B02 (Grinevich)

Project title
“Tackling the role of vasopressin in modulation of fear and pain”

Description
We have previously established the role of oxytocin pathways in the brain for fear and pain regulation. But what about its sister peptide arginine vasopressin (AVP)? Using a novel transgenic rat model, which grants genetic access to AVP neurons in the hypothalamus, we are now starting to expand our fear and pain research to this relatively understudied neuropeptide. Using viral vector-based tracing techniques, we have already discovered an intricate network of AVP connections throughout the brain, and are currently exploring their involvement in behavioural correlates of fear and pain sensations. We are looking for motivated and dedicated master students to assist us in these fast developing projects. We would prefer students who have already gathered previous experience in one or several of our main techniques. On the one hand, these are stereotaxic surgeries in rodents, in vivo optogenetics, in vivo calcium imaging (in particular fiber photometry or miniscope imaging) and behavioural fear- or pain-related paradigms in rodents. On the other hand, the projects also involve histology, immunofluorescence, light microscopy (i.e. fluorescent widefield slide scanner and confocal microscopy), and neuroanatomical analysis (spanning from manual annotation to 3D batch analysis using the IMARIS software). As an example for a current project in the scope of this larger endeavour, we recently used both anterograde AAV tracing and the retrograde monosynaptic Rabies virus technique to identify an axonal projection from AVP neurons mostly located in a caudal part of the supraoptic nucleus to the central amygdala. We hypothesized that this projection may represent the substrate for AVPergic modulation of fear behaviour, and are at the moment testing this hypothesis using optogenetic stimulation of AVP axons in central amygdala during fear recall after contextual fear conditioning.

Methods
Master students working with us on the AVP fear and pain projects can learn a combination of the following techniques:

- Application of the Cre/lox system to make use of our novel transgenic AVP-Cre rat model
- Stereotaxic surgeries in rats for viral vector applications and implantation of either fiber optic cannulas or miniscopes
- Behavioural paradigms to quantify the fear or pain-related behavioural roles of AVP circuits
- Histology and immunofluorescence including light microscopy and image analysis

Key publications

1. Iwasaki, M., Lefevre, A., Althammer, F., Creusot, E.C., Łąpieś, O., Petitjean, H., Hilfiger, L., Kerspern, D., Melchior, M., Küppers, S., Krablicher, Q., Patwell, R., Kania, A., Kirchner, M.K., Wimmer, M., Fröhlich, H., Dötsch, L., Schimmer, J., Herpertz, S.C., Ditzen, B., Schaaf, C.P., Schönig, K., Bartsch, D., Gugula, A., Trenk, A., Blasiak, A., Stern, J.E., Darbon, P., **Grinevich, V.,** Charlet, A. (2023): An analgesic pathway from parvocellular oxytocin neurons to the periaqueductal gray in rats. *Nature Communications,* 10.1038/s41467-023-36641-7
2. Tang, Y., Benusiglio, D., Lefevre, A., Hilfiger, L., Althammer, F., Bludau, A., Hagiwara, D., Baudon, A., Darbon, P., Schimmer, J., Kirchner, M.K., Roy, R.K., Wang, S., Eliava, M., Wagner, S., Oberhuber, M., Conzelmann, K.K., Schwarz, M., Stern, J.E., Leng, G., Neumann, I.D., Charlet, A., **Grinevich, V.** (2020): Social touch promotes inter-female communication via activation of parvocellular oxytocin neurons. *Nature Neurosci. 23,* 1125-1137. doi: 10.1038/s41593-020-0674.
3. Hasan, M.T., Althammer, F., da Silva Gouveia, M., Goyon, S., Eliava, M., Lefevre, A., Kerspern, D., Schimmer, J., Raftogianni, A., Wahis, J., Knobloch-Bollmann, H.S., Tang, Y., Liu, X., Jain, A., Chavant, V., Goumon, Y., Weislogel, J.-M., Hurlemann, R., Herpertz, S.C., Pitzer, C., Darbon, P., Dogbevia, G.K., Bertocchi, I., Larkum, M.E., Sprengel, R., Bading, H., Charlet, A. and **Grinevich, V.** (2019): A fear memory engram and its plasticity in the hypothalamic oxytocin system. *Neuron*, *103*, 133-146.

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