Characterization of a mouse model with a central knockout of BDNF

Assignment: T24 - Attention, Motivation, Emotion and Cognition
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Neurotrophins, such as brain-derived neurotrophic factor (BDNF), play a role in central functions of the brain like learning and memory (Leal et al. 2017, Monteggia et al. 2004), eating behaviour (Rios et al. 2013, Lebrun et al. 2006) and anxiety-related behaviour (Hashimoto 2007). Loss of BDNF or impairments in the BDNF-signalling are therefore linked with brain dysfunction. However, its role in the postnatal brain has remained difficult to assess, since the BDNF-null mutation is lethal (Rauskolb et al. 2010).
We therefore used C57Bl6/N conditional mutant mice floxed at the BDNF locus and with Cre expression in neurons expressing neurofilament L (BDNFflfl, cre+). NFL expression starts shortly after birth, to that these mice loose BDNF expression in pyramidal neurons, projection neurons, Purkinje cells, and motor neurons, but mice do survive. To assess whether the loss of central BDNF affects basic behaviour, we performed several behavioural test with BDNFflfl, cre+ and their control littermates (BDNFflfl, cre-): Open Field, Nest Building, Marble Burying, Dark/Light-Box, Elevated Plus Maze, and Novel Object Recognition (van Gaalen and Steckler 2000). We used female and male mice and performed every test with all mice at the age of three, six, and nine month to cover possible gender and age effect, respectively. Furthermore, we measured food intake and weight of the mice weekly.
We only saw differences between mice lacking BDNF in neurons expressing NFL (BDNFflfl, cre+) and their control littermates (BDNFflfl, cre-) in some of our analysis (i.e. Marble Burying). Interestingly, changes in behaviour of BDNF knock out mice increased with age. This may be due to the fact, that BDNF expression is highest immediately after birth and decreases with age. We suggest that young mice may cope better with a loss of central BDNF than old mice (i.e. through a higher expression of BDNF by glial cells).