Epileptic seizure propagation from the second somatic sensory area to the fronto-medial region, by insular redistribution. A case report and a connectome description

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SUMMARY

Introduction. The seizure propagation phenomenon by inducing remote symptoms brings several difficulties in finding the seizure onset and delineating the epileptic network which should be taken into consideration in epilepsy surgery. By demonstrating a difficult (MRI negative) epilepsy surgery case explored with invasive presurgical evaluation we highlight the importance to recognise the secondary sensory area and to explore the the parieto-opercular-insular-medial frontal network in certain cases. A further conclusion is the consideration of the redistributory role of the insula as a special structure in the cerebral connectome, having a role in epileptic network organisation.

Aims. To support the role of the insula in the organisation of an opercular – medial frontal epileptic network and to confirm Penfield’s the “second somatic sensory leg area” by way of a case report. We try to give an up to date exploration of our patient’s remote epileptic seizures by way of a connectome.

Methods. The epileptic disorder was studied with intensive video EEG monitoring and two times 3T MRI. Interictal FDG (fluorodeoxyglucose) PET was also undertaken. Beside the scalp EEG and computerized frequency analysis, the evaluation was performed by invasive EEG with 2 grids and 2 strips and an insular deep electrode in addition. Electrical cortical stimulation and cortical mapping were also undertaken.

Results. The video-EEG study revealed the complex seizure semiology. The left sided global somatosensory aura in the leg, followed supplementary motor area manifestations represented a remote seizure. The seizure onset zone and the symptomatogenic zone were localised by the invasive electrophysiology. With the insular deep electrode we succeeded to explore the propagation of ictal activity to the insula and later to frontal medial surface. The PET, the negative 3T MRI results and the postprocessing morphometry confirmed the lesional origin and localised the epileptogenic area to the second somato-sensory field where a dysgenesis was located.

Conclusions. By preoperative invasive video-EEG evaluation, the second somato-sensory leg area was delineated as the seizure onset zone. The resection of this area by IIb type cortical dysgenesis, resulted in a complete relief of the seizures. The invasive video-EEG revealed the peculiar role of the insula in the propagation of the epileptic seizure from the second sensory leg area to the ipsilateral fronto-medial supplementary motor area. Our results, confirm, that the insula has a relay or node function on the parietal opercular-fronto-medial epileptic network. The connectome of the insula is a further additive of the scale-free features of the remote epileptic networks.

Key words: second somatic sensory area • insular node-epileptic network • remote frontal lobe seizures • connectome
INTRODUCTION
The second sensory area of the cortex was identified after the electrical stimulation work of Penfield et al. (1954). It involves the lower part of the upper Sylvian bank and is placed in intimate proximity of the upper part of the insula itself (Tuxhorn et al., 2000). The semiological considerations of the functional role of this area shows slender interest. Contrasting to the sensory Jackson march originated from the postcentral convexity, our patient complained of one-sided „holistic” numbness or pain in the left arm or leg or body which may be linked with localized „spasmodic” clonus or tonic spasm (Young at al., 1983; Pandya et al., 1987). Primarily the sensory symptoms were intrinsically associated with face, mouth, and upper and lower extremity motor activity (Lüders et al., 1985). This symptomatological complexity raises usually several localizing questions between the second sensory area and the supplementary sensorimotor region (Tuxhorn et al., 2000).

Our case report provides an example for the localizational challenges of the somatosensory pain aura and about the seizure propagation through the network between the parieto-temporal operculum and the supplementary motor area. The network connections between the fronto-parieto-temporal operculum and the fronto medial region explain the mechanisms of such „remote” seizures where the somatosensory aura is followed by fronto medial postural seizure. During seizure semiology, it is difficult to differentiate the elemental somatosensory symptoms from the more complex sensorial events. The recognition of the „holistic” features of our patients pain aura provided possibility to overbridge the seeming localizatory contradictions and find the semiologic significance of her early seizure symptoms. Detection of the propagation network by exploring with invasive electrodes provided a possibility to interconnect the pain symptoms with her habitual postural seizures. That way we were able to show the connectivity inter-relationship between the parietal operculum and the frontomedial region.

METHODS
Our patient underwent presurgical evaluation and surgery. During her first video-EEG monitoring the scalp EEG was examined with frequency analysis (Micromed SystemPlus software). The invasive presurgical EEG was performed with subdural grids and strips and one insular deep electrode. Philips Achieva 3T MRI and interictal FDG-PET was conducted. Postoperative-ly quantitative postprocessing morphometry was also reconstructed. During the pre-operative phase, invasive electrophysiology with video-controlled electrical stimulation and cortical mapping was performed. Histology and immunhistology were also undertaken.

CASE HISTORY AND EVALUATION
Our 32 years old female patient suffered for 19 years from drug-resistant epilepsy. The patient’s seizures were discussed several years before operation (Balogh, 2011). The last therapy was since 2011 a valproate-carbamazepine-topiramate combination. Her left sided sleep seizures appeared nightly one or more times for the last three preoperative years. A brain MRI was undetaken on two separate occasions and showed no significant structural lesions. However, an interictal PET scan revealed clear hypometabolism on the right opercular parietal and insular region (fig. 1). EEG showed repeatedly right temporo-parietal interictal spike activity. The ictal scalp EEG and its computerized frequency analysis suggested that seizure onset was localized to the right parieto-temporal region and propagated to the right fronto-central electrodes (fig. 2 and fig. 3). The seizures awakened the patient and she used to shake her head violently, complaining and crying about her painfull spasm and numbness feeling in her left leg. The pain was occasionally substantially prolonged, principally on her left thigh or another occasion on her whole leg. This somatosensory symptoms were always followed by postural frontal seizure with preserved alertness and cognitive abilities. The patient was implanted by a 6×8 points right perisylvian grid, and a 2×10 points two sided re-

Figure 1. Right parietal and right insular FDG hypometabolismus on the interictal PET SCAN (from Balogh, 2011).
Figure 2. Ictal EEG-onset period: Right temporo-centro-parietal spike activity (followed ictal desynchronisation) predominantly on the right side associated with right sided priority followed by the clinical seizure (from Balogh, 2011).

Figure 3. Ictal EEG at time of the SMA period. The ictal activity is most significant on the right frontal region (repetitive spikes at Fp2;F4;C4;P4 electrodes) (from Balogh, 2011).
Figure 4. Seizure spread in the epileptic network: The electrode reconstruction shows the localisation of the low postcentral and insular seizure onset and the spread toward the supplementer motor area. The schematic insert illustrates the seizure spread from posterior opercular and insular structures toward the frontal medial surface supplementer motor area. On the left we show the results of the postprocessing morphometry based on a local (Budapest) and an international (general) database. The localisation of the electrical seizure onset and the bright spot showing aberrant structure is in good coincidence.
cording grid over both medial precentral frontal surface covering the supplementary motor regions. A further 8 points strip was placed over the right posterior cingular and 8 points two sided recording strips over the parietal medial surface. The implantation had been completed by an intracerebral 8 points deep electrode inserted from frontal direction into the structure of the insula. The invasive evaluation explored 18 spontaneous seizures. The seizure onset was revealed consequently from the postcentral opercular points of the perisylvian grid and in the same time from the insular electrode points, followed 1.5–2 s. later in the frontomedial surface (fig. 4). The cortical mapping activated heterogenous symptoms, but the leg somato-sensory experience was activated on S pole point where the red star is (fig. 5). With the results of the seizure semiology, PETscan, and complex electrophysiology, a surgical intervention have been planned and executed. Through a low postcentral craniectomy in the junction of lower part of the parietal lobe and the posterior insula, dysgenetic white matter became visible and palpable by the surgeon and this small territory was resected. Histological and immunohistological workup confirmed focal cortical dysplasia (IIb type). Since two years, from the day of her surgery the patient is seizure-free and for the last five month she is on topiramate monotherapy. Her only remaining symptom was a pareasthetic feeling of the whole left leg which was sucessfully cured with duloxetine for 7 month.

**DISCUSSION AND CONCLUSION**

This patient had peculiar somatosensory aura with left sided global pain, followed by frontal lobe seizures. Invasive ictal registration revealed a right parietal opercular seizure onset with propagation of the ictal activity to the posterior insular region, and after to the medial anterior frontal surface. She had an epilepsy with "remote"symptomatogenic zone. The feature of her sensory sensations were more complex than a primary sensory one. She never had jacksonian manner “Rolandic” somatic sensory symptoms, but she complained of prolonged pain mostly on her left thigh or on her whole left leg. Among the ictal leg pain symptoms, the thigh pain is known to have an indicated role (Trevathan et al.,...
1988). The invasive electrophysiological workup confirmed that the second sensory area is the seizure onset zone which was discovered during surgery and later confirmed by postprocessing quantitative morphometry-MAP07 general and MAP07 Budapest (fig. 4). This proved to be a dysgenetic tissue, confirmed by histology as type IIb, that is not always detectable by MRI. The propagation pattern of our patient’s seizures raised network and connectivity questions. As we can see, the onset zone is located to the inferior parietal lobe. The semiology of her seizures were postural frontal type. This “remote” epilepsy has been investigated with invasive electrophysiology and we were able to explore the network where the epileptic activity propagated. It is particularly interesting that after seizure onset, the next structure where the seizure spread was the insula (see on fig. 4). The special „node” function of the insula was analysed earlier in Epileptologia by us (Balogh, 2011). Its ability as a redistributor in the seizure network was described based on histological (Sanides, 1964; Sanides, 1970), structural (Afif et al., 2010) functional (electrophysiological) and surgical observations (Mesulam et al., 1982; Dupont et al., 2003; Isnard et al., 2004; Shelley et al., 2004; Isnard et al., 2008). Three insula related epileptic networks have been delineated: the insulo-temporo-opercular; the insulo-temporo-limbic and the insulo-frontal network (Munari et al., 1980; Isnard et al., 2000; Isnard et al., 2004; Ryvlin et al., 2005; Isnard et al., 2008; Nguyen et al., 2009).

In the above-mentioned case the challenge was to recognize the relationship between the parietal opercular epileptogenic area and the insular node and the symptomatogenic secondary sensory area. The invasive ictal EEG confirmed the seizure propagation to the insula where the redistribution by the insulo-fronto-medial network was occurring (Isnard et al., 2004; Ryvlin et al., 2005; Nguyen et al., 2009; Afif et al., 2010). Taking into consideration the three insular networks, the question is what factors influence the development of any one particular form? The given structural connections surely became superimposed by the functional epileptic connections and this can be influenced by the epileptogenic tissue transformations related to the epileptic lesion. The occasional conjoined structural networks configure the functional networks (Stam et al., 2012; Park et al., 2013). An epileptic network is formed by that pathological functional connections which are connected with the patients epileptic lesion (Lemieux et al., 2011; Varotto et al., 2012; Stamet al., 2012; Bartolomei et al., 2013). The spatial contexts of the epileptic processes are determined by the functional connectivity and this also explains the remote epileptic seizures. The redistributor function of the insular node raises the connectomic question: why the insulo-fronto-medial network has became the propagation trajectory? The repost is the effective connectivity (Friston, 1994; Wendling et al., 2010; Varotto et al., 2012; van Diessen et al., 2013). The effective connectivity means an actual influence of one region to other region of a concrete epileptic mechanism. In our patient the evolvement of the parieto-insular-fronto-medial network can be interpreted, that the epileptic propensity of this functional insular network was the strongest, compared to the other two insular functional networks.

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CONFLICT OF INTEREST
The authors declare that there are neither financial nor personal relationships that could inappropriately influence this study.

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