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Evaluating self-regulation in adolescents with conduct problems or severe disruptive behavior disorders - possible neural targets for future interventions

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Disruptive behavior is a common phenomenon in human nature and frequently occurs during adolescence. It is associated with conduct problems (CP) in healthy as well as clinical populations. When CP exceed the normal range and disruptive behaviors are severe, Disruptive Behavior Disorder (DBD), including Conduct Disorder (CD) and Oppositional Defiant Disorder (ODD), is often diagnosed. Individuals who fulfill diagnostic criteria of DBD also frequently display a conspicuous pattern of behavior that is characterized by a callous, uncaring and unemotional interpersonal style, including deficits in empathy, emotional affectivity and conscientiousness. These behaviors have been labeled the affective dimension of psychopathy or callous-unemotional traits (CU traits) in research. Overall, evidence-based psychological treatments for DBD (with and without increased CU traits) only reach small to moderate effect sizes and there is currently not enough evidence to support one specific form of treatment over another. To date, real-time functional magnetic resonance imaging (rtfMRI-NF) is increasingly considered as a promising tool for the training of brain self-regulation in order to treat psychiatric conditions. It has already been applied to train self-regulation of compromised inhibitory or emotional brain regions in clinical populations such as adult psychopaths and adolescents diagnosed with ADHD. For the purpose of investigating and evaluating new innovative forms of treatments for adolescents with DBD, this thesis followed a two-way approach. First (study 1), a large dataset of healthy young adolescents (mean age: 14.44 (0.41), range 13.08-15.72 years) with varying level of CP was analyzed with respect to possible neural correlates of frontal control over CP during affective processing of negative facial emotions. Second (study 2), an individualized rtfMRI-NF training aiming at the learning of self-regulation of emotional processing regions (amygdala or insula) and, as a result, at the improvement of both affective processing and clinical impairment, was conducted in adolescent patients (mean age: 14.62 (1.64), range: 12.04-17.99 years) diagnosed with DBD and elevated CU traits (ICU total score >20 in self-rating and/or >24 in parent-rating) over a course of 10 weeks and compared with a clinical TAU group.

In study 1, we observed no significant differences in brain responses to negative facial affect in adolescents with high versus low CP. However, regression analyses along the CP dimension across the groups revealed a significant nonlinear effect: left orbitofrontal cortex (OFC) responses increased with increasing CP up to the clinical range, and, decreased again only for the highest CP range. This increasing left OFC activity found during affective processing in an epidemiological adolescent sample with low to clinically relevant levels of CP might represent frontal control mechanisms preventing the outbreak of disruptive or conduct disorder despite the presence of CP.

In study 2, the NF and the TAU group showed comparable and significant clinical improvement on DBD-related behavioral scales over time, in line with non-inferiority. Within the NF group, successful learning of self-regulation in the target region was found for NF of the amygdala, but not for NF of the insula. Additional exploratory analyses also suggested involvement of prefrontal areas in the learning of self-regulation of emotion processing regions. However, clinical improvement in NF was not specific to the amygdala group. In the emotion matching task, both NF and TAU showed decreased activities after treatment in prefrontal emotion-regulation related areas, potentially indicating higher efficiency of processing affective stimuli after treatment. The results suggest clinical improvement and non-inferiority of rtfMRI-NF training compared to other treatment options for adolescents with diagnosis of DBD, but further studies are needed to clarify underlying mechanisms and cost effectiveness.

As a future perspective, further investigation of the role of structural and functional connections between subcortical and prefrontal areas with respect to the cognitive regulation of affective arousal might be

fruitful for the development of future specific treatment strategies aiming at the improvement of adaptive reactivity, emotion regulation and social behavior. Also, the OFC could form a promising target for further NF approaches aiming at the control of emotions.