Research of the Department of Behavioural Biology

Overview

The focus of professor Touma's research group is to generate and characterise clinically relevant animal models of inborn (trait) emotionality and stress reactivity in order to elucidate neurobiological, endocrine and molecular genetic mechanisms underlying affective disorders such as major depression. It is only with deep insight into these mechanisms that novel treatment strategies and promising targets for therapeutic interventions can be developed in the future.

The spectrum of our research includes projects at the genetic, proteomic and systemic level. We apply a variety of behavioural tests assessing emotionality, coping and cognitive functions along with neuroendocrine approaches to analyse neuropeptides and proteins involved in the activity and regulation of the hypothalamic-pituitary-adrenocortical (HPA) axis. Furthermore, we use paradigms addressing the interaction between genetic predispositions and environmental influences, shedding light on the epigenetic modification of behavioural traits and neurobiological endophenotypes.

Research interests:

- *Genes, Hormones and the Brain*
  - molecular genetic and neuroendocrine bases of behaviour
- *Function and Regulation of the Stress Hormone Systems*
  - focus: alterations in neurodegenerative and psychiatric disorders
- *Gene – Environment Interactions, Epigenetics*
  - modulation of genetic predispositions by social and non-social environmental factors
- *Regulation of Energy Metabolism and Neuronal Functions*
  - impact of metabolic changes on behavioural and neurobiological endophenotypes

Methods:

- Behavioural analysis and test paradigms
  - emotionality and coping styles
  - activity rhythms, learning and memory
  - social behaviour, parental care
- Neuroendocrine investigations
  - testing reactivity and feedback regulation of the HPA axis
  - hormone measurements in plasma samples and microdialysates from specific brain areas (quantifying steroids, neuropeptides and neurotransmitters)
  - non-invasive monitoring of steroid hormone metabolites in faecal samples
- Functional neuroanatomy and pharmacology
  - gene expression profiling in different brain areas (microarray, *in situ* hybridisation, real-time PCR)
  - neuronal plasticity measures and microdialysis
  - effects of neuromodulatory substances and drugs on emotionality and neuroendocrine responses

Study species:

- Laboratory mice
  - animal models of neurodegenerative and affective disorders (generated by selective breeding or targeted genetic manipulation)

Another branch of our research, headed by Rebecca Schulte, deals with host-parasite interactions. Parasites represent one of the strongest selective forces in evolution because:

- They are omnipresent. Every species has at least potential parasites.
- They reduce per definition host fitness, and thus the host should evolve to escape parasite attack.
- They usually have a stronger evolutionary potential than their host and can therefore adapt faster.

Host-parasite interactions are thus characterised by high evolutionary dynamics which should be highest if host and parasite coevolve.

But parasites may not only interact with their host. If parasites of different species or different strains attack the same host individual, it represents a limited resource for which the parasites compete. Alternatively, parasites may cooperate for more efficient host exploitation. Depending on the exact type of interaction between co-infecting parasites, the interaction between parasite and host will be influenced, for example on the virulence level.

We are studying host-parasite interactions and specifically interaction between co-infecting parasites using the model host *Caenorhabditis elegans* and its bacterial parasite *Bacillus thuringiensis*. This system allows us to study these interactions not only over one infection cycle, but also in the course of evolution. By using evolution experiments, phenotypic characterization and genome sequencing, we study for example the impact of multiple and single infections on the evolution of parasites and hosts, but also how hosts evolution affects the interaction between parasites.

Figure legend: The nematode *Caenorhabditis elegans* is ideally suited to study evolution in real time due to its short generation time of 2-3 days.

Selected Publications:

McIlwrick S, Rechenberg A, Matthes M, Burgstaller J, Schwarzbauer T, Chen A, **Touma C** (2016): Genetic predisposition for high stress reactivity amplifies effects of early-life adversity. *Psychoneuroendocrinology* 70: 85-97.

Bose J, **Schulte RD** (2014): Testing GxG interactions between coinfecting microbial parasite genotypes within hosts. *Front. Genet.* 5: 124.

Heinzmann JM, Kloiber S, Mattos GE, Bielohuby M, Schmidt MV, Palme R, Holsboer F, Uhr M, Ising M, **Touma C** (2014): Mice selected for extremes in stress reactivity reveal key endophenotypes of major depression: A translational approach. *Psychoneuroendocrinology* 49: 229-243.

Knapman A, Kaltwasser SF, Martins-de-Souza D, Holsboer F, Landgraf R, Turck CW, Czisch M, **Touma C** (2012): Increased stress reactivity is associated with reduced hippocampal activity and neuronal integrity along with changes in energy metabolism. *European Journal of Neuroscience* 35: 412-422.

Refojo D, Schweizer M, Kuehne C, Ehrenberg S, Thoeringer C, Vogl AM, Dedic N, Schumacher M, von Wolff G, Avrabos C, **Touma C**, Engblom D, Schütz G, Nave KA, Eder M, Wotjak CT, Sillaber I, Holsboer F, Wurst W, Deussing JM (2011): Glutamatergic and dopaminergic neurons mediate anxiogenic and anxiolytic effects of CRHR1. *Science* 333: 1903-1907.

Touma C, Gassen NC, Herrmann L, Cheung-Flynn J, Büll DR, Ionescu IA, Heinzmann JM, Knapman A, Siebertz A, Depping AM, Hartmann J, Hausch F, Schmidt MV, Holsboer F, Ising M, Cox MB, Schmidt U, Rein T (2011): FK506 binding protein 5 (FKBP5) shapes stress

responsiveness: modulation of neuroendocrine reactivity and coping behavior. *Biological Psychiatry* 70: 928-936.

Knapman A, Heinzmann JM, Hellweg R, Holsboer F, Landgraf R, **Touma C** (2010): Increased stress reactivity is associated with cognitive deficits and decreased hippocampal brain-derived neurotrophic factor in a mouse model of affective disorders. *Journal of Psychiatric Research* 44: 566-575.

Schulte RD, Makus C, Hasert B, Michiels NK, Schulenburg H (2010): Multiple reciprocal adaptations and rapid genetic change upon experimental coevolution of an animal host and its microbial parasite. *Proc Natl Acad Sci U S A* 107: 7359-64.

Touma C, Fenzl T, Ruschel J, Palme R, Holsboer F, Kimura M, Landgraf R (2009): Rhythmicity in mice selected for extremes in stress reactivity: behavioural, endocrine and sleep changes resembling endophenotypes of major depression. *PLoS ONE* 4 (1): e4325.

Touma C, Bunck M, Glasl L, Nussbaumer M, Palme R, Stein H, Wolferstätter M, Zeh R, Zimbelmann M, Holsboer F, Landgraf R (2008): Mice selected for high versus low stress reactivity: a new animal model for affective disorders. *Psychoneuroendocrinology* 33: 839-862.

Touma C, Ambrée O, Görtz N, Keyvani K, Lewejohann L, Palme R, Paulus W, Schwarze-Eicker K, Sachser N (2004): Age- and sex-dependent development of adrenocortical hyperactivity in a transgenic mouse model of Alzheimer's disease. *Neurobiology of Aging* 25: 893-904.

Touma C, Palme R, Sachser N (2004): Analyzing corticosterone metabolites in fecal samples of mice: a noninvasive technique to monitor stress hormones. *Hormones and Behavior* 45: 10-22.