Task-Set Switching Deficits in Early-Stage Huntington's Disease: Implications for Basal Ganglia Function

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Abstract

■ Executive functions are likely mediated by interconnected circuits including frontal lobe and basal ganglia structures. We assessed the executive function of task switching in patients with early-stage Huntington's disease (HD), a neurodegenerative disease affecting the basal ganglia. In two experiments, the HD patients had greater difficulty when switching than when repeating a task than matched controls, and this was true even when scaling for the overall slowing of the patients. In the first experiment, HD patients had a switching deficit even in a ''pure'' condition where they had to switch, predictably, and with substantial preparation time, between stimuli having only one possible response, indicating a switching deficit different from that for patients with Parkinson's disease or frontal lobe trauma, and possibly relating to inadequate activation of stimulus–response links or ''response set.'' In the more elaborate second experiment, we could not account for the switching deficit of the patients in terms of inadequate preparation in advance of a switch, deficient suppression of task-set processing from the preswitch trial, or impaired suppression of interference due to the presence of a competing task set. Instead, we found that part of the switching deficit was due to elevated reaction time and errors on switch trials for a repeated response (same button press as on preswitch trial) relative to an alternated response (different button press from preswitch trial). We argue that this elevated ''repetition effect'' for the HD patients is due to excessive inhibition of the just-performed response in advance of a switch. Alterations in the ''response-setting'' process alone (Experiment 1) and both the response-setting and ''response inhibition'' process (Experiment 2) probably arise from striatal pathology in HD, thus accounting for the task-switching deficits and showing how basal ganglia implemented response processes may underpin executive function. ■

INTRODUCTION

Executive processes enable performance of complex tasks requiring coordination of basic cognitive functions such as perception, memory, and action. Such control mechanisms are often impaired following dysfunction of the frontal lobes, having devastating effects on everyday planning and social behavior. Although the terms ''executive function'' and ''frontal function'' have often been used synonymously, it is mistaken to ascribe the neural implementation of ''executive function'' to a single brain region. Instead, what is referred to as ''executive function'' probably encompasses a variety of specialized subprocesses mediated by circuits intimately associated with the frontal cortex (e.g., fronto-parietal and fronto-striatal circuits) (Lawrence, Sahakian, & Robbins, 1998). We focus here on the latter circuits by studying executive functions in patients with early-stage Huntington's disease (HD)—an inherited neurodegenerative disease of the basal ganglia with characteristic motor, cognitive, and psychiatric symptoms.

We studied early-stage patients because they show few choreic movements (permitting performance of speeded reaction time [RT] tasks) and because their pathology is likely to be mainly restricted to the striatum (e.g., Rosas et al., 2001; Vonsattel & DiFiglia, 1998; Aylward et al., 1996). Neuropsychological testing has documented a ''dysexecutive'' deficit in HD (e.g., Lawrence et al., 1996) and this also has ecological validity as HD patients demonstrate difficulty organizing daily activities (Brandt & Butters, 1996). We studied executive function in these patients using task switching—an experimental paradigm measuring the consequences of reconfiguration operations required to change from one task to another (e.g., Goschke, 2000; Rogers & Monsell, 1995). The participant responds to a series of stimuli, but from time to time the task—the rules about what to do—changes. For instance, the stimuli might be visually displayed letters, and the task on some trials might be to name the letter (e.g., say ''em'') and on others to name the color (e.g., say ''red''). To perform

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either task, the participant must somehow chain together an appropriate set of processes linking sensory analysis to motor output, including ''categorizing'' sensory input with respect to the relevant attribute, ''mapping'' the attribute's value, using decision criteria, to one of a predetermined set of response categories via stimulus–response (S–R) links, and ''executing'' the motor response used to signal the response category (Rogers & Monsell, 1995). To change tasks, one or more components of this ''task set'' must be reconfigured. Effects of this reconfiguration are revealed by comparing performance on trials where the task changes to trials where it remains the same. There is usually a substantial ''switch cost''—longer RT and more errors on task switch than on task repetition trials. Moreover, where the task changes predictably every *n* trials, this immediate cost of a task switch is limited to the first trial after a switch (Monsell, Yeung, & Azuma, 2000; Rogers & Monsell, 1995).

Increasing the interval available for preparation after the previous reduces the switch cost (Meiran, 1996; Rogers & Monsell, 1995). The mean switch cost reduces as the interval increases up to 600 msec or so. This ''preparation effect'' is agreed to index effective reconfiguration, under endogenous control, in anticipation of the task change. With further increases in the preparation interval, the switch cost reaches a substantial asymptote, which remains even when there are 2 or 3 sec to prepare the upcoming task set. Although the source of this ''residual switch cost'' is controversial (see Monsell et al., 2000 for review), most task-switching experiments clearly require the participant to maintain two task sets in an active state, and there is no dispute that at least the endogenous component of control exerted at a task switch consists in one particular task set being facilitated and the other being inhibited. It seems plausible that any inhibitory processes required in task switching could be related to other types of inhibition already studied in HD (Georgiou, Bradshaw, Phillips, Bradshaw, & Chiu, 1995; Swerdlow et al., 1995; Lasker, Zee, Hain, Folstein, & Singer, 1987) and that switching deficits in HD patients could be partly attributed to deficient inhibition.

There has been one previous study of task switching in HD (Sprengelmeyer, Lange, & Homberg, 1995). In this experiment, there were three conditions of 50 trials each. On each trial, a letter and a number were presented at the same time, equidistant from the center on the left and right halves of the screen. Between trials the position of the letter and the number varied randomly. In the first condition, subjects responded to the letter (pressing the appropriate key corresponding to the left and right halves of the screen); in the second condition, subjects responded to the number; and in the third condition they alternated between letters and numbers. Although HD patients had a switching deficit relative to controls, the fact that switch and nonswitch trials were confined to separate blocks makes it possible that HD subjects' performance on switch relative to nonswitch trials was impaired by factors other than a switching deficit per se (e.g., arousal or strategy; see Rogers & Monsell, 1995).

By contrast with HD, there have already been a number of task-switching studies in Parkinson's disease (PD) patients. An initial study found no switching deficit (Rogers et al., 1998), while a later one did (Hayes, Davidson, & Keele, 1998). However, the interpretation is less than clear because of grossly elevated baseline RTs for PD patients. A clear-cut switching deficit was found by Cools, Barker, Sahakian, and Robbins (2001) who studied PD patients using the same task and method as our Experiment 1. PD patients showed increased switch costs compared with control subjects, but *only* in a ''cross-talk'' condition in which inhibition of competing (irrelevant task) information was necessary. Importantly, increased switch costs were not simply due to generalized slowing of the patients relative to the controls. Although HD is related to cell death in the striatum, whereas PD is related to the death of dopamine-containing cells which innervate the striatum, it seems likely that striatal dysfunction resulting from either disorder would result in problems with task switching. Therefore, although we expected a deficit in task switching for HD patients, we also designed our experiments to probe components of any task-switching impairment in more detail than hitherto achieved in studies of basal ganglia patients.

We performed two task-switching experiments with early-stage HD patients and matched control groups. The first of these experiments (using the same task and method as Cools et al., 2001; Rogers et al., 1998 for Parkinson's disease) was directed towards: (a) assessing whether there was an overall switching deficit in HD patients, (b) assessing whether such a deficit interacted with the presence of cross-talk trials (''bivalent trials,'' in which the stimulus has elements of both potential task sets), to explore the possibility that HD patients had difficulty inhibiting a response to an irrelevant stimulus element, and (c) whether there was evidence in trials following a bivalent stimulus of the putative need to suppress the irrelevant task on the previous trial. The second experiment, which required button presses rather than vocal responses, employed neutral (univalent), congruent (bivalent), and incongruent (bivalent) stimuli in cross-talk blocks only and manipulated preparation interval between blocks. This experiment was directed towards: (a) assessing how a putative switching deficit in HD patients interacts with preparation time, (b) exploring further the influence of stimulus congruency on the switch trial in terms of overcoming interference from the irrelevant task, and (c) assessing whether a disruption in ''response inhibition'' in HD could account for elevated switch costs.

EXPERIMENT 1: BACKGROUND NEUROPSYCHOLOGY AND TASK SWITCHING

Nineteen HD patients and 19 age- and IQ-matched controls participated (see Table 1). In addition to the test of task switching, the HD subjects received a battery of background neuropsychology tasks to assess general cognitive performance. For the switching experiment, the tasks used were letter and digit naming (see Figure 6A). Following Rogers et al. (1998), each stimulus consisted of a pair of characters displayed side by side. In the letter-naming task, one of the characters was a letter, in the digit-naming task one character was a digit. In ''no-cross-talk'' blocks of trials, the irrelevant character was drawn from a set of neutral characters (e.g., % or #), so that every character pair cued only digit naming or letter naming. In the ''cross-talk'' blocks, the irrelevant character was drawn from the neutral set on one-third of the trials, while on the other two-thirds the character pair comprised a letter and a digit thus cueing both tasks. On each trial, a word cue ''LETTER'' or ''NUMBER'' was shown above each character pair, which was randomly ordered. Successive trials followed an alternating-runs sequence so that two letter-naming trials were followed by two digit-naming trials (i.e., AABB). There was a 1000-msec interval between the subject's response and the next stimulus, and the cue–stimulus interval was also 1000 msec.

On the basis of previous findings with HD and PD patients, we expected the HD patients to have greater difficulty in the cross-talk blocks. These impose the need to select the appropriate action of the two cued by the stimulus, by suppressing either the analysis of the irrelevant stimulus category or the response tendency evoked by it. On the basis of Sprengelmeyer et al. (1995), we predicted an overall switching deficit for the HD patients. We were also interested in whether this deficit was especially marked in the cross-talk blocks, and whether we could detect less carry-over of cross-talk inhibition following a bivalent stimulus in the HD patients.

Table 1. Group Characteristics for Experiment 1

	HD	*Controls*
Male/female ratio	12:7	11:8
Age	46.9 (10.0)	49.4 (14.1)
PVIQ	110.9 (6.9)	112.4 (5.2)
MMSE (/30)	27.5 (1.7)	
ADL (/25)	21.7 (5.0)	
Duration of HD (years)	5.4 (2.8)	
BDI	6.2 (9.4)	4.1 (4.1)

PVIQ = predicted verbal IQ; MMSE = Mini Mental State Examination; ADL = Activities of Daily Living score from Unified Huntington's Disease Rating Scale (UHDRS); BDI = Beck Depression Inventory. Values shown are mean (SD).

Table 2. Background Neuropsychological Data for Experiment 1

	HD	*Control*	*Difference*
FAS	28.6 (11.5)	40.5 (10.5)	$t(36) = 3.3, p < .01$
SDMT	31.0 (11.5)	48.9 (11.9)	$t(35) = 4.6, p < .01$
Stroop			
Col	51.6 (11.5)	74.4 (16.6)	$t(35) = 4.9, p < .01$
Wd	70.4 (18.8)	98.1 (16.9)	$t(35) = 4.7, p < .01$
Col–Wd	31.3 (7.4)	53.1 (22.1)	$Z(35) = 3.7, p < .01$
Motor screen	1273 (256)	934 (159)	$t(36) = 4.9, p < .01$
Pattern			
% corr	83.3 (14.8)	91.9 (7.1)	$t(36) = 2.3, p < .05$
RT	3300 (1479)	1889 (444)	$Z(36) = 4.3, p < .01$
Spatial			
% corr	78.2 (13.0)	83.4 (10.0)	$t(36) = 1.4$, *ns*
RT	3255 (1188)	1943 (374)	$Z(36) = 4.2, p < .01$

FAS = Verbal Fluency Score; SDMT = Symbol Digit Modalities Test; Pattern = pattern recognition memory; Spatial = spatial recognition memory.

Results

Background Neuropsychological Tasks

Table 2 shows the performance of HD and control groups on the 5 background neuropsychological tests. In accordance with previous studies of HD, these patients were impaired on pattern and spatial recognition memory (Lawrence et al., 1996), verbal fluency (Rosser & Hodges, 1994), psychomotor speed, and Stroop interference (Brandt & Butters, 1996).

Task Switching

Switch costs in cross-talk and no-cross-talk blocks. Figure 1 shows RT and error data. Patients were significantly slower than controls, $F(1,34) = 42.7, p < .001$ [HD: 777 (183); controls: 477 (64)], and made more overall errors, $F(1,34) = 19.5, p < .001$ [HD: 2.9 (1.1); controls: 1.3 (1.1)]. There was a significant Trial-type (switch vs. nonswitch) × Group effect for RT, reflecting slower switching, $F(1,34) = 12.6, p = .001$, in patients compared with controls, and this was also the case for errors, $F(1,34) = 7.1, p = .01$, reflecting that HD patients made more errors on switch versus no-switch trials than did controls.

Comparing no-cross-talk with cross-talk blocks, there was a significant Trial-type × Group × Blocks interaction

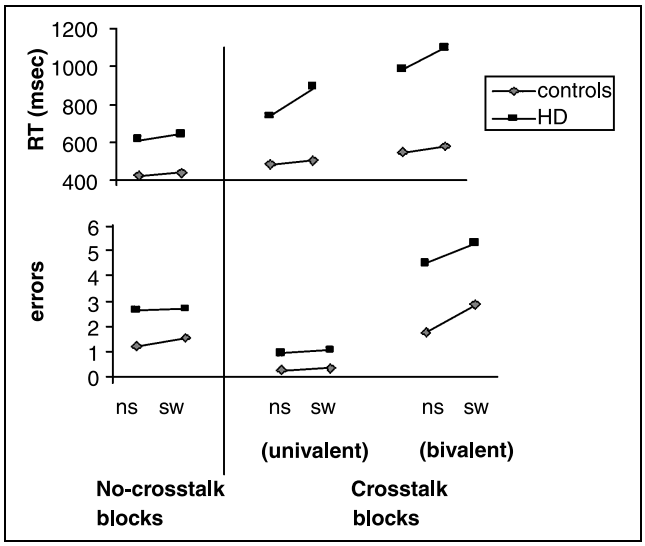

Figure 1. Switching deficit for HD patients for Experiment 1. No-cross-talk blocks only contained "univalent" stimuli, while cross-talk blocks contained both "univalent" and "bivalent" stimuli. Nonswitch (Ns) versus switch (Sw) values are shown for both errors and RT. HD patients are significantly slower on switch trials compared to nonswitch trials relative to controls, and this is exacerbated in cross-talk blocks, and especially when stimuli are bivalent (affording responses to both task sets).

for RT, $F(1,34) = 7.7$, $p = .01$, indicating that switching difficulty for patients relative to controls was particularly bad in cross-talk blocks, however, this was not the case for errors, $F < 1$. However, as simple interaction tests showed that the switching deficit of patients relative to controls held for both cross-talk blocks, $F(1,34) = 10.4$, $p < .01$, and non-cross-talk blocks, $F(1,34) = 8.3$, $p < .01$, the switching deficit of patients did not require the presence of cross-talk. Control subjects showed switch costs in both cross-talk blocks (29 msec), $F(1,17) = 15.3$, $p < .001$, and non-cross-talk blocks (9 msec), $F(1,17) = 15.6$, $p < .001$. An analysis of errors was possible within cross-talk blocks alone. An ANOVA with the factors Trial-type (switch vs. nonswitch) and Group showed there was a trend for HD patients to make more errors on switch versus nonswitch trials than controls for the cross-talk blocks alone, $F(1,34) = 2.2$, $p = .1$.

The much longer baseline RT for patients raises the possibility that their enhanced switch costs result from general slowing rather than an effect specific to task switching. As a conservative test (see, for discussion, Stuss et al., 1999), a further analysis compared the proportional or "scaled switch cost" (switch cost divided by nonswitch RT) between HD patients and controls. The scaled cost was greater for the patients, $F(1,34) = 11.0$, $p < .01$, and interacted with block type (cross-talk vs. no-cross-talk), $F(1,34) = 4.7$, $p < .05$. HD patients had significantly greater scaled switch costs for both no-cross-talk ($Z = 2.8$, $p < .01$) and cross-talk blocks ($Z = 3.2$, $p < .001$).

Effect of bivalence of present and preceding trial in cross-talk blocks. Stimuli in the cross-talk blocks could cue both tasks (bivalent) or only one (univalent). The difference between them provides a measure of the difficulty of suppressing processing of the irrelevant attribute or the response associated with it (cross-talk interference). HD subjects exhibited significantly more interference than controls for RT, $F(1,34) = 10.0$, $p < .01$, and errors, $F(1,34) = 6.5$, $p < .05$, but this did not interact with switching, $F(1,34) = 1.4$, *ns*, however, there was a trend for this interaction to be significant when scaled-switch costs were taken, $F(1,34) = 2.9$, $p = .1$. Goschke (2000) found that RTs tended to be slower on switch trials when the previous trial was bivalent (and incongruent) even though the response was different. This effect indexes a carry-over of suppression of the inappropriate S–R mapping or attribute that needs to be overcome when that mapping becomes appropriate. In order to assess this effect, we performed an ANOVA with the factors Previous trial valence (univalent vs. bivalent), Current trial valence (univalent vs. bivalent), and Switching (switch vs. no-switch). As this interaction was nonsignificant, $F(1,34) < 1$, we concluded that there was no reliable carry-over of inhibition onto the switch trial from prior processing of incongruent stimuli, and did not test group effects.

Correlations. For HD patients alone, we performed correlations for (i) clinical rating scale (UHDRS), (ii) medication status, (iii) activities of daily living (ADL), (iv) psychomotor speed (SDMT), (v) Stroop effect, (vi) pattern recognition memory, (vii) verbal fluency, and (viii) spatial recognition memory with overall RT, switch cost for RT, and switch cost for errors (switch errors minus nonswitch errors). Partially corrected for multiple comparisons ($\alpha = .01$), there was a significant negative correlation ($p < .001$) between ADL and overall RT (i.e., those subjects most impaired in daily living made the slowest RTs).

Summary. HD patients: (a) were impaired relative to controls on background neuropsychological measures, thus showing they were typical of the HD population, (b) were overall slower to respond and made more overall errors than controls on the principal test of switching, (c) had elevated overall switch costs relative to controls for RT (and errors) and this was still true when scaling for generalized slowing, (d) had elevated switch costs relative to controls for RT in no-cross-talk blocks even when scaling for generalized slowing, (e) had disproportionate switch deficits for RT (but not switch cost errors) on cross-talk relative to non-cross-talk blocks compared with controls, and this was still true when scaling for generalized slowing, and (f) showed greater interference from the irrelevant attribute (task set) than controls (increased RT on bivalent relative to univalent trials), but this effect was not reliably greater on switch than nonswitch trials.

Discussion

Unlike PD patients (Cools et al., 2001) or left-frontal patients (Rogers et al., 1998), the switching deficit of early-stage HD patients was not confined to ''cross-talk'' blocks as switch costs for patients were significantly greater than those for controls even in blocks where all stimuli cued only one of the two tasks. We argue in the General Discussion below that this indicates a ''pure'' switch deficit related to inadequate activation of relevant S–R mappings. Additionally, HD patients had disproportionately longer switch costs on cross-talk relative to no-cross-talk blocks compared to controls. Although HD patients showed more cross-talk interference than controls both in terms of RT and errors on bivalent relative to univalent trials, this did not robustly interact with switching, suggesting that the source of the HD switching deficit is not straightforwardly related to the presence of a stimulus that activates the currently inappropriate task on the switch trial (the so-called task-cueing effect; Rogers et al., 1998). Instead, we argue below that the presence of cross-talk within a block exacerbated the ''basic'' switch deficit related to inadequate activation of relevant S–R codes.

Overall, therefore, this first experiment provides evidence for a switching deficit of HD patients relative to control subjects under conditions of both noninterference and interference, with switching being particularly affected in the latter case. However, within cross-talk blocks, cross-talk interference did not interact with switching nor did processing of a bivalent stimulus on the previous trial. Therefore, the switching deficit of the HD patients could not be explained by inadequate suppression of the inappropriate task set or by inadequate carry-over suppression. Given that HD subjects perform worse than controls on the background neuropsychological tests (see Table 2), it is possible that the switching deficit is merely the reflection of more general memory or ''goal-neglect'' problems. Such an explanation, however, is unlikely for the following reasons. First, while those subjects with poor ADL scores made longer RTs, ADL did not correlate with switch cost. If it were true that the switching difficulty of HD patients is due to a general cognitive decline, one would expect the most (ecologically) impaired subjects to show the largest switch costs. Secondly, the background neuropsychological measures did not correlate with switch variables, therefore supporting the possibility that the switch deficit of HD patients may be due to impairment of specific mechanisms mediated by the striatum, such as those implementing various forms of inhibition. We further investigated such mechanisms in the following experiment by examining the effect of preparation on switch costs and by manipulating the congruency of the stimuli to dissociate inhibition of inappropriate responses from inhibition of inappropriate task sets.

Table 3. Group Characteristics for Experiment 2

	HD	*Controls*
Male/female ratio	11:6	9:8
Age	47.9 (9.6)	49.8 (10.9)
PVIQ	113 (5.6)	117 (5.5)
Duration of HD	8 (2.6) [1–10]	
ADL (/25)	22.1 (4.0)	
UHDRS	17.3 (10.2) [3–36]	
MOVEMENT	4.6 (3.9) [0–13]	

PVIQ = predicted verbal IQ; UHDRS = Unified Huntington's Disease Rating Scale. Duration of HD is in years since first symptoms were noted. MOVEMENT = neurological index of movement disorder from combining chorea and dystonia scores from UHDRS. Values shown are mean (SD). The range is shown in square brackets.

EXPERIMENT 2: TASK SWITCHING (WITHIN-BLOCK CONGRUENCY AND BETWEEN-BLOCK PREPARATION TIME)

Seventeen different HD patients and 17 different age- and IQ-matched controls participated (see Table 3). In addition to the test of task switching, we gathered neurological and other indices for the HD subjects based on the Unified Huntington's Disease Rating Scale (UHDRS).

The stimulus consisted of a letter string—LEFT, RIGHT, or XXXX, displayed inside an outline shape: a left facing arrow, a right facing arrow, or a rectangle (see Figure 6B). There were two tasks, both requiring the subject to press a left (index finger) or a right (middle finger) button with the right hand. For the word task, the word LEFT or RIGHT appeared in combination with one of the three outline shapes; the subject was to press the button on the side indicated by the word, ignoring the shape. For the arrow task, a left or right arrow shape was displayed containing one of the three letter strings, and the subject was to respond on the side pointed to by the arrow. The irrelevant attribute was equally often and randomly congruent (e.g., left arrow enclosing LEFT), incongruent (e.g., left arrow enclosing RIGHT), or neutral (e.g., rectangle enclosing LEFT, left arrow enclosing XXXX). The task changed predictably every three trials, and was cued in two ways. The position in which the stimulus was displayed was rotated clockwise around three positions, with the switch position clearly indicated. Also, immediately following the previous response, a cue word (''word'' or ''arrow'') was displayed just above the position in which the next stimulus was to be displayed after a response–stimulus interval (RSI) of 1500 or 100 msec (manipulated between blocks). Note that, unlike Experiment 1, all blocks contained all congruency conditions. The manipulation of between-block

preparation interval (RSI), and within-block congruency (incongruent, congruent, and neutral trials), and the use of button presses and an AAABBB sequence (two nonswitch trials for every switch trial) allowed us to extend the first experiment in several ways.

Hypothesis A: Inhibition of the just-performed response (response-related inhibition)

It is common to find, within a series of trials on the same task, that RT and error rate are reduced when the response is the same as the response produced on the previous trial, providing the time-lag between stimulus and next response is short. However, as some task-switching experiments have shown (e.g., Rogers & Monsell, 1995), on the switch trial, this situation reverses and response alternations are actually faster than response repetitions. While Rogers and Monsell (1995) suggest several possible hypotheses for this effect (see General Discussion), we assumed that some form of inhibition intervenes to suppress the response just made when a task switch is required. If this form of inhibition was deficient in HD, the just-performed response would not be properly suppressed and would interfere with the appropriate response on the current switch trial (taking longer to resolve); consequently, there would be a significant interaction between group, switch type (switch or nonswitch) and trial type (response repetition or alternation), so that the difference between response repetition and response alternations for switch versus nonswitch trials would be less for HD compared to controls.

Hypothesis B: Inhibition of irrelevant task set on current trial (task-cueing inhibition)

Greater switch costs for HD subjects may be due to the sort of exogenous driving of goal activation that is familiar in normal people as a ''capture error'' or observed in frontal patients as ''utilization behavior'' (Shallice, Burgess, Schon, & Baxter, 1989); that is, stimuli may evoke both inappropriate responses and inappropriate task sets associated with them. Experiment 1 already provided evidence for the conjecture that HD patients have difficulty with this from the fact that switching was particularly difficult for HD patients in cross-talk blocks where two-thirds of the stimuli afforded two conflicting responses, and the patients also showed greater interference from the irrelevant attribute when it afforded a conflicting response. However, in Experiment 1, we could not distinguish between inappropriate responses and inappropriate task sets. Experiment 2 allowed us to test this by comparing trials where the irrelevant attribute was associated with the other task but ''congruent'' (i.e., it was mapped to the currently appropriate task) with trials in which the irrelevant attribute had no association with either task

Table 4. Raw Data for Experiment 2

	HD		*Controls*	
	ns	*sw*	*ns*	*sw*
Short RSI				
incongruent	1221 (228)	1604.1 (299)	1076.5 (201)	1242.8 (206)
	8.2 (9.3)	22.7 (15.8)	11.3 (8.6)	14.5 (11.4)
congruent	1115 (192)	1423 (333)	919.1 (174)	1060.8 (147)
	1.4 (1.6)	1.2 (2.5)	0.2 (0.8)	1.2 (3.4)
neutral	1087.5 (176)	1421.3 (367)	889.4 (127)	1022.4 (138)
	1 (1.5)	3.1 (5.1)	0.4 (1.1)	1.6 (3.6)
Long RSI				
incongruent	844.8 (234)	992.7 (309)	657.5 (128)	705.9 (158)
	10.9 (9.6)	16.4 (11.2)	12.9 (6.1)	16 (10.5)
congruent	657.5 (155)	777.9 (213)	536 (94)	550.4 (112)
	1.2 (2.2)	0.8 (2.1)	0.4 (1.1)	0.4 (1.1)
neutral	660.5 (139)	772.9 (191)	531.2 (66)	600.9 (101)
	1 (1.5)	3.1 (4.6)	0.8 (1.4)	0.4 (1.6)

ns = nonswitch trials; sw = switch trials. RT and % errors are shown for each condition along with standard deviations in brackets.

or response (''neutral''). Therefore, we controlled for the nature of the response but varied whether one or two ''sets'' were triggered by the stimulus. Moreover, we assessed this effect in the context of switching. Therefore, if HD patients have difficulty in switching because of insufficient inhibition of the irrelevant task set, we would see longer RT on congruent relative to neutral trials compared to control subjects.

Hypothesis C: Inhibition of S–R links of irrelevant task on current trial (S–R inhibition)

In addition to examining how the entire task set may be activated by cueing the irrelevant task (i.e., comparing congruent with neutral trials), we can examine a more specific effect, the suppression of competing S–R links by contrasting congruent with incongruent trials. If HD patients have difficulty switching because of insufficient suppression of the irrelevant S–R links, then we would see longer RT on incongruent than congruent trials in switch relative to nonswitch trials.

Results

Overall

Table 4 contains RT and error data for the experiment. HD patients were significantly slower than controls, $F(1,30) = 16.6$, $p < .001$ [HD: 1009 (191); controls 800 (104)], but they did not make significantly more errors, $F(1,30) = 1.1$, *ns*. HD patients were particularly slow in the short preparation interval (RSI = 100) blocks compared to long preparation interval blocks (RSI = 1500) relative to controls, $F(1,30) = 4.3$, $p = .05$.

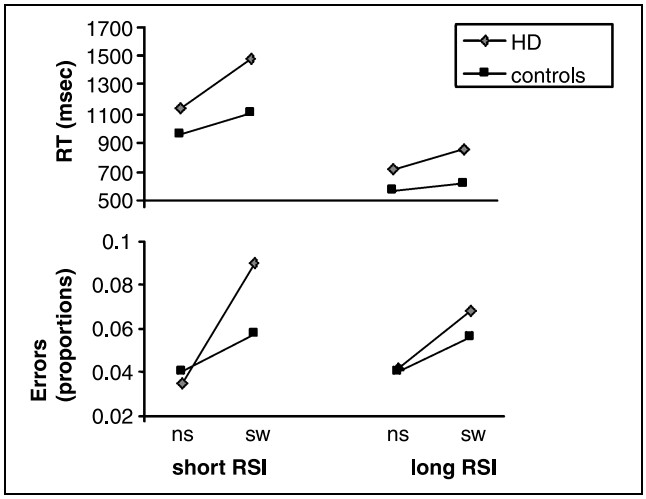

Figure 2. Switching deficit for HD patients for Experiment 2. HD subjects were overall slower and made more errors on switching (sw) relative to nonswitching (ns) compared to controls, and, for RT, this interacted further with RSI, so that the switching deficit of the patients was particularly bad at short RSI (short preparation interval). However, this further interaction was nonsignificant when scaling for the overall slowing of the patients (see text).

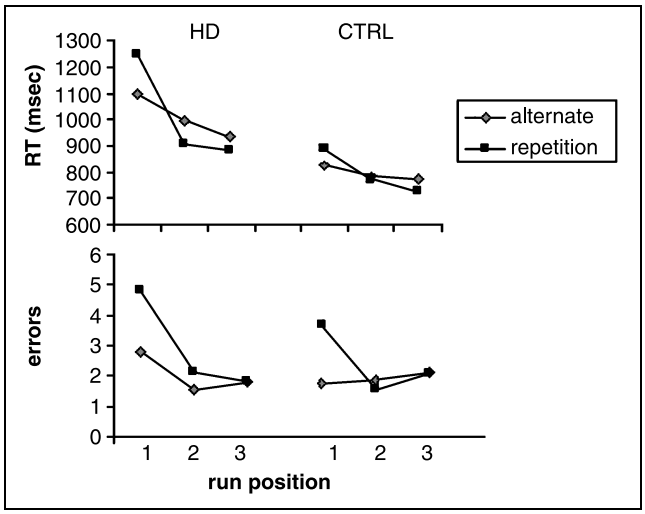

Figure 3. HD patients show an altered pattern of response repetitions versus alternations for switch versus no-switch trials. HD patients are slower to make a repeated response than an alternate one after a switch relative to a nonswitch compared to controls.

Switch Costs at Short and Long Preparation Intervals

As depicted in Figure 2, there was a significant Group × Switch interaction, $F(1,30) = 13.3$, $p = .001$, as well as a significant Group × Switch × RSI interaction, $F(1,30) = 4.0$, $p = .05$, indicating that the switching difficulty of the patients was particularly bad at short RSI. Simple interaction tests further revealed that HD patients were impaired on switching relative to controls for both long RSI, $F(1,30) = 6.2$, $p < .05$, as well as short RSI, $F(1,30) = 11.3$, $p < .01$. HD patients also made more switch-related errors than controls, $F(1,34) = 4.9$, $p < .05$, but this did not interact with RSI. Almost all errors occurred in the incongruent condition (82% of errors for HD, and 92% of errors for controls).

Response-related Inhibition

In order to assess Hypothesis A (response-related inhibition), ANOVAs for RT and errors were performed on the factors Run-position, Repetition-type, RSI, and Group. Figure 3 shows there was a significant effect of Run-position × Repetition-type for RT, $F(1,30) = 19$, $p < .001$, and errors, $F(1,30) = 6.9$, $p < .01$, and for RT this was qualified by a significant interaction with group, $F(1,30) = 4.0$, $p < .05$, but not a further interaction with RSI. These results therefore support Hypothesis A in suggesting a disruption to response-related inhibition in HD. However, the direction of the effect was opposite to that expected. If, in HD, the just-performed response is not properly suppressed, then one would expect it to lead to ''less'' interference on subsequent repetition, but in fact it putatively led to ''more.'' In order to simplify the analysis of this result and to relate it to other indices, we created a ''repetition-effect'' index by

subtracting the average of the difference between repeat and alternate RTs on nonswitch trials from the difference between repeat and alternate RTs on the switch trial. We regarded the repetition index as the RT cost associated with response-related inhibition. A t test showed the HD subjects had a significantly greater repetition effect than controls [$t(30) = 2.1$, $p < .05$]. In the interim, we interpreted this as implying that the HD subjects had ''increased response-related inhibition'' compared to controls—possibly accounting for their switching deficit (owing to elevated RT for repeated responses on the switch trial.)

Task-Cueing and S–R Inhibition

We assessed Hypothesis B regarding insufficient task-cueing inhibition in HD by performing an ANOVA with the factors Trial-type (switch vs. nonswitch), Congruency (congruent vs. neutral), RSI, and Group. Neither the Congruency × Group interaction nor the Congruency × Group × Switch interaction was significant. Therefore, Experiment 2 did not support the hypothesis of impaired task-cueing inhibition. We assessed Hypothesis C regarding inhibition of S–R links by analyzing the factors Trial-type (switch vs. nonswitch), Congruency (incongruent vs. congruent), RSI, and Group. There was a main effect of congruency, with incongruent trials significantly slower, $F(1,30) = 93$, $p < .001$, but neither the Congruency × Group interaction nor the Congruency × Group × Switch interactions were significant.

Scaling for Overall Slowing and Reanalyzing Switch Costs with Matched Groups

As HD patients were generally much slower than controls, a reanalysis of switch costs was undertaken, as before, by scaling for slowing. As before, we used the conservative method of dividing the switch cost by nonswitch RT (baseline). HD patients were still significantly impaired at overall switch, $F(1,30) = 6.5$, $p < .05$, but there was no longer a Group × Switch × RSI interaction, $F(1,30) = 1.6$, *ns*. Simple effects analysis showed, however, that HD patients still had a switching deficit relative to controls at both short, $F(1,30) = 5.1$, $p < .05$, and long, $F(1,30) = 4.3$, $p < .05$, preparation intervals.

A supplementary ANOVA was performed for Switch × RSI for HD and control groups matched for overall RT. The criteria for selection were minimum differences between groups with respect to (i) overall RT, (ii) predicted verbal IQ, and (iii) age. Within these constraints, a search was made for lower and upper bounds of overall RT that maximized the size of the groups. The ANOVA was performed on 7 HD patients (mean RT 946 msec, *SD* 76) and 7 control subjects (mean RT 890, *SD* 68). The difference between mean RT was nonsignificant, as were the differences between age and predicted verbal IQ for the groups. There was a significant Group × Switch interaction, $F(1,12) = 7.4$, $p < .05$, qualified by a further interaction with RSI, $F(1,12) = 6.3$, $p < .05$. Again, HD subjects had particular difficulty with the switch at short preparation interval. This supplementary analysis strongly suggests that even when groups are matched for speed of perceptual, selection, and response processes, HD subjects have a deficit specifically related to switching.

Correlations

For HD subjects, we performed correlations for the four measures of movement disorder, overall UHDRS score, ADL, and medication status with the three measures of the switch cost in terms of RT and errors, and the repetition effect. Partially corrected for multiple comparisons ($\alpha = .01$), there was a significant correlation between the repetition effect and the neurological movement disorder index ($r = .67$, $p = .005$), and between the repetition effect and time since onset of first symptoms ($r = .63$, $p = .01$).

Summary

HD patients: (a) were slower overall than controls, particularly when preparation interval was short, but they did not make more errors overall; (b) had greater overall switch costs than controls for both RT (even when scaling for overall slowing) and errors, and this interacted with preparation interval for RT, so that the switching difficulty of the patients was particularly bad when preparation interval was short (although this was not true when scaling for overall slowing); (c) showed a ''greater'' repetition effect, as evidenced by elevated RT on switch trials for repeated responses relative to controls, which we assumed to index excessive response-related inhibition, and those patients with the greatest response-related inhibition were also likely more progressed in the disease as judged by a worsened clinical movement index; and (d) did *not* show impaired inhibition related to task cueing, or the need to suppress S–R links.

GENERAL DISCUSSION

This second experiment replicated the finding in Experiment 1—an exaggerated switch cost in HD for cross-talk blocks—using different stimuli, manual instead of verbal responses, and a new pair of tasks generating Stroop-like interference in normal subjects. Again, the exaggerated switch cost survived scaling of RTs for overall slowing in the patients and a comparison between controls and a subgroup of HD patients matched for overall RT. In both experiments, we could exclude the possibility that the switching deficit was due to factors such as poor concentration, memory, psychomotor slowing, or medication status. In addition, Experiment 1 showed that HD patients had larger

switch costs even in no-cross-talk blocks. Having thus demonstrated a deficit in set switching in HD, we sought to account for the pattern of effects and relate them to striatal pathology.

Preparation Time

It is well established that the cost of a predictable switch is reduced if time for preparation is allowed before the next stimulus onset (Rogers & Monsell, 1995). The current experiment was no exception: Figure 2 shows that both groups reduced their switch costs by about half with preparation, and there was no significant interaction between group, switch-cost, and RSI when scaling for the overall slowing of the patients. Therefore, the patients' switching difficulty is unlikely to be explained by inadequate preparation during the RSI. (Figure 2 also shows a main effect of RSI: clearly, 100 msec is not enough time to move attention to the new location and prepare oneself for processing, whether switching tasks or not, but this more general preparation effect too appeared normal in the HD patients.)

Response-related Inhibition

Figure 3 demonstrates that HD patients show a larger switch cost than the controls, but only on response repetition trials. That is, the controls show the ''usual'' interaction—a larger switch cost for response repetition trials (Rogers & Monsell, 1995) but this is greatly exaggerated for the patients. When scaling the repetition effect for each subject by overall RT, there was no longer a reliable difference between groups [$t(30) = 1.4, p > .1$]. However, this is a very conservative correction which assumes that slowing of all cognitive processes is similar to overall slowing of RT. Instead, it is likely that the speed of cognitive processes underlying the repetition effect in HD patients is intermediate between that of healthy controls and that predicted by the conservative slowing assumption. Therefore, whatever causes the repetition effect is a strong candidate for explaining at least part of the HD switch deficit. This hypothesis is the more compelling as this interaction effect correlated highly with an index of movement disorder (itself a predictor of striatal pathology; Campodonico et al., 1998).

Central to our reasoning has been the assumption that the normal interaction between switch cost and response repetition is due to inhibition of any ongoing response when a task changes (Rogers & Monsell, 1995). However, alternative hypotheses for this effect have been suggested, including ''associative'' (Rogers & Monsell, 1995) and ''change signal'' (Thomas & Allport, 2000) accounts. The ''associative'' hypothesis suggests that the response most recently produced in the context of a particular task becomes associated with that task, and this ''binding'' has to be overcome when the task changes (cf. Allport & Wylie, 1999). This hypothesis would attribute the greater repetition effect in HD patients (elevated RT on the switch trial for repeated responses) to their greater difficulty in overcoming the binding of task-context to specific response. The ''change signal'' hypothesis, by contrast, maintains that detecting any change between trial $n - 1$ and trial n biases the subject towards performing a different response, and the presentation of a different task cue (as happens with a switch) is a salient change. On this account, HD patients show a greater repetition effect because they are *more* susceptible to such a bias (possibly because of weaker endogenous control of task set); hence, they have difficulty on switch trials that require a repeated response. One reason for preferring the response inhibition account is evidence from a different behavioral test conducted in the same group of HD patients as Experiment 2 (Aron, Barker, Sahakian and Robbins, unpublished observations), which we now summarize briefly.

Response Repetition and Stop-Signal Inhibition

In our version of Logan's (1994) stop-signal paradigm, subjects make a speeded left/right response on most trials, depending on the direction in which an arrow stimulus pointed, but tried to withhold their response if they heard a tone (stop trials). The majority of trials were go trials (no stop signal), to encourage rapid response initiation. The interval between arrow and stop-signal was manipulated dynamically to estimate stop-signal reaction time (SSRT)—an index of the efficiency of the process of inhibiting an imminent response. Although HD patients did *not* have significantly different SSRTs from controls (Aron et al., unpublished observations), they *did* differ in their speed of responding on a go trial as a function of whether the previous trial was a stop trial on which the subject had failed to suppress a response in time (''signal-respond'' trials in Logan 1994). In such sequences, go RT was elevated on response repetitions relative to response alternations for HD patients, but not for controls, and the interaction was reliable (this interaction was not, however, reliable following ''signal inhibit'' trials—possibly reflecting the fact that the influence of successful inhibition on subsequent processing would be less than unsuccessful inhibition owing to the differential timecourse). This effect of repeating a response to which inhibition has been applied (albeit unsuccessfully) is much like the one hypothesized for our task-switching data above. Figure 4 shows that for 17 HD patients, the repetition effect from the stop-signal experiment (repSS) correlated highly with the repetition effect from the task-switching experiment (repTS) at long preparation interval ($r = .64, p < .01$). This striking correlation between the two independent effects is suggestive of a related mechanism. Moreover, as we know that response inhibition is involved in the stop-signal paradigm, the repetition effect in task switching is better explained by a

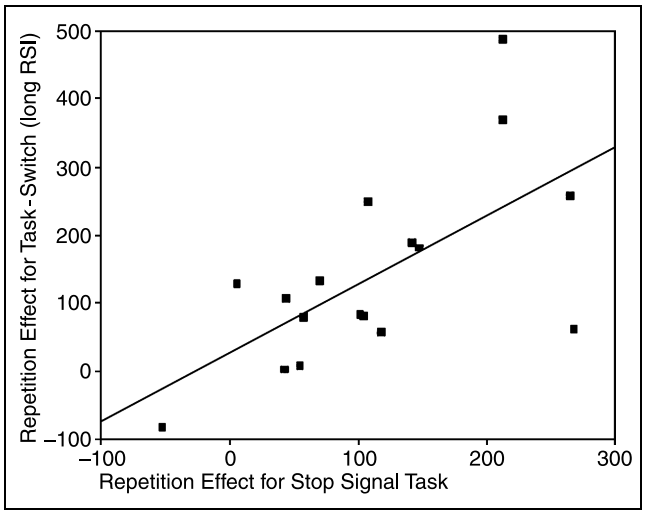

Figure 4. Evidence for excessive response inhibition in HD patients. The repetition effect for task switching (at long preparation interval) correlates with the repetition effect for the stop-signal paradigm.

response inhibition hypothesis rather than by ''associative'' or ''change signal'' accounts.

In summary, we speculate that the switching deficit for HD patients in Experiment 2 is due to ''excessive application of response inhibition or excessive persistence of response inhibition'' applied at a task switch. It is possible that the source of this inhibition normally arises from a prefrontal input to the subthalamic nucleus (STN), which in turn inhibits thalamocortical motor program generators (MPGs). In HD, striatal degeneration could lead to changes in the direct pathway from the striatum to the globus pallidus pars interna (Albin, Reiner, Anderson, Penney, & Young, 1990), which could lead to inappropriate increases in this inhibition, leading, in turn, to a switching deficit when responses must be repeated.

Cross-Talk Interference

While excessive response-related inhibition may therefore contribute to the switch deficit in HD, it cannot account for all of it. In Experiment 1, the HD subjects showed an elevated switch cost relative to controls, but responses were never repeated on switch trials (as these always involved a different set of spoken responses). Therefore, there must be an additional deficit in some other component of processing in order to account fully for the HD switch deficit. Rogers et al. (1998) suggested that greater switch costs for patient groups may be due to the fact that stimuli tend to evoke their associated task sets. They further postulated that a control mechanism is needed to intervene in such conditions of interference to ensure the correct task is selected, and when that intervening mechanism is damaged, it takes longer for the competition between task sets to be resolved. Unlike Experiment 1, where we found clear evidence for increased cross-talk interference for HD subjects, we did not find that in Experiment 2. This was possibly because subjects in the second experiment alone could use foreknowledge of the task to predict the spatial location of the relevant attribute (word task predicts inner region of the next stimulus locus, arrow task predicts outer region; whereas in the first experiment the spatial order of the relevant and irrelevant characters was random). There is evidence that facilitating attentional selection of the relevant attribute reduces strength of the endogenous control input needed to select competing S–R mappings when switching tasks (Yeung & Monsell, submitted). Regardless of the source of this discrepancy, in neither experiment was there a robust interaction between cross-talk interference and switching. Therefore, it is unlikely the switching deficit for HD patients was due to inadequate endogenous suppression of either inappropriate task-set or individual S–R associations, nor was there evidence of inadequate suppression of processing on the preswitch trial.

However, in Experiment 1, HD patients had significantly greater switch costs on cross-talk blocks, where they encountered numerous bivalent stimuli, than in the no-cross-talk blocks, where there were none, and this effect of block interacted with switching so that switch costs were greater for cross-talk blocks than no-cross-talk blocks relative to controls. However, this increase in switching difficulty was similar for univalent and bivalent trials in cross-talk blocks (it did not interact with switching ''within'' block). Moreover, HD patients had a small switching deficit in the no-cross-talk blocks themselves. Therefore, HD patients had a switch deficit even when they had to switch predictably on univalent trials, with adequate preparation interval, and without the possibility of response repetitions. This pattern contrasts with that for both PD patients (Cools et al., 2001) and frontal patients (Rogers et al., 1998), for whom the switching deficit was confined to ''cross-talk'' blocks alone. Below, we propose a model to account for these findings.

A number of authors have documented significant switch costs in control subjects performing predictable task switching with univalent stimuli (Ruthruff et al., 2001; Rogers & Monsell, 1995). Such switch costs may reflect the time required to activate the relevant S–R codes relative to the situation where they are already fully activated (Mayr, 2001). Figure 5 illustrates a simple model relating this to the findings of Experiment 1. On any one trial, the subject responds to the stimulus with a vocal response. Switching is completely regular (AABBAA) and is cued beforehand with ''digit'' or ''letter.'' We suppose that all potential response sets are in competition with each other via lateral inhibition (for which the striatum is a good candidate, see Graybiel & Kimura, 1995; Groves, 1983), and that motor output is specified by a winner-takes-all mechanism. We further suppose that the subject's expectancy (prompted by the

cue) consists in a top-down bias on a subset of response channels (i.e., the ''response set'' for digits). Upon arrival of the stimulus, the activation of the ''digit'' response set is higher than for the ''letter'' response set and a particular digit response wins. However, upon a switch, it requires time for the alternative ''response set'' to be suitably activated by the top-down effect. Moreover, when there is the possibility of interference from an irrelevant stimulus activating a member of the alternative response set (i.e., in cross-talk blocks), this can be counteracted by applying stronger bias to the selection of response set (cf. Yeung & Monsell, submitted). Therefore, in HD, the source of the switch deficit could plausibly be due to (a) a reduced input from the frontal cortex to the striatum which is less effective in preparing the new ''response set,'' or (b) an impairment in the proposed lateral inhibition-based striatal mechanism. We are currently investigating these possibilities by using fMRI to identify the relation between striatal activation change in HD patients and switching performance.

In summary, we have confirmed that early-stage HD constitutes a dysexecutive syndrome with respect to task switching (Sprengelmeyer et al., 1995) and shown that it has a different functional profile from that seen in either PD or frontal lobe trauma. The switch deficit of the HD patients did not appear to relate to deficits in endogenous or residual switching processes, or to inhibitory mechanisms modulating S–R links or entire task sets; instead, it was consistent with an impairment in a ''response-setting'' process, which we have argued is implemented by a fronto-striatal interaction, as well as an impairment in ''inhibition of the just-performed response'' prior to a switch. This form of inhibition does not obviously relate to other forms previously studied in HD such as inhibition of reflexive saccades (Lasker et al., 1987), prepulse inhibition (Swerdlow et al., 1995), or S–R compatibility (Georgiou et al., 1995); however, it does appear to relate to nogo inhibition, or at least the way in which nogo inhibition affects reactions on subsequent go trials—an interesting relation between two independent effects which clearly requires further research. Finally, we have suggested how deficits in both these components are compatible with striatal pathology. These results have significance for understanding how executive functions are implemented neurally, as well as suggesting a more concrete link between the control of cognitive processes and action. Apparent breakdown of ''high-level'' cognition as measured by RT methodology in frontal and basal ganglia patients may well owe more to specifically response-related processes than has hitherto been recognized, a factor which may, in turn, accelerate our specification of executive control.

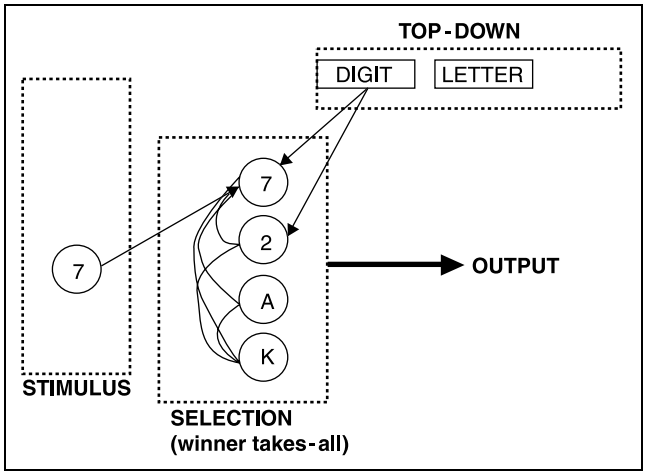

Figure 5. Schematic model illustrating how response set may be implemented by lateral inhibition in the striatum. All response nodes in the selection system mutually inhibit each other via lateral connections. In advance of the stimulus, the cue (digit or letter) activates a subset of response nodes (the ''response set''). Over time, the activation of these nodes exceeds that of the alternative nodes. Subsequently, a stimulus gives an advantage to just one of the response nodes in the ''response set'' and when its activation reaches some threshold there is a conversion to motor output (see text for further details).

METHODS

Experiment 1

Participants

Nineteen patients with clinically symptomatic and genetically confirmed HD and 19 control volunteers participated (see Table 1). Fourteen patients were unmedicated, 1 was taking antidopaminergic medication, 2 were taking an SSRI, and 2 were taking a tricyclic antidepressant. Patient and control groups did not differ significantly in terms of age [$t(36) = 0.64$], predicted verbal IQ [$t(36) = 0.75$], or Beck Depression Inventory (BDI) score [$t(35) = 0.5$].

Background Neuropsychology Tests

(a) Verbal fluency: Participants generated orally as many words as possible beginning with the letters ''F,'' ''A,'' and ''S'' for 60 sec each (Benton, 1968) (excluding proper nouns and variants of the same root word).
(b) Symbol Digit Modalities Test (SDMT): This test of psychomotor speed gave participants 90 sec to fill in boxes with the digit that corresponded to the symbol above it, according to a key alongside (Smith, 1968).
(c) Stroop Test: This comprised three subtests, namely, naming colors (red, green, blue), reading color words printed in black, and an interference condition where participants named the color of ink used to print a conflicting color word (e.g., the word red printed in green ink). The relevant measure was the number of correct responses within a 45-sec period (Stroop, 1935).

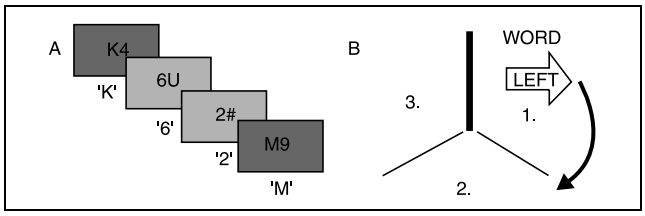

Figure 6. The tasks. (A) Experiment 1: The figure shows a sample of successive stimulus pairs and correct responses in a cross-talk block. The subject has to respond to the letter stimulus in the first trial, then to the numbers in the second and third trials and back to the letter in the fourth trial. A cue card, placed near the computer screen, reminds subjects that they should name the letter stimulus when the box on the computer screen is red (dark) and the number when the box is green (light). Color of cue was counterbalanced across subjects. (B) Experiment 2: The numbers denote run position after switch. Position of switch is denoted by the thick bar (which changes between blocks).

(d) Pattern and Spatial Recognition Memory: These two tasks evaluated recognition memory for abstract patterns and spatial locations separately (see Sahakian et al., 1988).

Task Switching

On each trial two characters were presented side-by-side in the center of a 12.5-cm-wide × 9.2-cm-high box, which was positioned in the middle of the computer screen (see Figure 6A). The characters were letters from the set {G, K, M, P, R, A, E, U}; digits from the set {2, 3, 4, 5, 6, 7, 8, 9}; or neutral (nonalphanumeric) characters {?, *, %, #}. Five pseudorandom strings of stimuli pairs were generated and assigned in a counterbalanced fashion within the two groups. No character appeared in adjacent trials and the relevant character (letter or number depending on currently appropriate task) was presented randomly in the left- and right-side locations. In the ''no-cross-talk'' blocks, the irrelevant character was always drawn from the set of neutral characters. In the ''cross-talk'' blocks, the irrelevant character was drawn from the neutral set on one-third of the trials. However, on the other two-thirds of trials, the character pair contained both a letter and a digit (see Figure 6A).

Subjects sat approximately 60 cm from the screen of a desktop computer. Each character pair remained on the screen until the subject responded by naming one of the characters. There then followed an RSI of 1000 msec before the next character was presented. Responses were collected with a purpose-built voice key. Between blocks, the word ''Ready'' was displayed until the experimenter started the next block. The first character pair appeared 2000 msec later. At the end of each block, average RT and number of errors were given to the subject as feedback. The session consisted in five rounds: (a) introductory training, (b) practice condition A, (c) test condition A, (d) practice condition B, and (e) test condition B. Introductory training consisted of four blocks of 24 trials, and stimulus pairs were always presented within a white box. Introductory Blocks 1 and 3 used letter and neutral pairs, while Blocks 2 and 4 used number and neutral pairs. Practice consisted of two successive blocks of 40 trials each in which task alternated every second trial (and was cued by red and green colors) while each trial consisted of a letter or number and neutral stimulus. Test conditions consisted of four blocks of 40 trials each. Conditions A and B were either cross-talk or no-cross-talk and the order of presentation was counterbalanced across the subjects in each group.

Data were analyzed from the test rounds only. The outcome of the trial (correct, error, or discarded trial) was recorded by the experimenter during testing and inserted into the computerized data file subsequently. The following trials were excluded from the analysis: the first four trials in each block, discarded trials, and the three trials following an error or discarded trial. Trials were discarded when the voice-switch was inappropriately triggered or RT was <300 or >3000 msec. Median correct RTs for valid trials, as well as percentage errors, were calculated for each subject. Corrupted data from one patient reduced the sample size of patients to 18. A single control subject was randomly selected and excluded from further analysis in order to balance group sizes.

Experiment 2

Participants

Seventeen different patients with early-stage clinically symptomatic and genetically confirmed HD and 17 control volunteers participated (see Table 3). There were no significant differences (for $\alpha = .05$) between groups in terms of age [$t(32) = 0.55$, *ns*] and predicted verbal IQ [$t(29) = 0.67$, $p = .093$]. Eleven of the patients were taking one or more forms of medication: 5 were taking antidopaminergic medication, 7 taking an SSRI, 2 were taking antiepileptics, and 2 were taking anxiolytics.

Tasks

A computer running ERTS (Berisoft, Germany) displayed a framework of three lines radiating 10 cm from the center at equal angles to form an ''inverted-Y.'' Each stimulus was displayed in one of the three sectors about 25 mm from the center (see Figure 6B). The position of the stimulus rotated clockwise from one trial to the next. Immediately following the previous response, a task cue word—''arrow'' or ''word''—was displayed about 14 mm above the position in which the next stimulus was then displayed following an RSI of 1500 or 100 msec, varied between blocks (as described below). The cue word, and hence the task, changed every three trials. The position associated with a task switch in that block was additionally indicated by the corresponding limb of the inverted-Y being a thicker bar. The position

of the switch trial was counterbalanced for each participant (between blocks) so that the direction of eye movements between trials would not be confounded with task or position-in-run. Each stimulus remained on the screen until the subject pressed ''a.'' If the participant made an incorrect response, a beep of 200 Hz sounded for 200 msec and the RSI was extended by 2000 msec. ''Left'' or ''Right'' responses were made with the index and middle fingers of the right hand on a keyboard interfaced so that RT was measured to 1 msec precision. For the word task, stimuli were randomly composed of a word (''left'' or ''right'') inside a shape (left arrow, right arrow, or rectangle). For the arrow task, stimuli were randomly composed of either a left or right arrow shape surrounding a letter string (LEFT, RIGHT, or XXX), allowing for three congruency conditions. Each block contained 36 experimental trials, one for each combination of task (Word, Arrow), run position (1, 2, or 3; see Figure 6B), response (left, right), and congruency (incongruent, neutral, or congruent). In addition, there were one, two, or three warm-up trials at the beginning of each block. Subjects were encouraged to minimize their RT while avoiding errors. After each block, the computer displayed a feedback graph, with successive blocks on the *x*-axis. Mean RT on the blocks so far completed was shown as diamonds linked by a line, with the error rate shown as a percentage above each point. An instruction screen was then displayed for the next block indicating the identity of the first task (e.g., ''Word''), and the RSI (short or long), and reminding the subject to respond as quickly and accurately as possible. Subjects were initially practiced in four single-task blocks, two for the word task alternating with two for the arrow task, each preceded by an instruction screen explaining the relevant response mappings for that task. In the practice blocks cues and stimuli were displayed in the successive positions indicated by the inverted-Y framework, but without the thick line which later demarcated the switch position. The RSI was 1000 msec. If the subject made an error, a beep was sounded and the RSI was extended by 2000 msec. There followed a demonstration of the switching concept, followed by one block of practice switching tasks for the long (1500 msec) and then the short (100 msec) RSI. The eight blocks of experiment proper consisted of alternating blocks with long and short RSIs, starting with the long. The thickened limb of the inverted-Y was initially upright, and moved one position clockwise after each block.

Exploratory data analysis indicated that one subject in the control group had extraordinarily long RTs. This subject was excluded, along with a patient who did not complete the test. Mean correct RTs and error rates were computed for each cell (Task × Run position × RSI × Congruence) excluding practice and warm-up trials, trials following an error on either of the preceding two trials, RTs smaller than 300 msec or greater than 3000 msec. Where contrasts between ''switch'' and ''nonswitch'' trials are reported, the latter is the average performance on the second and third trials of a run.

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