



Emotional face recognition deficits and medication effects in pre-manifest through stage-II Huntington's disease

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ABSTRACT

Facial emotion recognition impairments have been reported in Huntington's disease (HD). However, the nature of the impairments across the spectrum of HD remains unclear. We report on emotion recognition data from 344 participants comprising premanifest HD (PreHD) and early HD patients, and controls. In a test of recognition of facial emotions, we examined responses to six basic emotional expressions and neutral expressions. In addition, and within the early HD sample, we tested for differences on emotion recognition performance between those 'on' vs. 'off' neuroleptic or selective serotonin reuptake inhibitor (SSRI) medications. The PreHD groups showed significant ($p < 0.05$) impaired recognition, compared to controls, on fearful, angry and surprised faces; whereas the early HD groups were significantly impaired across all emotions including neutral expressions. In early HD, neuroleptic use was associated with worse facial emotion recognition, whereas SSRI use was associated with better facial emotion recognition. The findings suggest that emotion recognition impairments exist across the HD spectrum, but are relatively more widespread in manifest HD than in the premanifest period. Commonly prescribed medications to treat HD-related symptoms also appear to affect emotion recognition. These findings have important implications for interpersonal communication and medication usage in HD.

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1. Introduction

Huntington's disease (HD) is an autosomal-dominant neurodegenerative disorder caused by an expanded CAG-repeat in the *Huntingtin* gene. HD is characterised by the gradual onset and progression of motor impairments, cognitive decline and psychiatric symptoms. Formal diagnosis is dependent on the motor signs, however these signs are preceded by subtle cognitive deficits (Lawrence et al., 1998; Lemiere et al., 2004; Paulsen et al., 2006; Duff et al., 2007; Tabrizi et al., 2009, 2011, 2012; Stout et al., 2012). Among the many cognitive deficits reported in HD, an

intriguing and consistent finding has involved impairments in emotion recognition, which has mostly been examined by asking subjects to identify the emotion associated with a photo of an emotionally expressive face (Sprengelmeyer et al., 1996; Gray et al., 1997; Milders et al., 2003; Hennenlotter et al., 2004; Montagne et al., 2006; Sprengelmeyer et al., 2006; Hayes et al., 2007, 2009; Johnson et al., 2007; Kipps et al., 2007; Henley et al., 2008; Snowden et al., 2008; Aviezer et al., 2009; Calder et al., 2010). However, despite the large number of previous reports, the specific nature of emotional face recognition impairments across the spectrum of HD remains unclear.

Earlier reports suggested that emotion recognition deficits in HD predominantly involve the emotion of disgust; however, the balance of evidence from more recent studies suggests either more global impairments across all emotions or particular deficits in negative emotions. For example, in *manifest HD*, emotion

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recognition deficits have been found for disgusted faces (Wang et al., 2003; Montagne et al., 2006), disgusted and angry faces (Snowden et al., 2008; Aviezer et al., 2009), all negative emotional faces (Milders et al., 2003), all negative and surprised faces (Sprengelmeyer et al., 1996; Hayes et al., 2009) and disgusted, angry, fearful, and surprised faces but not sad or happy faces (Henley et al., 2008). A more recent study reported impairments across all six basic emotional faces (Calder et al., 2010). Similarly, in subjects with *premanifest HD (PreHD)*, emotion recognition impairments have been reported for disgusted faces (Gray et al., 1997; Hennenlotter et al., 2004; Sprengelmeyer et al., 2006), happy faces (Henley et al., 2008), and, in a very large study, in all negative (angry, fear, sadness and disgusted) faces (Johnson et al., 2007).

There has been limited evidence for whether emotion recognition deficits are progressive across different disease stages in HD. Previously, longitudinal studies have been few (Sprengelmeyer et al., 1996, 2006) and the sensitivity of these studies to detect progressive change has been limited due to small sample sizes ($n=22$ and $n=13$) and the short nature of the longitudinal intervals (i.e., months rather than years). However, we have recently reported deterioration in recognition of negative emotions in a large longitudinal sample involving both premanifest ($n=243$) and early stage HD ($n=233$) at both 12- and 24-month follow-up time points (Tabrizi et al., 2011, 2012; Stout et al., 2012). Because we presented the emotion recognition data in the context of numerous other measures, however, the findings reported in these publications were limited to only a single combined negative emotion variable, and did not allow for the consideration of individual emotions (including neutral expressions). Besides our studies, only two other studies (Milders et al., 2003; Henley et al., 2008) have examined premanifest and manifest HD groups, and neither of these included neutral expressions. These studies were cross-sectional, involved small sample sizes (e.g., 21 PreHD and 40 early HD; Henley et al., 2008) and yielded mixed results. Thus, there is limited evidence as to whether the emotion recognition deficits in HD vary or remain stable through the progression from the premanifest through to the early manifest stages of the disease. Better study designs involving all emotions, larger sample sizes and both premanifest and manifest stage groups are needed to clearly define the nature of these emotion recognition deficits in HD.

An important clinical issue is whether those patients taking medications commonly used to treat HD-related symptoms, especially neuroleptics and selective serotonin reuptake inhibitors (SSRIs), respond differentially to emotional cues compared to those not taking such medications. In HD, neuroleptic and SSRI medications are often used for the treatment of motor problems and neuropsychiatric symptoms (see reviews; De Marchi et al., 2001; Bonelli and Hofmann 2007; Adam and Jankovic 2008; van Duijn 2010). That is, neuroleptics are used in HD most often to treat chorea and behavioural disturbances such as irritability and anger outbursts, and less often for psychotic symptoms. SSRIs are used in HD most often for depression and anxiety-related symptoms, but also for behavioural disturbances such as irritability and aggression (see reviews; De Marchi et al., 2001; Bonelli and Hofmann 2007; Adam and Jankovic 2008; van Duijn 2010). The effects of these medications on emotional processes have not yet been studied in HD. Limited evidence has indicated that SSRIs are associated with improved facial emotion recognition in healthy controls (Harmer et al., 2003; Browning et al., 2007) and in people with depression (Tranter et al., 2009). Interestingly, in other clinical disorders not involving HD, both neuroleptics and SSRIs have been linked to detrimental effects on emotion-related behaviours, with these medications being associated with affective indifference, emotional blunting, reduced facial

expressiveness, and reduced intensity and frequency of emotional experiences (Delay and Deniker 1956; Sommers 1985; Schneider et al., 1992; Heinz et al., 1998; Price 1998; Opbroek et al., 2002; Whitaker 2004; Mizrahi et al., 2007; Fakra et al., 2008). The latter evidence forms the basis for the rationale for investigating the effects of medication on emotion recognition in the current study. That is, whereas neuroleptics and SSRIs are prescribed to HD patients for their movement and psychiatric-related symptoms, no study to date has reported on the relationships between these drugs and cognitive emotional processes such as emotion recognition in HD.

Although emotion recognition impairments are known in HD, the evidence about individual emotions impaired across the premanifest to manifest disease spectrum have been unknown. Comparing across studies has been difficult because of the small sample sizes and the differences between studies, for example, in the inclusion criteria, sample characteristics and types of emotions used. To date, no single study has looked at emotion recognition performance across the spectrum of HD involving multiple disease stages, large sample sizes and all types of emotional expressions in a single experimental design. Furthermore, no studies to date have addressed how medications commonly used in HD influence emotion recognition ability.

Therefore, our study aims were two-fold. First, using the TRACK-HD study cohort, we aimed to present a comprehensive cross-sectional picture of the emotion recognition performance across the spectrum of HD by examining the individual (six emotional and one neutral) and combined negative emotion recognition impairments across four disease stages of HD (ranging from those more than 11.5 years from disease onset to those in Stage 2 HD). Although we have previously described the combined negative emotion variable as part of a larger report on cognitive, motor, and psychiatric domains from the TRACK-HD study (Tabrizi et al., 2009, 2011, 2012; Stout et al., 2012), these previous reports did not permit a more comprehensive picture of emotion recognition for the individual emotion types. Secondly, we aimed to further extend these findings by examining whether medications, specifically neuroleptics and SSRIs, play a role in emotion recognition ability. Because it is during the manifest stages of HD that relatively more people with HD are medicated, we only had sufficient sample sizes in the early manifest groups, but not in the premanifest groups, to examine these medication effects. Overall for emotion recognition, we expected to observe impairments in both premanifest and manifest stages of HD based on prior evidence. We further hypothesised that the impairments would progress in a step-wise deterioration across the four disease stages studied, whereby the premanifest groups would show relatively selective emotion recognition impairments, whereas more comprehensive impairments across all emotions would be more apparent after disease diagnosis. Based on evidence from other clinical disorders showing detrimental effects of neuroleptics and SSRIs on emotional behaviours such as emotional blunting, reduced facial expressiveness and reduced intensity of emotions experiences, we expected that in the early diagnosed stages, the use of neuroleptic or SSRI medication would be associated with detrimental effects on emotion recognition accuracy.

2. Methods

2.1. Participants

We report on baseline data from 344 premanifest (PreHD) and early HD participants and controls, who completed a facial emotion recognition task across four sites (Paris, London, Vancouver and Leiden) as part of a multidisciplinary, multi-site, longitudinal study known as TRACK-HD (for study details see Tabrizi et al., 2009). Five out of the approximately 30 premanifest participants recruited

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