Social Cognitive and Affective Neuroscience (SCAN)

## Supplementary Information

# Underconnectivity of the Superior Temporal Sulcus predicts Emotion recognition deficits in Autism

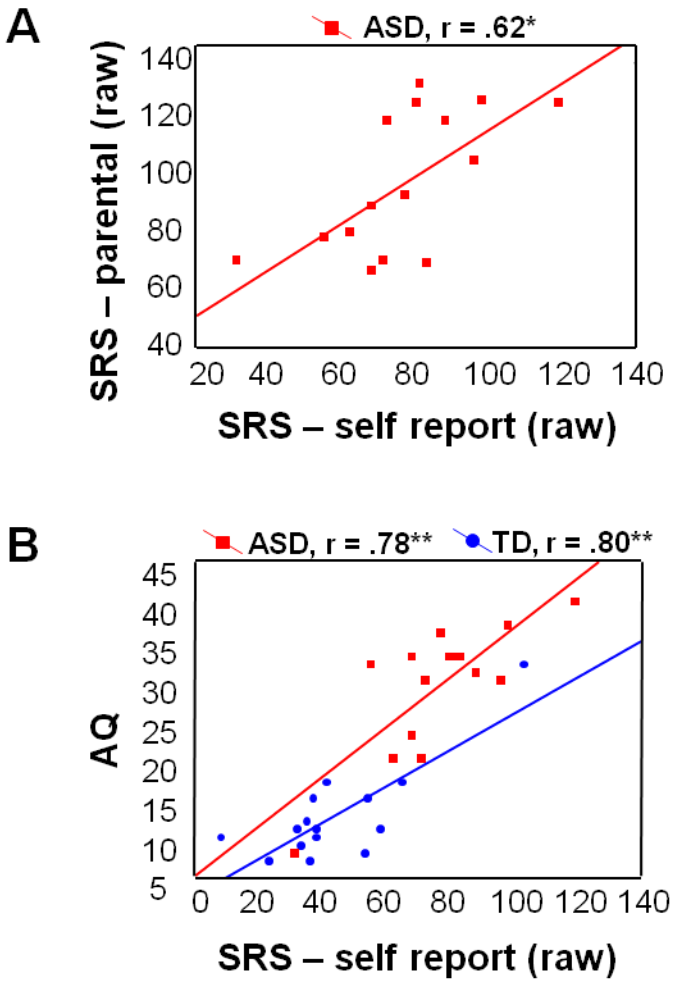
**Kaat Alaerts, Daniel G. Woolley, Jean Steyaert,**

**Adriana Di Martino, Stephan P. Swinnen, Nicole Wenderoth**

### Supplementary Figures, Tables and Movies

## Supplementary Figure 1

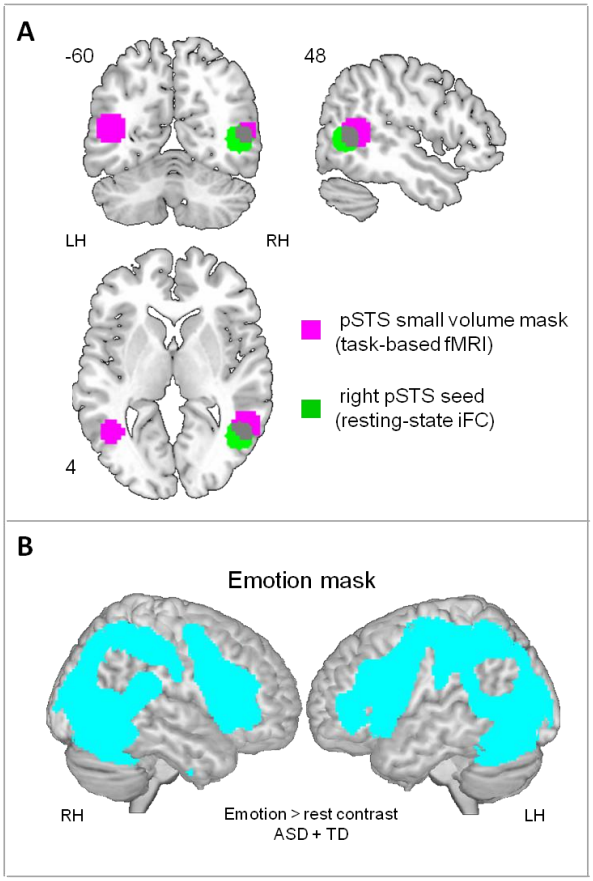
Relationship between total SRS - self report scores (raw) at time of study and (**A**) earlier total SRS - parental scores (raw); and (**B**) scores on the Autism Quotient Questionnaire (AQ). Relationships and Pearson correlation r-values are displayed separately for the ASD- (red) and TD-group (blue). SRS: Social Responsiveness Scale. * P < 0.05; ** P < 0.001.



## Supplementary Figure 2

**Panel A** displays (i) **in violet**: the small-volume mask used to threshold the task-based fMRI analyses, consisting of two 10-mm radius spheres centered on literature-based coordinates for right pSTS (53,-53,9) and left pSTS (-43,-58,11); and (ii) **in green**: the right pSTS-seed used to calculate resting-state intrinsic functional connectivity (iFC) between right pSTS and all other voxels in the brain. The right pSTS-seed was a 10-mm radius sphere centered around MNI-coordinates (47,-60,4), and was created using task-based fMRI coordinates that were relevant to emotion recognition in both groups. Specifically, the right pSTS seed was centered around the peak coordinates within right the pSTS-region that were identified from the task-based fMRI contrast 'emotion recognition>fixation **across all participants** (conjunction of ASD and TD one-sample t-maps). The task-based fMRI scans - which are collected independently but from the same group of participants - therefore served as a functional localizer for the resting-state fMRI analyses. As shown in the figure, the resting-state pSTS-seed (green) partly overlapped with the right pSTS small-volume (violet) used to threshold the task-based fMRI analysis.

**Panel B** displays the emotion mask used to specifically explore pSTS resting-state iFC with regions that are relevant to PLD emotion recognition. The mask was created based on the task-based fMRI results and encompassed brain regions that were activated during emotion recognition (>rest) in both groups [whole brain, one-sample t-test across ASD and TD groups, p<0.05, corrected].

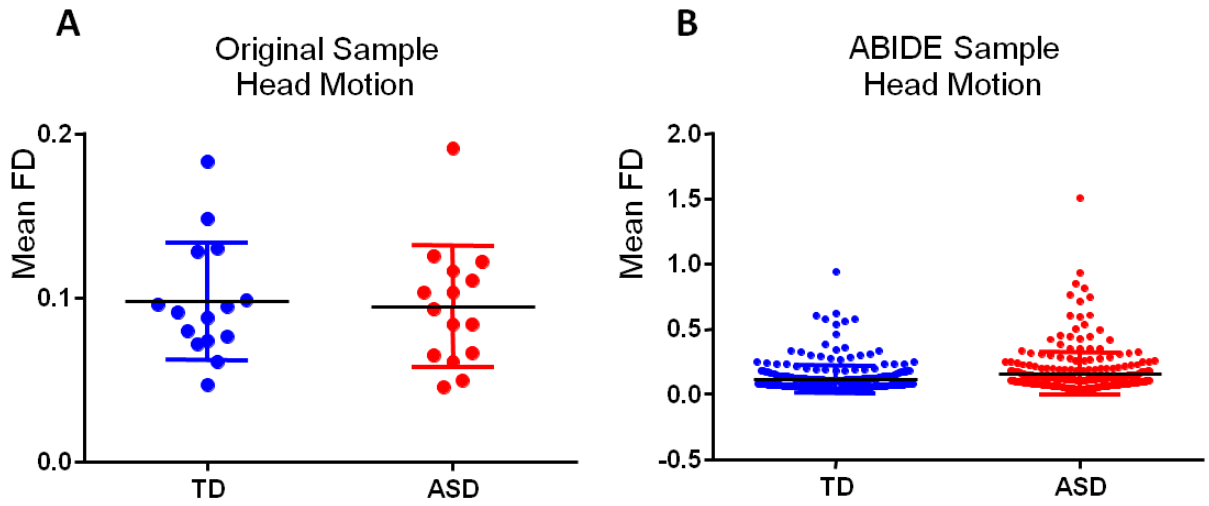


## Supplementary Figure 3

Mean frame-wise displacement (mean FD) was assessed for each participant over the entire resting-state fMRI scan (Art Repair). Each individual's values and group mean and standard deviations are displayed.

For the original sample (**panel A**), mean FD was not significantly different between groups (ASD, TD) [t(28)=0.25; p=0.81].

For the ABIDE replication sample (**panel B**), mean FD was greater within the ASD- compared to the TD-group [F(1, 566)= 4.23, p=.041], albeit group mean FD was below .2 mm for both ASD and TD groups.

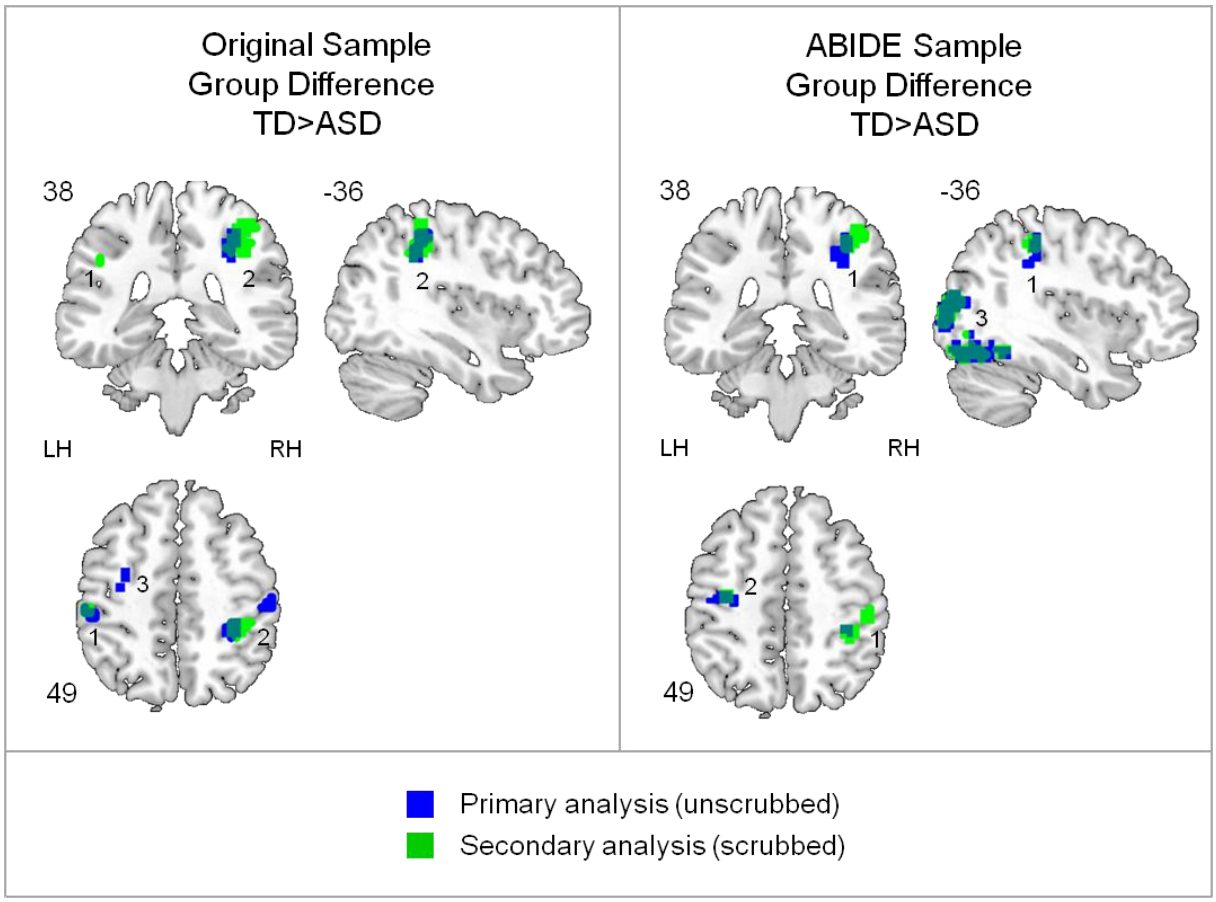


## Supplementary Figure 4

Considering that even small amounts of movement can produce spurious increases or decreases in iFC (Satterthwaite *et al*., 2013; Van Dijk *et al*., 2012; Yan *et al*., 2013), primary analyses were repeated on 'scrubbed' data (i.e., censoring frames with FD> 0.5 mm or DVARS> 0.5). Clusters with significant group-differences (TD>ASD) emerging from primary analyses ('unscrubbed; blue) are superimposed on those emerging from the secondary analyses ('scrubbed'; green) using the same statistical threshold [p<.05 cluster-wise corrected].

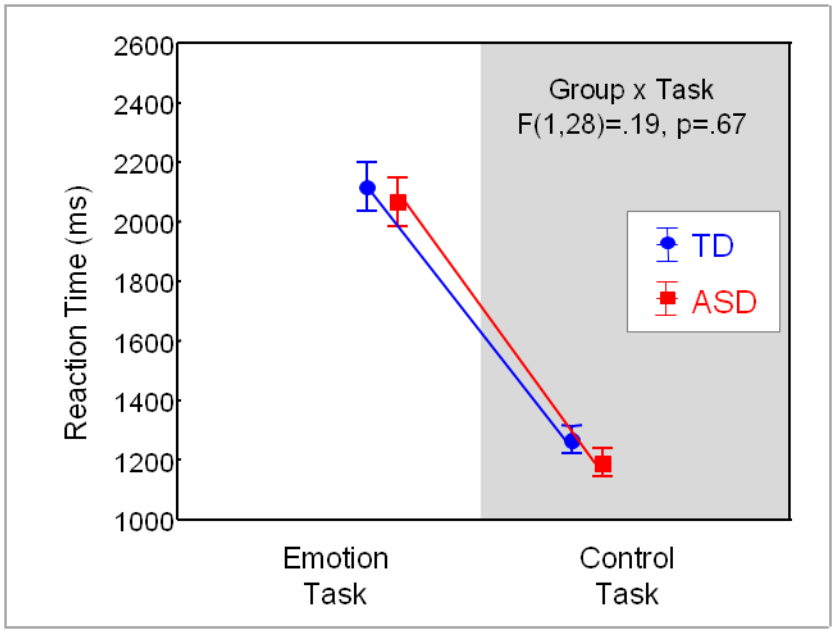
For the original sample (**panel A**), robust clusters with reduced pSTS-iFC in the ASD-group were revealed in bilateral inferior parietal lobule (1,2), whereas primary findings of reductions in pSTS-iFC with left inferior frontal gyrus (not shown) and premotor (3) were only identified at uncorrected statistical thresholds.

For the ABIDE sample (**panel B**), TD>ASD group differences remained similar for the scrubbed data, showing reductions in pSTS iFC with right IPL (1), left premotor (2), and bilateral fusiform-superior occipital gyrus (3).



## Supplementary Figure 5

Reaction times on the emotion recognition and control tasks were comparable across groups (ASD – TD).



## Supplementary Table 1

To test for reproducibility, intrinsic functional connectivity analyses were conducted on 584 resting-state fMRI datasets (278 ASD/306 TD) retrospectively aggregated across 9 sites participating in the 'Autism Brain Imaging Data Exchange' (ABIDE) release (Di Martino *et al.*, 2013).

Basic descriptive subject data are provided separately for each site and combined across sites (mean (SD)), including information on gender, age, full-scale IQ, head motion (mean frame-wise displacement (mean FD)) and total ADOS-scores (assessed using modules 3 or 4). Additional information on the diagnostics and scan procedures/parameters are publicly available via the ABIDE release website (http://fcon_1000.projects.nitrc.org/indi/abide/index.html).

ABIDE
Autism Brain Imaging Data Exchange

The ABIDE Consortium was founded to publicly release large samples of previously collected resting-state fMRI datasets (ASD and TD) to advance discovery science and data sharing in the broader scientific community.

| ABIDE - Contributing site | | ASD | TD | |
|---|---|---|---|---|
| Olin, Institute of Living at Hartford Hospital | **N** | 19 | 16 | |
| | **Gender** | 16 Male | 14 Male | |
| | **Age in years** | 16.6 (1.2) | 16.9 (1.3) | t(33) = -.30; p = .77 |
| | **Full Scale IQ** | 111.9 (3.7) | 114.9 (3.8) | t(31) = -.50; p = .62 |
| | **Mean FD** | 0.27 (0.32) | 0.24 (0.16) | t(33) = .44; p = .66 |
| | **ADOS** | | | |
| | - Total | 14.53 (4.55) | | |
| | **ADI-R** | | | |
| | - Social | 4.47 (1.31) | | |
| | - Communication | 10.05 (3.78) | | |
| | - RRB | - | | |
| Oregon Health and Science University | **N** | 11 | 15 | |
| | **Gender** | 11 Male | 15 Male | |
| | **Age in years** | 11.1 (1.6) | 10.1 (1.3) | t(24) = 1.68; p = .11 |
| | **Full Scale IQ** | 106.0 (4.6) | 115.7 (3.9) | t(24) = -1.48; p = .15 |
| | **Mean FD** | 0.084 (0.024) | 0.15 (0.09) | t(24) = -2.11; p = .05 |
| | **ADOS** | | | |
| | - Total | 12.18 (4.77) | | |
| | **ADI-R** | | | |
| | - Social | 19.64 (6.70) | | |

| | | | | |
|---|---|---|---|---|
| | - Communication | 17.09 (5.77) | | |
| | - RRB | 7.36 (3.20) | | |
| Trinity Centre for Health Sciences  | **N** | 24 | 25 | |
| | **Gender** | 24 Male | 25 Male | |
| | **Age in years** | 17.3 (1.0) | 17.1 (1.0) | t(47) = .19; p = .85 |
| | **Full Scale IQ** | 109.3 (3.1) | 111.7 (3.2) | t(45) = -.61; p = .54 |
| | **Mean FD** | 0.16 (0.15) | 0.12 (0.11) | t(47) = 1.03; p = .30 |
| | **ADOS** | | | |
| | - Total | 10.54 (2.87) | | |
| | **ADI-R** | | | |
| | - Social | 4.54 (1.45) | | |
| | - Communication | 8.79 (2.40) | | |
| | - RRB | 1.85 (1.72) | | |
| University of Utah, School of Medicine  | **N** | 56 | 43 | |
| | **Gender** | 56 Male | 43 Male | |
| | **Age in years** | 22.1 (0.7) | 21.4 (0.8) | t(97) = .49; p = .62 |
| | **Full Scale IQ** | 100.0 (2.0) | 115.1 (2.3) | t(97) = -4.97; p < .001 |
| | **Mean FD** | 0.19 (0.19) | 0.13 (0.09) | t(97) = 1.94; p = .06 |
| | **ADOS** | | | |
| | - Total | 13.32 (3.29) | | |
| | **ADI-R** | Administered, but scores not available | | |
| Yale Child Study Center  | **N** | 26 | 28 | |
| | **Gender** | 18 Male | 20 Male | |
| | **Age in years** | 12.7 (1.0) | 12.7 (1.0) | t(52) = -.01; p = .99 |
| | **Full Scale IQ** | 95.7 (3.0) | 105.1 (2.9) | t(51) = -1.76; p = .09 |
| | **Mean FD** | 0.15 (0.14) | 0.11 (0.07) | t(52) = 1.43; p = .16 |
| | **ADOS*** | | | |
| | - Total (Gotham) | 11.92 (3.25) | | |
| | **ADI-R** | | | |
| | - Social | 21.75 (5.76) | | |
| | - Communication | 17.75 (4.05) | | |
| | - RRB | 5.80 (3.91) | | |
| University of Leuven: Sample 2  | **N** | 13 | 17 | |
| | **Gender** | 10 Male | 13 Male | |
| | **Age in years** | 13.9 (1.4) | 14.5 (1.2) | t(28) = -1.12; p = .27 |
| | **Full Scale IQ** | Not provided | Not provided | |

| | | | | |
|---|---|---|---|---|
| | **Mean FD** | 0.14 (0.09) | 0.10 (0.03) | t(28) = 1.42; p = .17 |
| | **ADOS** | Not administered | | |
| | **ADI-R** | Not administered | | |
| NYU Langone Medical Center  | **N** | 78 | 104 | |
| | **Gender** | 67 Male | 78 Male | |
| | **Age in years** | 14.5 (0.6) | 15.8 (0.5) | t(180) = -1.23; p = .21 |
| | **Full Scale IQ** | 108.3 (1.8) | 113.5 (1.5) | t(174) = -2.29; p = .02 |
| | **Mean FD** | 0.11 (0.065) | 0.07 (0.04) | t(180) = 4.43; p < .001 |
| | **ADOS** | | | |
| | **-** Total | 11.39 (4.07) | | |
| | **ADI-R** | | | |
| | - Social | 19.22 (5.97) | | |
| | - Communication | 15.25 (5.81) | | |
| | - RRB | 5.36 (2.93) | | |
| University of California, Los Angeles: Sample 1  | **N** | 41 | 33 | |
| | **Gender** | 35 Male | 29 Male | |
| | **Age in years** | 13.1 (0.8) | 13.2 (0.9) | t(72) = -.24; p = .81 |
| | **Full Scale IQ** | 102.8 (2.4) | 105.2 (2.6) | t(72) = -.86; p = .39 |
| | **Mean FD** | 0.24 (0.28) | 0.16 (0.19) | t(72) = 1.46; p = .15 |
| | **ADOS** | | | |
| | **-** Total | 10.24 (3.56) | | |
| | **ADI-R** | | | |
| | - Social | 20.24 (4.85) | | |
| | - Communication | 16.66 (4.38) | | |
| | - RRB | 7.41 (2.32) | | |
| University of Michigan: Sample 2  | **N** | 11 | 24 | |
| | **Gender** | 10 Male | 23 Male | |
| | **Age in years** | 14.6 (1.6) | 16.6 (1.1) | t(33) = -1.51; p = .14 |
| | **Full Scale IQ** | Not provided | Not provided | |
| | **Mean FD** | 0.11 (0.077) | 0.11 (0.11) | t(33) =.03; p = .98 |
| | **ADOS** | | | |
| | **-** Total | 10.30 (3.37) | | |
| | **ADI-R** | | | |
| | - Social | 17.18 (5.40) | | |
| | - Communication | 15.82 (2.86) | | |
| | - RRB | 6.36 (3.35) | | |

| | | | | |
|---|---|---|---|---|
| Total Sample (9 sites) | N | 278 | 306 | |
| | Gender | 246 Male | 258 Male | |
| | Age in years | 15.9 (6.2) | 15.9 (5.7) | F(1, 566)= .23, p=.63 |
| | Full Scale IQ | 104.4 (17.3) | 111.9 (13.9) | F(1, 494)= 17.3, p<.001 |
| | Mean FD | 0.16 (0.11) | 0.12 (0.18) | F(1, 566)= 4.23, p=.041 |

ASD, autism spectrum disorder; TD, typically developed; IQ, intelligence quotient; Mean FD, framewise displacement (micro head motion); ADOS, Autism Diagnostic Observation Schedule; ADI-R, Autism Diagnostic Interview-Revised; RRB, Restricted Repetitive Behaviors.
***** Total ADOS score was based on the algorithm described by Gotham et al. (2009), resulting from the sum of the scaled scores (Social affective and Repetitive restricted behavior). For the remaining sites the ADOS total score (Lord et al., 1999) is provided resulting from the sum of the Social and Communication scaled sub-scores. For more information, please see: (http://fcon_1000.projects.nitrc.org/indi/abide/index.html)

Information regarding **medication status** was provided by the following ABIDE sites: Olin, Trinity, NYU, UCLA and University of Michigan. Of these five sites, 29 % of the participants with ASD were on medication within the month prior to the scan. Specific information on the medication class and whether stimulants were used at the time of the scan is provided in Di Martino *et al.,* 2013 or on the ABIDE website (http://fcon_1000.projects.nitrc.org/indi/abide/index.html).

## Supplementary Table 2

Regression models testing the relationship between emotion recognition accuracy (dependent variable) and the independent variables (i) pSTS-activity and (ii) pSTS-functional connectivity. Regression model 1 shows the regression results when only 'pSTS-activity' is included as an independent variable. Regresson model 2-6 show the regression results for adding 'pSTS-connectivity' (to right IPL, left IPL, left premotor, left SMA and left IFG) as an additional independent variable into the model. For models 2-6 the change in variance explained compared to model 1 is reported ($R^2$-change).

| dependent variable<br>Emotion recognition accuracy | Independent variables<br>pSTS activity | Connectivity to right IPL | Connectivity to left IPL | Connectivity to left premotor | Connectivity to left SMA | Connectivity to left IFG | Connectivity to | Whole model |
|---|---|---|---|---|---|---|---|---|
| Model 1 | ß=.61,<br>t(28)=4.11* | | | | | | | $R^2$=.37; F(1,28)=16.92; p=.0003 |
| Model 2 | ß=.42,<br>t(27)=2.75* | ß=.38,<br>t(27)=2.48* | | | | | | $R^2$=.49; F(2,27)=13.10; p=.0001<br>**$R^2$-change=11.5%*** |
| Model 3 | ß=.47,<br>t(27)=2.80* | | ß=.27,<br>t(27)=1.62 | | | | | $R^2$=.43; F(2,27)=10.27; p=.0004<br>**$R^2$-change=5.5%*** |
| Model 4 | ß=.41,<br>t(27)=1.84 | | | ß=.26,<br>t(27)=1.19 | | | | $R^2$=.41; F(2,27)=9.29; p=.0001<br>**$R^2$-change=3.0%** |
| Model 5 | ß=.53,<br>t(27)=3.61* | | | | ß=.31,<br>t(27)=2.14* | | | $R^2$=.47; F(2,27)=11.82; p=.0002<br>**$R^2$-change=9.0%*** |
| Model 6 | ß=.51,<br>t(27)=3.54* | | | | | ß=.36,<br>t(27)=2.54* | | $R^2$=.50; F(2,27)=13.33; p=.0001<br>**$R^2$-change=12.0%*** |

## Supplementary Table 3

Between-group differences in resting-state functional connectivity with right pSTS (posterior Superior Temporal Sulcus) based on 278 ASD and 306 TD resting-state fMRI samples of the 'Autism Brain Imaging Data Exchange' (ABIDE) release

**Bold regions** were previously identified in the original sample of 30 participants (15 ASD/ 15 TD).

| | Cluster size | Area | Hemi | *x* | *y* | *z* | *t* |
|---|---|---|---|---|---|---|---|
| **TD >ASD** | 1075 | Fusiform Gyrus | R | 36 | -78 | -18 | 4.96 |
| | | Superior Occipital Gyrus | R | 22 | -94 | 6 | 4.72 |
| | | | R | 24 | -76 | 30 | 4.52 |
| | 710 | Fusiform Gyrus | L | -40 | -82 | -14 | 4.28 |
| | | | L | -42 | -64 | -14 | 4. 05 |
| | | | L | -36 | -72 | -14 | 3.87 |
| | 349 | Superior Occipital Gyrus | L | -20 | -78 | 24 | 4.04 |
| | | | | -16 | -94 | 18 | 3.76 |
| | 75 | **Precentral Gyrus (BA 6)** | L | -34 | -16 | 52 | 3.53 |
| | | | L | -30 | -22 | 58 | 3.00 |
| | 86 | **Inferior Parietal Lobule** | R | 32 | -36 | 40 | 3.20 |
| | | | R | 38 | -36 | 48 | 3.00 |
| **ASD >TD** | 158 | Thalamus | L | -10 | -16 | 12 | 4.98 |
| | | | | -6 | -14 | 12 | 4.41 |
| | 167 | IFG (pars Triangularis) (BA 45) | R | 50 | 30 | 10 | 3.70 |
| | | | | 60 | 26 | 10 | 3.50 |

BA refers to putative Brodmann Area; L and R refer to left and right hemispheres; x, y, and z refer to the MNI (Montreal Neurological Institute) coordinates corresponding to the left-right, anterior-posterior, and inferior-superior axes, respectively; cluster size denotes number of voxels; t refers to the highest t-score within a region [p<.05, cluster-wise corrected].

pSTS: posterior Superior Temporal Sulcus - IFG: Inferior Frontal Gyrus

## Supplementary Table 4

All participants of the original sample (N=30), were debriefed about their experience during the acquisition of the resting-state scan. In the questionnaire, participants indicated the percentage (%) of time they spend thinking about something (part 1 and part 3) and provided a score (0-6) to describe their experience in the scanner (6 being highest score) (part 2). The table displays mean (percentage) scores within each group (SD). are were compared between groups using two-sample t-tests.

No significant group-differences in experience or spontaneous thoughts were revealed based on the adopted questionnaire (two-sample t-tests, all p>.05).

| | ASD | TD | | |
|---|---|---|---|---|
| **PART1**<br>% of time spend thinking about: | mean (SD) | mean (SD) | t-value | p |
| experience within scanner | 41.93 (34.52) | 51.25 (24.39) | 0.86 | 0.40 |
| life in general | 43.07 (35.55) | 45.00 (25.50) | 0.17 | 0.86 |
| past | 26.96 (27.67) | 13.88 (13.35) | -1.68 | 0.10 |
| present | 46.79 (31.90) | 59.38 (26.39) | 1.18 | 0.25 |
| future | 19.11 (23.07) | 25.50 (20.67) | 0.80 | 0.43 |
| myself | 43.21 (31.48) | 55.94 (27.94) | 1.17 | 0.25 |
| others | 42.50 (31.30) | 44.69 (27.96) | 0.20 | 0.84 |
| **PART 2**<br>Score 0-6 to describe your experience inside the scanner | | | | |
| anxiousness | 0.50 (0.85) | 1.19 (1.33) | 1.66 | 0.11 |
| eye-open instruction | 2.71 (2.20) | 2.88 (2.36) | 0.19 | 0.85 |
| being comfortable in scanner | 3.79 (1.81) | 2.84 (1.41) | -1.60 | 0.12 |
| lie-still instruction | 1.07 (1.27) | 1.75 (1.44) | 1.36 | 0.18 |
| duration of the scanner | 3.29 (2.20) | 4.19 (1.60) | 1.30 | 0.21 |
| sleepiness | 3.21 (2.39) | 4.25 (1.84) | 1.34 | 0.19 |
| thoughts about others | 3.36 (1.86) | 2.88 (1.67) | -0.75 | 0.46 |
| conversations with others | 3.14 (1.96) | 2.38 (1.59) | -1.19 | 0.25 |
| things to-do | 3.29 (2.05) | 3.56 (1.71) | 0.40 | 0.69 |
| things done today | 2.21 (1.67) | 3.13 (1.86) | 1.40 | 0.17 |
| things to-do today | 2.64 (2.10) | 3.50 (1.59) | 1.27 | 0.21 |
| things to-do this week | 2.57 (2.31) | 1.81 (1.76) | -1.02 | 0.32 |
| tiredness | 2.71 (2.16) | 3.69 (2.12) | 1.24 | 0.22 |
| irritation about duration of scan | 2.86 (2.41) | 3.56 (1.90) | 0.90 | 0.38 |
| **PART 3**<br>% of time spend thinking about: | | | | |
| family | 10.71 (16.27) | 4.33 (9.04) | -1.32 | 0.20 |
| friends | 8.50 (12.89) | 13.33 (9.94) | 1.14 | 0.27 |
| acquaintances | 4.64 (11.51) | 1.40 (5.15) | -0.99 | 0.33 |
| pets | 0.36 (1.34) | 0.00 (0.00) | -1.04 | 0.31 |
| fysical comfort | 14.14 (22.76) | 12.67 (13.21) | -0.22 | 0.83 |
| past events | 10.00 (14.81) | 7.87 (9.40) | -0.47 | 0.64 |
| personal things | 2.07 (5.08) | 4.53 (9.09) | 0.89 | 0.38 |
| noise of the scanner | 18.14 (21.32) | 17.13 (14.94) | -0.15 | 0.88 |
| future travel plans | 2.86 (6.11) | 0.00 (0.00) | -1.81 | 0.08 |
| financial problems | 0.71 (2.67) | 0.00 (0.00) | -1.04 | 0.31 |
| novel ideas | 3.57 (5.35) | 2.00 (5.61) | -0.77 | 0.45 |
| things to-do | 10.00 (17.87) | 11.67 (12.49) | 0.29 | 0.77 |
| mental comfort | 2.50 (5.10) | 3.33 (6.99) | 0.36 | 0.72 |
| future events | 4.64 (6.64) | 7.07 (9.82) | 0.77 | 0.45 |
| interpersonal conflicts | 1.29 (4.03) | 1.33 (3.52) | 0.03 | 0.97 |
| other | 1.57 (5.88) | 12.33 (24.27) | 1.61 | 0.12 |

## Supplementary Movie 1

One trial of the emotion recognition task.

The emotional state of the blue-bordered point light display (PLD) had to be indicated relative to a baseline PLD (yellow-bordered) that always showed a neutral emotional state. The emotional state could be indicated as happy, sad, angry, or neutral (sad in this example).

## Supplementary Movie 2

One trial of the control task.

Point light displays (PLD) of the **control task** were identical to those presented during the emotion recognition task, except participants were required to indicate color changes in the moving point lights.

One of the dots in the yellow-bordered PLD briefly changes color to either red or green and participants had to indicate the number of dots (0-1-2-3) that changed into the same color in the blue-bordered PLD (2 in this example).

## Supplementary References

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