



Sensory hyper-responsivity mediates intrinsic brain connectivity in Autism Spectrum Condition (ASC) and their parents



Yang-Teng Fan^{1,2,3}, Ming-Chu Chung⁴, Ling Chu⁵, Yawei Cheng⁵, Chung-Hsin Chiang⁶, Chih-Mao Huang^{1,2,3}, Chien-Te Wu^{4,7}, Ovid J. L. Tzeng^{1,2,3,8,9}

1. Department of Biological Science and Technology, National Chiao Tung University, Taiwan; 2. Center for Intelligent Drug Systems and Smart Bio-devices (IDS²B), National Chiao Tung University, Taiwan; 3. Cognitive Neuroscience Laboratory, Institute of Linguistics, Academia Sinica, Taiwan; 4. School of Occupational Therapy, National Taiwan University, Taiwan; 5. Institute of Neuroscience and Brain Research Center, National Yang-Ming University, Taiwan; 6. Department of Psychology and Research Center for Mind, Brain and Learning, National Chengchi University, Taiwan; 7. Department of Psychiatry, National Taiwan University Hospital, Taiwan; 8. College of Humanities and Social Sciences, Taipei Medical University, Taiwan; 9. Department of Educational Psychology and Counseling, National Taiwan Normal University, Taiwan

Background

1. Aberrant sensory responsivity has been reported since early descriptions of ASC, however, historically were thought to represent secondary consequences of social-communication differences (Robertson and Baron-Cohen, 2017).
2. ASC is a highly-heritable neurodevelopmental condition; however, the concordance in sensory features between parent and child dyads within ASC families is mostly unknown (Donaldson et al., 2017 & Glod et al., 2017 & Uljarević et al., 2016; Uljarević et al., 2014).
3. Such endophenotype-based research can help disentangle the nature of sensory features in individuals with ASC and have implications for early detection and potential future interventions for ASC.

Research purposes

1. To investigate the group differences (ASC vs. control (CON) and parents of ASC (P-ASC) vs. parents of control (P-CON)) in performance and neural activity (resting-state fMRI and task-induced fMRI).
2. To investigate the similarities and differences in neurobehavioral patterns of sensory responsiveness in dyads of ASC and their unaffected biological parents.
3. To investigate the roles of sensory responsiveness in intrinsic brain connectivity within ASC families.

Methods

1. We recruited 30 ASD and 23 matched controls (CON), and 45 their unaffected parents (27 P-ASD and 18 P-TDC).
2. Autistic symptoms: Autism Diagnostic Observation Schedule (ADOS) and Autism-Spectrum Quotient (AQ)
3. Sensory responsivity: (1) Questionnaires-based sensory evaluations (the Adolescent/Adult Sensory Profile (AASP) and the Sensory Over-Responsivity Inventory (SORI)); (2) Lab- and neural-based sensory measures (Figure 1)

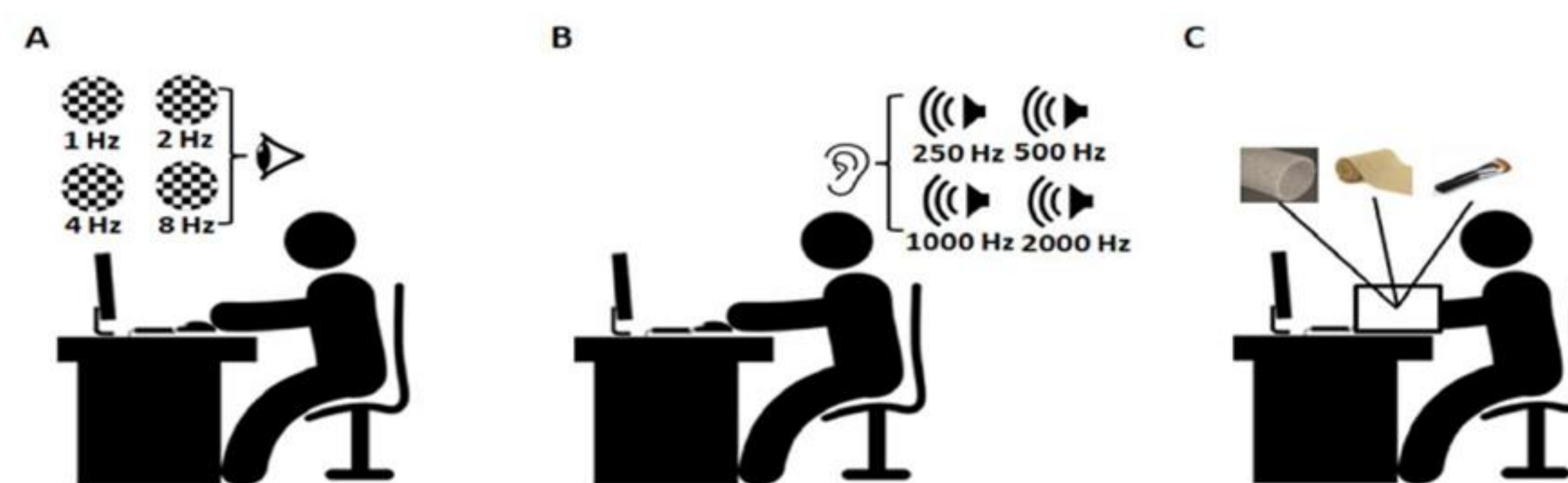


Figure 1: Illustration of the current lab-based sensory tasks.

Results

1. Behaviorally, ASC and the P-ASC exhibited hyper-responsiveness to the sensory stimuli than the CON and the P-CON, respectively.
2. Similar levels of agreement were only observed within ASC parent-child dyads on most of the sensory domain scores (visual, activity level, and tactile subscale scores, and total scores of the AASP, as well as the SORI total scores).
3. Correlation analyses showed that the total AASP score was positively correlated with both the ADOS and AQ scores in ASC group (Figure 2).
4. ASC relative to the CON was associated with greater activation within the primary sensory cortices during the sensory tasks, and furthermore our findings indicate that the response within these sensory cortices itself also differs significantly between the P-ASC and the P-CON individuals (Figure 3).
5. The conjunction of group-difference maps showed that greater activation was evident when comparing ASC and P-ASC with CON and P-CON, respectively (ASC > CON ∩ P-ASC > P-CON), at these primary sensory cortices.

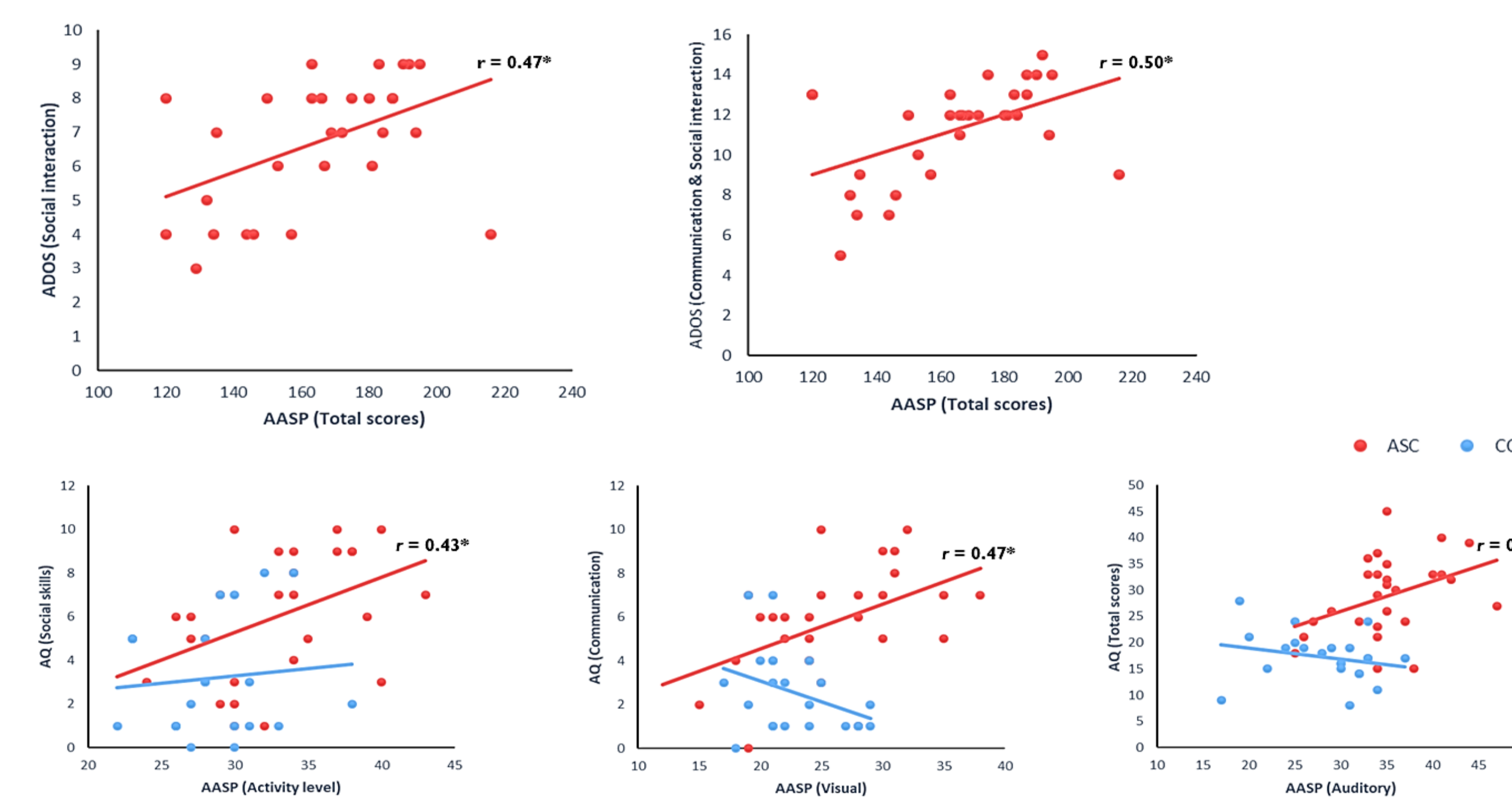


Figure 2: Correlations between sensory responsiveness and autistic symptoms.

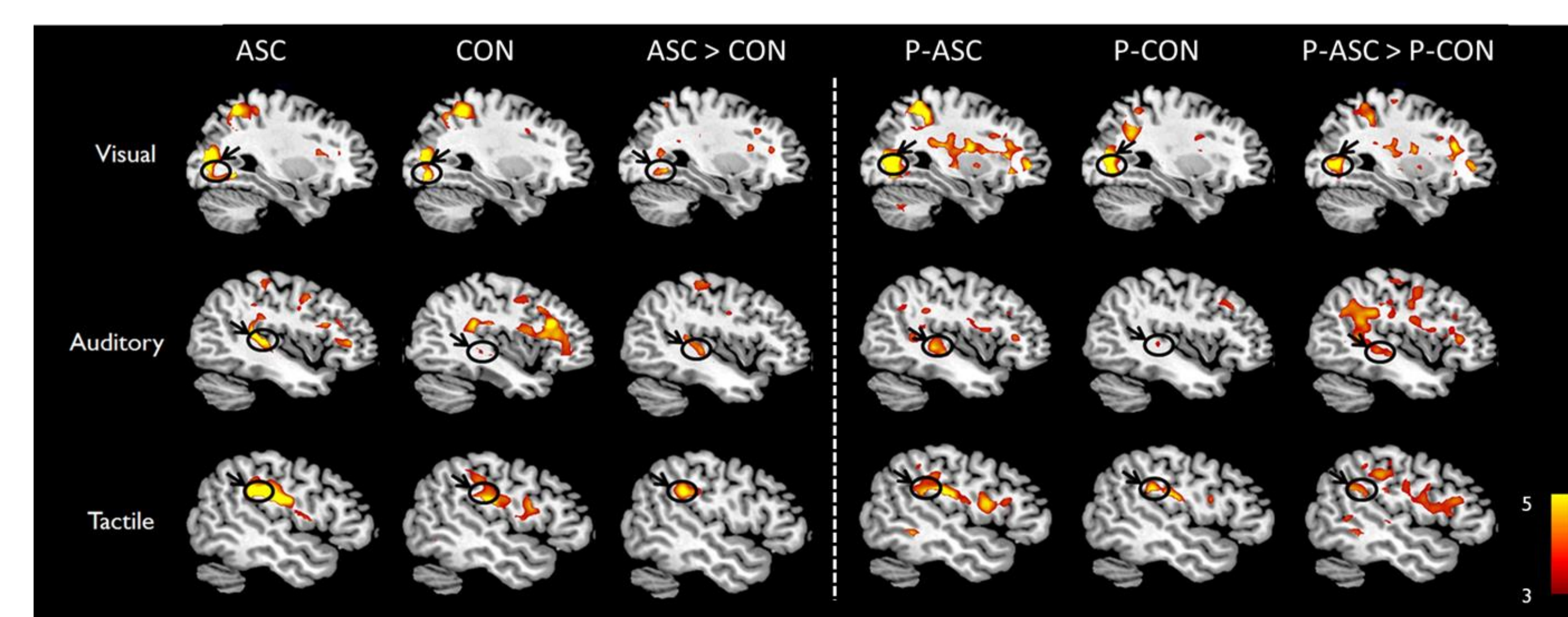


Figure 3: Hemodynamic responses to the sensory stimuli (visual, auditory, and tactile) within and between groups.

Results (Cont'd)

6. For the resting-state fMRI data, mediation analysis revealed that sensory hyper-responsiveness specific to ASC and P-ASC significantly mediated the association between occipital-hippocampus connectivity and autistic symptoms (Figure 4).

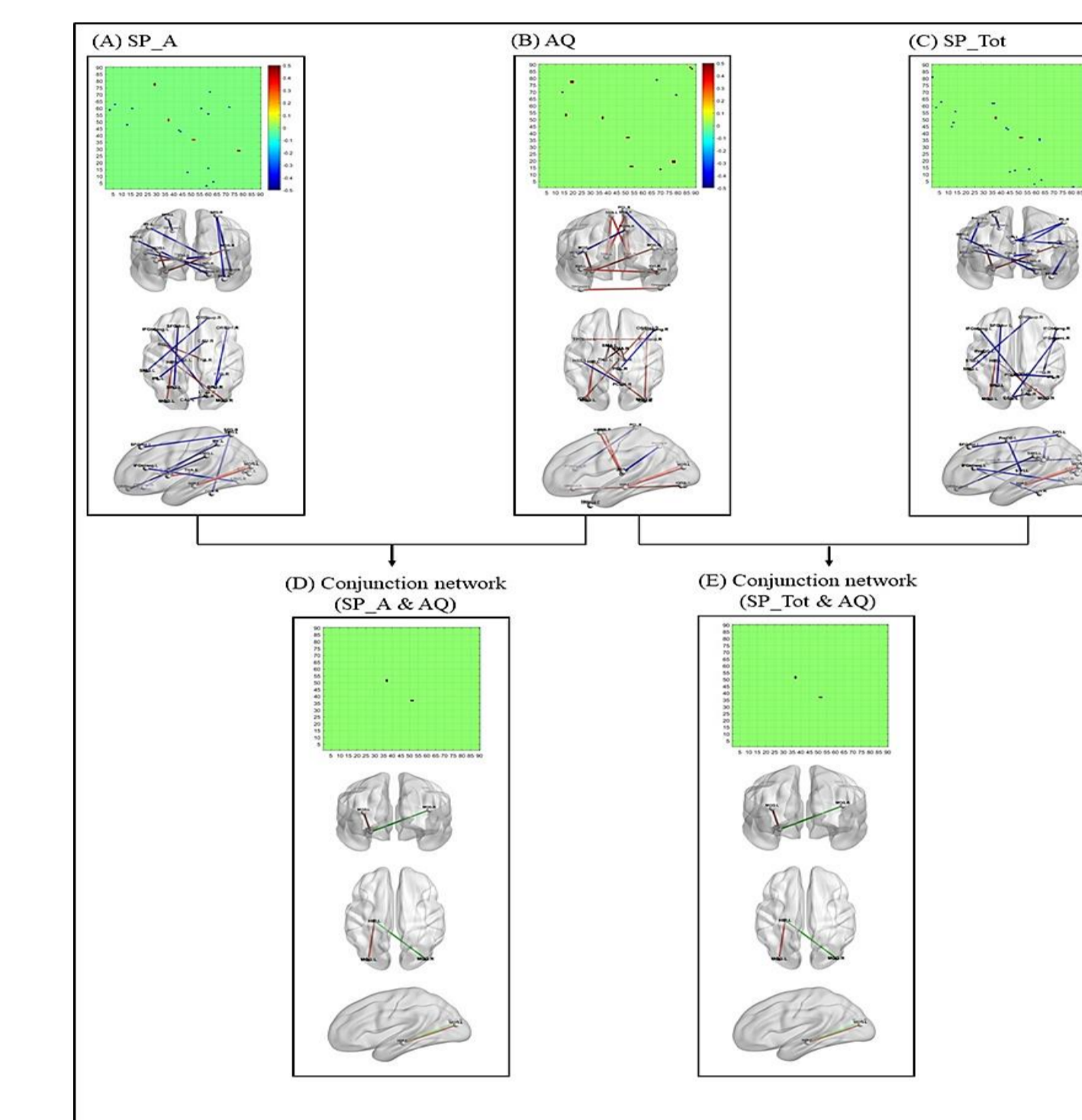


Figure 4. The column of (A), (B), (C) showed the matrix and the brain map of behavioral connectivity networks of auditory subscales of the AASP (SP_A), AQ scores, total scores of the AASP (SP_Tot) when pooling the data of ASC and P-ASC group together. The red and blue voxels/connections represented the positive and negative correlation, respectively. The column of (D), (E) showed the common networks between AQ, SP_A and SP_Tot. The red connections in the brain map of (D), (E) represented the connection (occipital-hippocampus) was a mediator in the relationship between them.

Conclusions

These results support the idea that ASC and their unaffected parents share similar sensory features in both behavioral performance and neural indices, and such sensory hyper-responsiveness aberrantly mediates the association between intrinsic brain connectivity and autistic traits. The findings have significant implications for early detection of ASC and, ultimately, to targeted ASC interventions.

References

1. Donaldson, C. K., Stauder, J. E., & Donkers, F. C. (2017). Increased sensory processing atypicalities in parents of multiplex ASD families versus typically developing and simplex ASD families. *J Autism Dev Disord*, 47, 535-548.
2. Glod, M., Riby, D. M., Honey, E., & Rodgers, J. (2017). Sensory atypicalities in dyads of children with autism spectrum disorder (ASD) and their parents. *Autism Res*, 10, 531-538.
3. Uljarević, M., Carrington, S., & Leekam, S. (2016). Brief report: effects of sensory sensitivity and intolerance of uncertainty on anxiety in mothers of children with autism spectrum disorder. *J Autism Dev Disord*, 46, 315-319.
4. Robertson, C. E., & Baron-Cohen, S. (2017). Sensory perception in autism. *Nat Rev Neurosci*, 18, 671.
5. Uljarević, M., Prior, M. R., & Leekam, S. R. (2014). First evidence of sensory atypicality in mothers of children with autism spectrum disorder (ASD). *Mol Autism*, 5, 26.

Acknowledgments

This study was supported by the Ministry of Science and Technology (MOST 106-2410-H-009-059-MY2; 108-2410-H-009-020-MY3), and supported by the Center for Intelligent Drug Systems and Smart Bio-devices (IDS²B) from The Featured Areas Research Center Program within the framework of the Higher Education Sprout Project by the Ministry of Education (MOE) in Taiwan.

Email: Yang-Teng Fan (yangtengfan@nctu.edu.tw)