Altered functional connectivity consistent with associated language impairment in rolandic epilepsy

René Besseling[1], Jacobus Jansen[1], Geke Overvliet[2], Sylvie van der Kruijs[3], Johannes Vles[2], Saskia Ebus[3], Paul Hofman[1], Anton de Louw[3], Albert Aldenkamp[3], and Walter Backes[1]

[1]Radiology, Maastricht University Medical Center, Maastricht, Limburg, Netherlands, [2]Neurology, Maastricht University Medical Center, Maastricht, Limburg, Netherlands, [3]Epilepsy Centre Kempenhaeghe, Heeze, Noord-Brabant, Netherlands

Target audience: Neuroscientists interested in (task and) resting-state functional MRI analysis in general and those working on (cognitive impairment in) (childhood) epilepsy in particular.

Purpose: Rolandic epilepsy (RE) is classically considered a benign and transient disorder, however recent studies have raised awareness for associated cognitive impairments, among which are language disorders[1]. Thus far it remains unknown how seizures originating from the rolandic (sensorimotor) areas affect the language system. The aim of the current study is to identify functional networks involving the rolandic areas and to link potential network abnormalities to language impairment.

Methods: Twenty-two children with RE (age, mean±SD: 11.4±2.0 years, 16 boys) and 22 age-matched healthy controls (10.3±1.7 years, 11 boys) underwent resting-state fMRI (3T Philips Achieva, TE/TR=35/2000 ms, 195 dynamics, acquisition time 6.5 min). Probabilistic group independent component analysis[2] (gICA) was applied to the concatenated data using FSL's MELODIC and the resting-state network involving (among others) the rolandic areas (see inset Fig 1) was selected as network of interest, and mapped to the individual subject level using FSL's dual regression[3]. Permutation testing (N=5000) was performed to test for regions of aberrant functional connectivity with this rolandic network in patients compared to controls. To facilitate the interpretation of findings in the context of language impairment, language task fMRI was performed (word generation and reading tasks, standard block design with 30s intervals, MR setting equal to the resting-state scan) as well as neuropsychological testing of language performance (Clinical Evaluation of Language Fundamentals for children; CELF-4).

Results: The network of interest extended beyond the rolandic areas, and involved perisylvian regions including the bilateral superior temporal gyri (Fig 1). Voxel-wise trends of aberrant rolandic network connectivity (permutation testing) suggested reduced connectivity in children with RE compared to controls for the left inferior frontal gyrus (IFG_L), which coincided with the region of interest (ROI) defined from the pooled word generation activation map (MNI-coordinate [48,7,26] mm, radius 10 mm); this local reduction in rolandic functional connectivity was significant at the ROI level (2-sided t-test, p=0.011).
Language performance was reduced in patients compared to controls according to the CELF-4 (e.g. reduced core language score; 95±18 vs 105±11; p=0.03). No correlations were found between language performance and IFG_L rolandic network connectivity.

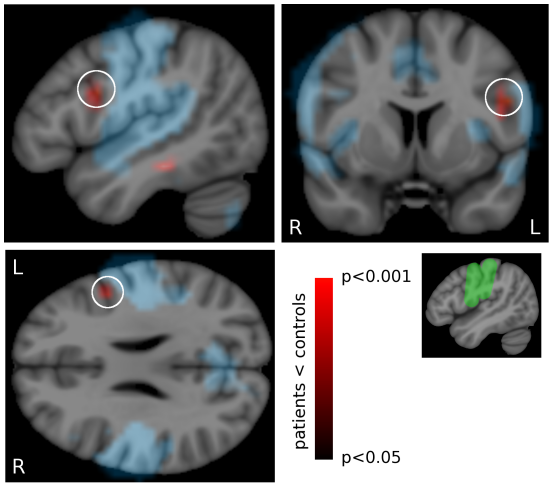

Fig 1: Average rolandic resting-state network of the patients in blue (multiple-comparisons corrected), voxel-wise trends of reduced rolandic network connectivity in red, ROI for word generation activation in the IFG_L as a white circle. The reduction in rolandic network connectivity was significant at the ROI level. The rolandic areas are given in green in the inset.

Discussion: This study represents a task-informed resting-state analysis, in which language task fMRI was used to allocate functionality to (abnormalities of) the network of intrinsic (resting-state) connectivity of interest. We found reduced functional connectivity between the rolandic resting-state network and the expressive language area in the IFG_L. Our findings might represent aberrant functional connectivity within this integrative network, and provide a link between seizures/epileptiform activity originating from the rolandic cortex and language impairment in RE.

Conclusion: For the first time, functional abnormalities have been found in RE that are topologically consistent with language impairment. This result adds to the increased awareness that RE might be benign with respect to its (relatively mild) seizure semiology, but not with respect to cognitive aspects[1,4]. For future research, it remains to be resolved whether the functional abnormalities resolve after seizure remission and whether abnormalities in functional brain organization might be prevented by e.g. the use of anti-epileptic drugs or specific speech therapy.

[1]Massa R et al, EEG criteria predictive of complicated evolution in idiopathic rolandic epilepsy. Neurology 2001; 57: 1071-1079. [2]Beckmann, C.F. et al, Investigations into resting-state connectivity using independent component analysis. Philos Trans R Soc Lond B Biol Sci 2005; 360: 1001-1013. [3]Filippini et al, Distinct patterns of brain activity in young carriers of the APOE-epsilon4 allele. Proc Natl Acad Sci U S A 2009; 106: 7209-7214. [4]Hughes J, Benign epilepsy of childhood with centrotemporal spikes (BECTS): To treat or not to treat, that is the question, Epilepsy & Behavior 2010; 19: 197–203