Dual task performance may be a better measure of cognitive processing in Huntington's disease than traditional attention tests

Eleftheria Vaportzis[a], Nellie Georgiou-Karistianis[a], Andrew Churchyard[a,b], Julie C. Stout[a,*]

[a]School of Psychological Sciences, Faculty of Medicine, Nursing and Health Sciences, Monash University, Clayton, Victoria 3800, Australia.

[b]Department of Neurology, Monash Medical Centre, Clayton, Victoria 3800, Australia.

Address correspondence to Julie C. Stout, School of Psychological Sciences, Monash University, Wellington Road, Clayton, Victoria 3800, Australia.

E-mail: julie.stout@monash.edu

Note. Eleftheria Vaportzis is now a postdoctoral research associate in the School of Life Sciences, Heriot-Watt University, Edinburgh, Scotland, UK.

Keywords: Attention allocation; Divided attention; Dual task; Huntington's disease; Visual search.

Abstract

BACKGROUND:

Past research has found cancellation tasks to be reliable markers of cognitive decline in Huntington's disease (HD).

OBJECTIVE:

The aim of this study was to extend previous findings by adopting the use of a dual task paradigm that paired cancellation and auditory tasks.

METHODS:

We compared performance in 14 early stage HD participants and 14 healthy controls. HD participants were further divided into groups with and without cognitive impairment.

RESULTS:

Results suggested that HD participants were not slower or less accurate compared with controls; however, HD participants showed greater dual task interference in terms of speed. In addition, HD participants with cognitive impairment were slower and less accurate than HD participants with no cognitive impairment, and showed greater dual task interference in terms of speed and accuracy.

CONCLUSIONS:

Our findings suggest that dual task measures may be a better measure of cognitive processing in HD compared with more traditional measures.

INTRODUCTION

Dual tasking is an essential and routine element of everyday life that can be compromised in individuals with neurodegenerative disorders. Dual task performance has been studied extensively in various populations, such as Parkinson's disease and healthy ageing (1-3); however, dual task research in Huntington's disease (HD) has been sparse. The limited studies that have been conducted have shown that HD patients performed dual tasks slower and less accurately than controls on tasks administered within dual task contexts (4), and HD patients' accuracy decreased with task difficulty compared with controls (5, 6). Performing concurrent tasks has often been a source of complaint from patients and their family members, establishing the relevance of dual processing research in HD. This and previous studies (5, 6) attempted to determine what combinations of dual tasks may be better or worse off in HD patients. Understanding better the challenges that HD patients face when dual tasking, will assist us in developing strategies to manage symptoms.

The profile of cognitive performance in HD shows progressive decline of attention, executive function, working memory and processing speed. Longitudinal studies have reported deterioration in early HD from baseline at 12, 24 and/or 48 month follow ups using tasks such as the Symbol Digit Modality Test (SDMT), Stroop test, circle tracing, months forward and backward, and Trail Making Test (TMT) A; performance on some tests was very poor even at baseline levels (e.g., TMT B) (7-11). Interestingly, some evidence suggests that the most sensitive markers of cognitive change were low rather than high cognitive demand tasks (11, 12). For example, on the traditional Stroop test (13) simple word reading and colour naming were more sensitive markers of cognitive change than the more challenging interference tasks of colour naming of incongruous colour words. Reciting months of the year was also a sensitive cognitive marker, unlike the more challenging recitation of months in backward order (11). In addition, compared with controls, HD participants showed increased tapping variability on a simple finger tapping task, and increased variability of bimanual vs. unimanual tapping (12). Overall, these results point towards an inverse relationship between cognitive demands and sensitivity to cognitive change in HD.

Past research with various populations has implemented various tasks to examine dual task performance including choice RT (3, 4, 14), digit forward and backward (3), auditory (4, 14), tracing (15), peg placement (16), balance (17) and cancellation (18). Cancellation tasks are of great interest due to a number of reasons. For example, they engage essential mechanisms required for cognitive processing in a person's environment because they depend upon selection of relevant stimuli while ignoring irrelevant stimuli (19). Furthermore, they have been found to be reliable markers of cognitive decline in HD (7).

Bachoud-Lévi et al. (7) conducted a longitudinal study to investigate the progression of cognitive deficits in early HD. They employed one-, two-, and three-digit, *and* figure cancellation tasks to assess attention and executive functions. Participants were presented with a panel of strings and had to cancel one, two, and three digits *or* figures. Overall, compared with controls, HD participants' performance was worse; however, some tasks (e.g., one digit *and* one figure cancellations) were too easy, and others too hard (e.g., three digit *and* three figure cancellations) for the HD participants. As a result of the poor baseline performance on the hard tasks, performance on these tasks did not decline as for the easy tasks in subsequent visits. The results of Bachoud-Lévi et al. (7) suggest that performance depends on disease stage, and cancellation tasks may assess the progression of HD at an early stage. They may also suggest that performance differences in HD may emerge under different levels of task difficulty.

The effect of adding a second task on a cancellation task in HD has not been studied. In an ageing study that investigated dual tasking using cancellation tasks with auditory digit span *and* letter fluency, results suggested that older participants with cognitive deficits had greater dual task interference compared with controls (18). Discriminant function analysis suggested that the dual task measures used were more accurate and better at discriminating older adults with cognitive deficits from healthy controls compared with more traditional neuropsychological measures, which were the same measures performed on their own (i.e., single tasks).

A prominent theory that has attempted to explain dual task interference is the Multiple Resources Theory (20). The Multiple Resources Theory postulates that attention has *multiple separate resource pools* (e.g., a visual resource pool, an auditory resource pool), each of which can be divided among concurrent tasks. According to this theory two tasks that share common resources on these four dichotomous dimensions, are performed less efficiently as divided attention deteriorates (20, 21). Thus, cross-dimensional tasks (e.g., visual-auditory) should lead to more efficient processing than uni-dimensional tasks (e.g., visual-visual).

To extend past research in HD and to test the Multiple Resources Theory, our dual task paradigm employed cancellation and auditory tasks that were performed at two difficulty levels: easy and hard. This combination of tasks is likely to be processed by separate modalities-responses (i.e., visual-manual for the cancellation task, and auditory-vocal for the auditory task), therefore leading to minimal interference. In light of the Multiple Resources Theory, we expected minimal interference between the two tasks in the control group; however, in the HD group, we expected dual task interference. Previous dual task studies in HD have found participants to be slower and less accurate compared with controls (5, 6), therefore, not supporting the Multiple Resources Theory. A similar study with older adults (18) also did not support the Multiple Resources Theory.

We expected all participants to be slower and error rates to be higher with increased task difficulty; differences in performance were expected to be more pronounced in HD participants. Finally, we were interested to investigate whether dual task performance was a sensitive indicator of cognitive impairment in HD. A number of studies suggested that the Montreal Cognitive Assessment (MoCA; 22) is a useful instrument for assessing cognitive performance and providing insight into the cognitive status of HD patients (23-25). Therefore, we expected HD participants with cognitive impairment, as suggested by the MoCA, to be slower and less accurate than HD participants with no cognitive impairment.

METHOD

Participants and measures

Participants were 16 patients in the early stages of HD and 14 healthy controls. Two patients were excluded due to inability to perform some of the tasks. The final sample comprised 14 HD participants and 14 controls. Demographics are presented in Table 1. Controls were recruited via word-of-mouth, online advertisements on the Monash University website, and retirement villages around Melbourne, and were group matched to HD participants by age, sex and education. HD participants were recruited from an existing patient database, and were diagnosed by an experienced neurologist (AC). HD participants were assessed using the Unified Huntington's

Disease Rating Scale (UHDRS; 26). We report the total motor score with greater scores indicating more impaired motor function (highest possible score = 124); and the oculomotor score (ocular pursuit, saccade initiation and velocity) with greater scores indicating more impaired oculomotor function (highest possible score = 24). HD participants also self-reported total functional capacity with greater scores indicating higher functioning (highest possible score = 13).

INSERT TABLE 1 ABOUT HERE

Other measures included the Montreal Cognitive Assessment (MoCA;22), Wechsler Test of Adult Reading [WTAR; (27) and Inventory of Depressive Symptomatology-Self-Report (IDS-SR; 28). The MoCA is a 30-point cognitive test designed to detect cognitive impairment. The suggested cut-off point for mild impairment is 26 (22). All control participants performed over 26 on the MoCA. We used MoCA as a covariate in all analyses. The WTAR is a premorbid estimate of IQ, and is composed of 50 words that have irregular letter to sound translations. The IDS-SR is a 30-item questionnaire that assesses the severity of depression within the past 7 days for all symptom domains within major depression according to the Diagnostic and Statistical Manual-IV (29). Higher scores indicate more severe depressive symptoms (highest possible score = 84). Education level was assessed using the International Standard Classification of Education (ISCED; 30), according to which 0 indicates pre-primary education and 6 second stage tertiary education.

To investigate cognition-related differences within our HD sample, we divided the HD participants into low-MoCA (<26) and high-MoCA (>26) groups (see Table 2 for demographics). The low-MoCA HD group had significantly more impaired motor function as indicated by the UHDRS motor score, and significantly more symptoms of major depression as indicated by the IDS-SR scores.

Monash University Human Research Ethics Committee provided ethical approval for the study (Project number: CF09/3246 – 2009001766), and therefore, this study has been performed in accordance with the Declaration of Helsinki. Participants gave written informed consent, were fluent in English and self-reported that they had normal or corrected-to-normal vision and hearing, and were free of upper limb impairments (e.g., difficulty in pressing keyboard buttons). In addition, controls self-reported that they were free of neurological disease and psychological disorders, and their MoCA scores were within the normal range.

INSERT TABLE 2 ABOUT HERE

Dual task description and procedure

For the dual task procedure, participants performed letter cancellation with auditory tasks, each of which had two difficulty levels: easy and hard. The cancellation task required participants to scan randomly dispersed letters on a sheet of paper and circle the target letter O amongst distractor letters. In the easy condition, distractors were other letters of the alphabet; in the hard condition, distractors were the letter Q, which is visually similar to the target letter O (Fig.1). The cancellation task comprised one practice, and four trial forms, each printed on a separate A4 white page. All forms had 70 distractor letters; target letters ranged between 15 and 17. All letters were printed in Arial 20 uppercase font and were arranged randomly. We recorded completion time in seconds and errors of omission expressed as a percentage. Completion time was the time taken from the moment the researcher said ‘Start’ and started a stopwatch until participants ticked off a box at the bottom right corner on each form, which prompted the researcher to stop the stopwatch. Thus, completion time reflects participants’ speed. Participants had as much time as they required finding all target letters. Errors of omission were the number of target letters not circled for each form separately. Bachoud-Lévi et al. (7) found that cancelling out one digit or figure was too easy for HD participants. Despite that, we still decided to use this paradigm as combining two tasks is more challenging for participants; we prioritised having single tasks that were not very challenging on their own to be suitable combination with another task. Previous studies found that although up to 35% of participants performed without error in single tasks, in harder dual task conditions no participants performed perfectly (6).

INSERT FIGURE 1 ABOUT HERE

The auditory task required participants to report the number of high-pitched sounds from a series of intermittent sounds. This task was controlled by a Lenovo ThinkPad® X61 (Morrisville, NC, USA) laptop running E-Prime software (31). The laptop was placed at close proximity to the participants with the screen facing away from them. When participants indicated that they were ready, the researcher started the auditory task by pressing the spacebar on the keyboard. In the easy condition, all sounds were high-pitched (100ms); in the hard condition, sounds were high- and low-pitched (300ms). The interstimulus interval varied between 1000ms and 2000ms. The auditory task comprised one practice and four trials. When the auditory task was performed on its own (i.e., single tasks) it lasted 15 s. In the easy trials, the number of high-pitched sounds ranged between 9 and 11. In the hard trials, the number of sounds (both high- and low pitched) was always 10, and the number of high-pitched sounds (i.e., targets) ranged between 4 and 6. Participants verbally reported the number of high-pitched sounds that they heard at the end of each trial. When the auditory task was performed concurrently with the cancellation task (i.e., dual tasks), its duration depended upon the duration of the cancellation task: the experimenter ended the auditory task when the participants ticked off the box on the cancellation task form. We recorded error rates expressed as a percentage. Error rates were defined as the absolute difference between the reported and actual values of high-pitched sounds.

Following previous studies (32-35), *dual task costs* for *completion time* and *error rates* were computed using the following formula: dual task cost = (single task−dual task)/single task, to calculate the relative ratio of single task to dual task completion time (or error rates), controlling for single task completion time (or error rates). For error rates in the cancellation and auditory tasks, we added a value of one to each data point prior to computing dual task costs due to a large number of participants not committing any errors in the single tasks. Negative dual task costs for completion time indicate that slower performance in the dual tasks compared with the single tasks, whereas for error rates they indicate lower accuracy.

Design

Participants first performed four single tasks: (1) easy cancellation, (2) hard cancellation, (3) easy auditory, and (4) hard auditory. Then, for the dual task conditions, participants performed every possible combination between the cancellation and auditory tasks (1) easy cancellation with easy auditory, (2) easy cancellation with hard auditory, (3) hard cancellation with easy auditory, and (4) hard cancellation with hard auditory. The cancellation with auditory dual task set was one of four sets of tasks that participants performed as part of a larger study. The order of the four sets was counterbalanced across participants; however, the order of the conditions was not counterbalanced for a number of reasons. Firstly, a full permutation with all the different conditions for the four sets of tasks was impractical due to the large number of conditions within each set of tasks, and would have required a much larger sample size. Secondly, since there is a learning component for these tasks it was appropriate for the hard tasks to be preceded by easy tasks. Finally, by presenting the easier tasks and task combinations first, we could maintain some control over the participants' previous task experiences, which could benefit them similarly when they reached the harder levels.

Statistical analyses

Completion time and *error rates* for the cancellation task and *error rates* for the auditory task were calculated. The Schweinle method was used to remove outliers at or over 3.5 standard deviations from the mean. This method multiplies the standard deviation to determine the new upper limit of the score range, and remove scores above that limit. There were no data with values over 3.5 standard deviations from the individual's mean; thus, no data were removed prior to analyses.

For the cancellation task, we computed 2 X 2 X 3 mixed-model ANCOVAs with the between factor, Group (HD, controls), and two within factors, Cancellation task difficulty (easy, hard), and Auditory task difficulty (none, easy, hard) for completion time and error rates separately. For the auditory task, we also computed 2 X 2 X 3 mixed-model ANCOVAs with the between factor, Group (HD, controls), and two within factors, Auditory task difficulty (easy, hard), and Cancellation task difficulty (none, easy, hard) for error rates. We also computed dual task costs in order to quantify participants' ability to perform two concurrent tasks. We used 2 X 2 X 2 mixed-model ANCOVAs with the between factor, Group (HD, controls), and two within factors, Cancellation task difficulty (easy, hard), and Auditory task difficulty (easy, hard) for all dependent variables separately: cancellation task completion time and error rates, and auditory task error rates. Finally, we ran the same analyses with between factor low- and high-MoCA HD participants.

For all analyses, we examined main effects, two- and three-way interactions. Significant interactions were followed up with appropriate post hoc analyses: pairwise comparisons or simple main effects. We report Greenhouse-Geisser corrected degrees of freedom due to violations of the sphericity assumption. A Bonferroni adjustment was applied. Alpha was set at .05.

RESULTS

In the following section, we first present the results between HD participants and controls, followed by performance between low- and high-MoCA HD participants. Within each of these sections, we describe cancellation task performance in terms of completion time and error rates, followed by auditory task performance in terms of error rates.

Dual task performance in HD participants and controls

Using *completion time* in the cancellation task as the dependent variable, a three-way ANCOVA revealed a significant two-way interaction between Cancellation and Auditory tasks, $F(1.84, 46.08) = 3.66$, $p = .037$, $\eta^2 = .13$. Pairwise comparisons revealed that the easy cancellation tasks were performed significantly ($p < .001$)

faster compared with the hard cancellation tasks. In addition, the easy cancellation task was performed significantly (p = .002) faster on its own (no auditory) than when performed with the hard auditory task.

The same model for *dual task costs* for *completion time* showed a significant main effect of Group with HD participants having significantly greater costs compared with controls, $F(1,25) = .414$, $p = .044$, $\eta^2 = .15$. We also found a significant interaction between Cancellation and Auditory tasks, $F(1,25) = 7.00$, $p = .014$, $\eta^2 = .21$. Pairwise comparisons showed significantly ($p < .001$) greater costs when auditory tasks (easy or hard) were performed with easy cancellation tasks compared with hard cancellation tasks. We found no interactions involving Group.

Using *error rates* in the cancellation task as the dependent variable, a three-way ANCOVA revealed a significant interaction between Cancellation and Auditory tasks, $F(1.95,48.86) = 89.66$, $p = .002$, $\eta^2 = .22$. Pairwise comparisons revealed significantly ($p < .01$) more errors in the hard cancellation tasks compared with the easy cancellation tasks. In addition, there were significantly (p = .015) more errors in the hard cancellation task when performed with the easy auditory task than when performed on its own (no auditory). The same model for *dual task costs* for *error rates* in the cancellation tasks showed no significant main effects or interactions.

Using *error rates* in the auditory task as the dependent variable, a three-way ANCOVA revealed a significant main effect of Group with HD participants making significantly more errors than controls, $F(1,25) = 5.64$, $p = .026$, $\eta^2 = .18$. We also found a significant two-way interaction between Auditory and Cancellation tasks, $F(1.67,41.83) = 4.63$, $p = .02$, $\eta^2 = .16$. Pairwise comparisons revealed that there were significantly ($p < .05$) more errors in the dual tasks compared with the single tasks (no cancellation) with one exception: there were no significant (p = .88) differences between the easy and hard auditory tasks when performed with the hard cancellation task. We found no interactions involving Group.

HD participants with low vs. high MoCA scores

Using *completion time* in the cancellation task as the dependent variable, a three-way ANOVA revealed a significant three-way interaction between Group, Cancellation and Auditory tasks, $F(1.57,18.91) = 4.70$, $p = .029$, $\eta^2 = .28$ (Fig.2).Post hoc analysis of the simple main effects revealed that the low-MoCA group was significantly ($p < .05$) slower than the high-MoCA group in the easy and hard cancellation single tasks (i.e., no auditory), and also when the hard cancellation task was performed with the easy auditory task. Both groups were significantly ($p < .05$) slower when performing the hard cancellation tasks compared with the easy cancellation tasks.

INSERT FIGURE 2 ABOUT HERE

The same model for *dual task costs* for *completion time* showed a significant three-way interaction between Group, Cancellation and Auditory tasks, $F(1,12) = 8.25$, $p = .014$, $\eta^2 = .41$ (Fig.3). Post hoc analysis of the simple main effects showed that the high-MoCA group had significantly ($p < .05$) greater costs than the low-MoCA group when the easy cancellation task was performed with the easy auditory task. Overall, both groups showed significantly ($p < .05$) greater costs in the easy cancellation tasks compared with the hard cancellation tasks except when the low-MoCA group performed the easy auditory task with the easy *or* hard cancellation task ($p = .082$).

INSERT FIGURE 3 ABOUT HERE

Using *error rates* in the cancellation task as the dependent variable, a three-way ANOVA revealed a significant two-way interaction between Group and Auditory tasks, $F(1.83,22.03) = 4.15$, $p = .032$, $\eta^2 = .26$ (Fig.4). Pairwise comparisons revealed that the low-MoCA group made significantly ($p < .05$) more errors than the high-MoCA group in the easy auditory tasks compared with the hard auditory tasks and also compared with the single tasks (no auditory). We also found a significant main effect of Cancellation task, $F(1,12) = 22.93$, $p < .001$, $\eta^2 = .66$, with greater error rates in the hard cancellation tasks compared with the easy cancellation tasks. The same model for dual task costs for error rates showed a significant main effect of Group, $F(1,12) = 6.84$, $p = .023$, $\eta^2 = .36$, with the low-MoCA group showing greater dual interference compared with the hard-MoCA group.

INSERT FIGURE 4 ABOUT HERE

Using *error rates* in the auditory task as the dependent variable, a three-way ANOVA revealed a significant main effect of Cancellation, $F(1.74,20.88) = 21.13$, $p < .001$, $\eta^2 = .64$, with fewer errors in the single auditory tasks compared with the dual auditory tasks. We found no significant main effects or interactions for *dual task costs* for *error rates* in the auditory tasks.

DISCUSSION

Our results showed that HD participants were not slower or less accurate compared with controls; however, HD participants were disproportionately compromised in the dual task conditions in terms of speed, as suggested by their greater costs for completion time on the cancellation tasks. In any case, the current findings show some resource sharing between two apparently different tasks, therefore suggesting that the visual and auditory modalities *and* the manual and vocal responses are not entirely separate as the Multiple Resources Theory postulates.

Our findings may be explained, although not conclusively, by the Unitary Resource Theory, which posits that attention is a *single, limited capacity resource* that can be allocated to a single task or divided between different tasks, and can be affected by task difficulty (36). This theory holds that dual task performance deteriorates if one task is difficult and requires a large proportion of this limited attentional resource, because there is not much left to support the other task's performance. When the demand exceeds the amount of attentional capacity, allocation strategies are used to establish on which tasks the attention resource should be allocated. Our results showed that with increased task difficulty performance of both groups deteriorated. In further support of the Unitary Resource Theory, performance of HD participants was disproportionately slower in the dual task conditions compared with the single task conditions of the cancellation task. It is possible that unlike controls, with the addition of the auditory task, HD participants reached a point where attentional resources were not enough to perform the dual tasks as quickly as they performed the single tasks. However, we found HD-related dual task interference in terms of speed, but not error rates. Thus, our study highlights the importance of taking into account speed and accuracy measures, as the relationship between HD and these measures may vary with task difficulty.

Neuroimaging studies have provided some support for the Unitary Resource Theory as they found dual tasks to activate some brain regions (i.e., prefrontal cortex) to a greater extent than the same tasks performed in isolation (37, 38). Therefore, higher cognitive load due to dual task performance generates increased brain activity in specific brain regions. These findings suggest that dual task interference occurs due to a competition for the same processing resources between two tasks, and the prefrontal cortex may be the locus for this competition. Another explanation may be that aberrant interactions between the frontal cortex and the striatum caused a response processing bottleneck that slowed task performance in HD participants. However, this possibility needs to be further explored by a study giving higher priority to one of the tasks and lower priority to the other one.

As the prefrontal cortex has been implicated in both HD and older age, one might expect similar results in HD and older participants. We note that although the Multiple Resources Theory does not make any predictions related to brain mechanisms, it is possible that striatal degeneration in HD may result in compromised dual task performance in HD participants due to signal crosstalk from divergent brain areas and/or erroneous distribution of signals to control processes. Therefore, any differences between HD participants and controls may be due to pathological changes in the HD brains. For example, Rosas et al. (39) reported white matter abnormalities in the corpus callosum in premanifest and early HD, which correlated with performance on distinct cognitive measures (e.g., Stroop test, SDMT). These findings suggest an important role for disrupted inter-hemispheric information transfer in the clinical symptoms of HD upon which dual task processing may rely.

In the past, some dual task studies suggested that attention is not a unitary phenomenon [4,16]. For example, both Sprengelmeyer et al. [4] and Müller et al. [16] used the same visual-auditory dual task paradigm: participants pressed a button to specific stimuli and a different button to discriminative stimuli. Overall, HD participants were slower and less accurate than controls when tasks were administered within dual task contexts. These studies endorsed the notion that attention is a multidimensional system of related, but semi-independent processes. However, the input of the tasks was cross-dimensional (i.e., visual-auditory), and the output uni-dimensional (i.e., motor-motor); therefore, it is difficult to draw conclusions on the Multiple Resources Theory.

Posner and Petersen (40) proposed a distributed network model of attention including a posterior automatic attention system, which involves the posterior parietal cortex, pulvinar nuclei of the thalamus, and superior colliculi. This system is thought to be activated when a person is required to allocate attention to visual space, select a stimulus location and shift attention from one stimulus to another. Studies have reported cortical atrophy in the parietal cortex in HD (41, 42). It is possible that attentional processes, such as shifting attention, are more affected in HD participants with cognitive impairment, causing slowness and more errors in performance on the cancellation tasks.

Contrary to the present study, previous studies that used different combinations of tasks (i.e., circle tracing with serial subtraction, *and* choice reaction time tasks with digit forward and backward tasks) found differences between HD participants and controls in terms of speed and/or accuracy (5, 6). These studies paired motor with verbal tasks, unlike this study that paired motor with auditory tasks. It is possible that verbal tasks are more cognitively demanding for HD participants than auditory tasks when performed concurrently with another task. Despite that, the present study found that HD participants showed some dual task interference compared with controls. Interference was notable in terms of speed on the cancellation task. While group performance was comparable when the tasks where administered alone, it seems that introducing a concurrent auditory task forced the HD participants to perform above their capacity of attentional resources. We note that the cancellation task required visual processing, and oculomotor abnormalities were evident in some participants as suggested by the UHDRS oculomotor score. These abnormalities may have become more pronounced under the dual task conditions.

Movement impairment is the most visible symptom of basal ganglia pathologies in HD. Decline in psychomotor speed is sensitive to striatal dysfunction, and may be one of the earliest indicators of HD onset (43, 44). However, there is converging evidence about the basal ganglia involvement in cognitive domains, such as attention (45), working memory (46), and processing speed (47). HD patients have been found to be consistently impaired in tasks tapping different types of attention (48, 49) and working memory (50), as well as processing speed (43, 44). In addition, greater declines were found on less cognitively demanding tasks; a finding that presumably reflects changes in HD that occur for effortful, speed- and time-based tasks (11).

A conceptual problem when assessing performance in HD has been that measures of psychomotor processing derive from a variety of tasks incorporating both motor and cognitive aspects (e.g., SDMT, TMT). Dual tasks may provide a means to distinguish between motor and cognitive aspects of processing by characterizing changes in cognitive performance under single (e.g., cognitive task) and dual task (e.g., cognitive and motor tasks) conditions. Therefore, dual task research may shed light upon specific cognitive impairments in HD. In addition, it may assist in understanding better the function of the basal ganglia. Dual task interference in people with HD may be explained by disruptions of basal ganglia functions, such as the striatum, which is a major site of neurodegeneration in HD. Models of basal ganglia thalamo-cortical circuitry suggest that the striatum receives topographically organized input from the cerebral cortex (e.g., dorsolateral prefrontal cortex), and through the globus pallidum/substantia nigra and thalamus it influences motor and sensory control *and* cognitive function (51, 52). Dual task research may provide more information about the specific role of the basal ganglia in cognitive and motor functions. For example, a paradigm that requires non-timed verbal responses may permit attentional components to be assessed independently and not confounded by motor impairments, which are prevalent in HD.

In line with our predictions, HD participants with low MoCA scores were slower and less accurate than HD participants with high MoCA scores. In addition, the low-MoCA group experienced greater costs for error rates compared with the high-MoCA group. Previous studies revealed dual task difficulties in HD compared with controls (4, 5). The results of the current study extend our knowledge on the association between dual task performance and cognitive processing in HD, and suggest that the ability to perform two concurrent tasks may be a better measure of cognitive processing in HD than more traditional measures (e.g., Stroop test). This is an important point as it may suggest that there is a window for HD patients that are not cognitively impaired to be able to learn strategies for dual tasking to improve quality of life. Our results also support previous findings that showed that MoCA may offer a great tool for the screening of cognitive impairment in HD (53). The current study did not investigate the clinical validity of the cancellation-auditory dual task; therefore, future studies may consider how dual task measures relate to other more traditional attention measures.

Limitations of this study include the small sample size; therefore, absence of significant interactions may be due to low statistical power. Despite that, some non-significant interactions approached statistical significance, suggesting that the current findings warrant future investigation with a larger sample size that will supply sufficient power. In addition, our conclusions must be considered in light of possible order effects since; for practical reasons, we did not counterbalance single and dual tasks. However, we found that participants' performance worsened in the harder conditions, which were performed later. Thus, counterbalancing would most likely have further strengthened our results.

In summary, although HD participants were not slower or less accurate compared with controls, all participants were slower and less accurate with increased task difficulty. Differences were more pronounced in HD participants in terms of speed only. These results provide partial support to the Unitary Resource Theory. In addition, we found HD participants with cognitive impairment to show greater dual task interference relative to HD participants with no cognitive impairment. We propose that dual task measures may be a better measure of cognitive processing in HD, and may provide information that is not readily available from other neuropsychological measures.

ACKNOWLEDGMENTS

This research was supported by the School of Psychological Sciences, Monash University. We thank our participants and their families for their time and effort.

CONFLICT OF INTEREST

The authors have no conflict of interest to report.

ETHICAL STANDARD

This study has been approved by the appropriate ethics committee, and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

REFERENCES

[1] Fuller RL, Van Winkle EP, Anderson KE, Gruber-Baldini AL, Hill T, Zampieri, C, Weiner WJ, Shulman LM. Dual task performance in Parkinson's disease: A sensitive predictor of impairment and disability. Parkinsonism Relat Disord. 2013; 19: 325-328.

[2] Plotnik, M, Giladi N, Hausdorff JM. Bilateral coordination of gait and Parkinson's disease: The effects of dual tasking. J Neurol Neurosurg Psychiatry. 2009; 80: 347-350.

[3] Vaportzis E, Georgiou-Karistianis N, Stout JC. Dual task performance in normal aging: A comparison of choice reaction time tasks. PLoS One. 2013; 8: e60265.

[4] Müller SV, Jung A, Preinfalk J, Kolbe H, Ridao-Alonso M, Dengle R, Münte TF. Disturbance of "extrinsic alertness" in Huntington’s disease. J Clin Exper Neuropsych. 2002; 24: 517-526.

[5] Vaportzis E, Georgiou-Karistianis N, Churchyard A, Stout JC. Effects of task difficulty during dual task circle tracing in Huntington’s disease. J Neurol. 2015; 262: 268-276.

[6] Vaportzis E, Georgiou-Karistianis N, Churchyard A, Stout JC. Dual task performance in Huntington’s disease: A comparison of choice reaction time tasks. Neuropsychology. (in press).

[7] Bachoud-Lévi AC, Maison P, Bartolomeo P, Boisse MF, Dalla Barba G, Ergis A. M, Baudic S, Degos J-D, Cesaro P, Peschanski M. Retest effects and cognitive decline in longitudinal follow-up of patients with early HD. Neurology. 2001; 56: 1052-1058.

[8] Tabrizi SJ, Scahill RI, Durr A, Roos RAC, Leavitt BR, Jones R, Landwehrmeyer GB, Fox NC, Johnson H, Hicks SL, Kennard C, Craufurd D, Frost C, Langbehn DR, Reilmann R, Stout JC, the TRACK-HD investigators. Biological and clinical changes in premanifest and early stage Huntington’s disease in the TRACK-HD study: The 12-month longitudinal analysis. Lancet Neurol. 2011; 10: 31-42.

[9] Tabrizi SJ, Reilmann R, Roos RAC, Durr A, Leavitt B, Owen G, Jones R, Johnson H, Craufurd D, Hicks SL, Kennard C, Landwehrmeyer L, Stout JC, Borowsky B, Scahill RI, Frost C, Langbehn DR, the TRACK-HD investigators. Lancet Neurol. 2012; 11: 1-12.

[10] Stout JC, Jones R, Labuschagne I, O'Regan AM, Say MJ, Dumas EM, Queller S, Justo D, Dar Santos R, Coleman A, Hart EP, Dürr A, Leavitt BR, Roos RA, Langbehn DR, Tabrizi SJ, Frost C. Evaluation of longitudinal 12 and 24 month cognitive outcomes in premanifest and early Huntington's disease. J Neurol Neurosurg Psychiatry. 2012; 83: 687-694.

[11] Snowden JS, Craufurd D, Griffiths H, Thompson J, Neary D. Longitudinal evaluation of cognitive disorder in Huntington’s disease. JINS. 2001; 7: 33-44.

[12] Thompson JC, Poliakoff E, Sollom AC, Howard E, Craufurd D., Snowden JS. Automaticity and attention in Huntington's disease: When two hands are not better than one. Neuropsychologia. 2010; 48: 171-178.

[13] Stroop JR. Studies of interference in serial verbal reactions. J Exp Psych Health. 1935; 18: 643-662.

[14] Sprengelmeyer R, Lange H, Hömberg V. The pattern of attentional deficits in Huntington's disease. Brain. 1995; 118: 145-152.

[15] Vaportzis E, Georgiou-Karistianis N, Stout JC. Age and task difficulty differences on dual tasking using circle tracing and serial subtraction tasks. Aging Clin Exp Res. 2014; 26: 201-211.

[16] Brown RG, Jahanshahi M, Marsden CD. The execution of bimanual movements in patients with Parkinson's, Huntington's and cerebellar disease. J Neurol Neurosurg Psychiatry. 1993; 56: 295-297.

[17] Mendelson DN, Redfern MS, Nebes RD, Jennings JR. Inhibitory processes relate differently to balance/reaction time dual tasks in young and older adults. Aging Neuropsychol C. 2010; 17: 1-18.

[18] Holtzer R, Burright RG, Donovick PJ. The sensitivity of dual-task performance to cognitive status in aging. JINS: 2004; 10: 230-238.

[19] Amieva H, Lafont S, Dartigues JF, Fabrigoule C. Selective attention in Alzheimer's disease: Analysis of errors in Zazzo's cancellation task. Brain Cognition. 1999; 40: 26-100.

[20] Wickens CD, McCarley JS. (2008). Applied attention theory. Boca Raton: Taylor & Francis.

[21] Wickens CD. (2002). Multiple resources and performance prediction. TIES. 2002; 3: 159-177.

[22] Nasreddine ZS, Phillips NA, Bédiriam V, Charbonneau S, Whitehead V, Collin I, Cummings JL, Chertkow H. The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. J Am Geriatr Soc. 2005; 53: 695-699.

[23] Bezdicek O, Majerova V, Novak M, Nikolai T, Ruzicka E, Roth J. Validity of the Montreal Cognitive Assessment in the detection of cognitive dysfunction in Huntington's disease. Appl Neuropsychol Adult. 2013; 20, 33-40.

[24] Gluhm S, Goldstein J, Brown D, Van Liew C, Gilbert PE, Corey-Bloom J. Usefulness of the Montreal Cognitive Assessment (MoCA) in Huntington's disease. Movement Disord. 2013; 28: 1744-1747.

[25] Videnovic A, Bernard B, Fan W, Jaglin J, Leurgans S, Shannon K. The Montreal Cognitive Assessment as a screening tool for cognitive dysfunction in Huntington's disease. Movement Disord. 2010; 25: 402-404.

[26] Huntington Study Group. Unified Huntington's Disease Rating Scale: Reliability and consistency. Movement Disord. 1996; 11: 136-142.

[27] Wechsler D. (2001). Wechsler Test of Adult Reading. San Antonio: The Psychological Corporation.

[28] Rush AJ, Carmody T, Reimitz P-E. The Inventory of Depressive Symptomatology (IDS): Clinician (IDS-C) and Self-Report (IDS-SR) ratings of depressive symptoms. Int J Methods Psychiatr Res. 2006; 9: 45-59.

[29] American Psychiatric Association (1994). Diagnostic and statistical manual of mental disorders 4th ed. Washington, DC: American Psychiatry Association.

[30] UNESCO (1997). International Standard Classification of Education. Available from http://www.uis.unesco.org/ev.php?ID=7433_201&ID2=DO_TOPIC

[31] Schneider W, Eschmann A, Zuccolotto A. (2002). E-Prime user's guide. Pittsburgh, PA: Psychology Software Tools, Inc.

[32] Kemper S, Herman RE, Lian CHT. The costs of doing two things at once for young and older adults: Talking while walking, finger tapping, and ignoring speech or noise. Psychol Aging. 2003; 18: 181-192.

[33] Swanenburg J, de Bruin ED, Hegemann S, Uebelhart D, Mulder T. Dual tasking under compromised visual and somatosensory input in elderly fallers and non-fallers. TOREHJ. 2010; 3: 169-176.

[34] McDowd JM, Craik FIM. Effects of aging and task difficulty on divided attention performance. J Exp Psychol Human. 1998; 14: 267-280.

[35] de Ribaupierre A, Ludwig C. Age differences and divided attention: Is there a general deficit? Exp Aging Res. 2003; 29: 79-105.

[36] Kahneman D. (1973). Attention and effort. New Jersey: Prentice-Hall.

[37] Ohsugi H, Ohgi S, Shigemori K, Schneider EB. Differences in dual-task performance and prefrontal cortex activation between younger and older adults. BMC Neurosci. 2013; 14: 10.

[38] Klingberg T. Limitations in information processing in the human brain: Neuroimaging of dual task performance and working memory tasks. Prog Brain Res. 2000; 126: 95-102.

[39] Rosas HD, Lee SY, Bender AC, Zaleta AK, Vangel M, Yu P, Fischl B, Pappu V, Onorato C, Cha J-H, Salat DH, Hersch SM. Altered white matter microstructure in the corpus callosum in Huntington's disease: Implications for cortical "disconnection". Neuroimage. 2010; 49: 2995-3004.

[40] Posner MI, Petersen SE. (1990). The attention system of the human brain. Annu Rev Neurosci. 1990; 13: 25-42.

[41] Nopoulos PC, Aylward EH, Ross CA, Johnson HJ, Magnotta VA, Juhl AR, Pierson RK, Mills J, Langbehn DR, Paulsen JS, the PREDICT-HD Investigators Coordinators of HSG. Cerebral cortex structure in prodromal Huntington disease. Neurobiol Disease. 2010; 40: 544-554.

[42] Rosas HD, Tuch DS, Hevelone ND, Zaleta AK, Vangel M, Hersch SM, Salat DH. Diffusion tensor imaging in presymptomatic and early Huntington's disease: Selective white matter pathology and its relationship to clinical measures. Movement Disord. 2006; 21: 1317-1325.

[43] Aylward EH, Sparks BF, Field KM, Yallapragada V, Shpritz BD, Rosenblatt A, Brandt J, Gourley LM, Liang K, Zhou H, Margolis RL, Ross CA. Onset and rate of striatal atrophy in preclical Huntington disease. Neurology: 2004; 63: 66-72.

[44] Snowden JS, Craufurd D, Thompson J, Neary D. Psychomotor, executive, and memory function in preclinical Huntington's disease. J Clin Exp Neuropsychol. 2002; 24: 133-145.

[45] van Schouwenburg MR, den Ouden HEM, Cools R. The human basal ganglia modulate frontal-posterior connectivity during attention shifting. J Neurosci. 2010; 30: 9910-9918.

[46] Voytek B, Knight RT. Prefrontal cortex and basal ganglia contributions to visual working memory. Proc Natl Acad Sci. 2010; 107: 18167-18172.

[47] Rhein C, Mühle C, Richter-Schmidinger T, Alexopoulos P, Doerfler A, Kornhuber J. Neuroanatomical correlates of intelligence in healthy young adults: The role of basal ganglia volume. PLoS One. 2014; 9: e93623.

[48] Couette M, Bachoud-Levi A-C, Brugieres P, Sieroff E, Bartolomeo P. Orienting of spatial attention in Huntington's disease. Neuropsychologia. 2008; 46: 1391-1400.

[49] Delval A, Krystkowiak P, Delliaux M, Dujardin K, Blatt J-L, Destée A, Derambure P, Defebvre L. Role of attentional resources on gait performance in Huntington's disease. Movement Disord. 2008; 23: 684-689.

[50] Georgiou-Karistianis N, Stout JC, Dominquez JF, Carron SP, Ando A, Churchyard A, Chua P, Borowsky B, Egan GF, Stout JC. Functional magnetic resonance imaging of working memory in Huntington's disease: Cross-sectional data from the IMAGE-HD study. Hum Brain Mapp. 2014; 35: 1847-1864.

[51] DeLong MR, Wichmann T. Circuits and circuit disorders of the basal ganglia. Arch Neurol. 2007; 64: 20-24.

[52] Alexander GE, DeLong MR, Strick PL. Parallel organization of functionally segregated circuits linking basal ganglia and cortex. Annu Rev Neurosci. 1986; 9: 357-381.

[53] Mickes L, Jacobson M, Peavy G, Wixted JT, Lessig S, Goldstein JL, Corey-Bloom J. A comparison of two brief screening measures of cognitive impairment in Huntington's disease. Movement Disord. 2010; 25: 2229-2233.

Table 1

Demographics' descriptives for HD participants and controls

	HD (n = 14)	Controls (n = 14)	p
Sex (F:M)	4:10	4:10	
Montreal Cognitive Assessment			
Mean(SD)	24.93(2.89)	28.14(1.46)	.001
Range	20-29	26-30	
Age			
Mean(SD)	57.86(8.94)	58.64(11.39)	
Range	41-73	39-73	
CAG			
Mean(SD)	42.38(1.85)		
Range	40-47		
Diagnosis (years)			
Mean(SD)	4.57(1.91)		
Range	2-7		
Motor score			
Mean(SD)	21.20(8.82)		
Range	7-34		
Total functional capacity			
Mean(SD)	10.10(3.04)		
Range	6-13		
Oculomotor score			
Mean(SD)	2.47(3.34)		

Range	0-11		
Wechsler Test for Adult Reading			
Mean(SD)	109.21(6.50)	111.50(7.25)	.39
Range	99-118		
Inventory of Depressive Symptomatology-Self-Report			
Mean(SD)	14.21(9.50)	11.07(6.41)	.31
Range	2-32	5-29	
International Standard Classification of Education			
Mean(SD)	4.14(.770)	4.43(1.08)	.43
Range	3-6	3-6	

Note. Groups were compared using independent samples *t*-tests.

Table 2

Demographics' descriptives for low- and high-MoCA HD participants

	Low-MoCA HD (n = 8)	High-MoCA HD (n = 6)	*p*
Sex	3:5	1:5	
Montreal Cognitive Assessment			
Mean(SD)	22.17(1.60)	27.00(1.51)	<.001
Range	20-24	26-29	
Age			
Mean(SD)	60.83(11.61)	55.63(6.23)	.299
Range	41-73	42-61	
CAG			
Mean(SD)	41.60(.89)	42.88(2.16)	.243
Range	40-42	40-47	
Diagnosis (years)			
Mean(SD)	5.00(1.89)	4.25(1.98)	.489
Range	3-7	2-7	
Motor score			
Mean(SD)	8.83(4.16)	4.13(3.39)	.038
Range	6-17	0-9	
Total functional capacity			
Mean(SD)	8.33(3.32)	11.13(2.16)	.081
Range	7-13	6-13	
Oculomotor score			
Mean(SD)	2.83(2.99)	2.22(3.70)	.070

Range	0-8	0-11	
Wechsler Test for Adult Reading			
Mean(SD)	109.50(6.83)	109.00(6.72)	.893
Range	99-117	99-118	
Inventory of Depressive Symptomatology-Self-Report			
Mean(SD)	20.67(11.43)	9.38(3.46)	.021
Range	0-33	4-14	
International Standard Classification of Education			
Mean(SD)	4.17(.98)	4.13(.64)	.925
Range	3-6	3-5	

Note. Groups were compared using independent samples *t*-tests.

FIGURE CAPTIONS

Fig. 1. Example forms of the (a) easy, and (b) hard cancellation tasks.

Fig. 2. Completion time on the cancellation tasks as a function of Group, Cancellation and Auditory tasks. E = Easy; H = Hard. Standard error bars included.

Fig. 3. Dual task costs (completion time) on the cancellation tasks as a function of Group, Cancellation, and Auditory tasks. E = Easy; H = Hard. Standard error bars included.

Fig. 4. Error rates on the cancellation tasks as a function of Group and Auditory tasks. E = Easy; H = Hard. Standard error bars included.

Fig. 1

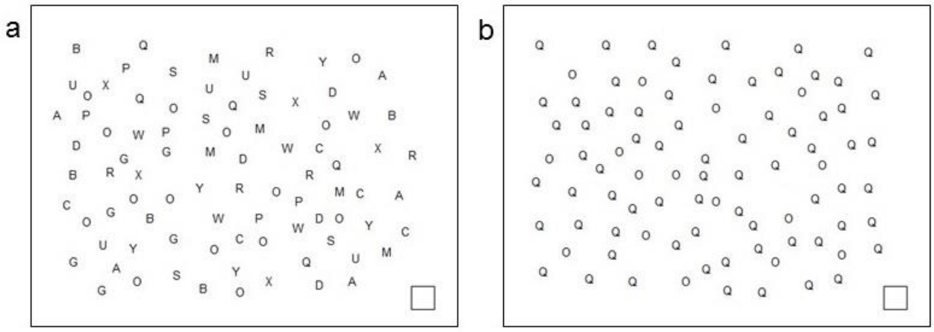


Fig 2.

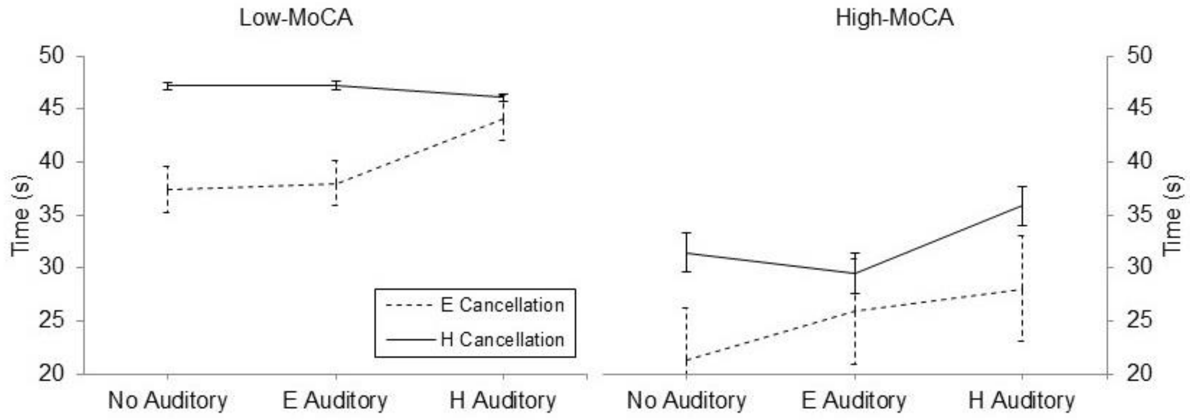

Low-MoCA
High-MoCA
Time (s)
50
45
40
35
30
25
20
No Auditory
E Auditory
H Auditory
E Cancellation
H Cancellation

Fig 3.

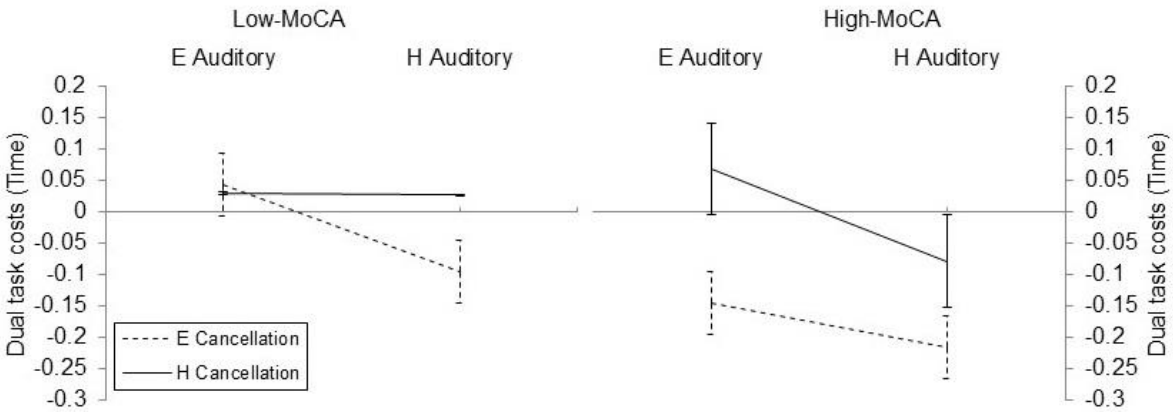
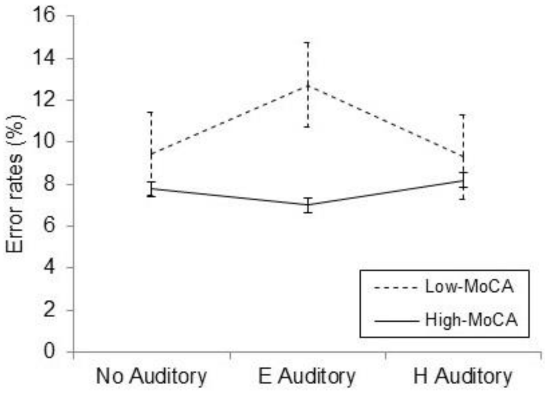

Low-MoCA
High-MoCA
E Auditory
H Auditory
E Auditory
H Auditory
Dual task costs (Time)
0.2
0.15
0.1
0.05
0
-0.05
-0.1
-0.15
-0.2
-0.25
-0.3
E Cancellation
H Cancellation
Dual task costs (Time)

Fig 4.



16
14
12
10
8
6
4
2
0
Error rates (%)
Low-MoCA
High-MoCA
No Auditory
E Auditory
H Auditory