Onset symptoms in 510 patients with Huntington's disease

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Abstract

The onset of Huntington's disease (HD) is preceded or accompanied by events and symptoms which contribute to the natural history of the disease. Data obtained from the first 510 completed 'Questionnaires for Affected Individuals', recorded by the National Huntington's Disease Research Roster (NHDRR) were analysed. The following features were evaluated: (1) neurological and psychiatric onset symptoms; (2) the precipitating effect of stressful events and drugs; (3) the modification after onset of smoking and alcohol consumption. The most frequent psychiatric onset symptom was depression. Stressful events in the year before onset occurred in 43% of patients. However, onset age was the same in patients with and without previous stressful events. Smoking and especially alcohol consumption showed a decreasing trend after onset.

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Huntington's disease (HD) has a slow and insidious onset. The most frequently observed symptoms are choreic movements and psychiatric disturbance. The onset of choreic movements generally leads to the diagnosis of HD although psychiatric disturbance may be noted as early as a decade or more before these movements begin. This initial stage of HD is important because the first neurological symptoms and the first behaviour and mood changes, together with the preceding external events in patients' lives, may give some insight into an important and still unexplained feature, the wide range in onset age characteristic of HD. Only a few studies have given a detailed description of onset symptoms of HD in a large population.[1(table 5:1)-3]

The National Huntington's Disease Research Roster (NHDRR), Indiana University School of Medicine, collects clinical and genetic data pertaining to HD patients and families. Onset symptoms from a sample of NHDRR patients were examined.

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Patients and methods

When a patient with HD is registered with the Roster, in most cases a first degree relative is asked to fill in a questionnaire ('Affected Questionnaire', AQ) containing a number of questions about the patient's clinical history. Relatives receive the AQ at home and nearly 40% of them complete and return the questionnaire. In a small percentage of cases the patient himself completes the AQ.

In 1987, at the start of this study, the Roster had collected data from 1338 families and 64 329 subjects including 6884 patients with HD. Of these patients 1365 had returned AQs to the NHDRR. Questionnaires are not sent to those who have no living first degree relative who can complete the form. In this study, the data contained in the first 510 AQs available in February 1987 and recorded at the Roster were analysed. The analysis does not include patients from the huge Venezuelan family[3]

Table 1 Persons completing the questionnaire.

	No	%	Sex	
			M	F
Spouse	173	34·0	—	—
Daughter/son	154	30·3	38	116
Sib	67	13·3	29	38
Parent	49	9·7	3	46
Ex-spouse	6	1·2	—	—
In laws (daughter/son)	13	2·6	0	13
Patient	23	4·5	—	—
Others	23	4·5	—	—
Not reported	2	0·4		
Total	510	100	70	213

Table 2 Onset symptoms recorded in the questionnaire: analysis of patients with one symptom.

	No of patients
Physical symptoms (total 133, 69%)	
Involuntary movements (chorea)	97
Trouble in walking	9
Clumsiness, imbalance	15
Unsteadiness	7
Trouble holding objects	2
Speech difficulty	3
Weight loss	0
Difficulty with bladder control	0
Difficulty with bowel control	0
Changes in sleep patterns	0
Mental and emotional symptoms (total 61, 31%)	
Sadness	0
Depression	35
Lack of motivation	12
Difficult to get along with	3
Sexual problems	1
Memory loss	1
Intellectual decline	2
Delusions or hallucinations	2
Suspiciousness, paranoia	5
Total	194

Table 3 Presenting symptoms of HD (n=510 AQs).

Persons completing the question "What were the first symptoms?" = 472
(A) One onset symptom = 260
(B) Two or more onset symptoms = 212
Imprecise symptoms, approximately described, not included in the established categories = 157 (A = 66; B = 91)
A = 260 − 66 = 194
B = 212 − 91 = 121
} useful answers 315

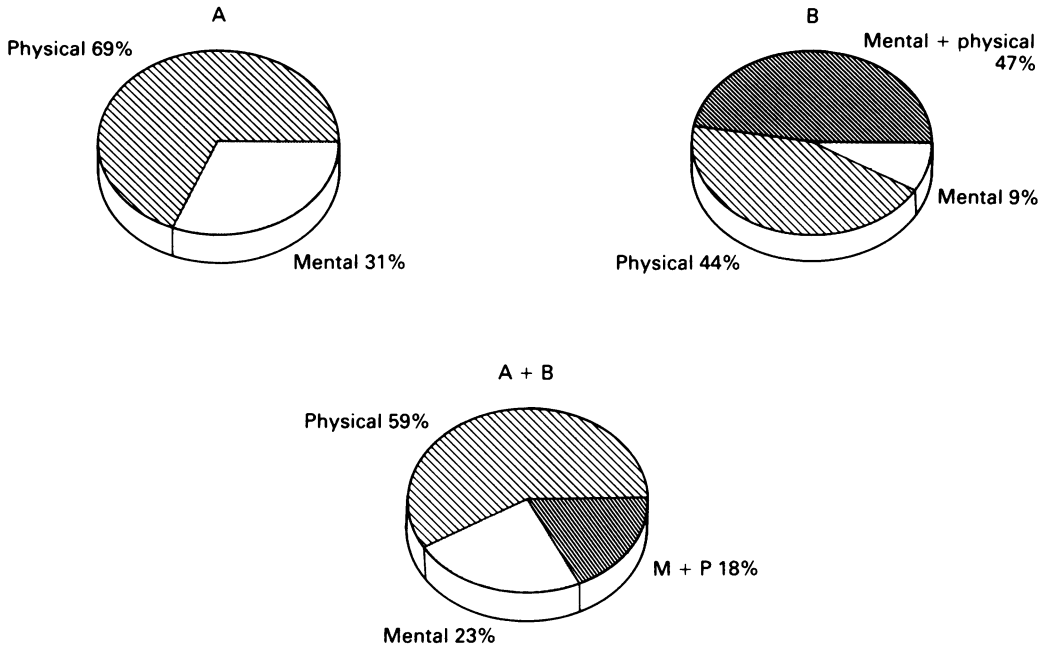

Figure 1 Distribution of mental and physical onset symptoms in HD patients. (A) One onset symptom (194 patients). (B) Two or more onset symptoms (121 patients). (A+B) One and two or more onset symptoms (315 patients).

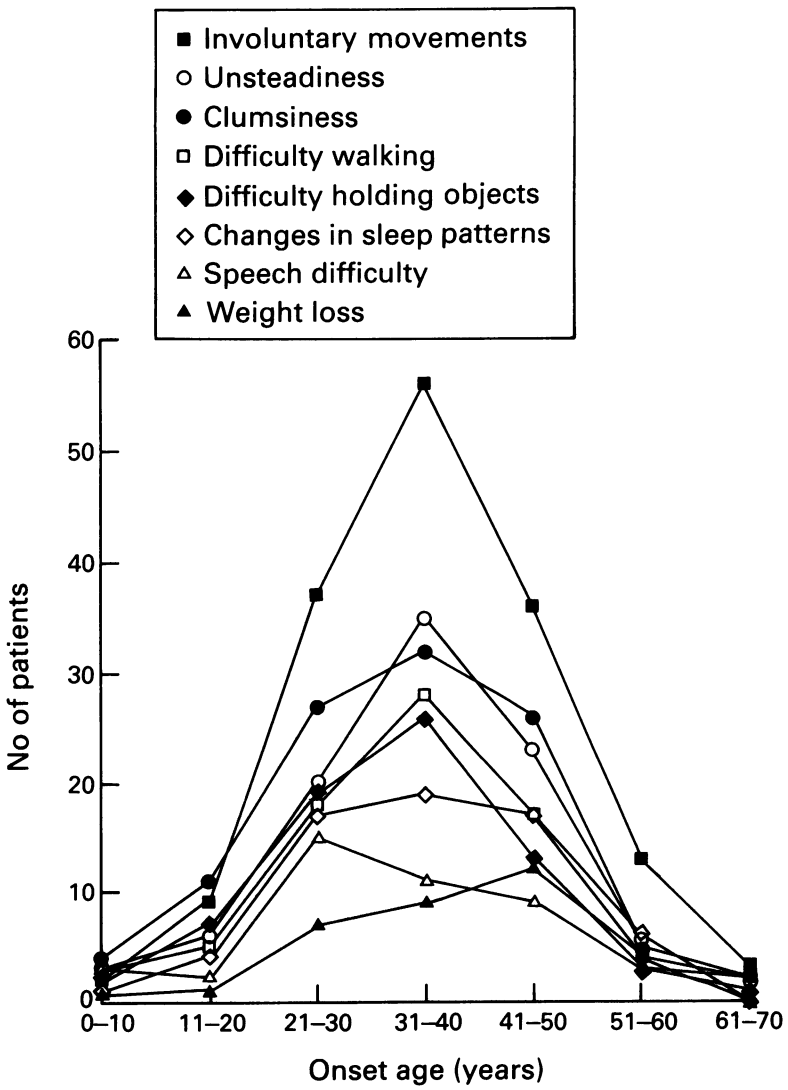

Figure 2 Physical symptoms in the first year of illness. Difficulty with bladder/bowel control was not reported during the first year of illness.

which is also collected and maintained at Indiana University.

An analysis of the persons who completed the AQ is shown in table 1. In most cases (65%), the patient's spouse or child completed the questionnaire. In all categories, the majority of the completed questionnaires were answered by women.

In the present study, only a small portion of the questions included in the AQ was analysed. They concerned onset age, type of presenting symptoms, and social history (Sections: Symptoms of HD and the year before the symptoms appeared; Use of alcohol, cigarettes, tranquillisers and non-prescribed drugs). In particular, persons completing the AQ had to indicate which of 10 neurological and nine psychiatric symptoms appeared within one, two to five, six to 10, or more than 10 years after disease onset. A list of these 19 symptoms is reported in table 2. Other questions concerned illnesses, stressful events, or medication during the year before the symptoms appeared. Consumption of alcohol, cigarettes, tranquillisers, and non-prescribed drugs before and after disease onset was also compared.

These data were extracted from the Roster data base, managed by MEGADATS-3M computer program.[4]

Results

The first question in the questionnaire concerned onset symptoms. In table 3 an analysis of the answers obtained is shown. A further description of the single onset symptoms is reported in table 2. Fig 1 shows a comparison of the occurrence of physical or mental symptoms in the patients with one *v* two or more onset symptoms, and an overall evaluation of the 315 patients with classifiable answers.

The second question that was examined

read: "At what age did the symptoms first appear?". These answers were compared with those given to the question: "What was the age of the patient when HD was diagnosed?". These data were available for 348 patients of the 510 questionnaires analysed. Mean onset age was 37·0 (SD 10·6) years with a range of 4 to 70 years. Mean age at diagnosis was 43·3 (SD 11·8) years, with a mean interval between onset and diagnosis of 6·3 years.

Persons completing AQs had to report the occurrence of symptoms at different times during the course of the illness. To have a better idea of the presenting symptoms, ones occurring during the first year after onset were evaluated. The occurrence of physical and psychiatric symptoms is reported in figs 2 and 3. In order to determine if a presenting symptom occurred more or less frequently at different onset ages, each symptom was plotted in 10 year intervals of onset age. All physical and psychiatric symptoms are given as presenting symptoms at different onset ages. A slight shift of weight loss and sexual problems towards advanced age classes was observed, while a contrary trend was seen for speech disturbances. However, these symptoms occurred during the first year of illness in a relatively small group of patients. The height of each curve in figs 2 and 3 is proportional to symptom frequency.

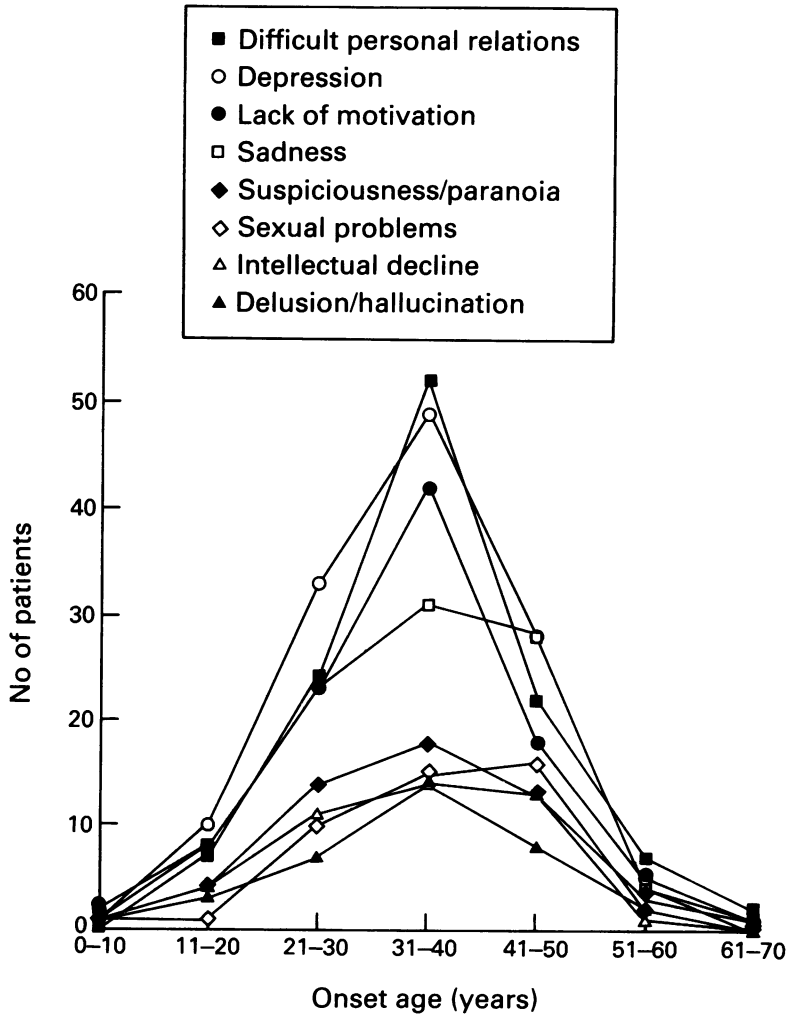

Figure 3 Psychiatric symptoms in the first year of illness. Memory loss was not reported during the first year of illness.

Another question concerned the occurrence of illnesses other than HD and stressful events during the year before the onset of HD. Two hundred and sixteen AQs (43%) reported one or two stressful events in the year before onset. Table 4 shows the subdivision of 161 patients with one stressful event into nine main groups. In the other 55 patients, two stressful events occurred, generally belonging to the same nine groups.

To verify whether a stressful event might anticipate onset age, groups of patients with and without stress in the year before onset were compared. In some patients in both groups onset age was not available and thus was not included in the analysis. In the first group (stressful event(s) before onset, n = 206) mean onset age was 37·1 (SD 10·9) years; in the second group (no stressful event(s), n = 142) mean onset age was 36·9 (SD 10·5). The difference between the two groups is not significant.

The AQs provided 337 answers concerning the use of medication in the year before onset. Two hundred and forty-five respondents reported no use of medication. Among the 92 positive answers the most frequent groups of drugs were anxiolitics (32%) and analgesics (17%).

Alcohol and cigarette consumption decreased after the onset of HD (fig 4). This trend was less evident for smoking than for alcohol. Five patients used non-prescribed drugs before and four patients after HD onset.

Discussion

In most cases this study used the answers given by family members of patients with HD rather than the patient himself. Generally, family members are the main source of information concerning onset age and symptoms. Data concerning onset symptoms in this study are very similar to those reported in other studies. Hayden[1(table 5.1)] reported the following figures, which are the means of eight studies:

Onset symptoms	Hayden[1] (%)	Current study (%)
Neurological	46 (22–65)*	59
Psychiatric	36 (24–51)	23
Combined	18 (10–42)	18

* (range in brackets).

Table 4 Stressful events in the year before disease onset.

	No	%
One stressful event		
Death of a family member/friend	32	20
Conjugal problems	28	17
Health problems (except HD)	24	15
Employment problems	22	14
Family problems (children)	14	9
Accidents	11	7
Financial problems	1	0·6
Academic problems	1	0·6
Arrest/problems with law	0	0
Others	28	17
Total	161	100
Two stressful events		
Association of two of the above	55	
Total	216	

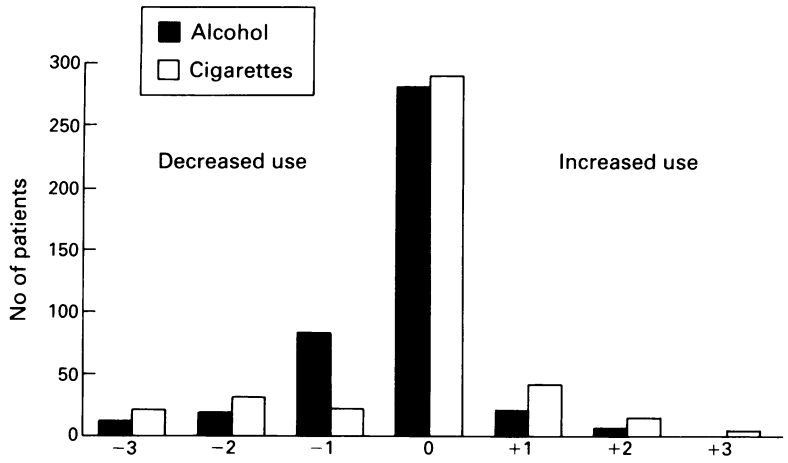

Figure 4 Alcohol (black bars) and cigarette (white bars) consumption. Numbers on horizontal axis show the transition from one score to another after disease onset. According to an arbitrary scale, patients might vary by 1, 2, or 3 points towards decreased or increased consumption after disease onset, independently of their previous classification as light or heavy drinkers or smokers. Zero bars include patients who did not change their previous habit. An analysis by χ^2 of these data showed a significant trend towards decrease for both habits (alcohol $\chi^2 = 37{\cdot}04$, $p < 0{\cdot}01$; cigarette $\chi^2 = 37{\cdot}82$, $p < 0{\cdot}01$; no of patients analysed: alcohol = 423, cigarettes = 425).

In this study only psychiatric symptoms seem to be reported less frequently by relatives than in previous studies. Onset age in this sample is very close to that reported by Conneally[5] in a sample of 999 patients analysed in another study of the NHDRR (36·1 years).

Analysis of the distribution of onset symptoms in different age classes suggests that in most patients HD starts with the same type of symptoms at all ages. In other words, there are no age specific onset symptoms. These data agree with the assumption that HD has a similar clinical picture over the wide age range of onset.

Some authors emphasise the possible precipitating role of stressful events in onset of HD, suggesting that this might explain the wide range of onset age.[6 7] Stressful events, although frequently reported in the year before onset, do not seem to accelerate HD onset. They are more likely a consequence of the first behavioural changes caused by the disease rather than a precipitating factor.

There is a trend towards decreased alcohol and cigarette consumption after disease onset. The cause of these changes in habit is not clear, but might be related to the patient's sensation of these substances' negative effects on dyskinesias or psychiatric symptoms.

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