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An integrated fMRI, SEPs and MEPs approach for assessing functional organization in the malformed sensorimotor cortex

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Summary
Purpose: Malformations of cortical development are often accompanied by an abnormal cortical pattern. Due to its propensity to involve discrete cortical areas, polymicrogyria represents an interesting model for assessing the reorganization of cortical function in relation to the disrupted anatomy. Functional MRI, TMS and SEPs can provide a highly complementary, multimodal approach to map noninvasively the functional rearrangement of sensorimotor functions in the polymicrogyric cortex, and to obtain a coherent modelling. We report here an illustrative case which is included in a patients series under study using a block design 3 T fMRI, short-latency SEPs as identified on the basis of their latency, polarity, and scalp distribution and an assessment of the area and volume of the motor maps and the relative position of the center of gravity and hot spot.
Results: A 15 years old girl, with drug-resistant epilepsy and left perisylvian polymicrogyria that was part of a large epileptogenic network including also the mesial aspect of the left frontal lobe, exhibited a normal distribution of somatomotor responses in the expected anatomic sites, with a dissociation between motor functions, which were slightly impaired in the malformed hemisphere, and bilaterally normal sensory responses. In this patient, a large resection of epileptogenic zone, sparing eloquent areas as previously identified, should be planned in order to improve seizure outcome.

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Conclusions: An integrated fMRI, TMS and SEP mapping approach helps defining the relationship between epileptogenic zones and somatomotor areas. Studies of greater number of patients will be necessary in order to identify the general rules that determine the functional representation in the malformed cortex.
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Introduction

Malformations of cortical development are accompanied by a remarkable rearrangement of the cortical pattern. To what extent cortical representation of functions is likewise reorganized, is an intriguing question, which is difficult to address in that many patients are either too young or cognitively impaired and, consequently unable to perform functional studies. Polymicrogyria, however, provides an interesting model for studying anatomo-functional reorganization due to its propensity to involve discrete cortical areas. The term polymicrogyria defines an excessive number of abnormally small gyri that produce an irregular cortical surface. The gyral pattern is often abnormal with involvement of primary and secondary sulci in the affected areas. Polymicrogyria can be localized to a single gyrus, involve portions of a hemisphere, be bilateral and asymmetrical, bilateral and symmetrical or diffuse. Sometimes, it is associated with deep clefts that might extend through the entire cerebral mantle to comunicate with the lateral ventricle(schizencephaly).

Extent and location of the cortical abnormality influence the severity of neurologic manifestations (Guerrini et al., 2008). Numerous observations have linked polymicrogyria with a spectrum of epilepsy phenotypes and severity, including cases with good outcome and spontaneous remissions, even after a period of intractability (Guerrini et al., 1998). Diffuse epileptogenesis is frequently encountered, even with seemingly limited abnormalities (Guerrini et al., 1992). Intracranial recordings suggest large epileptogenic networks which extend well beyond the limits of the visible abnormality (Guerrini et al., 1992; Chassoux et al., 2008). Consequently, surgical treatment of epilepsy is applicable to a very limited number of patients in whom large resections are feasible and remission of epilepsy is not expected (Guerrini et al., 1998; Chassoux et al., 2008).

In order to select patients to be included in presurgical evaluation protocol, the assessment of functional organization of polymicrogyric cortex and the correlation between the epileptogenic zone and the eloquent areas is essential. Some studies suggest that polymicrogyric cortex may preserve at least partly somatomotor functions while according to other authors generalization of findings to the entire population of patients with polymicrogyria might be inappropriate, in view of its causal heterogeneity and high degree of histopathologic variability (Guerrini et al., 1992). Differences in cortical representation, have been noticed in relation to the involved modality (Guzzetta et al., 2007).

Functional MRI (fMRI) studies indicate that the polymicrogyric language and motor areas tend to preserve functionality in the expected sites (Araujo et al., 2006). Combined transcranial magnetic stimulation and fMRI studies in one patient with hemiparesis and fronto-temporo-parietal polymicrogyria without clefts demonstrated a preserved primary motor representation of the paretic hand in the contralateral (malformed) hemisphere (Staudt et al., 2004). Conversely, when polymicrogyria was associated with schizencephalic clefts or was part of complex malformations, both putative participation as nonprimary motor areas in an abnormal motor network and the absence of any functional participation were possible (Staudt et al., 2004).

Normal organization of visual areas and processing of visual information has been observed in patients with bilateral parieto-occipital polymicrogyria (Guerrini et al., 1997; Dumoulin et al., 2007).

MEG studies exploring somatosensory reorganization in polymicrogric cortex yielded more challenging results. Burneo et al. (2004) showed that in patients with polymicrogyria, the somatosensory function remained localized in the polymicrogyric rolandic cortex. Conversely, if anatomy was distorted by a schizencephalic cleft, the primary sensory cortex was located in the perirolandic area as long as it was present. When the anatomic area for the rolandic cortex was not present, function was located in the hemisphere ipsilateral to the stimulation in expected anatomic locations (Burneo et al., 2004). Accordingly, somatosensory evoked responses were preserved and originated within the polymicrogyric cortex in patients with bilateral perisylvian polymicrogyria, but the locations of some source components can be grossly shifted (Paetau et al., 2004). In five patients with unilateral polymicrogyria, Ishitobi et al. (2005) reported that the N20m and P38m sources were localized in a normal somatotopic arrangement in the unaffected as well as in the dysplastic hemisphere. However, potential amplitude and dipole orientation were abnormal in the malformed hemisphere, with a high grade of variability, possibly related to variations in extent and distribution of polymicrogyria among patients (Ishitobi et al., 2005). Conversely, a SEP (somatosensory evoked potential) study performed by multichannel recordings, did not find any N20/P20 response in polymicrogyric cortex but the first cortical response was a positive wave that appeared predominantly over the centroparietal area (Saito et al., 2000). These different findings may be partly explained by the different techniques utilized since MEG, provides higher spatial resolution for source analysis than SEP mapping but it can hardly detect the radially oriented dipoles.

The interpretation of SEP findings in patients with polymicrogyria is further challenged by uncertainties about the localization of SEP generators. Short-latency SEPs by median nerve stimulation have been supposed to originate either exclusively in post-central regions (Goff et al., 1977; Allison et al., 1989a, 1991; Valeriani et al., 1998, 2000; Barba and Valeriani, 2004) or also in motor areas (Rossini et al., 1989; Kanovsky et al., 2003; Balzamo et al., 2004) on the basis of scalp and intracranial recordings. By comparing the

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