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Research report

Suicidal ideation in a European Huntington's disease population

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ABSTRACT

Background: Previous studies indicate increased prevalences of suicidal ideation, suicide attempts, and completed suicide in Huntington's disease (HD) compared with the general population. This study investigates correlates and predictors of suicidal ideation in HD.
Methods: The study cohort consisted of 2106 HD mutation carriers, all participating in the REGISTRY study of the European Huntington's Disease Network. Of the 1937 participants without suicidal ideation at baseline, 945 had one or more follow-up measurements. Participants were assessed for suicidal ideation by the behavioural subscale of the Unified Huntington's Disease Rating Scale (UHDRS). Correlates of suicidal ideation were analyzed using logistic regression analysis and predictors were analyzed using Cox regression analysis.
Results: At baseline, 169 (8.0%) mutation carriers endorsed suicidal ideation. Disease duration (odds ratio [OR]=0.96; 95% confidence interval [CI]: 0.9–1.0), anxiety (OR=2.14; 95%CI: 1.4–3.3), aggression (OR=2.41; 95%CI: 1.5–3.8), a previous suicide attempt (OR=3.95; 95%CI: 2.4–6.6), and a depressed mood (OR=13.71; 95%CI: 6.7–28.0) were independently correlated to suicidal ideation at baseline. The 4-year cumulative incidence of suicidal ideation was 9.9%. Longitudinally, the presence of a depressed mood (hazard ratio [HR]=2.05; 95%CI: 1.1–4.0) and use of benzodiazepines (HR=2.44; 95%CI: 1.2–5.0) at baseline were independent predictors of incident suicidal ideation, whereas a previous suicide attempt was not predictive.
Limitations: As suicidal ideation was assessed by only one item, and participants were a selection of all HD mutation carriers, the prevalence of suicidal ideation was likely underestimated.
Conclusions: Suicidal ideation in HD frequently occurs. Assessment of suicidal ideation is a priority in mutation carriers with a depressed mood and in those using benzodiazepines.
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1. Introduction

Huntington's disease (HD) is an autosomal dominant progressive neurodegenerative disease (Walker, 2007). The underlying genetic defect is an unstable and expanded CAG repeat on the short arm of chromosome 4, which causes an expanded polyglutamine chain in the huntingtin protein (Hoogeveen et al., 1993). The disease is characterized by motor abnormalities, cognitive decline, and both behavioural problems and psychiatric disorders. George Huntington first described the tendency to suicide as an important aspect of the disease in 1872 (Huntington, 1872). Recent studies have reported that completed suicide rates among HD mutation carriers are four to eight times higher compared with the general population (Farrer, 1986; Robins Wahlin et al., 2000; Schoenfeld et al., 1984), and increased prevalences of suicidal ideation and attempted suicide, of up to 20%, have been reported (Hubers et al., 2012; Wetzel et al., 2011).

Previous cross-sectional studies have shown that both socio-demographic characteristics such as having no offspring (Baliko et al., 2004; Lipe et al., 1993) or being unemployed (Almqvist et al., 1999), and clinical characteristics such as the presence of a

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depressed mood (Hubers et al., 2012; Wetzel et al., 2011), aggression (Wetzel et al., 2011), or having a psychiatric history (Almqvist et al., 1999) are associated with suicidal ideation, suicide attempts, or completed suicide in HD. Some of these studies only included a small number of participants (Lipe et al., 1993) or used data obtained from family members (Di Maio et al., 1993). Also, several of these studies only investigated the effect of undergoing genetic testing on suicide risk (Almqvist et al., 1999; Farrer, 1986; Robins Wahlin et al., 2000), without investigating correlates or predictors of suicidal ideation during disease progression.

Despite the high suicide risk in HD, only two prospective studies have been carried out (Fiedorowicz et al., 2011; Hubers et al., 2012). One study investigating both suicide attempts and completed suicide in 735 prodromal HD mutation carriers during a median follow-up of 3.5 years, reported presence of depression and a history of suicide attempts as relevant predictors (Fiedorowicz et al., 2011). However, there were only 13 incident events, which limited study power (Fiedorowicz et al., 2011). The other longitudinal study, in which 100 mutation carriers were assessed for both suicidal ideation and suicide attempts, reported 7 participants who developed suicidal ideation or attempted suicide after two years follow-up. This study also found depressed mood as a predictor for suicidal ideation and attempts in HD (Hubers et al., 2012).

The present study aimed to identify correlates and predictors of suicidal ideation in a large well-monitored European cohort of HD mutation carriers.

2. Method

2.1. Participants

The study cohort consisted of 2106 European HD mutation carriers participating in the REGISTRY study prior to February 2011. Our study included only monitored data of REGISTRY participants who had a Unified Huntington's Disease Rating Scale (UHDRS) (Huntington Study Group, 1996) behavioural assessment. REGISTRY is a large prospective, observational study of the European Huntington's Disease Network (EHDN) describing the natural course of HD in many European countries (Orth et al., 2010). More detailed information can be found at http://www.euro-hd.net/html/registry.

In the study cohort, participants from 15 European countries were included: Austria ($n=58$), Belgium ($n=3$), Czech Republic ($n=29$), Finland ($n=23$), France ($n=158$), Germany ($n=493$), Italy ($n=181$), The Netherlands ($n=215$), Norway ($n=74$), Poland ($n=222$), Portugal ($n=65$), Spain ($n=160$), Sweden ($n=18$), Switzerland ($n=21$) and the United Kingdom ($n=386$). Full ethical approval for REGISTRY was obtained in each of the participating countries and all participants gave written informed consent after the study procedure had been fully explained. The first behavioural assessment according to the behavioural subscale of the Unified Huntington's Disease Rating Scale (UHDRS-b) (Huntington Study Group, 1996) was taken as baseline visit. Follow-up data from mutation carriers free of suicidal ideation at baseline ($n=1,937$) were used in the longitudinal analyses. Of these mutation carriers, 992 participants dropped out because they had no follow-up measurements. This resulted in 945 eligible mutation carriers for follow-up assessment (Fig. 1).

2.2. Instruments

Assessment of suicidal ideation: Suicidal ideation was examined using the UHDRS-b (Huntington Study Group, 1996). The behavioural subscale of the UHDRS assesses frequency and severity of 11 neuropsychiatric symptoms (Huntington Study Group, 1996). The item 'Suicidal thoughts' of the UHDRS-b (Huntington Study Group, 1996) measures frequency and severity of suicidal thoughts in the month preceding the interview. The frequency score ranges from 0 through 4: a score of 0 indicates suicidal thoughts are never present, a score of 1 indicates seldom presence, a score of 2 indicates suicidal thoughts are sometimes present, a score of 3 indicates frequent presence, and a score of 4 indicates suicidal thoughts are often present. The severity score also ranges from 0 through 4: a score of 0 indicates absence of suicidal ideation, a score of 1 indicates there are no current suicidal thoughts, but the participant considers suicide as a potential option, a score of 2 indicates presence of fleeting suicidal ideation, a score of 3 indicates the participant seriously considered suicide but has no plan, and a severity score of 4 indicates the participant has a plan and is actively preparing (Huntington Study Group, 1996). The total score was computed by multiplying the frequency and severity scores (range 0–16 points) (Wetzel et al., 2011). Based on clinical experience, a total score >1 point on this item was used to characterize presence of suicidal ideation, meaning that participants scoring a total score of 1 on the 'suicidal ideation' item were not considered to have suicidal ideation, since suicidal ideation is then 'not currently and seldom' present according to the participant or interviewer. When participants had fleeting suicidal thoughts, although 'seldom' (less than once per month), they scored 2 points on the 'suicidal ideation' item, and were considered to have suicidal ideation. This cut-off value also implies that participants that consider suicide as a potential option for the future, and 'seldom' think about this, were not considered to have suicidal ideation.

Assessment of neuropsychiatric characteristics: The presence of depressed mood, anxiety, apathy, irritability, and aggression was also assessed with the UHDRS-b (Huntington Study Group, 1996). Total scores for these separate items were computed by multiplying their severity (range 0–4 points) and frequency (range 0–4 points) scores. Based on clinical experience, a total score >1 point on such an item

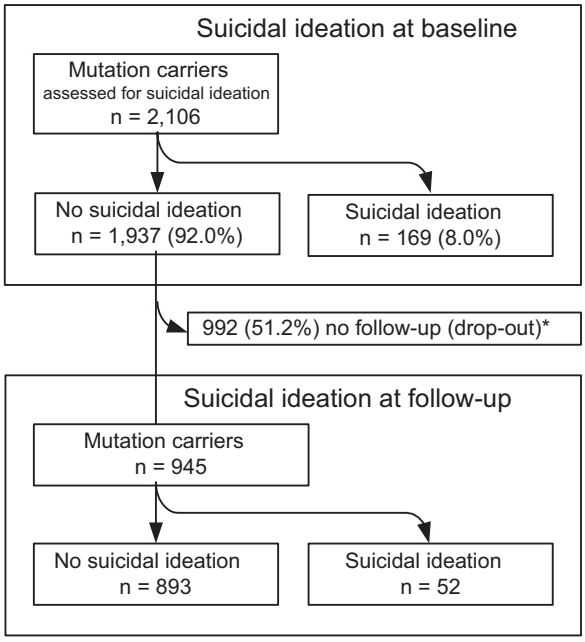

Fig. 1. Flowchart of drops-outs. * drop-outs had a significantly longer estimated duration of disease, lower Total Functioning Capacity (TFC) score and higher Unified Huntington's Disease Rating Scale (UHDRS)-motor score. No significant difference in any of the neuropsychiatric characteristics.

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