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Short communication

Altered subjective fear responses in Huntington's disease☆

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ABSTRACT

Patients with Huntington's disease (HD) have been shown to exhibit impairment in the recognition of facial expressions such as disgust, as well as deficits in disgust responses to olfactory and gustatory stimuli. The present study investigated whether HD is associated with changes in emotional responses to a variety of visual and verbal stimuli selected to elicit core disgust, moral disgust, fear and happiness. Thirteen patients with HD and twelve controls provided emotional ratings after both reading emotion eliciting scenarios and viewing pictures from the International Affective Picture System database. Patients with HD exhibited executive dysfunction. In comparison to controls, they gave similar ratings for happy stimuli and did not differ significantly in response to core disgust or moral disgust stimuli. However, they did exhibit lower fear ratings in response to both sets of fear stimuli (pictures and scenarios), and higher anger ratings than controls in response to fear pictures. These differences in fear response could reflect dysfunction within frontostriatal pathways involving the amygdala. Changes to fear responses in HD may impair decision making and lead to increased risk-taking behaviour with significant personal or social consequences.

1. Introduction

Patients with Huntington's disease (HD) demonstrate impairments in recognising facial expressions of disgust [1]. The characteristic facial expression of disgust involves constriction of the mouth and nose, signalling resistance to ingestion. Core disgust is typically experienced in response to an unpleasant taste or smell, is associated with nausea, and has been linked to the insula [2], a neural region critical for the awareness of bodily sensations. Core disgust enables organisms to avoid harmful contact with potential contaminants such as rotting food or body products. Disgust deficits have been revealed in HD using pictures, olfactory and gustatory stimuli [3]. Snowden et al. [4] showed that patients with HD can exhibit poor recognition of vocally expressed disgust and reduced disgust responses in response to written scenarios that elicited this emotion in control participants.

While some authors argue difficulties with disgust are disproportionate compared to recognition of other emotional expressions [1,3], studies have revealed deficits in the recognition of a range of negative emotional facial expressions in HD [5] and one study found greater impairment in the recognition of fearful facial expressions [6]. However, it is generally assumed that positive emotions including happiness are unaffected.

Sprengelmeyer et al. [7] showed that poor recognition of fearful facial expressions was accompanied by reductions in two HD patients' emotional experience of fear. This may be because the neural regions involved in emotion recognition in others are implicated in the experience of that emotion [2]. As patients with HD exhibit difficulties recognising certain emotions, their subjective experience of those emotions may differ to neurologically intact individuals. The current study therefore aimed to assess a range of emotional reactions of patients with HD, through the use of stimuli associated with fear and disgust.

One complication when investigating the experience of disgust lies in the range of stimuli that elicit this emotion. For example, disgust may be elicited by some moral (e.g. antisocial or criminal) offences [8]. While many previous investigations have focused on

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core disgust, the current study may be the first to investigate moral disgust in patients with HD.

Previous research investigating emotional processing in HD mainly focused on patients' recognition of emotional facial expressions, with limited attention to whether changes in one's own emotional experience were a feature of HD. For example, it could be that changes in the recognition of others' disgust are accompanied by changes in the experience of disgust in HD. We investigated subjective emotional responses to pictures and scenarios selected to elicit core disgust, moral disgust, fear and happiness, comparing patients with clinical HD to healthy controls. It was expected that patients with HD would show reduced disgust responses to both core and moral disgust stimuli, and to a lesser extent reduced fear responses to fear stimuli, but that reactions to happiness stimuli would be unaffected.

2. Methods

This study was granted ethical approval by a local Ethics Committee. All participants gave written informed consent.

2.1. Participants

Thirteen outpatients (8 males) with clinical HD were recruited from the Queen Elizabeth Psychiatric Hospital, Birmingham. None exhibited a Mini Mental State Examination score of less than 24/30, or evidence of dementia as assessed by their experienced Consultant (HER). One had clinically significant evidence of depression and one had an anxiety disorder. Patients' mean age was 53.1 years and mean years of education were 13.3 years. Twelve neurologically intact controls (6 males, mean age: 53.1 years, mean years of education: 14) also participated.

Patients with HD exhibited a characteristic neuropsychological profile involving executive dysfunction, performing significantly more poorly than controls on tasks assessing verbal fluency (FAS test total score: $t(23) = -4.265$, $p < .001$), working memory (digit ordering maximum span: $t(23) = -8.942$, $p < 0.001$) and inhibition (Stroop errors: $t(15.944) = 2.690$, $p = 0.016$).

2.2. Procedure

Three investigators selected stimuli for each emotional category (fear, happiness, core disgust and moral disgust). Control participants' ratings (Tables 1 and 2) indicated that stimuli were appropriate, as the target emotion for each individual category was always rated highly. Moral disgust stimuli did not feature imagery which may elicit core disgust (e.g. blood).

2.2.1. Emotive pictures

Twenty emotive pictures were selected from the International Affective Picture System [9]. There were four sets of five pictures selected to elicit happiness (e.g. children laughing), fear (e.g. a masked man with a knife), core disgust (e.g. a dirty toilet) or moral disgust (e.g. a drug addict after injecting).

Participants viewed each stimulus and rated their emotional response in terms of six basic emotions; anger, sadness, surprise, fear, happiness and disgust. The rating scale ranged from 0 to 9, with 0 indicating the participant felt the emotion was not relevant and 9 indicating that they felt the emotion was completely relevant.

Table 1
Mean and standard deviation of emotional ratings given by patients with HD and controls in response to pictures within the four emotional categories.

Rated emotion	Group	Emotional category (pictures)			
		Fear*	Happiness	Core disgust	Moral disgust
Happiness	Patients	1.49 (1.11)	**8.62 (0.88)**	0.51 (0.80)	0.14 (0.24)
	Controls	0.35 (0.53)	**8.17 (1.14)**	0.05 (1.73)	0.00 (0.00)
Sadness	Patients	1.00 (1.57)	0.32 (0.64)	1.62 (2.25)	3.69 (2.67)
	Controls	1.45 (1.13)	0.12 (0.28)	1.15 (0.96)	4.67 (2.54)
Surprise	Patients	4.26 (2.71)	1.43 (2.35)	4.18 (2.96)	3.95 (2.92)
	Controls	4.08 (3.00)	0.50 (1.01)	4.55 (2.78)	3.72 (2.41)
Fear	Patients	**5.51 (3.06)**	0.46 (0.89)	4.85 (2.96)	3.95 (2.92)
	Controls	**8.00 (0.84)**	0.13 (0.46)	2.98 (1.53)	3.77 (1.72)
Disgust	Patients	2.69 (2.32)	0.28 (0.83)	**5.51 (2.44)**	**6.11 (2.13)**
	Controls	1.62 (1.10)	0.00 (0.00)	**6.52 (1.13)**	**7.07 (1.42)**
Anger	Patients	3.77 (2.94)	0.26 (0.68)	2.95 (3.54)	5.48 (2.71)
	Controls	1.00 (1.14)	0.00 (0.00)	1.48 (1.16)	5.83 (1.73)

KEY: Mean (standard deviation).
Target emotions for each category are shown in bold.
*Significant group interaction $p < .003$ (adjusted for multiple comparisons).

Table 2
Mean and standard deviation of emotional ratings given by patients with HD and controls in response to scenarios within the four emotional categories.

Rated emotion	Group	Emotional category (scenarios)			
		Fear*	Happiness	Core disgust	Moral disgust
Happiness	Patients	0.12 (0.35)	**8.25 (1.25)**	0.05 (0.17)	0.00 (0.00)
	Controls	0.00 (0.00)	**8.60 (0.52)**	0.00 (0.00)	0.00 (0.00)
Sadness	Patients	1.47 (2.27)	0.10 (0.35)	1.93 (2.40)	2.85 (2.90)
	Controls	1.17 (1.56)	0.05 (0.17)	1.67 (2.27)	4.80 (2.55)
Surprise	Patients	4.75 (2.43)	4.45 (2.37)	4.03 (2.94)	3.75 (2.77)
	Controls	6.45 (2.40)	6.72 (1.33)	4.38 (2.84)	4.63 (2.69)
Fear	Patients	**6.50 (2.70)**	1.17 (0.42)	2.33 (2.98)	3.12 (3.87)
	Controls	**8.57 (0.64)**	0.70 (1.71)	1.22 (1.42)	3.00 (2.29)
Disgust	Patients	2.72 (3.17)	0.07 (0.23)	**6.80 (2.12)**	**6.42 (2.15)**
	Controls	1.13 (1.65)	0.00 (0.00)	**7.63 (1.05)**	**7.87 (1.04)**
Anger	Patients	4.43 (3.41)	0.05 (0.17)	5.00 (2.27)	7.23 (2.00)
	Controls	2.25 (2.23)	0.08 (0.29)	4.38 (2.05)	7.95 (1.23)

KEY: Mean (standard deviation).
Target emotions for each category are shown in bold.
*Significant group interaction $p < .003$ (adjusted for multiple comparisons).

2.2.2. Emotive scenarios

Twenty short vignettes were used, designed to predominantly elicit each of the following four emotions (five in each set); happiness (e.g. winning the lottery), fear (e.g. encountering a ferocious dog), core disgust (e.g. being vomited on by a drunk) and moral disgust (e.g. witnessing violence against an old woman). Fear, happiness and core disgust scenarios were written so that the reader was the subject of the experience. For moral disgust scenarios, adapted from stimuli used by Moll et al. [8], the reader witnessed another's experience as participants may have had difficultly imagining themselves partaking in morally aversive activities.

Participants read each vignette. They received the same instructions and used the same rating system and scale as described for the emotive pictures.

2.2.3. Statistical analysis

SPSS version 17 was used for statistical analysis. Split plot ANOVAs were conducted for pictures in each of the four emotional categories (between participants variable = group, within participants variable = emotion) for pictures and scenarios. Pair-wise comparisons were made using two-tailed independent samples *t*-tests and Pearson's correlations were calculated.

In order for the results of an ANOVA with a repeated measures factor to be trustworthy, the assumption of sphericity (equalities of variance for different levels of the within participants variable) must not be violated. When Mauchly's test for sphericity indicates this cannot be assumed, the Greenhouse-Geisser correction can be applied to correct for sphericity, by altering the degrees of freedom and so the significance value of the *F*-ratio. Greenhouse-Geisser correction has therefore been applied to the results of the current study where appropriate. Bonferroni correction for multiple comparisons has also been applied. As 15 comparisons were considered for each picture/scenario (all pair-wise comparisons between the six emotions), the significance value was adjusted to $p < .003$.

3. Results

Patients and controls did not differ significantly for age or education.

3.1. Emotive pictures

Table 1 shows the mean and standard deviation of the six emotion ratings (anger, sadness, surprise, fear, happiness and disgust) from patients and controls for emotive pictures by category (fear, happiness, core disgust and moral disgust). There was a main effect of emotion for each category (fear: $F(3.52, 23) = 40.65$, $p < 0.001$; happiness: $F(1.49, 23) = 324.00$, $p < 0.001$; core disgust: $F(2.91, 23) = 25.18$, $p < 0.001$; moral disgust: $F(3.49, 23) = 59.42$, $p < 0.001$). The target emotion for each category was given the highest mean rating by both patients and controls. Patients with HD showed more variation in emotional ratings for fear, core disgust and moral disgust stimuli than controls.

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For fear pictures there was no significant main effect of group on emotional ratings, but there was a significant interaction, $F(3.52, 23) = 6.64$, $p < 0.001$. *T*-tests indicated that patients' fear ratings were significantly lower for fear pictures than controls', $t(13.95) = -2.82$, $p = 0.014$. Their anger ratings were significantly higher, $t(15.78) = 3.15$, $p = 0.006$. However, these latter results are not significant with Bonferroni correction applied.

There were no significant main effects of group for happiness, core disgust, or moral disgust pictures. There were also no significant interactions.

3.2. Emotive scenarios

Table 2 shows the mean and standard deviation of the six emotions rated by patients and controls for scenarios by category. One patient did not complete this task.

There was a main effect of emotion for each emotional category (fear: $F(3.03, 22) = 64.08$, $p < 0.001$; happiness: $F(2.17, 22) = 330.27$, $p < 0.001$; core disgust: $F(3.23, 22) = 56.44$, $p < 0.001$; moral disgust: $F(3.23, 22) = 56.44$, $p < 0.001$). The target emotion for stimuli selected to elicit fear, happiness or core disgust was rated highest by control participants. For moral disgust scenarios, anger was the emotion rated highest overall by patients and controls; although controls' mean rating for the target emotion disgust was almost equivalent.

For fear scenarios there was no main effect of group, but there was a significant interaction, $F(3.03, 22) = 5.93$, $p = 0.001$. Patients' ratings for fear were lower than controls', $t(12.22) = -2.58$, $p = 0.024$, although this finding is not significant with Bonferroni correction applied. Patients' anger ratings were also higher for fear scenarios, although this difference was not significant.

There were no significant main effects of group for happiness, core disgust, or moral disgust scenarios. There were also no significant interactions.

3.3. Correlations

Pearson correlations were conducted to identify whether patients' lower fear ratings were linked to performance on executive tasks. With Bonferroni correction applied, there were no significant correlations.

4. Discussion

We report evidence of altered subjective fear responses in HD. Patients with HD were similar to controls in that they rated the target emotions for each emotional category higher than other emotions. However, there were significant differences between the groups for fear pictures and scenarios. Patients gave lower fear ratings than controls for pictures and scenarios selected to elicit this emotion. They also gave higher anger ratings in response to fear pictures.

Patients with HD gave lower disgust ratings for core and moral disgust stimuli, but these differences did not reach significance. This may be due to the sensitivity of the disgust stimuli used, or small sample size. Although the strongest emotion elicited in controls by core disgust stimuli was disgust, these ratings were not as high as those of fear for fear stimuli. The investigation of moral disgust may have been complicated by the high anger ratings given by both groups in response to moral disgust stimuli.

The consistency of fear deficits across the patient group was striking, especially as such difficulties are not thought to be an obvious consequence of striatal dysfunction. Recognition of fearful facial expressions is not as reliably impaired as recognition of disgusted expressions in HD (but see Ref. [5]). However, Sprengelmeyer et al. [7] found that two patients' self-assessment of their emotional experience indicated reduced fear experience. These patients also confused fearful and disgusted expressions and misreported disgusted faces as angry. It could be that patients in the current study exhibited higher anger ratings than controls for fear stimuli because they confused feelings of fear and anger. However, it is also possible that increased anger ratings could be linked to some of the emotional changes seen in HD, such as irritability and aggression. One limitation of the study was the lack of an instrument which assessed irritability and aggression in addition to anxiety and depression, which could also be linked to changes in emotional responsivity.

The reduced fear responses exhibited by patients with HD in the current study could reflect dysfunction of the amygdala. Lesions to this structure reduce fear in primates [10] and can affect the appraisal of pictures from the IAPS selected to elicit fear, in association with alterations in skin conductance responses [11]. The current study did not assess patients' skin conductance responses and it would be useful to do this in future research. However, the possibility of amygdala dysfunction in HD is supported by studies reporting structural changes to this region [12]. The amygdala projects to the ventral striatum, so possible amygdala dysfunction in HD could further implicate changes in frontostriatal pathways involving ventromedial prefrontal cortex, a region important for social cognition.

Another possibility is that patients' fear deficits reflect altered functioning of lateral orbitofrontal cortex. While one limitation of the current study is that patients' recognition of emotional expressions was not assessed, Henley et al. [5] found that poor fear recognition of fearful expressions in HD was associated with lateral orbitofrontal degeneration. This cortical region could play a role in the subjective appreciation of one's own fear as it is thought to be important for learning in relation to negative reinforcement. Lateral OFC is likely to form part of frontostriatal pathways involving the caudate, that is, the primary site of degeneration early in HD. Dysfunction of this region could therefore explain changes to fear responses in early stage patients.

The reduced subjective fear responses exhibited by patients with HD in the present study could be linked to difficulties recognising fear expressed by others. Some patients with HD exhibit increased irritability and outbursts of aggression, and a poor appreciation of others' negative emotional reactions to these disruptive behaviours could further impair patients' social interaction. The implications of these findings could therefore include poor correction of inappropriate social behaviour, and increased risk-taking due to inadequate emotional feedback.

In conclusion, patients with HD show reduced subjective fear responses to stimuli which elicit this emotion in controls. Further research should investigate whether deficits in fear experience are accompanied by changes in skin conductance response or impaired recognition of fear in others, and seek to determine the precise neural underpinnings of these changes.

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