Social Cognition, Executive Functions and Self-Report of Psychological Distress in Huntington’s Disease

Ida Unmack Larsen, Tua Vinther-Jensen, Jørgen Erik Nielsen, Anders Gade, Asmus Vogel

Abstract

Objective: Huntington’s disease (HD) is characterized by motor symptoms, psychiatric symptoms and cognitive impairment in, inter alia, executive functions and social cognition. The aim of this study was to investigate the relationship between subjective feeling of psychological distress using a self-report questionnaire and performances on tests of executive functions and social cognition in a large consecutive cohort of HD patients.

Method: 50 manifest HD patients were tested in social cognition and executive functions and each answered a self-report questionnaire about current status of perceived psychological distress (the Symptom Checklist-90-Revised (SCL-90-R)). Correlation analyses of test performance and SCL-90-R scores were made as well as stepwise linear regression analyses with the SCL-90-R GSI score and test performances as dependent variables.

Results: We found that less psychological distress was significantly associated with worse performances on social cognitive tests (mean absolute correlation .34) and that there were no significant correlations between perceived psychological distress and performance on tests of executive functions. The correlations between perceived psychological distress and performance on social cognitive tests remained significant after controlling for age, Unified Huntington’s Disease Rating Scale-99 total motor score and performance on tests of executive functions.

Conclusions: Based on previous findings that insight and apathy are closely connected and may be mediated by overlapping neuroanatomical networks involving the prefrontal cortex and frontostriatal circuits, we speculate that atrophy of the prefrontal cortex and/or impaired executive functions may mediate the relationship between psychological distress and social cognition in this study.

Funding Statement

Ida Unmack Larsen and Tua Vinther-Jensen are both supported by grants from Copenhagen University. Jørgen Erik Nielsen is supported by a research grant from the Novo Nordisk Foundation. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Introduction

Huntington’s disease (HD) is an autosomal dominantly inherited neurodegenerative disorder caused by an expanded CAG repeat on chromosome 4 and characterized by motor symptoms, psychiatric symptoms and cognitive decline. Once onset of motor symptoms has occurred, cognitive and/or psychiatric symptoms also tend to be present. The cognitive deterioration in HD is thought to be related to dysfunction of the frontostriatal circuits due to gradual degeneration of the striatum. Accordingly, the first signs of cognitive impairment are observed in cognitive functions associated with the prefrontal cortex such as executive functions and social cognitive functions. Psychiatric symptoms are also commonly found even in the presymptomatic and earliest stages in HD, and a wide variety of psychiatric symptoms such as apathy, depression, irritability, anxiety, mania and obsessive compulsive symptoms can be seen.

Performance on tests of social cognition and executive functions are often affected by psychopathology. Associations between social cognitive functions, executive functions and psychiatric symptoms have been investigated in both psychiatric and neurological disorders such as schizophrenia, depression, bipolar disorder, Parkinson’s disease (PD) and frontotemporal dementia (FTD). The most common finding being that greater degree of psychiatric symptoms are associated to worse performance on tests of executive functions and social cognition.

In two previous studies we have investigated performance on tests of executive functions and social cognition in a large cohort of HD patients in early-moderate disease stage and found a high frequency of impaired performances on tests of executive functions and social cognition. Based on the associations between the presence of psychiatric symptoms and impairments in...
executive functions and social cognition found in other patient groups we wanted to investigate how subjective experience of psychological distress as reported by patients with Huntington's disease is related to performance on tests of social cognition and executive functions.

Therefore the aim of this study was to investigate the relationship between self-report of perceived psychological distress and performances on a battery of tests of executive functions and social cognition in a large consecutive cohort of HD patients. We wanted to investigate: 1) whether performances on tests of social cognition and executive functions are correlated, and 2) whether performances on tests of social cognition and executive functions are associated with degree of self-reported psychological distress. To our knowledge, this is the first study to compare performance on a large battery of tests of social cognition and executive functions to self-report of psychological distress in HD.

Methods

Participants

Participants were recruited from January 2012 to March 2013 from the Neurogenetics Clinic, Danish Dementia Research Centre, Rigshospitalet. Fifty HD patients with a CAG repeat \( \geq 39 \), a Unified Huntington's Disease Rating Scale-99 total motor score (UHDRS-TMS) of \( >51 \), a Mini-Mental State Examination (MMSE) score \( \geq 24 \), and a Montreal Cognitive Assessment (MoCA)\(^1\) score \( \geq 20 \) were included in the study. Exclusion criteria were other neurological illness, ongoing alcohol or drug abuse and having a native language other than Danish. Table 1 shows the background information for the HD patients. All patients had gone through genetic counseling and had been informed of their genetic status prior to (and independently from) study enrolment. We have previously published results from the same cohort\(^2-4,5,21\) also including premanifest HD carriers, but since we found no impairments in social cognitive functions in our premanifest subjects we did not include them in the present study.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Manifest HD gene-expansion carriers N=50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (m/f)</td>
<td>30/20</td>
</tr>
<tr>
<td>Age (years)</td>
<td>51 (24-75)</td>
</tr>
<tr>
<td>Education index</td>
<td>13 (8-17)</td>
</tr>
<tr>
<td>MMSE(^1)</td>
<td>28 (24-30)</td>
</tr>
<tr>
<td>MoCA(^1)</td>
<td>26 (21-30)</td>
</tr>
<tr>
<td>CAG-repeat(^3)</td>
<td>43 (40-53)</td>
</tr>
<tr>
<td>UHDRS total motor score(^2)</td>
<td>20 (6-41)</td>
</tr>
<tr>
<td>SCL-90-R GSI score(^2)</td>
<td>56 (34-76)</td>
</tr>
</tbody>
</table>

Table 1. Background information. Results shown as median (range)

Procedure

The study was approved by the Ethics Committee of the Capital Region of Denmark(H2-2011-085), and written informed consent was obtained from each participant before enrollment. All participants had a minimum of two planned visits. At one visit psychiatric screening and neurological examinations were performed. At the other visit neuropsychological testing was performed. The same physician and the same neuropsychologist performed all examinations. The examination by the physician and the examination by the neuropsychologist were performed blinded to one another.

Neuropsychological Testing

All participants were tested with an extensive three-hour battery of neuropsychological tests, including tests of attention, memory, visuospatial functions, executive functions and social cognition. For this study only tests of executive functions and tests of social cognition are included. The tests were administered in a fixed order. The education index score (range 8-17) was
Emotion Hexagon (EH)\textsuperscript{23}: This test consists of 30 cards with pictures of morphed facial expressions of the six basic emotions: happiness, surprise, fear, sadness, anger and disgust. Each of the six emotions was represented with four pictures; each picture was morphed with either 10% or 30% of the neighboring emotions (e.g. happiness is morphed with either 10% or 30% anger or surprise). Between two neighboring emotions was a picture morphed with 50% of each emotion; these were not counted in the total raw score. A card with the six emotion words was presented, and each of the six emotions was explained before the pictures were shown to the participants and remained visible for them during the test. The pictures were shown in random order, and the participants were asked to choose which of the six emotions best described the facial expression. The pictures were shown only once, and no feedback was given. The test was scored as the total number of correct responses (0-24).

Emotion Evaluation Task (EET)\textsuperscript{24}: The EET consists of 28 short videotaped vignettes (15-60 seconds) of actors interacting in everyday situations. In some of the scenes there is one actor only, and in other scenes there are two (the participant was then told on whom to focus). The participants were asked to choose whether the actor was displaying one of the six basic emotions: happiness, surprise, sadness, anger, fear or disgust or no particular emotion (neutral). The EET does not exist in a Danish version and therefore the video clips were shown without sound in order to exclude any influence of differences in English language abilities. Each video was shown once, and no feedback was given. The test was scored as the total number of correct responses (0-28).

Social Inference – Minimal (SI-M)\textsuperscript{24,51}: The SI-M (Danish version: Bliksted, Fagerlund, Weed, Frith, & Videbech, 2014) consists of short (15-53 seconds) videotaped vignettes with professional actors interacting in everyday situations. The exchanges are either sincere or sarcastic. The sarcastic vignettes are either with simple sarcasm, meaning that they are acted in such a way as to imply the opposite meaning to what is actually being said, or with paradoxical sarcasm meaning that the exchange of words is meaningless unless one understands that one of the actors is being sarcastic. After each video, the participant was asked four yes/no questions about the interaction. Correct answers to the questions for the sarcastic videos required interpretation of paralinguistic cues such as tone of voice and non-verbal cues such as posture and facial expressions. The test comprises part A2 and part B2. Part A2 consists of five videos of paradoxical sarcasm and ten vignettes that are either sincere or with simple sarcasm. Part B2 consists of exactly the same dialogue as the ten sincere or simple sarcastic videos from part A2 but with sincerity and sarcasm switched. For this study the participants were shown all 25 videos. Each video was shown once, and no feedback was given. Total number of correct yes/no answers (0-100) was used in the present study.

Reading the Mind in the Eyes Test (RME)\textsuperscript{25}: The RME revised version consists of 36 photos of eyes expressing different emotional states. The participants were given four choices of words and were asked to pick the word that best described what the eyes expressed (e.g., serious, ashamed, alarmed or bewildered). In order to pick the correct emotion the participant needed to be able to attribute mental states to others thereby using Theory of Mind (ToM). The participants were also given a list of explanations of all the words in the test and were encouraged to look up the words if they felt uncertain of the meaning of a word. The number of correct responses was recorded (0-36).

Semantic fluency\textsuperscript{26}: The participants were asked to name as many different animals as they could think of within one minute. It was emphasized that all types/categories of animals would be correct. Categories (e.g., birds) as well as specific animals (e.g., eagle) were accepted. The number of different animals named was recorded.

Lexical fluency\textsuperscript{26}: The participants were asked to produce as many words as possible within one minute beginning with each of the letters F, A or S. It was emphasized that it could be all words in Danish except proper nouns. The number of different words produced with F, A and S were recorded and added together for a total score.

Lexical alternating fluency. This fluency test was developed by the researchers based on a category that was thought to be very broad and one of the most common first-letters in Danish apart from S, F, K and B. The participants were asked to produce as many different words as possible within one minute alternating between words beginning with the letter K and words beginning with the letter B. It was emphasized that it could be all types of words except proper nouns. The number of correct responses was recorded, and improper alternations were counted as incorrect.

Semantic/lexical alternating fluency. This fluency test was developed by the researchers based on a category that was thought to be very broad and one of the most common first-letters in Danish apart from S, F, K and B. The participants were asked to produce as many different words as possible within one minute alternating between types of food and words beginning with the letter D. They were told that the former could be “anything you can eat”, and that the latter covered all words beginning with the letter D except proper nouns. The number of correct responses was recorded; improper alternations were counted as incorrect.

Trail Making Test B (TMT B)\textsuperscript{27}: The participants were asked to connect circles alternating between numbers in numeric order and letters in alphabetical order. The time to completion was recorded.

Stroop interference test\textsuperscript{28}: This 100-word version of the Stroop test consisted of a simple reading task and an interference test. In the interference test the name of the color and the color of the ink did not correspond, for example the word ‘blue’ could
be written in green ink, and the participants were asked to name the colors instead of reading the words. Participants were instructed to complete the test as quickly as possible and to correct their mistakes. Only the time to completion for the interference test was used for analysis.

**Self-report of psychological distress**

**Symptom Checklist -90-Revised (SCL-90-R)²⁹:** The SCL-90-R is a 90 item self-report inventory designed to reflect the current status of perceived psychological distress. The participant is asked to rate each of the 90 items on a five-point Likert scale ranging from “not at all” to “very often” according to how much they experienced each symptom in the preceding week. The scoring is based on nine primary symptom dimensions: somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism. Added together these yield three global indices of distress: Global Severity Index (GSI), Positive Symptoms Distress Index and Positive Symptom Total. For the current study raw scores were converted into T-scores standardized to a normative Danish sample stratified by gender⁶⁰. Higher T-scores indicate greater degree of psychological distress. Only the GSI score was used for the association analyses in current study.

**Statistical analysis**

Results for the background variables are presented as medians and ranges. Pearson’s r and Spearman’s Rho (rs used for skewed distributions) were used to assess the level of significance of correlations between the cognitive tests and the SCL-90-R GSI scores and also to investigate the level of significance of associations between performances on tests of social cognition and executive functions. Lastly stepwise linear regression analyses were used with SCL-90-R GSI score as the dependent variable and scores on each of the social cognitive tests that were significantly associated with SCL-90-R GSI score as independent variables. For each regression analysis performances on all of the executive tests (Lexical fluency, Semantic fluency, Lexical alternating fluency, Semantic/lexical alternating fluency, Stroop test and TMT B), age and UHDRS-TMS were also included as independent variables. Plots of residuals were used as model control and the alpha level was set to .05 (two-tailed).

**Results**

Table 2 shows the median and interquartile range for performance on all tests of executive functions and social cognition, as well as the median and interquartile range for the standardized T-scores on the GSI and the nine symptom dimensions of the SCL-90-R.

<table>
<thead>
<tr>
<th>Domain</th>
<th>Test</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social Cognition</td>
<td>Emotional Hexagon²</td>
<td>15 (13-17)</td>
</tr>
<tr>
<td></td>
<td>Reading the Mind in the Eyes²</td>
<td>19 (15-23)</td>
</tr>
<tr>
<td></td>
<td>Emotion Evaluation Test²</td>
<td>19 (15-22)</td>
</tr>
<tr>
<td></td>
<td>Social Inference-Minimal total²</td>
<td>77 (65-85)</td>
</tr>
<tr>
<td>Executive functions</td>
<td>Lexical fluency²</td>
<td>27 (20-34)</td>
</tr>
<tr>
<td></td>
<td>Semantic fluency²</td>
<td>15 (13-23)</td>
</tr>
<tr>
<td></td>
<td>Stroop test¹</td>
<td>166 (137-221)</td>
</tr>
<tr>
<td></td>
<td>Semantic/lexical Alternating Fluency²</td>
<td>7 (6-10)</td>
</tr>
<tr>
<td></td>
<td>Lexical Alternating Fluency²</td>
<td>10 (7-12)</td>
</tr>
<tr>
<td></td>
<td>Trail Making Test B¹</td>
<td>121 (85-163)</td>
</tr>
<tr>
<td></td>
<td>Global Severity Index³</td>
<td>56 (47-61)</td>
</tr>
<tr>
<td></td>
<td>obsessive-compulsive³</td>
<td>58 (50-64)</td>
</tr>
<tr>
<td></td>
<td>depression³</td>
<td>55 (47-61)</td>
</tr>
</tbody>
</table>
Table 2. Scores for HD carriers on the cognitive tests and the Symptom Checklist-90-Revised Global Severity index and the nine primary symptoms dimensions. Results shown as median (interquartile range).

Table 3 shows the correlations between social cognitive tests and tests of executive functions. As expected we found that performances on all four social cognitive tests were significantly correlated with each other. Performances on all four social cognitive tests were also significantly associated with performances on tests of executive functions (mean correlation .24).

Table 3. Correlations between tests of executive functions and tests of social cognition. Results shown as Spearmans Rho.

Table 4 shows the correlations between the SCL-90-R GSI score and the UHDRS-TMS and the tests of executive functions and social cognition. We found a significant correlation between the SCL-90-R GSI score and scores on three of the four social cognitive tests (the SI-M total, the EET and the RME), such that better test performance was related to more perceived psychological distress. The mean overall correlation was .34. By contrast, none of the correlation coefficients between the SCL-90-R GSI score and the tests of executive functions reached significance. Motor symptoms were not significantly correlated to SCL-90-R GSI score, but were significantly correlated to performance on most tests of executive functions and social cognition.

<table>
<thead>
<tr>
<th>Domain</th>
<th>Test</th>
<th>Emotional Hexagon</th>
<th>Reading the Mind in the Eyes</th>
<th>Emotion Evaluation Test</th>
<th>Social Inference-Minimal total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social cognition</td>
<td>Emotional Hexagon</td>
<td>0.45**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Reading the Mind in the Eyes</td>
<td>0.45**</td>
<td>0.66**</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Emotion Evaluation Test</td>
<td>0.51**</td>
<td>0.45**</td>
<td>0.64**</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Social Inference-Minimal total</td>
<td>0.45**</td>
<td>0.55**</td>
<td>0.64**</td>
<td></td>
</tr>
<tr>
<td>Executive functions</td>
<td>Lexical fluency</td>
<td>0.31*</td>
<td>0.29*</td>
<td>0.41**</td>
<td>0.17</td>
</tr>
<tr>
<td></td>
<td>Semantic fluency</td>
<td>0.49**</td>
<td>0.42**</td>
<td>0.45**</td>
<td>0.36*</td>
</tr>
<tr>
<td></td>
<td>Stroop test</td>
<td>-0.40**</td>
<td>-0.46**</td>
<td>-0.63**</td>
<td>-0.58**</td>
</tr>
<tr>
<td></td>
<td>Semantic Lexical Alternating Fluency</td>
<td>0.26</td>
<td>0.26</td>
<td>0.48**</td>
<td>0.28*</td>
</tr>
<tr>
<td></td>
<td>Lexical Alternating Fluency</td>
<td>0.24</td>
<td>0.42**</td>
<td>0.36*</td>
<td>0.12</td>
</tr>
<tr>
<td></td>
<td>Trail Making Test B</td>
<td>-0.56**</td>
<td>-0.59**</td>
<td>-0.59**</td>
<td>-0.46*</td>
</tr>
</tbody>
</table>

*p<0.05, **p<0.01, 1 seconds to completion

<table>
<thead>
<tr>
<th>Domain</th>
<th>Test</th>
<th>SCL-90-R GSI score</th>
<th>UHDRS - TMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychological distress</td>
<td>SCL-90-R GSI score</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Motor symptoms</td>
<td>UHDRS - TMS</td>
<td>-0.099</td>
<td>-</td>
</tr>
<tr>
<td>Social Cognition</td>
<td>Social Inference-Minimal total</td>
<td>$r_s = 0.41^{**}$</td>
<td>$r_s = -0.54^{**}$</td>
</tr>
<tr>
<td></td>
<td>Emotion Evaluation Test</td>
<td>$r_s = 0.40^{**}$</td>
<td>$r_s = -0.49^{**}$</td>
</tr>
<tr>
<td></td>
<td>Reading the Mind in the Eyes</td>
<td>$r = 0.35^*$</td>
<td>$r = -0.45^{**}$</td>
</tr>
<tr>
<td></td>
<td>Emotional Hexagon</td>
<td>$r_s = 0.21$</td>
<td>$r_s = -0.55^{**}$</td>
</tr>
<tr>
<td>Executive functions</td>
<td>Lexical fluency</td>
<td>$r = -0.20$</td>
<td>$r = -0.40^{**}$</td>
</tr>
<tr>
<td></td>
<td>Semantic fluency</td>
<td>$r = -0.02$</td>
<td>$r = -0.60^{**}$</td>
</tr>
<tr>
<td></td>
<td>Stroop test</td>
<td>$r = -0.18$</td>
<td>$r = 0.58^{**}$</td>
</tr>
</tbody>
</table>
that loss of insight and flattening of affect in oneself may be associated with less sensitivity to others' emotional states as well,
cortex particular, the parietal cortex, superior temporal sulcus, limbic areas, striatum and orbital and medial areas in the prefrontal
cortex particular, the parietal cortex, superior temporal sulcus, limbic areas, striatum and orbital and medial areas in the prefrontal
research in neuroscience has supported the view of common representation networks between self and other involving, in
research in neuroscience has supported the view of common representation networks between self and other involving, in
Social developmental research has long posited the idea that representations of the self and other are closely connected
Social developmental research has long posited the idea that representations of the self and other are closely connected
emotion recognition as has been demonstrated in related disorders
emotion recognition as has been demonstrated in related disorders
feeling less psychologically distressed themselves was associated to worse performance on tests of the ability to recognize
feeling less psychologically distressed themselves was associated to worse performance on tests of the ability to recognize
progression performing worse and reporting fewer psychological symptoms since the associations remained significant after
progression performing worse and reporting fewer psychological symptoms since the associations remained significant after
distress and performance on social cognitive tests does not seem to be an artefact of those being furthest in the disease
distress and performance on social cognitive tests does not seem to be an artefact of those being furthest in the disease
distress and tests of executive functions were non-significant. Furthermore, the correlations between psychological
distress and tests of executive functions were non-significant. Furthermore, the correlations between psychological
correlations between SCL-90-R GSI score, UHDRS – TMS and test of executive functions, social cognition.
correlations between SCL-90-R GSI score, UHDRS – TMS and test of executive functions, social cognition.
Table 5 shows the result from the stepwise linear regression analysis. We found that the correlation between score on SCL-90-
Table 5 shows the result from the stepwise linear regression analysis. We found that the correlation between score on SCL-90-
Table 5 shows the result from the stepwise linear regression analysis. We found that the correlation between score on SCL-90-
Dependent model predictor variables $b_i$ Standard error $p$ value $R^2$
SCL-90-R GSI score Age -0.283 0.101 0.008 0.240
SCL-90-R GSI score Reading the mind in the eyes 0.569 0.276 0.045
SCL-90-R GSI score Emotion Evaluation task 1.411 0.379 0.001 0.369
SCL-90-R GSI score Trail Making Test B 0.065 0.025 0.013
SCL-90-R GSI score Age -0.237 0.097 0.019
SCL-90-R GSI score Social Inference-Minimal total 0.266 0.106 0.015 0.270
SCL-90-R GSI score Age -0.249 0.102 0.018
SCL-90-R=Symptom Checklist-90-Revised
SCL-90-R=Symptom Checklist-90-Revised
SCL-90-R=Symptom Checklist-90-Revised
Each stepwise linear regression model included SCL-90-R as dependent variable and either Reading the mind in the eyes, Emotion Evaluation task or Social Inference-Minimal total score plus the following independent variables: Lexical fluency, Semantic fluency, Stroop test, Semantic/lexical Alternating Fluency, Trail Making B, Unified Huntington Disease Rating Scale total motor score and age. Only the statistically significant relationships are shown.
Table 5. Stepwise linear regression results

Discussion
This study investigated whether performances on tests of social cognition and executive functions were associated with perceived psychological distress in a group of HD patients. Since greater degree of psychiatric symptoms such as depression has been negatively associated with both social cognitive skills and executive functions, we were surprised that more perceived psychological distress was significantly associated with better performances on social cognitive tests and that less perceived psychological distress was associated with worse performance on social cognitive tests. The correlations between psychological distress and tests of executive functions were non-significant. Furthermore, the correlations between self-reported psychological distress and performance on social cognitive tests does not seem to be an artefact of those being furthest in the disease progression performing worse and reporting fewer psychological symptoms since the associations remained significant after controlling for age, UHDRS-TMS and performance on tests of executive functions. This means that for our cohort of HD patients feeling less psychologically distressed themselves was associated to worse performance on tests of the ability to recognize emotions, ToM and sarcasm in others. This is an interesting finding that may help to understand the interpersonal problems often associated with HD. It may be helpful for clinicians and caregivers to know that feeling little psychological distress oneself may also influence the ability to recognize distress in others.

We used a self-report measure of psychological distress, and it is important to remember that self-report of psychological distress in HD may be influenced by poor insight, which is a common feature of HD. This means that although the patients themselves do not report having psychiatric symptoms this might not be true from a clinician or caregiver perspective. This means that our findings do not necessarily indicate that poor social cognition is genuinely associated with fewer psychiatric symptoms in patients with HD from an outside perspective. Instead, our findings may reflect a relationship between insight and emotion recognition as has been demonstrated in related disorders and a close connection between our understanding of the self and others.

Social developmental research has long posited the idea that representations of the self and other are closely connected, and research in neuroscience has supported the view of common representation networks between self and other involving, in particular, the parietal cortex, superior temporal sulcus, limbic areas, striatum and orbital and medial areas in the prefrontal cortex. Since representations of others are closely connected to our representation of the self, it could be speculated that loss of insight and flattening of affect in oneself may be associated with less sensitivity to others' emotional states as well,
leading to a state of being ‘comfortably numb’. We speculate that an alternative explanation of our results may be that a flattening of affect (from here on referred to as ‘apathy’) and impaired insight has led to low self-report of psychological distress in our cohort and that this was related to the weaker understanding of others (i.e. poor social cognitive skills including emotion recognition).

Impaired insight and apathy are well-known features of HD and other psychiatric and neurological disorders affecting the prefrontal cortex and frontostriatal circuits such as schizophrenia, PD and FTD. Apathy ratings have been associated with white matter changes in the orbitofrontal cortex in HD, and in both PD and FTD apathy has been associated with areas of the striatum and frontostriatal circuits. In schizophrenia negative symptoms have been inversely associated with striatal activation. These studies suggest that social cognition, insight and apathy may in part be mediated by overlapping neuroanatomical networks involving the prefrontal cortex and frontostriatal circuits. Thus HD may be a relevant condition in which such associations can be studied.

Studies of patients with HD, schizophrenia and FTD suggest a reciprocal relationship between insight and apathy (or negative symptoms), such that higher scores of apathy or negative symptoms have been associated with impaired awareness of these symptoms. In fact, impaired insight has been associated with better mood in both HD and schizophrenia meaning that patients with less awareness of illness and symptoms has been associated with fewer symptoms of depression, whereas greater self-awareness has been associated with higher depression scores. These findings support the view that apathy and lack of insight are closely connected and they also point in the direction of patients with symptoms of apathy being expected also to have poor self-awareness and therefore to report neither apathetic symptoms nor psychological distress in general.

Impaired insight and higher apathy scores have been found to be associated with worse performances on social cognitive tests in FTD, PD and schizophrenia. One study in FTD found that patients’ own ratings of apathy were positively correlated to ToM whereas the caregivers’ apathy ratings were negatively associated to ToM performance, indicating that greater awareness of apathetic symptoms was associated with better social cognitive skills. This finding may reflect the close connection between representations of the self and other and is in line with our results indicating that patients with better self-awareness also have a better understanding of others’ emotional states and vice versa. We found no associations between self-report of psychological distress and performance on tests of executive functions. This was somewhat surprising since psychiatric symptoms such as depression has often been associated to impairment in executive functions. There may be several different explanations for this finding. It may be that the tests used in this study are not sensitive to the type of executive dysfunction associated with psychiatric symptoms. It could also be that the types of psychiatric symptoms that are associated with executive dysfunctions are not well measured by the SCL-90-R. In a study by Thompson et al. they found that only apathy was significantly associated with impairment in executive functions in HD.

No other studies that we know of have found significant correlations between self-report of psychological distress and performance on social cognitive tests in HD. Two studies have investigated the correlation between alexithymia and emotion recognition and ToM in HD but found no significant correlations, and one other study found no significant associations between performance on a ToM task and psychiatric symptoms on the Positive And Negative Syndrome Scale in HD. Discrepancies between our results and previous findings may be explained by different methodological approaches, and these previous studies had small sample sizes compared to our study.

**Limitations**

There are several limitations to our study. In an exploratory study like this was, there can be quite a lot of statistical comparisons and thus a chance of false positive findings. The use of a self-report measure of perceived psychological distress may have been misleading, since some HD patients are known to show poor awareness of their symptoms. Future research should add ratings from caregivers or clinicians to overcome this problem and to get more information about the relationship between social cognitive performances and insight in HD. Also an apathy rating scale or a scale for rating negative symptoms, would have helped to clarify the mechanisms for our findings. Future studies should apply apathy ratings to investigate the association between social cognition and apathy in HD.

Other limitations to the study relate to the tests used. The Danish version of TASIT was developed for research purposes and it has not been standardized and validated. This must, of course, lead to caution when interpreting results. Sarcasm as a part of everyday interaction is somewhat culture specific and thus generalization to all other cultures may be limited. The EET of the TASIT does not exist in a Danish version and thus was used without sound. The clinical impression of performances on this test was that it was still meaningful and there were no significant differences between healthy controls and premanifest HD carriers on performances on the EET in a previously published study (ref). Although our evaluation was that the test was still meaningful, the different use of the test from its original form requires caution when interpreting the results.

**Conclusions**

We found significant associations between self-report of psychological distress and performances on social cognitive tests but not on tests of executive functions. According to our findings HD patients that feel less psychologically distressed themselves...
perform worse on tests of the ability to recognize emotions, ToM and sarcasm in others. This is an interesting finding that may be of importance for understanding the interpersonal problems often associated with HD. We speculate that one mechanism for this finding may be that shared representations of self and other as well as insight and apathy may be closely connected and may be mediated by overlapping neuroanatomical networks involving the prefrontal cortex and frontostriatal circuits. Therefore we speculate that a flattening of affect or apathy and impaired insight has led to low self-report of psychological distress in our cohort and that this was related to the weaker understanding of others (i.e. poor social cognitive skills including emotion recognition).

Competing Interests Statement
The authors have declared that no competing interests exist

Data Availability Statement
All relevant data are within the manuscript.

Corresponding Author
Ida Unmack Larsen (ida.unmack.larsen.01@regionh.dk)

References


51. The Awareness of Social Inference Test (TASIT): Danish Translation Copyright © (2008) by Skye McDonald, Sharon Flanagan and Jennifer Rollins, published by Pearson Assessment; Copyright © 2011 by Skye McDonald, Sharon Flanagan and Jennifer Rollins. Reproduced with permission from Pearson Assessment. All rights reserved.