Letter to the Editor

Mild forms of focal cortical dysplasia: how certain are we?

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The study by Fauser and colleagues on subtypes of focal cortical dysplasia (FCD) and their impact on post-surgical outcome in focal epilepsies (Fauser et al., 2004) focussed on reports of milder forms of FCD, i.e. focal cortical dysplasia type I (Type 1-FCD) and mild malformations of cortical development (mMCD) according to a recent classification system (Palmini et al., 2004). These entities were compared with cases with dysmorphic neurons and balloon cells on histopathology (Type 2-FCD).

The histopathological features used for tissue diagnosis and some of the clinical characteristics reported for Type 1-FCD and mMCD deserve comment. The issue of milder forms of FCD—in particular what tissue findings are needed for diagnosis and whether these categories are useful at all—are matters of ongoing debate in epileptology (Palmini and Lüders, 2002; Palmini et al., 2004). For the presumed milder FCD variants, the uncertainties were emphasized and the hope expressed that ‘the use of the proposed classification scheme in every day practice and for research purposes will refine and validate its usefulness’ (Palmini et al., 2004). The large series presented by Fauser et al. (2004) missed an opportunity to clarify these classifications further since it diverges from the Palmini classification.

It would have been useful for the histological features of FCD 1a and 1b to be specified and reported in more detail. For FCD 1a, Fauser et al. (2004) refer to the finding of ‘dyslamination’ but leave open the definition. A columnar arrangement of cortical neurons as shown in Fig. 1A, however, is perfectly normal in many brain areas, especially temporal gyri (Economo, 1927; Kasper et al., 1999). Some authors even state the loss of vertical architecture as a sign of FCD (Babb et al., 1998). A columnar cellular arrangement could theoretically indicate pathology when found in areas not normally displaying this kind of architecture, but such studies have not been performed. ‘Oligodendrogial clusters’ as shown in Fig. 1B are not mentioned in Palmini’s classification and, to my knowledge, have not yet been described. They are clearly different from the oligodendrogial clusters reported in epilepsy pathology (Kasper et al., 1999), which are located along white matter vessels. Therefore, we do not know which features constituted ‘dyslamination’ and how often they were seen. For the cases diagnosed with FCD 1b (defined by presence of ‘giant’ or ‘immature’ neurons), a more detailed description is needed, especially because immature neurons were not illustrated by Palmini and colleagues. In Fig. 1C, low magnification and missed labelling leave open the precise morphology of the presumed immature neurons. This makes it difficult to establish how often these features were seen alone or in combination.

The definition of the other sub category, mMCD as proposed by Palmini and colleagues (Palmini and Lüders 2002; Palmini et al., 2004), includes more features than neuron counts within the molecular layer and subcortical white matter. It remains unexplained why these two criteria only were chosen to define mMCD by Fauser et al. (2004). Regarding the diagnostic value of these two features, studies on epilepsy molecular layer neuronal counts have not reported any increase in epilepsy cases compared with normal subjects (Jung et al., 1996; Thom et al., 2001). Although an increase in white matter neuronal counts is a consistent finding in morphological studies on temporal lobe epilepsy (TLE) (Rojiani et al., 1996; Emery et al., 1997; Kasper et al., 1999; Thom et al., 2001), this does not necessarily imply a dysplastic pathogenesis of the phenomenon. As discussed previously, the systematic shift towards higher counting values in TLE patient groups compared with controls is also compatible with a secondary pathogenesis related to white matter volume loss (Emery et al., 1997; Kasper et al., 1999). Furthermore, neurons are physiologically present in cerebral white matter, which is particularly pronounced...
within temporal lobes (Rojiani et al., 1996). In summary, it seems inappropriate to classify an individual epilepsy case as dysplastic only by the presence of white matter or molecular layer neurons, or observation of columnar cortical architecture only.

Looking at the clinical data in the Fauser series, it was surprising to find nearly all cases with milder forms of FCD to have been detected by MRI. In contrast, Palmini and Lüders (2002) and Palmini et al. (2004) stated that these are not visible and it is unclear whether they can be visualized by clinical imaging. This discrepancy is left undiscussed, as are the imaging findings. The imaging characteristics of Type-1 FCD and mMCD and the differences between Type 2- and the milder FCDs, which could be used for presurgical differentiation, need to be known. TLE due to hippocampal sclerosis (HS) not uncommonly presents with anterior temporal lobe abnormalities on MRI mimicking some features of FCD. Without the structural basis of these signal changes having been identified (Ryvlin et al., 2002), however, it is not certain that the MRI abnormalities described by Fauser et al. (2004) depend on the histological findings cited. A ‘typical’ MRI showing temporal lobe Type 1-FCD as defined by Fauser et al. (2004) would have been useful.

Finally, the authors’ remarks on dual pathology are confusing. Dual pathology was defined as ‘FCD in temporal location associated with HS’. HS was defined by histology according to Wyler (Wyler et al., 1992). First, it seems inaccurate to include all extratemporal cases in the ‘no dual pathology’ group as the hippocampal formation was not available for tissue examination; but MRI results were not provided. Secondly, in order to draw conclusions about the influence of dual pathology on outcome in TLE, comparison to a group with FCD/no HS and pure HS is necessary. We need to know how many TLE cases displayed classical HS on MRI and how many patients with extratemporal epilepsy had hippocampal changes on MRI. Wieser et al. (2004) recently emphasized that there is no accepted definition of dual pathology and the concept as such needs clarification. A more accurate report of results by Fauser et al. (2004) could have contributed to this important issue.

In summary, it seems premature to draw conclusions on surgical outcome given the uncertainties about presumed milder forms of FCD.

References