

## The multiple phenotypes of Tourette syndrome and attention-deficit hyperactivity disorder

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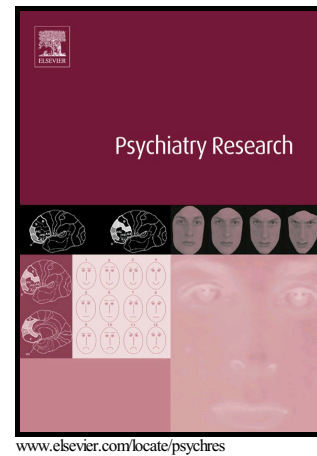
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# Author's Accepted Manuscript

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# The multiple phenotypes of Tourette syndrome and attention-deficit hyperactivity disorder

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## To the editors

We read with interest the recent Letter to the Editor by Mao and Yang (Mao and Yang, 2017) and we are pleased that our study on the impact of co-morbid attention deficit hyperactivity disorder (ADHD) on cognitive function in male children with Tourette syndrome (TS) (Termine et al., 2016) elicited praise and comments. In summary, our participants included four matched groups of 6- to 15-year-old male children who were not taking medications: TS (n=13), TS+ADHD (n=8), ADHD (n=39), healthy controls (n=66). All participants underwent a standardised psychometric battery of neuropsychological tests, in addition to clinical assessment. We found that problems in executive functions were more common in patients with neurodevelopmental disorders (TS and/or ADHD) than healthy controls. Moreover, the TS+ADHD group was the most severely affected, followed by the ADHD group and the TS group, particularly in the neuropsychological tests tapping into planning ability, inhibitory function, working memory, and visual attention. Overall, our preliminary findings suggested that a specific set of executive function deficits could be more strongly related to the presence of co-morbid ADHD symptoms than core TS symptoms.

The problem of the relative contribution of tic symptoms and ADHD symptoms to cognitive deficits in patients with TS is an under-investigated research area posing considerable challenges, which were only partially addressed by our controlled study paradigm. Specifically, we agree with the points raised by Mao and Yang (Mao and Yang, 2017) that further research is needed to confirm our preliminary findings and to better disentangle the relative contributions of tics and ADHD symptoms to cognitive function in male children with uncomplicated TS and TS+ADHD, in comparison to children with ADHD and healthy controls. Of particular interest is the observation that both TS and ADHD are heterogeneous neurodevelopmental conditions characterised by a spectrum of clinical presentations or discrete phenotypes (Bernfeld, 2012; Martino et al., 2013). Although it has not been established whether there is a definite link between one particular ADHD subtype and specific cognitive deficits, it is likely that future studies with more in-depth characterization of the clinical samples will add key contributions to our understanding of the cognitive

profiles of TS+ADHD populations, as well as their underlying neurobiological correlates (Mao and Yang, 2017). For example, the findings of a recent study suggested that executive function patterns are different in children with different ADHD subtypes, as the combined ADHD subtype appears to be associated with more significant problems in the perseveration and response inhibition domains (Ahmadi et al., 2014). Current evidence shows that the existence of multiple phenotypes is an important aspect of TS research, as chronic tic disorders have increasingly been re-conceptualized as clinically heterogeneous disorders spanning a motor-behavioural-cognitive continuum. Different clinical phenotypes have been shown to preferentially affect different aspects of health-related quality of life (Eddy et al., 2012) and there is the possibility that impulsivity as a feature of specific subtypes of both TS and ADHD predicts the presence of selective neuropsychological deficits (Frank et al., 2011). Likewise, the standardized characterization of ADHD symptom severity, as well as tic severity, is likely to provide one of the missing pieces of the multifaceted jig-saw of neurocognitive function in young patients affected by both conditions.

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