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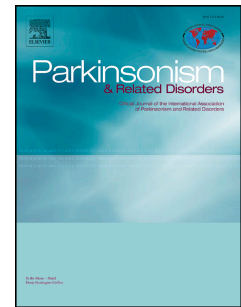
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No evidence of impaired visual and tactile metacognition in adults with Tourette disorder

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ABSTRACT

Introduction. Premonitory urges in Tourette disorder are often linked to altered somatosensory processing, which might include deficits in metacognition. We explored tactile and visual metacognitive ability in people with Tourette disorder and healthy control participants. **Methods.** Patients with Tourette disorder and healthy control participants completed a tactile and a visual metacognitive task. On each trial, participants did a forced choice discrimination and then rated their confidence in their decision. To quantify metacognitive ability, we used *m-ratio* — a bias-free measure that allows for comparisons across modalities. Correlations between severity of tics and premonitory urges with tactile metacognitive sensitivity were also performed. **Results.** Metacognitive ability in both tactile and visual domains was comparable between adults with Tourette disorder and healthy controls. We also found no evidence for correlations between tactile metacognitive ability and severity of premonitory urges or tic severity. **Conclusions.** Tactile and visual metacognition is not impaired in adults with Tourette disorder. These results question the role of altered tactile metacognition in pathophysiology of tic disorders.

INTRODUCTION

Tics are brief, sudden and repetitive movements or sounds that appear out of context. In the clinical setting, tics are most commonly encountered as part of the spectrum of primary tic disorders, including Tourette disorder (TD). One of the distinguishing characteristics of tics compared to other hyperkinetic movement disorders such as chorea or myoclonus, is that they are often preceded and even driven by an unpleasant sensation known as the “premonitory urge” (PU). An increase in the perceived intensity of PUs typically leads to tics. Phenomenologically, PUs are often described not only with motor qualities (energy build-up, urge to move, sense of incompleteness)[1], but also as a wide range of somatosensory phenomena (tension, pressure, urge to stretch, itching, burning, etc.)[2]. This suggests that dysfunctional somatosensory processes may play a role in tic generation [3]. However, despite several attempts to date, the pathophysiological underpinnings of the neurocognitive mechanisms that lead to PUs remain elusive [4].

According to one line of research, some symptoms that people with tic disorders and TD experience might result from a dissociation between sensory processing, measured objectively,

and patients' subjective reports. For example, although patients with TD describe their subjective experience as an increased sensitivity to external stimuli such as cutaneous or olfactory stimuli, objective perception thresholds for these stimuli were not found to differ compared to a sample of healthy volunteers [5], [6]. And while patients report having more tics after a period of tic suppression, there is no objective increase in tic frequency [7]. Precisely these kinds of dissociations are studied by metacognition research, where subjective introspective reports are often operationalized as confidence ratings about the accuracy of a perceptual decision. Metacognitively well-calibrated individuals generally report higher confidence following correct responses, and lower confidence when they err; whereas in poorly-calibrated individuals this association is less clear. We hypothesized that altered somatosensory metacognition in people with TD could underlie PUs generation.

To test this hypothesis, we quantified metacognitive performance in TD patients, defined as their capacity to adjust subjective confidence reports according to performance during a discrimination task, on a trial-by-trial basis. We compared metacognitive performance in a tactile and in a visual task between a group of patients and healthy control volunteers. Because visual and tactile metacognitive performance are correlated in the general population [8], this design allowed us to test whether potential metacognitive deficits are specific to the tactile domain, or reveal general impairments in metacognitive monitoring. Following a pre-registered plan, we expected to find poorer metacognitive efficiency in TD patients, as compared to a healthy control (HC) group. Further, we expected this impairment to be specific, or more pronounced, in the somatosensory domain, close to description of PUs, as compared to the visual domain. Finally, we expected a negative relationship between the severity of the disease (i.e., intensity of PUs and tic severity) and tactile metacognitive efficiency.

METHODS

Participants

Twenty-six TD patients (diagnosed according to the DSM-5 diagnostic criteria, 5 female and 21 male) and 24 HC participants (6 female and 18 male) completed the study and were included in the initial analysis. After exclusions due to pre-registered thresholds of performance (see *Supplementary Material: Data Analysis and Statistical Methods* for more details), 4 patients were excluded in the TD group in from each modality, one HC participants was excluded from the tactile task and 5 participants were excluded from the visual task. The final sample

consisted of 22 TD patients in the tactile task and 22 in the visual task, and 23 HC participants in the tactile task and 19 in the visual task. HC participants with no pre-existing neurological or psychiatric conditions were matched to the TD population sample for age (mean (M) (\pm standard deviation (SD)): HC: 29.42 (\pm 7.32); TD: 27.84 (\pm 9.84)), sex, and education (M (\pm SD): HC: 18.08 (\pm 3.74); TD: 16.69 (\pm 3.83), Table 1). Twelve TD patients were taking psychoactive medication (Table 1), while none of the HC participants did. We used the Yale Global Tic Severity Scale (YGTSS) and Premonitory Urge for Tics Scale (PUTS) to assess patients with TD. The study was approved by the Charité Ethics Committee (EA2/082/18) and adhered to the Declaration of Helsinki. All participants gave written informed consent.

*** *Insert Table 1 here* ***

Procedure

The experimental procedure was based on a previous study [8]. Each participant completed two metacognitive tasks (visual and tactile). After calibration, training, and practice trials, each task consisted of 240 trials, split over four blocks of 60 trials each. For both tasks, each trial followed the same basic structure: A two-alternative forced-choice (2AFC) discrimination judgement using a computer keyboard followed by a confidence rating on a continuous scale from “very sure” to “very unsure”, using a computer mouse (Figure 1.A). For the visual task, participants discriminated which of two gratings had the stronger contrast. In the tactile task, participants discriminated which of two small actuators vibrated more strongly. For both the training and main experimental blocks, we titrated task difficulty using an online adaptive 2-down-1-up staircasing procedure (aiming at approximately 71% correct trials).

Data Analysis and Statistical Methods

Confirmatory analysis

The data analysis plan was pre-registered after data from first 20 TD and 20 HC participants were collected (but not analysed in regard to the main hypotheses) and is available under <https://osf.io/3djxs/>, as well as the analysis scripts and anonymized experimental data.

We used *m-ratio* (*meta-d'/d'*), a signal detection theory (SDT)-based measure to quantify metacognitive efficiency for each participant and task. *M-ratio* quantifies the sensitivity of subjective second-order reports relative to objective first-order task performance.

More details about the participants, procedure, analysis, the measure of choice (*M-ratio*), and exclusion criteria can be found in the Supplementary Materials.

*** *Insert Figure 1 here* ***

RESULTS

First-order performance

We first analyzed first-order performance in the tasks, as measured with d' . A 2X2 mixed-design ANOVA revealed no statistically significant effects of group ($F(1,34) = 2.77$, $p = 0.11$, $\eta^2 = 0.045$, $BF_{10} = 0.78$; Figure 1.B), modality ($F(1,34) = 1.73$, $p = 0.29$, $\eta^2 = 0.014$, $BF_{10} = 0.40$) or their interaction ($F(1,34) = 2.56$, $p = 0.12$, $\eta^2 = 0.030$, $BF_{10} = 0.97$) on d' (Figure 2A). On average, d' was indistinguishable between TD patients and HC in both tactile (M (\pm SD): TD: 1.38 (\pm 0.24); HC: 1.23 (\pm 0.10)) and visual (HC: 1.34 (\pm 0.18); TD: 1.37 (\pm 0.22)) tasks. In other words, objective, first-order performance did not differ significantly between tasks or groups. This shows the response accuracy was well controlled with an online adaptive staircase. See Supplementary Results for a confirmation that the stimulus difficulty levels also did not differ between groups.

M-ratios

In line with our hypothesis, we expected to find a difference in *m-ratios* between the groups, and a further interaction effect between task and group — a more pronounced difference between groups in the tactile task as compared to the visual task. Against our expectations, we found no evidence for an interaction effect of group and modality when we ran a 2X2 mixed-design ANOVA with *m-ratios* ($F(1,34) = 1.84$, $p = 0.18$, $\eta^2 = 0.022$, $BF_{10} = 0.73$; Figure 1.C), or for the effect of group ($F(1,34) = 0.95$, $p = 0.34$, $\eta^2 = 0.016$, $BF_{10} = 0.42$). However, contradicting previous results, we found a significant effect of modality ($F(1,34) = 10.08$, $p = .003$, $\eta^2 = 0.016$) (more details in Supplementary Results). Overall, *m-ratios* were higher in the tactile (M (\pm SD): TD: 0.785 (\pm 0.33); HC: 0.89 (\pm 0.33, $BF_{10} = 16.71$) than in the visual task (TD: 0.66 (\pm 0.36); HC: 0.63 (\pm 0.26)). This result does not support our hypothesis about poorer metacognitive ability in tactile modality in TD patients as compared to HC.

Correlations between m-ratios and clinical scores

To test whether more severe tics and more intense PUs are associated with worse tactile metacognitive ability, we correlated the individual PUTS and YGTSS (total) scores with *m-ratios* in the tactile task. Individual tactile *m-ratios* did not correlate with the PUTS score (Figure 1.D, skipped correlation Pearson's $r = -0.06$, $CI = [-0.48 \ 0.30]$, $n = 21$, $BF_{10} = 0.29$), or with the YGTSS score (Figure 1.E, skipped correlation Pearson's $r = -0.01$, $CI = [-0.34 \ 0.31]$, $n = 22$, $BF_{10} = 0.26$).

DISCUSSION

We investigated a specific role of tactile metacognitive ability in the phenomenology of PUs and tics in adults with TD. We used an experimental paradigm that allowed us to measure metacognitive ability independently of performance confounds. We asked participants to complete two tasks (a visual and a tactile), in order to test whether tactile metacognition was impaired, and whether this potential deficit was general or specific. Against our pre-registered hypothesis however, we found no evidence for impaired tactile or visual metacognitive ability in TD patients; or any correlations between individual tics severity and intensity of PUs and tactile metacognitive ability, which would be expected if metacognitive deficits were linked to the TD symptoms. Moreover, Bayesian statistics provided support for some of these null hypotheses. Taken together, these results suggest that metacognitive monitoring mechanisms in the somatosensory and visual domain are intact in TD patients, challenging the metacognitive hypothesis of abnormal somatosensory processing in TD. Thus, this study contributes to the existing literature by discarding a proposed pathogenesis for TD, rooted on failures of metacognitive insight.

It could be argued that differences between the tactile stimulation we used and PU sensations could explain the absence of differences in our findings: The vibratory tactile stimulation we used may have different phenomenological or statistical properties than the sensations accompanying PUs (which can influence metacognitive estimates [9]), and it may not capture attention in the same way as real PUs do. However, while it remains possible that the lack of ecological validity of the paradigm did not allow us to detect subtle differences in metacognitive efficiency between groups, we argue that the clear behavioural and phenomenological aspects of tics in TD should lead to large and detectable differences between

groups, using methods that have been shown to be sensitive to metacognitive deficits in other patient populations (e.g. patients with obsessive-compulsive disorder or addiction [10]).

Neuropsychiatric disorders and their transdiagnostic dimensions may relate differentially to global self-beliefs than to local metacognitive ability (measured through trial-by-trial measures, as we do here)[11]. This differentiation might apply to TD, too: While one previous study reported a link between tic severity and global metacognitive ability (measured through responses to a questionnaire to gauge general beliefs about patients' own tics) [12], we found no evidence for a link between local tactile metacognitive ability and tic severity. In the same way, PU intensity does not correlate with a local measure of metacognitive ability of interoception, while global bodily self-beliefs do correlate with PUTS scores [13]. Thus, our study suggests that local (trial-by-trial) perceptual metacognition in TD is not impaired and hence cannot explain PUs or tics. Speculatively, this might differ from global self-beliefs about bodily sensations in people with chronic tics. Alternatively, within the framework of predictive processing, PUs may emerge as the result of pathological active inference, whereby sensation changes as the result of an action made to match expectations [14]. In this case, TD may present differences to the healthy population in somatosensory processing (metacognitive or not) solely in the context of motor intentions.

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Author roles

(1) A. the conception and design of the study, or B. acquisition of data, or C. analysis and interpretation of data, (2) A. drafting the article or B. revising it critically for important intellectual content, (3) final approval of the version to be submitted.

P.A.: 1C, 2AB, 3

S.G.: 1B, 2B, 3

C.K.: 1, 2B, 3

L.K.: 1B, 2B, 3

N.F.: 1AC, 2B, 3

A.A.K.: 1A, 2B, 3

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S.G. has nothing to declare.

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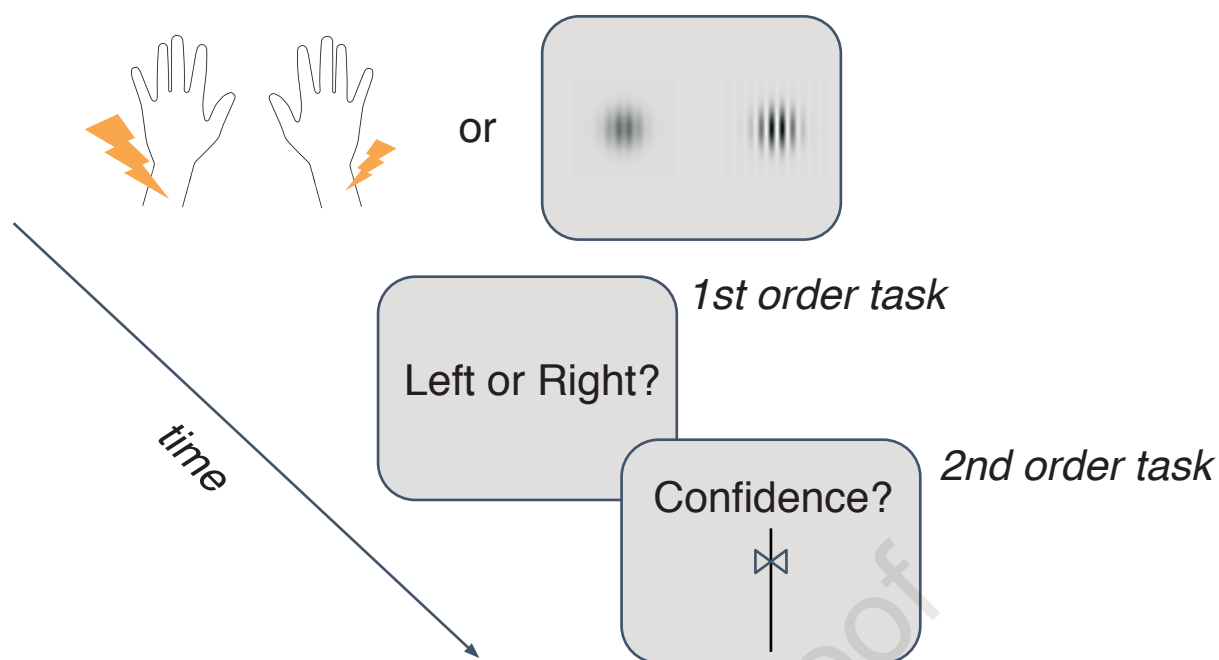
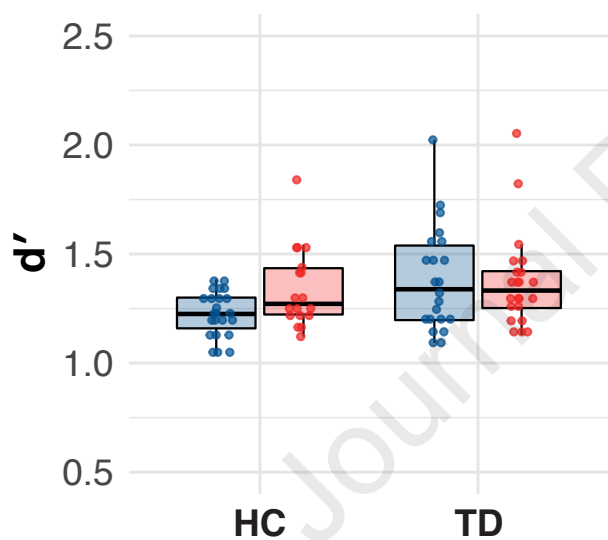
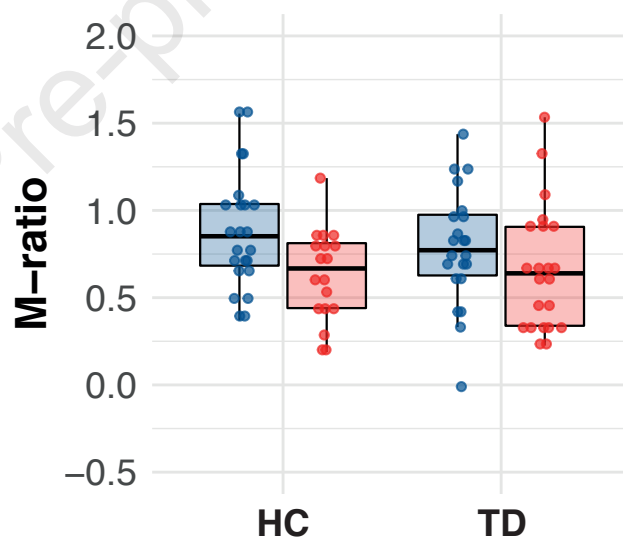


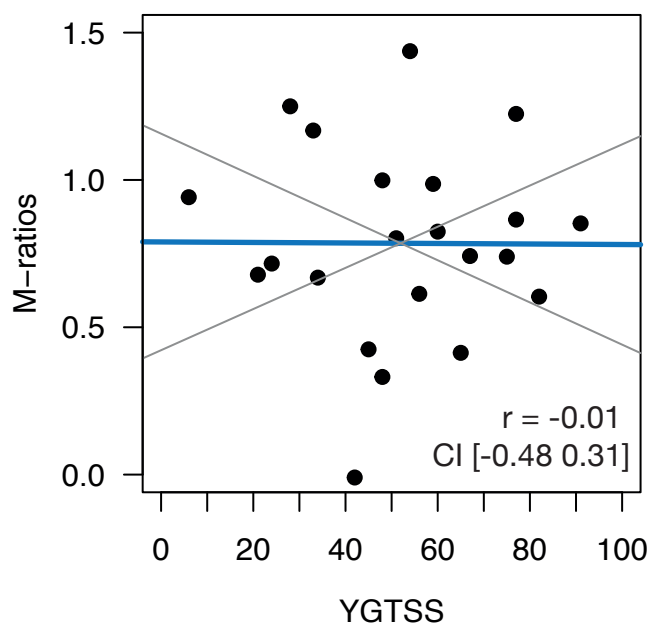
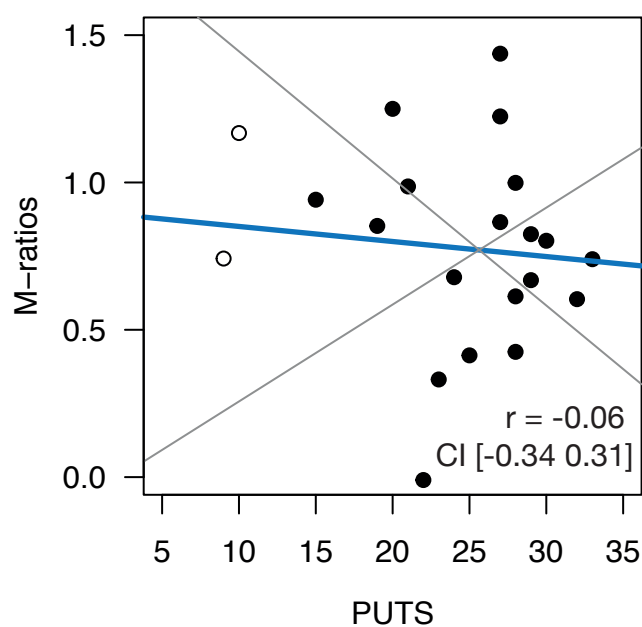
TABLES

Table 1. Demographics of the TD patient group.

Patient No	Age	Sex	Education (years)	YGTSS (total)	PUTS	Medication	Comorbidities	Tasks Included in Analysis: Tactile (T) Visual (V)
1	24	M	13	77	27	Methylphenidate, Escitalopram	ADHD, Depression	T, V
2	22	M	17	54	27	Aripiprazole	None	T, V
3	26	M	18	75	33	Aripiprazole	ADHD, OCD	T, V
4	57	F	25	24	N/A	None	None	T, V
5	45	M	10	48	23	Botulinum Toxin Ramipril/Opipramol	None	T, V
6	26	F	15	55	29	Botulinum Toxin	None	V
7	18	M	13	36	26	Aripiprazole	None	V
8	40	M	20	82	32	None	None	T, V
9	22	M	15	45	28	None	None	T, V
10	24	M	16	21	24	None	None	T, V
11	22	M	16.5	65	25	Aripiprazole	ADHD, Depression	T, V
12	24	M	15	33	10	Tetrabenazine, Rivotril, Lorazepam, Paroxetine	Depression, Anxiety Disorder	T, V
13	24	M	18	22	21	Botulinum Toxin	None	V
14	19	F	12	56	28	Fluoxetine	Depression, Social Anxiety Disorder	T, V
15	28	M	19	60	29	Aripiprazole	None	T, V
16	26	M	10	51	30	L-Thyroxine	ADHD	T
17	32	M	18	28	20	None	None	T, V
18	19	M	11	67	9	Tiaprider, Cannabinol	ADHD	T, V
19	28	F	20	34	29	Antidepressant (SSRI)	ADHD, OCD, Anxiety Disorder	T
20	42	M	16	77	27	Metocarbamol, Formoterol, Salbutamol	None	T
21	27	M	16	48	28	Finasteride	None	T, V
22	29	F	23	6	15	None	None	T, V

23	30	1	17	59	21	None	ADHD, Anxiety Disorder, Panic Disorder, Agoraphobia, Depression	T, V
24	33	1	18	42	22	Aripiprazole, Topiramate	None	T, V
25	35	1	21	91	19	None	None	T, V

Figure 1. A. Trial structure. On each trial of the tactile task, participants first indicated on which wrist they had felt the stronger vibration. On each trial of the visual task, participants discriminated which side of the screen the grating with the stronger contrast had appeared. Immediately after each discrimination decision, participants reported confidence on a visual analogue scale. We quantified performance using signal detection theoretic measures. Performance in the discrimination (first-order) task was quantified with the sensitivity measure d' . The accuracy of confidence ratings (second-order task), was quantified with $meta-d'$, which corresponds to how well confidence ratings can discriminate correct from incorrect first-order responses. We obtained one estimate of m -ratio (metacognitive efficiency, $meta-d'/d'$) for each participant and task. **B.** First-order performance as measured by d' . **C.** Metacognitive efficiency (m -ratio). In panels B and C dots show individual data points, boxes show interquartile range (IQR), median and whiskers extend to the highest or lowest values that are no further than the 1.5 of the IQR from the top or the bottom of the box. **D.** Relationship between tic severity scores (YGTSS, total score) and tactile metacognitive efficiency in the TD group. **E.** Relationship between premonitory urges scores (PUTS) and tactile metacognitive efficiency in the TD group. In panels D and E blue lines represent the model II regression line, fitted with the major axis method. Grey lines represent 95% CIs of the parametric slope estimates for the line of best fit, drawn through the centroid of the bivariate distribution. Empty dots in panel E represent outliers that were excluded from the correlation analysis and line of best fit estimation by the robust correlation procedure.

A**B****C**modality  tactile  visual**D****E**

HIGHLIGHTS

- Tactile and visual metacognition are likely intact in adults with Tourette disorder”
- Tactile metacognitive ability is not associated with tics severity
- Tactile metacognitive ability is not associated with severity of premonitory urges