The hierarchy of brain networks is related to insulin growth factor-1 in a large, middle-aged, healthy cohort: a magnetoencephalography study
P. Sorrentino1,2, D. Nieboer3, J.W.R. Twisk4, C.J. Stam1, L. Douw5,6, A. Hillebrand1

1Department of Clinical Neurophysiology and MEG Center, VU University Medical Center, Amsterdam, The Netherlands 2Istituto di diagnosi e cura Hermitage Capodimonte, Naples, Italy 3Department of Methodology and Applied Biostatistics, Faculty of Earth and Life Sciences, VU University Amsterdam, Amsterdam, The Netherlands 4Department of Epidemiology and Biostatistics, VU University Medical Center, Amsterdam, The Netherlands 5Department of Anatomy and Neurosciences, VU University Medical Center, Amsterdam, The Netherlands 6Department of Radiology, Athinoula A. Martinos Center for Biomedical Imaging / Massachusetts General Hospital, Boston (MA), United States of America

Background: Studies with structural magnetic resonance imaging (MRI) have shown that in healthy elderly lower serum levels of insulin growth factor-1 (IGF-1) relate to brain atrophy and to greater risk for Alzheimer’s disease (AD). We hypothesized that the study of functional brain networks can detect the effects of IGF-1 earlier. To test this hypothesis, we studied the relationship between IGF-1 and magnetoencephalography–based functional network characteristics in a middle-aged population.

Methods: We estimated serum levels of IGF-1, and analyzed eyes-closed resting-state magnetoencephalographic signals in a healthy Dutch cohort (The Amsterdam growth and health longitudinal study). Functional connections between brain areas were estimated for the canonical frequency bands using the phase lag index (PLI). The topology of the frequency-specific networks was characterized calculating the minimum spanning tree. We computed the tree hierarchy (T_h), capturing the balance between node–overload and efficient communication, and the leaf fraction, studying network integration. These measures were regressed with IGF-1, correcting for gender and for systemic effects of IGF–1. In the frequency bands where the T_h and the leaf fraction related to IGF-1, the betweenness centrality, a nodal measure, was compared between subjects with high and low serum levels of IGF-1 (median split) by permutation analysis corrected for multiple comparison across regions.

Results: IGF-1 serum levels regressed positively with the tree hierarchy (β:.2;p:.01) and leaf fraction (β.18;p:.037) in the beta band and with the leaf fraction (β:.18; p:.03) in the theta band. The correlations remained significant when correcting for gender and systemic effects of IGF-1. We could not find any relationship between IGF-1 serum levels and betweenness centrality.

Conclusions: Our results imply that lower levels of serum IGF-1 relate to a less integrated functional network. Thus, IGF-1 seems to have a direct effect on the topology of functional brain networks. We found a correlation between IGF-1 serum levels and global parameters, despite the fact that no specific region showed direct involvement. This study allowed the early detection of effect of a risk factor for neurodegeneration, and might improve risk stratification and our understanding of neurodegeneration.