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(a) Narrative academic profile

The focus of our work has been on a mechanism-based approach to mental disorder with an emphasis on the role of learning and memory processes and associated brain plasticity. The initial focus of this work was on memory and learning processes such as operant and classical conditioning as well as psychobiological interventions in chronic pain, but progressed to disorders such as addiction, borderline personality disorder, posttraumatic stress disorder, depression and dysfunctional aging since my arrival at the ZI in 2000, where a broader integrative concept that could involve cooperations across the institute and in Heidelberg was needed.

We have established Collaborative Research Center 636, where I was the spokesperson, with a focus on learning and brain plasticity in psychopathology, which was funded by the German Research Foundation from 2004 to 2016 and involved many research groups in Heidelberg and at the ZI. This mechanistic approach to mental disorder on the basis of core psychobiological constructs such as fear or reward learning predated the National Institutes of Mental Health Research Domain Criteria Initiative with a similar focus. It was also the bases of the EU-funded IMAGEN (Reinforcement-related behaviour in normal brain function and psychopathology) project, where we longitudinally follow 2000 adolescents since 2004 to determine who develops a mental disorder, and assess core neuropsychological and behavioral constructs as well as brain imaging and genetic data. A large number of influential publications have resulted from this ongoing project, where I am still a principal investigator.

Collaborative Research Center 636 was followed by Collaborative Research Center 1158 on brain circuits involved in the chronicity process in pain disorders, which was jointly initiated by Rohini Kuner and me, and which has been funded since 2015 (last funding phase application is in progress). There again, learning and memory processes and related brain plasticity are at the center of the research. Important discoveries in this area were that memory processes and associated brain changes play an important role in the development of chronic musculoskeletal pain as well as phantom limb pain. We have published this work in high impact scientific outlets and have also written review articles in Nature Reviews Neuroscience or Lancet Neurology. Based on this work, novel behavioral treatments such as mirror therapy, sensory discrimination training or virtual-reality based methods were developed. These interventions have also been incorporated in national and international treatment guidelines. For posttraumatic stress disorder and addiction, we discovered the important role of context conditioning and contextual modulation, which are now viewed as core mechanistic constructs in these disorders. Our work on phantom limb pain was also funded by a European Research Council Advanced Grant and cortical reorganization as a major mechanism behind phantom limb pain has made entry in textbooks of pain as well as neuroscience. A Koselleck Award by the German Research Foundation funded interventions based on the concept of improving brain plasticity by sensorimotor training and virtual reality applications. This importance of this work was also acknowledged by two honorary doctorates (Free University Amsterdam, Aalborg University) and this work received numerous prizes such as the Lifetime Achievement Award of the German Psychological Association, the Max Planck Research Prize, the Research Prize of the State of

Baden-Württemberg, the International Myopain Award and the SmithKlineBeecham Research Prize, among others as well as a membership in the National Academy Leopoldina and the Academia Europaea. Our research also contributed to the definition of a third type of pain “nociplastic pain” (in addition to nociceptive pain and neuropathic pain), which refers to pain based on central alterations in the nervous system without structural injury. I was also involved in the latest definition of pain by the International Association for the Study of Pain, where I served and serve in many leadership functions. This also includes editorial functions in journals and the organization of international scientific meetings.

We were also very active in educating researchers and clinicians alike by setting up several graduate programs in the realm of translational neuroscience as well as a training program for psychological psychotherapists (ZPP, Center for Psychological Psychotherapy, located as a core facility at my Institute). A large number of young researchers have completed their dissertation or habilitation in my Institute and many of them have moved on to their own professorships (e.g., Christiane Hermann, Michèle Wessa, Susanne Becker, Frauke Nees, Kati Thieme, Carsten Diener, Patric Meyer, Martin Diers). My group is also responsible for the Medical Psychology curriculum at the Medical Faculty Mannheim of Heidelberg University and we participate in the Graduate School for Social Sciences at the University of Mannheim and the Master in Translational Medicine at the Medical Faculty Mannheim of Heidelberg University. We have established many fruitful collaborations at the ZI, in the Medical Faculty Mannheim, the University of Heidelberg and the University of Mannheim (where I am an adjunct professor) as well as with international cooperation partners, including joint grants in Denmark, France, England and Australia.

My group has contributed to the ZIPP (Center for Innovative Psychiatry and Psychotherapy Research) by participating in the grant proposals for the center, where we led the application for the Virtual Reality Laboratory, were Co-PI on the proposal for the Magnetoencephalography Center and contributed to the Magnetic Resonance Imaging and Positron Emission Tomography applications. We also set up the Brain Stimulation Laboratory and greatly contributed to the EEG and Peripheral Physiology Laboratory at the ZIPP. I served as a PI for the application for the German Center for Mental Health, where I brought in neuropsychological and clinical psychological expertise. This expertise has also been entered in the ZI wide cohort studies that are being conducted.

At the moment our work has a focus on translation with emphasis on mechanistic brain-based interventions building on solid theoretical concepts in psychobiology. We are especially interested in novel interventions in augmented and virtual reality, where we have a new cooperation with Engineering in Darmstadt within the Graduate Program LokoAssist. Virtual Reality applications are also a topic for a cooperation with the Research Laboratory of TSG Hoffenheim on the use of virtual and augmented reality in sports and rehabilitation with s special focus on counteracting immobility and improving memory and attention. This work is also funded by the Hector Foundation. A new ERC grant in this area is in preparation as well as a proposal to the Fresenius-Kröner Foundation. I will retire in 9/2023 but plan to continue research in the position of a senior professor of the University of Heidelberg.

(b) Key output of the years 2020-now (700 words):

1. Andoh, J., Milde, C., Diers, M., Bekrater-Bodmann, R., Trojan, J., Fuchs, X., Becker, S., Desch, S., & Flor, H., (2020). Assessment of cortical reorganization and preserved function in phantom limb pain: a methodological perspective. Scientific Reports, 10, 11504.

   This study shows that methodological differences explain two opposing theories of phantom limb pain.

2. Heinz, A., Kiefer, F., Smolka, M.N., Endrass, T., Beste, C., Beck, A., Liu, S., Genauck, A., Romund, L., Banaschewski, T., Bermpohl ,F., Deserno, L., Dolan, R.J., Durstewitz, D., Ebner-Priemer, U., Flor, H., Hansson, A.C., Heim, C., Hermann, D., Kiebel, S,, Kirsch, P., Kirschbaum, C., Koppe, G., Marxen, M., Meyer-Lindenberg, A., Nagel, W.E., Noori, H.R., Pilhatsch, M., Priller, J., Rietschel, M., Romanczuk-Seiferth, N., Schlagenhauf, F., Sommer, W.H., Stallkamp, J., Ströhle, A., Stock, A.K., Winterer, G., Winter, C., Walter, H., Witt, S., Vollstädt-Klein, S., Rapp, M.A., Tost, H., & Spanagel, R.. (2020). Addiction Research Consortium: Losing and regaining control over drug intake (ReCoDe)-From trajectories to mechanisms and interventions. Addiction Biology, 25:e12866.

   This article outlines the key constructs of a new collaborative research center on addiction, which should greatly move the field forward,

3. Löffler, M., Gamroth, C., Becker, S., & Flor, H., (2020). Chronic Pain as a Neglected Core Symptom in Mitochondrial Diseases. Neurology, 94, 357-359.

   This study was initiated by a patient with mitochondrial disease who is a co-author of the study. He was sure that pain is a key symptom and we indeed found that this is the case. This study should make it into textbooks and treatment guidelines.

4. Makin, T., & Flor, H., (2020) Brain (re)organisation following amputation: implications for phantom limb pain. NeuroImage, 218, 116943.

   This is a theoretical and review paper that should set the stage for further research on this topic.

5. Flor, H., Lautenbacher, S., & Kunz, M. (2021) Neuropsychologie des chronischen Schmerzes [Neuropsychology of Chronic Pain], Fortschritte der Neuropsychologie, Band 22 [Advances in neuropsychology, Vol. 22], Hogrefe Verlag, Göttingen.

   This book was written for neuropsychologists to educate them about characertistics, assessment and treatment of pain.

6. Grasby, K.L., et. al. Alzheimer's Disease Neuroimaging Initiative; CHARGE Consortium; EPIGEN Consortium; IMAGEN Consortium; SYS Consortium; Parkinson's Progression Markers Initiative, Flor, H., Enhancing NeuroImaging Genetics through Meta-Analysis Consortium (ENIGMA)—Genetics working group.(2020). The genetic architecture of the human cerebral cortex. *Science,* 367, 6484.

   This study used a genome-wide association meta-analysis of brain magnetic resonance imaging structural brain data from 51,665 individuals and identified 199 significant loci. Variation in cortical structure was genetically correlated with cognitive function, Parkinson's disease, insomnia, depression, neuroticism, and attention deficit hyperactivity disorder.

7. Kammler-Sucker, K. I., Loffler, A., Kleinbohl, D., & Flor, H. (2021). Exploring Virtual Doppelgangers As Movement Models To Enhance Voluntary Imitation. IEEE

transactions on neural systems and rehabilitation engineering: a publication of the IEEE Engineering in Medicine and Biology Society, 29, 2173–2182.

This is our first publication out of the VR lab und shows the feasibility of avatars for modelling
movement.

8. Löffler, M., Levine, S. M., Usai, K., Desch, S., Kandić, M., Nees, F., & Flor, H. (2022). Corticostriatal circuits in the transition to chronic back pain: The predictive role of reward learning. Cell Reports Medicine, 3, 100677

   This study shows that the connectivity of prefrontal and limbic regions that was shown to predict the development of chronic pain is mediated by reward-related learning processes that explain a large percentage of the transition to chronic pain.

9. Nees, F., Ditzen, B., & Flor, H., (2022). When shared pain is not half the pain: enhanced central nervous system processing and verbal reports of pain in the presence of a solicitous spouse. PAIN, 163(9):e1006-e1012.
   This study showed that the presence of spouse as a discriminative cue in the laboratory augments both pain perception and pain site-specific brain activation in patients with chronic pain, reinforcing again an operant view of pain.

10. Raja, S.N., Carr, D.B:, Cohen, M., Finnerup, N.B., Flor, H., Gibso, S., Keefe, F.J., Mogils, J.S., Ringkamp, M., Sluka, K.A., Song, X.-J., Stevens, B., Sullivan, M.D., Tutelman, P.R., Ushida, T., & Vader, K. (2020). The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. Pain, 161, 1975-1982.
    This is a result of the work of a task force that redefined pain with a large emphasis on psychological variables.