Early Huntington’s Disease: Impulse Control Deficits but Correct Judgment Regarding Risky Situations

Victor Galvez, Juan Fernandez-Ruiz, Leo Bayliss, Adriana Ochoa-Morales, Carlos R. Hernandez-Castillo, Rosalinda Díaz and Aurelio Campos-Romo

Abstract

Background: Huntington’s disease (HD) patients show alterations in decision making tasks. However, it is still uncertain if these deficits are due to poor judgment regarding risky situations, or to impulse control deficits.

Objective: To elucidate whether decision-making in patients is related to genuine risk behavior or to impulse control deficits.

Methods: To test between these two alternative possibilities, we evaluated the performance of 19 prodromal HD patients and 19 matched healthy controls in the Cambridge Gambling Task (CGT). This task assesses decision-making while dissociating between genuine risk-taking behaviors (ascending condition) from impulsive behavior (descending condition).

Results: The results showed that patients and controls had the same performance during all trials in the ascending condition, reflecting a correct judgment regarding risky situations; however, during the descending condition, patients responded before the controls in all trials, making a significantly larger number of higher bets. Unlike the control group, they did not wait for more optimal subsequent options.

Conclusion: These results suggest impulse control deficits in HD gene carriers, but unimpaired risk-taking judgment.

Keyword: Huntington Disease, decision making, judgment, impulse control, risk-taking

INTRODUCTION

Making decisions in everyday life involves planning, assessing risks and controlling impulses. Decision making processes are carried out by a brain network that integrates these variables to obtain profits and desired benefits [1, 2]. Huntington Disease
(HD) affects a number of brain regions that participate in the decision making process, like caudate nucleus, putamen and globus pallidus [3, 4]. However, decision making findings in HD patients are heterogeneous. An initial study using the Cambridge Gambling Task (CGT) suggested that there are no decision making deficits in HD patients, despite finding impaired performance in a visuospatial task [5]. Later studies, however, proposed that HD patients engaged in risk taking behavior even at early stages of the disease. For example, in the Iowa Gambling Task (IGT), HD patients have problems maintaining a pattern of advantageous choices across the task. Their IGT scores correlate positively with measures of learning, memory and conceptualization, proving that poor performance could be more related to these cognitive impairments rather than a genuine propensity for risky behavior [6]. Moreover, it has also been demonstrated that HD patients’ poor performance on this task could be linked to increased recklessness and impulsivity [7].

Therefore, it is not yet clear whether early HD patients have congruent judgment deficits in risky situations, or if the behavioral alterations are consequence of impairments in planning, working memory, insensitivity to high losses or impulsivity [8]. Here we specifically tested if inhibitory control deficits could help explain HD impairment in decision making. To test this hypothesis, we assessed the performance of early HD patients in the CGT and analyzed the ascending and descending bet conditions independently of each other. This distinction is important because performance differences in these conditions have different conceptual interpretations. Performance in the ascending condition is related with genuine risk behavior in the sense that to place higher riskier bets, implying bigger risks to lose their points, participants would have to wait longer. Unlike the ascending condition, in the descending condition participants are free to bet high amounts at the beginning of the trial, regardless of the winning odds, therefore they have to be able to inhibit their responses in order to wait for better conditions [9]. This analysis in the CGT allows dissociating between genuine risk behaviors from impulsivity deficits, as has been shown in opiate and amphetamine abusers, patients with prefrontal cortex damaged and healthy population [9–11]. The CGT also has low working memory and learning demands unlike others task, like IGT, where the low performance is biased by alterations from these cognitive resources and not as consequence of genuine impairment to making decision [3].

MATERIALS AND METHOD

Participants

A total of 38 participants were recruited for this study; 19 HD gene carriers with null (5 patients) or low disease clinical manifestations (14 patients), defined as Stage I and II according to the scores obtained in the total functional capacity scale (TFC) from the Unified Huntington’s Disease Rating Scale (UHDRS); seven patients were pharmacologically treated (4 = haloperidol, 1 = valproate + amitriptyline, 1 = olanzapine + metformin, 1 = sertraline + clonazepam) and 19, age, education and sex matched controls, that reported no history of neurological, psychiatric symptoms or to be under any pharmacological treatment. General characteristics of the groups are given in Table 1. All the participants gave their signed informed consent after the purpose of the study was explained. The study was performed according to the Declaration of Helsinki [12] and approved by health and ethics committees from Instituto Nacional de Neurología y Neurocirugía “MVS” and the Universidad Nacional Autónoma de México.

Cambridge gambling task

All participants were evaluated with the CGT from the Cambridge Neuropsychological Test Automated Battery (CANTAB) software version Eclipse [13]. On each trial, participants were presented with a row of ten boxes across the top of the screen, some of which were red and some of which were blue. At the bottom of the screen were rectangles containing the words ‘Red’ and ‘Blue’. Participants had to guess whether

<table>
<thead>
<tr>
<th>Table 1</th>
<th>General demographic information of the participants</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
</tr>
<tr>
<td>Male/Female ratio</td>
<td>8:11</td>
</tr>
<tr>
<td>Age (years)</td>
<td>45 ± 13 (26–67)</td>
</tr>
<tr>
<td>Education (years)</td>
<td>15 ± 3 (7–21)</td>
</tr>
<tr>
<td>CAG repeat length</td>
<td>–</td>
</tr>
<tr>
<td>Duration of symptoms (years)</td>
<td>–</td>
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<tr>
<td>UHDRS motor score</td>
<td>–</td>
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<tr>
<td>TFC</td>
<td>–</td>
</tr>
<tr>
<td>MoCA</td>
<td>27.5 ± 1.9 (21–30)</td>
</tr>
<tr>
<td>CES-D</td>
<td>8.6 ± 5.3 (0–19)</td>
</tr>
</tbody>
</table>

HD: Huntington disease group; UHDRS: Unified Huntington’s Disease Rating Scale; TFC: Total Functional Capacity score; MoCA: Montreal Cognitive Assessment; CES-D: Center for Epidemiologic Studies Depression Scale; ±, standard deviation.
Fig. 1. Diagram explaining the Cambridge Gambling Task.

A yellow token was hidden in a red box or a blue box. In the gambling stages participants started with a number of points. The points were displayed in either rising or decreasing order in a second box on the screen. They could select a portion of these points to gamble depending on the confidence of their judgement. A stake box on the screen displayed the current amount of the bet. The participants had to try to accumulate as many points as possible. The distribution ratio of the two colors was varied on different trials: 5:5, 6:4, 7:3, 8:2 and 9:1 while the yellow token location was pre-specified and pseudo-randomized. After they indicated their decision by touching a response panel marked as ‘Red’ or ‘Blue’, a bet was made. Patients were shown every 5 s consecutive bet values which varied from 5, 25, 50, 75 or 95% of the running total of points held by the subject. Then either a yellow token accompanied by a ‘You win!’ message and short raising musical scale, or a ‘You lose!’ message and a low tone were shown depending on the bet outcome.

Correct choices increased the participant’s total points, while incorrect choices decreased them for the next trial. Subjects were given a fixed number of points at the start of each block, and they tried to maximize their points during the nine consecutive block trials. After an introductory practice session, two sets of four blocks were completed. On the first set, bet values were offered in ascending order, starting at 5% of current total (ascending condition); in the second set, they were offered in descending order, starting at 95% (descending condition) (Fig. 1).

**Statistical analysis**

Three variables were analyzed from the CGT. The first variable was the most likely outcome, which consisted of selecting the color of the majority of the boxes in each trial; the second variable was the choice response time for trials when the most probable outcome was selected; and the third variable was the bet size, which was the percentage of the bet, out of their total points, in each trial. The mean values of these three variables were obtained across blocks at each ratio of colored boxes (6:4, 7:3, 8:2 and 9:1), and for the two conditions (ascending and descending). Then a Linear mixed model was performed to determine differences in the rate of change of each of these variables between groups in the ratios and both conditions, taking into account the results even if the participants did not hit the color where the yellow token finally appeared. This model is adequate to analyze repeated measures obtained from each individual, since random intercepts and random slopes can be assumed in the analysis [14]. Finally, it was carried out a box plot to reveal if the statistical differences come from a few individuals or is apparent in a significant proportion of the HD patients.
RESULTS

Most likely outcome

HD patients and the control group chose the most probable outcome in 86.4% and 87.9% of trials, respectively. The analysis showed no group effect \([F(1, 106.6) = 0.162, p = 0.688]\), nor a group by ratio interaction \([F(1, 112) = 0.074, p = 0.787]\) (Fig. 2A).

Choice response time

The reaction time to make a decision between the two colors was 3002 ± 1666 ms for the control group, and 3742 ± 2079 ms for the HD group. The analysis showed that there were no group differences \([F(1, 44.68) = 1.54, p = 0.220]\) nor a significant group by ratio interaction \([F(1, 112) = 0.057, p = 0.813]\) (Fig. 2B).

Percentage of bet size

The statistical analysis did not show a group effect \([F(1, 101) = 0.848, p = 0.359]\). However, there was a significant group by condition interaction \([F(1, 260.1) = 13.6, p < 0.0002, d = −0.68]\), revealing that the HD group selected their bets earlier than the control group only during the descending condition (Fig. 2C). That is, only during the descending condition, a high proportion of HD patients did not wait longer in the trial to place their bets as the controls did (Fig. 2D).

The significant difference between the HD and the control group in the CGT performance suggests that patients placed similar bets to those of the controls during the ascending condition. However, the results also suggest that the HD patients had an impaired performance during the descending condition, selecting larger bets than controls during all the trials regardless of the odds.

DISCUSSION

Here we tested if impulse control deficits played a role in the decision-making outcome in prodromal HD patients performing a gambling task. Our results in early HD patients clearly showed a congruent judgment regarding their odds of winning, as can be appreciated by their behavior in the ascending bet condition. However, they also show that HD patients couldn’t wait for better betting options when highest
that they don’t show a genuine risk behavior, as has been suggested by previous reports based on this task [9, 10].

Unlike other paradigms of decision-making, the use of CGT allowed clarification regarding how HD patients make decisions, dissociating aspects between genuine risky behavior and impulsivity while minimizing the presence of biases unrelated to the decision-making process that affect the performance of the task. For example, participants do not have the need to generate long-term strategies, so, decisions were made solely by the probabilities associated with winning trial by trial according to the box ratios; thus, the attentional, learning and working memory requirements were less strongly linked to the optimal performance during the whole task. This lead to higher sensitivity in the identification of alterations pertaining to the decision-making process, versus other tasks. For instance, it has been suggested that HD patients’ poor performance in IGT, is linked to deficits in working memory, learning and concept formation rather than a genuine propensity for risk taking behavior [6, 7].

Based on our results and previous reports, it is possible to speculate that the correct performance during the ascending bet condition could be associated with the relative integrity of the ventromedial prefrontal cortex in early HD. This area, whose activity has been linked with the successful performance in CGT [17], is a component of the Stimulus Encoding System, necessary for optimal evaluation during the decision process according to the neuroanatomical model of decision-making [3]. Furthermore, the ventral striatum, which is part of the orbitofrontal cortex loop [18], and part of the same Stimulus Encoding System [1, 2], is typically affected only in the later stages of the disease [19].

One limitation of this study is the lack of a second instrument assessing the patients’ impulsivity, as has been reported in other studies [20]. Also, although the working memory requirements are lower in the CGT than other tasks as mentioned earlier, we cannot completely rule out some influence on the subjects’ performance. Further studies should look into this possible relation. We also suggest that future studies related to decision making would benefit from measurements of autonomous system responses to elucidate whether HD patients show or not insensitivity to the losses.

CONCLUSION

Our results suggest that early Huntington’s disease patients have an impaired impulse control;
however, the correct judgment about risky situations is preserved. Within HD gene carriers, these results contribute to clarify important personality changes during early stages of the disease, which could help in the development of effective rehabilitation strategies and pharmacological treatments in relation to the impulsivity.

ACKNOWLEDGMENTS

Special thanks to all the patients and their families for the cooperation provided. This study was supported in part by: CONACYT grant No. 220871 and PAPIIT-UNAM grant No. IN214716 to JFR and CONACYT Ph.D. scholarship No. 369794 to VG.

FUNDING AGENCIES

This study was supported in part by: CONACYT grant No. 220871 and PAPIIT-UNAM grant No. IN214716 to JFR and CONACYT Ph.D. scholarship No. 369794 to VG.

CONFLICT OF INTEREST

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REFERENCES