Neuroplasticity of nucleus accumbens suggested by resting state connectivity in Nerve Growth Factor Beta mutation carriers.

H. van Ettinger-Veenstra¹,²,³ I. Perini¹,² I. Morrison¹,²,³

¹IKE, Linköping University, Linköping, Sweden ² CSAN, Linköping University, Linköping, Sweden. ³CMIV, Linköping, Sweden.

Background: Deficits in stimulus-appropriate behavioral responses to pain and affective touch caused by a reduction in thin-diameter sensory afferents including C nociceptors and C-tactile afferents are linked to a rare mutation of the human nerve growth factor beta (NGFB). Mutation carriers show more pain and pleasant touch indifference compared to controls, however this effect was highly variable [1,2]. We are the first to investigate functional connectivity in heterozygous NGFB mutation carriers, and explored two functional regions of interest that were implied in carriers' pain-related deficits in the right anterior insula (rAI) and middle cingulate cortex (MCC) [3].

Methods: We scanned 12 NGFB heterozygous mutation carriers and 12 controls. Resting state fMRI of 10 min was obtained at a Philips 3T Ingenia, SENSE head coil, single-shot EPI gradient echo, TR/TE/FA/resolution = 2s/30ms/30°/3.4mm³, whole-brain coverage. Preprocessing in SPM12 (Wellcome Trust Centre for Neuroimaging, London, UK) for realigned, normalized and smoothed images (8mm FWHM). A ROI-to-ROI and voxel-to-voxel fc analysis (with CONN-toolbox [4]) was employed with CONN ROIs at p<0.05 FDR corrected, exploration of 10 mm radius spheres at rAI and MCC at p<0.05 uncorr.

Results: Functional connectivity between the nucleus accumbens (NAc) and the left temporal fusiform was higher for NGFB mutation carriers compared to controls. Main group effect showed a larger amount of connections with the rAI respectively the MCC for the NGFB mutation carriers.

Conclusions: The role of the NAc is suggested to be the integration of cognitive and affective information in order to engage in action selection, rather than the classical attributed role of a reward center [5]. The fusiform gyrus has been proposed to integrate multisensory input including tactile information [6,7] and receives input from the amygdala to augment reaction to multisensory emotional input [8]. The NGFB mutation carriers may have a functional reorganization to compensate for impaired processing of affective information originating from sensory afferents.