients with obsessive-compulsive disorder would also be of interest. If these results are replicated in a clinical sample, study of community samples will be useful to avoid the possible effects of Berkson's bias (23).

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