Loss of white matter network organization is associated with cognitive decline in chronic epilepsy

Poster No:
184

On Display:
Monday, June 27 & Tuesday, June 28

Stand-By Time:
Monday, June 27: 13:00 – 15:30

Authors:
Maarten Vaessen\textsuperscript{1,2,3}, Jaap Jansen\textsuperscript{1,2}, Marielle Vlooswijk\textsuperscript{2,4}, Paul Hofman\textsuperscript{1,2}, Marjan Majoie\textsuperscript{3,4}, Albert Aldenkamp\textsuperscript{2,3,4}, Walter Backes\textsuperscript{1,2}

Institutions:
\textsuperscript{1}Radiology, Maastricht University Medical Centre, Maastricht, Netherlands, \textsuperscript{2}School for Mental Health and Neurosciences, Maastricht University, Maastricht, Netherlands, \textsuperscript{3}Kempenhaeghe Epilepsy Center, Heeze, Netherlands, \textsuperscript{4}Neurology, Maastricht University Medical Centre, Maastricht, Netherlands

Introduction:
Patients with chronic epilepsy frequently display cognitive co-morbidity (Elger, 2004). From MRI studies on whole brain structural and functional networks, it appears that network efficiency plays an important role in intelligence (Li et al., 2009; van den Heuvel et al., 2009). It is increasingly shown that epilepsy patients might have widespread network abnormalities outside of the epileptic zone (Meador, 2010), which might affect a variety of cognitive functions and global intelligence. Most studies focus on the role of the grey matter. To study the role of the white matter as a neuronal correlate of the cognitive co-morbidity, the relation between deviant white matter connectivity and global intelligence (and intellectual decline) was investigated in a group of patients with chronic epilepsy with varying degrees of cognitive impairment. Fiber tractography and graph theoretical analysis (Bullmore, 2009) were used to study tract volume weighted networks.

Methods:
Subjects: 39 patients (19 men, 20 woman, age 40±12y, IQ 95±15) with non-symptomatic localization-related epilepsy and 23 age-matched healthy controls (9 men, 14 women, age 40±13y, IQ 113±15) were included. All subjects had a neuropsychological assessment, including an IQ test. Patients were classified into a cognitively non-impaired (n=32) and an impaired (n=7) group based on an estimation of IQ discrepancy (Schoenberg, 2002). MRI: Diffusion tensor imaging (DTI) data was acquired on a 3T MRI system (voxel size=2x2x2 mm, TE=62 ms, TR=6600 ms, SENSE=2, 15 directions at b=800 s/mm\textsuperscript{2}, one b=0 s/mm\textsuperscript{2}). Tract volumes were calculated from a number of processing steps: (i) fitting of a tensor model incorporating uncertainty in fiber orientation (Parker, 2003), (ii) whole brain probabilistic fiber tractography, (iii) registration of n=90 cortical and sub-cortical regions (AAL atlas) to the individual brain, (iv) network construction by calculating the volume of each tract connecting any two regions. Last, only fiber tracts that could be reconstructed in all subjects were analyzed (k=1224). Structural connectivity: From the tract volume weighted networks the cluster coefficient (C)
and path length (L) were calculated. C and L were compared between the control, non-impaired and impaired patients (Student's t-test) and partial correlation analyses (corrected for age and gender) between C and L and IQ were performed.

Results:
C was significantly lower for the impaired group compared to the control group (p<0.04) and the non-impaired group (p<0.02). The impaired group had significantly higher L compared to the control group (p<0.05) and the non-impaired group (p<0.04); see Fig 1. C was associated with FSIQ (r=0.58, p<0.001), L was associated with FSIQ (r=-0.57, p<0.001). IQ discrepancy was also found to be correlated with C (r=0.37, p<0.028) and negatively correlated with L (r=-0.31, p<0.068), see Fig 2. On the regional level, several sub-cortical and posterior regions displayed significantly lower C (control - impaired patients), controlled for multiple comparison; see Fig. 3. At the level of single connections, no significant differences or correlations were found. We found no significant relation between whole brain white matter volume and IQ in our population.

Conclusions:
This study reveals neurobiological evidence for impaired white matter connectivity which is associated with cognitive co-morbidity in patients with chronic epilepsy. C and L appeared abnormal in epilepsy patients with cognitive impairment and were strongly correlated with (lowered) IQ scores. As whole brain white matter in itself was not correlated with IQ, it is not the total volume of the white matter that is deviant in epilepsy patients or associated with FSIQ, but it is the network topology in terms of volume contribution of different white matter fiber bundles, that is important. Our results imply that in-vivo measurement of brain network efficiency is a sensitive markers for cognitive decline in chronic epilepsy.

Disorders of the Nervous System:
Epilepsy

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<th>Partial correlation table, controlled for age &amp; gender</th>
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Fig. 2: Partial correlation table showing correlation values between C and L and FS-IQ. Pre-morbid IQ and IQ discrepancy, controlled for age and gender.
Abstract Information

References


Neuropsychology, 16(4):426-37