Exploring three levels of interoception in people with Functional Motor Disorders.

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Abstract

Introduction: A three-level model of interoception has recently been defined. We aim to study the interoceptive processing in individuals with functional motor disorder (FMD).

Methods: Twenty-two patients with FMD were compared to 23 healthy controls. They underwent a protocol measuring different levels of interoception including: accuracy (an heart-beat tracking task), awareness (participant's confidence level) and sensibility (the Body Awareness Questionnaire-BAQ). Depression, anxiety and alexithymia were assessed by means of validated clinical scales.

Results: The FMD group showed a lower cardiac interoceptive accuracy and sensibility than healthy controls but they did not differ in terms of awareness ($p=0.03$ and 0.005 respectively). They were aware of their poor performance in the accuracy task. Cardiac interoceptive accuracy positively correlated with the BAQ sub-scales "Predict Body Reaction" ($r=0.49$, $p=0.001$) and "Sleep-Wake Cycle" ($r=0.52$, $p<0.001$). A mediation analysis showed a significant indirect effect of group on cardiac interoceptive accuracy through BAQ "Predict Body Reaction" ($b=-2.95$, 95% BCa CI[-7.2;-0.2]). The direct effect of group on "Predict Body Reaction" was still significant ($b=- 6.95$, $p=0.02$, 95% CI[-13.18;-0.73]). Conclusions: People with FMD have impaired cardiac interoceptive accuracy and sensibility but no difference in metacognitive interoception compared to healthy controls.

Keywords

Functional Neurological Disorder; Functional Movement Disorder; Interoception; Metacognition; Bayesian Models.

Introduction

In the last decade, the interplay between brain and heart has gained increasing attention in both the healthy population and in people with neurological and psychiatric conditions [1]. Interoception refers to the interaction between peripheral sensors and effectors of autonomic function and the central nervous system. It encompasses homeostatic mechanisms, conscious awareness and appraisal of autonomic activity and the influence of such activity on cognitive processes such as emotion and action [2].

A three-level model of interoception has recently been defined, where *interoceptive accuracy* refers to the performance on objective test of detection of one's bodily signal (e.g. the Heartbeat Detection Task)*; interoceptive sensibility* indicates a subjective report of one's ability to detect body signals (mostly evaluated through confidence questions and self-report questionnaires); *interoceptive awareness* refers to the metacognitive awareness of one's interoceptive accuracy, usually calculated as the correspondence between accuracy and confidence [3]. Previous work suggested that patients with functional neurological disorders, such as Functional Motor Disorders (FMD) and functional seizures have disturbances in interoceptive processing and specifically in interoceptive accuracy [4, 5], although this has not always been confirmed [6]. However, neither interoceptive sensibility nor metacognitive aspects of interoception have been explored in these patients to date. Investigating higher-order beliefs and body representation in this population may be crucial, as highlighted in other clinical studies [7].

In people with FMD, prior beliefs or expectations, and attention towards the body, are thought to be key mechanisms within a predictive coding aetiological framework of FMD [8]. However, FMD patients are as susceptible as healthy controls to bodily illusions such as the Rubber Hand Illusion, suggesting that multisensory integration processes and their sense of body ownership are not impaired [9]. The present study aims to deepen our knowledge about FMD patients' metacognition and bodily awareness, by assessing interoceptive sensibility and awareness together with interoceptive accuracy. We hypothesized that patients with FMD would have poorer cardiac interoceptive accuracy and sensibility compared to healthy controls.

Materials and Methods

Twenty-two patients with a diagnosis of FMD and 23 healthy controls (HC), matched for age and gender consented to participate and were included in this study. Patients were included if they had "clinically established and documented" FMD according to Fahn & Williams criteria (Supplementary material for reference). Healthy controls were visitors to the hospital and hospital staff. Exclusion criteria for both groups were as follows: language difficulties, learning disability, concurrent neurological, cardiologic or medical conditions, and treatment with medications with direct cardiac effects. Participants signed an informed consent form before starting the procedure. Institutional ethics approval was obtained and the experiment was conducted in accordance with the Declaration of Helsinki.

Socio-demographic and clinical information were gathered, including: age, educational level, current and former illness, medications taken and, for the patients, information on disease onset, progression and duration and description of symptoms. Body weight and height were measured.

Three levels of interoception were explored as follows:

1. *Cardiac interoceptive accuracy*: the Heartbeat Detection Task was performed according to the protocol described by Schandry [10] and detailed in Ricciardi et al. [4].

2. *Interoceptive sensibility:* (i) Confidence in the perceived accuracy of performance at the Heartbeat Detection Task: immediately after each trial participants were asked: "how confident are you in your answer?" and had to reply with a number ranging from 0 ("Total guess/No heartbeat awareness") to 10 ("Complete confidence/Full perception of

heartbeat"), as in [3; 7]. Participants did not receive any feedback about their performance. (ii) Body Awareness Questionnaire (BAQ), an 18-items self-report scale, with a α >0.77, measuring beliefs about one's sensibility to physiological, non-emotive body processes (Supplementary material for reliability analysis and reference). The BAQ includes four subscales: "Note Response/Changes in Body Process", measuring the ability to read one's own body reaction to food, fatigue, weather, and changing in energy levels; "Predict Body Reaction", assessing the ability to predict one's own body state from actual body signal; "Sleep-Wake Cycle", assessing bodily signals related to circadian rhythm; "Onset of Illness", assessing the ability to recognize illnesses signals.

3. Metacognitive interoceptive awareness was explored performing confidence-accuracy correlations (i.e. Pearson's r) during heartbeat tracking.

All the participants also completed the following questionnaires: (i) Toronto Alexithymia Scale (TAS-20) assessing: difficulties identifying feelings (DIF), difficulties describing feelings (DDF) and externally-oriented thinking (EOT); (ii) Hospital Anxiety and Depression Scale. (Supplementary material for references).

In order to control for a deficit in executive functions (in particular attention and inhibition) that might have influenced the accuracy task performance, all participants were assessed with the Stroop Color and Word Test (SCWT). Two variables were extracted: time in naming the colour of the ink, regardless of the word, which is a measure of attention; and accuracy in naming the word, regardless of the colour of the ink which is a measure of inhibition of automatic response.

Severity of functional motor symptoms was assessed with the Simplified FMD Rating Scale (S-FMDRS) [11].

Statistical analysis

Cardiac interoceptive accuracy was calculated using the following formula [4; 9]: 1/3 ∑ [1 – (|recorded heartbeats – counted heartbeats|/recorded heartbeats)]. This formula allows obtaining a score ranging from 0 (the worst estimation of heartbeats) to 1 (the best estimation of heartbeats). To calculate the interoceptive awareness, the within-participant Pearson correlation, r, between confidence rating and cardiac interoception accuracy was computed.

When Kolmogorov-Smirnov test showed that the distribution of the values of each variable, within each group, was normal ($p > 0.05$), independent sample t-tests were employed and degrees of freedom reflect the Greenhouse-Geisser correction where sphericity was violated. Otherwise, non-parametric Mann Whitney U test was employed. Categorical variables were assessed with Chi-square analysis. To evaluate a possible relationship between depression, anxiety, alexythimia and interoception (accuracy, awareness and sensibility) we performed Spearman's correlation analyses. Correlations between measures of interoception and demographic (age) and clinical variables (disease duration, S-FMDRS) were investigated using Spearman's bivariate correlations.

Simple mediation analysis was run to examine the presence of a possible mediating factor (interoceptive accuracy) in the relationship between Group and interoception sensibility, as we hypothesized that possible differences between groups in interocepitive sensibility (BAQ) might be related to differences in interoceptive accuracy. In other words, interoceptive accuracy would be the underlying mechanism of the relationship between groups and interoceptive sensibility (BAQ): X (group) → M (Interoceptive Accuracy) → Y (Interoceptive Sensibility). It was performed with PROCESS tool for Statistical Package for Social Sciences (SPSS), v4.3 by Andrew F. Hayes. The index of the indirect effect are considered statistically significant if the 95% CI does not include zero.

All the analyses were conducted in SPSS 25. All reported results are based on two-tailed p-values. Cut-off for statistical significance was set at $p < 0.05$.

Results

There was no difference between groups in age, gender and BMI (Table 1). FMD illness duration was 55.5±42.2 months and average score on the S-FMDRS was 11±9.3. Demographical, clinical and psychophysiological data, together with statistical indexes, are presented in Table 1.

FMD patients had lower cardiac interoceptive accuracy (p=0.03) than HC. They also showed lower interoceptive sensibility than HC, both as measured by the BAQ (BAQ Total Score, p=0.005; Predict Body Reaction sub-score, p=0.003; Sleep-Wake Cycle sub-score, p<0.001; Onset of Illness sub-score, p=0.004), and by confidence levels (p=0.008); however metacognitive interoceptive awareness was not significantly different between groups (p=0.2).

FMD patients were more depressed (p=0.01) and more alexithymic than HC (p=0.02).

There was no significant difference between groups at the SCWT (all p>0.05), suggesting no significant difference in attention and executive functions.

To evaluate a possible relationship between depression, anxiety, alexythimia and interoception (accuracy, awareness and sensibility) we performed Spearman correlation analyses. There was no significant correlation between any measure of interoception and any psychological variable neither when looking at the whole sample nor when taking into account only the FMD group (Supplementary Table 1).

In the whole sample, cardiac interoceptive accuracy positively correlated with the BAQ "Predict Body Reaction" (ρ=0.39, p=0.011) and "Sleep-Wake Cycle" (ρ=0.44, p=0.003). Interoceptive awareness negatively correlated with Predict Body Reaction (ρ=-0.51, p=0.004) and “Sleep-Wake Cycle” (ρ=-0.374, p=0.042); interoceptive awareness also negatively correlated with BAQ Total Score (ρ=-0.4, p=0.025). In the FMD patients group severity of symptoms (S-FMDRS) correlated with interoceptive awareness (ρ=0.888, p<0.001), while disease duration did not correlate with measures of interoception (all p>0.05).

Given that Group has an effect on both Interoceptive Accuracy and “Predict Body reaction”, and that Interoceptive Accuracy and “Predict Body reaction” are correlated, a mediation analysis was run with Group as predictor, “Predict Body Reaction” score as Dependent Variable, and Interoceptive Accuracy as Mediator. A significant indirect effect of Group on Interoceptive Accuracy through “Predict Body Reaction” emerged (b=-2.95, 95% BCa CI[-7.2;-0.2]). The direct effect of Group on “Predict Body Reaction” was still significant (b=-6.95, p=0.02, 95% CI[-13.18;-0.73]), therefore the relationship between Group and “Predict Body Reaction” is partially mediated by interoceptive accuracy. Detailed coefficients are reported in Figure 1.

Discussion

Our results showed that patients with FMD have lower cardiac interoceptive accuracy and lower interoceptive sensibility than healthy controls; specifically they have lower ability to predict their body reactions and are less confident than healthy controls about their ability to perceive their heart rate. Our mediation analysis showed that one of the reasons why people with FMD have lower ability to predict their body reactions is their impaired interoceptive accuracy.

Our findings can be interpreted in the context of the hierarchic Bayesian predictive model of FND according to which abnormal top-down predictions or priors of the symptoms emerge in particular conditions (such as the presence of a physical or psychological precipitating event) [6, 12]. When attention is turned towards the body, these top-down predictions overwhelm any bottom-up sensory information that might change them, with the subsequent production of physical symptoms related to the abnormal top-down prediction. Here we make a step further hypothesizing that the deficit in interoceptive accuracy observed in patients with FMD might predispose constitutionally to down-weighing bottom-up interoceptive signalling and subsequently to a reliance on top-down predictions. This means that if these top-down predictions are abnormal and inaccurate they cannot be updated or adjusted by bottom up information, further fostering a vicious circle where the entire system is compromised. This model also supports the result of our mediation analysis, according to which the lower ability to predict body reactions seen in patients with FMD is partially due to lower interoceptive accuracy. Moreover, this model has recently been extended also to specific interoceptive symptoms such as chronic pain and fatigue, potentially explaining the frequent co-occurrence of these symptoms with FMD [13] and providing a rationale for specific treatment options, such as motor rehabilitation programme for FMD which is based in part on challenging and changing expectations about symptoms [14].

As assessed in the current study, we found no evidence of impairment in FMD patients' metacognitive interoceptive awareness, suggesting that they are aware of their poor performance on the Heartbeat Detection Task. Poor metacognitive ability has been suggested as a key mechanism underlying cognitive functional disorders [15] and in one study in 10 patients with motor conversion disorders [16] using a motor task, however our study is the first one evaluating metacognitve awareness of internal signals and this might account for our apparently contrasting results.

We acknowledge our study limitations: first, the small sample size, which might limit the generalization of the results and did not allow us to perform secondary analysis looking for differences between different phenotypes of FMD; second, the use of the Heartbeat

Detection Task as a measure of interoceptive accuracy which has been recently criticized [17] which however to date is still the most validated and widely-used method to quantify interoception; third, the lack of a test evaluating sustained attention to control for the role of a potential attentional deficit, although our populations did not differ in performance at the Stroop test which is a measure of attention and inhibition; finally we did not control for the potential confound of the medication use in the patients group and we did not perform a structured psychiatric interview for depression and anxiety but we used self-administered questionnaires.

In conclusion, our findings showed that patients with FMD have lower interoceptive accuracy and lower interoceptive sensibility than healthy controls. We propose an interpretation of our findings within the framework of the hierarchic Bayesian predictive model of FMD. Future studies are encouraged to further explore interoception as a potential transdiagnostic biomarker which can be used to guide novel therapeutic approaches for patients with FMD.

Tables

Table 1 – Demographic, clinical and psychometric data of the two study population

	HC	FMD	t/chi/U	df	95% CI	effect size	p-value
Age	41.5 [15]	44.8 [14.8]	- 0.7	41	[-12.5; 5.9]	0.2	0.5
Gender	9 M, 14 F	3 M, 19 F	3.7	1	N/A	0.3	0.053
BMI	22.7 [3]	24.4 [3.6]	-1.6	42	[-3.6; 0.4]	0.5	0.1
Interoceptive Accuracy	0.645 [.218]	0.489 [0.266]	2.2	43	[0.01; 0.3]	0.6	**0.037**
BAQ -Total	87.4 [17.7]	70.3 [19.3]	3	40	[5.6; 28.7]	0.9	**0.005**
BAQ - Note Response / Changes In Body Process	28.5 [7.8]	22.1 [10.8]	1.9	40	[-0.2; 10.8]	0.6	0.06
BAQ - Predict Body Reaction	32.4 [7.80]	21.5 [12.5]	3.2	34.7	[3.6; 16.1]	1	**0.003**
BAQ - Sleep-Wake Cycle	31.1 [5.1]	19.9 [11.5]	3.9	28.5	4.9; 15.6]	1.3	**<0.001**
BAQ - Onset Of Illness	19.9 [3.898]	13.8 [7.5]	3.1	31.2	[1.9; 9]	1	**0.004**
Confidence level	5.1 [2.1]	3 [2.8]	2.8	42	[0.6; 3.5]	0.8	**0.008**
Interoceptive Awareness	0.1 [0.7]	0.4 [0.7]	- 1.2	31	[-0.8; 0.2]	0.4	0.2
HADS-D	4.1 [3.3]	7.1 [4]	- 2.7	40	[-5.2; -0.7]	0.8	**0.01**
HADS-A	6.3 [3.9]	8.6 [5.3]	- 1.7	40	[-5.2; 0.5]	0.5	0.1
TAS-20 Total	43.3 [10.6]	52.2 [13.3]	- 2.4	40	[-16.3; -1.5]	0.7	**0.02**
TAS-20 DDF	10.9 [4.3]	13.8 [4.8]	- 2	38	[-5.9; -0.01]	0.6	**0.049**
TAS-20 DIF	14 [5.7]	18.5 [8.3]	- 2	38	[-9; -0.01]	0.6	**0.049**
TAS-20 EOT	17.9 [5.6]	19.8 [4.5]	- 1.2	38	[-5.2; 1.4]	0.4	0.2
Stroop_C	59.6 [16.2]	63.18 [13.8]	284	44	N/A	0.02	0.3
Stroop_CW	104.6 (10.8)	98.1 (18.8)	199.5	44	N/A	0.02	0.3

Abbreviations: BAQ – Body Awareness Questionnaire; BMI = Body Mass Index; Effect size: Cohen's d/Cramer's V / η^2 measure of effect size for t-test, Chi Square and Mann-Whitney U test, respectively; CI: Confidence Interval;; df: degrees of freedom; DDF = Difficult Describing Feeling; DIF = Difficult Identifying Feelings; EOT = Externally Oriented Thinking; FMD = Functional Movement Disorder; HC = Healthy Controls; p = p value; t / χ / U = statistical index for t-test, chi square and Mann-Whitney U test, respectively; Stroop_C = Stroop Color and Word Test, Color reading condition; Stroop_CW: Stroop Color and Word Test, fColor-Word condition; TAS-20: Toronto Alexithymia Scale-20 Items. Significant differences are depicted in bold.

Legend Figure 1:

Model of group as predictor of interoceptive sensibility measured via Body Awareness Questionnaire, subscale: “Predict Body Reaction”, mediated by Interoceptive Accuracy. The confidence Interval for the indirect effect is a BCa bootstrapped CI based on 5000 samples.

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Authors' Contribution

LR: Designed and conceptualized the study, interpreted the data, drafted the manuscript.

VN, EA, JMC, LPK, LC: collected, analysed and interpreted the data; drafted the manuscript.

BD, MY, FM, AF, ME: Conceptualized the study, revised the manuscript for intellectual content.

All the authors approved the version to be submitted.