

## Qualitative H-Reflex Testing in Huntington's Disease

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**Summary.** The occurrence of H-reflexes over both the anterior tibial muscle and the thenar muscle on both sides was investigated in 15 patients suffering from Huntington's disease, 8 clinically inconspicuous offspring, and 30 healthy normal controls. The following results were obtained:

1. An obvious H-reflex over the anterior tibial muscle was found in 12 of 15 patients; there was no H-reflex in only 3 patients.
2. After stimulation on the median nerve there was an H-reflex in 12 of 13 patients investigated.
3. In 5 of 8 clinically inconspicuous offspring there was an H-reflex after peroneal [4] or median [5] nerve stimulation.
4. In 30 normal controls, 1 displayed a weak H-reflex over the anterior tibial muscle; 9 showed a weak H-reflex after median nerve stimulation.
5. The possibility is discussed that an abnormal H-reflex might be an early sign of central reflex disinhibition in otherwise asymptomatic offspring.

**Key words:** Huntington's disease – Asymptomatic offspring – H-reflex – Early detection

**Zusammenfassung.** Das Vorkommen von H-Reflexen im M. tibialis anterior und Thenar beidseits wurde an 15 Patienten mit Chorea Huntington, 8 klinisch unauffälligen Nachkommen und 30 Normalpersonen untersucht. Es fand sich

1. bei 12 von 15 Patienten im M. tibialis anterior beidseits ein eindeutiger H-Reflex, nur bei 3 Choreapatienten war kein H-Reflex nachweisbar,
2. bei 12 von 13 untersuchten Choreapatienten ein- oder beidseitig ein H-Reflex nach Medianusreizung,
3. bei 5 von 8 klinisch unauffälligen Nachkommen ein eindeutiger H-Reflex nach Reizung des N. peroneus (4) bzw. Medianus (5),
4. bei 1 von 30 Normalpersonen ein schwacher H-Reflex über dem M. tibialis anterior bzw. bei 9 von 30 Normalpersonen ein schwacher H-Reflex nach Medianusreiz.

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Dedicated to Heinrich Oepen on the occasion of his 60th birthday

Es wird diskutiert, ob ein abnormer H-Reflex im N. peroneus bei sonst gesunden Huntingtonnachkommen auf eine zentrale Reflexenthemmung bei beginnender Chorea Huntington hinweisen kann. Der alleinige Nachweis nach Medianusreizung ist wegen seines Vorkommens in ca. 30% der Normalpersonen dafür nicht verwertbar.

**Schlüsselwörter:** Chorea Huntington – Asymptomatische Nachkommen – H-Reflexe – Früherkennung

## Introduction

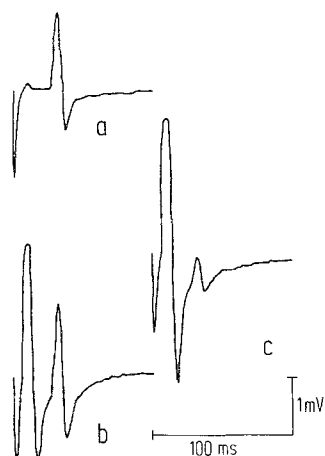
The investigation of the Hoffmann or H-reflex in man, a reflex elicited by nerve stimulation with an electric shock, has been established since its first description by Paul Hoffmann [6]. H-reflex testing may give useful diagnostic hints in several diseases of the CNS. Different findings were reported in pyramidal and extrapyramidal lesions [4, 5, 10, 12, 16, 17, 19], cerebellar disorders [13, 21] and spinal shock [1, 3], but quantitative analysis of H-reflexes or of conditioned recovery curves is difficult because of the numerous influences on H-reflex amplitude [9]. The occurrence of an H-reflex in muscles where it is usually not obtainable seems to be a reliable feature in detecting lesions of the CNS [1, 3, 5, 10, 19]. Such qualitative testing is of interest in the preclinical diagnosis of Huntington's disease (HD) with regard to genetic counseling or selection for therapeutic trials [9, 11, 14], since the gene carrier remains inconspicuous until post-adolescence [2]. To date no feature has been proved to predict if an offspring will develop the disease, although investigation of eye movements [14, 15] might show some early abnormalities in asymptomatic carriers. Administration of L-dopa to relatives of those affected may elicit choreiform movements, but because of the high suicidal rate in this patient group [2], this method should be avoided.

H-reflex testing is not molesting and may reveal abnormalities of motor system. After previous reports on this subject [10, 16] the purpose of this study was to determine alterations in the H-reflex in patients with manifest HD and to demonstrate their diagnostic validity for early detection of the disease in unaffected relatives.

## Patients and Methods

A study was made of 15 right-handed patients suffering from HD, as diagnosed by a definite family history and characteristic symptoms, and 8 clinically inconspicuous first-generation offspring. The mean age of the patients was  $44.1 \pm 9.3$  years ( $\bar{x} \pm \text{SD}$ ), with a range of 28 to 65 years. The 8 right-handed first-generation descendants derived from 8 different families; their mean age was  $33 \pm 6.1$  years ( $\bar{x} \pm \text{SD}$ ), with a range of 24 to 45. The control group comprised 30 normal subjects. Technical details and reference values for the H-reflex recovery cycles were given in a recent study [17]. Since neuroleptic drugs do not affect results [10], medication of patients with HD was not interrupted. For qualitative H-reflex testing, the subjects sat relaxed in armchairs in a slightly darkened, quiet room, with eyes closed and arms flexed at the elbow. Percutaneous electrical stimuli to the peroneal nerve near the fibular head on both sides and to the median nerve at the wrist were delivered by a bipolar stimulating electrode fixed by an elastic tape. Rectangular stimuli of 0.2 ms duration were generated in series by a Tönnies stimulation unit type

**Fig. 1 a-c.** Original recording (on average 16 stimuli) of H-reflexes from the thenar muscle after median nerve stimulation in a first-generation relative: 30-year-old asymptomatic daughter of a Huntington patient. **a.** Clear H-reflex with low stimulus intensity, **b.** increasing M-response with increasing stimulus intensity, **c.** decreasing H-reflex with further increasing stimulus intensity



D with an isolation unit using constant-current stimulus. Placement of the electrodes was considered adequate if a threshold stimulus was eliciting a direct M-response. The reflex responses were recorded by two silver disc surface electrodes, placed at the upper third of the anterior tibial muscle (active electrode) and on the distal tibial crest (reference electrode) for peroneal nerve stimulation; for median nerve stimulation at the wrist the active electrode was placed on the thenar muscle, the reference electrode on the dorsal side of the thumb. The frequency, duration, and intensity of stimulation were according to Hugon et al. [8]. The rectangular stimuli of 0.2 ms duration were applied every 5 s, with an intensity ranging from zero to supramaximal for the M-response (see Fig. 1). The M-response and the H-wave, if present, were averaged 16 times by a 200-point averager (Data Laboratories, England) and recorded by an xy-plotter. These examinations were repeated twice on the right and left peroneal nerve as well as on the right and left median nerve.

An H-wave was considered to be present when its amplitude increased simultaneously with the M-response as the intensity of the stimulus increased. With further increase of intensity, the H-wave decreases and finally disappears. However, the F-wave does not decrease in amplitude with increasing stimulus intensity [10, 18]. H-waves considered in this study met these criteria (see Fig. 1).

## Results

In 30 normal persons, 1 showed a weak unilateral H-reflex after peroneal nerve stimulation, 9 after median nerve stimulation (four times on the right side, five times on the left, twice bilaterally). Central nervous system abnormality was not indicated in subjects with obtainable H-reflexes.

All 15 patients with manifest HD had H-reflexes over the anterior tibial or thenar muscle. However, after stimulation of the median nerve, 1 patient had no H-reflexes, and 2 patients underwent severe involuntary muscle spasms, so an investigation was not possible. The H-reflex obtained in 7 patients after left median nerve stimulation was more pronounced than contralaterally, while 3 patients showed more pronounced H-reflexes on the right thenar muscle and 2 had similar H-reflexes on both sides (see Table 1).

**Table 1.** Occurrence of H-reflex in the anterior tibial and thenar muscles, classified as marked (m), weak (w), and absent (a). The number of recordings is indicated for each classification; in bilateral evaluation the clearer H-reflex was considered for classification; interindividual overlap occurs. For more details see text

		Peroneal nerve stimulation			Median nerve stimulation		
		Right	Left	Bilat- erally	Right	Left	Bilat- erally
Patients with HD (n = 15)	m	10	7	7	5	8	3
	w	2	5	5	7	3	8
	a	3	3	3	1	2	2 <sup>a</sup>
Healthy offsprings (n = 8)	m	2	2	2	3	2	2
	w	3	2	3	4	2	5
	a	3	4	3	1	4	1
Normal controls (n = 30)	m	0	0	0	0	0	0
	w	0	1	0	4	5	2
	a	30	29	30	26	25	28

<sup>a</sup> Two patients not investigated

After peroneal nerve stimulation, 12 patients showed marked H-reflexes over the anterior tibial muscle: 5 patients showed more pronounced H-reflexes on the left side, 6 on the right side, while 1 patient had H-reflexes on both sides. The H-reflex recovery curve [17] of the patient with the least involuntary movement indicated late facilitation at 250 ms above the level of the normal controls [8, 17].

In eight offsprings, five inconspicuous first-generation relatives showed an H-reflex after median (5 times) or peroneal (4 times) nerve stimulation, or both (3 times). Two had marked H-reflexes in the thenar and anterior tibial muscle, one had similar reflexes on both sides, and one had emphasis on the left side. Two showed weak H-reflexes after median peroneal nerve stimulation, with emphasis of the right side. One showed H-reflexes only after median nerve stimulation; H-reflexes after peroneal nerve stimulation alone were not observed. In the remaining three, an H-reflex was observed in the thenar muscle (twice) and the anterior tibial muscle (once), but it was not continuous and was thus regarded as nonreproducible. In three offspring the H-reflex recovery curve [17] was investigated. In one with nondetectable H-reflexes after median nerve and peroneal nerve stimulation, no abnormality was found; however, the curves of the other two with obtainable H-reflexes showed an increased late facilitation at 250 ms, with minor depression following facilitation in comparison to the controls (for methodological details see [17]).

**Discussion**

This study confirms that H-reflexes occur in all patients with clinically manifest HD [10]. An H-reflex does not usually occur in the anterior tibial [7, 10] or thenar

muscle [19], although weak but reproducible H-reflexes were found after median nerve stimulation in about 30% of normal controls. Nevertheless, this phenomenon could be cautiously interpreted as a sign of central nervous system abnormality, while the occurrence of an H-reflex in the anterior tibial muscle is a more reliable feature of Huntington's disease.

The change in motor activity of the CNS is also reflected in the H-reflex recovery curves. We found an increased late facilitation at 250 ms, comparable to that reported in spasticity [17] and Parkinson's disease [16, 20]. Similar, slightly elevated facilitation in HD is reported by Sax et al. [16], but less pronounced than in Parkinson's disease. These authors suggest that "the clinical picture in the extrapyramidal disorders forms a continuum of neuronal muscle system activity rather than distinct and opposite phenomena (too much versus too little) as suggested by the initial clinical observations" [16]. The lack of tonic motor inhibition due to striate degeneration could explain the facilitation of H-reflexes in certain muscles [10, 18]. While the H-reflex is usually obtainable after posterior tibial nerve stimulation [6, 8, 10, 17] and can be found up to the age of 6 months in the muscles of the hand [5], it is then suppressed by the development of the pyramidal tract. In patients with hemispherical or upper brainstem lesions, the H-reflex was reported to reappear and be demonstrable in the forearm and brachioradialis muscles of the majority of patients tested [19]. Also, in normal subjects an H-reflex is obtainable during voluntary contraction in the upper and lower extremity muscles [6, 18], a finding we confirmed in preliminary tests. Even though great care was taken to ensure maximal relaxation in a supine position, a weak H-reflex occurred in about 30% of normal controls, which could be due to incomplete relaxation.

In Sydenham's chorea, an H-reflex in the hypothenar muscle was found in four patients with active chorea, and it was still present 3–4 months after cessation of choreiform movements, disappearing only after 4 months [5]. Thus correlation of an H-reflex with the presence of choreic behavior suggests that this reflex may be useful in the detection of subclinical chorea. The occurrence of an H-reflex in offspring after median or peroneal nerve stimulation may mean subclinical HD. As one offspring with saccadic oculomotor disturbances [14] and three patients showed bilateral H-reflexes only after median nerve stimulation, the detection of motor abnormalities may be augmented by the investigation of both thenar muscle and anterior tibial muscle.

Although these abnormalities may be an early sign of fully developed HD, they may also represent a neurologic abnormality in some offspring as an expression of partial penetration of the HD gene [11]. Only a planned follow-up study will prove whether the offspring develop the disease.

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