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The ultimate aim is to help the translation of most relevant research findings into every-day clinical practice. These contributions are written in house by the journal's editorial team or commissioned by the Section Editor (no more than 1000 words, short unstructured abstract, four key-words, one Table or Figure and up to ten references).

Paolo Brambilla, *Section Editor*

Basal ganglia and restricted and repetitive behaviours in Autism Spectrum Disorders: current status and future perspectives

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This editorial offers a concise overview of the recent structural magnetic resonance imaging studies that evaluate the basal ganglia (BG) volumes in autism spectrum disorders (ASD). The putative relationship between the repetitive or stereotyped behaviours of ASD and BG volumes is also explored, with a focus on possible translational approaches.

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Under the umbrella category of autism spectrum disorder (ASD) are included neurodevelopmental conditions with a high genetic and phenotypic heterogeneity, but shared by a symptom dyad: (1) deficits in social communication and interactions; and (2) repetitive patterns of behaviour, interests and activities (Diagnostic and Statistical Manual of Mental Disorders, DSM-5; American Psychiatric Association, 2013). The modifications of the diagnostic criteria included in the current version of DSM have enhanced the role of the second domain: in fact, the restricted and repetitive behaviours (RRB), once considered non-ASD specific and subordinate to the socio-communication deficit, are now required for an ASD diagnosis.

Recent ASD research attempted to investigate whether the social communication and RRB dimensions are correlated with distinct endophenotypes and genotypes. In fact, a number of family studies in ASD have shown that genes controlling RRB are independent of genes controlling social or communication impairments (Mandy & Skuse, 2008). Similarly, among the neuroanatomical correlates of ASD

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Table 1. *Summary of studies published between 2005–2013 investigating basal ganglia volumetry in patients with autism spectrum disorders (ASD) compared with control subjects*[a]

Study	Subjects	Age in years (SD)	Full-scale IQ	MRI methods	Significant BG findings in ASD relative to controls	Brain–behaviour correlation in ASD
Hollander *et al.* (2005)	17 ASD 17 TD	28.4 (11.3) 29.4 (9.1)	97.1 (25.4) 111.5 (14.2)	1.5 T; ROI manual tracing	Enlargement in right caudate and putamen volumes (TBV as covariate)	Positive correlation between RRB assessed through the ADI-R and right caudate volume
Haznedar *et al.* (2006)	17 ASD 17 TD	27.7 (11.3) 28.8 (9.4)	97.1 (25.3) 111.5 (14.3)	1.5 T; ROI manual tracing	Enlargement in right caudate volume (TBV as covariate)	n.r.
Rojas *et al.* (2006)	24 AD 23 TD	20.8 (10.6) 21.4 (10.9)	94,7 (20,6) 118,7 (11,2)	1.5 T; VBM	Enlargement in caudate volumes (TGMV as covariate)	Positive correlation between RRB assessed through the ADI-R and caudate volumes
Voelbel *et al.* (2006)	38 ASD 12 BD 13 TD	10.2 (1.9) 10.1 (1.3) 10.7 (1.5)	99.4 (16.1) 102.2 (12.2) 115.1 (9.4)	1.5 T; ROI manual tracing	Enlargement in caudate volumes (TBV as covariate)	Negative correlation between executive functions assessed through WCST and caudate volumes
Langen *et al.* (2007)	(a) 21 HFA 21 TD (b) 21 HFA 21 TD	11.1 (2.2) 10.4 (1.8) 20.1 (3.1) 20.3 (2.2)	106,5 (13,7) 107.6 (13.4) 114,9 (19,2) 112.6 (10.2)	1.5 T; ROI manual tracing	Enlargement in caudate volumes for (a) and (b) samples (TBV as covariate) and in putamen volumes for sample (a)	No significant correlations between RRB assessed through the ADI-R and BG structures
Langen *et al.* (2009)	99 HFA 89 TD	12.9 (4.4) 12.4 (4.8)	107.6 (13.6) 109.9 (12.8)	1.5; ROI manual tracing and VBM	Enlargement in caudate volumes (specifically in head of the caudate nucleus) (TBV as covariate)	Negative correlation between insistence on sameness cluster of ADI-R and caudate volumes, particularly evident in the younger age group
Estes *et al.* (2011)	45 ASD 14 DD 25 TD	47.4 (4.2) months 47.5 (5.6) months 47.4 (6.9) months	59.1 (20.6) 56.9 (14.4) Evaluated, but n.r.	1.5; ROI manual tracing	Enlargement in bilateral thalami, striatum, caudate, and left globus pallidus in comparison to DD group (TBV as covariate)	Negative correlation between RRB assessed through the ADOS and right globus pallidus, right and left putamen, right striatum, left thalamus (no TBV as covariate)
Langen *et al.* (in press)[b]	49 HFA 37 TD	12.1 (2.3) 10.8 (1.8)	107,5 (18,6) 111.9 (15.0)	1.5; ROI manual tracing	Increase in the growth rate of caudate volumes (TBV as covariate)	Positive correlation between RRB (insistence on sameness) assessed through the ADI-R and striatal growth
Wolff *et al.* (2013)	30 iAD 41 FXS 16 FXS + AD	4.7 (0.7) 4.6 (0.8) 4.8 (0.8)	70.5 (32.1) 55.7 (16.6) 46.3 (14.1)	1.5; semi-automated 3D segmentation	Reduction in caudate volumes with respect to FXS and FXS + AD (TBV as covariate)	Positive correlation between compulsive/ritual behaviours and bilateral caudate volumes; positive correlation between self-injurious behaviour and left caudate volume (RRB assessed through RBS-R)

AD, autistic disorder; ADI-R, Autism Diagnostic Interview-Revised; ADOS, Autism Diagnostic Observation Schedule; ASD, autism spectrum disorders; BD, bipolar disorder; BG, basal ganglia; DD, developmental delay; FXS: fragile X syndrome; FXS + AD, fragile X syndrome with autistic disorder; HFA, high-functioning autism; iAD. idiopathic autistic disorder; n.r., not reported; RBS-R, Repetitive Behaviour Scales-Revised; RRB, restricted and repetitive behaviours; TBV, total brain volume; TD, typically developing control subjects; TGMV, total grey matter volume; VBM, voxel-based morphometry; WCST, Wisconsin Card Sorting Test.

[a]Due to the editorials guideline of limited number of references, only the most recent MRI studies on basal ganglia volumetry in ASD were considered, starting from year 2005.

[b]Longitudinal study.

symptoms (Bellani *et al.* 2013*a*, *b*), RRB have been frequently associated with structural alterations of the basal ganglia (BG), the deep grey matter structures that include the caudate nucleus, the putamen and the *globus pallidus*. Several structural magnetic resonance imaging (sMRI) studies have investigated the BG volumetry in patients with ASD and its correlation with the RRB severity. The association between BG structure and RRB symptom expression has been frequently, but not always (Hardan *et al.* 2003), found (see Table 1) and calls for further inquiry. First, (a) since the RRB domain encompasses a broad range of symptoms, ranging from repetitive motor behaviours ('lower order' RRB) to restricted behaviours and resistance to change ('higher order' RRB), future studies should investigate if different RRB phenotypes are related to different neuroanatomical underpinnings. Second, BG alterations are present in other neuropsychiatric conditions (e.g. attention deficit-hyperactivity disorder, social anxiety or obsessive-compulsive disorders): studies that compare ASD individuals with those affected by the above-mentioned disorders could contribute to define the specific characteristics of BG involvement in ASD; and finally, the effect of potentially significant factors other than RRB (age, gender, cognitive and adaptive functioning, ASD symptom severity, comorbid psychopathology, psychotropic medications and pattern of ASD onset) on BG volumes of ASD patients has not been clearly elucidated yet: longitudinal research designs in larger sample of carefully assessed subjects could contribute to this aim.

In addition to the fact that RRB are socially inappropriate and stigmatising, they also interfere with acquisition of adaptive and social skills. Moreover, RRB affect considerably day-to-day functioning and can jeopardise optimal academic and vocational placement. Recent research has focused on methods for reducing RRB, by triggering a positive cascade of effects on other behaviours. Therefore, elucidating the neurobiological underpinnings of the RRB will increase our understanding of the system involved and would eventually facilitate the development of effective intervention strategies. First, since BG volumetry is related to RRB severity, future longitudinal studies should explore the potential use of BG sMRI analysis as an adjunct method for monitoring the response to intervention aimed at reducing RRB. Second, additional research is needed to identify the brain circuitry associated with different functions of RRB in individuals with ASD (e.g. self-stimulation, modulation of anxiety) in order to define tailored treatment strategies that target those pathways. Third, the integration of results from different MRI techniques (i.e. Diffusion Tensor Imaging, proton spectroscopy, resting state fMRI and functional MRI) or newer imaging analysis methods (e.g. Support Vector Machines) applied to the same subjects could enhance our knowledge on symptom-specific neurobiological underpinnings, paving the way for treatment development.

In conclusion, research into the contribution of BG abnormalities to RRB pathogenesis and pathophysiology is an emerging and challenging new area that compliments and extends the search for ASD neuroanatomical correlates, with the final aim of translating laboratory findings into clinical practice.

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Conflict of Interest

None.

Ethical Standard

The authors declare that no human or animal experimentation was conducted for this work.

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