The multiple phenotypes of Tourette syndrome and attention-deficit hyperactivity disorder
Termine, Cristiano; Luoni, Chiara; Fontolan, Stefania; Selvini, Claudia; Perego, Livia; Pavone, Francesca; Rossi, Giorgio; Balottin, Umberto; Cavanna, Andrea E.

DOI: 10.1016/j.psychres.2017.03.002
License: Creative Commons: Attribution-NonCommercial-NoDerivs (CC BY-NC-ND)

Document Version
Peer reviewed version

Citation for published version (Harvard):

Link to publication on Research at Birmingham portal

General rights
Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

• Users may freely distribute the URL that is used to identify this publication.
• Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
• User may use extracts from the document in line with the concept of ‘fair dealing’ under the Copyright, Designs and Patents Act 1988 (?)
• Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

Take down policy
While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact UBIRA@lists.bham.ac.uk providing details and we will remove access to the work immediately and investigate.
The multiple phenotypes of Tourette syndrome and attention-deficit hyperactivity disorder

Cristiano Termine, Chiara Luoni, Stefania Fontolan, Claudia Selvini, Livia Perego, Francesca Pavone, Giorgio Rossi, Umberto Balottin, Andrea E. Cavanna

PII: S0165-1781(17)30362-1
DOI: http://dx.doi.org/10.1016/j.psychres.2017.03.002
Reference: PSY10369

To appear in: Psychiatry Research
Accepted date: 2

Cite this article as: Cristiano Termine, Chiara Luoni, Stefania Fontolan, Claudia Selvini, Livia Perego, Francesca Pavone, Giorgio Rossi, Umberto Balottin and Andrea E. Cavanna, The multiple phenotypes of Tourette syndrome and attention-deficit hyperactivity disorder, Psychiatry Research, http://dx.doi.org/10.1016/j.psychres.2017.03.002

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting galley proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.
The multiple phenotypes of Tourette syndrome and attention-deficit hyperactivity disorder

Cristiano Termine, Chiara Luoni, Stefania Fontolan, Claudia Selvini, Livia Perego, Francesca Pavone, Giorgio Rossi, Umberto Balottin, Andrea E. Cavanna

Child Neuropsychiatry Unit, Department of Experimental Medicine, University of Insubria, Varese, Italy
Child Neuropsychiatry Unit, Ospedale di Circolo & Macchi Foundation, Varese, Italy
Department of Child Neurology and Psychiatry, IRCCS "C. Mondino" Foundation, University of Pavia, Italy
Department of Neuropsychiatry, BSMHFT and University of Birmingham, United Kingdom
School of Life and Health Sciences, Aston University, Birmingham, United Kingdom
Sobell Department of Motor Neuroscience and Movement Disorders, UCL and Institute of Neurology, London, United Kingdom

*Corresponding author at: Department of Neuropsychiatry, National Centre for Mental Health, 25 Vincent Drive, Birmingham B15 2FG, United Kingdom. Tel.: +44 121 3012280. a.cavanna@ion.ucl.ac.uk

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 (Bernfled, 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 jigsaw of neurocognitive function in young patients affected by both conditions.

**References**


Mao, S., Yang, R., 2017. Do ADHD subtypes related to specific impairment of cognitive functions in boys with TS? Psychiatry Res. in press.
