



Centre de Neurosciences Psychiatriques

CNP SEMINARS

ANNOUNCEMENT

Friday, March 18, 2022, 11:00 – 12:00

Neuronal plasticity and neurotrophin signaling as the common mechanism for antidepressant effect

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Neuronal plasticity has for a long time been considered important for the recovery from depression and for the antidepressant drug action, but how the drug action is translated to plasticity has remained unclear. Brain-derived neurotrophic factor (BDNF) and its receptor TRKB are critical regulators of neuronal plasticity and have been implicated in the antidepressant action. We have recently found that many, if not all, different antidepressants, including serotonin selective SSRIs, tricyclic as well as fast-acting ketamine, directly bind to TRKB, thereby promoting TRKB translocation to synaptic membranes, which increases BDNF signaling. We have previously shown that antidepressant treatment induces a juvenile-like state of activity in the cortex that facilitates beneficial rewiring of abnormal networks. We recently showed that activation of TRKB receptors in parvalbumin-containing interneurons orchestrates cortical activation states and is both necessary and sufficient for the antidepressant-induced cortical plasticity. Our findings open a new framework how the action of antidepressants act: rather than regulating brain monoamine concentrations, antidepressants directly bind to TRKB and allosterically promote BDNF signaling, thereby inducing a state of plasticity that allows re-wiring of abnormal networks for better functionality.

Invited by Ron.stoop@chuv.ch

Selected recent publications:

Casarotto P.C., Girysh M., Fred S.M., Kovaleva, V., Moliner R., Enkavi G., Biojone C., Cannarozzo C., Sahu, M.P., Kaurinkoski, K., Brunello C.A., Steinzeig A., Winkel F., Patil S., Vestring S., Serchov T., Diniz C.R.A.F., Laukkanen L., Cardon I., Antila H., Rog T., Piepponen, T.P., Bramham C.R., Normann C., Lauri S.E., Saarma M., Vattulainen I., Castrén E. Antidepressant drugs act by directly binding to TRKB neurotrophin receptors. (2021) Cell 184, 1299–1313, <https://doi.org/10.1016/j.cell.2021.01.034>.

Winkel F., Ryazantseva M., Voigt M.B., Didio G., Lilja A., Llach Pou M., Steinzeig A., Harkki J., Englund J., Khirug S., Rivera C., Palva S., Taira T., Lauri S.E., Umemori J. and Castrén E. T Pharmacological and optical activation of TrkB in Parvalbumin interneurons regulates intrinsic states to orchestrate cortical plasticity. (2021) Mol. Psychiatry, <https://doi.org/10.1038/s41380-021-01211-0>

Lesnikova, A., Casarotto, P. C., Fred, S. M., Voipio, M., Winkel, F., Steinzeig, A., Antila, H., Umemori, J., Biojone, C., and Castrén, E. (2020). Chondroitinase and antidepressants promote plasticity by releasing trkb from dephosphorylating control of PTP α in parvalbumin neurons. (2020) J. Neurosci. 41(5):972-980. <https://www.jneurosci.org/content/41/5/972>.

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Link for videoconference

<https://chuv.webex.com/chuv/j.php?MTID=m9f74837024d3ecc9f0929f2592e935f8>