

## Research Area 1

### **Targeting diversity in trajectories of mental and somatic disorders and their interaction across the lifespan**

We have developed new interdisciplinary approaches, including ecological momentary assessments and sensor-based technology to measure the impact of sex/gender, (epi)genetic and early life stress and trauma, as well as environmental, behavioral and social diversity on mental health and its relationship with somatic disorders across the lifespan (Heuser and Lambers, 2003; Heinz et al., 2020; Schiele et al., 2020). We also have focused on the reciprocal interaction between mental and somatic disorders, aiming to leverage a better understanding of the underlying mechanisms to improve both aspects of health (Correll et al., 2017; Gold et al., 2020). We have several large-scale projects on developmental programming of health and disease, identifying biological mechanisms of risk relating to adversity in prenatal, postnatal and childhood periods (Entringer et al., 2011; Heim et al. 2019). Additionally, we have researched trajectories from clinical-high risk states in youth and adults to fully established severe mental health disorders and within individuals with established illness, including substance use disorders, psychotic and mood disorders (Cornblatt et al. 2015; Heinz et al., 2020). Furthermore, we have established a Centre for Population Neuroscience and Precision Medicine that is coordinating large neuroimaging and (epi)genetic studies embedded in deep-phenotyping prospective cohorts (IMAGEN, <http://www.imagen-europe.com/>, Global Initiative for Imaging Genetics/GIGA, [www.giga.org](http://www.giga.org)) (Ing et al., 2019; Schumann et al., 2019; Mascarell Maricic et al., 2020).

#### Selected References (PIs in bold):

- Cornblatt, B. A., Carrión, R. E., Auther, A., McLaughlin, D., Olsen, R. H., John, M., & **Correll, C. U.** (2015). Psychosis Prevention: A Modified Clinical High Risk Perspective from the Recognition and Prevention (rap) Program. *American Journal of Psychiatry*, 172(10), 986–994.
- Correll, C. U.**, Robinson, D. G., Schooler, N. R., Brunette, M. F., Mueser, K. T., Rosenheck, R. A., Marcy, P., Addington, J., Estroff, S. E., Robinson, J., Penn, D. L., Azrin, S., Goldstein, A., Severe, J., Heinssen, R., & Kane, J. M. (2014). Cardiometabolic Risk in Patients With First-Episode Schizophrenia Spectrum Disorders: Baseline Results From the RAISE-ETP Study. *JAMA Psychiatry*, 71(12), 1350–1363.
- Correll, C. U.**, Solmi, M., Veronese, N., Bortolato, B., Rosson, S., Santonastaso, P., Thapa-Chhetri, N., Fornaro, M., Gallicchio, D., Collantoni, E., Pigato, G., Favaro, A., Monaco, F., Kohler, C., Vancampfort, D., Ward, P. B., Gaughran, F., Carvalho, A. F., & Stubbs, B. (2017). Prevalence, Incidence and Mortality from Cardiovascular Disease in Patients with Pooled and Specific Severe Mental Illness: A Large-Scale Meta-Analysis of 3,211,768 Patients and 113,383,368 Controls. *World Psychiatry*, 16(2), 163–180.
- Entringer, S.**, de Punder, K., Overfeld, J., Karaboycheva, G., Dittrich, K., Buss, C., Winter, S. M., Binder, E. B., & **Heim, C.** (2015). Immediate and Longitudinal Effects of Maltreatment on Systemic Inflammation in Young Children. *Development and Psychopathology*, 27(2), 553–566.
- Entringer, S.**, Epel, E. S., Kumsta, R., Lin, J., Hellhammer, D. H., Blackburn, E. H., Wüst, S., & Wadhwa, P. D. (2011). Stress Exposure in Intrauterine Life Is Associated with

- Shorter Telomere Length in Young Adulthood. *Proceedings of the National Academy of Sciences*, 108(33), E513.
- Gold, S. M.**, Köhler-Forsberg, O., Moss-Morris, R., Mehnert, A., Miranda, J. J., Bullinger, M., Steptoe, A., Whooley, M. A., & **Otte, C.** (2020). Comorbid Depression in Medical Diseases. *Nature Reviews Disease Primers*, 6(1), 1–22
- Graham, A. M., Rasmussen, J. M., **Entringer, S.**, Ben Ward, E., Rudolph, M. D., Gilmore, J. H., Styner, M., Wadhwa, P. D., Fair, D. A., & Buss, C. (2019). Maternal Cortisol Concentrations During Pregnancy and Sex-Specific Associations with Neonatal Amygdala Connectivity and Emerging Internalizing Behaviors. *Biological Psychiatry*, 85(2), 172–181.
- Heim, C. M.**, **Entringer, S.**, & Buss, C. (2019). Translating Basic Research Knowledge on the Biological Embedding of Early-Life Stress into Novel Approaches for the Developmental Programming of Lifelong Health. *Psychoneuroendocrinology*, 105, 123–137.
- Heim, C. M.**, Mayberg, H. S., Mletzko, T., Nemeroff, C. B., & Pruessner, J. C. (2013). Decreased Cortical Representation of Genital Somatosensory Field After Childhood Sexual Abuse. *American Journal of Psychiatry*, 170(6), 616–623.
- Heim, C. M.**, Newport, D. J., Heit, S., Graham, Y. P., Wilcox, M., Bonsall, R., Miller, A. H., & Nemeroff, C. B. (2000). Pituitary-Adrenal and Autonomic Responses to Stress in Women After Sexual and Physical Abuse in Childhood. *JAMA*, 284(5), 592–597.
- Heinz, A. J., Beck, A., Meyer-Lindenberg, A., **Sterzer, P.**, & **Heinz, A.** (2011). Cognitive and Neurobiological Mechanisms of Alcohol-Related Aggression. *Nature Reviews Neuroscience*, 12(7), 400–413.
- Heinz, A.**, Kiefer, F., Smolka, M.N., Endrass, T., Beste, C., Beck, A., Liu, S., Genauck, A., Romund, L., Banaschewski, T., Birmphohl, 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., Stalkamp, 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(2), e12866.
- Heuser, I.**, & Lammers, C.-H. (2003). Stress and the Brain. *Neurobiology of Aging*, 24, S69–S76.
- Houtepen, L. C., Vinkers, C. H., Carrillo-Roa, T., Hiemstra, M., van Lier, P. A., Meeus, W., Branje, S., **Heim, C. M.**, Nemeroff, C. B., Mill, J., Schalkwyk, L. C., Creighton, M. P., Kahn, R. S., Joëls, M., Binder, E. B., & Boks, M. P. M. (2016). Genome-Wide DNA Methylation Levels and Altered Cortisol Stress Reactivity Following Childhood Trauma in Humans. *Nature Communications*, 7(1), 10967.
- Ing, A., Sämann, P., Chu, C., Tay, N., Biondo, F., Robert, G., Jia, T., Wolfers, T., Desrivieres, S., Banaschewski, T., Bokde, A.L.W., Bromberg, U., Büchel, C., Conrod, P.J., Fadai, T., Flor, H., Frouin, V., Garavan, H., Spechler, P.A., Gowland, P.A., Grimmer, Y., **Heinz, A.**, Ittermann, B., Kappel, V., Martinot, J.L., Meyer-Lindenberg, A., Millenet, S., Nees, F., van Noort, B., Orfanos, D.P., Martinot, M.P., Penttilä, J., Poustka, L., Quinlan, E.B., Smolka, M.N., Stringaris, A., Struve, M., Veer, I.M., **Walter, H.**, Whelan, R., Andreassen, O.A., Agartz, I., Lemaitre, H., Barker, E.D., Asguburner, J., Binder, E., Buitelaar, J., Marquand, A., Robbins, T.W., Schumann, G.; IMAGEN Consortium. (2019). Identification of Neurobehavioural Symptom Groups Based on Shared Brain Mechanisms. *Nature Human Behaviour*, 3(12), 1306–1318.
- Jia, T., Ing, A., Quinlan, E. B., Tay, N., Luo, Q., Francesca, B., Banaschewski, T., Barker, G. J., Bokde, A. L. W., Bromberg, U., Büchel, C., Desrivieres, S., Feng, J., Flor, H., Grigis, A., Garavan, H., Gowland, P., **Heinz, A.**, Ittermann, B., Martinot, J.-L., Paillere Martinot, M.-L., Nees, F., Papadopoulos Orfanos, D., Paus, T., Poustka, L., Fröhner, J.H., Smolka, M.N., **Walter, H.**, Whelan, R., **Schumann, G.**, IMAGEN Consortium.

- (2020). Neurobehavioural Characterisation and Stratification of Reinforcement-Related Behaviour. *Nature Human Behaviour*, 4(5), 544–558.
- Klengel, T., Mehta, D., Anacker, C., Rex-Haffner, M., Pruessner, J. C., Pariante, C. M., Pace, T. W. W., Mercer, K. B., Mayberg, H. S., Bradley, B., Nemeroff, C. B., Holsboer, F., **Heim, C. M.**, Ressler, K. J., Rein, T., & Binder, E. B. (2013). Allele-Specific FKBP5 DNA Demethylation Mediates Gene-Childhood Trauma Interactions. *Nature Neuroscience*, 16(1), 33–41.
- Lindsay, K. L., Buss, C., Wadhwa, P. D., & **Entringer, S.** (2019). The Interplay Between Nutrition and Stress in Pregnancy: Implications for Fetal Programming of Brain Development. *Biological Psychiatry*, 85(2), 135–149.
- Lupien, S. J., McEwen, B. S., Gunnar, M. R., & **Heim, C. M.** (2009). Effects of Stress Throughout the Lifespan on the Brain, Behaviour and Cognition. *Nature Reviews Neuroscience*, 10(6), 434–445.
- Mascarell Maričić, L., **Walter, H.**, Rosenthal, A., **Ripke, S.**, Quinlan, E. B., Banaschewski, T., Barker, G. J., Bokde, A. L. W., Bromberg, U., Büchel, C., Desrivières, S., Flor, H., Frouin, V., Garavan, H., Itterman, B., Martinot, J.-L., Martinot, M.-L. P., Nees, F., Orfanos, D. P., Paus, T., Poustka, L., Hohmann, S., Smolka, M.N., Fröhner, J.H., Whelan, R., Kaminski, J., **Schumann, G.**, **Heinz, A.**; IMAGEN Consortium. (2020). The IMAGEN Study: A Decade of Imaging Genetics in Adolescents. *Molecular Psychiatry*, 25(11), 2648–2671.
- Moog, N. K., **Entringer, S.**, Rasmussen, J. M., Styner, M., Gilmore, J. H., Kathmann, N., **Heim, C. M.**, Wadhwa, P. D., & Buss, C. (2018). Intergenerational Effect of Maternal Exposure to Childhood Maltreatment on Newborn Brain Anatomy. *Biological Psychiatry*, 83(2), 120–127.
- Pathak, S., Jiang, Y., DiPetrillo, L., Todtenkopf, M. S., Liu, Y., & **Correll, C. U.** (2020). Course of Psychosis in Schizophrenia With Alcohol Use Disorder: A Post Hoc Analysis of the Clinical Antipsychotic Trials of Intervention Effectiveness in Schizophrenia Phase 1 Study. *The Journal of Clinical Psychiatry*, 81(2).
- Rasmussen, J. M., **Entringer, S.**, Kruggel, F., Cooper, D. M., Styner, M., Gilmore, J. H., Potkin, S. G., Wadhwa, P. D., & Buss, C. (2017). Newborn Insula Gray Matter Volume Is Prospectively Associated with Early Life Adiposity Gain. *International Journal of Obesity*, 41(9), 1434–1439.
- Rudolph, M. D., Graham, A. M., Feczko, E., Miranda-Dominguez, O., Rasmussen, J. M., Nardos, R., **Entringer, S.**, Wadhwa, P. D., Buss, C., & Fair, D. A. (2018). Maternal IL-6 During Pregnancy Can Be Estimated from Newborn Brain Connectivity and Predicts Future Working Memory in Offspring. *Nature Neuroscience*, 21(5), 765–772.
- Scheidt-Nave, C.**, Kamtsiuris, P., Gößwald, A., Hölling, H., Lange, M., Busch, M. A., Dahm, S., Dölle, R., Ellert, U., Fuchs, J., Hapke, U., Heidemann, C., Knopf, H., Laussmann, D., Mensink, G. B., Neuhauser, H., Richter, A., Sass, A.-C., Rosario, A. S., ... Kurth, B.-M. (2012). German Health Interview and Examination Survey for Adults (DEGS)—Design, Objectives and Implementation of the First Data Collection Wave. *BMC Public Health*, 12(1), 730.
- Schiele, M. A., Gottschalk, M. G., & **Domschke, K.** (2020). The Applied Implications of Epigenetics in Anxiety, Affective and Stress-Related Disorders—A Review and Synthesis on Psychosocial Stress, Psychotherapy and Prevention. *Clinical Psychology Review*, 77, 101830.
- Scholaske, L., Buss, C., Wadhwa, P. D., & **Entringer, S.** (2018). Acculturation and Interleukin (il)-6 Concentrations Across Pregnancy Among Mexican-American Women. *Brain, Behavior, and Immunity*, 73, 731–735.
- Vancampfort, D., Stubbs, B., Mitchell, A. J., Hert, M. D., Wampers, M., Ward, P. B., Rosenbaum, S., & **Correll, C. U.** (2015). Risk of Metabolic Syndrome and Its Components in People with Schizophrenia and Related Psychotic Disorders, Bipolar Disorder and Major Depressive Disorder: A Systematic Review and Meta-Analysis. *World Psychiatry*, 14(3), 339–347.

- Verner, G., Epel, E., Lahti-Pulkkinen, M., Kajantie, E., Buss, C., Lin, J., Blackburn, E., Räikkönen, K., Wadhwa, P. D., & **Entringer, S.** (2020). Maternal Psychological Resilience During Pregnancy and Newborn Telomere Length: A Prospective Study. *American Journal of Psychiatry*, appi.ajp.2020.1.
- Xu, J., Liu, X., Ing, A., Li, Q., Qin, W., Guo, L., Huang, C., Cheng, J., Wang, M., Geng, Z., Zhu, W., Zhang, B., Liao, W., Qiu, S., Zhang, H., Xu, X., Yu, Y., Gao, B., Han, T., Cui, G., Chen, F., Miao, Y., Yuan, F., Lui, S., Zhang, X., Xu, K., Zhang, L., Ye, Z., Banaschewski, T., Barker, G.J., Bokde, A.L., Quinlan, E.B., Desrivieres, S., Flor, H., Grigis, A., Garavan, H., Gowland, P., **Heinz, A.**, Brühl, R., Martinot, J., Artiges, E., Nees, F., Orfanos, D.P., Lemaitre, H., Paus, T., Poustka, L. Hohmann, S., Fröhner, J.H., Smolka, M.N., **Walter, H.**, Whelan, R., Goldblatt, R., Patrick, K., Calhoun, V., Junli, M., Liang, M., Gong, P., Barker, E.D., Clinton, N., Yu, L., Yu, C., **Schumann, G.**, the CHIMGEN and IMAGEN Consortia. (2019). Satellite Imaging of Global Urbanicity Relate to Adolescent Brain Development and Behavior. *Biorxiv*, 781674.