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Review

Social cognition in Huntington's disease: A meta-analysis

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HIGHLIGHTS

- ToM and recognition of emotions from vocal and facial stimuli in Huntington's disease is impaired.
- Social cognitive deficits in Huntington's disease is already evident before the onset of motor symptoms.
- Illness progression is associated with decline in emotion recognition and ToM abilities.

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ABSTRACT

Neurocognitive impairment in Huntington's disease (HD) frequently includes deficits in emotion recognition, and recent studies have also provided evidence for deficits in theory of mind (ToM). There have been conflicting reports regarding the extent of emotion recognition and ToM deficits before the onset of motor symptoms in HD. In this meta-analysis, ToM and emotion recognition performances of 2226HD or pre-manifest HD and 998 healthy controls were included in the meta-analysis. Meta-regression analyses were conducted to investigate the relationship between social cognition deficits and demographic, cognitive and clinical features in HD. HD patients were significantly less accurate than controls in ToM and across all emotions in response to both facial and vocal stimuli. ToM ($d = 1.72$) and recognition of negative emotions ($d = 1.20–1.33$), especially anger, disgust and fear ($d = 1.26–1.52$) were severely impaired. Pre-manifest HD was also associated with impairment in social cognition. The severity of emotion recognition impairment was significantly associated with disease burden, proximity of onset of motor symptoms and cognitive impairment. Social cognition impairments are potential biomarkers of disease onset and progression in HD.

Contents

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1. Introduction

Huntington's disease (HD) is an autosomal-dominant neurodegenerative disorder characterized by the gradual emergence and progression of motor impairment, neurocognitive deficits and psychiatric symptoms. Subtle neurocognitive deficits and psychiatric symptoms precede the emergence of motor symptoms, and the ultimate diagnosis of HD, in many cases [17,23,24]. HD is caused by expanded CAG-repeat (CAG-exp) in the Huntingtin gene and the number of repeats is inversely correlated with the age of onset of symptoms.

Neurocognitive impairment in HD not only includes deficits in abilities assessed by traditional neuropsychological batteries such as memory and executive functioning [17,48], but also often features impairments in social cognition [35]. One aspect of social cognition, the recognition of emotion from faces, has been investigated in a relatively large number of studies within the last 20 years [35]. Evidence also suggests that emotion recognition deficits are evident in response to stimuli other than faces (vocal, body language) [14,19]. Early studies investigating emotion recognition reported that most profound deficit in HD is an inability to recognize disgust, which may be related to dysfunction in the basal ganglia and insula [50,51,61,65,72]. Other studies reported that deficits in the recognition of disgust, but not other emotions, might be evident in pre-manifest HD [62]. However, many more recent studies were not in agreement with the notion of a disproportionate disgust deficit in HD [35]: these studies suggested that HD is associated with either a global deficit in emotion recognition or particular deficits in the recognition of all negative emotions. Another aspect of social cognition is theory of mind (ToM), which is the ability to attribute mental states (feelings, beliefs, intentions, and desires) to others and understand and predict others' behavior based on their mental states. Severe ToM impairment is one of the core features of frontotemporal dementia and less pronounced deficits are also evident in other neurodegenerative diseases such as Alzheimer's and Parkinson' diseases [11,12]. ToM is not an entirely homogeneous concept, and some authors have suggested ToM includes both affective and cognitive components [2,58], involved in reasoning *vs.* decoding of mental states [9]. Functional imaging studies have suggested overlapping activity in medial prefrontal cortex and the posterior temporoparietal junction in response to different aspects of ToM, but considerable activation differences in brain regions occur depending on the task used [15,56,58]. HD is associated with widespread neuroanatomical changes [21] including regions involved in ToM. Recent studies have begun to investigate ToM in HD, and these early studies have suggested that ToM is also impaired in HD [25,27,28,59].

Both ToM and emotion recognition abilities are critical for adaptive and effective social functioning. ToM and emotion recognition deficits are likely to be clinically relevant, as difficulties in social interaction, communication and poor insight frequently occur in HD and deficits in social cognition have been associated with poor social functioning and insight in other neuropsychiatric disorders [9,10,16,20,23,24,54,71].

Another important consideration is the timing of the emergence of social cognitive deficits. If social cognitive deficits exist before the onset of motor symptoms, they may potentially also serve as biomarkers of disease progression, and thus contribute to the decision-making process regarding future early intervention with disease-modifying treatments. Studies investigating social cognition in HD have reported conflicting findings. A number of studies have not reported significant between-group differences between HD and healthy controls [2,40,55]. The number of participants in existing individual social cognitive studies in pre-manifest HD has been small, and most of these studies are likely to be underpowered to show moderate deficits in social cognition before the onset of motor symptoms.

A meta-analysis of the emotion recognition and ToM findings to date can help to resolve a number of conflicting findings, including most specific social cognition deficits and that social cognitive deficits occur before the onset of motor symptoms. It also offers the means to examine the influence of cognitive deficits, demographic confounders, and clinical stage. The goal of the current meta-analysis was to investigate emotion recognition and ToM deficits and their relationship with key clinical variables including disease state, motor symptoms, disease burden and neuropsychological impairment

2. Method

2.1 Study selection

PRISMA guidelines were used in conducting this meta-analysis [47]. A literature search was conducted using the databases Pubmed, PsycINFO and Scopus to identify the relevant studies (January 1990–August 2015) using the combination of keywords as follows: Huntington's disease; emotion recognition; theory of mind and social cognition. Reference lists of published reports were also reviewed for additional studies. Inclusion criteria were studies that:

Examined emotion recognition abilities.

(1) Reported sufficient data to calculate the effect size and standard error of the ToM and emotion recognition measure including results of parametric statistics (*i.e.* *t* and *F* values).
(2) Compared the performances of patients with HD or pre-manifest HD and healthy controls.
(3) The selection process is summarized in supplementary Fig. 1. We contacted authors of papers that did not report sufficient data to calculate effect sizes. Studies investigating emotion recognition abilities with methods other than facial or vocal recognition were excluded as only a few studies used such methods (*i.e.* body language, scenes). Studies were excluded if they were overlapping with other studies included in the current meta-analysis. A total of 37 studies (53CAG-exp (manifest or pre-manifest HD) *vs.* control comparisons) consisting of 2226HD or pre-manifest HD (57.8% females) and 998 healthy controls (54.1% females) were included in the meta-analysis (Table 1). There was no significant difference in age between the CAG-exp group and controls ($d = 0.11$, CI = −0.03–0.25, $Z = 1.6$, $p = 0.11$).

2.1. Social cognitive tasks

Some studies investigated facial emotion recognition with multiple methods (different sets of images of faces, emotion hexagon, and short-video format). In these studies, data from facial pictures were preferred as the majority of studies used this stimulus (most commonly the Ekman set of images) rather than other methods. However, three studies included in the meta-analysis used only emotion hexagons and one study used a 3 s video of the face to investigate emotion recognition. Two of these studies included Ekman pictures with different intensities across stimuli. Vocal emotion recognition tasks included either short non-verbal vocal sounds or "nonsense" word prosody. Reading the mind in the Eyes test (RMET) and recognition of faux pas [7,63] were the most commonly used ToM tests. Other than these two tasks, different versions of ToM stories and ToM cartoons were used in the studies included (Table 1).