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Abnormal postural behavior in patients with functional movement disorders during exposure to stress

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ABSTRACT

Background: Patients affected by functional (psychogenic) movement disorders (FMD) have abnormal processing of stress responses. However, little is known about the influence of this abnormal stress processing on automatic motor defense behavior, such as freeze response. Our aim was thus to investigate stress-induced postural motor responses in FMD.
Methods: Nine FMD patients and thirteen healthy controls were engaged in the Trier Social Stress Test, while we measured the movement of their body by means of accelerometers and gyroscopes attached to the thorax. Standard deviation of thorax acceleration, reflecting the variability of movement amplitude (body sway), was compared across groups over time in a 2 × 2 ANOVA design. Higuchi's fractal dimension (HFD), reflecting the complexity of movement pattern over time, was also analyzed. Salivary cortisol and α-amylase samples were collected before and after the experiment, as stress biomarkers. Pearson's correlation coefficients were calculated between these biomarkers and movement parameters.
Results: A significant interaction effect was found, showing that healthy controls reduced their thorax sway over time during exposure to stress (from $0.027 \pm 0.010\,m/s^2$ to $0.023 \pm 0.008\,m/s^2$, effect size of Cohen's $d = 0.95$), whereas patients with FMD did not. This change in body sway in controls over time negatively correlated with salivary cortisol values ($\rho = -0.67$, $p = 0.012$). A significant group effect revealed that FMD patients had an overall larger body sway ($0.038 \pm 0.013\,m/s^2$) compared to controls ($0.025 \pm 0.009\,m/s^2$ – effect size of Cohen's $d = 1.29$) and a lower HFD (1.602 ± 0.071) than controls (1.710 ± 0.078 – Cohen's $d = 1.43$).
Conclusions: Patients with FMD failed to show a reduction of body sway over time, i.e., freeze response observed in the controls, thus suggesting an impairment in the automatic defense behavior. Moreover, our analysis found a lower complexity of movement (HFD) in FMD, which deserves future research in order to verify whether this could represent a characteristic trait of the disorder.

1. Introduction

Functional (psychogenic) neurological disorders or conversion disorders consist of neurological symptoms that occur in the absence of visible lesions of the nervous system (Espay et al., 2018). Up to 18% of the neurological patients presenting with "unexplained" symptoms are currently diagnosed with functional neurological disorders (Stone et al., 2009b). One of the most common clinical presentations is functional movement disorders (FMD), characterized by motor symptoms such as paralysis or paresis, tremor or dystonia (Stone and Carson, 2015; Voon et al., 2010). Given the neuropsychiatric nature of these disorders, the understanding of their underlying mechanisms challenges both neurologists and psychiatrists (Stone et al., 2011; Voon et al., 2010).

Neuroimaging studies have related functional symptoms to abnormal activation patterns of the limbic system (hypothalamus and amygdala) (Aybek et al., 2014), the periaqueductal grey matter (PAG)

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(Aybek et al., 2015), the anterior cingulate cortex and some regions of the medial prefrontal cortex (Vuilleumier, 2014), as well as the posterior parietal cortex and other sub-cortical areas (for an extensive review, see (Perez et al., 2012)). Interestingly, this overlaps with brain areas involved in the regulation of the stress system (Roelofs and Spinhoven, 2007).

Stress is indeed a key aspect of FMD, as the onset of motor symptoms has been linked to both psychological (Nicholson et al., 2016) and physical stressors (Pareés et al., 2014; Stone et al., 2009a). Although FMD patients do not always report stress or traumatic events in their past history (Roelofs and Pasman, 2017), previous research has confirmed higher rates of adverse life experiences in FMD patients (Ludwig et al., 2018), suggesting that psychological stressors act as risk factors for FMD. Indeed, hyperactivity of the central stress systems, i.e., the hypothalamic–pituitary–adrenal (HPA) axis (probed with salivary cortisol) and the sympathetic-adrenal-medullary (SMA) system (probed with salivary α-amylase), as well as dissociation between perceived and objective levels of stress, and a correlation of stress biomarkers with life adversities have been recently found in patients affected by FMD (Apazoglou et al., 2017).

A possible automatic response to stress with phylogenetic roots has been suggested to account for FMD (Kozlowska, 2007). In an experiment where participants were exposed to either pleasant or threatening visual stimuli while maintaining a constant force with their hand (measured with a hand grip device), a decay of force was observed in healthy controls during both types of emotional stimuli. In FMD patients, no such a decay was observed during the threatening condition, suggesting an abnormal mechanism of automatic motor control under stressful conditions (Blakemore et al., 2016). An fMRI study exposing participants to pictures of faces with negative valence (sad or fearful) showed an increased brain activity in FMD patients, as compared to healthy controls, in a network involving the PAG (Aybek et al., 2015), which is an area known to respond to defensive motor behavior (Hermans et al., 2013).

The analysis of postural behavior under stress has been well studied in healthy subjects, and has highlighted a specific motor pattern, known as "freeze response", characterized by a decreased body sway, often associated with bradycardia (Roelofs et al., 2010), in response to threatening stimuli (e.g., angry faces (Roelofs et al., 2010) or threatening movie scenes (Hagenaars et al., 2014)) but, up to date, little research has been conducted on such a motor behavior in FMD. Recent advances in the analysis of standing postural behavior using inertial sensors, e.g., gyroscopes and accelerometers, have highlighted the importance of non-linear dynamic metrics, such as the fractal dimension (Martinez-Mendez et al., 2012), which offer the possibility to study movement patterns that evolve over time, and therefore give complementary information to standard, static measures of body sway. Higuchi's fractal dimension (HFD), for instance, is an index that represents the geometrical structure of non-linear time series. HFD estimates the dimensional complexity of a time-signal, describing thus its degree of roughness or regularity (Higuchi, 1988; Newman et al., 2017). It ranges from 1 to 2, where 1 represents high regularity (e.g., smooth oscillatory movements) and 2 describes an irregular/random movement pattern (Higuchi, 1988; Paraschiv-Ionescu and Aminian, 2009). If classic static measures of body movement mainly investigate *how much* movement is recorded, fractality focuses on *how* the movement is dynamically performed. Fractality has already been found to be altered in neurological (Manabe et al., 2001; Newman et al., 2017) and psychiatric disorders (Bolbecker et al., 2011), with patients showing higher regularity of the movement pattern, compared to controls in Huntington's disease (Hausdorff et al., 1997), dyskinesia (Newell et al., 1993), Parkinson disease (Sekine et al., 2004), bipolar disorders (Bolbecker et al., 2011) or stereotypical movement disorders (Bodfish et al., 2001). This underlies the importance of studying postural behavior under pathological conditions not only as movement variability (e.g., body sway), but also as regularity of movement.

In this paper, we investigated standing postural sway in FMD patients and healthy controls (HC), by looking at differences in motor behavior between the two groups, as well as correlations between motor activity and stress biomarkers (i.e., salivary cortisol and α-amylase). To this end, we engaged our participants in the Trier Social Stress Test (TSST) (Kirschbaum et al., 1993), a well-recognized test to measure stress response under ecological conditions, while we measured their body movement by means of accelerometers and gyroscopes attached to the thorax. Our main hypotheses were: 1) FMD patients show higher variability of body movement, compared to HC, when exposed to stress (impaired freeze response), and 2) FMD patients show higher regularity of movement (higher smoothness or roughness) compared to HC.

2. Methods

2.1. Participants

Nine patients with FMD (eight female, mean age = 43.7, SD = 14.7) were recruited from the Neurology Department of Geneva University Hospital. The diagnosis was established according to the DSM-5 criteria of conversion disorder (functional neurological symptom) (American Psychiatric Association, 2013), motor subtype (F44.4), and a board-certified neurologist confirmed the presence of positive signs for FMD. Five patients had negative symptoms (weakness) and four of them positive (tremor or jerks). Further details on the clinical population are described in Table 1. Thirteen HC (eleven female, mean age = 40.0, standard deviation = 14.1) were recruited through public advertisement. Exclusion criteria for both groups were: presence of a comorbid neurological disorder, major psychiatric disorders such as acute severe mood disorder, risk of suicidality, psychosis, history of present or past substance abuse. The presence of other psychiatric symptoms (such as minor depression, anxiety, or panic attacks) did not lead to exclusion, as they are frequent in FMD (Lehn et al., 2016). Medication and subjective symptom severity for the patients' group are detailed in Table 1.

Table 1
Demographics for the FMD patients group. BZD = Benzodiazepines, Severity = self-reported ratings of symptom severity, where 0 represents no symptom, and 10 severe symptoms.

ID	Age at time of examination	Gender	Main functional symptoms	Severity (0 – 10)	Medication conditions
1	21	female	Tremor and left arm dystonia	0	
2	53	female	Tremor	8	Antidepressant
3	40	female	Weakness (right or left paroxystic hemiparesis)	9	Antidepressant
4	48	female	Weakness (right hemiparesis)	4	BZD
5	23	female	Weakness (paraparesis)	6	
6	58	female	Weakness (right leg)	9	
7	62	female	Jerks (generalized)	6	BZD
8	36	male	Jerks (generalized)	5	
9	52	female	Weakness (left hemiparesis)	5	

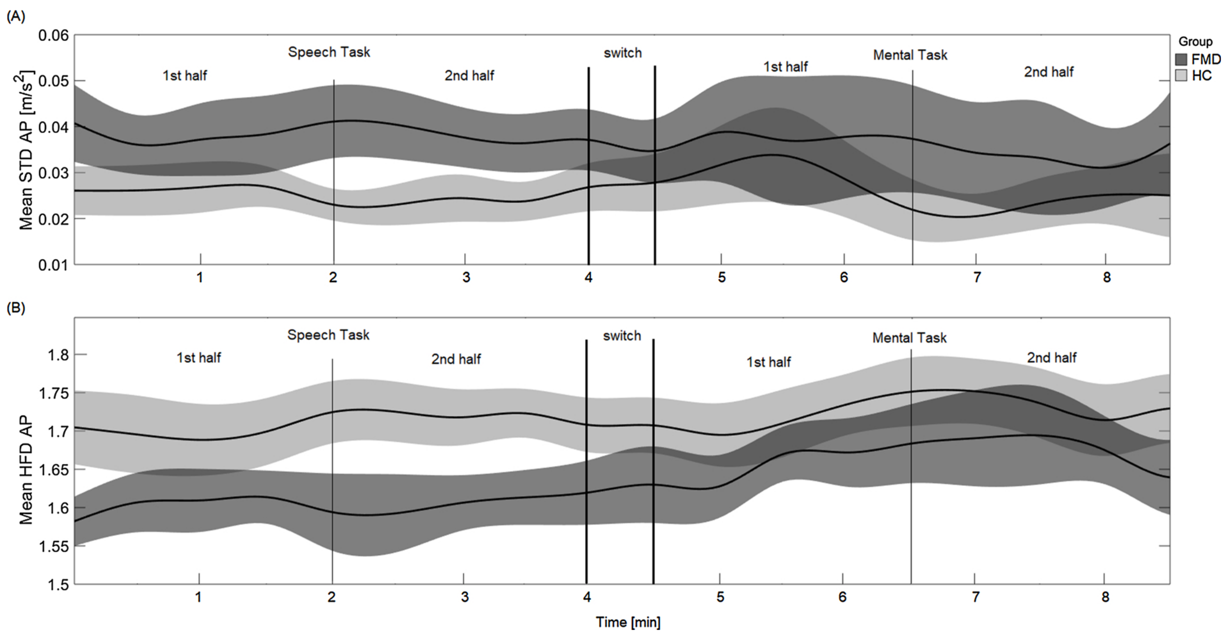

Fig. 1. Example of movement parameters over time, in the anterior-posterior (AP) direction.
(A) Mean STD AP for the entire duration of the experiment, in FMD patients and HC. (B) Mean HFD AP for the entire duration of the experiment, in FMD patients and HC. The solid lines represent the mean values, shades represent the standard error of the mean.

The study was carried out in accordance with the latest version of the Declaration of Helsinki. Ethical Approval was provided by the Ethics Committee of Canton Geneva (Swissethics, CH). Prior to the study, all participants gave written informed consent.

2.2. Experimental setup

The experimental setup is described in details in (Apazoglou et al., 2017). In short, participants were first invited to a room where they were prepared for the experiment. Small wearable devices (Physilog, Gait Up SA, CH) with inertial sensors (tri-axial accelerometer and tri-axial gyroscope) were attached to the thorax of the participants with elastic belts. Saliva samples were collected with a cotton-swab (Salivette, Sarstedt AG & Co, DE). After the preparation, participants were taken to a second room, where they were engaged in the TSST (Kirschbaum et al., 1993). During the TSST, participants were standing in front of two examiners, a microphone was placed in the middle of the room and a camera behind the examiners, facing the participants. The participants were first required to calibrate the wearable device by lifting their arms for five seconds and then resting them along the body. They were then required to perform two tasks. In the first one, called Speech Task, they had to simulate the speech for a job application with a committee of managers for five minutes. If they finished their speech in less than five minutes, the examiners encouraged them to continue through standardized questions. In the second task, called Mental Task, participants had to count back from 1022 to 0 in steps of 17 as fast and accurately as possible for five more minutes. On every failure, they had to restart at 1022 with one member of the committee interfering "Wrong, start again at 1022". The participants were told that the two examiners were experts in non-verbal communication and body language. Furthermore, during the experiment, the examiners provided no verbal or non-verbal feedback in order to induce an uncertainty component and reliably increase cortisol and α-amylase (Nater et al., 2005). After ten minutes, the experiment was stopped, and the participants were taken back to the first room, where they were explained the purpose of the study. A second saliva sample was collected, with the same procedure described above. Thereafter, participants could rest for 30–60 min before leaving.

2.3. Data analysis

The analysis of the saliva samples is described in details in (Apazoglou et al., 2017), and followed the guidelines of the international ISO-15189 norms.

The movement of the participants was extracted from the data recorded with the inertial sensors. The data (3D acceleration and 3D angular velocity) were sampled on 16 bits at a frequency of 200 Hz, low-pass filtered at 17 Hz, and then recorded on a micro-SD card before transferring to the PC for off-line processing. Subsequently, data were processed to align sensor axes with respect to gravity and to extract parameters characterizing body movement, in the anterior-posterior (AP) and the medial-lateral (ML) directions, separately. In particular, we measured the Standard Deviation of the thorax acceleration (STD) as a measure of the variability of the amplitude of body movement (Demura et al., 2008), defined as:

$$\mathrm{STD}=\sqrt{\frac{\sum_{i=1}^{N_{samples}}(a_i-\bar{a})^2}{N_{samples}}}$$

where a_i is the current acceleration sample, $\bar{a}$ is the mean of all acceleration samples in one direction, and $N_{samples}$ is the total number of acquired samples; and the Mean HFD, computed according to Higuchi's algorithm (Higuchi, 1988). The algorithm measures the length of a curve L, at different sampling periods k, with k ranging from 1 to half of the number of samples in the time series. If the signal examined is fractal, the L(k) is proportional to k^{-HFD} (Newman et al., 2017).

A qualitative plot of the Mean STD AP and the Mean HFD AP during the experiment is shown in Fig. 1, where the minutes 0–4 correspond to the Speech Task, the minutes 4 to 4.5 to the time when the participants were asked to switch to the Mental Task, and the minutes 4.5–8.5 correspond to the Mental Task.

2.4. Statistical analysis

In order to capture a change of movement pattern over time, the movement data were divided into 1st and 2nd half of the Speech and Mental Task, respectively.

After checking for normality of data, for each task, Mean STD, AP and ML, and Mean HFD, AP and ML, were entered in four separated repeated measure Analyses of Variance (rmANOVAs) with TIME (1st half, 2nd half) as within-subject factor, and GROUP (FMD patients, HC) as between-subject factor. Tukey's HSD tests were used for post-hoc comparisons. Effect size was calculated as Cohen's d (Cohen, 1988), where d ≈ 0.20 is considered small, d ≈ 0.50 is considered medium, and d ≈ 0.80 large effect size.

Changes in salivary cortisol and α-amylase, defined as the difference between the values at the end and at the beginning of the experiment (Delta Cortisol and Delta Amylase), were correlated with the changes in the movement parameters, Delta STD, AP and ML, and Delta HFD, AP and ML, defined as the difference between the values during the 2nd and the 1st half of the Speech and Mental Task, respectively. Pearson's correlation coefficient was then computed. For all statistics, the significance p-value was set at 0.050.

3. Results

3.1. Mean STD

3.1.1. Speech task

For the AP direction, during the Speech Task, the Mean STD AP showed a significant main effect of GROUP (see Table 2 for detailed statistics). FMD patients exhibited a larger thorax sway (mean ± SD = 0.038 ± 0.013 m/s^2) compared to HC (0.025 ± 0.009 m/s^2). This difference corresponded to a large effect size, according to (Cohen, 1988) (see Table 2 for details). An interaction (GROUP x TIME) effect was also observed, with HC showing a significantly lower sway in the 2nd half of the task (0.023 ± 0.008 m/s^2, Fig. 2a) compared to the 1st half (0.027 ± 0.010 m/s^2), whereas FMD patients did not show this pattern (1st half: 0.038 ± 0.014 m/s^2, 2nd half: 0.039 ± 0.013 m/s^2).

For the ML direction, the same significant GROUP and interaction (GROUP x TIME) effects were found (see detailed statistics in Table 2).

3.1.2. Mental task

No significant effects were found for the Mean STD AP during the Mental Task (Table 2 and Fig. 2b). In the ML direction, during the mental task, a significant main effect of TIME was found for the Mean STD ML, with both FMD patients and HC reducing their thorax sway over time (1st half: 0.024 ± 0.013 m/s^2, 2nd half: and 0.018 ± 0.015 m/s^2).

3.1.3. Correlations with stress parameters

The correlation analysis during the Speech Task evidenced that the change in Mean STD AP (Delta STD AP) negatively correlated with the change in cortisol levels (Delta Cortisol) in HC ($r = -0.67$, $p = 0.012$ – Fig. 3a), i.e., the more the reduction in body sway, the higher the increase in cortisol, but not in FMD patients ($r = -0.24$, p = n.s. – Fig. 3b). No significant correlations between Delta STD AP and the change in α-amylase levels (Delta Amylase) were found. No significant correlations were found during the Mental Task between Delta STD AP and Delta Cortisol or Delta Amylase.

No significant correlations were found in the ML direction, for any of the studied parameters.

3.2. Mean HFD

3.2.1. Speech task

For both the AP and ML directions, during the Speech Task, the Mean HFD showed a significant main effect of GROUP (see Table 3 for detailed statistics), with FMD patients presenting a lower fractality (AP: 1.602 ± 0.071) than HC (AP: 1.710 ± 0.078 – see Fig. 2c for the AP direction). Effect size were large for both AP and ML directions (see Table 3 for further details).

3.2.2. Mental task

A similar main effect of GROUP was found during the Mental Task, in both AP and ML directions (see Fig. 2d for the AP direction and Table 3 for detailed statistics). In addition, a significant main effect of TIME was observed in the Mean HFD ML during the Mental Task, with both groups increasing their fractality from 1.732 ± 0.0667 to 1.784 ± 0.0762.

3.2.3. Correlations with stress parameters

For the Speech Task, no significant correlations were found, in any of the other studied parameters.

4. Discussion

The central finding of this study is that FMD patients exhibited an abnormal postural behavior during stress. They did not exhibit the same pattern of freeze response (decrease in body sway), as observed in HC during the second part of the Speech Task, in line with hypothesis 1. The second finding is that FMD patients showed a smooth and more regular pattern of movement, compared to controls, with a lower HFD, in line with hypothesis 2.

4.1. Mean STD: group differences in the variability of body sway

Social stress, as targeted by the TSST, is known to affect postural sway (Mascret et al., 2016). Our data showed that FMD patients moved with a globally higher variability of body sway, compared to HC, during the Speech Task, and this is consistent with previous literature on movement disorders in neuropsychiatric conditions (Bolbecker et al., 2011), including FMD (Lempert et al., 1991). In particular, bipolar patients have shown an increased sway area when tested with eyes closed, and this is indicative of reduced postural control (Bolbecker et al., 2011), whereas FMD patients have shown high fluctuations of stance and gait (equivalent to our Mean STD), excessive slowness or hesitation of locomotion, and a build-up of sway amplitudes after a silent latency (Lempert et al., 1991). However, during the Mental Task, no differences in body sway were observed between FMD patients and HC.

Previous research has suggested that the Speech and Mental Task elicit different psychological stress. In particular, the Speech Task, i.e., the simulation of a job interview, seems to engage a higher degree of

Table 2
Results of the rmANOVA and effect size on the Mean STD, in the AP and ML direction, during the Speech and Mental Task, respectively. * depicts significant effects.

Mean STD		Speech Task			Mental Task		
		F(1,20)	p-value	Cohen's d	F(1,20)	p-value	Cohen's d
AP Direction	GROUP	8.37	0.009*	1.29	1.96	0.177	–
	TIME	1.54	0.230	–	3.90	0.062	–
	interaction	4.41	0.049*	0.95	1.23	0.281	–
ML Direction	GROUP	7.11	0.015*	1.19	4.18	0.054	–
	TIME	1.88	0.185	–	11.62	0.003*	1.52
	interaction	4.71	0.042*	0.97	2.35	0.141	–

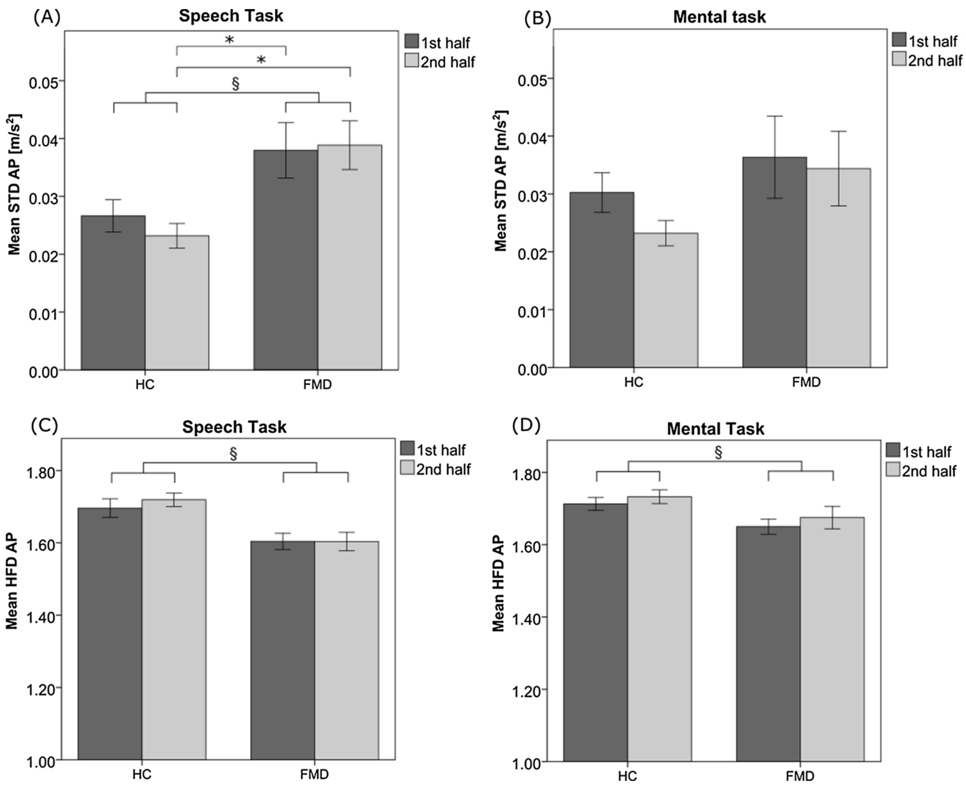

Fig. 2. Results of the movement parameters in the anterior-posterior (AP) direction.
(A) Mean STD AP during the Speech Task. (B) Mean STD AP during the Mental Task. (C) Mean HFD AP during the Speech Task. (D) Mean HFD AP during the Mental Task. Error bars represent the standard error of the mean. § depicts significant GROUP differences at rmANOVA. * depicts significant ($p < 0.05$) differences at Tukey's HSD post hoc tests. STD = standard deviation of the thorax acceleration; HFD = Higuchi fractal dimension; AP = anterior-posterior; HC = healthy controls; FMD = functional movement disorders.

ego involvement (Kirschbaum et al., 1993), compared to the arithmetic calculations of the Mental Task, and is known to have a high impact on psychological stress (Mason, 1968). It is then possible that the Speech Task triggered higher stress in our participants than the Mental Task, and affected postural behavior more. The Mental Task, less stressful than the previous one, might have acted as a classic dual task (Stins et al., 2015; Wuehr et al., 2016), where distraction could have accounted for the normalization of the motion pattern in the FMD group, in line with our hypothesis that stress is responsible for the abnormal motor responses in FMD.

4.2. Mean STD: a possible impairment in the freeze response mechanism

The significant effect of interaction GROUP x TIME revealed that, while HC decreased the variability of their movement over time, patients maintained their motor activity in a pathologically high state. This suggests that HC adopted a freeze response mechanism, which seems to be impaired in FMD. An impaired freeze response was first suggested by Kozlowska to account for FMD (Kozlowska, 2007). This line of research was further investigated in an fMRI study that examined the brain areas activating during exposure to stress, in FMD patients and HC (Aybek et al., 2015). The main finding was that FMD patients showed abnormal activation patterns in areas commonly associated with freeze response, as compared to HC. More recent research showed that FMD patients maintained their hand force constant during exposure to stress, whereas HC decreased it over time (Blakemore et al., 2016). This pointed to a link between psychological stressors, defensive behavior, and motor function in FMD. Our results support these findings as we showed that FMD patients maintained their Mean STD in a pathologically high state during exposure to stress, whereas HC decreased it. Although a direct comparison with these studies is not possible, due to the different outcome measures used (e.g., fMRI, force strength, body motion), all these findings seem to share a common element: an impairment in the freeze response mechanism in FMD, which could potentially account for symptom production.

Our results also show a freeze response mechanism in HC that persists over minutes, as we compared the body sway between the first and the second half of the stressful Speech Task, over a total period of

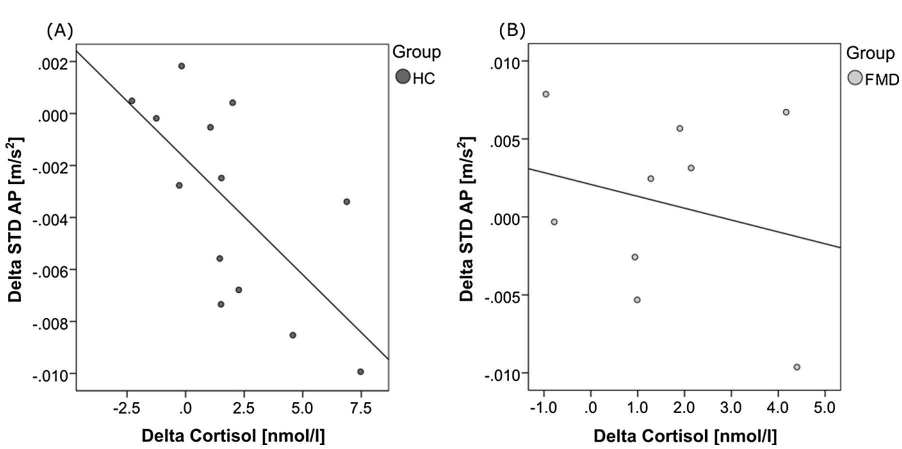

Fig. 3. Results of the correlation analysis between the change in cortisol levels (Delta Cortisol) and the movement parameters for the Speech Task.
(A) Results of the Delta STD in HC. (B) Results of the Delta STD in FMD patients. STD = standard deviation of the thorax acceleration; AP = anterior-posterior; HC = healthy controls; FMD = functional movement disorders.

Table 3
Results of the rmANOVA and effect size on the Mean HFD, in the AP and ML direction, during the Speech and Mental Task, respectively. * depicts significant effects.

Mean HFD		Speech Task			Mental Task		
		F(1,20)	p-value	Cohen's d	F(1,20)	p-value	Cohen's d
AP Direction	GROUP	10.26	0.004*	1.43	4.47	0.047*	0.95
	TIME	1.64	0.215	–	3.10	0.094	–
	interaction	1.81	0.193	–	0.04	0.835	–
ML Direction	GROUP	4.69	0.043*	0.97	6.58	0.018*	1.15
	TIME	1.78	0.196	–	13.09	0.002*	1.62
	interaction	1.92	0.181	–	0.90	0.354	–

about 5 min. One could argue that freezing is an acute reaction lasting few seconds (Azevedo et al., 2005; Roelofs et al., 2010), but evidence of a sustained reduction of body movements has been shown in both human (Hagenaars et al., 2014) and animal (Vianna and Carrive, 2005) studies, in support to our findings.

Moreover, our correlation analysis between the movement parameters and the stress biomarkers seems to confirm a link between stress and freeze response mechanism in HC (reduced movement with the increase in cortisol release), but not in FMD patients. HC showed a negative correlation between Delta STD AP and the cortisol release (Delta Cortisol) over time, in line with previous research that also observed increased indicators of freezing (e.g., bradycardia) associated with higher cortisol levels (Niermann et al., 2017). We found no such a correlation in FMD patients.

FMD is characterized by abnormal levels of cortisol, and we recently showed that the baseline levels of cortisol are higher in FMD than in HC, and that both groups increase their cortisol levels when exposed to the psychosocial stress of the TSST (Apazoglou et al., 2017). It is then possible that life stressors, commonly observed in the past history of FMD patients (Kranick et al., 2011), influenced the stress levels in the present time (as reflected by overall elevated levels of cortisol and α-amylase described in (Apazoglou et al., 2017)), and play a role in disrupting the physiological freeze response.

4.3. Mean HFD: differences in the type of movement

An abnormal postural behavior in FMD patients was visible not only in the variability of body sway, but also in the type, as evidenced by the group differences in the Mean HFD AP for the Speech Task. The lower fractality of body sway might indicate that FMD patients moved in a more regular and smooth pattern, compared to HC.

Although our approach was methodologically different from classic posturography, where participants typically stand still with the arms resting on their hips, our results show several similarities with existing studies on postural control (Bodfish et al., 2001; Bolbecker et al., 2011), reporting higher variability of movement (corresponding to our Mean STS), and higher regularity (corresponding to our Mean HFD) in patients, compared to controls. In classic posturography, the regularity of the movement is interpreted as an indicator of the "degrees of freedom" for postural control, in the way that highly irregular movement sequences require a higher number of degrees of freedom to use, conversely, more regular movements indicate the use of fewer degrees of freedom (Newell and Corcos, 1993). In this biomechanical framework, it is possible that FMD patients, who showed more regular movements, used less degrees of freedom to control their motor behavior. A speculative explanation for this might be the weak multisensory integration of visual, vestibular, and proprioceptive systems, typical of such disorders (Voon et al., 2010), and essential for the control of sway (Bolbecker et al., 2011).

Interestingly, the group differences observed during the Speech Task remained significant during the Mental Task as well, despite both groups tended to evolve their movement pattern towards higher fractality over time (main effect of TIME for Mean HFD ML). Even if FMD patients again attempted to habituate to stress, it seems that their movement pattern was not influenced by the stress currently experienced, as the lack of correlation between Delta HFD AP and Delta Cortisol evidenced. Albeit speculative, one possible interpretation of such results is that the fractal pattern of body sway is a characteristic trait of the disorder.

No correlation was found for the movement parameters with the Delta Amylase, in any of the studied groups. This is not surprising, as previous research conceptualized the major stress response as occurring in two stages: a fast response mainly driven by the SAM system (and measured with the α-amylase), and a slower one depending on the HPA axis (measured with the cortisol) (Takai et al., 2004). The design of our analysis of postural behavior did not account for very brief adaptation to stress and computed changes of movement over minutes in the first and second half of the stress induction task.

4.4. Limitations

Our study has several limitations, the first one being the measurement setup that differed from classic posturography, as our participants were free to move their body and arms as they would do in real life conditions. We chose not to restrain any movement, because this could ecologically reproduce the stressful situation induced by the TSST and, in turn, reveal the freezing response behavior, that could potentially be masked if tested under laboratory conditions. Although our focus was on the difference in the movement pattern during exposure to stress, one improvement to the current setup could be to measure the movement pattern at rest, i.e., before the TSST, which could have served as baseline assessment. A second limitation was the small sample size, which was due to the complexity of the experimental settings. We based the decision of collecting data from 22 participants (9 FMD patients and 13 HC) on previous studies on postural behavior, which engaged a similar number of participants. (Stins et al., 2015; Wuehr et al., 2016). The between-subject heterogeneity of our FMD group (Table 1), as evidenced in the larger standard deviation on the movement parameters, as compared to HC, could have affected our results. This heterogeneity may be due to the different symptoms, ranging from jerks to weakness, coexisting psychiatric illnesses, commonly observed in FMD (Lehn et al., 2016), as well as by the different medication conditions, which are difficult to statistically account for (Bolbecker et al., 2011). We did not control for this because of the small sample size, however, even though the studied differences might be due to the different symptoms that change over time due to the increasing stress, this still represents an advance in understanding postural behavior in FMD, as the stress-induced aggravation of the symptoms could be the reason why patients showed a different movement pattern compared to controls. Moreover, our results showed an effect size that can be considered large (Cohen, 1988), at all studied group differences. This means that our results are robust enough to suggest that there is a difference in postural behavior between FMD patients and HC during exposure to stress, and that the heterogeneity in our patients' sample minimally affected our results. In order to generalize our results to all subtypes of symptoms, however, further longitudinal research with a higher control over the different types of FMD and medication, and a larger sample size may be of interest to elucidate these effects on postural behavior in FMD. Another possible improvement in the current setup is to measure salivary cortisol and α-amylase at several points in time during the experiment, for instance in between the Speech and Mental Task. We decided not to interrupt the Speech and Mental tasks to collect saliva during the experiment, as this would have negatively affected the ecological validity of the TSST. However, cortisol level has a slow response time, and previous research has shown a linear increase of cortisol during stress for at least 10 min (Kirschbaum et al., 1993). This time is in line with the duration of our experiment. We could then assume that our TSST constantly increased cortisol levels during both the Speech and Mental Task, and that the peak could have occurred at the end of the experiment, when cortisol was measured. In future research, the use of physiological data, such as heart rate, could also be taken into account in order to confirm the hypothesis of a freeze response in healthy controls.

5. Conclusions

In conclusion, while HC showed a change in motor response proportional to their level of stress, FMD patients did not, suggesting an impairment of the physiological freeze response to a stressful situation. Moreover, FMD patients differed from the HC in the complexity of their movement pattern, suggesting the use of a low amount of "degrees of freedom" to control movement, which could potentially be considered as a trait biomarker of the disorder.

Declaration of interest

None.

Contributors

Zito GA conducted the main analysis of the results, the discussion of the findings, and the writing of the manuscript. Apazoglou K contributed to the analysis of the results and interpretation of the data. Paraschiv-Ionescu A contributed to the extraction and analysis of the movement parameters and supervised the data collection. Aminian K contributed to the technical development of the study. Aybek S designed the experiment, guided the discussion of the results, and led the overall study. All Authors contributed to drafting and revising of the submitted version of the manuscript.

Conflict of interest

None

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