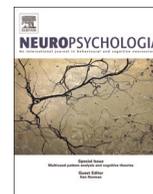




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# Impairments in negative emotion recognition and empathy for pain in Huntington's disease families



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## ABSTRACT

Lack of empathy and emotional disturbances are prominent clinical features of Huntington's disease (HD). While emotion recognition impairments in HD patients are well established, there are no experimental designs assessing empathy in this population. The present study seeks to cover such a gap in the literature. Eighteen manifest HD patients, 19 first-degree asymptomatic relatives, and 36 healthy control participants completed two emotion-recognition tasks with different levels of contextual dependence. They were also evaluated with an empathy-for-pain task tapping the perception of intentional and accidental harm. Moreover, we explored potential associations among empathy, emotion recognition, and other relevant factors – e.g., executive functions (EF). The results showed that both HD patients and asymptomatic relatives are impaired in the recognition of negative emotions from isolated faces. However, their performance in emotion recognition was normal in the presence of contextual cues. HD patients also showed subtle empathy impairments. There were no significant correlations between EF, empathy, and emotion recognition measures in either HD patients or relatives. In controls, EF was positively correlated with emotion recognition. Furthermore, emotion recognition was positively correlated with the performance in the empathy task. Our findings highlight the preserved cognitive abilities in HD families when using more ecological tasks displaying emotional expressions in the context in which they typically appear. Moreover, our results suggest that emotion recognition impairments may constitute a potential biomarker of HD onset and progression. These results contribute to the understanding of emotion recognition and empathy deficits observed in HD and have important theoretical and clinical implications.

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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 (Conneally, 1984), classically characterized by a triad of symptoms including cognitive, motor, and behavioral abnormalities, and associated with neuronal loss within corticostriatal circuits (Lawrence et al., 1998). Neuropathological and neuroimaging studies (Della Nave et al., 2010; Muhlau et al., 2007; Nopoulos et al., 2010) have revealed selective gray matter atrophy in HD, with the earliest changes progressing from the dorsolateral

to the ventromedial portions of the neostriatum. Furthermore, the cerebral cortex is selectively affected with early involvement of the operculum. Subsequently, progressive atrophy involves the insula, primary sensory, motor, and visual cortices, and then the primary auditory cortex. Finally, atrophy extends to the entorhinal cortex and higher order cortical regions. Importantly, structural and functional abnormalities in the basal ganglia and the insula (Hennenlotter et al., 2004; Ille et al., 2011; Kipps et al., 2007) as well as in the frontostriatal pathways (Joel, 2001) have been associated with social cognition impairments in HD.

HD patients are typically impaired in their social functioning, partly due to emotional disturbances and lack of empathy (Kirkwood et al., 2001; Snowden et al., 2003). While emotion recognition impairments are well documented in HD patients (Henley et al., 2012; Johnson et al., 2007; Mitchell et al., 2005; Trinkler et al., 2013), only one study (Trinkler et al., 2013) has assessed empathy in these individuals and none has assessed this domain in first-degree relatives. This comes as a surprise, since lack of empathy is a prominent clinical feature of HD (Bodden et al., 2010; Kirkwood et al., 2001; Williams et al., 2009).

To cover such a gap, this study evaluated the performance of HD patients and first-degree asymptomatic relatives on empathy and emotion recognition tasks with different levels of contextual dependence. Moreover, we explored potential associations among empathy, emotion recognition, and other relevant factors – e.g., executive functions (EF).

Emotion recognition is essential for successful social interaction. Neuroanatomically, this process has been linked to regions in the temporal lobe, such as the fusiform gyrus, together with a network involving amygdala, orbitofrontal cortex, and cingulate structures (Adolphs, 2001). However, dissociations in the recognition of different facial expressions (e.g. Blair et al., 1999; Lawrence et al., 2007; Williams et al., 2009) suggest that different neural systems are specialized, at least in part, for the recognition of particular emotions. For instance, the amygdala appears to link perceptual representations to cognition and behavior on the basis of the emotional value of the stimuli (Adolphs, 2001). Thus, it appears to be involved in processing the emotional salience of both positive and negative stimuli, with a special role in coding signals of fear (Adolphs, 2001; Britton et al., 2006). The recognition of sadness expressions has been particularly associated with the right inferior and middle temporal gyrus (Blair et al., 1999; Rosen et al., 2006), while disgust recognition has been linked to the insula and the basal ganglia (Adolphs, 2002; Calder et al., 2000; Couto et al., 2013; Ibanez et al., 2010; Wang et al., 2003).

Emotion recognition has been systematically studied in HD. In manifest HD patients, anger recognition appears to be most consistently impaired, closely followed by recognition of disgust and fear (Aviezer et al., 2009; Henley et al., 2012; Milders et al., 2003; Montagne et al., 2006; Snowden et al., 2008). On the contrary, recognition of other emotions, such as happiness, sadness, or surprise, is rarely affected (Calder et al., 2010; Hayes et al., 2009). Some studies on pre-manifest HD (Gray et al., 1997; Hennenlotter et al., 2004; Sprengelmeyer et al., 2006) have reported a selective deficit in disgust recognition, whereas others (Johnson et al., 2007; Tabrizi et al., 2009) have found impairments across negative emotions. These findings and those of large longitudinal studies (Paulsen et al., 2006; Tabrizi et al., 2009) suggest that emotion recognition might be a sensitive biomarker of disease onset and progression in HD.

Most of the studies investigating facial emotion recognition in HD have relied on tasks involving isolated faces. However, real-life facial expressions are typically embedded in a rich, informative context. Recent reports (Barrett and Kensinger, 2010; Barrett et al., 2007; Van den Stock et al., 2007) have shown that facial expression recognition is a context-sensitive process. Visual scenes,

voices, bodies, other faces, and even words influence how an emotion is perceived in a face (Barrett et al., 2011). Indeed, under certain conditions, context can modify the emotional category recognized in basic facial expressions (Aviezer et al., 2008). These findings notwithstanding, only one study (Aviezer et al., 2009) has assessed the recognition of facial expressions embedded within an emotional body and scene context in HD mutation carriers. This study showed that HD patients display relatively preserved processing of facial expressions when these are embedded in a given context. However, one limitation of this work concerns the employment of static, as opposed to dynamic stimuli. In this sense, the use of dynamic stimuli to assess facial emotion recognition in HD may provide a more realistic and sensitive measure, as these more closely resemble the moving faces encountered in everyday life (Mendoza et al., 2011; Russell et al., 2007; Schaefer et al., 2010).

Unlike emotion recognition, empathy has been scarcely studied in patients with HD. Empathy comprises the capacity to share and understand the subjective experience of others in reference to oneself (Decety, 2011). This complex construct involves (1) affective components: sharing and responding to the emotional experience of others (Decety and Jackson, 2004), which facilitates somatic, sensory, and motor representation of other people's mental states (Nummenmaa et al., 2008); (2) cognitive components: understanding the intentions and internal mental states of others (Blair, 2005); and (3) aspects related to the moral evaluation: judging the actions of a perpetrator or the punishment deserved (Decety and Jackson, 2004; Decety et al., 2012).

Only one study in HD patients (Trinkler et al., 2013) has assessed empathy, evidencing normal scores in self-report questionnaires. Here we implemented a novel paradigm with naturalistic stimuli that measures empathy for others' physical pain. This type of paradigm has been widely used due to the robustness of pain in inducing empathic responses (Bernhardt and Singer, 2012), and the well characterized neural circuit of empathy (Akitsuki and Decety, 2009). Neuroimaging studies on empathy for pain have systematically evidenced a neural network that is implicated in the experience of physical pain, and involved in the perception or imagination of another individual in pain (Jackson et al., 2006; Melloni et al., 2014). This neural network includes the supplementary motor area, the anterior cingulate cortex, the amygdala, and the anterior insula extending into the inferior frontal gyrus (Bernhardt and Singer, 2012; Decety et al., 2012; Singer and Lamm, 2009).

We employed an adaptation of an empathy for pain task (EPT) previously validated with behavioral measures, eye-tracking and fMRI (Decety et al., 2012). This adapted version has been used in the assessment of other neuropsychiatric populations (Baez et al., 2012, 2013, 2014; Baez and Ibanez, 2014; Sedeno et al., 2014). The task evaluates empathy in the context of intentional/accidental harms, and consists of three different scenarios: (1) intentional or (2) accidental harms in which one person is in a painful situation intentionally or accidentally caused by another, and (3) neutral or control situations. The EPT evaluates the following components: (A) comprehension of the accidental or deliberate nature of the action and the intention of the perpetrator to hurt (cognitive components); (B) the empathic concern, the degree of discomfort for the victim, and the valence behavior of the active performer (affective components); and (C) the correctness of the action and the punishment for the perpetrator (moral aspects). Note that the cognitive components of empathy assessed in this study have been associated to theory of mind (ToM) (Blair, 2005; Zaki and Ochsner, 2012; Ibanez et al., 2013), a fundamental ability to empathize with others by considering their mental states. Impairments in this ability have also been reported in HD patients. These individuals show a tendency to draw faulty inferences from social situations,

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