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Review

Emotion recognition in Huntington's disease: A systematic review

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ABSTRACT

There is increasing interest in the nature of the emotion recognition deficit in Huntington's disease (HD). There are conflicting reports of disproportionate impairments for some emotions in some modalities in HD.

A systematic review and narrative synthesis was conducted for studies investigating emotion recognition in HD. Embase, MEDLINE, PsychINFO and Pubmed were searched from 1993 to 2010, and citations and reference lists were searched. 1724 citations were identified.

Sixteen studies were included. In manifest HD evidence of impaired recognition of facial expressions of anger was found consistently, although recognition of all negative emotions (facial and vocal) tended to be impaired. In premanifest HD impairments were inconsistent, but are seen in all facial expressions of negative emotion. Inconsistency may represent the variability inherent in HD although may also be due to between-study differences in methodology.

Current evidence supports the conclusion that recognition of all negative emotions tends to be impaired in HD, particularly in the facial domain. Future work should focus on using more ecologically-valid tests, and testing inter-modality differences.

Contents

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1. Introduction

Huntington's disease (HD) is an autosomal dominant neurodegenerative disorder caused by an expanded CAG repeat on chromosome 4. It is classically characterised by involuntary movements and cognitive and psychiatric deficits, with the onset of motor signs usually occurring in mid-adulthood. There is, however, often evidence for subtle cognitive and behavioural deficits ahead of these motor features (Lawrence et al., 1998; Snowden et al., 2002).

The ability to recognise emotions in others is a key social skill, and much work has focused on studying the expression and recognition of canonical emotions (happiness, sadness, fear, surprise, anger and disgust) which appear to be cross-cultural, and which it is argued have a biological basis (Ekman, 1992, 1993). More recently, attempts have been made to elucidate the neural substrates of emotion recognition, with lesion studies and functional brain imaging providing new insights into the pathways underlying this skill (e.g., Calder et al., 2004; Phillips et al., 1998; Scott et al., 1997); for a review see Adolphs (2002).

Over the last two decades there has been increasing interest in emotion recognition deficits in people with HD, and this interest is justified on both clinical and neurobiological grounds. HD is relatively common (Harper, 2002; Novak and Tabrizi, 2010) and has the potential for presymptomatic diagnosis (and therefore early intervention with disease-modifying therapies). These factors lend particular urgency to the search for biomarkers of brain dysfunction in HD, and emotion recognition is a promising candidate (Paulsen et al., 2006; Stout et al., 2011; Tabrizi et al., 2009). In addition, HD has contributed to the literature on models of emotion recognition, as associations are made between the behavioural deficits seen in the disease, and the affected brain regions.

An initial finding of disproportionately impaired recognition of facial expressions of disgust was found in people with early symptoms of the disease (Sprengelmeyer et al., 1996). This was followed by suggestions that facial disgust recognition might also be affected in premanifest gene carriers (Gray et al., 1997), and that recognition of disgust in other modalities, such as voices, taste and odours (Hayes et al., 2007; Mitchell et al., 2005), was also impaired. However other work has failed to replicate the disproportionate impairment in disgust recognition, instead suggesting that recognition of all negative emotions is broadly affected in HD (Henley et al., 2008; Johnson et al., 2007; Milders et al., 2003). The aim of this review was therefore to disambiguate the pattern of emotion recognition deficits in HD through a systematic appraisal of previous reports.

This review is warranted to better understand the nature and progression of cognitive impairment in HD, and how it might impact on people with HD and their carers. A better conceptualisation of the emotion recognition deficits in HD is important to improve understanding of the social interaction problems that occur in the disease. From this, more refined strategies for managing these problems might be developed. More fundamentally, the emotion processing deficit in HD and its brain mechanism may hold important clues to the pathophysiology of the disease. In particular, a selective deficit of emotion comprehension would (if substantiated) potentially predict a relatively specific pathophysiological and anatomical substrate which could in turn targeted as a biomarker of disease modification in future therapeutic trials (Henley et al., 2005; Tabrizi et al., 2009).

The purpose of this review was to appraise systematically the reported impairments in emotion recognition in HD. Such a review is warranted in order to assess the nature of the deficits reported, and to investigate whether differences in findings can be explained by disease-related factors, such as stage or CAG repeat length. The review aims to ask what conclusions can be drawn from the current literature about which emotions people with HD struggle to recognise, and in which modalities, as well as to identify areas for future research.

2. Methods

2.1. Criteria for considering studies for this review

2.1.1. Types of studies

In order to be eligible for inclusion in the review studies had to compare emotion recognition in a group of participants with Huntington's disease with a control group (i.e., quasi-experimental design). Emotion recognition was defined as any task in which

stimuli conveying emotional information were presented, and for which participants were asked to state or choose which emotion they thought was represented by the stimuli. The stimulus could be of any modality (e.g. visual, vocal) and of any form (e.g. static faces, videos). Any target emotions were considered. Studies in which participants were asked to match emotions within a modality were excluded (e.g. selecting a happy face in response to a happy face stimulus); success on this task might be achieved using perceptual features alone. Studies in which participants were asked to match emotions across a modality (e.g. selecting an angry face in response to an angry voice) were included as this cannot be solved purely on the basis of the perceptual features of the stimuli.

Studies looking exclusively at "mood" or emotion production, or semantic knowledge (e.g. about situations that might be expected to induce emotions) were excluded. Editorials, reviews, commentaries, letters or other articles that contained no original data were excluded.

2.1.2. Types of participants

The patient group had to consist of participants carrying the gene coding for Huntington's disease (Huntington's Disease Collaborative Research Group, 1993), confirmed by genetic analysis. This excluded any studies done before genetic testing was available, but ensured that findings were specific to this population.

Studies of both manifest (showing hard motor signs of HD) and premanifest (not yet showing hard motor signs of HD) participants were included. Manifest HD is conventionally defined as the point at which gene carriers develop hard motor signs. Clinically, this can be a useful way in which to define disease onset, although in practice more subtle motor, cognitive and behavioural deficits are usually present many years before this point (Huntington Study Group, 1996; Paulsen et al., 2008). The control group had to be neurologically normal participants. Studies of any participants aged 18 or over were included. Participants with onset prior to this age are likely to have very high CAG repeat lengths and a rapidly progressing disease process as well as immature emotion processing mechanisms, which may be qualitatively dissimilar to those in adults (Gao and Maurer, 2010; Kremer, 2002, pp. 43–44).

2.1.3. Types of measures

Studies must have reported a quantitative measure of emotion recognition.

2.2. Search methods for identification of studies

2.2.1. Electronic searches

Searches were run in the following databases: Embase (1993–July 2010), MEDLINE (1993–July 2010), PsychINFO (1993–July 2010) and PubMed (1993–July 2010).

Searches were limited from 1993 to the present day, as studies carried out prior to this would necessarily have included participants without genetically-confirmed HD.

The search used keywords "(Huntington* AND (emotion* OR cogniti* OR neuropsycho*)) NOT (mouse OR rat OR mice)". Using Ovid the search was run on Embase, MEDLINE and PsychINFO simultaneously and results were then deduplicated (a function within Ovid).

Only peer-reviewed published articles were accepted for inclusion in the review. Attempts were made to contact corresponding authors of all articles included in the review, either to ask for access to more demographic or experimental data, or to check queries about the study.

2.2.2. Searching other resources

For each study included in the review, manual searches of reference lists were conducted and a citation search was also conducted to identify further potential studies.

2.3. Data collection and analysis

2.3.1. Selection of studies

The initial searches identified 1724 citations (after deduplication). The title and abstract of each citation were examined independently by both SMDH and MJUN against the pre-specified inclusion and exclusion criteria listed above.

104 citations could not be excluded on the basis of the title and abstract alone (a proportion of these did not have an abstract available). The full text of these citations was obtained by SMDH to assess whether they fully met inclusion criteria. One additional citation was identified from the reference list and citation search.

2.3.2. Data extraction and management

Data were extracted to a standardised data collection form. This covered demographic information, details of emotion recognition tests, any background tests, results, and technical assessment.

2.3.3. Technical assessment

Study structure and technical characteristics were assessed according to a number of criteria: sample size and power analysis; the nature of the control group; reporting of demographic data, the nature of stimuli, stimulus presentation and response options; ways in which potential confounding variables were measured and addressed; appropriate statistics; and reporting of quantitative outcome data. Demographic data considered necessary in order to be able to compare groups adequately between studies were: age, gender, some measure of estimated IQ or educational level, and additionally in the gene-positive group, CAG repeat length, and some estimate of disease course e.g. disease duration, UHDRS motor score or an estimate of time to motor onset in premanifest subjects (e.g., Langbehn et al., 2004). (Note that these demographic data were considered desirable in order to assess studies fully, but these were not criteria for inclusion in the review overall.)

2.3.4. Data synthesis

Given that the data reviewed here were quantitative a meta-analytic approach was considered. Ultimately, however, a narrative synthesis was undertaken for two reasons. Firstly, although attempts were made to contact representatives of all the studies included in the review, some authors could not be contacted and this meant that quantitative results were not available for all studies. Secondly, the ways in which the HD cohorts varied between studies were not always clear (e.g. measures such as IQ, CAG repeat length, disease severity and duration were not always reported). This meant that it would not be possible to determine the extent to which differences in effect size were attributable to differences in these factors between the cohorts studied.

3. Results

3.1. Description of studies

3.1.1. Results of the search

Sixteen reports met full inclusion criteria. Appendix A summarises reasons for which 89 studies that met initial inclusion criteria were excluded after the full text was examined. Of the sixteen studies included, one or more individual experiments from five of them were subsequently excluded for not meeting criteria (see Appendix B).

3.1.2. Included studies

See Table 1
for characteristics of included studies.

3.1.2.1. Studies of facial emotion recognition. The majority of studies (14/16) included at least one test of facial emotion recognition (exceptions were Hayes et al. (2007) and Mitchell et al. (2005)). The two most commonly used face stimulus sets were 60 (or 24) static black and white images from the Ekman and Friesen battery (Ekman and Friesen, 1976), 10 (or four) each for happiness, sadness, surprise, disgust, anger and fear, henceforth "Ekman Faces"; and the set of 30 face images[1] morphing between these six canonical emotions from the FEEST (Young et al., 2002). In this latter test, the "Emotion hexagon", presentation of the 30 face stimuli is repeated over six blocks, with results from the first block subsequently discarded as practice trials. Three studies also included neutral face stimuli in at least one test (Johnson et al., 2007; Snowden et al., 2008; Tabrizi et al., 2009).

Two studies used the same brief (24-stimulus) version of Ekman Faces (Gray et al., 1997; Henley et al., 2008). Some researchers opted to replace or supplement these tests with their own stimuli in a similar format (e.g., Aviezer et al., 2009; Snowden et al., 2008). One study used colour video clips made by morphing between neutral and emotional still photographs (Montagne et al., 2006).

One study also included a test of emotion recognition from eye regions only (Snowden et al., 2008).

3.1.2.2. Studies of auditory emotion recognition. Five studies included tests of emotion recognition in the auditory modality, testing either short non-verbal vocal sounds (e.g. laughter, growls) or prosody of spoken phrases constructed from non-words. Three of these studies (Calder et al., 2010; Snowden et al., 2008; Sprengelmeyer et al., 2006) used stimuli taken from the same set of non-verbal vocal sounds (Scott et al., 1997). One study used their own non-verbal stimuli (Hayes et al., 2007), and two studies used the same "nonsense" word prosody recognition task (Sprengelmeyer et al., 1996, 2006).

3.1.2.3. Studies of emotion recognition in other modalities. One study included a test of emotion recognition of static black and white pictures portraying body language (Aviezer et al., 2009) and one, looking specifically at disgust recognition, tested recognition of pleasant and disgusting tastes and odours (Mitchell et al., 2005).

3.1.2.4. Response options. All the studies, with the exception of Mitchell et al. (2005) (investigating taste and odour perception) used a forced choice response paradigm, in which participants were given a limited set of written verbal emotion terms and asked to pick the one that best described the stimulus.

3.1.2.5. Study populations. Eight studies included a sample of premanifest HD gene carriers, and 10 included a sample of people with manifest HD (i.e., unequivocal motor signs). One study included both premanifest and manifest participants in the patient group (Aviezer et al., 2009).

Study populations were drawn from a range of countries, including the United Kingdom (7), Australia (4), Germany (3), Canada (3), The Netherlands (2), France (1) and the United States (1). Ethnicities of participants in each country were not reported in any study. Culturally, this is a relatively restricted sample, based almost entirely on Western/European (the majority English-speaking) countries.

[1] These images were based on the face known as 'JJ' from the Ekman and Friesen set.

3.2. Assessment of methodological factors

Study methodology was assessed in four distinct categories: choice of control group; reporting of key demographic data and results; stimulus type, presentation and response options; and reporting of statistical analysis, including discussion of power, potential confounding variables and the issue of multiple comparisons (Table 2).

3.2.1. Reporting of key demographic data and results

Huntington's disease is highly heterogeneous, and clinical presentation is known to depend on age and CAG repeat length (and their interaction); these explain some of the variance in age of motor onset (see e.g., Mahant et al., 2003; Rosenblatt et al., 2006). It is therefore important to be able to rule out differences in the clinical characteristics of cohorts as a potential cause of differences between study findings. In addition, factors such as age, education and intelligence, and possibly gender, may affect performance on cognitive tasks in both HD and control groups. The impact of these factors both within studies (between patient and control groups) and between studies needs to be taken into account when assessing differences in outcome. Consequently it is important for studies to report summary data for each of these variables, so that the effects (if any) of these potential confounders can be judged.

Four studies were considered to have reported adequate demographic data: age, gender, an index of intellectual ability, CAG repeat length, and an index of disease severity (Henley et al., 2008; Hennenlotter et al., 2004; Sprengelmeyer et al., 1996, 2006). Most others reported most of the above variables but many did not have CAG repeat data available; in these cases although participants had undergone genetic testing for confirmation of diagnosis, researchers had not always requested (or been granted access to) the exact CAG data. Some lacked an estimate of intelligence or educational level, although some authors were able to provide the extra data on request.

Also of note is the fact that studies varied in their definition of pathological CAG repeat length. Typically alleles of up to 35 repeats are considered normal, whilst alleles with 40 or more repeats are fully penetrant and the carrier is likely to show signs of HD within a normal lifespan. The intermediate repeat numbers (36–39) are not fully penetrant but there have been reports of 36 CAG repeats leading to the disease, and of people living into their 90s with 39 CAG repeats and no signs of HD (Rubinsztein et al., 1996). Whilst the majority of studies tend to include participants with a CAG repeat length of 40 or above, at least two included participants with CAG repeat lengths between 36 and 39 (Aviezer et al., 2009; Tabrizi et al., 2009), and not all report their criteria. This raises the possibility that some participants may not be representative of the more general HD population.

The majority of studies reported their findings in full (i.e., gave quantitative measures of central tendency and spread in each of the groups tested). A number of authors made their raw data available on request if they were not available in the published paper. Some authors preferred to report composite scores (Sprengelmeyer et al., 2006; Tabrizi et al., 2009), and were able to justify this, although this makes it difficult to draw direct comparisons between individual tests.

3.2.2. Choice of control group

Control groups were of three different kinds. Ten studies used healthy volunteers as controls; five used gene-negative controls from an HD environment (either people who had been at risk and tested negative for the HD gene, or partners of gene-positive participants); and one study used at-risk gene-negative controls who were unaware of their negative gene status when they completed the study tests.

Table 1
Characteristics of included studies.

Study	Demographic data				Stimuli & response options
		Control	*HD (premanifest & mild)*		
Aviezer et al. (2009) Expt. 1[a]	*N*	27	21		(1) 6 b&w pictures of body language, shown 3 times on computer; 6AFC, no time limit
	Age	49.2 (10.0)	48.3 (10.1)		(2) 40 Ekman faces, shown once on computer; 6AFC, no time limit
	Gender (%F)	56%	57%		
	CAG		42.85 (3.69)		
	Estimated IQ	–	–		
	UHDRS Motor		8.26 (8.02)		
	Country	Canada			
		Control	*Manifest HD*		(1) 60 Ekman faces, shown on computer for up to 3 s; 6AFC, no time limit
Calder et al. (2010) Study 1[b]	*N*	Varies from 20 to 52	21 (20 for morphs)		(2) 30 b&w morphs "Emotion Hexagon"; 5 blocks of 30 (plus practice block), each morph shown on computer for 5 s; 6AFC, no time limit
	Age	"Matched"	50.43 (8.7)		(3) 60 non-verbal vocal sounds; 6AFC, no time limit
	Gender (%F)	Varies	43%		
	CAG		Genetically confirmed in most participants		
	Estimated IQ	"Matched"	107.38 (8.40)		
	UHDRS Motor		30.45 (13.10)		
	Country	United Kingdom			
		Control	*Premanifest HD*		
Gray et al. (1997)	*N*	23	17 (2 early manifest)		(1) 24 Ekman faces, shown on card after 6 practice items; 6AFC, no time limit
	Age	38.26 (11.82)	38.53 (11.24)		
	Gender (%F)	–	–		
	CAG		–		
	Estimated IQ	–	–		
	UHDRS Motor		–		
	Country	United Kingdom			
		Control	*Manifest HD*		
Hayes et al. (2007)	*N*	14	14		(1) 40 non-verbal vocal sounds; 4AFC, no time limit
	Age	51.3 (9.25)	54.6 (11.16)		
	Gender (%F)	43%	43%		
	CAG		–		
	Years in education	11.8 (2.04)	11.8 (2.12)		
	Disease duration		6.7 (5.21)		
	Country	Australia			
		Control	*Manifest HD*		
Hayes et al. (2009)	*N*	14	14		(1) Emotion Hexagon (see Calder et al. entry, above)
	Age	51.8 (8.37)	54.6 (11.17)		(2) 35 b&w morphs based on Ekman faces, at different intensities ranging from 0 to 150%, 5 blocks of 35 (plus 5 practice stimuli), each morph shown on computer; 6AFC
	Gender (%F)	50%	43%		
	CAG		–		
	Years in education	11.8 (1.81)	11.8 (2.12)		
	Disease duration		6.7 (5.21)		
	Country	Australia			
		Control	*Premanifest*	*Manifest*	
Henley et al. (2008)	*N*	20	21	40	(1) 24 Ekman faces, shown on card after 6 practice items; 6AFC, no time limit
	Age	44.9 (10.5)	37.2 (7.9)	48.5 (9.6)	
	Gender (%F)	65%	52%	50%	
	CAG		42.2 (1.8)	43.7 (2.4)	
	Estimated IQ	106.2 (11.6)	103.2 (9.3)	105.3 (13.0)	
	UHDRS Motor	1.1 (0.9)	3.6 (4.0)	28.9 (12.6)	
	Country	United Kingdom			
		Control	*Premanifest HD*		
Hennenlotter et al. (2004)	*N*	9	9		
	Age	"Matched"	37.4 (5.4)		(1) Emotion Hexagon (see above)
	Gender (%F)	44%	44%		
	CAG		43.7 (1.7)		
	Estimated IQ	"Matched"	112.9 (11.1)		
	UHDRS Motor				
	Country	Germany			
		Control	*Premanifest HD*		
Johnson et al. (2007)	*N*	57	464		(1) 70 Ekman faces, shown on computer touch screen for up to 4 s after 7 practice trials using verbal labels instead of faces; 7AFC, up to 8 s to respond using touch screen
	Age, yr	43.01 (10.13)	41.43 (9.63)		
	Gender (%F)	61%	63%		
	CAG	<30	>39		
	Years in education	15.11 (2.29)	14.48 (2.59)		
	UHDRS Motor				
	Country	United States, Canada, Australia			

Table 1 (*Continued*)

Study	Demographic data				Stimuli & response options
		Control	*Premanifest HD*		
Kipps et al. (2007)	*N*	13	17		(1) Emotion Hexagon (see above)
	Age, yr	42.0 (11.4)	43.8 (10.0)		
	Gender (%F)	31%	47%		
	CAG	20 (3.3)	41 (2.8)		
	Estimated IQ	–	–		
	UHDRS Motor	3.6 (1.8)	6.4 (3.9)		
	Country	Australia			
		Control	*Premanifest*	*Manifest*	
Milders et al. (2003)	*N*	20	20	20	(1) 60 Ekman faces, shown on card; 6AFC, no time limit
	Age, yr	47.9 (9.3)	38.4 (9.5)	47.6 (8.45)	
	Gender (%F)	40%	65%	40%	
	CAG		–	–	
	Estimated IQ	109.0 (6.0)	110.1 (6.1)	105.8 (7.41)	
	Disease duration			6.5 (3.2)	
	Country	United Kingdom			
		Control	*Manifest HD*		
Mitchell et al. (2005)[c]	*N*	8 (6 for odours)	8 (6 for odours)		(1) 5 disgusting & 5 pleasant odours, presented once for up to 5 seconds; rate odour on 10 cm anchored line scale from very pleasant to very disgusting
	Age, yr	49.25 (4.86)	53.25 (7.25)		
	Gender (%F)	50%	50%		
	CAG		–		
	Estimated IQ	–	–		(2) 6 everyday foods, presented individually and then in 4 appropriate & 4 inappropriate pairings; rate taste as for expt. 1 above
	UHDRS Motor		–		
	Country	United Kingdom			
		Control	*Manifest HD*		
Montagne et al. (2006)	*N*	30	7		(1) colour videos (4 sets of 9 different intensities for each of 6 emotions), made by morphing stills from actors, presented in 9 blocks of increasing intensity (20–100%); 6AFC, no time limit
	Age, yr	39.0 (11.1)	46.4 (11.2)		
	Gender (%F)	53%	29%		
	CAG		–		
	Estimated IQ	–	–		
	UHDRS Motor		17.1 (6.2)		
	Country	The Netherlands			
		Control	*Manifest HD*		
Snowden et al. (2008)[d]	*N*	12	10		(1) 60 Ekman faces; 6AFC, no time limit
	Age, yr	57 (9)	47 (9)		(2) 60 Ekman faces; 2AFC, no time limit
	Gender (%F)	33%	50%		(3) 120 non-verbal vocal sounds (20 for each of 6 emotions); 6AFC, no time limit
	CAG		–		
	Estimated IQ	108.0 (6.7)	103.6 (10.7)		(4) 35 b&w faces, "Manchester" set (5 for each of 7 emotions plus 5 practice items); 7AFC, no time limit
	UHDRS Motor				
	Country	United Kingdom	20.6 (8.2)		(5) 35 b&w eye regions, "Manchester" set (as (4)); 7AFC, no time limit
		Control	*Manifest HD*		
Sprengelmeyer et al. (1996)	*N*	17	13 (11 for expts 2 & 3)		(1) Emotion Hexagon (see above)
	Age, yr	50.7 (14.3)	45.0 (7.6)		(2) 60 Ekman faces, shown on computer for up to 3 s; 6AFC, no time limit
	Gender (%F)	47%	54%		
	CAG		45.2 (4.9) ($N = 11$)		(3) 60 "nonsense" sentences spoken with emotional prosody; 6AFC, no time limit
	Estimated IQ	107.5 (10.0)	105.6 (10.7)		
	Disease duration		6.6 (2.5)		
	Country	Germany			
		Control	*Premanifest HD*		
Sprengelmeyer et al. (2006)	*N*	8 (6)[e]	14 (12)[e]		(1) 60 Ekman faces, shown on computer for up to 3 s; 6AFC, no time limit
	Age, yr	38.3 (14.5)	31.0 (8.5)		
	Gender (%F)	75%	64%		(2) Emotion Hexagon (see above)
	CAG	20.4 (3.8)	45.1 (4.0)		(3) 60 "nonsense" sentences spoken with emotional prosody; 6AFC, no time limit
	Estimated IQ	108.8 (9.7)	113.2 (8.1)		
	UHDRS Motor				(4) 60 non-verbal vocal sounds; 6AFC, no time limit
	Country	Germany			

Table 1 (*Continued*)

Study	Demographic data				Stimuli & response options
		Control	*Premanifest*	*Manifest*	
Tabrizi et al. (2009)[f]	*N*	123	120	123	(1) 70 Ekman faces, shown on computer touch screen for up to 4 s after 7 practice trials using verbal labels instead of faces; 7AFC, up to 8 s to respond using touch screen
	Age, yr	46.1 (10.2)	40.8 (8.9)	48.8 (9.9)	
	Gender (%F)	55%	55%	54%	
	CAG		43.1 (2.4)	43.7 (3.0)	
	Years in education[g]	4.0 (1.3)	3.9 (1.2)	3.6 (1.3)	
	UHDRS Motor		2.5 (1.6)	23.7 (10.8)	
	Country	Canada, France, The Netherlands, United Kingdom			

Note: "Ekman faces" are always black & white (see text) A hyphen denotes data not reported; an empty cell denotes variable not applicable; AFC = Alternative Forced Choice Attempts were made to contact representatives of all studies included in the review to resolve queries; responses were received from all authors other than Drs Hayes, Hennenlotter and Sprengelmeyer.

[a] CAG and UHDRS motor data provided by Dr Hillel Aviezer (personal communication).
[b] Discrepant age data and CAG confirmation provided by Prof Andy Calder (personal communication).
[c] Age and gender data provided by Dr Ian Mitchell (personal communication).
[d] IQ data provided by Dr Julie Snowden and Dr Jennifer Thompson (personal communication).
[e] Figures in brackets denote *N* at timepoints 2 and 3; data are given for all subjects at timepoint 1.
[f] CAG repeat length and UHDRS motor score provided by Prof Sarah Tabrizi and the Track-HD team (personal communication).
[g] UNESCO International Standard Classification of Education: Level 3 qualifications typically start at the end of compulsory education (after 11 years of schooling in the UK).

The rationale for using gene-negative or partner controls is that these people live in a similar social and emotional environment to people with HD; interacting with family members whose emotion recognition, and possibly expression, is impaired may impact on the controls' expression and recognition of emotion, and they are more likely than unrelated volunteers to be subject to similar stresses, and therefore have similar levels of anxiety and depression. In support of this, gene-negative controls in some studies have been shown to perform below "healthy" control level at facial emotion recognition (Gray et al., 1997; Henley et al., 2008; Sprengelmeyer et al., 2006). Use of a gene-negative control group therefore aims to minimise group differences attributable to social or emotional factors.

3.2.3. Stimulus type, presentation and response options

As mentioned above, the majority of studies used very similar stimulus sets. Facial stimuli were usually based on the Ekman and Friesen set (Ekman and Friesen, 1976). However there are a number of variations of this: whether simple faces or the Emotion Hexagon are used, whether or not neutral faces are included, and the overall number of stimuli used. Only two studies included non-Ekman facial stimuli, one using a similar black and white static set (Snowden et al., 2008) and one making their own colour videos from actors (Montagne et al., 2006).

Similarly, studies of vocal emotion recognition tended to use stimuli drawn from the same set (either a set of non-verbal vocal sounds, see Scott et al. (1997), Calder et al. (2004), or the prosodic stimuli used by Sprengelmeyer et al. (1996)). One exception was Hayes et al. (2007) where it seems that novel non-verbal vocal stimuli were used.

There were a number of subtle variations of presentation and response options, particularly pertinent to facial stimuli as these are not naturally time-limited (as auditory stimuli are). Some faces were presented for a limited time, others were presented until participants had made a choice. As mentioned above, in the Emotion Hexagon test each stimulus is repeated six times (responses from the first presentation being discarded as practice items), whereas in simple face tests each stimulus is presented only once.

Most studies did not impose a fixed time to respond, but two limited the time available in which a response could be made (Johnson et al., 2007; Tabrizi et al., 2009). All studies of facial and vocal emotion recognition used an alternative forced choice (AFC) response paradigm, but they varied in the choices given. Most gave the same number of response options as there were emotion categories (e.g. if six different emotions were presented, there would be six response options). One deliberately reduced the number of responses (Snowden et al., 2008) in order to evaluate performance when task demands were decreased. One study used a 6AFC response when only four different emotions were represented in the stimuli (Aviezer et al., 2009).

3.2.4. Statistical analysis

3.2.4.1. Power analysis and sample size. Only two studies reported considerations of power and sample size calculation (Johnson et al., 2007; Tabrizi et al., 2009). These were the two largest studies (over 100 participants in the patient groups), and both had calculated that they were adequately powered to detect relatively small effects in premanifest and manifest HD populations. Sample sizes in the remaining studies ranged from six (Mitchell et al., 2005, odour test) to 40 (Henley et al., 2008).

3.2.4.2. Potential confounding variables. Potential confounding variables were dealt with in a number of different ways. Almost all studies reported gender, age and some measure of estimated premorbid intelligence or educational level. Most of these reported that groups were "matched" for one or more of these variables, and some, but not all, reported a statistic to confirm that there were no statistically significant differences between groups. Four studies included some or all of these variables as covariates in their analysis (Henley et al., 2008; Johnson et al., 2007; Milders et al., 2003; Tabrizi et al., 2009).

Almost all studies that tested facial emotion recognition included a standard test of face recognition[2] and sometimes a test of visual acuity or contrast sensitivity, and other visual or face processing tasks (the exception was Tabrizi et al. (2009), which was designed to assess potential biomarkers, rather than to test facial emotion recognition *per se*). One study excluded two participants with poor acuity (Aviezer et al., 2009), and no other studies reported impairments in basic visual skills. Six studies reported that performance on the Benton Facial Recognition Test was significantly worse in HD groups than control groups. Two took this into account in their analysis: one adjusted for facial recognition ability by including Benton score as a covariate in the analysis (Henley et al., 2008) and one investigated whether Benton scores correlated with emotion recognition scores (Snowden et al., 2008). The others did not take poor Benton performance into account in the emotion recognition analysis although mean (SD) Benton data in most cases

[2] Benton Facial Recognition Test (Benton et al., 1978).

Table 2
Technical assessment.

Study	Control type	Power analysis / sample size	Normality of data considered	Multiple comparisons addressed	Confounders measured and controlled for
Aviezer *et al.* 2009	■	■	■	■	■
Calder *et al.* 2010	■	■	■	■	■
Gray *et al.* 1997	■	■	■	■	■
Hayes *et al.* 2007	■	■	■	■	■
Hayes *et al.* 2009	■	■	■	■	■
Henley *et al.* 2008	■	■	■	■	■
Hennenlotter *et al.* 2004	■	■	■	■	■
Johnson *et al.* 2007	■	■	■	■	■
Kipps *et al.* 2007	■	■	■	■	■
Milders *et al.* 2003	■	■	■	■	■
Mitchell *et al.* 2005	■	■	■	■	■
Montagne *et al.* 2006	■	■	■	■	■
Snowden *et al.* 2008	■	■	■	■	■
Sprengelmeyer *et al.* 1996	■	■	■	■	■
Sprengelmeyer *et al.* 2006	■	■	■	■	■
Tabrizi *et al.* 2009	■	■	■	■	■

Control type: ■ = gene-negative/spouses; ■ = gene negative unaware of status; ■ = healthy volunteers.
Power analysis/sample size: ■ = analysis performed; ■ = no analysis performed.
Normality of data considered: ■ = discussed, and stats adapted accordingly; ■ = stats adjusted for inhomogeneity of variance only; ■ = not discussed.
Multiple comparisons addressed: ■ = discussed and addressed; ■ = not discussed.
Confounders measured and controlled for: ■ = effect of potentially confounding variables taken into account in analysis; ■ = effect of some potentially confounding variables taken into account in analysis; ■ = not considered.

suggest that some participants may have been fallen into the "moderately impaired" range. In two studies in which a group difference was not found on the Benton, some HD participants still scored in the "moderate impairment" or "severe impairment" range although this is not commented on (Aviezer et al., 2009; Gray et al., 1997). In addition to those studies that reported group differences in Benton score, one study included Benton as a covariate in the main analyses although did not report whether group differences were statistically significant (Johnson et al., 2007).

Studies that included auditory stimuli did not report testing auditory perception. The one study that investigated taste and olfactory recognition tested olfactory identification and threshold and excluded two HD participants from the olfactory experiment on the basis of poor performance (Mitchell et al., 2005).

Overall, potential confounding variables were not always dealt with satisfactorily. Very few studies adjusted for demographic variables despite the fact that non-statistically significant between-group differences in demographic variables can still materially impact on between-group differences in other variables (Johnson et al., 2007). Additionally, in some cases it seems likely that poor facial recognition skills in one or two HD participants may have impacted on the emotion recognition scores for the group as a whole.

3.2.4.3. Normality of data. The majority of studies noted that data did not meet assumptions needed for parametric statistics. Many cited ceiling effects and used non-parametric tests (e.g. techniques such as Mann-Whitney tests, or using bootstrap confidence intervals), whilst some just acknowledged heterogeneity of residual variance between groups and used appropriate statistics for this.

Five studies used parametric statistics and did not discuss whether the data were normally distributed (Aviezer et al., 2009; Hayes et al., 2007; Milders et al., 2003; Mitchell et al., 2005; Montagne et al., 2006). One study used non-parametric statistics for behavioural data, but opted to use parametric statistics for analysis of untransformed mean reaction time data, although it would seem likely that such data might have been positively skewed (Sprengelmeyer et al., 2006).

3.2.4.4. Multiple statistical comparisons. All studies reported several statistical comparisons. Three studies reported Bonferroni-corrected results (controlling the false positive rate across a number of comparisons) (Calder et al., 2010; Hayes et al., 2007; Milders et al., 2003). Three studies discussed the increased risk of false positives but preferred to maximise power by reporting uncorrected results (Henley et al., 2008; Snowden et al., 2008; Sprengelmeyer et al., 2006). The remaining ten studies did not discuss this issue.

3.2.4.5. Reporting of analysis and results. The majority of studies reported their analysis and test results clearly. Most studies reported two-tailed tests. Four studies chose to use one-tailed tests for some or all of their comparisons based on *a priori* predictions that the HD group would, on average, do worse than controls (Gray et al., 1997; Hennenlotter et al., 2004; Kipps et al., 2007; Sprengelmeyer et al., 2006) although Sprengelmeyer et al. (2006) still report one test in which the HD group outperformed the control group.

3.3. Outcomes

Outcomes are described separately for manifest and premanifest populations as this is how the majority of studies were designed. As discussed above, this is a somewhat arbitrary distinction, based on an assessment of motor symptoms. There is inevitably variation between clinicians with regard to when symptoms are judged sufficient to make a diagnosis of manifest disease, and different studies use different cut-off points to define this. Aviezer et al. (2009) included both manifest and premanifest participants in a single group in their study. Examination of their data shows that nine out of 21 participants who completed the study had a UHDRS motor score of five or less, a cut-off used elsewhere to discriminate between manifest and premanifest participants (Tabrizi et al., 2009). Therefore since the majority of participants had clear signs of the disease, Aviezer et al.'s results are reported below as representing manifest HD.

Outcomes are described as statistically significant if they were reported as such in the original study. The majority of studies set $p < 0.05$ as the cut-off for statistical significance. As reported above, studies varied as to whether or not they adjusted this cut-off for multiple comparisons. Therefore in studies that opted to use a Bonferroni-type correction larger effect sizes will have been required in order for a result to be reported as statistically significant, relative to studies that did not opt to use this correction.

3.3.1. Facial emotion recognition

In participants with manifest HD the most consistent evidence of impairment was shown for recognition of facial anger: statistically significant effects were found in every study that included a test for it. Evidence of disgust recognition impairment was also found in almost every study that tested it. The only exception was Snowden et al. (2008) in a task in which they gave a two-alternative forced choice response option to the Ekman faces, instead of the usual six (i.e., they reduced task demands); anger and fear recognition were still impaired in this condition. Evidence that fear recognition was impaired was often found, although only using Ekman stimuli (not moving facial stimuli (Montagne et al., 2006), or a non-Ekman stimulus set, the "Manchester" set, a different, locally-made set of black-and-white static emotion faces (see Snowden et al., 2008)). Sadness and surprise recognition were found to be impaired less often, whilst a statistically significant impairment in happiness recognition was only found by two groups (Calder et al., 2010; Hayes et al., 2009) (Table 3).

In premanifest participants a statistically significant impairment in disgust recognition was most frequently reported and was seen in five out of eight studies. Three of these reported evidence that disgust was selectively impaired (Gray et al., 1997; Hennenlotter et al., 2004; Sprengelmeyer et al., 2006), whilst two found an impairment across negative emotions (Johnson et al., 2007; Tabrizi et al., 2009). Sprengelmeyer et al. (2006) also reported evidence of a deficit in surprise recognition at the third of three timepoints tested. The remaining three studies found no evidence of impairment at all in premanifest participants, although one study explained a finding of impaired happiness recognition as an artefact of the ceiling effect in controls for that emotion (Henley et al., 2008).

Snowden et al. (2008) found evidence that manifest HD participants were impaired at recognising sadness and disgust from the eye regions alone (Table 3).

3.3.2. Vocal emotion recognition

In manifest participants evidence of an impairment in vocal disgust recognition was found consistently (four out of four studies) for both short non-verbal vocal sounds and speech prosody. Anger recognition was found to be statistically significantly impaired in the three studies using non-verbal vocal sounds, but not for prosody. Evidence of an impairment in fear recognition was also found in three out of four studies, including both non-verbal vocal sounds and prosody. Using prosodic stimuli, statistically significant impairments were also reported for recognising surprise and happiness (Sprengelmeyer et al., 1996) although no other studies reported evidence of deficits in these emotions. No studies reported statistically significant impairments in recognising sadness from vocal sounds (Table 4).

Only one study tested vocal emotion recognition in a premanifest cohort (Sprengelmeyer et al., 2006) and reported no evidence of impairments at any of three timepoints tested, using a combined score from sounds and prosodic stimuli (Table 4).

3.3.3. Recognition of emotion in other modalities

Aviezer et al. (2009) found no evidence that their HD population was impaired at recognising sad, disgusted or angry body language. Some of the body language stimuli contained semantic clues (dirty underwear for disgust, and a gravestone for sadness). It is possible that people with HD were able to label the images based

Table 3
Facial emotion recognition results.

Population	Study	Stimuli	Ha	Sa	Su	Di	An	Fe	Ne
Manifest HD	Aviezer et al. (2009)	Ekman faces	○	○		●	●		
	Calder et al. (2010)	Ekman faces	●	●	●	●	●	●	
		Emotion hexagon	●	●	●	●	●	●	
	Hayes et al. (2009)	Emotion hexagon	○	●	●	●	●	●	
		Ekman faces at different intensities	○	●		●	●	●	
	Henley et al. (2008)	Ekman faces	○	○	●	●	●	●	
	Milders et al. (2003)	Ekman faces	○	●	○	●	●	●	
	Montagne et al. (2006)	Videos at different intensities	○	○	○	●	●	●	
	Snowden et al. (2008)	Ekman faces (6AFC)	○	●	●	●	●	●	
		Ekman faces (2AFC)	○	○	○	○	●	●	
		Manchester faces	○	○	○	●	●	○	○
	Sprengelmeyer et al. (1996)	Emotion hexagon	○	●	●	●	●	●	
		Ekman faces	○	●	●	●	●	●	
	Tabrizi et al. (2009)	Ekman faces	(○)	(●)	(○)	(●)	(●)	(●)	(○)
Manifest HD	Snowden et al. (2008)	Manchester eyes	○	●	○	●	○	○	○
Premanifest HD	Gray et al. (1997)	Ekman faces	○	○	○	●	○	○	
	Henley et al. (2008)	Ekman faces	●	○	○	○	○	○	
	Hennenlotter et al. (2004)	Emotion hexagon	○	○	○	●	○	○	
	Johnson et al. (2007)	Ekman faces	○	●	○	●	●	●	○
	Kipps et al. (2007)	Emotion hexagon	○	○	○	○	○	○	
	Milders et al. (2003)	Ekman faces	○	○	○	○	○	○	
	Sprengelmeyer et al. (2006)[a]	Ekman faces + Emotion hexagon	○	○	(●)	●	○	○	
	Tabrizi et al. (2009)[b]	Ekman faces	(○)	(●)	(○)	(●)	(●)	(●)	(○)

Key: Ha = happiness; Sa = sadness; Su = surprise; Di = disgust; An = anger; Fe = fear; Ne = neutral. ● = between-group difference; ○ = no between-group difference; blank = not tested.

[a] Result in brackets only found at timepoint 3.

[b] Composite "negative emotion" score tested.

on previously acquired semantic knowledge, rather than recognition of the emotion conveyed by the body postures of the models. Mitchell et al. (2005) reported that their manifest HD cohort tended to rate unpleasant odours and taste combinations as less disgusting than controls, and that this difference was statistically significant. However this study differed from those for the facial and vocal modalities in using subjective ratings, rather than categorisation of an objective stimulus; mean ratings suggest that participants with HD were still able to discriminate between pleasant and less pleasant stimuli, which makes it hard to draw inferences about more specific recognition impairments in this paradigm (Table 5).

3.3.4. Cross-modal comparisons

Several studies included tests of emotion recognition in more than one modality, although they only report independent statistics for group differences in each modality (i.e., they do not directly statistically compare performance between modalities). Aviezer et al. (2009) reported that anger and disgust recognition from Ekman faces was statistically significantly impaired in the absence of impairments in recognising emotional body language. Calder et al. (2010) found evidence of a global impairment in recognising the six canonical emotions from Ekman faces, but evidence that only disgust, anger and fear recognition were impaired from non-verbal vocal sounds. A similar pattern was shown by Snowden et al. (2008) using the same face stimuli: recognition of all emotions except happiness was statistically significantly impaired with facial stimuli, whilst only disgust, anger and fear were impaired with non-verbal vocal sounds. However using a different set of faces Snowden et al. (2008) reported evidence of impairment only for disgust and anger recognition. In the study of Sprengelmeyer et al. (1996) subjects showed evidence of impaired recognition of surprise, disgust and fear from both facial expressions and prosody, but impaired sadness and anger recognition only from facial expressions. In a premanifest cohort, evidence of a selective impairment recognising the facial expression of disgust was found in the absence of impairments for the other five canonical facial emotions, or any deficits in recognising emotions from sounds or prosody (Sprengelmeyer et al., 2006).

3.3.5. Disproportionate deficits in recognition of specific emotions

Early reports suggested that HD gene carriers (both manifest and premanifest) were disproportionately impaired at recognising disgust, both using faces and prosody (Gray et al., 1997; Sprengelmeyer et al., 1996). Sprengelmeyer et al. (1996) tested this statistically, expressing manifest HD scores as a proportion of the mean score in controls (to adjust for emotion difficulty)

Table 4
Vocal emotion recognition results.

Population	Study	Stimuli	Ha	Sa	Su	Di	An	Fe	Ne
Manifest HD	Calder et al. (2010)	Non-verbal vocal sounds	○	○	○	●	●	●	
	Hayes et al. (2007)	Non-verbal vocal sounds		○		●	●	○	
	Snowden et al. (2008)	Non-verbal vocal sounds	○	○	○	●	●	●	
	Sprengelmeyer et al. (1996)	Prosody	●	○	●	●	○	●	
Premanifest HD	Sprengelmeyer et al. (2006)	Prosody + non-verbal vocal sounds	○	○	○	○	○	○	

Key: Ha = happiness; Sa = sadness; Su = surprise; Di = disgust; An = anger; Fe = fear; Ne = neutral. ● = between-group difference; ○ = no between-group difference; blank = not tested.

Table 5
Emotion recognition in other modalities.

Population	Study	Stimuli	Ha	Sa	Su	Di	An	Fe	Ne
Manifest HD	Aviezer et al. (2009)	Body language		○		○	○		
	Mitchell et al. (2005)	Odours				●			
		Tastes				●			

Key: Ha = happiness; Sa = sadness; Su = surprise; Di = disgust; An = anger; Fe = fear; Ne = neutral. ● = between-group difference; ○ = no between-group difference; blank = not tested.

and comparing disgust recognition with the next worst recognised emotion, fear. Disgust recognition was statistically significantly worse than fear recognition for Ekman Faces, Emotion Hexagon, and prosodic stimuli; HD participants scored at or below chance level. Sprengelmeyer et al. (2006) also report that in a premanifest cohort facial disgust recognition was the only emotion to be statistically significantly impaired relative to controls, and that 5/12 gene carriers were only impaired (judged by z scores) at disgust, whilst the other seven participants were either unimpaired, or globally impaired. Three other studies report selective or disproportionate impairments in disgust recognition. Gray et al. (1997) and Hennenlotter et al. (2004) both found evidence that facial disgust recognition was the only emotion impaired in premanifest cohorts, although this was not assessed statistically in relation to other emotions. Hayes et al. (2007) reported that more HD participants had *z* scores of >−1.56 (and more scored at levels judged consistent with chance) for non-verbal vocal disgust recognition than for any other vocal emotion, although again, differences between emotions were not assessed statistically.

Most other studies do not report selective or disproportionate impairments in disgust recognition. Hayes et al. (2009) tested differences between emotions and found no evidence that one was more impaired than any other (Ekman Faces and Emotion Hexagon). Henley et al. (2008) compared emotion recognition performance statistically (adjusting for control scores) and found recognition of anger to be disproportionately impaired (Ekman Faces). Milders et al. (2003) found evidence that recognition of disgust was less impaired than recognition of anger, fear and sadness (Ekman Faces). Snowden et al. (2008) reported either no evidence of impairment of disgust recognition (Ekman Faces with 2AFC), or that no patient got their worst scores at disgust recognition (Ekman Faces with 6AFC); when assessed statistically, disgust recognition in their HD group was no worse (and in one case was better) than fear and anger recognition both for the Manchester faces and eyes set (see Section 3.3.1), and for non-verbal vocal sounds. Other studies did not test inter-emotion differences statistically but argued that the pattern of findings did not support a disproportionate impairment of disgust recognition (e.g., Aviezer et al., 2009; Calder et al., 2010, who found a greater number of HD participants impaired at anger across all tasks; Johnson et al., 2007; Montagne et al., 2006).

3.3.6. *Within-modality stimulus type comparisons*

Many studies used both the "Ekman Faces" set, as well as the "Emotion Hexagon". Calder et al. (2010) reported similar deficits (across all emotions except happiness) with both stimulus sets. Hayes et al. (2009) found evidence that sadness, surprise, disgust, anger and fear recognition were impaired using both the Emotion Hexagon, and Ekman Faces at varying intensities, although happiness was only impaired on the Ekman Faces set, and no impairment was seen for 25% and 50% sad Ekman Faces. Snowden et al. (2008) compared the Ekman Faces set 6AFC, with 2AFC, an alternative face set, and eye regions only. They reported a statistically significant recognition deficit across all emotions except happiness using Ekman Faces, reduced to anger and fear recognition deficits when the task was simplified (2AFC), whilst only disgust and anger recognition were impaired on the alternative "Manchester" set, and sadness and disgust recognition using eye regions only.

3.3.7. *Summary*

Disgust, anger and fear recognition were most often impaired in manifest HD populations, across modalities. For face recognition, the most frequently tested modality with the most consistency in stimulus presentation, a deficit in anger recognition was found in all the studies in which it was tested. In premanifest populations deficits are more commonly seen for disgust recognition than any other emotion, but only in the facial modality. Whilst disgust recognition appears disproportionately impaired in some HD populations, this is not true of all populations tested, nor across modalities. Outcome varies depending on the type of stimulus used (even within a modality).

4. Discussion

Certain general conclusions emerge from this review of studies of emotion recognition in HD. Considering firstly the most widely used emotional stimulus (facial expressions), anger recognition appears to be most consistently impaired in manifest HD populations, closely followed by recognition of disgust and fear, whereas recognition of sadness and surprise are less consistently affected, and recognition of happiness only rarely affected. Individuals with pre-manifest HD may exhibit no detectable deficit; however, if there is an impairment of emotion recognition this is likely to affect disgust or recognition of negative facial emotions more generally. Deficits of facial emotion recognition become more likely, more severe and more widespread with the conversion from premanifest to manifest disease. However, the lack of uniformity in measures of disease stage and severity across studies precludes a precise statement about the time course or profile of these deficits; this is one of the biggest weaknesses in the literature. HD is known to be highly heterogeneous, and clearly this natural clinical variability may underlie many of the inter-study differences reported here, meaning that where differences do exist, they are not necessarily contradictory. Nevertheless, between-group differences in levels of potential confounds (e.g. CAG repeat length, or severity) may also underlie differences in behavioural findings, and until these confounds are reported consistently this will be impossible to judge.

In line with early work in the field, initial evidence suggested that that impaired recognition of facial expressions of disgust occurs early in HD (Gray et al., 1997; Hennenlotter et al., 2004; Sprengelmeyer et al., 2006); however, two large studies have suggested that this deficit may occur in the context of a more widespread impairment affecting negative emotions, even early in the course of premanifest stages of disease (Johnson et al., 2007; Tabrizi et al., 2009). In manifest HD, most studies do not suggest a disproportionate defect of a particular emotion when recognition of different emotions is compared directly, though negative emotions are generally affected more severely than the positive/ambiguous emotions of happiness and surprise. Taken together the evidence

suggests that recognition of various negative emotions may be affected from an early stage in HD, and that impairments worsen across emotions as disease evolves.

Information about recognition of emotions via other sensory channels in HD remains too limited for firm conclusions to be drawn. However, at least for vocal emotion recognition, the picture emerging is broadly convergent with the data for facial expressions. In studies of manifest HD recognition of vocal disgust is consistently impaired, although recognition of vocal anger and fear are often also impaired. Evidence concerning the relative degree of impairment for particular vocal emotions is conflicting (Calder et al., 2010; Hayes et al., 2007; Snowden et al., 2008; Sprengelmeyer et al., 1996). The few data available for premanifest HD have not provided evidence of an early deficit of vocal emotion recognition. This pattern suggests that, as for facial expression, impaired recognition of vocal expressions in HD may become more salient with evolving disease and may be more marked for negative than for positive emotions. It is likely that there are modality-specific factors here: for example, the apparent preservation of recognition of vocal (in contrast to facial) expressions of sadness may mean that sadness is intrinsically easier to recognise from auditory than from visual cues (Rohrer et al., 2010) or that different sensory modalities are differentially affected in HD. However, inter-modality differences have yet to be evaluated statistically.

These findings have important clinical implications. One key implication is that emotion recognition could potentially serve as a biomarker of disease onset and progression in HD. Emotion scores (both composites and individual emotions) are already included in the two largest ongoing longitudinal studies, PREDICT-HD (Paulsen et al., 2006) and Track-HD (Tabrizi et al., 2009) and further work should demonstrate how sensitive emotion recognition is at tracking decline over time, relative to other potential markers.

From the perspective of the individual patient with HD, these results clearly show that manifest HD is associated with impaired recognition of negative emotions. Furthermore, subtle impairments of emotion processing can be detected many years before motor onset. There is little formal evidence concerning the impact of emotional deficits on the social functioning of people with HD. However, the results of this analysis suggest the potential for some compensation if multiple (especially non-facial) channels can be used to convey emotional information to people with HD.

There are important limitations on an analysis of this kind. The review was limited to peer-reviewed publications: an important potential source of bias in attempting to estimate the overall significance of emotion recognition deficits in HD. In addition, the size and comprehensiveness of the studies included in the review varied widely. Small studies are potentially under-powered to detect small effects or to adjust for confounding factors (particularly for non-standard data distributions), whilst in large studies it may be more difficult to tailor assessments to particular kinds of deficits or to assess deficits comprehensively. A further source of variation between studies is linked to the different paradigms used to assess emotion recognition, even within a modality (e.g., facial expressions); using different stimulus sets does lead to divergent findings (Snowden et al., 2008) and our understanding of emotion processing mechanisms remains too rudimentary to offer a principled account of this.

This review suggests certain clear directions for further work. There is a need for large, longitudinal studies of emotion comprehension in HD that are informed by emerging neurobiological data and which use consistent measures of disease stage and overall severity as well as uniform assessment instruments. In future studies it will be important to compare emotion processing in different sensory modalities statistically, and at different levels of response (autonomic as well as cognitive); and to extend the assessment to include more ecological kinds of emotion processing beyond the relatively artificial scenario of the forced-choice recognition protocol. There is also a need to understand how these deficits, and the other cognitive difficulties noted in this disease, impact on patients' everyday lives. The data that are currently available suggest that there is no 'magic bullet' of selective emotional impairment that is specific or selective for HD. On the other hand, the data provide grounds for some optimism that emotion comprehension is a useful paradigm of disease onset and progression in HD. Like other diseases, HD will almost certainly benefit from the exciting progress currently being made in the basic neuroscience of human emotion. However, the study of patients with HD could also inform this enterprise, and the structural and functional anatomical bases for altered emotion processing in HD should be addressed in hypothesis-led studies motivated by the neuropsychological data. As neuropsychological metrics of clear relevance to patients' everyday lives, there is an overarching need further to evaluate emotion processing measures as potential biomarkers for symptomatic and disease-modifying therapies in this devastating disease.

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Appendix A. Articles that did not meet search criteria

Reference	Reason for exclusion
Nabilone shows potential for symptomatic relief of Huntington's disease (2008). *Pharmacy in Practice, 18,* 183.	RCT for drug treatment, No emotion recognition tasks in battery.
Abel, C. G., Stein, G., Arakaki, T., Mancuso, M., Nano, G., Garretto, N. et al. (2007). Decision making ability assessment in patients with basal ganglia and cerebellum subcortical syndromes: Parkinson, Huntington and isolated degenerative cerebellar diseases. [Spanish]. *Revista Neurologica Argentina, 32,* 20-34.	Includes social cognition tests but they are Theory of Mind and gambling, not emotion recognition.
Arango-Lasprilla, J. C., Rogers, H., Lengenfelder, J., Deluca, J., Moreno, S., & Lopera, F. (2006). Cortical and subcortical diseases: do true neuropsychological differences exist? *Arch.Clin.Neuropsychol., 21,* 29-40.	No emotion recognition tasks in battery.

Appendix A (*Continued*)

Reference	Reason for exclusion
Bachoud-Levi, A. C., Maison, P., Bartolomeo, P., Boisse, M. F., Dalla, B. G., Ergis, A. M. et al. (2001). Retest effects and cognitive decline in longitudinal follow-up of patients with early HD. *Neurology, 56,* 1052-1058.	No emotion recognition tasks in battery.
Baker, J. G. (1996). Memory and emotion processing in cortical and subcortical dementia. *J.Gen.Psychol., 123,* 185-191.	Summary of old research, nothing novel.
Bales, K. R. (2004). Neurodegenerative disease research in the 21st century. *Drug Discovery Today, 9,* 553-556.	Conference review.
Bamford, K. A., Caine, E. D., Kido, D. K., Cox, C., & Shoulson, I. (1995). A prospective evaluation of cognitive decline in early Huntington's disease: functional and radiographic correlates. *Neurology, 45,* 1867-1873.	No emotion recognition tasks in battery.
Barquero-Jimenez, M. S. & Gomez-Tortosa, E. (2001). [Cognitive disorders in patients with Huntington's disease]. *Rev.Neurol., 32,* 1067-1071.	No emotion recognition tasks in battery.
Baudic, S., Maison, P., Dolbeau, G., Boisse, M. F., Bartolomeo, P., Dalla, B. G. et al. (2006). Cognitive impairment related to apathy in early Huntington's disease. *Dement.Geriatr.Cogn Disord., 21,* 316-321.	No emotion recognition tasks in battery.
Berrios, G. E., Wagle, A. C., Markova, I. S., Wagle, S. A., Rosser, A., & Hodges, J. R. (2002). Psychiatric symptoms in neurologically asymptomatic Huntington's disease gene carriers: a comparison with gene negative at risk subjects. *Acta Psychiatr.Scand., 105,* 224-230.	No emotion recognition tasks in battery.
Blackmore, L., Simpson, S. A., & Crawford, J. R. (1995). Cognitive performance in UK sample of presymptomatic people carrying the gene for Huntington's disease. *J.Med.Genet., 32,* 358-362.	No emotion recognition tasks in battery.
Bodner, T., Jenner, C., Benke, T., Ober, A., Seppi, K., & Fleischhacker, W. W. (2001). Intoxication with riluzole in Huntington's disease. *Neurology, 57,* 1141-1143.	Case report.
Bonelli, R. M. & Kapfhammer, H. P. (2003). Why minocycline is helpful in Huntington's disease. *J.Psychopharmacol., 17,* 461.	Drug report.
Boxer, A. L. & Yoon, G. (2007). Reply from the authors [6]. *Neurology, 68,* 1325.	Reply to query about juvenile HD.
Brandt, J., Inscore, A. B., Ward, J., Shpritz, B., Rosenblatt, A., Margolis, R. L. et al. (2008). Neuropsychological deficits in Huntington's disease gene carriers and correlates of early "conversion". *J.Neuropsychiatry Clin.Neurosci., 20,* 466-472.	No emotion recognition tasks in battery.
Brandt, J., Leroi, I., O'Hearn, E., Rosenblatt, A., & Margolis, R. L. (2004). Cognitive impairments in cerebellar degeneration: a comparison with Huntington's disease. *J.Neuropsychiatry Clin.Neurosci., 16,* 176-184.	No emotion recognition tasks in battery.

Appendix A (*Continued*)

Reference	Reason for exclusion
Brandt, J., Shpritz, B., Codori, A. M., Margolis, R., & Rosenblatt, A. (2002). Neuropsychological manifestations of the genetic mutation for Huntington's disease in presymptomatic individuals. *J.Int.Neuropsychol.Soc., 8,* 918-924.	No emotion recognition tasks in battery.
Campodonico, J. R., Codori, A. M., & Brandt, J. (1996). Neuropsychological stability over two years in asymptomatic carriers of the Huntington's disease mutation. *J.Neurol.Neurosurg.Psychiatry, 61,* 621-624.	No emotion recognition tasks in battery.
de Boo, G. M., Tibben, A., Lanser, J. B., Jennekens-Schinkel, A., Hermans, J., Maat-Kievit, A. et al. (1997). Early cognitive and motor symptoms in identified carriers of the gene for Huntington disease. *Arch.Neurol., 54,* 1353-1357.	No emotion recognition tasks in battery.
de Gelder, B., Van den Stock, J., Balaguer, R. D., & Bachoud-Levi, A. C. (2008). Huntington's disease impairs recognition of angry and instrumental body language. *Neuropsychologia, 46,* 369-373.	Emotion matching (within modality), not explicit emotion recogntion, labelling or cross-modality matching.
Derouesne, C. (2004). [Cognitive disorders at the onset of Huntington disease]. *Psychol.Neuropsychiatr.Vieil., 2,* 226-227.	Editorial, no novel data.
Duff, K., Beglinger, L. J., Theriault, D., Allison, J., & Paulsen, J. S. (2010). Cognitive deficits in Huntington's disease on the Repeatable Battery for the Assessment of Neuropsychological Status. *J.Clin.Exp.Neuropsychol., 32,* 231-238.	No emotion recognition tasks in battery.
Fletcher, L. (1997). Computer 'games' diagnose early Huntington's disease. *Mol.Med.Today, 3,* 48-49.	Focuses on CANTAB as diagnostic tool for HD, not emotion recognition.
Giordani, B., Berent, S., Boivin, M. J., Penney, J. B., Lehtinen, S., Markel, D. S. et al. (1995). Longitudinal neuropsychological and genetic linkage analysis of persons at risk for Huntington's disease. *Arch.Neurol., 52,* 59-64.	No emotion recognition tasks in battery.
Gomez-Anson, B., Alegret, M., Munoz, E., Monte, G. C., Alayrach, E., Sanchez, A. et al. (2009). Prefrontal cortex volume reduction on MRI in preclinical Huntington's disease relates to visuomotor performance and CAG number. *Parkinsonism Relat Disord., 15,* 213-219.	No emotion recognition tasks in battery.
Gomez-Anson, B., Alegret, M., Munoz, E., Sainz, A., Monte, G. C., & Tolosa, E. (2007). Decreased frontal choline and neuropsychological performance in preclinical Huntington disease. *Neurology, 68,* 906-910.	No emotion recognition tasks in battery.
Gomez-Tortosa, E., del, B. A., Garcia Ruiz, P. J., Pernaute, R. S., Benitez, J., Barroso, A. et al. (1998). Severity of cognitive impairment in juvenile and late-onset Huntington disease. *Arch.Neurol., 55,* 835-843.	No emotion recognition tasks in battery.

Appendix A (*Continued*)

Reference	Reason for exclusion
Hahn-Barma, V., Deweer, B., Durr, A., Dode, C., Feingold, J., Pillon, B. et al. (1998). Are cognitive changes the first symptoms of Huntington's disease? A study of gene carriers. *J.Neurol.Neurosurg.Psychiatry, 64,* 172-177.	No emotion recognition tasks in battery.
Halligan, P. W. (1998). Inability to recognise disgust in Huntington's disease. *Lancet, 351,* 464.	Commentary, no novel data.
Hoth, K. F., Paulsen, J. S., Moser, D. J., Tranel, D., Clark, L. A., & Bechara, A. (2007). Patients with Huntington's disease have impaired awareness of cognitive, emotional, and functional abilities. *J.Clin.Exp.Neuropsychol., 29,* 365-376.	No emotion recognition tasks in battery.
Jacobs, D. H., Shuren, J., & Heilman, K. M. (1995). Impaired perception of facial identity and facial affect in Huntington's disease. *Neurology, 45,* 1217-1218.	Includes emotion testing but tests matching and discriminating, not labelling/explicit recognition; also no controls.
Jason, G. W., Suchowersky, O., Pajurkova, E. M., Graham, L., Klimek, M. L., Garber, A. T. et al. (1997). Cognitive manifestations of Huntington disease in relation to genetic structure and clinical onset. *Arch.Neurol., 54,* 1081-1088.	No emotion recognition tasks in battery.
Jurgens, C. K., van de, W. L., van Es, A. C., Grimbergen, Y. M., Witjes-Ane, M. N., Van Der, G. J. et al. (2008). Basal ganglia volume and clinical correlates in 'preclinical' Huntington's disease. *J.Neurol., 255,* 1785-1791.	No emotion recognition tasks in battery.
Lawrence, A. D., Hodges, J. R., Rosser, A. E., Kershaw, A., Ffrench-Constant, C., Rubinsztein, D. C. et al. (1998a). Evidence for specific cognitive deficits in preclinical Huntington's disease. *Brain, 121,* 1329-1341.	No emotion recognition tasks in battery.
Lawrence, A. D., Watkins, L. H., Sahakian, B. J., Hodges, J. R., & Robbins, T. W. (2000). Visual object and visuospatial cognition in Huntington's disease: implications for information processing in corticostriatal circuits. *Brain, 123,* 1349-1364.	No emotion recognition tasks in battery.
Lawrence, A. D., Weeks, R. A., Brooks, D. J., Andrews, T. C., Watkins, L. H., Harding, A. E. et al. (1998b). The relationship between striatal dopamine receptor binding and cognitive performance in Huntington's disease. *Brain, 121,* 1343-1355.	No emotion recognition tasks in battery.
Lemiere, J., Decruyenaere, M., Evers-Kiebooms, G., Vandenbussche, E., & Dom, R. (2002). Longitudinal study evaluating neuropsychological changes in so-called asymptomatic carriers of the Huntington's disease mutation after 1 year. *Acta Neurol.Scand., 106,* 131-141.	No emotion recognition tasks in battery.
Lemiere, J., Decruyenaere, M., Evers-Kiebooms, G., Vandenbussche, E., & Dom, R. (2004). Cognitive changes in patients with Huntington's disease (HD) and asymptomatic carriers of the HD mutation–a longitudinal follow-up study. *J.Neurol., 251,* 935-942.	No emotion recognition tasks in battery.

Appendix A (*Continued*)

Reference	Reason for exclusion
Lichter, D. G. & Hershey, L. A. (2010). Before chorea. Pre-Huntington mild cognitive impairment. *Neurology.75,* 490-491.	Commentary, no novel data.
Morris, M. (1995). Dementia and cognitive changes in Huntington's disease. *Adv.Neurol., 65,* 187-200.	Review, no data.
Nehl, C. & Paulsen, J. S. (2004). Cognitive and psychiatric aspects of Huntington disease contribute to functional capacity. *J.Nerv.Ment.Dis., 192,* 72-74.	No emotion recognition tasks in battery.
Paulsen, J. S. & Conybeare, R. A. (2005). Cognitive changes in Huntington's disease. *Adv.Neurol., 96,* 209-225.	Review, no data.
Paulsen, J. S., Hayden, M., Stout, J. C., Langbehn, D. R., Aylward, E., Ross, C. A. et al. (2006). Preparing for preventive clinical trials: the Predict-HD study. *Arch.Neurol., 63,* 883-890.	Same data are presented (but with slightly more participants) in the Johnson et al., 2007 paper which is included in review (Julie Stout, personal communication)
Paulsen, J. S., Langbehn, D. R., Stout, J. C., Aylward, E., Ross, C. A., Nance, M. et al. (2008). Detection of Huntington's disease decades before diagnosis: the Predict-HD study. *J.Neurol.Neurosurg.Psychiatry, 79,* 874-880.	No emotion recognition tasks in battery.
Paulsen, J. S., Wang, C., Duff, K., Barker, R., Nance, M., Beglinger, L. et al. (2010). Challenges assessing clinical endpoints in early Huntington disease. *Mov Disord., 25,* 2595-2603	No emotion recognition tasks in battery.
Pierrot-Deseilligny, C. (2001). Actualites American Academy of Neurology Philadelphie, 5-11 mai 2001* compte-rendu du congres. [French]. *Revue Neurologique, 157,* 578-600.	Congress account, no data.
Pillon, B., Dubois, B., & Agid, Y. (1996). Testing cognition may contribute to the diagnosis of movement disorders. *Neurology, 46,* 329-334.	Review, no data.
Redondo, V. L., Brown, R. G., & Chacon, J. (2001). [Executive dysfunction in Huntington's disease]. *Rev.Neurol., 32,* 923-929.	No emotion recognition tasks in battery.
Robins Wahlin, T. B., Lundin, A., & Dear, K. (2007). Early cognitive deficits in Swedish gene carriers of Huntington's disease. *Neuropsychology, 21,* 31-44.	No emotion recognition tasks in battery.
Rodrigues, G. R., Souza, C. P., Cetlin, R. S., de Oliveira, D. S., Pena-Pereira, M., Ujikawa, L. T. et al. (2009). Use of the frontal assessment battery in evaluating executive dysfunction in patients with Huntington's disease. *J.Neurol., 256,* 1809-1815.	No emotion recognition tasks in battery.
Roger, K. S. (2005). Exploring memory loss: A study starts. *Journal of Dementia Care, 13,* 36.	Commentary.
Rogers, D. (1993). Movement disorders. *Current Opinion in Psychiatry, 6,* 113-116.	Review, no data.
Roitberg, B. (2004). Research news and notes. *Surgical Neurology, 61,* 106-108.	Commentary.
Rosas, H. D., Salat, D. H., Lee, S. Y., Zaleta, A. K., Pappu, V., Fischl, B. et al. (2008). Cerebral cortex and the clinical expression of Huntington's disease: complexity and heterogeneity. *Brain., 131,* 1057-1068.	No emotion recognition tasks in battery.

Appendix A (*Continued*)

Reference	Reason for exclusion
Rosas, H. D., Tuch, D. S., Hevelone, N. D., Zaleta, A. K., Vangel, M., Hersch, S. M. et al. (2006). Diffusion tensor imaging in presymptomatic and early Huntington's disease: Selective white matter pathology and its relationship to clinical measures. *Mov Disord., 21,* 1317-1325.	No emotion recognition tasks in battery.
Rosenberg, N. K., Sorensen, S. A., & Christensen, A. L. (1995). Neuropsychological characteristics of Huntington's disease carriers: a double blind study. *J.Med.Genet., 32,* 600-604.	No emotion recognition tasks in battery.
Rupp, J., Blekher, T., Jackson, J., Beristain, X., Marshall, J., Hui, S. et al. (2010). Progression in prediagnostic Huntington disease. *J.Neurol.Neurosurg.Psychiatry, 81,* 379-384.	No emotion recognition tasks in battery.
Sawa, A. & Snyder, S. H. (2005). Two genes link two distinct psychoses. *Science, 310,* 1128-1129.	Genes for psychosis.
Sax, D. S., Powsner, R., Kim, A., Tilak, S., Bhatia, R., Cupples, L. A. et al. (1996). Evidence of cortical metabolic dysfunction in early Huntington's disease by single-photon-emission computed tomography. *Mov Disord., 11,* 671-677.	No emotion recognition tasks in battery.
Simpson, S. A. (2004). The management of Huntington's disease. *Practical Neurology, 4,* 204-211.	Review, no data.
Snowden, J. S., Craufurd, D., Thompson, J., & Neary, D. (2002). Psychomotor, executive, and memory function in preclinical Huntington's disease. *J.Clin.Exp.Neuropsychol., 24,* 133-145.	No emotion recognition tasks in battery.
Soliveri, P., Monza, D., Piacentini, S., Paridi, D., Nespolo, C., Gellera, C. et al. (2002). Cognitive and psychiatric characterization of patients with Huntington's disease and their at-risk relatives. *Neurol.Sci., 23 Suppl 2,* S105-S106.	No emotion recognition tasks in battery.
Solomon, A. C., Stout, J. C., Weaver, M., Queller, S., Tomusk, A., Whitlock, K. B. et al. (2008). Ten-year rate of longitudinal change in neurocognitive and motor function in prediagnosis Huntington disease. *Mov Disord., 23,* 1830-1836.	No emotion recognition tasks in battery.
Sprengelmeyer, R., Young, A. W., Sprenglemeyer, A., Calder, A. J., Rowland, D., Perrett, D. et al. (1997). Recognition of facial expressions: Selective impairment of specific emotions in Huntington's disease. *Cognitive Neuropsychology, Vol.14,* 839-879.	Two case studies.
Sprengelmeyer, R. (2007). The neurology of disgust. *Brain, 130,* 1715-1717.	Commentary.
Stout, J. C., Weaver, M., Solomon, A. C., Queller, S., Hui, S., Johnson, S. A. et al. (2007). Are cognitive changes progressive in prediagnostic HD? *Cogn Behav.Neurol., 20,* 212-218.	No emotion recognition tasks in battery.

Appendix A (*Continued*)

Reference	Reason for exclusion
Thieben, M. J., Duggins, A. J., Good, C. D., Gomes, L., Mahant, N., Richards, F. et al. (2002). The distribution of structural neuropathology in pre-clinical Huntington's disease. *Brain., 125,* 1815-1828.	No emotion recognition tasks in battery.
Thompson, J. C., Poliakoff, E., Sollom, A. C., Howard, E., Craufurd, D., & Snowden, J. S. (2010). Automaticity and attention in Huntington's disease: when two hands are not better than one. *Neuropsychologia, 48,* 171-178.	No emotion recognition tasks in battery.
Thompson, J. C., Snowden, J. S., Craufurd, D., & Neary, D. (2002). Behavior in Huntington's disease: dissociating cognition-based and mood-based changes. *J.Neuropsychiatry Clin.Neurosci., 14,* 37-43.	No emotion recognition tasks in battery.
Timman, R., Tibben, A., & Roos, R. A. (2003). Nonlinear effects in behavioural changes in Huntington disease. *Cogn Behav.Neurol., 16,* 82.	Letter, no novel data.
Tost, H., Wendt, C. S., Schmitt, A., Heinz, A., & Braus, D. F. (2004). Huntington's disease: phenomenological diversity of a neuropsychiatric condition that challenges traditional concepts in neurology and psychiatry. *Am.J.Psychiatry, 161,* 28-34.	Case study.
van Oostrom, J. C., Dekker, M., Willemsen, A. T., de Jong, B. M., Roos, R. A., & Leenders, K. L. (2009). Changes in striatal dopamine D2 receptor binding in pre-clinical Huntington's disease. *Eur.J.Neurol., 16,* 226-231.	No emotion recognition tasks in battery.
van Walsem, M. R., Sundet, K., Retterstol, L., & Sundseth, O. (2010). A double blind evaluation of cognitive decline in a Norwegian cohort of asymptomatic carriers of Huntington's disease. *J.Clin.Exp.Neuropsychol., 32,* 590-598.	No emotion recognition tasks in battery.
Verny, C., Allain, P., Prudean, A., Malinge, M. C., Gohier, B., Scherer, C. et al. (2007). Cognitive changes in asymptomatic carriers of the Huntington disease mutation gene. *Eur.J.Neurol., 14,* 1344-1350.	No emotion recognition tasks in battery.
Veyssier-Belot, C. (2005). Psychiatric disorders and systemic diseases. [French]. *Revue de Medecine Interne, 26,* 682-685.	Review, no novel data.
Videnovic, A., Bernard, B., Fan, W., Jaglin, J., Leurgans, S., & Shannon, K. M. (2010). The Montreal Cognitive Assessment as a screening tool for cognitive dysfunction in Huntington's disease. *Mov Disord., 25,* 401-404.	No emotion recognition tasks in battery.
Wang, K., Hoosain, R., Yang, R. M., Meng, Y., & Wang, C. Q. (2003). Impairment of recognition of disgust in Chinese with Huntington's or Wilson's disease. *Neuropsychologia, 41,* 527-537.	Genetic confirmation not available (Wang, personal communication).
Ward, J., Sheppard, J. M., Shpritz, B., Margolis, R. L., Rosenblatt, A., & Brandt, J. (2006). A four-year prospective study of cognitive functioning in Huntington's disease. *J.Int.Neuropsychol.Soc., 12,* 445-454.	No emotion recognition tasks in battery.

Appendix A (*Continued*)

Reference	Reason for exclusion
Wetter, S., Peavy, G., Jacobson, M., Hamilton, J., Salmon, D., & Murphy, C. (2005). Olfactory and auditory event-related potentials in Huntington's disease. *Neuropsychology, 19,* 428-436.	Investigates odour perception but not emotion or disgust.
Wetter, S. R. (2003). *Olfactory psychophysics and electrophysiology in huntington's disease.*	Thesis—based on same concepts as Wetter et al. (2005), above.
Wexler, A. (2006). Huntington disease [2]. *Journal of the Royal Society of Medicine, 99,* 53.	Letter, no novel data.
Wild, E. J. & Tabrizi, S. J. (2006). Predict-HD and the future of therapeutic trials. *Lancet Neurology, 5,* 724-725.	Commentary.
Wilkinson, D. & Halligan, P. (2004). The relevance of behavioural measures for functional-imaging studies of cognition. *Nat.Rev.Neurosci., 5,* 67-73.	Commentary.
Williams, R. (2006). Hunting for huntingtin modification. *Nature Reviews Neuroscience, 7,* 503.	Research highlights, no novel data.
Witjes-Ane, M. N., Mertens, B., van Vugt, J. P., Bachoud-Levi, A. C., van Ommen, G. J., & Roos, R. A. (2007). Longitudinal evaluation of "presymptomatic" carriers of Huntington's disease. *J.Neuropsychiatry Clin.Neurosci., 19,* 310-317.	No emotion recognition tasks in battery.
Witjes-Ane, M. N., Vegter-Van, D., V, van Vugt, J. P., Lanser, J. B., Hermans, J., Zwinderman, A. H. et al. (2003). Cognitive and motor functioning in gene carriers for Huntington's disease: a baseline study. *J.Neuropsychiatry Clin.Neurosci., 15,* 7-16.	No emotion recognition tasks in battery.
Young, A. W., Sprengelmeyer, R., Phillips, M., & Calder, A. J. (1997). Response from Young, Sprengelmeyer, Phillips and Calder. [References]. *Trends in Cognitive Sciences, Vol.1,* 322-325.	Response to comments about original Sprengelmeyer paper, no novel data.
Zakzanis, K. K. (1998). The subcortical dementia of Huntington's disease. *J.Clin.Exp.Neuropsychol., 20,* 565-578.	Review, no novel data.
Zihl, J. (2004). Clear indications of emotion depend on vivid stimuli. *Journal of Neurology, Neurosurgery and Psychiatry, 75,* 1658-1659.	Comment on emotion recognition testing.

Appendix B. Individual studies (from included references) that did not meet search criteria

Study and reference	Reason for exclusion
Aviezer et al. (2009): Experiment 2	Participants were asked to identify facial emotion expressions that were superimposed on body images portraying a different emotion and thus the experiment was not assessing "pure" emotion recognition in either modality.
Calder et al. (2010): Study 2	Participants were asked to match photographs of different "types" of disgust recognition with a written scenario, i.e., was too specific for this review.

Appendix B (*Continued*)

Study and reference	Reason for exclusion
Hayes et al. (2007): Experiments 1, 3, 4, 5, 6, 7	These experiments did not include an overt recognition component. Expt. 1 required participants to describe situations that would induce emotions, in Expt. 3 participants had to categorise emotional words, in Expt. 4 they had to categorise emotion-inducing scenes, all of which might rely solely or in part on semantic knowledge. In Expt. 5 their experience of disgust was assessed using a questionnaire, and in Expts. 6 and 7 they were asked to rate odours and tastes but this did not include the explicit label "disgust".
Milders et al. (2003): Test 2	Test 2 involved matching facial expressions and therefore did not meet criteria for explicit emotion recognition.
Snowden et al. (2008): Tasks 1, 2, 3, 6, 7	Task 1 required participants to define emotion labels, Task 2 asked participants to pick synonyms or link emotion words with specific scenarios, and Task 3 repeated Task 2 but with reduced response options; thus these tasks were not examining explicition recognition of emotional stimuli. Task 6 was a facial expression matching task, and Task 7 assessed facial identity matching.

References

Adolphs, R., 2002. Neural systems for recognizing emotion. Curr. Opin. Neurobiol. 12, 169–177.

Aviezer, H., Bentin, S., Hassin, R.R., Meschino, W.S., Kennedy, J., Grewal, S., Esmail, S., Cohen, S., Moscovitch, M., 2009. Not on the face alone: perception of contextualized face expressions in Huntington's disease. Brain 132, 1633–1644.

Benton, A.L., Sivan, A.B., Hamsher, K., Varney, d., Spreen, N.R.O., 1978. Benton Facial Recognition. Test Psychological Assessment Resources Inc., Lutz, FL.

Calder, A.J., Keane, J., Lawrence, A.D., Manes, F., 2004. Impaired recognition of anger following damage to the ventral striatum. Brain 127, 1958–1969.

Calder, A.J., Keane, J., Young, A.W., Lawrence, A.D., Mason, S., Barker, R.A., 2010. The relation between anger and different forms of disgust: implications for emotion recognition impairments in Huntington's disease. Neuropsychologia 48, 2719–2729.

Ekman, P., Friesen, W.V., 1976. Pictures of Facial Affect Consulting Psychologists. Press, Palo Alto, CA.

Ekman, P., 1992. Are there basic emotions? Psychol. Rev. 99, 550–553.

Ekman, P., 1993. Facial expression and emotion. Am. Psychol. 48, 384–392.

Gao, X., Maurer, D., 2010. A happy story: developmental changes in children's sensitivity to facial expressions of varying intensities. J. Exp. Child Psychol. 107, 67–86.

Gray, J.M., Young, A.W., Barker, W.A., Curtis, A., Gibson, D., 1997. Impaired recognition of disgust in Huntington's disease gene carriers. Brain 120, 2029–2038.

Harper, P., 2002. The epidemiology of Huntington's disease. In: Bates, G., Harper, P., Jones, L. (Eds.), Huntington's Disease. , 3rd. ed. Oxford University Press, Oxford, pp. 3–27.

Hayes, C.J., Stevenson, R.J., Coltheart, M., 2007. Disgust and Huntington's disease. Neuropsychologia 45, 1135–1151.

Hayes, C.J., Stevenson, R.J., Coltheart, M., 2009. The processing of emotion in patients with Huntington's disease: variability and differential deficits in disgust. Cogn. Behav. Neurol. 22, 249–257.

Henley, S.M., Bates, G.P., Tabrizi, S.J., 2005. Biomarkers for neurodegenerative diseases. Curr. Opin. Neurol. 18, 698–705.

Henley, S.M., Wild, E.J., Hobbs, N.Z., Warren, J.D., Frost, C., Scahill, R.I., Ridgway, G.R., MacManus, D.G., Barker, R.A., Fox, N.C., Tabrizi, S.J., 2008. Defective emotion

recognition in early HD is neuropsychologically and anatomically generic. Neuropsychologia 46, 2152–2160.
Hennenlotter, A., Schroeder, U., Erhard, P., Haslinger, B., Stahl, R., Weindl, A., von Einsiedel, H.G., Lange, K.W., Ceballos-Baumann, A.O., 2004. Neural correlates associated with impaired disgust processing in pre-symptomatic Huntington's disease. Brain 127, 1446–1453.
Huntington Study Group, 1996. Unified Huntington's Disease Rating Scale: reliability and consistency Huntington Study group. Mov. Disord. 11, 136–142.
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Johnson, S.A., Stout, J.C., Solomon, A.C., Langbehn, D.R., Aylward, E.H., Cruce, C.B., Ross, C.A., Nance, M., Kayson, E., Julian-Baros, E., Hayden, M.R., Kieburtz, K., Guttman, M., Oakes, D., Shoulson, I., Beglinger, L., Duff, K., Penziner, E., Paulsen, J.S., 2007. Beyond disgust: impaired recognition of negative emotions prior to diagnosis in Huntington's disease. Brain 130, 1732–1744.
Kipps, C.M., Duggins, A.J., McCusker, E.A., Calder, A.J., 2007. Disgust and happiness recognition correlate with anteroventral insula and amygdala volume respectively in preclinical Huntington's disease. J. Cogn. Neurosci. 19, 1206–1217.
Kremer, B., 2002. Clinical neurology of Huntington's disease. In: Bates, G., Harper, P., Jones, L. (Eds.), Huntington's Disease. , 3rd ed. Oxford University Press, Oxford, pp. 28–61.
Langbehn, D.R., Brinkman, R.R., Falush, D., Paulsen, J.S., Hayden, M.R., 2004. A new model for prediction of the age of onset and penetrance for Huntington's disease based on CAG length. Clin. Genet. 65, 267–277.
Lawrence, A.D., Sahakian, B.J., Robbins, T.W., 1998. Cognitive functions and corticostriatal circuits: insights from Huntington's disease. Trends Cogn. Sci. 2, 379–389.
Mahant, N., McCusker, E.A., Byth, K., Graham, S., 2003. Huntington's disease: clinical correlates of disability and progression. Neurol 61, 1085–1092.
Milders, M., Crawford, J.R., Lamb, A., Simpson, S.A., 2003. Differential deficits in expression recognition in gene-carriers and patients with Huntington's disease. Neuropsychologia 41, 1484–1492.
Mitchell, I.J., Heims, H., Neville, E.A., Rickards, H., 2005. Huntington's disease patients show impaired perception of disgust in the gustatory and olfactory modalities. J. Neuropsychiatry Clin. Neurosci. 17, 119–121.
Montagne, B., Kessels, R.P., Kammers, M.P., Kingma, E., de Haan, E.H., Roos, R.A., Middelkoop, H.A., 2006. Perception of emotional facial expressions at different intensities in early-symptomatic Huntington's disease. Eur. Neurol. 55, 151–154.
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