

# A Multimodal Approach toward the Biological Categorization of Autism

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligens försvaras i Arvid Carlsson-salen, Medicinaregatan 3, Göteborg, den 9e december 2022, klockan 13:00.

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## Avhandlingen baseras på följande delarbeten

- I. **Sarovic D.** A framework for neurodevelopmental disorders: Operationalization of a pathogenetic triad. (Preprint) PsyArXiv 2019. Doi:10.31234/osf.io/mbeqh
- II. **Sarovic D**, Hadjikhani N, Schneiderman JF, Lundström S, Gillberg C. Autism classified by magnetic resonance imaging: A pilot study of a potential diagnostic tool. International Journal of Methods in Psychiatric Research, 2020; e1846. Doi:10.1002/mpr.1846
- III. **Sarovic D**, Hadjikhani N, Schneiderman JF, Lundström S, Riaz B, Orekhova E, Khan S, Gillberg C. Pareidolia as a probe for early and late face processing components in autism: A magnetoencephalographic study. (Under review)
- IV. Orekhova, EV, Stroganova, TA, Schneiderman, JF, Lundström, S, Riaz, B, **Sarovic, D**, Sysoeva, OV, Brant, G, Gillberg, C, Hadjikhani, N. Neural gain control measured through cortical gamma oscillations is associated with sensory sensitivity. Human Brain Mapping 2018; 1–11. Doi:10.1002/hbm.24469

**SAHLGRENSKA AKADEMIN**  
**INSTITUTIONEN FÖR NEUROVETENSKAP OCH**  
**FYSIOLOGI**



# A Multimodal Approach toward the Biological Categorization of Autism

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## Abstract

Autism Spectrum Disorder (ASD) is an umbrella term for a group of neurodevelopmental disorders (NDD) which are behaviorally defined by the presence of difficulties with social communication, and behavioral rigidity and repetitiveness, including sensory disturbances. The overarching aim of this thesis was to improve the categorization of autism through the development of a theoretical framework and a multivariable classification method, and identify biomarkers which together would aid in the understanding of autism and be used in ASD classification.

*Paper I* presents a theoretical framework for the pathogenesis of ASD and other NDDs. The framework conceptualizes and operationalizes a three-factor model: (1) a *disorder personality type* that is specific for each NDD diagnostic category, but extends across the threshold for diagnosis and is not maladaptive in and of itself; (2) *cognitive capacity* as the ability of the individual to compensate for issues that may arise from of a “pronounced” personality type; (3) *neuropathological burden* which is conceptualized as the inhibition of neural and cognitive development resulting from the presence of neurodevelopmental risk factors. It is concluded that such a framework may contribute to an improved understanding of pathogenetic mechanisms underlying NDDs, including ASD.

Papers II-IV are based on a structural and functional brain imaging study of a group of adult males with ASD, and an age- and IQ-matched group of neurotypical controls. *Paper II* is a morphometric study that presents a multivariable classification method which showed up to 79% accuracy for diagnostic status, and outperformed machine learning algorithms on the same dataset. *Paper III* investigated the magnetoencephalographic source space activation in the right fusiform gyrus in response to faces and face-like objects and found only late post-stimulus group differences, potentially relating to differences in top-down cognitive mechanisms. *Paper IV* compared the change in occipital magnetoencephalographic power in the gamma range in response to moving stimuli and showed a relationship with self-reported sensory sensitivity across both the ASD and control groups.

In summary, the thesis presents a theoretical framework that proposes pathogenetic mechanisms for ASD and other NDDs, a simple classification method for multivariable categorization using quantitative data, and biomarkers for face processing and sensory sensitivity. **Keywords:** Autism, Classification, Biomarker, Theoretical Framework, Magnetoencephalography, Magnetic Resonance Imaging, Morphometry