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Neurobiological correlates of Attention-Deficit/Hyperactivity Disorder (ADHD) and impulsivity – a developmental perspective

Autor: Anna Kaiser
Institut / Klinik: Zentralinstitut für Seelische Gesundheit Mannheim (ZI)
Doktorvater: Prof. Dr. D. Brandeis

The current thesis addresses neurobiological characteristics associated with Attention-Deficit/Hyperactivity Disorder and the transdiagnostic symptom dimension of impulsivity. A special focus was set on developmental effects in brain-behavior relationships for a more detailed understanding of the relevance of identified neuromarker-candidates within distinct maturational stages. Further, the current work took into account the highly relevant topic of electroencephalographic data quality as an essential prerequisite for validly translating neurophysiological study results into clinical practice. Due to its ease of administration, its high tolerability, and the rather low costs, electroencephalography was the focus of most of the current work.

Therefore, three meta-analytical or empirical studies were conducted and reviewed within this thesis: first, our meta-analysis on event-related potential-differences between patients with Attention-Deficit/Hyperactivity Disorder (n=1576) and healthy controls (n=1794) in childhood, adolescence, and young adulthood was presented. We identified relevant medium to large effect sizes between patients diagnosed with Attention-Deficit/Hyperactivity Disorder and healthy controls ($-0.32<d<-0.57$), mainly regarding later cognitive event-related potentials (P300, Contingent Negative Variation, and error-related positivity), indicating deficits in higher-order cognitive functioning (study 1). Second, results on electroencephalographic data quality were reported from our ESCAlife trial exploring Attention-Deficit/Hyperactivity Disorder patients in childhood (n=184), adolescent (n=39), and young adult (n=57) age compared to a small sample of healthy controls in school-age (n=25). We were able to show that participant-related characteristics, especially age and symptoms of hyperactivity/impulsivity, affect electroencephalographic data quality subsequently impacting on results obtained from spectral power analyses (study 2). And finally, we introduced our analyses on the large population-based IMAGEN-cohort of healthy adolescents (n=2034) assessed longitudinally into young adulthood (n=1383). We found that measures of different facets of impulsivity are related to brain activity in the pre-supplementary motor area and inferior frontal gyrus during inhibitory control during adolescence and in the ventral striatum during reward anticipation in young adulthood with distinct effects for different age groups. Associations between brain activity and impulsivity change substantially from adolescence to young adulthood, especially due to maturational changes on a neural level (study 3). Across all studies relevant developmental effects were identified.

The studies presented here indicate that a variety of neurobiological characteristics and processes can be related to Attention-Deficit/Hyperactivity Disorder and impulsivity from either a categorical or a dimensional perspective and possibly represent promising biomarker-candidates. However, the current findings are in line with previous literature highlighting that no single biomarker might be sufficient to characterize aspects of healthy as well as deviant, clinically relevant human behavior. Future large-scale longitudinal studies using multidimensional assessment methods are needed to disentangle effects and further prove sensitivity and specificity of already identified neuromarker-candidates, thereby combining categorical and dimensional approaches. Additionally, data quality should be in the focus of future work to ensure a valid translation of neuroscientific study results into clinical practice. Specifically, developmental effects need to be explicitly taken into account. Further, future studies should address the predictive value of the neuromarker-candidates identified and prove their effectiveness as targets of neuromodulation-treatment within a personalized-medicine framework.