ORIGINAL CONTRIBUTION

The Startle Pattern in the Minor Form of Hyperekplexia

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Background: The major and minor forms of hereditary hyperekplexia (HE) are characterized by excessive startle responses, which are accompanied by transient stiffness only in major HE; patients with major HE also have continuous stiffness during infancy. A point mutation has been identified for major HE in the gene encoding the α_1 subunit of the glycine receptor but not for minor HE.

Objective: To measure startle reflexes and autonomic responses in the major and minor forms of HE in the original Dutch HE pedigree.

Design: Startle reflexes and autonomic responses were studied with 3 series of 20 auditory stimuli with intervals of 10 seconds (at 90 and 113 dB) and 60 seconds (at 113 dB).

Setting: A university hospital neurologic department.

Patients: Four patients with minor and 9 patients with major HE (patient groups) (a part of the Dutch HE family pedigree) and 20 healthy controls (control group).

Main Outcome Measures: Startle movements were quantified with latencies and areas of electromyographic bursts of the following 4 muscles: the orbicular muscle of the eye, the sternocleidomastoid muscle, the biceps muscle of the arm, and thenar muscles. Autonomic reactions were measured with psychogalvanic responses.

Results: The 4 muscles contracted in similar order in the groups. The onset latencies of the orbicular muscle of the eye, the sternocleidomastoid muscle, and the biceps muscle of the arm were significantly prolonged in patients with minor HE ($P<.006$). The frequencies of occurrence of the electromyographic bursts were not different in the minor HE and major HE groups, but they were significantly higher in both patient groups compared with those in the control group ($P<.001$). The magnitude of the startle responses did not differ between the 2 patient groups ($P=.4$), but it was larger in both patient groups than in the control group ($P<.001$). Startle habituation in the minor HE group was much weaker than in the major HE group ($P<.001$) or in the control group ($P<.001$). The size of psychogalvanic responses ($P=.1$) and the degree of habituation ($P=.24$) in the minor HE group did not differ from those in the major HE group. Compared with that in the control group, the size of psychogalvanic responses in the minor HE group was larger ($P<.001$) and they habituated stronger ($P<.001$).

Conclusions: The differences in the startle pattern between major HE and minor HE agree with the clinical and genetic findings: only major HE constitutes part of the HE phenotype. The cause of the minor HE is, as yet, unknown.

Arch Neurol. 1996;53:608-613

HEREDITARY hyperekplexia (HE), or startle disease, is an autosomal dominant disorder characterized by exaggerated startle reactions to unexpected, particularly auditory, stimuli. Suhren et al[1] and Tijssen at al[2] described the syndrome in a large Dutch family, and subsequent studies[3-10] confirmed its familial occurrence. In the Dutch family, 2 clinical forms of HE were recognized. The major form of HE (hereafter, major HE) is characterized by excessive startle reactions followed by a short period of generalized stiffness, during which voluntary movements are impossible. Consciousness remains clear during the response. Patients with major HE show an extreme generalized stiffness immediately after birth, which normalizes during the first years of life. The minor form of HE (hereafter, minor HE) is also characterized by excessive startle reactions but without stiffness. In the original description of this pedigree, both forms of HE were supposed to reflect the same gene defect.[1] In other HE pedigrees,[4,10-12] the occasional occurrence of minor HE has been confirmed.

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SUBJECTS AND METHODS

SUBJECTS

Four patients (all female; mean age, 41 years; age range, 26-57 years) with minor HE and 9 patients (6 male; mean age, 45 years; age range, 33-54 years; and 3 female; mean age, 51 years; age range, 28-66 years) with major HE from the Dutch HE family were included in the study.[1,3] In all patients, genetic testing had been performed; the patients with minor HE did not have the gene defect, while those with major HE did.[3] Twenty healthy controls were studied: 10 men (age range, 26-65 years; mean age, 40.5 years) and 10 women (age range, 26-63 years; mean age, 40.3 years). Five patients with major HE were taking medication (clonazepam [n=3], diazepam [n=1], and phenobarbital [n=1]). The study was approved by the Medical Ethical Committee of the Leiden University Hospital in the Netherlands, and informed consent was obtained from all participants of the study.

METHODS

Startle responses were elicited by binaural tones delivered through earphones. Subjects were standing at rest, wore a parachute harness attached to the ceiling to prevent injury in case of a fall, and were instructed to count the stimuli to remain alert.

Three series of auditory stimuli were given: (1) 20 tones at 90 dB delivered every 10 seconds, (2) 20 tones at 113 dB with intervals of 10 seconds, and (3) 20 tones at 113 dB every 60 seconds. The 3 series were executed in identical order, with at least a 5-minute pause between the series. These series enabled effects of stimulus intensity and stimulus interval on habituation to be investigated.

EMG Recording

Electromyographic activity was recorded with silver–silver chloride cup electrodes, using the belly-tendon system, from the following 4 muscles: the orbicular muscle of the eye, the sternocleidomastoid muscle, the biceps muscle of the arm, and the thenar muscle on the right side. Electromyographic signals were acquired with a 4-channel EMG apparatus (Viking II, Nicolet, Madison, Wis), with a bandpass filter of 20 Hz to 20 kHz. Signals of 250-millisecond periods were sampled and stored for later analysis. The beginning and the end of the EMG bursts were determined, and the area of the bursts was noted, as was onset latency. The *frequency of occurrence of a response* was defined as the percentage of all 60 stimuli that evoked an EMG burst in a muscle.

Autonomic Recording

Psychogalvanic responses were recorded with silver–silver chloride cup electrodes fastened to the palm and back of the right hand. The signal was recorded on paper with an electroencephalographic apparatus. The gain of the PGR recording was adjusted during the test according to the magnitude of the response. Because PGR activity showed spontaneous fluctuations, it was quantified by measuring the difference between minimum and maximum peaks during 8 seconds after the stimulus.

Data Analysis

In our previous study on patients with major HE (unpublished data, 1995), it was found that the use of medication significantly influenced the onset latencies and the frequency of occurrence of the EMG bursts. No significant influence of medication was found on the area of the burst, the degree of startle response habituation, and the amount and degree of habituation of the PGRs. Therefore, for the comparisons of the onset latencies and the frequency of occurrence of the EMG bursts between the patient groups, only patients who did not take medication were examined.

Differences in onset latencies of EMG bursts of the 4 muscles among the 3 study groups were assessed, using analysis of variance (ANOVA), with study groups and 3 series of stimuli as factors. For analysis of the onset latencies, only the first response of each series of stimuli was used. The Duncan post hoc test was used to investigate differences between the groups. *Frequency of occurrence of bursts*, defined as the percentage of all responses of all subjects in a group, was compared between the study groups paired as follows: minor HE vs major HE, minor HE vs control, and major HE vs control, using the χ^2 test. Differences in areas of EMG responses among the groups were analyzed with repeated measures ANOVA (RM-ANOVA). Areas of EMG responses proved to be skewed and were transformed to their square roots before analysis. An RM-ANOVA was performed for the 3 series of stimuli combined with the areas of the 4 muscles during the series of stimuli as response variable comparing 2 groups at a time (minor HE vs major HE, minor HE vs control, and major HE vs control). The PGRs were also evaluated with RM-ANOVA.

The gender composition of the 3 study groups differed strongly. The minor HE group comprised female patients only; the major HE group comprised both male and female patients, but all the female patients were taking medication. Therefore, part of the statistical analysis performed in the major HE group (onset latencies and frequencies of occurrence of the EMG bursts) was based on male patients only. It was not possible to determine whether gender had an influence on the results in the 2 patient groups because of the composition of both groups. Analysis of differences in results between men and women was restricted to the control group (10 men and 10 women). Any differences within the control group were assumed to apply also to the patient groups.

The NCSS package (Number Cruncher Statistical Systems, Kaysville, Utah) was used for all analyses. A P value of less than .05 was considered significant.

The genetic defect of hereditary HE has been located in the α_1 subunit of the glycine receptor on chromosome 5q33-q35.[3,13] This locus and the abnormality of the glycine receptor have been confirmed only for major HE in the Dutch HE pedigree.[3] Patients with minor HE did not have this point mutation, prompting the question of whether minor HE is an integral part of HE. It was hypothesized that exaggerated, but normal,

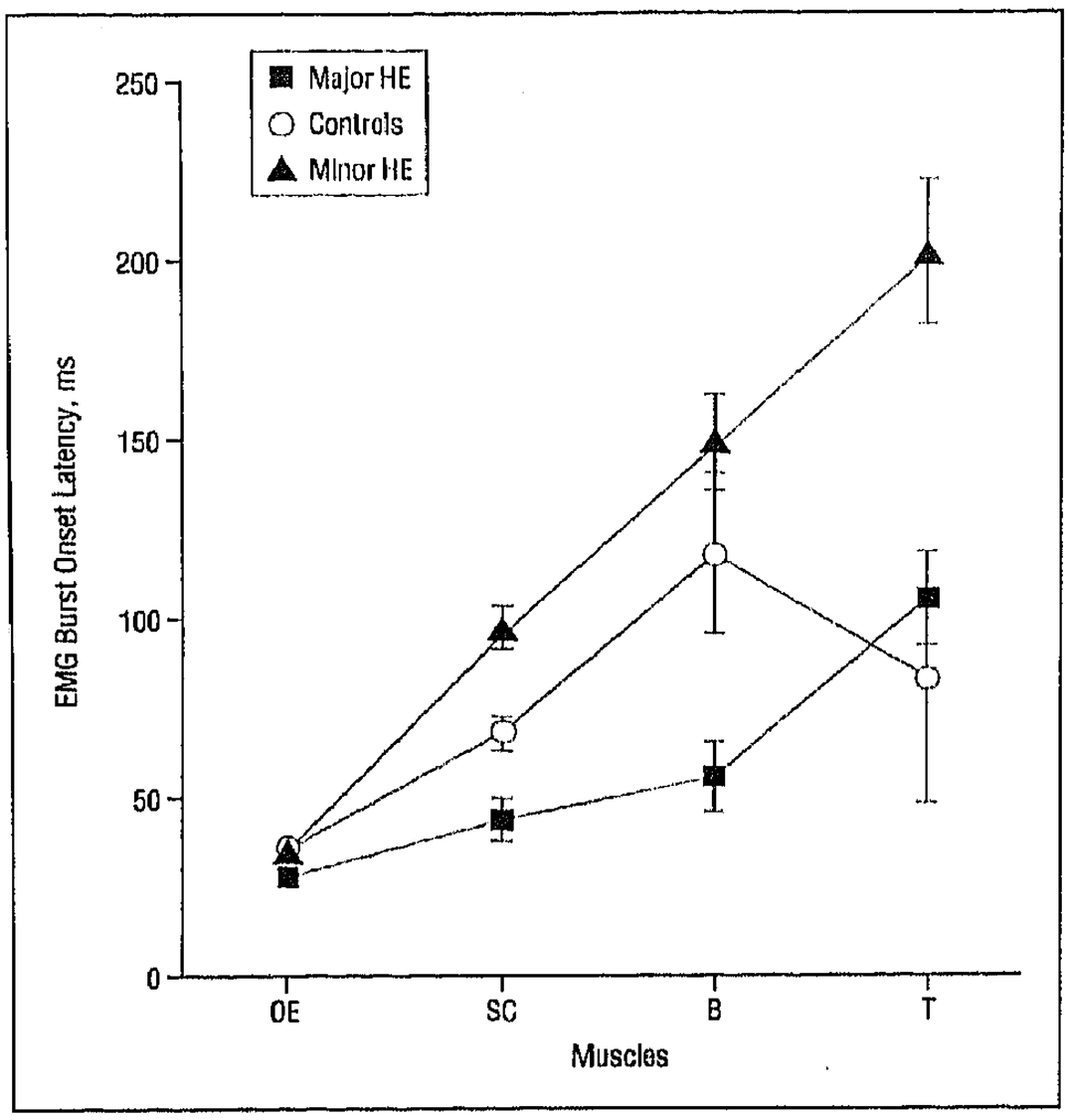

Figure 1. *Onset latencies (±SEM) of the electromyographic (EMG) bursts of the 4 muscles in patients with the minor and major forms of hyperekplexia (HE) and in controls for the response to the first stimulus of all 3 series of stimuli (series 1, 20 tones at 90 dB and 10-second intervals; series 2, 20 tones at 113 dB and 10-second intervals; and series 3, 20 tones at 113 dB and 60-second intervals). (The SEMs below 2 are not shown.) The latencies increase in the 4 muscles in the following order: orbicular muscle of the eye (OE), sternocleidomastoid (SC) muscle, biceps (B) muscle, and thenar (T) muscle in the 2 patient groups (major HE and minor HE). Note that the intervals between the onset latencies of the muscles in minor HE are long and that the thenar muscle response in the control group refers to very few responses.*

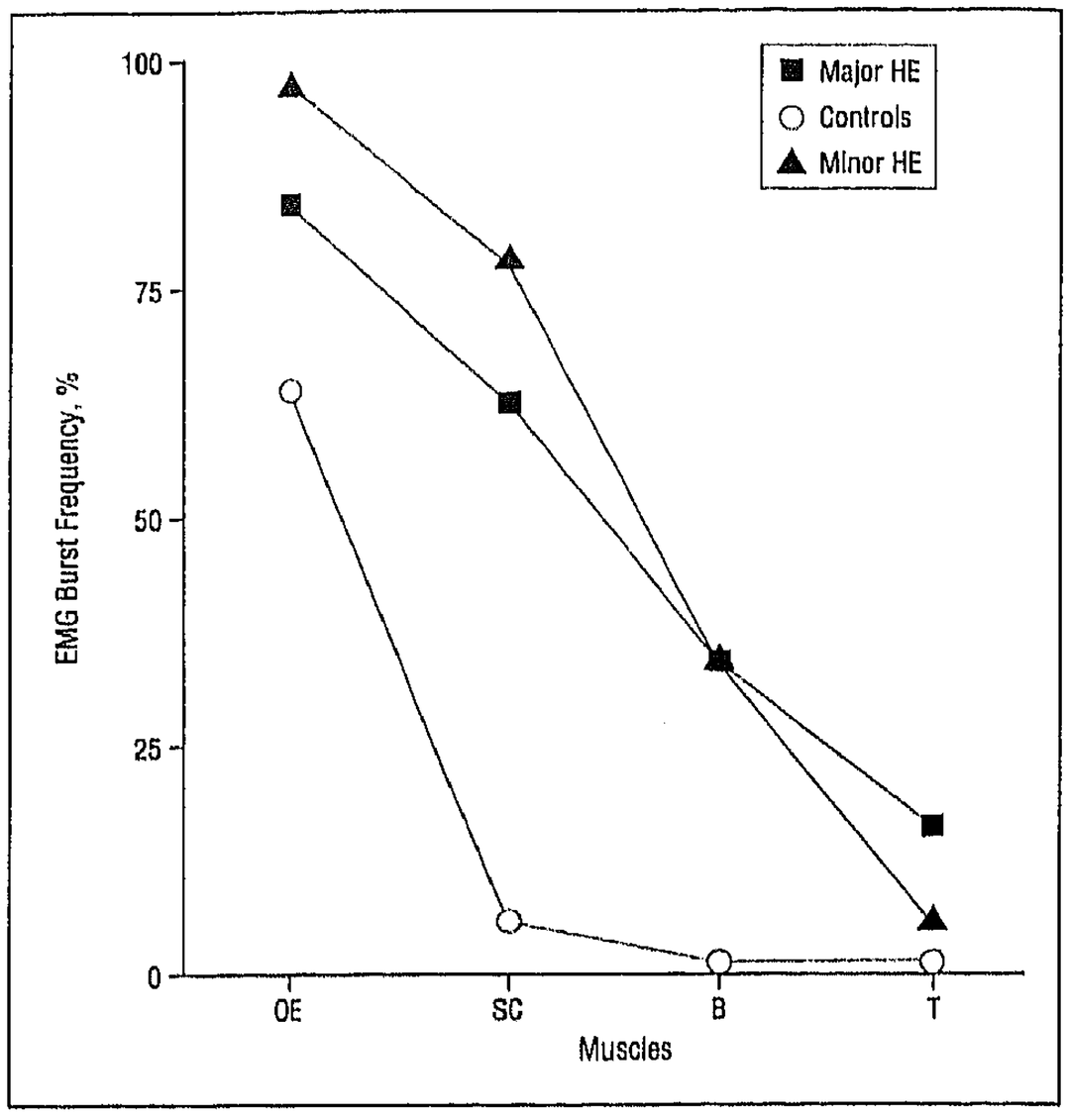

Figure 2. *Frequency of occurrence of electromyographic (EMG) bursts of the 4 muscles (orbicular muscle of the eye [OE], sternocleidomastoid [SC] muscle, biceps [B] muscle, and thenar [T] muscle) in patients with the minor and major forms of hyperekplexia (HE) and in controls (denoting the percentage of all stimuli that were followed by EMG responses to all 3 series of stimuli (series 1, 20 tones at 90 dB and 10-second intervals; series 2, 20 tones at 113 dB and 10-second intervals; and series 3, 20 tones at 113 dB and 60-second intervals). The frequency of occurrence of EMG bursts is not significantly different in minor HE and major HE except for the thenar muscles (P=.001). In the controls, almost no responses were registered in the biceps and thenar muscles.*

startle reactions might erroneously be considered abnormal because startle responses are well known in the HE pedigrees.

Electromyographic (EMG) studies in patients with HE[10,14] revealed a pattern of muscular activity that is similar to the startle reaction in normal subjects, except for its larger magnitude. These findings were confirmed for patients with major HE in the Dutch HE family, but, in contrast to our previous studies (unpublished data), the startle reflex to repetitive stimuli habituated stronger than in controls. Autonomic reactions, measured by the psychogalvanic response (PGR), were enlarged in patients with major HE, but with a reduced degree of habituation (unpublished data.) Electromyographic and autonomic responses of minor HE have never, to our knowledge, been investigated.

Electromyographic startle reflex studies were performed to investigate the magnitude of the motor and autonomic responses and their degree of habituation in the minor HE group in comparison with those in the major HE and control groups.

RESULTS

EMG FINDINGS

Mean values of onset latencies increased in the 4 muscles in the following order: the orbicular muscle of the eye, the sternocleidomastoid muscle, the biceps muscle of the arm, and the thenar muscle in the 2 patients groups (**Figure 1**). In the control group, the onset latency of the thenar muscles was shorter than that of the biceps muscles. The onset latencies of the orbicular muscle of the eye ($P<.001$), sternocleidomastoid muscle ($P<.001$), and the biceps muscle of the arm ($P=.006$) were significantly different among the 3 groups. The differences were statistically significant between the minor HE and major HE groups for the 3 muscles and between the minor HE group and the control group for the sternocleidomastoid muscle (Duncan test). The onset latencies of the thenar muscles were not significantly different ($P=.22$) among the groups. The paucity of responses of the biceps and thenar muscles in the control group (<1%) made their analysis less reliable. Within the control group, the onset latencies were not significantly different between sexes for the orbicular muscle of the eye ($P=.14$) and for the sternocleidomastoid muscle ($P=.06$). For the biceps and thenar muscles, only 2 responses were registered in the female subgroup and none in the male subgroup of the control group.

The frequency of occurrence of an EMG burst was not significantly different between the minor HE and major HE groups, except for the thenar muscles, in which the frequency of EMG burst occurrence was significantly higher in the major HE group ($P=.001$) (**Figure 2**). Compared with the control group, the minor HE group had higher frequencies for all 4

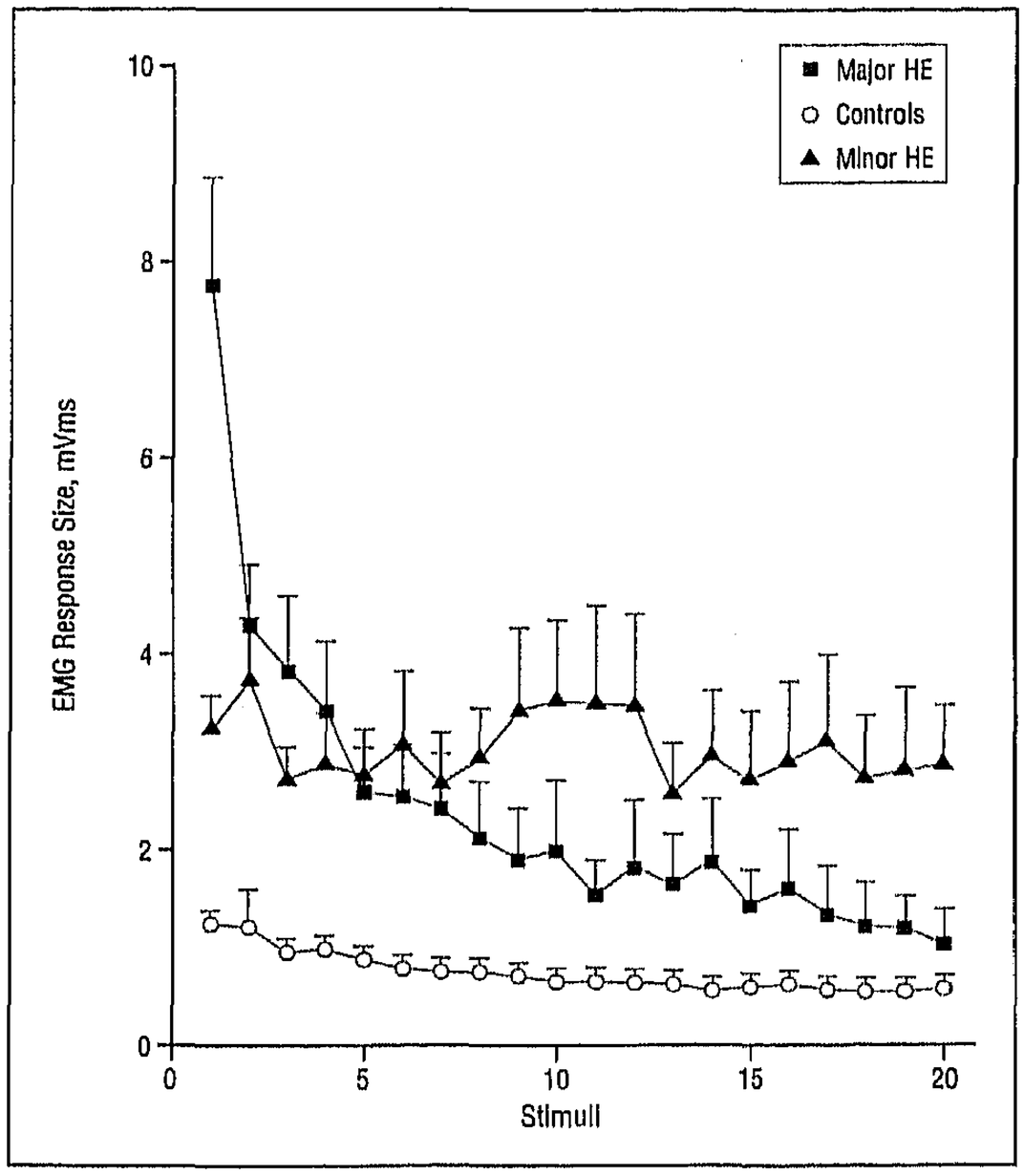

Figure 3. *The summed areas of electromyographic (EMG) bursts (±SEM) of the orbicular muscle of the eye, sternocleidomastoid muscle, biceps muscle, and thenar muscle in patients with the minor and major forms of hyperekplexia (HE) and in controls for the combined series of stimuli (series 1, 20 tones at 90 dB and 10-second intervals; series 2, 20 tones at 113 dB and 10-second intervals; and series 3, 20 tones at 113 dB and 60-second intervals). The EMG response refers to response size expressed as the square root of the summed area. Areas of summed EMG bursts are larger in both forms of HE compared with those in controls, and they habituate in the major HE group and in the control group, but not in the minor HE group.*

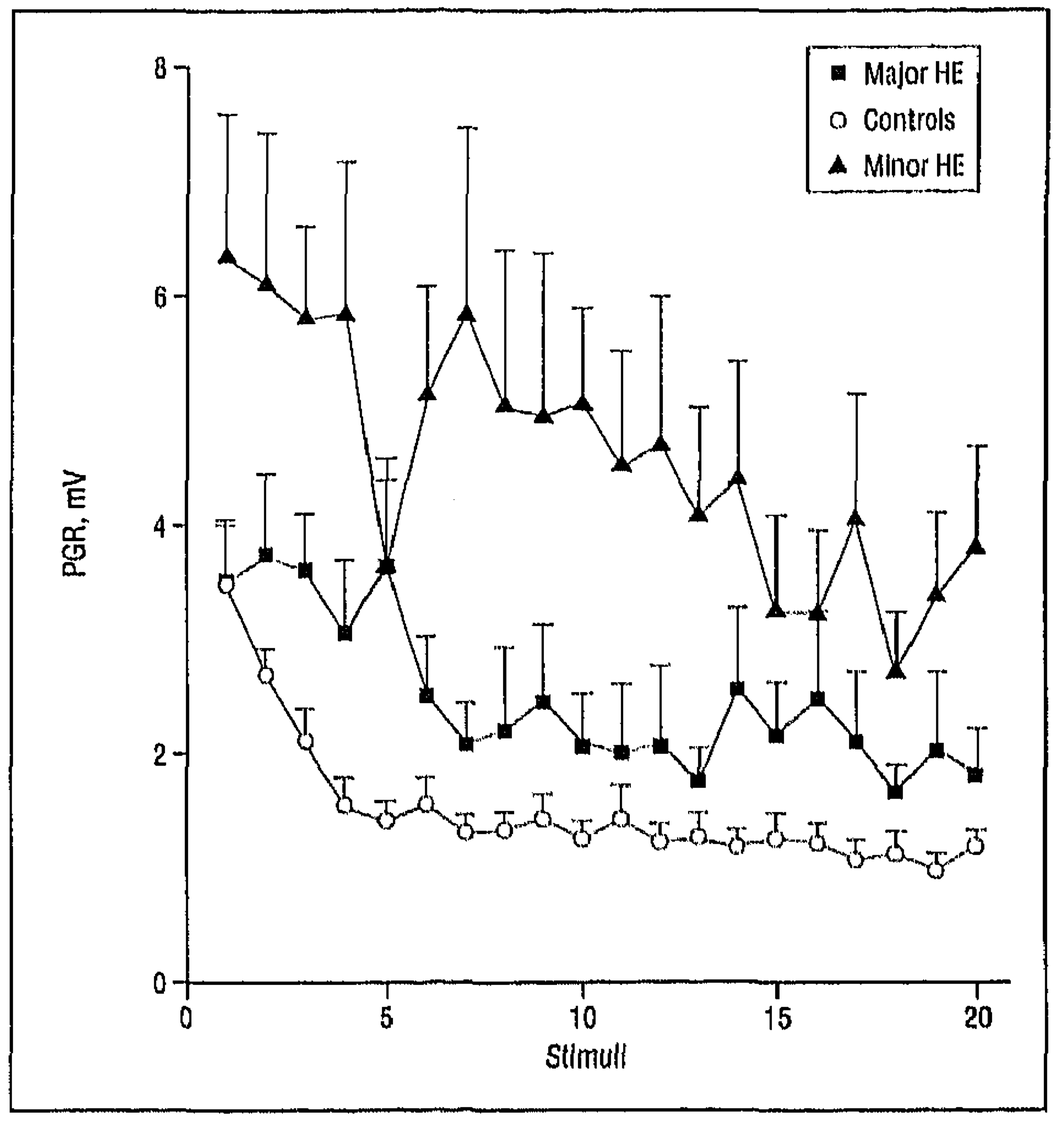

Figure 4. *The psychogalvanic responses (PGRs) (±SEM) in patients with the minor and major forms of hyperekplexia (HE) and in controls for the combined series of stimuli (series 1, 20 tones at 90 dB and 10-second interval; series 2, 20 tones at 113 dB and 10-second intervals; and series 3, 20 tones at 113 dB and 60-second intervals). The PGR size and the degree of habituation of the PGRs are not significantly different in the 2 patient groups, but they are larger in the 2 patient groups compared with those in the control group.*

muscles ($P<.001$). Within the control group, the frequencies of EMG burst occurrence in the orbicular muscle of the eye were 58% in men and 68% in women ($P<.001$); in the sternocleidomastoid muscle they were 4% in the male subgroup and 7% in the female subgroup ($P=.01$); and in the biceps and thenar muscles, responses occurred in less than 1% in both the male and female subgroups. The significant difference in frequency of occurrence in the orbicular muscle of the eye and the sternocleidomastoid muscles might have positively influenced the results in the minor HE group for the orbicular muscle of the eye but certainly not for the sternocleidomastoid muscle.

The 3 different series of stimuli did not influence the magnitude and habituation of the startle responses in the 3 groups to any relevant degree. Further analysis was based on pooled data. For the 3 series of stimuli combined, the summed area of the 4 muscles did not differ significantly between the minor HE and major HE groups ($P=.4$), but the area changed in significantly different ways during the series of stimuli in both patient groups ($P<.001$): the startle responses were enlarged in both patient groups, but the degree of their habituation was stronger in the major HE group (**Figure 3**). The difference in summed area between the minor HE group and the control group was significant ($P<.001$), as was the change of the area during the series of stimuli ($P<.001$) (Figure 3). This meant that startle responses in the minor HE group were enlarged and habituated less than in the control group. Within the control group, the summed area of the 4 muscles did not differ significantly between the male and female subgroups for the 3 series of stimuli combined ($P=.6$), but the area changed in significantly different ways during the series of stimuli ($P<.001$): the degree of startle response habituation was greater in the male than in the female subgroup. These results in the control group cannot explain the differences in results between the patient groups (major HE and minor HE groups) because a lack of habituation was found in the minor HE group, consisting of women only.

AUTONOMIC RESPONSES

The PGR magnitude was significantly different in the 3 groups: it was larger in the minor HE than in the major HE group, and it was larger in both patient groups than in the control group ($P<.001$, for each of the 3 series of stimuli) (**Figure 4**). The change of the PGRs during the series of stimuli was also significantly different among the 3 groups (for each of the 3 series of stimuli): it decreased more in the minor HE than in the major HE group, and also more in the control group than in the major HE group ($P<.001$ in both cases) (Figure 4). A comparison between the 2 patient groups showed that they did not differ in the magnitude of PGRs ($P=.1$), or in the degree of habituation ($P=.24$). Compared with those in the control group, the PGRs in the minor HE group were greater ($P<.001$) and showed a

greater degree of habituation ($P<.001$). Within the control group, no significant difference was found in the PGR magnitude between the female and male subgroups for each of the 3 series of stimuli ($P>.08$), but the change during the series of stimuli was significantly different between sexes ($P\leq.02$): PGR habituation was greater in the male than in the female subgroup. These differences do not significantly influence the results; the comparison among the 3 groups showed more PGR habituation in the minor HE group (women).

COMMENT

As expected, motor startle responses were larger in both patient groups than in the control group, which is compatible with other studies.[10,14] As we found previously (unpublished data), the startle response habituation was stronger in the major HE group than in the control group. A new finding of the present study was that habituation of startle responses was virtually absent in patients of the minor HE group. These results might explain why a reduced degree of habituation had been reported earlier in one of the HE studies[10]; in that study, hereditary and symptomatic minor HE and major HE had been combined.

Besides a lack of habituation of the startle responses, patients with minor HE in the present study had prolonged onset latencies for the orbicular muscle of the eye, the sternocleidomastoid muscle, and the biceps muscles compared with those in patients with major HE. The difference in onset latency was also significant for the sternocleidomastoid muscle compared with that in the control group. The paucity of responses of the biceps and thenar muscles made the comparison less reliable. The onset latencies of the orbicular muscle of the eye were not prolonged in the minor HE compared with those in the control group, but their analysis is complicated because they comprise 2 types of reflexes: the startle reflex and the blink reflex.[15] Prolonged onset latencies in a patient with the hereditary minor HE were also described by Brown et al.[10] Mean onset latencies increased in the 4 muscles in the following order: the orbicular muscle of the eye, the sternocleidomastoid muscle, the biceps muscle, and the thenar muscle in the 2 patient groups in our study, which may be caused by the innervation of the muscles from the startle generator.[10] In the control group, the onset latency of the thenar muscle was shorter than that of the biceps muscle, but this may be caused by the small number of thenar responses. The onset latencies in the minor HE group were too long to be compatible with a startle response; the same refers to the differences in latencies between the sternocleidomastoid and the biceps muscles (51.8 milliseconds) and between the biceps and thenar muscles (53.2 milliseconds).[10,15]

Thompson et al[16] investigated voluntary stimulus-sensitive jerks in patients and controls and found that it was possible to distinguish voluntary jerks from the stereotyped electrophysiological characteristics of the startle response of brain-stem origin. The onset latencies were prolonged in these voluntary excessive jerks, and the jerks to repetitive stimuli habituated stronger,[16] in contrast to those in minor HE. The resemblance of the delayed excessive responses with the voluntary stimulus-sensitive jerks suggests that the startle response in minor HE is a partially voluntary response. Obviously, excessive startle responses are well known in families with HE. An argument in favor of this theory is that the clinical manifestations in minor HE do not start at birth, but rather, later in childhood.[1]

The PGR magnitude was also increased in patients with minor HE and major HE. However, in contrast to the motor response, the PGRs do habituate in both forms of HE in similar fashion. In patients with major HE, habituation of the motor startle response was larger, while habituation of the autonomic response was decreased compared with that in controls (unpublished data). The enlarged autonomic response in minor HE may be a result of increased alertness.

In summary, the motor startle responses in the patients with minor HE are, in comparison with those in the controls, enlarged, delayed, occurring more frequently, and not habituating to repeated stimuli. Minor HE differs from major HE in that startle responses are delayed and do not habituate. The neurophysiological findings are, therefore, in accordance with the clinical and genetic results found in this HE family pedigree: the characteristics of the startle response also point toward a different origin of the startle response in the 2 forms of HE. The hereditary minor HE is rare and, except for the large Dutch HE family, only small pedigrees with both major HE and minor HE have been described.[4,10-12] The supposed existence of a hereditary minor HE was based on this Dutch HE family, because a patient with what seemed to be minor HE had offspring with major HE. Because this patient later was proved to have had stiffness related to the startle responses, he is now considered to have major HE.[2] The smaller families with both major HE and minor HE, described by others,[17] probably concern a recessive type of major HE, as has recently been found in 1 woman.[17] The larger studies on minor HE[18] included mostly sporadic cases. There is, therefore, no proof of a hereditary nature of minor HE. Obviously, a genetic cause cannot be excluded in the Dutch HE pedigree, but, if included, this would imply that there are 2 different genes involved in 1 pedigree, which is unlikely. The cause of the excessive startle responses in minor HE remains unproven.

Based on the results of this study, we suggest 2 contrasting hypotheses. First, the excessive nonhabituating startle response in minor HE could result from a different influence of the cerebellar vermis on the startle response. It was previously described[19,20] that the cerebellar vermis is essential for the habituation of the startle response. The lack of habituation of the startle responses in the patients with minor HE would then be an effect of altered cerebellar influences. Second, the resemblance of the startle responses to voluntary startling strengthens our previous assumption[3] that, although startle responses are well known in this pedigree, pronounced (but normal) startle reactions are considered abnormal. However, not all the characteristics of the voluntary jerks were found in minor HE: the

jerks habituated stronger to repetitive stimuli. Further neurophysiological studies are necessary to discriminate between these 2 hypotheses. A previous study on patients with major HE showed augmented long-loop responses.[21] It would be of interest to measure these long-loop responses in minor HE.

Accepted for publication March 27, 1996.

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REFERENCES

1. Suhren O, Bruyn GW, Tuynman A. Hyperexplexia: a hereditary startle syndrome. *J Neurol Sci.* 1966;3:577-605.
2. Tijssen MAJ, Shiang R, van Deutekom J, et al. Molecular genetic reevaluation of the Dutch hyperekplexia family. *Arch Neurol.* 1995;52:578-582.
3. Shiang R, Ryan SG, Zhu Y, Hahn AF, O'Connell P, Wasmuth JJ. Mutations in the α_1 subunit of the inhibitory glycine receptor cause the dominant neurologic disorder, hyperekplexia. *Nat Genet.* 1993;5:351-357.
4. Andermann F, Keene DL, Andermann E, Quesney LF. Startle disease or hyperekplexia: further delineation of the syndrome. *Brain.* 1980;103:985-997.
5. Morley DJ, Weaver DD, Garg BP, Markand O. Hyperekplexia: an inherited disorder of startle response. *Clin Genet.* 1982;21:388-396.
6. Shahar E, Brand N, Uziel Y, Barak Y. Nose tapping test inducing a generalized flexor spasm: a hallmark of hyperekplexia. *Acta Paediatr Scand.* 1991;80:1073-1077.
7. Hayashi T, Tachibana H, Kajii T. Hyperekplexia: pedigree studies in two families. *Am J Med Genet.* 1991;40:138-143.
8. Saenz-Lope E, Herranz-Tanarro FJ, Masdeu JC, Chacon Pena JR. Hyperexplexia: a syndrome of pathological startle responses. *Ann Neurol.* 1984;15:36-41.
9. Ryan SG, Dixon MJ, Nigro MA, et al. Genetic and radiation hybrid mapping of the hyperekplexia region on chromosome 5q. *Am J Hum Genet.* 1992;51:1334-1343.
10. Brown P, Rothwell JC, Thompson PD, Britton TC, Day BL, Marsden CD. The hyperekplexias and their relationship to the normal startle reflex. *Brain.* 1991;114:1903-1928.
11. Dooley JM, Andermann F. Startle disease or hyperekplexia: adolescent onset and response to valproate. *Pediatr Neurol.* 1989;5:126-127.
12. Pascotto A, Coppola G. Neonatal hyperekplexia: a case report. *Epilepsia.* 1992;33:817-820.
13. Shiang R, Ryan SG, Zhen Zhu R, et al. Mutational analysis of familial and sporadic hyperekplexia. *Ann Neurol.* 1995;38:85-91.
14. Matsumoto J, Fuhr P, Nigro M, Hallett M. Physiological abnormalities in hereditary hyperekplexia. *Ann Neurol.* 1992;32:41-50.
15. Brown P, Rothwell JC, Thompson PD, Britton TC, Day BL, Marsden CD. New observations on the normal auditory startle reflex in man. *Brain.* 1991;114:1891-1902.
16. Thompson PD, Colebatch JG, Brown P, et al. Voluntary stimulus-sensitive jerks and jumps mimicking myoclonus or pathological startle syndromes. *Mov Dis.* 1992;7:257-262.
17. Rees MI, Andrew M, Jawad S, Owen MJ. Evidence for recessive as well as dominant forms of startle disease (hyperekplexia) caused by mutations in the α_1 subunit of the inhibitory glycine receptor. *Hum Mol Genet.* 1994;12:2175-2179.
18. Gastaut H, Villeneuve A. The startle disease or hyperekplexia: pathological surprise reaction. *J Neurol Sci.* 1967;5:523-542.
19. Loplano L, De'Sperati C, Montarolo PG. Long-term habituation of the acoustic startle response: role of the cerebellar vermis. *Neuroscience.* 1990;35:79-84.
20. Leaton RN, Supple WF. Cerebellar vermis: essential for long-term habituation of the acoustic startle response. *Science.* 1986;4:513-515.
21. Markand ON, Garg BP, Weaver DD. Familial startle disease (hyperekplexia). *Arch Neurol.* 1984;41:71-74.