



Multidimensional Approaches in the Study of Autistic Traits using Behavioral and Imaging Data

Angeline Mihailov, Cathy Philippe, Antoine Grigis, Vincent Guillemot, Charles Laidi, Camille Piguet, Hervé Abdi, Josselin Houenou, Vincent Frouin

► To cite this version:

Angeline Mihailov, Cathy Philippe, Antoine Grigis, Vincent Guillemot, Charles Laidi, et al.. Multidimensional Approaches in the Study of Autistic Traits using Behavioral and Imaging Data. Organization of Human Brain Mapping, Jun 2019, Rome, Italy. cea-02289422

HAL Id: cea-02289422

<https://cea.hal.science/cea-02289422>

Submitted on 16 Sep 2019

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Multidimensional Approaches in the Study of Autistic Traits using Behavioral and Imaging Data

Angeline Mihailov¹, Cathy Philippe¹, Antoine Grigis¹, Vincent Guillemot⁵, Charles Laidi^{1,2}, Camille Piguet^{1,3}, Hervé Abdi⁴, Josselin Houenou^{1,2}, Vincent Frouin¹

¹Neurospin CEA, Saclay, France; ²INSERM, U955, Translational Psychiatry Team, 94000, Créteil, France; ³University of Geneva, Geneva, Switzerland; ⁴University of Texas at Dallas, Dallas, U.S.A; ⁵Institut Pasteur, Paris, France



Introduction

- Autism spectrum disorder (ASD) is a complex array of neurodevelopmental conditions, typically characterized by social interaction and communication impairments, and restricted and repetitive behaviors¹.
- Patients exhibit widespread heterogeneity in behavior, biological phenotypes, and genetics.
- Scientific literature has reported gross neuroanatomical inconsistencies, possibly due to classically adopted case-control approaches lumping together these heterogeneities.
- We propose a gradual shift toward experimental designs focused on subtyping ASD before further case-control investigations.
- Objective:** Uncover ASD cortical phenotypes after subgrouping autistic traits by A) age, and B) behavioral phenotypes.

Results

Part 1: Score Distribution

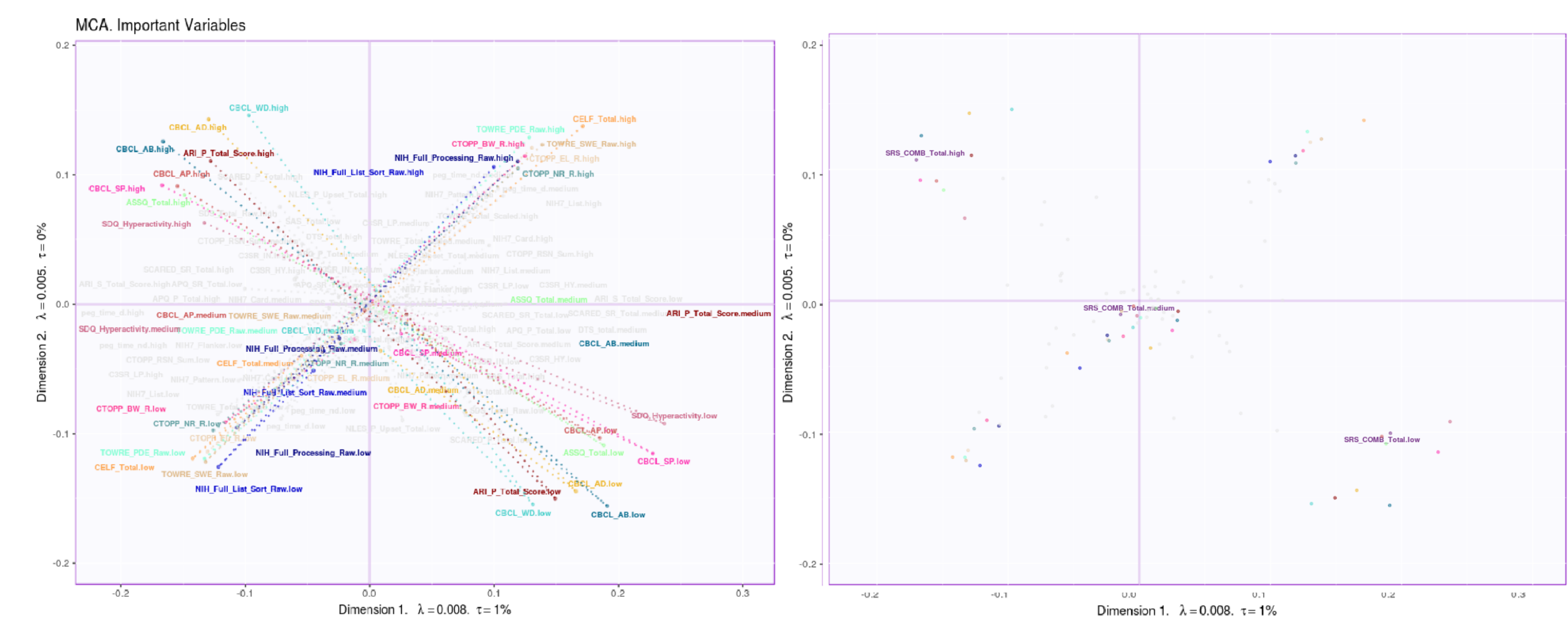


Figure 1: MCA plot. Correlation between several behavioral and cognitive scores (left). To better interpret correlation with SRS, score labels removed and only SRS projected onto plot (right). Showed SRS closely correlates with scores representing aggression, hyperactivity, attention deficits, depression, reactivity, and anxiety.

Part 2: Cortical Structures in Children and Adults

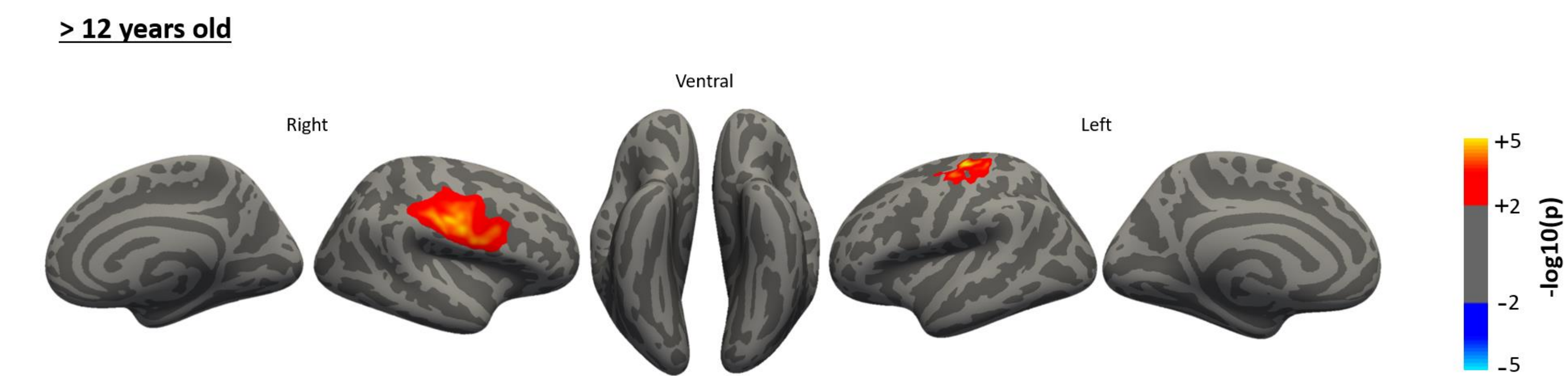


Figure 2: Age Effect in Cortical Structure. Comparing high vs. low autistic traits in adults yielded bilateral increases in gyrification in precentral and frontal regions of right hemisphere ($p < 0.01$), and in precentral region of left hemisphere ($p < 0.01$). Same contrast run in children (below 12 years old) with no results.

Part 3: Cortical Comparisons in Behavioral Subgroups

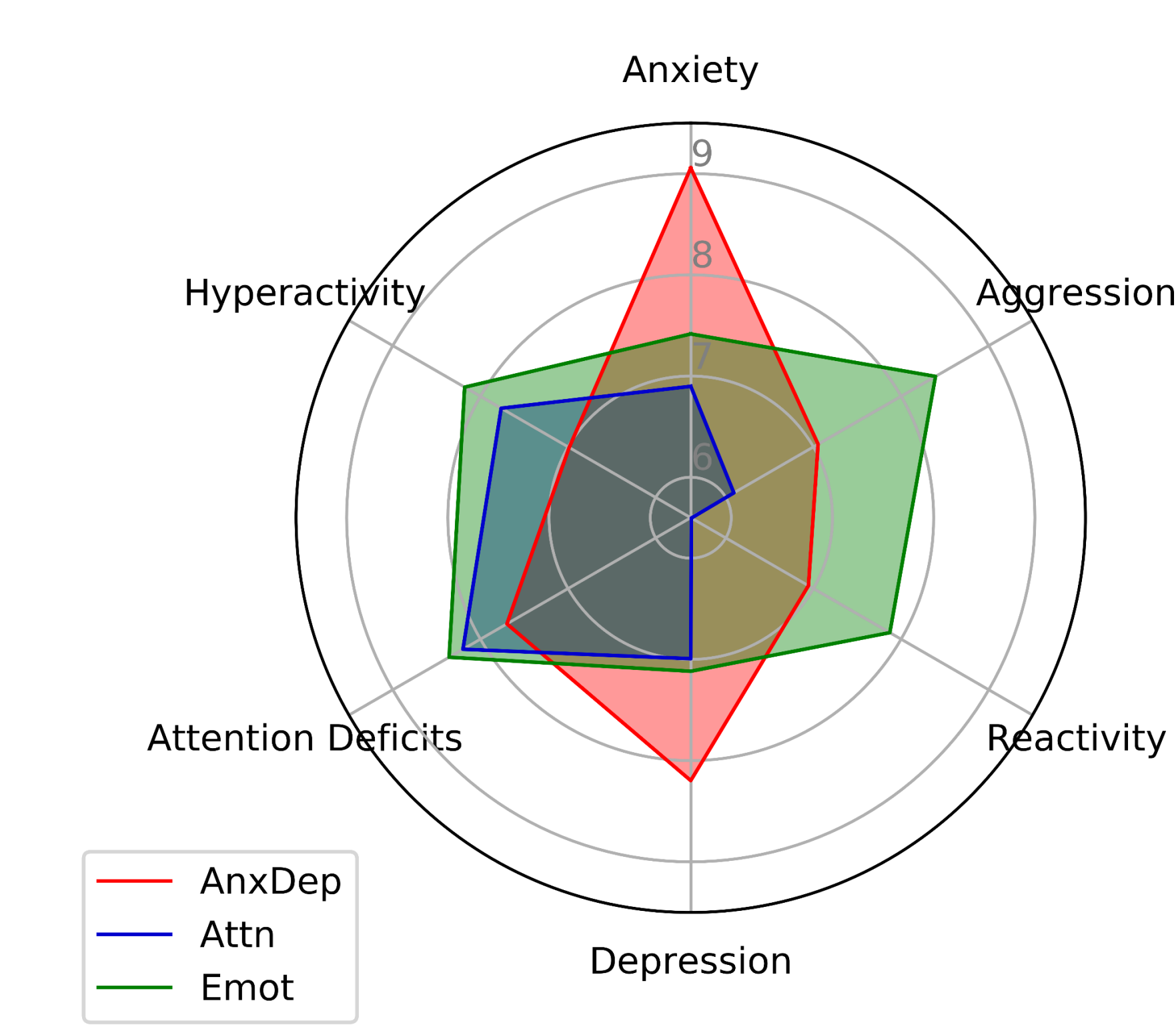


Figure 3: Radar Plot of High Autistic Traits Subgroups. Clustering analysis yielded 9 subgroups varying in behavioral composition. From these, 3 exhibited high SRS. First subgroup (AnxDep) exhibited high levels of anxiety and depression, second (Attn) showed ADHD-like tendencies, and third (Emot) had ADHD-like tendencies with strong emotional dysregulation (high aggression and reactivity levels).

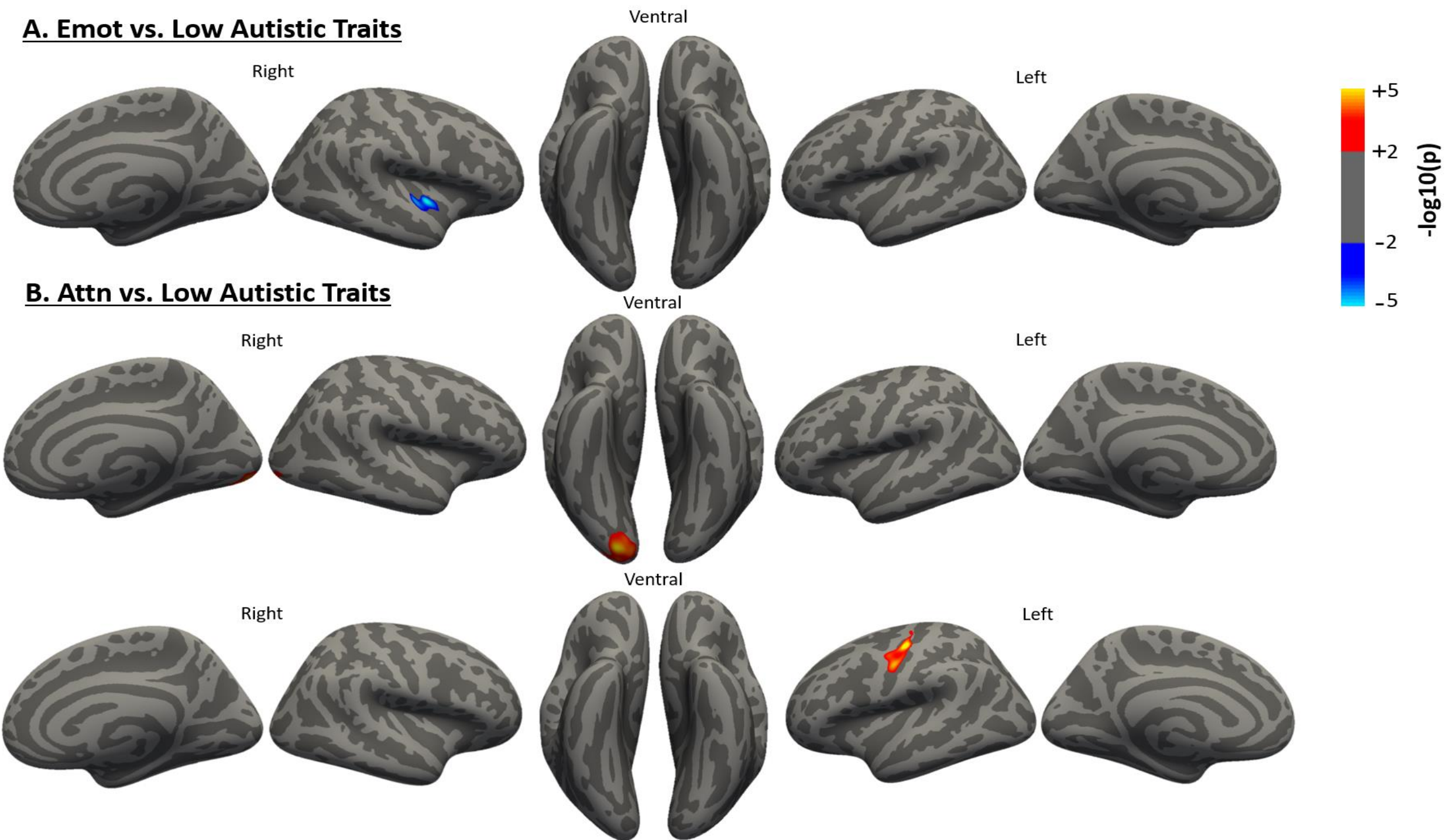


Figure 4: Comparing Surface Features Between each Subgroup and Clinical Controls. A) Comparing Emot subgroup against control group yielded decreases in cortical thickness in right insula ($p < 0.005$). B) Comparisons between Attn subgroup and controls showed increases in gyrification in right lateraloccipital ($p < 0.005$), and in surface area in left precentral region ($p < 0.005$). AnxDep showed no results.

Conclusions

- Wide range of data in the HBN cohort allowed to observe autistic traits correlation to several behaviors by means of MCA analysis (**Part 1**)(Fig. 1).
- Could also finely investigate structural differences in 2 conditions: high vs. low autistic traits in children and in adults (**Part 2**), and differences between behaviorally distinct subgroups and controls (**Part 3**).
- Presence of surface structure signatures in adults, but not in children (Fig. 2).
- Showed that behavioral traits distribute differently thereby isolating autistic traits subgroups (Fig. 3). Affected brain regions in each subgroup are associated to functions spanning ASD^{7,8,9} (Fig. 4).
- Perspectives:** To emphasize the importance of ASD stratification in the search of biological phenotypes. We demonstrated that though subtypes (age, behavior, etc.) show cortical signatures, **combining them into one collective and heterogeneous autistic traits group does not reveal structural brain differences.**

Methods and Materials

Cohort

- Used the Healthy Brain Network (HBN) cohort² comprised of children and youth that are either diagnosed or at risk for psychiatric illnesses.

- Contains wide variety of clinical scores, neuroimaging data, and genetics.

- Age range: 5-21 years old, n = 1753, M:F ratio = 1111:642

Part 1: Score Distribution

- Conducted a Multiple Correspondence Analysis³ (MCA) to determine variance of the Social Responsiveness Scale⁴ (SRS) among behavioral scores.

Part 2: Cortical Structure in Children and Adults

- Intersection between high and low SRS groups, QC images, IQ>70, yielded n= 319 (age 5-18; 58% males).

- First compared participants with high SRS to those with low SRS, then further divided into two age groups: children (below 12; n=195, 61% males) and adults (above 12; n=120, 55% males) and compared high vs. low SRS again within each age group.

- Scans quality checked manually and with euler metric⁵.

- FreeSurfer pipeline⁶ and vertex-wise analysis to look at cortical thickness, gyrification, and surface area by running a GLM at each vertex. Covariates considered: age, gender, IQ, and site.

Part 3: Cortical Comparisons in Behavioral Subgroups

- 1092 subjects (aged 5-18, m=11.1 | M:F = 681:411) based on score availabilities in **social impairment, anxiety, reactivity, hyperactivity, aggression, attention deficits and depression.**

- Conducted k-means clustering analysis on behavioral scores to find high autistic traits subgroups based on **high SRS**. BIC method suggested a k=9 optimal cluster level.

- 549 subjects had good quality T1 scans.

- First, ran cortical morphology comparison between all subgroups combined (one heterogeneous high autistic traits group) and controls. Second, compared each autistic trait subgroup to controls.

- FreeSurfer pipeline⁶ and vertex-wise analysis to look at cortical thickness, gyrification, and surface area by running a GLM at each vertex. Covariates considered: age, gender, IQ, and site.

References

- American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders – 5 (5th edn), American Psychiatric Association (2013)
- http://hbn-1000.projects.cimr.org/hbn/cimr_healthy_brain_network/sharing_phenotype.html
- Abdi H & Bera M, (in Press), ‘Correspondence Analysis’, Alhajj and J. Rokne (Eds.), Encyclopedia of Social Networks and Mining (2nd Edition), New York: Springer Verlag
- Constantino JN, et al., (2003), ‘Validation of a Brief Quantitative Measure of Autistic Traits: Comparison of the Social Responsiveness Scale with the Autism Diagnostic Interview Revised’. J. Autism Dev. Disord. 33:427-433
- Rosen AFG, et al., (2018), ‘Quantitative Assessment of Structural Image Quality’. Neuroimage 169:407-418
- Dale AM, Fischl B, Sereno MI (1990), ‘Cortical Surface Analysis. I. Segmentation and Surface Reconstruction’. Neuroimage 9:179-194
- Jung M, et al., (2019), ‘Decreased Structural Connectivity and Resting-State Brain Activity in the Lateraloccipital Cortex is Associated with Social Communication Deficits in Boys with Autism Spectrum Disorder’. Neuroimage 190:205-212
- Nebel MB, et al., (2014), ‘Disruption of Functional Organization within the Primary Motor Cortex in Children with Autism’. Hum. Brain. Mapp. 35:567-580
- Silani et al., (2008), ‘Levels of Emotional Awareness in Autism: an fMRI Study’. Soc. Neurosci. 3(2):97-112