Ruprecht-Karls-Universität Heidelberg
Medizinische Fakultät Mannheim
Dissertations-Kurzfassung

Cross-brain neural synchronization examined by fMRI-hyperscanning as a biomarker of human social interaction

Autorin: Edda Bilek
Institut / Klinik: Zentralinstitut für Seelische Gesundheit Mannheim (ZI)
Doktorvater: Prof. Dr. A. Meyer-Lindenberg

Social interactions are important for human health and essential human skills and basic abilities such as language are acquired only through interaction with others. Neuroimaging studies have discovered a brain-wide network functionally specialized in the processing of social information, as well as the planning, execution, and monitoring of social behavior; i.e., the social brain. The right temporoparietal junction has been highlighted as a central hub of this network, holding brain-wide connections and integrating socially meaningful data for successful interaction with the environment. Research has struggled to investigate the biological mechanisms underlying social behavior due to prior methodological constraints, especially missing procedures to simultaneously acquire multi-subject data during true social contact and appropriate analyses for the study of multi-brain processes. Considering the varying subject behavior and cognition for real versus computerized task partners and the differential behavioral and neural outcome measures derived from two-person studies, appropriate neuroimaging approaches were greatly needed. However, study designing is challenging due to the complex and unpredictable social processes and requires the consideration of the subjects' engagement in the task (passive observation to interaction), the reciprocity of the interaction (single one-way to dynamic), and ecologic validity (artificial task to real-life interaction).
We have advanced pioneering two-person neuroscience approaches, termed *hyperscanning*, to a study environment for the simultaneous functional magnetic resonance imaging of two subjects during true interaction. Two identical scan labs with synchronized hardware allowed for real-time data transmission including a continuous live video stream of the partner. Our first study describes the development of the scan environment and a generalizable analysis routine for hyperscanning data based on two independent samples of healthy subject dyads; 13 pairs of both sexes, and 25 female pairs for replication. Subjects completed a Joint Attention task, representing a very basic, cooperative, and early learned interaction type in humans. Here, subjects are required to repeatedly interact via eye-gaze and hereby transfer information in order to successfully complete a task trial. Conventional analyses were abandoned and a tailored routine for two-person data handling was developed, remaining largely data-driven and with minimal a-priori assumptions on derived parameters. The analysis included blind source separation of neuroimaging data (group independent component analysis), identification of interaction-related brain regions (components), determination of a measure of cross-brain coherence between these areas (i.e., neural coupling), and provided permutation-based comparisons that demonstrated uniqueness of neural coupling to true interaction (comparison to non-interacting permutated pairs). This revealed information flow between the sender's and receiver's brain systems, temporally and spatially highly specific to true interaction and right temporoparietal junction function. After replication in the second sample, the procedure was validated by demonstrating a relation of the cross-brain parameter to a key real-world measure of social expertise (the complexity of the social network). While speculative, this measure may represent the mechanism underlying successful social contact and we expect neural coupling to prove as highly valuable for a biology-based understanding of the formation of social bonds and relationship-defining variables such as interpersonal sympathy. In the second study, the approach was applied in the context of Borderline Personality Disorder where disturbed interpersonal functioning is a core symptom, manifesting in difficulties in cooperation and trust, the maintenance of relationships, and continuous feelings of exclusion. We investigated 60 female subject pairs each including a healthy subject and either a patient currently fulfilling diagnostic criteria for Borderline Personality Disorder (N=23), a patient in remission (N=17), or a second healthy subject (N=20). All data were analyzed as described above for study 1. Neural coupling was found to be sensitive to disorder state: while healthy pairs showed

synchronized neural responses in the right temporoparietal junction, subject pairs including a current patient exhibited significantly lower neural coupling, with the group mean just above permutation-based levels. Surprisingly, neural coupling in pairs involving a patient in remission indicated normalization of the measure. Group comparisons showed no differences to healthy pairs, but significantly higher group means compared to pairs involving patients with a current diagnosis. The neural coupling in patients was furthermore associated with a widely used measure of risk for the disorder, the quantification of childhood adverse events. Post-hoc tests investigating brain-wide structural and functional group differences failed to provide a plausible cause for above differences, supporting neural coupling as a novel state-dependent neuroimaging marker of human social interaction. These results challenge the current classification of Borderline diagnosis. By definition, personality disorders (and thus the underlying neurobiological mechanisms) remain largely stable across the lifespan. Conversely, we find restored neurobiology to accompany remission, suggesting a requirement to adjust diagnosis definition.

It is noteworthy that our approach identified a cross-brain measure of interaction based on a conservative analysis routine, and a number of other measures may be similarly fit to investigate cross-brain interactions (e.g., correlation, wavelet transformation, granger causality). In addition, we present data from cooperative interaction only and confirmation of its relevance for a variety of interaction types such as competition or trust is pending, likewise the investigation in multiple psychiatric conditions of impaired social processes. Despite, the sensitivity of neural coupling to disorder states suggest the usage in clinical care for individualized therapy, for the modulation of temporoparietal junction function, and/or for the improvement of the patient-therapist relationship.

Summarizing, our findings support a central role of human-specific cortical areas in the dynamics of dyadic interactions and provide an approach for the non-invasive examination of the neural basis of healthy and disturbed human social behavior.