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LETTER TO THE EDITOR

Forward model deficits and enhanced motor noise in Tourette syndrome?

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Sir,

We read with great interest the manuscript entitled 'Impaired forward model updating in young adults with Tourette syndrome' by Kim *et al.* (2019). Based on our own previous work (Ostendorf *et al.*, 2010) and common practice in the literature, we wish to highlight three aspects of their study design in light of which the authors' main conclusion of 'less precise forward models [...] in individuals with Tourette syndrome' (Kim *et al.*, 2019) may be premature.

Kim *et al.* (2019) compared performance of adolescents with Tourette syndrome versus healthy matched control subjects in a variant of a classic oculomotor paradigm (Hallett and Lightstone, 1976), the double-step task, which they adapted for pointing movements of the arm. They asked participants to point to the remembered location of a briefly presented visual target and then return to the remembered starting position of that movement. As movement kinematics inevitably vary from one repetition to the next, the second, return movement relied on monitoring metrics of the first. Given that hands were occluded from sight, the authors assumed this monitoring depended on estimates provided by an internal forward model. In support of this proposition, healthy subjects compensate for targeting errors of the first eye movement in oculomotor double-step tasks by adjusting second saccade metrics (Joiner, 2010), an ability that is impaired with dysfunctional internal monitoring pathways (Sommer and Wurtz, 2004; Ostendorf *et al.*, 2010).

While endpoint accuracy and variability of the first, outward movement were not significantly different between patients and controls, endpoints of the second, return movement were significantly less accurate and more variable in patients [a statistical test of a group (patients, controls) × movement (outward, return) interaction effect was not reported, i.e. a confirmation that any performance deficit in Tourette syndrome is indeed specific to the second movement]. The authors interpreted these results as reflecting a deficit in estimating the endpoint of the first, outward movement via an internal forward model. An additional analysis demonstrated that the second, return movement partially compensated for trial-by-trial variability in first movement errors. Crucially, this correction did not differ between patients and control subjects (i.e. non-significant interaction of group × error-estimate-type), hampering strong conclusions on forward model deficits in patients with Tourette syndrome.

Forward models are considered critical for accurate, precise and adaptive motor control (Shadmehr *et al.*, 2010; Franklin and Wolpert, 2011). Given that our motor commands are subject to noise, and motor execution is often perturbed, e.g. by a heavier-than-expected load, ongoing movements have to be monitored and, if necessary, corrected in order to fulfil their goals. However, due to sensory conduction delays, any correction that relies purely on sensory feedback is potentially outdated by the time it takes effect (Franklin and Wolpert, 2011). An internal model of the mechanics of our body and the environment, on the other hand, can simulate kinematics and dynamics that

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result from a given motor command and provide estimates in real time (Miall *et al.*, 2007; Wagner and Smith, 2008).

This is particularly useful for online corrections to movements whose duration is in the order of, or even shorter than, sensory conduction delays, such as in the case of saccadic eye movements (Shadmehr *et al.*, 2010). Experimental evidence indeed demonstrates that accurate and precise execution of the second saccade in an oculomotor double-step task relies on internal monitoring signals (Sun and Goldberg, 2016; Wurtz, 2018). However, sensory feedback (i.e. proprioceptive inflow) may increasingly be used for larger saccade sequences (Poletti *et al.*, 2013) or longer time intervals between eye movements (Rath-Wilson and Guitton, 2015).

Kim *et al.*'s (2019) study placed only loose temporal constraints on movement execution. Participants had up to 3 s to complete each of the two successive movements (of ~12–18 cm), which could therefore be initiated and executed relatively slowly. These loose temporal constraints limit interpretation of the findings in several ways.

First, it seems implausible that internal estimates of arm position derived from a forward model played a dominant role in the planning of the second, return movement. This is because the task gave participants enough time to sense the final position of their hand at the end of the outward movement before initiating the return movement (via proprioception). Thus, Kim *et al.*'s task (2019) stands in contrast to classic oculomotor double-step tasks that tightly controlled the information available for saccade planning to ensure a dominance of forward model estimates. In Kim *et al.*'s study this dominance is unlikely given that sensory information was readily accessible within the time available for planning the second movement.

Second, slow movements allow for online corrections. Motor control studies that aim to avoid these often ask participants for fast, ballistic movements, whose peak velocities are typically in the order of 30–70 cm/s (Tseng *et al.*, 2007). In the present study, the authors included movements as slow as 5 cm/s. As a result, it is likely that outward as well as return movements had a strong feedback component, i.e. that motor commands were updated as movements were unfolding. Changes in accuracy and precision of return movements in Tourette syndrome, as indexed by movement endpoints, could thus reflect differences in feedback corrections, and may not at all be related to the process of monitoring the first movement.

Finally, with loose temporal constraints, more time elapses between the initial, brief visual target presentation and execution of the return movement. Thus, in Kim *et al.*'s (2019) study, integrity of a memory trace of target location and starting position over time becomes more relevant. The authors argue that the absence of significant differences in accuracy and precision of the first, outward movement indicates that there is no confounding effect of any group differences in working memory. However, as memory decays with time (Peterson and Peterson, 1959), impaired working memory would be expected to affect the second, return movement more strongly than the first. Because differences in working memory between the two groups are likely, given the prevalence of co-morbid ADHD symptoms in this cohort, these differences could thus provide an alternative explanation for Kim *et al.*'s findings. That is, patients may have been less precise in their return movement because they were less certain of the remembered starting position they had to return to by the time they were planning that movement. Indeed, the pattern of clinical correlations supports this view: severity of ADHD but not tics was associated with imprecision of return movements.

Notwithstanding these limitations, Kim *et al.*'s (2019) research questions are highly relevant and topical, in particular regarding the mechanism they propose to underlie deficient forward modelling in Tourette syndrome, namely enhanced 'sensorimotor' noise. Indeed, several lines of research draw on the idea of enhanced noise in the motor system in Tourette syndrome, to explain either an altered subjective experience of volition in Tourette syndrome (Ganos *et al.*, 2014) or tic generation (Misirlisoy *et al.*, 2015). In healthy individuals, random fluctuations have been proposed to contribute to the decision 'when' to execute a voluntary movement (Schurger *et al.*, 2012). It is conceivable that this mechanism could also contribute to the perception of an urge to execute a tic movement when such fluctuations are enhanced (Ganos *et al.*, 2014).

However, direct evidence of enhanced noise in the motor system in Tourette syndrome is pending. One could argue that the absence of any significant difference in accuracy and precision of outward movements in Kim *et al.*'s study dismisses the idea of enhanced motor noise in Tourette syndrome. However, by design, their task is not optimized for quantifying motor noise, for two reasons.

First, in Kim *et al.*'s (2019) study, movement variability was highly task-relevant. Task-relevant and irrelevant movement variability are regulated differently (Todorov and Jordan, 2002; van Beers *et al.*, 2012). Thus, Kim *et al.*'s findings do not exclude the possibility of a subtle, or latent, increase in motor noise, which patients may be able to suppress reasonably well when the task at hand calls for high precision—hence their preserved (coarse) motor skills in everyday life, and the relatively unimpaired outward movement in Kim *et al.*'s study. Motor noise may rather surface and critically contribute to the generation of tic behaviours in situations that require no specific motor task.

Second, to estimate motor noise via movement kinematics, any potentially confounding influence of online feedback corrections on movement variability should be minimized, e.g. by emphasizing fast movements (Wu *et al.*, 2015). The loose temporal constraints in Kim *et al.*'s study (2019) thus limit interpretation of their findings also with respect to the level of motor noise in Tourette syndrome.

Taken together, Kim *et al.* (2019) ask questions that are highly relevant to our understanding of the pathophysiology of Tourette syndrome. It remains to be further clarified, however, whether sensorimotor noise is indeed enhanced in Tourette syndrome, and forward modelling impaired, with strong potential implications to our pathophysiological understanding of tic behaviours in Tourette syndrome.

Data availability

Data sharing is not applicable to this article as no new data were created or analysed in this study.

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Competing interests

The authors report no competing interests.

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