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Short communication

Quantitative Sensory Testing in adults with Tourette syndrome

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ABSTRACT

Introduction: Abnormal sensory perceptions, for instance hypersensitivity to certain external stimuli or premonitory urges preceding tics, are core features in Gilles de la Tourette syndrome (GTS). Aberrant awareness of externally applied stimuli in terms of altered sensory perception thresholds might contribute to these sensory phenomena in GTS.
Methods: We used the well-established and standardized "Quantitative Sensory Testing" (QST) battery (German Research Network on Neuropathic Pain) to investigate 13 sensory parameters including thermal, mechanical/tactile and pain thresholds in 14 GTS patients without clinically significant comorbidities and 14 healthy controls matched for age and gender.
Results: There were no relevant group differences in any of the 13 QST parameters and no specific QST pattern in GTS patients. There was no correlation between QST parameters and "Premonitory Urge for Tics scale" (PUTS) scores.
Conclusion: Our data show that the perceptual threshold detection of externally applied sensory stimuli is normal in adults with GTS. This indicates that other perceptual mechanisms, such as abnormal central sensorimotor processing and/or aberrant interoceptive awareness might underlie the clinically significant sensory abnormalities in GTS.

1. Introduction

Gilles de la Tourette syndrome (GTS) is a hyperkinetic movement disorder defined by the presence of multiple motor and phonic tics [1]. Tics differ from other hyperkinesias in that they share most neurophysiological and phenomenological properties of voluntary actions and can be inhibited on demand for variable periods of time. In the majority of GTS patients, particularly adults, tics are preceded by sensory phenomena referred to as premonitory sensations [2]. These aversive somatic experiences preceding the tic are often described rather abstract or generalized as an inner urge/impulse to tic, increased tension, anxiety or restlessness, but in some patients they may resemble rather localized somatic sensations such as ache, itching, tingling/burning, numbness or coldness [2]. Often, the execution of a tic gives relief to the preceding disturbing sensation [2].

It has been suggested that premonitory sensations could be the result of increased somatic sensitivity due to heightened perception of signals arising within (interoception) and/or outside the body (exteroception) [3,4]. Indeed, for the interoceptive system, a recent study has provided first direct experimental evidence to link interoceptive awareness with premonitory sensations [5]. GTS adults who were better able to detect their heartbeats reported higher premonitory sensations to tic. However, the contribution of the exteroceptive system to tic-related sensory phenomena remains unclear. GTS patients are often hypersensitive towards particular external tactile stimuli (e.g. clothing tags, tight neckline) [4] and structural neuroimaging findings have demonstrated abnormalities within the primary somatosensory system [6]. Therefore, perception of externally applied stimuli (exteroception) might

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be altered in GTS patients and might contribute to the development of stimulus hypersensitivity and premonitory sensations.

To date, there have been only two attempts to evaluate sensory thresholds to external stimuli in GTS adults with mixed findings [4,7]. However, the examined samples comprised patients with potentially confounding comorbidities, such as attention-deficit hyperactivity disorder (ADHD) and obsessive-compulsive behavior/disorder (OCD), and no more than two sensory modalities were assessed (olfactory [4] and tactile [4,7]). Importantly, although both studies emphasized the role of the somatosensory system in premonitory urges, neither provided clinical information on their presence or their relation to sensory findings.

To further explore the potential contribution of the exteroceptive, but also nociceptive systems to tic-related sensory phenomena in GTS, we systematically assessed a battery of somatosensory functions by means of the established "Quantitative Sensory Testing" (QST) battery (German Research Network on Neuropathic Pain = "Deutscher Forschungsverbund Neuropathischer Schmerz", DFNS) [8]. Our study sample comprised 14 well-characterized uncomplicated adults with GTS and without clinically significant comorbidities and age- and gender-matched healthy controls. Using QST information about peripheral (e.g. large and small fiber functions) and central mechanisms (e.g. sensitization/disinhibition) can be captured in addition to determining sensory thresholds.

Using this technique we aimed to obtaining potentially disease specific sensory profiles and to comparing them to age- and gender-matched healthy subjects and the DFNS reference values. Based on the patients' unusual sensory experiences (e.g. sensory hypersensitivity), we hypothesized reduced sensory thresholds, particularly to tactile/mechanical external stimuli. We further aimed at exploring the relationship between sensory thresholds and premonitory urges.

2. Methods

2.1. Participants

The study was approved by the local ethics committee and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all study participants who were told to be free to withdrawal from the study at any time. GTS participants were assessed in the outpatient clinic in the Department of Neurology, University Medical Center Hamburg-Eppendorf, Germany. GTS participants were diagnosed by neurologists specialized in movement disorders (A.M. or C.G.) using DSM-IV-TR criteria [1]. Only adult (>18 years) individuals with uncomplicated GTS (i.e. without ADHD or OCD) were included in the study to avoid confounding factors that might influence study results, for example inattention or OCD-related sensory phenomena.

Adult healthy control subjects not taking any medication other than contraceptives were recruited locally and matched by age and gender. GTS patients without apparent comorbidity were recruited from the GTS clinics of one of the authors (A.M.). Subsequently, a semi-structured neuropsychiatric interview with a particular view to the DSM-IV-TR criteria of ADHD, OCD and depression was conducted (C.G., D.S.) and confirmed the absence of clinically relevant comorbidities. None of the subjects suffered from a chronic pain disorder.

2.2. Questionnaires and Quantitative Sensory Testing (QST)

Sensory phenomena were assessed based on Kwak et al. [2] and quantified by means of the German version of the Premonitory Urge for Tics Scale (PUTS [9]). QST was performed using an established battery and the standard equipment according to the DFNS [8]. All QST experimenters were specially trained by the DFNS to perform QST according to a standard protocol.

As we did not expect differences in laterality, all subjects were investigated at their right dorsal hand. 13 QST parameters were determined: cold and warm detection thresholds, thermal sensory limen (perception of changing temperatures from warm to cold and vice versa), paradoxical heat sensations (participant experiences cold as heat), cold and heat pain thresholds, mechanical detection and pain thresholds, mechanical pain sensitivity (sensitivity to pinprick stimuli), pressure pain threshold, vibration detection thresholds, mechanical allodynia (experience of pain during non-painful stimulation) and the wind-up ratio (temporal pain summation = ratio of pain ratings of a series of painful stimuli/pain ratings of a single painful stimulus). The room temperature was kept between 20 and 25 °C.

2.3. Statistical analyses

Statistical analyses were performed using the Equista software provided by the DFNS (http://www.neuro.med.tu-muenchen.de/dfns/arzt/qstform.html) and using IBM SPSS software version 20.0 (http://www-01.ibm.com/software/analytics/spss/). Initially, using Equista, raw values of both groups were log-transformed to establish normal distribution and mapped onto the distribution of the DFNS reference group [8,10] consisting of 180 healthy subjects using z-transformation ($z\text{-score}_{Participant} = ((QST_{Participant} - QST_{Reference})/\text{standard deviation}_{Reference})$). This method assured comparability of QST results as z-scores were adjusted to sex, age and tested body site of the published reference group [8,10] and has been used in a recent study [11]. A z-score > 0 indicated high and a z-score < 0 low sensitivity to the external stimulus applied. Z-scores exceeding 95% of the confidence interval of the reference group (±1.96 standard deviation (SD)) are considered as pathologic. As there were no paradoxical heat sensations or allodynia in both groups, analyses proceeded with only 11 out of 13 QST parameters.

For between group analyses, mean z-scores were compared between GTS and control group using parametric student's t-test. Furthermore, group mean z-scores and individual z-scores were compared with the published reference data [8,10] and analyzed with a view to neurobiological (topodiagnostic) mechanisms assessing, for example, the function of different types of nerve fibers (e.g. A delta, A beta or C fibers) or more central mechanisms such as sensitization [12]. Finally, z-scores were correlated with PUTS scores using Pearson's correlation coefficients.

3. Results

14 GTS patients without relevant comorbidities (mean age 31.7 ± SD 7.8 years) and 14 healthy control subjects (32.7 ± 7.8 years) matched by age ($t(26) = -0.339$, $p = 0.737$) and gender (each group: 2 female) were included in the study. Patient characteristics are given in Table 1 (see also supplementary table 1). All patients reported tic-related premonitory sensations as given in Table 1.

Initial group comparisons of single QST parameters' mean z-scores revealed a significant difference for the cold detection threshold (CDT, $t(26) = 4.175$; $p < 0.001$) even after Bonferroni correction with a gain of function for cold detection in GTS patients (mean z-score 0.61 ± SD 0.63) and a loss of function in healthy subjects (mean z-score −0.68 ± SD 0.97). However, CDT mean z-scores of both groups ranged within ±1.96 SD of the DFNS reference group. All other QST parameters did not differ significantly between both groups (all $p > 0.15$, see Fig. 1, part A and supplementary table 1). None of the patients or controls experienced allodynia or