Ideomotor limb apraxia in Huntington’s disease: implications for corticostriate involvement

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Abstract

Ideomotor limb apraxia, a disorder of goal-directed movement, has been attributed to lesions in the frontal and parietal lobes, but the role of subcortical structures is less certain. In order to determine its prevalence in a disorder affecting the basal ganglia and corticostriatal connections, we examined imitation of hand gestures in Huntington’s disease (HD) patients. We also assessed the relationship between apraxia and cognitive and motor dysfunction in an effort to better understand the neural underpinnings of apraxia in HD. If damage restricted to the basal ganglia produces ideomotor limb apraxia, then we would expect to find evidence of apraxia in patients who were early in the disease course when selective striatal damage is most common. Such a pattern, however, was not found in our sample. Instead, patients with greater neurological impairment and with a longer duration of disease were more likely than less affected patients to demonstrate apraxia. Apraxia was not related to severity of chorea, but was associated with greater impairment in eye movements, voluntary movements, and verbal fluency. These findings suggest that apraxia in HD results from damage to the corticostriate pathways and the basal ganglia rather than from damage restricted to the basal ganglia.

Keywords: Apraxia; Motor programming; Corticostriatal circuits; Basal ganglia

1. Introduction

Although the neuroanatomical substrates for goal-directed movements are not fully delineated, frontoparietal circuits are crucial for controlling a variety of actions that require the storage and retrieval of motor programs [18,21,35]. Ideomotor limb apraxia, a deficit in the performance of complex gestures (e.g. flipping a coin), has also been associated with damage to the frontoparietal circuits [13]. More specifically, Haaland and colleagues [13] report that damage to the area around the left intraparietal sulcus, encompassing Brodmann areas 7, 39 and 40, and the left middle frontal gyrus, including Brodmann areas 9, 46 and 6, produced spatiotemporal gestural deficits that are the hallmark of ideomotor limb apraxia. These same regions are activated when healthy adults pantomime tool use [30] supporting their role in the production of goal-directed movement.

The subcortical substrates of goal-directed movement are not well understood, but the frontoparietal circuits do not operate independently of subcortical structures, such as the basal ganglia. The frontal and parietal lobes have reciprocal interconnections with the basal ganglia [1,27,37], and imaging data support their functional relationship [6,47]. Furthermore, diseases of the basal ganglia, such as Huntington’s disease (HD) and Parkinson’s disease (PD), are known to cause deficits in higher-order motor functioning, such as sequencing and motor programming [10,14,16,19,48]. A breakdown in either skill could produce apraxia by interfering with the execution of the spatiotemporal aspects of the movements or disrupting access to the stored motor programs that specify those spatiotemporal features.

The literature on the role of the basal ganglia for praxis is sparse and inconsistent, likely due to methodological variations, such as different etiologies of basal ganglia disruption or different criteria for diagnosing limb apraxia [31]. A
comprehensive review of the frequency of ideomotor limb apraxia in PD found that 27% of the patients who were examined were apraxic in both hands and demonstrated spatiotemporal errors in transitive movements [25] that were similar to those seen in patients with left frontal or parietal damage [13]. The only group study to examine the rate of ideomotor limb apraxia in HD patients reported that 33% (i.e. 3/9) of the patients met criteria for ideomotor apraxia, and the authors suggested that apraxia in HD was caused by primary basal ganglia damage rather than damage to the cerebral cortex [38].

However, a recent review of the incidence of apraxia following focal subcortical lesions concluded that damage to basal ganglia structures (i.e. caudate, putamen, globus pallidus) does not cause apraxia unless additional involvement of the periventricular, in particular peristriatal, white matter has occurred [31]. This report calls into question the conclusion that apraxia in HD can be caused by neuropathology in the basal ganglia alone. The HD sample studied by Shelton and Knopman [38] was in an advanced disease state, characterized by illness duration greater than 9 years and significant functional disability and cognitive deficits. The three apraxic patients were among the most severely affected. Imaging data in HD patients with similar disability has documented frontal white matter involvement [2], suggesting that the HD neuropathology in the Shelton and Knopman sample was not likely confined to the basal ganglia. Because Shelton and Knopman [38] examined a small number of patients (n = 9), formal comparisons between apraxic and nonapraxic patients were not possible so differences in the characteristics (e.g. level of global dementia, severity of motor impairment) of the apraxic and nonapraxic patients could not be examined.

If ideomotor limb apraxia occurs in diseases of the basal ganglia because of primary damage to these structures, then impaired gestural imitation would be expected in patients who are relatively early in the disease course. However, if ideomotor apraxia in HD is caused by damage to the basal ganglia plus direct damage to the corticostriate circuits that interconnect the basal ganglia with the cerebral cortex, then ideomotor apraxia would be expected only in more advanced patients who have more widespread neuropathology [2,4,17,22,40]. The current study was designed to determine if apraxia is present in earlier stages of HD, when selective striatal damage is most common [45], by examining a larger sample of HD patients with a greater range of disease severity than the Shelton and Knopman sample [38]. Further, we used the same apraxia assessment battery used in a previous study that identified ideomotor limb apraxia resulting from left frontal or parietal lobe lesions [13]. Unlike the battery utilized by Shelton and Knopman, our assessment did not include examples of buccofacial apraxia because neuoroanatomical substrates of buccofacial apraxia differ from those involved with ideomotor limb apraxia [43]. We also assessed a variety of cognitive skills that are compromised by HD to determine if apraxia was associated with specific cognitive deficits, and we used a standardized neurological examination commonly used to assess the severity of HD (i.e. the Quantified Neurological Examination (QNE)) to explore the relationship between apraxia and other neurological symptoms of HD.

2. Methods

2.1. Subjects

Twenty HD patients recruited from the Baltimore Huntington’s Disease Research Center at the Johns Hopkins University (n = 14) or the Cognitive Neuroscience Research Program at the Albuquerque Veterans Affairs Medical Center (n = 6) and 40 healthy age- and education-matched control subjects were assessed with a limb apraxia test. All subjects were right-handed. The control subjects’ data have been previously reported as part of a group of 75 normal control subjects [13], and their demographic data are presented in Table 1. Twenty additional control subjects were included to provide a comparison group for the HD patients’ neuropsychological test performance. These cognitive control subjects are not presented in Table 1, but they were age-matched (mean = 48.6; S.D. = 15.1), education-matched (mean = 14.0; S.D. = 2.6), and gender-matched (45% women) to the HD patients. Informed consent was obtained according to the Declaration of Helsinki, and the Institutional Review Boards of the Albuquerque Veterans Affairs Medical Center, University of New Mexico, and Johns Hopkins University approved this research.

HD was diagnosed by neurologists or neuropsychiatrists based on a positive family history of HD, the presence of abnormal movement consistent with HD, and genetic testing for the mutation that causes HD. Exclusionary criteria included substance dependence at the time of testing or the presence of a neurological condition other than HD. No participants had a psychotic disorder. As expected, most patients were taking psychotropic medications either alone or in combination to treat the symptoms of their HD, including antidepressants (n = 8), neuroleptics (n = 4), benzodiazepines (n = 1), sympathomimetics (n = 1), and perphenazine/amitriptyline (n = 1). Four patients were participating in a double-blind clinical trial of remacemide and coenzyme Q10 at the time of testing, but whether they were receiving drug or placebo is unknown.

HD patients were examined using the Quantified Neuropsychological Examination [9], yielding measurements of ocular motor deficits (Eye Movement Scale), choreiform movements (Chorea Scale), and general motor impairment (MIS). Subtests were examined individually because they have been found to assess motor skills that show different patterns of deterioration as HD progresses [8,23]. The Eye Movement Scale assesses smoothness and range of gaze, saccades, forceful eye closure, and gaze persistence. The
Table 1
Huntington’s disease (HD) and Control groups’ demographic information

<table>
<thead>
<tr>
<th></th>
<th>Apraxic HD (n = 7)</th>
<th>Nonapraxic HD (n = 13)</th>
<th>Control subjects (n = 40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>48.3 (18.2)</td>
<td>50.3 (14.5)</td>
<td>55.1 (12.0)</td>
</tr>
<tr>
<td></td>
<td>22–69</td>
<td>25–70</td>
<td>31–71</td>
</tr>
<tr>
<td>Education</td>
<td>13.0 (2.8)</td>
<td>13.5 (2.2)</td>
<td>14.3 (2.5)</td>
</tr>
<tr>
<td></td>
<td>10–17</td>
<td>12–19</td>
<td>8–20</td>
</tr>
<tr>
<td>Sex (% women)</td>
<td>71</td>
<td>31</td>
<td>38</td>
</tr>
<tr>
<td>QNE total score</td>
<td>54.6 (14.8)</td>
<td>33.5 (13.0)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>26–75</td>
<td>a 19–52</td>
<td>NA</td>
</tr>
<tr>
<td>Chorea Scale</td>
<td>11.6 (5.4)</td>
<td>8.4 (4.1)</td>
<td>11.6 (5.4)</td>
</tr>
<tr>
<td></td>
<td>5–19</td>
<td>a 0–13</td>
<td>5–19</td>
</tr>
<tr>
<td>MIS</td>
<td>11.3 (4.6)</td>
<td>7.5 (5.0)</td>
<td>11.3 (4.6)</td>
</tr>
<tr>
<td></td>
<td>5–16</td>
<td>a 1–14</td>
<td>5–16</td>
</tr>
<tr>
<td>Eye Movement Scale</td>
<td>8.0 (1.3)</td>
<td>4.0 (1.0)</td>
<td>8.0 (1.3)</td>
</tr>
<tr>
<td></td>
<td>6–10</td>
<td>a 1–7</td>
<td>6–10</td>
</tr>
<tr>
<td>MMSE</td>
<td>23.4 (2.9)</td>
<td>25.5 (3.6)</td>
<td>23.4 (2.9)</td>
</tr>
<tr>
<td></td>
<td>10–26</td>
<td>10–30</td>
<td>10–26</td>
</tr>
<tr>
<td>Duration of illness</td>
<td>9.7 (3.9)</td>
<td>4.5 (3.0)</td>
<td>9.7 (3.9)</td>
</tr>
<tr>
<td></td>
<td>5–15</td>
<td>a 1–11</td>
<td>5–15</td>
</tr>
<tr>
<td>Praxis performance errors</td>
<td>6.2 (1.3)</td>
<td>2.5 (1.1)</td>
<td>6.2 (1.3)</td>
</tr>
<tr>
<td></td>
<td>4–7.5</td>
<td>a 1–4.5</td>
<td>4–7.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0–4</td>
<td></td>
</tr>
</tbody>
</table>

Values shown are mean (S.D.) range. Note: QNE, Quantified Neurological Examination; MIS, Motor Impairment Scale; MMSE, Mini Mental State Examination; NA, not administered.

* n = 12.

Chorea Scale assesses severity of choreiform movements when the patient is in various positions and states (e.g. arms out, under stress). Finally, the MIS assesses movement speed, motor persistence, speech clarity, plantar responses, motor smoothness, dysdiadochokinesis, and gait. One nonapraxic HD patient was not rated with the QNE, so data are presented for 19 subjects. Global cognitive status was assessed in the HD patients using the Mini Mental State Examination (MMSE) [7].

2.2. Procedure

The HD group and the apraxia control group completed a 15-item ideomotor limb apraxia test [15] in which participants imitated the examiner performing meaningless (e.g. thumb to forehead), intransitive (e.g. wave goodbye), and transitive (e.g. flip a coin) movements. These three types of movement were examined because they differ in the degree to which they rely on stored representations. Additionally, transitive movements require integration between an imaginary object and limb placement, and they appear to be the most sensitive to apraxia in patients with cortical lesions [13,33].

Praxis performance errors were videotaped and scored by two independent raters. Because of the visibly obvious signs of HD, raters were not blind to diagnosis. Errors made by the HD group were discounted if both independent raters attributed them to choreiform movements or bradykinesia (i.e. slowed movement initiation or execution). The ratings were done by the consensus of the two raters so interrater reliability is not reported.

Apraxia was examined in both hands in the HD group, and the data analyzed were the average of the errors made with each hand. In the majority of patients (18/20), the right-hand was tested first, but there were no significant practice effects (mean errors from first hand tested = 3.70 ± 2.34 versus mean errors from second hand tested = 3.95 ± 2.46; P > 0.6), and there were no significant differences between performances with the right or left-hand (mean errors for the right hand = 3.80 ± 2.33; mean errors for the left hand = 3.85 ± 2.48, P > 0.9). Twenty of the 40 were tested with their left-hand only and 20 with their right-hand only.

There were no significant differences between the control groups in number of total praxis performance errors or number of errors for each movement type (P > 0.5). Since there were no significant differences in right- and left-hand performance, the two control groups were pooled into a single group.

Table 2
Huntington’s disease and control groups’ cognitive performance

<table>
<thead>
<tr>
<th></th>
<th>Apraxic HD (n = 6)</th>
<th>Nonapraxic HD (n = 13)</th>
<th>Control subjects (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WAIS-R Vocabulary Scaled Score</td>
<td>8.3 (2.3)</td>
<td>9.5 (2.8)</td>
<td>10.4 (1.9)</td>
</tr>
<tr>
<td></td>
<td>8.3 (2.3)</td>
<td>9.5 (2.8)</td>
<td>10.4 (1.9)</td>
</tr>
<tr>
<td>WAIS-R Block Design Scaled Score</td>
<td>6.0 (1.0)</td>
<td>6.6 (2.3)</td>
<td>11.1 (2.5)</td>
</tr>
<tr>
<td></td>
<td>6.0 (1.0)</td>
<td>6.6 (2.3)</td>
<td>11.1 (2.5)</td>
</tr>
<tr>
<td>Controlled Oral Word Association Test</td>
<td>17.2 (11.5)</td>
<td>23.3 (7.6)</td>
<td>36.2 (6.5)</td>
</tr>
<tr>
<td></td>
<td>17.2 (11.5)</td>
<td>23.3 (7.6)</td>
<td>36.2 (6.5)</td>
</tr>
<tr>
<td>Hopkins Verbal Learning Test total recall</td>
<td>19.3 (4.7)</td>
<td>20.2 (4.4)</td>
<td>26.5 (4.9)</td>
</tr>
<tr>
<td></td>
<td>19.3 (4.7)</td>
<td>20.2 (4.4)</td>
<td>26.5 (4.9)</td>
</tr>
<tr>
<td>Stroop Color-Word Interference t-Score</td>
<td>35.3 (22.2)</td>
<td>32.4 (6.7)</td>
<td>45.8 (8.3)</td>
</tr>
<tr>
<td></td>
<td>35.3 (22.2)</td>
<td>32.4 (6.7)</td>
<td>45.8 (8.3)</td>
</tr>
<tr>
<td>Trail Making Test, Part A (s)</td>
<td>51.0 (9.1)</td>
<td>49.0 (16.4)</td>
<td>28.9 (8.0)</td>
</tr>
<tr>
<td></td>
<td>51.0 (9.1)</td>
<td>49.0 (16.4)</td>
<td>28.9 (8.0)</td>
</tr>
<tr>
<td>Trail Making Test, Part B (s)</td>
<td>153.8 (55.6)</td>
<td>154.2 (114.3)</td>
<td>80.1 (22.8)</td>
</tr>
<tr>
<td></td>
<td>153.8 (55.6)</td>
<td>154.2 (114.3)</td>
<td>80.1 (22.8)</td>
</tr>
</tbody>
</table>

Values shown are mean (S.D.).

* n = 5.

* n = 12.
The HD patients were considered apraxic if they made four or more spatiotemporal errors on the 15 movements with each hand (i.e. subjects making at least four errors in one hand, but less than four in the other were coded as nonapraxic). This criterion of at least four errors represents a two standard deviation departure from the apraxia control group’s mean error rate. Table 1 provides the descriptive data for the apraxic and nonapraxic HD groups and the apraxia control group.

The HD and the cognitive control groups completed a brief neuropsychological test battery that included the Wechsler Adult Intelligence Scale-Revised (WAIS-R) Vocabulary and Block Design subtests [46], the Hopkins Verbal Learning Test [5], Controlled Oral Word Association Test [3], Trail Making Test, Parts A and B [32], and the Stroop Interference Test [12]. These tests were chosen because with the exception of the WAIS-R Vocabulary subtest, they assess cognitive abilities frequently impaired in HD. Tests were administered according to their standardized instructions. Some HD patients were unable to complete the cognitive battery, and the exact number completing each test is detailed in Table 2.

3. Results

Thirty-five percent (7/20) of the HD patients were apraxic (i.e. made four or more praxis performance errors with each hand). The apraxic and nonapraxic HD groups were demographically similar and did not differ from the pooled NC group in age, educational attainment, or sex distribution, as detailed in Table 1. Despite lack of significant group differences in sex, it is apparent that the HD apraxic group included a higher proportion of women compared to the nonapraxic HD group. However, separate comparisons of the number of praxis performance errors produced by men and women in all HD patients (men’s mean = 3.2 ± 2.1 and women’s mean = 4.6 ± 2.0) and in all control subjects (men’s mean = 1.1 ± 1.3 and women’s mean = 0.93 ± 0.96) demonstrated no significant differences for either group. The apraxic HD group had a greater duration of illness than the nonapraxic group (P < 0.01), but there were no differences in severity of dementia as rated by the MMSE. Nonapraxic patients were more likely to be taking antidepressants (7/13) compared to apraxic patients (1/7), but other psychotropic medications were prescribed to patients in the two groups with roughly the same frequency.

As seen in Table 2, there were also no differences in performance on any of the cognitive measures between the two HD groups, but both groups were impaired relative to the control group on all cognitive measures (all P < 0.05 except the WAIS-R Vocabulary Scaled Score (P > 0.7). In addition, compared to the nonapraxic HD patients, the apraxic HD patients demonstrated greater neurological impairment on the QNE (P < 0.001) due primarily to greater impairment in eye movements (P < 0.001) rather than general motor impairment (P = 0.12) or chorea severity (P = 0.17).
Control subjects made no praxis performance errors on the intransitive movements so the following overall analysis of variance (ANOVA) did not include those movements (see Fig. 1). A Group (apraxic HD, nonapraxic HD, control) x Movement (meaningless, transitive) mixed-model ANOVA showed that the number of praxis performance errors reliably varied across the groups \(F(2, 57) = 41.14; P < 0.001\) due to the apraxic HD group’s poorer performance relative to the nonapraxic HD group \(P < 0.001\) and to the control group \(P < 0.001\), as well as to the nonapraxic HD group’s poorer performance relative to the control group \(P < 0.01\). In addition, while all groups made a greater number of errors on transitive than meaningless movements \(F(1, 57) = 40.89; P < 0.001\), this effect was particularly marked for the apraxic group, as evidenced by a significant interaction \(F(2, 57) = 16.48; P < 0.001\). More specifically, the apraxic patients performed worse than the control subjects for both movement types \(P < 0.001\) but worse than the nonapraxic group for the transitive movements only \(P < 0.001\). The nonapraxic patients and the control subjects made a comparable number of errors of performance on meaningless and transitive items \(P > 0.05\). A separate comparison of intransitive performance by the two HD groups demonstrated no significant differences, similar to the pattern for meaningless movements.

The relationship between praxis performance errors and motor dysfunction was examined in the entire HD group with Pearson correlations and is illustrated in Fig. 2. Patients who made a greater number of praxis performance errors had greater general neurological impairment on the QNE \(r = 0.59, P < 0.01\). More specifically, there was a significant relationship between praxis performance errors and the Eye Movement Scale \(r = 0.74, P < 0.001\) and the MIS \(r = 0.48, P < 0.05\) of the QNE, but there was no significant relationship with the Chorea Scale \(r = 0.06, P = 0.81\). Thus, apraxia was associated with eye movement impairment and voluntary motor deficits, but not with severity of chorea. Finally, the relationship between cognitive test performance and apraxia demonstrated that only letter fluency was related to the severity of apraxia in the HD patients \(r = -0.49, P < 0.05\).

4. Discussion

4.1. Incidence of limb apraxia in HD

This study demonstrated that spatiotemporal errors in gestural imitation, the hallmark of ideomotor limb apraxia, are present in HD at a sufficiently high rate to diagnose apraxia in 35% of the patients examined. Roughly the same incidence was reported in a small group of more severely affected HD patients [38], and consistent with those results, the apraxia identified in the current sample was independent of chorea. Thus, ideomotor limb apraxia can be separated from chorea, further supporting the role of the corticostriatal system in higher-order motor processing.

The incidence of apraxia in our HD sample (35%) was somewhat smaller than in a group of left hemisphere stroke patients (41%) but much larger than in a group of right hemisphere stroke patients (8%) [13]. Like patients with lesions in the left middle frontal gyrus and intraparietal sulcus [13], apraxia in these HD patients was most evident when they mimicked transitive movements compared to intransitive or meaningless movements. This pattern suggests a breakdown in overlearned movements that are dependent on the selection of stored representations and/or the normality of these representations. The differential impairment of transitive movements (i.e. movements demanding the manipulation of an imagined object) may have occurred because unlike intransitive and meaningless movements they require the integration of extrapersonal and personal space, suggesting that disruption of striatoparietal or frontoparietal circuits may impact praxis in HD.

4.2. Relationship to disease severity

While ideomotor limb apraxia is frequently associated with left hemisphere lesions in the frontal and parietal...
cognitive and functional impairment. In contrast, chor-
assessed by the MIS of the QNE has been related to greater
of HD, and increased difficulty performing the movements
V oluntary motor control also declines linearly with duration
ficulty maintaining steady fixation, are features of early HD
ments, particularly initiation of voluntary saccades and dif-
related to oculomotor deficits (Eye Movement Scale) and
apraxia was not related to chorea severity, it was strongly
severity influences the level of apraxia. We found that while
axia is highly sensitive to cognitive impairment
impaired scores on the QNE (67.8 ± 8.2) and longer dis-
5.8) [2]. Our apraxic patients were comparable to the moderately
neuroanatomical substrate.
Correlational analyses support the conclusion that disease
axia was not related to chorea severity, it was strongly
related to oculomotor deficits (Eye Movement Scale) and
general motor impairment (MIS). These relationships can-
not be explained simply by these scales’ dependence on
movement initiation and speed because errors caused by
bradykinesia were excluded from the final apraxia score.
Furthermore, it is unlikely that perceptual problems due to
oculomotor abnormalities (e.g. gaze impersistence and
disengagement deficits) affected the patients’ imitation of
movements because the apraxic and nonapraxic HD patients
only differed in their abilities to perform transitive, not in-
transitive or meaningless, movements. Perceptual problems
would be expected to affect all three movement types to a
similar degree. Rather, these relationships are more likely
due to the differential pattern of deterioration in the QNE
measures as HD progresses. Abnormalities in eye move-
ments, particularly initiation of voluntary saccades and dif-
ficulty maintaining steady fixation, are features of early HD
that show linear worsening as disease state advances [23].
Voluntary motor control also declines linearly with duration
of HD, and increased difficulty performing the movements
assessed by the MIS of the QNE has been related to greater
cognitive and functional impairment [8]. In contrast, chor-
eform movements are reported early in the course of HD,
but they plateau and may actually resolve in later stages [8].
Therefore, the lack of relationship between chorea severity
and apraxia results, in part, from our exclusion of errors
caused by chorea in the final determination of its diagnosis,
but also from the nonlinear progression of chorea.
Importantly, while we are suggesting that apraxia in HD
occurs with greater neuropathology in the corticostriatal cir-
cuits, it is not caused by global dementia or an inability to
understand the requirements of the task. Our apraxic and
nonapraxic patients performed comparably on the MMSE
and the cognitive tests that were administered, and these tests
have been shown to be highly sensitive to cognitive impair-
ment in HD [34]. Furthermore, apraxic patients were capa-
bile of mimicking meaningless and intransitive movements as
well as nonapraxic patients indicating that they were able to
understand the task. Finally, only transitive movements dif-
ferentiated apraxic from nonapraxic patients, which would
not be expected if the apraxia was due to global cognitive
deficits.

4.3. Implications for neuroanatomical substrates of goal-directed movement

The strong relationship between eye movement abnor-
malities and apraxia suggests the possibility that the two
rely upon the same neural structures. However, the QNE
Eye Movement Scale assesses many different types of
eye movement (e.g. saccades, voluntary gaze, nystagmus),
which have multiple neuroanatomical substrates. Because
different HD patients can be impaired on different items
in the scale and obtain the same overall eye movement
score, it is problematic to conclude that the strong corre-
lation between limb apraxia and the Eye Movement Scale
is indicative of a common neuroanatomical substrate. This
is particularly true considering the multidimensional char-
acter of the Eye Movement Scale, which would predict
multiple neuroanatomical correlates rather than a single
neuroanatomical substrate.

Two recent reviews of the role of the basal ganglia in
controlling saccadic eye movements [29] and voluntary
movement [29] have described the caudate nuclei as gates
that moderate response choice by selectively inhibiting
competing input from the cortex. Basal ganglia lesions may
disrupt the organized production of purposeful movement
by flooding the system with competing response options.
Presumably, apraxia in HD may result from an inability to
effectively gate competing motor programs, which would
overwhelm the system and lead to aberrant motor responses.
However, this conclusion would predict that all HD patients
should show such difficulty since caudate involvement is
present early in the disease’s progression. Yet only HD
patients with longer disease duration demonstrate deficits
on the eye movement and the limb praxis scales suggesting
that these deficits are independent of this gating mechanism
or the gating mechanism is dependent on damage to the
caudate plus surrounding white matter. The latter possibility is more likely given the strong neuroanatomical evidence of corticostriatal circuits [1,27].

The empirical determination of whether lesions in the cortex, the basal ganglia, or the interconnections between the structures cause apraxia in HD is beyond the scope of this paper. However, the circuit that includes the caudate nuclei and dorsolateral prefrontal cortex may be quite important in suberving functions that have been attributed to the prefrontal cortex, including response selection [35,36] and working memory [11,27,39]. Disruption of the flow of information from the prefrontal cortex through the caudate could produce apraxia by interfering with the selection of the correct motor representation, which specifies the spatiotemporal sequence of responses. The significant relationship between apraxia severity and performance on the MIS of the QNE suggests that impaired selection and inhibition of motor programs may contribute to apraxia in HD. However, this speculation requires additional study, along with the identification of the underlying cognitive mechanisms that produced these interrelationships.

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