



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

Eye tracking as a diagnostic tool in autism spectrum disorder

Autor: Nico Müller
Institut / Klinik: Zentralinstitut für Seelische Gesundheit Mannheim (ZI)
Doktorvater: Prof. Dr. med. Dr. rer. nat. T. Banaschewski

Social functioning deficits in autism spectrum disorder (ASD) were explained by aberrant social cognition and empathy. It is largely unknown how deviating neurocognitive processes like theory of mind or emotion recognition contribute to aberrant social cognition and empathy, although their developmental effects likely moderate later symptom outcome. Patterns of neurocognitive processes might also explain distinctive profiles of social cognition and empathy, which would aid in a subgrouping of ASD and conduct disorder (CD). Further subgrouping by endophenotypes would lead to valid diagnoses boosting research in pathogenic mechanisms and efficient interventions. We proposed a theoretical framework with eye tracking as linking method to relate aberrant social cognition and empathy with neurocognitive processes and potential endophenotypes. Eye tracking is largely tolerated even by younger clinical groups as it requires no intrusive elements.

However, adequate tests of social cognition and empathy in adolescence were lacking to investigate our theoretical framework. Recent findings favored naturalistic assessments as questionnaire measures were of insufficient external validity. First, the current dissertation adapted naturalistic measures of social cognition and empathy for adolescent age ranges (Movie for the Assessment of Social Cognition – Revised = MASC-R, Multifaceted Empathy Test – Junior Revised = MET-JR) with a thorough assessment of psychometric quality. These rather ecologically-valid measures exhibited good validity and sufficient reliability. They were superior or of equal power in discriminating clinical groups from controls compared to conventional questionnaires. Further utility was provided by clinical cut-offs of cognitive and emotional empathy.

Second, as key evidence of our theoretical framework, we identified fixation duration on eye regions as substantial predictor of social-cognition performance, which was moderated by ASD diagnosis. Furthermore, we retrieved reduced pupil dilation in the ASD group during (but not before) the social-cognition test. Reduced fixation duration was an indicator of derailed social attention, while diminished pupil dilation reflected diminished physiological arousal, related to a hypoactivation of the nucleus coeruleus that controls the neuromodulation of norepinephrine and triggers attention towards salient environmental stimuli. Both findings delivered evidence for the developmental theory of low social motivation in ASD and indicated potential endophenotypes. These findings will be further explored in a subsequent study by relating fMRI data of locus-coeruleus activity to pupil-dilation data (EU-AIMS LEAP).

Third, we replicated divergent empathy profiles in ASD and CD with unaffected emotional empathy in ASD and reduced emotional empathy in CD, but extended previous findings by substantially reduced cognitive empathy in ASD and slightly reduced cognitive empathy in CD. In addition, clinical empathy profiles were related to broader and disjoint empathy continua in a larger community sample. Thus, empathic deficits were not specific to both disorders but reflected behavioral-trait variation within the normal population even reaching clinical cutoffs. Functional neural networks of empathy were discussed as endophenotype, which is further investigated in a subsequent study of moderating effects of oxytocin on MET-JR empathy (ASD-NET).

Fourth, additional eye-tracking measures as potential endophenotypes were explored in a literature review arguing for the application of machine learning and temporal data analysis to utilize the richness of eye-tracking data. This will be applied in future analyses to identify oculomotor metrics that could contribute to a valid subgrouping of the autism spectrum (EU-AIMS LEAP).

As a limitation, we did not replicate the multidimensionality of social cognition and did not retrieve sufficient fits of empathy for proposed structure equations, which suggested that we did not assess all required processes to reflect the multifacetedness of social cognition and empathy. But, our empirical data indicated that emotion recognition and cognitive empathy are congruent processes that could be subsumed under social cognition, while condensing empathy to emotional empathy. This would

reduce the conceptual overlap of social cognition and empathy, which could aid in reducing conflicting findings in future research.

Overall, we refined the naturalistic assessment of social cognition and empathy in adolescence. Our empirical data delivered evidence that eye tracking is a promising method to relate distinctive neurocognitive processes to associated behavioral assessments of broader psychological concepts. Our approach might assist in endophenotype identification by extending neurocognitive processes to associated neural networks and pathogenic mechanisms like neurochemical imbalances reflected in eye-tracking data. Small sample sizes limit the representativeness of our findings, but encouraged us that eyes are sufficient 'windows to the souls' to refine and replicate our hypotheses in ongoing research projects by larger and better samples.