Christian Schmahl

My research agenda "Experimental Psychopathology and Psychotherapy - Mechanisms and Treatment of Impaired Emotion Regulation" aims at significantly improving the mechanistic understanding and psychotherapeutic treatment of patients with impaired emotion regulation. For disorders such as borderline personality disorder (BPD), post-traumatic stress disorder (PTSD) or eating disorders, disorder-specific psychotherapies are significantly better than wait-list comparisons, but still on average only every second patient benefits from such an approach, even in combination with pharmacotherapy. One of the main reasons for the non-response to psychotherapy is, on the one hand, our lack of understanding of basic mechanisms of emotion regulation and its relation to social interaction and identity problems, that are not only key to understanding normal and disturbed personality, but also for developing targeted therapies. On the other hand, a further improvement of psychotherapeutic processes can only be achieved in the long term by establishing individualized therapies for each patient based on psychological or biological predictors.

My research in the last two decades has focused on emotion dysregulation, non-suicidal self-injury (NSSI) and dissociation as well as the interaction of neurobiology and psychotherapy in Borderline Personality Disorder (BPD) and Posttraumatic Stress Disorder. I have a broad background in psychiatry, psychotherapy and experimental psychopathology, with specific training and expertise in key research areas such as neuroimaging or pharmacological and psychological modulation of stress- and trauma-related processes. From 2015-2018, I was the spokesperson of a Clinical Research Unit (KFO 256) which comprised eight individual projects on the neurobiology of BPD, where I administered the projects, collaborated with other researchers, and produced several peer-reviewed publications from each project. Since 2018, I am the spokesperson of a Research Training Group (GRK 2350) on the consequences of adverse childhood experiences. Coordinating larger research programs and supervising junior researchers has been my favorite academic occupation throughout the last decade and I have received very positive feedback about my leadership qualities in our department and in the research consortia. I have organized our departments` research activity in six groups, one headed by myself and the others headed by an experienced junior researcher, with postdocs and doctoral researchers in each group. There is very close interaction between these groups (with regular group leader meetings and research conferences) and also between our department´s research and other groups at the CIMH, e.g. in the field of neuroimaging. To reach the above-mentioned goals, my research broadly follow three lines: (1) Neurobiology of trauma-related disorders, (2) Mechanism-based psychotherapy research, (3) Neuromodulation with focus on the amygdala.

1. Neurobiology of trauma-related disorders BPD and PTSD

The aim of this line of research is the elucidation of pathological mechanisms in patients with BPD with a focus on emotion dysregulation and non-suicidal self-injury. This line of research follows an experimental psychopathology approach with phenomenological characterization of behavioral alterations (e.g. NSSI), elucidation of underlying neurobiological mechanisms and development of therapeutic interventions based on these mechanisms. It started with script-driven imagery neuroimaging studies and studies on neural pain processing. The Clinical Research Unit (KFO 256) helped to characterize the dysfunctional processing of emotions and social interactions in BPD and to clarify their neural basis. The projects

focused on deficient sensory integration and its relation to dissociation, dysfunctional processing of emotional stimuli, and NSSI as a form of dysfunctional emotion regulation. Another focus is the function of the amygdala: The amygdala has a central role in stress- and trauma-related psychopathology. In PTSD, threat-related hyperarousal is one of the hallmarks of the disorder and associated with amygdala hyperactivity and prefrontal dysfunction. In PTSD and BPD, we could meta-analytically demonstrate amygdala hyperreactivity to negatively valenced stimuli.

Our training program for MD and PhD candidates, GRK 2350, focuses on the psychosocial and somatic consequences of early traumatic stress (abuse and neglect) and comprises 25 young researchers. The experience of violence in childhood and adolescence, e.g. in the form of physical or sexual abuse, is a massive stressor and has been proven to have long-lasting negative consequences for mental and somatic health. Projects from different areas such as addiction, public health, or obstetrics focus on the elucidation of the mechanisms and the development of trauma-targeted treatments. The close collaboration between the field of mental disorders, psychotherapy and somatic medicine in GRK 2350 enables the strengthening of up-and-coming research talents and the expansion of its scientific focus in the field of stress-related diseases.

2. Mechanism-based psychotherapy research

In patients with trauma-related disorders, particularly in Borderline Personality Disorder (BPD) and PTSD, psychotherapy has so far been more successful than pharmacotherapy in improving emotion regulation in these conditions. Dialectical Behavior Therapy (DBT) has been demonstrated to be among the most efficacious treatments for BPD. We have continuously been developing and disseminating DBT programs for nearly two decades in residential and outpatient setting. Our group evaluated the effects of DBT in adults and adolescents with BPD and developed DBT for PTSD, which showed superiority to Cognitive Processing Therapy in patients with complex PTSD, particularly in a subgroup with comorbid BPD. Besides classical psychotherapy studies, e.g. randomized controlled trials in patients with BPD and PTSD, my research is particularly focusing on the neurobiological correlates and predictors of treatment success. We could demonstrate that amygdala dysfunction was normalized in responders to DBT in two trials in BPD and PTSD. Volumetric and functional alterations in limbic regions were shown to be predictors of psychotherapy success.

3. Neuromodulation with focus on the amygdala

My research in the last decade has been very active in the field of neuromodulation with a focus on the amygdala and amygdala-prefrontal regulation circuits. In this field, we have received numerous grants by federal funding agencies (German Research Foundation) as well as from industry and private foundations. Given the central role of amygdala hyperreactivity in stress- and trauma-related psychopathology, it is of central importance to tailor treatments around this mechanism helping those afflicted with these conditions to improve modulation of amygdala-based neurocircuitry. There is an urgent need for the development of additional therapeutic options for the improvement of emotion regulation in stress- and trauma-related psychopathology. Besides classical psychotherapeutic approaches, more specific, mechanism-based interventions such as neurofeedback are needed. We have developed and tested a four-session fMRI amygdala-NF training,

administered to female patients with BPD and observed down-regulation of amygdala activation and increased functional connectivity between amygdala and prefrontal cortex. While this study demonstrated feasibility and good tolerance by patients who participated in a DBT-based psychotherapy program in parallel, the second study extends previous findings with significant down-regulation of amygdala. After training, patients indicated less feeling of inner tension and negative emotions, as well as lower BPD symptoms and lower hour-to-hour variability in these measures assessed in everyday life with ambulatory assessment. We are currently starting a DFG-funded multicenter trial to test the efficacy of amygdala neurofeedback in patients with BPD, which was funded in the DFG clinical studies program. Since fMRI-based neurofeedback is not easy to disseminate for larger use, we are also testing aymgdala-focused EEG neurofeedback options for adolescents and adults with trauma-related disorders.

Two other approaches focusing on amygdala dysfunction are novel pharmacotherapies targeting amygdala-based emotion dysregulation (in collaboration with the pharmacoceutical industry) and exploring options for amygdala deep-brain stimulation.

Key output:

Ad 1) Neurobiology of trauma-related disorders BPD and PTSD

a. Sicorello M, Herzog J, Wager TD, Ende G, Müller-Engelmann M, Herpertz SC, Bohus M, Schmahl C, Paret C, Niedtfeld I: Affective neural signatures do not distinguish women with emotion dysregulation from healthy controls: A mega-analysis across three task-based fMRI studies. Neuroimage: Reports 1:100019 (2021)

This article from my group, which was published in a special issue on negative findings, investigated whether patients with BPD have neural patterns in response to affective stimulation. In three different samples, however, we could not demonstrate evidence for a specific amygdala-prefrontal neural signature of emotion dysregulation or differences between patients with BPD and/or PTSD compared to healthy controls. Publishing negative findings is of high importance for scientific progress and this article has already received much feedback in the scientific community.

b. Störkel L, Karabatsiakis A, Hepp J, Kolassa IT, Schmahl C, Niedtfeld I: Salivary beta-endorphin in non-suicidal self-injury: an ambulatory assessment study. Neuropsychopharmacology 46(7):1357-1363 (2021)

This article is a good example of our experimental psychopathology approach, where we could demonstrate that NSSI leads to an elevation of beta-endorphins directly after the self-injury, using a novel approach of opioid measurements in saliva in combination with ambulatory assessment.

c. “The long shadow of trauma”. Scientific American, January 2022, 48-55.

This gives an in-depth depiction of BPD for the scientifically interested broader audience, based on a longer stay of a science journalist in our clinical and research units.

d. In 2012, I founded the journal “Borderline Personality Disorder and Emotion Dysregulation” together with Martin Bohus and John Oldham as editors-in-chief. It is a free-access online journal published by SpringerNature. Number of publications and impact of the journal have continuously risen throughout the last ten years. In 2021, there were 556,232 article downloads. It is a great pleasure and an honor to receive, process and publish the latest high-quality research in a broad field of psychopathology, neurobiology and treatment of BPD and related fields such as PTSD, eating disorders, and ADHD.

Ad 2) Mechanism-based psychotherapy research

a. Bohus M, Stoffers-Winterling J, Sharp C, Krause-Utz A, Schmahl C*, Lieb K*: Borderline Personality Disorder. Lancet 398:1528-1540 (2021)

This article gives a state-of-the-art overview of psychopathology and treatment of BPD. It has already been cited 13 times in the first half of 2022. Its predecessor, published 2004 also in Lancet, has been cited 898 times.

b. Bohus M, Kleindienst N, Hahn C, Müller-Engelmann M, Ludäscher P, Steil R, Fydrich T, Kuehner C, Resick PA, Stiglmayr C, Schmahl C, Priebe K: Dialectical Behavior Therapy for PTSD (DBT-PTSD) Compared to Cognitive Processing Therapy (CPT) for Posttraumatic Stress Disorder in Adult Survivors of Childhood Abuse - A Randomized Clinical Trial. JAMA Psychiatry 77:1235-1245 (2020)

After conducting an RCT of the newly developed DBT-PTSD in the residential treatment setting, this publication is an important step n the evaluation of the efficacy of DBT-PTSD, as this RCT showed not only a superiority in comparison to a standard PTSD treatment but also very high effect sizes for the treatment of patients with comorbid BPD and PTSD. Accompanying neuroimaging studies revealed normalization of pathologically high amygdala activity in an emotional stroop paradigm after therapy.

c. In 2021, I published a book “Selbstverletzung” [Self-Injury] together with Christian Stiglmayr in Hogrefe “Blaue Reihe”, which is an important and widely distributed periodical for practitioners in the fields of psychiatry, psychosomatic medicine and psychotherapy. It gives an easy-to-read overview of the psychopathology and treatment of this very frequent aberrant behavior in adolescents and adults.

Ad 3) Neuromodulation with focus on the amygdala

In this field, we have published several methodological, review and conceptual articles in the last years and successfully conducted pilot trials in real-time fMRI and EEG neurofeedback. We will soon start several larger clinical trials in neurofeedback and pharmacotherapy of amygdala-based emotion dysregulation. Key outputs in 2020-2022 were several symposia at international conferences such as European Society for the Study of Personality Disorders (ESSPD), European College of Neuropsychopharmacology (ECNP) and American College of Neuropsychopharmacology (ACNP).