Startle responses in functional jerky movement disorders are increased but have a normal pattern

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ABSTRACT

Background: Exaggerated startle reactions have been frequently described in patients with functional movement disorders (FMD). Long onset latencies and inconsistent recruitment pattern are thought to be a hallmark in these patients. The auditory startle reflex has not been systematically assessed though.

Objectives: Assessing the frequency and pattern of the early and late component of the auditory startle response in patients with functional jerky movement disorders.

Methods: A case-control design was used to study 17 patients with functional jerky movement disorders and 15 healthy gender- and age-matched control subjects. The auditory startle reflex was elicited by 108 dB loud tones and assessed with electromyography in multiple muscles.

Results: Response probability of the early and the late response were significantly enlarged in patients with FMD. The early response showed a normal muscle recruitment pattern whereas the late response revealed a more variable pattern compared to controls. The early and late responses showed normal habituation in both groups. Remarkably, a high response rate of the abdominal muscle was noted especially in patients suffering from abdominal jerks.

Conclusions: This study shows enlarged, but normally patterned early startle responses in FMD. The high response frequency of the late responses found in these patients reflects a behavioral component. Hypersensitivity to external stimuli, often noted in FMD is supported by high response probabilities of both components of the auditory startle response.

1. Introduction

Functional (psychogenic) movement disorders (FMD) refer to a heterogeneous category of movement disorders not caused by a known underlying neurological disease [1]. They are commonly seen in daily neurological practice and jerky movements are one of the most prevalent (15%) phenomenologies [2].

The cause of FMD is largely unknown. There appears to be a discrepancy between perception of the movements as involuntary by the patient, while the clinical and neurophysiologic characteristics, such as distractibility, entrainment, and the readiness potential, suggest volitional control. In the clinical setting, abnormal sensory processing is reflected by hypersensitivity to external stimuli and exaggerated startle reactions [3,4]. Although often mentioned as a clinical hallmark of FMD, the prevalence and characteristics of exaggerated startle reactions have not been well described in the literature nor systematically assessed.

The auditory startle reflex (ASR) can be used as an objective neurophysiological measure of the affective system [5]. It is one of the fastest responses of the fear system and consists of two parts. The first motor response involves generalized muscle activation with short onset latencies (<100–120 ms) and a fixed recruitment pattern [6]. This early part is the motor startle reflex, meant to gain maximal postural stability. It is mediated by the caudal brainstem [7]. The second part of the startle response - also called the ‘orienting response’ - occurs with longer onset latencies (>400 ms) and is characterized by posture adjustment and orientation towards the startling stimulus, accompanied by autonomic changes [8]. This second response is influenced by psychological and behavioral processes and is much more variable in pattern and size [9].

So far, only one small electrophysiological study on the startle response in five FMD patients has been conducted [10]. It showed long and variable onset latencies.
The aim of the present study was to systematically assess the ASR in patients with functional jerks. We studied different parameters of the ASR, including the response rate, onset latencies, recruitment pattern and habituation. We hypothesized that patients would reveal predominantly second responses with long and variable onset latencies. Analyzing the startle reflex in a systematic manner, distinguishing the early and late phase, might help further delineate the origin and substrate of exaggerated startle reactions in FMD.

2. Methods

2.1. Participants

The study was performed in patients with either focal or generalized jerks, consecutively included from the outpatient clinic (n = 17). Two movement disorders specialists (MT or JK) evaluated the patients. Only patients who met Fahn and Williams criteria of ‘clinically probable, established, or documented FMD’ were included [11]. To support the diagnosis patients underwent EEG-EMG co-registration to demonstrate the presence of a Bereitschaftspotential (BP) [12]. Furthermore, all subjects were screened for co-morbid psychiatric disorders based on the DSM-IV using the Mini International Neuropsychiatric Interview - PLUS (MINI-PLUS) [13]. In the context of a trial in which the majority of participating patients (n = 15) were enrolled the Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI) were conducted. Both are widely quantitative self-report scales assessing symptoms of general anxiety and depression. In total 15 healthy age- and gender-matched controls participated. Control subjects who used psychiatric medication, or had neurologic or psychiatric disorders were excluded. Further, patients and controls with a hearing defect were excluded. The local Medical Ethics Committee of the AMC approved this study and all participants gave written informed consent.

2.2. Study procedure

Subjects were instructed to sit in an upright position on a bed and were asked to sit quietly and relaxed and keep their eyes open. They were instructed to listen to a series of beeps through headphones.

2.3. Paradigm

The ASR was recorded with 16 bipolar active cutaneous Ag-AgCl EMG electrodes (Active One System; Biosemi, Amsterdam, The Netherlands) over the right orbicularis oculi, masseter, sternocleidomastoid, deltoid, abductor pollicis brevis, rectus abdominis and quadriceps muscle. The psychogalvanic reflex (PGR) was recorded as the difference in potential between the palm and the dorsum of the right hand. The impedance of all electrodes was checked to be below 10 kΩ. For further details on data acquisition we refer to a previous study conducted by our research group [5]. Headphones were used to present 8 consecutive binaural auditory stimuli of 100 Hz with a duration of 55 ms and loudness of 110 dB. Stimuli were presented with a varying interval of 1.5–3 min, using the same order in all subjects.

2.4. Data processing

Data analysis was performed off-line using Brain Vision Analyzer version 2.0 (Brain Products GmbH). For a detailed description of data preprocessing see Bakker et al., 2009 [5]. We specifically distinguished between the first and second response of the ASR by quantifying different parameters of the ASR for two different time windows [14]. A time window of 1–100 ms and 101–1000 ms for the orbicularis oculi, masseter and sternocleidomastoid muscle and 1–120 ms and 121–1000 ms in the remaining muscles was used to discriminate the early and late components. One researcher (YD) visually inspected and marked response occurrence at a constant scale sensitivity (200 μV) for all subjects. EMG criteria for a response were pre-defined as an increase in EMG activity of a minimal duration of 30 ms and amplitude of 30 μV. Unreliable EMG segments (caused by ECG or other artefacts) were not included in the analysis. Response probabilities and onset latencies were determined for all muscles. Further, a total response probability was calculated using the average response probabilities of all muscles.

To be able to quantify the PGR channels were re-segmented (–100 ms before and 8000 ms after stimulus) and baseline corrected (0–900 ms). The PGR, defined as the largest increase in amplitude from baseline after stimulation within 4–5 s, was calculated and standardized to the intra-individual maximum (0%–100%) [5,15].

2.5. Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (IBM SPSS version 23). A Student’s T-test or Mann-Whitney U test (where applicable) was used in order to test for differences in onset latencies and response probabilities of individual muscles. Differences in onset latencies were only tested when there was a sufficient response rate. A level of p < 0.05 was considered significant. Because the distribution of the response probability revealed a positively skewed distribution, a negative binomial regression model was most appropriate to analyze group differences in terms of frequency and habituation (General Estimation Equation method type III Wald chi-square statistics with robust estimator as covariance matrix). In order to perform this analysis the combined response probability was converted from percentage to number of responses (counts). A repeated measures analysis was performed to analyze group difference between the groups of the PGR (Linear mixed model with fixed effects). Possible confounding factors, i.e. age, disease duration, medication use and co-morbid anxiety disorders, were added to the different models to assess their influence on the different startle parameters.

3. Results

3.1. Patient characteristics

Baseline characteristics are summarized in Table 1. As expected, groups did not significantly differ in terms of age and gender. The median FMD disease duration of patients was 36 months with a range between 2 and 372 months. All patients but one had a disease duration of at least one year. Within the patient group 9 patients (53%) had abdominal, 6 (35%) had limb jerks and 2 (12%) had both. The history of 2 patients stated increased startle responses, accompanied by non-verbal vocalizations in one of them. Twelve subjects (71%) in the patient group were on medication with influence on the central nervous system (Table 1). In 8/17 patients (47%) a BP preceding the jerks was found. In 6 other patients (24%) other polymyographic characteristics supported FMD, such as disappearance of jerks with distraction and variability in muscle jerk recruitment pattern. In one patient a BP could not be recorded due to infrequency of the jerks. Finally, in 2 patients both the BP preceding the jerks as well as the voluntary movement, was lacking. This has been reported in FMD patients before [16]. Three patients (18%) had a current anxiety and three (18%) a current depressive disorder. Self-report scores of 15 patients on depression
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