# Supplementary Information

## Supplementary Results

### Robustness of dysconnectivity in ASD boys to the inclusion of dysregulation as an additional covariate

Comparisons of ASD and TD boys accounting for dysregulation levels (as an additional covariate) using MDMR identified multiple clusters, with similar patterns but less spatial involvement. These clusters included bilateral pre-post central gyri (Somatomotor), and left IFG (FPN) (Supplementary Figure 3A and Supplementary Table 3).

*Post-hoc* seed-based analyses also exhibited similar patterns with the results of diagnostic group comparisons without adjusting for dysregulation, but with decreased spatial involvements. Specifically, the left postcentral cluster exhibited reduced connectivity with the right insula (involving Salience/VAN extending to Somatomotor Network) in the ASD group. ASD had reduced interhemispheric connectivity between homologous pre-postcentral areas (Somatomotor). In ASD, the left IFG cluster demonstrated reduced connectivity with the Salience/VAN and DAN hubs (bilateral anterior insula-putamen and dACC extending to right FEF), and the right inferior parietal lobule (IPL in FPN) (Supplementary Figure 3B and Supplementary Table 2).

## Supplementary Discussion

Beyond conventional diagnostic group comparisons, our results indicate that the inter-individual variability in dysregulation levels, which have been largely overlooked in the neuroimaging literature (Vasa et al., 2016), further complicates the matter of characterizing dysconnectivity in ASD. Benchmarking group comparisons covarying CBCL-DP scores against the conventional model without statistically controlling for dysregulation levels, we observed sparser spatial distributions in dysconnectivity patterns of ASD. Specifically, only bilateral pre-postcentral gyri and the left IFG clusters were significantly identified by the MDMR controlling for dysregulation levels; connectivity patterns associated with ASD yielded from follow-up analyses also altered (see topographical differences between Figure 1 and Supplementary Figure 3). In the present study, the magnitude of dysregulation in the ASD group was similar to those reported in earlier studies on emotion dysregulation (Samson, Huber, & Gross, 2012;

Samson et al., 2014), with regards to effect sizes relative to the TD. The current sample also consisted of relatively 'pure' ASD, as participants had a lower ratio of confirmed co-occurring psychiatric disorders (only 23% of the participants had psychiatric comorbidity) (Lai, Lombardo, & Baron-Cohen, 2014). Together with intellectually able features, these demographic characteristics endorse the current sample is similar to cohorts published in most of the rs-fMRI literature (Hull et al., 2016). Notably, at odds with reports by Samson and colleagues (2012; 2014), we did not identify a significant association of dysregulation levels with core autistic symptoms, except a weak correlation between scores of the CBCL-DP and the Communication domain in the ADI-R. Our finding of a significant dysregulation effect in the between-diagnosis comparison model, if replicated independently, highlights the need of considering the inter-individual variability of impaired self-regulation when searching for brain differences in ASD (Ni et al., 2018). This approach might also help overcome some levels of phenotypic heterogeneity, which partly contributes to the inconsistency in dysconnectivity patterns associated with ASD.

**Supplement Table 1.** Co-occurring psychiatric disorders and methylphenidate use in individuals with autism spectrum disorder (ASD)

| | ASD+Dysregulation (n = 36) | ASD-Dysregulation (n = 16) | Statistics |
|---|---|---|---|
| ASD only | 27 | 13 | $p = 0.622$ |
| Co-occurring ADHD only | 5 | 1 | |
| Co-occurring learning disorders only | 2 | 1 | |
| Co-occurring tic disorder only | 0 | 0 | |
| Co-occurring ADHD and ODD | 0 | 1 | |
| Co-occurring ADHD and tic disorder | 1 | 0 | |
| Co-occurring learning disorder and tic disorder | 1 | 0 | |
| Co-occurring anxious adjustment reaction | 4 | 2 | |
| Current methylphenidate use | 5 | 2 | $p = 0.896$ |

ADHD, attention-deficit/hyperactivity disorder; ODD, oppositional defiant disorder

**Supplementary Table 2.** Altered resting-state functional connectivity in boys with autism spectrum disorder (ASD), with adjusting for individual dysregulation levels

| Region | Network | MNI coordinates[†] | | | Size | Max z[‡] | Connections (Rz[*]) | |
|---|---|---|---|---|---|---|---|---|
| | | x | y | z | ($mm^3$) | | ASD | TD |
| **Left pre-postcentral gyrus**[§] | Somatomotor | -32 | -24 | 44 | 3776 | 3.35 | | |
| | **ASD<TD** | | | | | | | |
| Right insula | Salience/ Ventral attention-Somatomotor | 44 | -12 | 16 | 11968 | 3.38 | 0.316 (0.256) | 0.484 (0.239) |
| Right pre-postcentral gyrus-supplementary motor area | Somatomotor | 44 | -28 | 64 | 28160 | 5.79 | 0.348 (0.267) | 0.622 (0.257) |
| **Right pre-postcentral gyrus** | Somatomotor | 44 | -28 | 52 | 4864 | 3.35 | | |
| | **ASD<TD** | | | | | | | |
| Left pre-postcentral gyrus- supplementary motor area | Somatomotor | -36 | -24 | 56 | 27584 | 5.66 | 0.522 (0.267) | 0.786 (0.272) |
| **Left inferior frontal gyrus** | Frontoparietal | -40 | 16 | 20 | 2880 | 3.35 | | |
| | **ASD<TD** | | | | | | | |
| Left anterior insula-putamen | Salience/ Ventral attention | -20 | 0 | 44 | 8640 | 4.59 | 0.265 (0.238) | 0.455 (0.216) |
| Right anterior insula-putamen | Salience/ Ventral attention | 24 | 4 | 60 | 10048 | 4.49 | 0.053 (0.245) | 0.219 (0.198) |
| Dorsal anterior cingulate cortex-frontal eye field | Salience/ Ventral attention-Dorsal attention | -4 | 20 | 40 | 11392 | 3.72 | 0.403 (0.283) | 0.558 (0.252) |
| Right inferior parietal lobule | Frontoparietal | 56 | -32 | 52 | 9472 | 3.81 | 0.118 (0.262) | 0.239 (0.195) |

[†]Peak voxel coordinates.

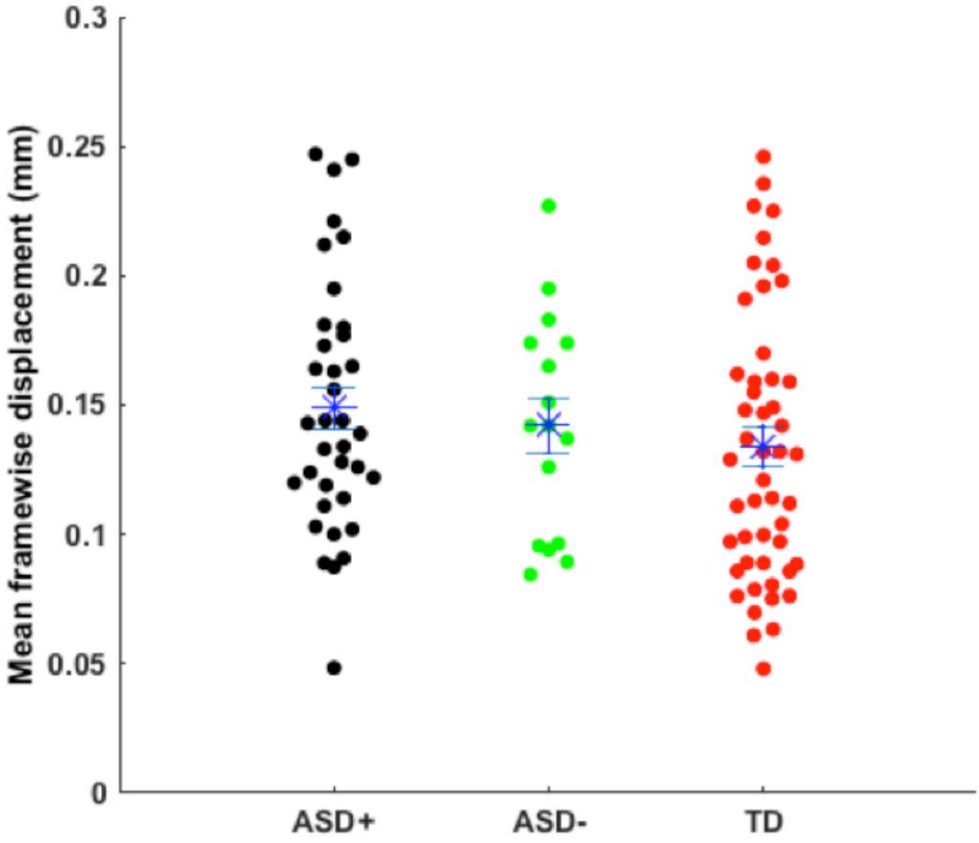
[‡]Absolute values.

[*]z-transformed correlational values.

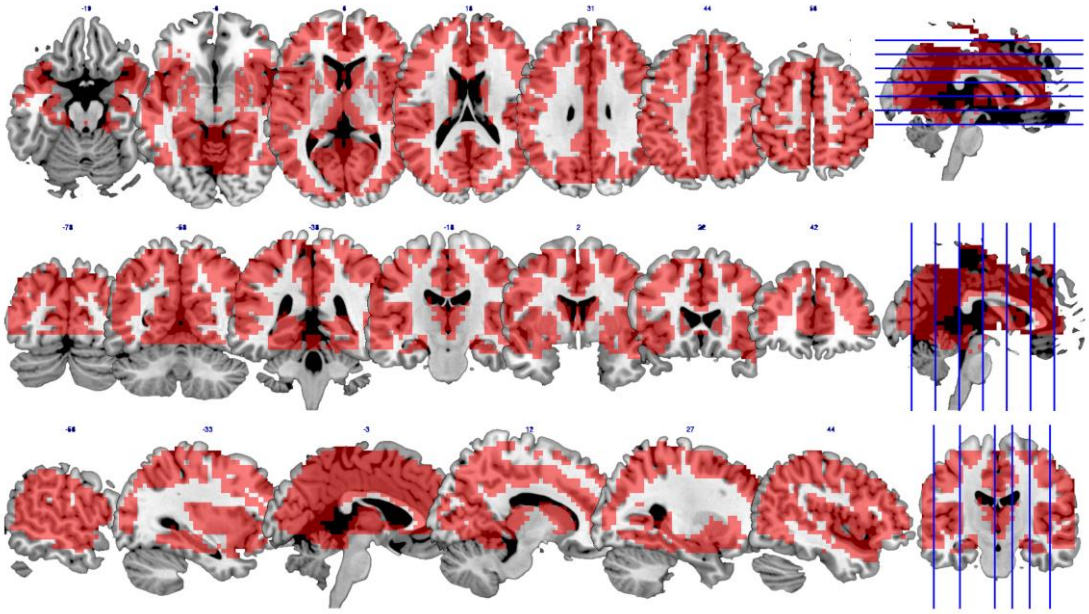
[§]The row with the gray background indicates the information of clusters identified by Multivariate Distance-based Matrix Regression. The following rows with transparent background indicate the information of clusters identified by follow-up seed-based analysis.

Abbreviation: MNI=Montreal Neurological Institute; TD=typically developing.

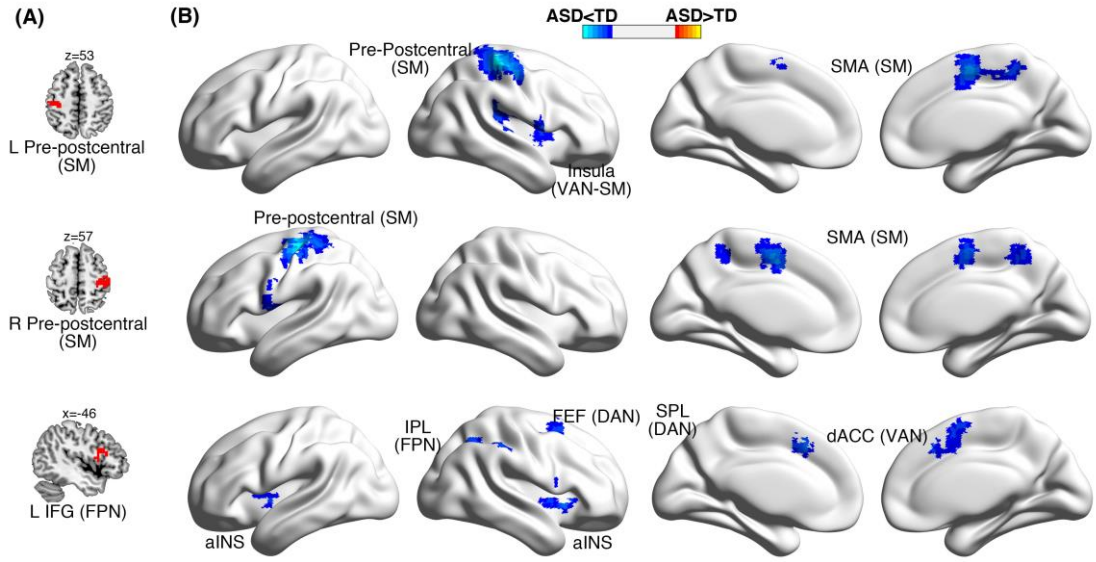
**Supplementary Figure 1.** In-scanner motion levels of individual participants based on mean framewise displacement [Jenkinson et al., 2002]. Blue asterisks denote mean, while blue bars correspond to standard error of group-wise mean framewise displacement. ASD+=ASD with Dysregulation; ASD-=ASD without Dysregulation; TD=typically developing.



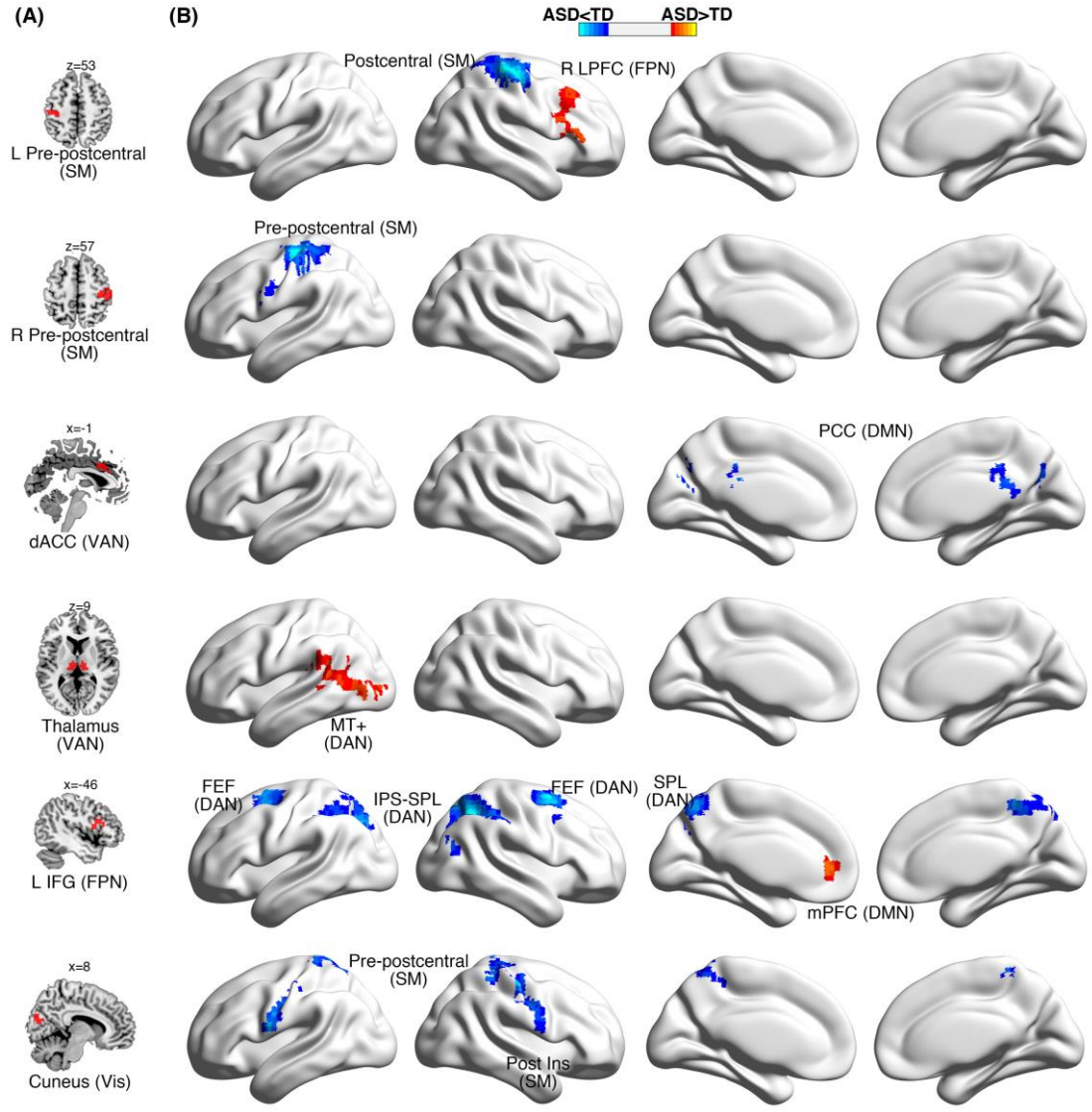
**Supplementary Figure 2.** The spatial coverage of our group-specific gray matter mask. The gray matter mask is overlaid on the ch2better template in MRIcron.



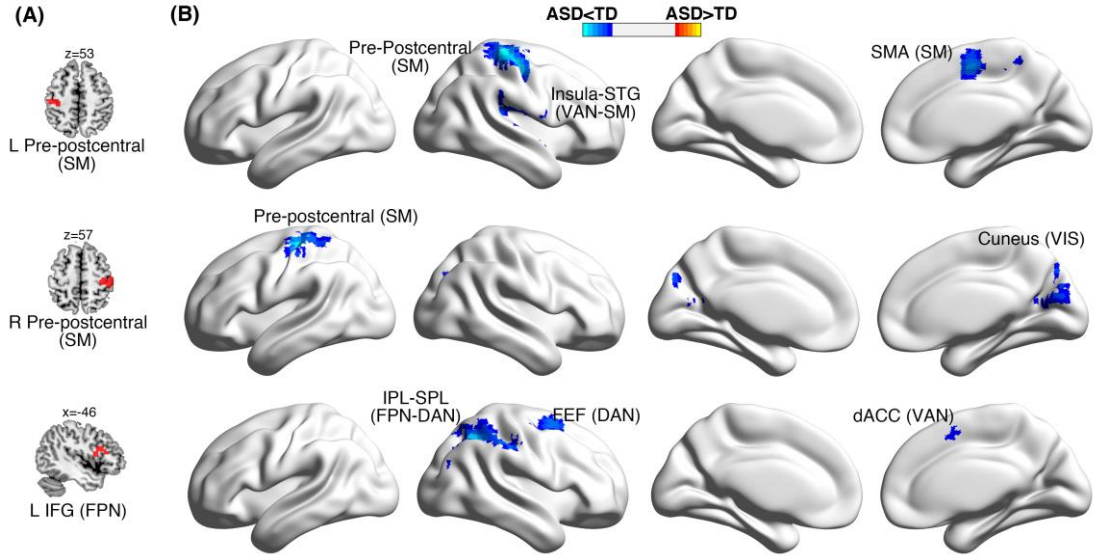
**Supplementary Figure 3.** Dysconnectivity patterns in ASD boys adjusting for the individual dysregulation level were altered, as compared to models without covarying dysregulation as shown in Figure 1. (A) MDMR identified multivariate patterns of dysconnectivity in left (L) and right (R) pre-postcentral gyrus, and left inferior frontal gyrus (IFG). (B) Follow-up seed-based analyses based on each MDMR-identified cluster also exhibited substantial differences as compared to corresponding sectors in Figure 1, in terms of spatial distribution. Other abbreviations: aINS=anterior insula; SPL=superior parietal lobule; IPL=inferior parietal lobule; dACC=dorsal anterior cingulate cortex; VAN=ventral attention network; SM=somatomotor network; FPN=frontoparietal network; DAN=dorsal attention network; SMA=supplementary motor area.



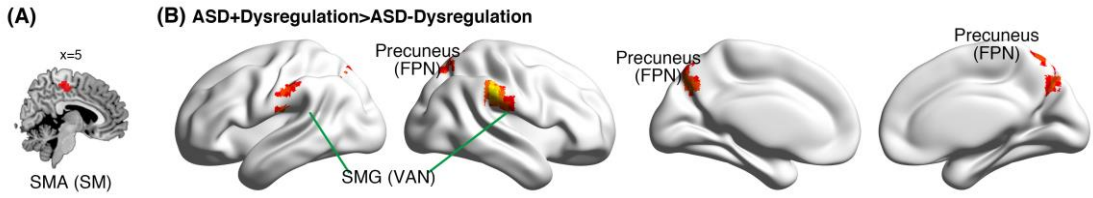
**Supplementary Figure 4.** Altered RSFC in ASD boys, without adjusting for the individual dysregulation level, with additionally covarying age square term and ADHD comorbidity. (A) MDMR identified multivariate patterns of dysconnectivity in the left (L) and right (R) pre-postcentral gyrus (somatomotor, SM), thalamus (ventral attention network, VAN), dACC (Salience/VAN), left IFG (FPN), and cuneus (Visual network, Vis). Brain patterns in each column of (B) illustrate specific connections contributing to the observed multivariate result in each cluster of the same column of (A). Other abbreviations: DAN=dorsal attention network; LPFC=lateral prefrontal cortex; PCC=posterior cingulate cortex; MT+=middle temporal motion complex; FEF=frontal eye field; mPFC=medial prefrontal cortex.



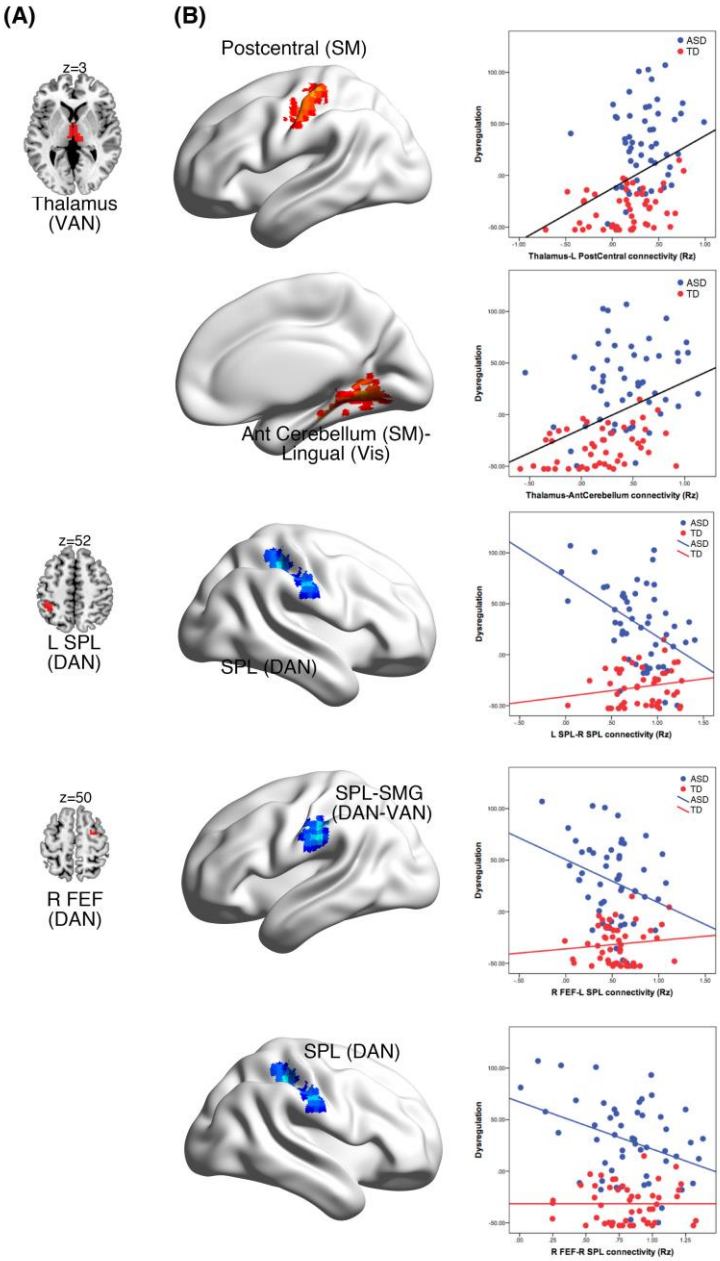
**Supplementary Figure 5.** Dysconnectivity patterns in ASD boys adjusting for the individual dysregulation level, with additionally covarying age square term and ADHD comorbidity. (A) MDMR identified multivariate patterns of dysconnectivity in left (L) and right (R) pre-postcentral gyrus, and left inferior frontal gyrus (IFG). Other abbreviations: aINS=anterior insula; SPL=superior parietal lobule; IPL=inferior parietal lobule; dACC=dorsal anterior cingulate cortex; VAN=ventral attention network; SM=somatomotor network; FPN=frontoparietal network; DAN=dorsal attention network; VIS=visual network; SMA=supplementary motor area; STG=superior temporal gyrus.



**Supplementary Figure 6**. Different RSFC between ASD boys with and without dysregulation, with additionally covarying age square term and ADHD comorbidity. (A) MDMR identified multivariate pattern of difference in the supplementary motor area (SMA) in somatomotor network (SM) between the ASD+Dysregulation and ASD-Dysregulation groups. (B) Follow-up seed-based analyses based on the SMA showed that the ASD+Dysrguelation group had increased connectivity between the SMA and supramarginal gyrus (SMG of Salience/ VAN), and between the SMA and medial dorsal-posterior precuneus (FPN).



**Supplementary Figure 7**. Distinct and shared dimensional neural correlates of dysregulation in autism ASD and TD boys, with additionally covarying age square term and ADHD comorbidity MDMR identified multivariate patterns of dimensional neural correlates of dysregulation in the dorsal anterior cingulate cortex (dACC) (Salience/ventral attention network, VAN), thalamus (VAN), left superior parietal lobule (L SPL in the dorsal attention network, DAN), and right frontal eye field (R FEF, DAN) (B) Follow-up seed-based analyses interrogates specific connections contribute to these multivariate patterns. Scatterplots at each row illustrate the brain-behavior relationship of the related cluster. The scale of dysregulation levels had been mean-centered. Other abbreviatation: Ant=anterior; Rz= Fisher-z-transformed correlation coefficient; SM=somatomotor network.



**Supplementary Figure 8**. Dimensional neural correlates of dysregulation based on previously identified neuroanatomical clusters (Ni et al., 2018). The scale of dysregulation levels had been mean-centered. Abbreviations: LPFC=lateral prefrontal cortex, Ins=insula; FPN=frontoparietal network; VAN=ventral attention network; mPFC=medial prefrontal cortex; DMN=default mode network; VAN=ventral attention network; IFG=inferior fronal gyrus; Rz= Fisher-z-transformed correlation coefficient.