

FLUMAZENIL BINDING AND CORTICAL MALFORMATIONS

Central Benzodiazepine Receptors in Malformations of Cortical Development: A Quantitative Study

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PURPOSE: We calculated [^{11}C]flumazenil volume of distribution ($[^{11}\text{C}]\text{FMZ-}V_d$) after correction for partial volume effect in 10 patients with malformations of cortical development (MCDs) and partial seizures, to quantify the γ -aminobutyric acid (GABA_A)-central benzodiazepine receptor complex.

METHODS: Abnormal grey matter and adjacent or overlying cortex were outlined individually and added to an individualized anatomic template for correction for partial volume effect.

RESULTS: Nine of 10 patients showed single or multiple increases or decreases in $[^{11}\text{C}]\text{FMZ-}V_d$ in or around MCDs. Two of three patients with band heterotopia showed multiple increases in the overlying cortex. In three of four patients with subependymal nodular heterotopia, nodules had lower $[^{11}\text{C}]\text{FMZ-}V_d$ than the overlying cortex, which was normal. Decreases in $[^{11}\text{C}]\text{FMZ-}V_d$ were found in two of three clefts and one of six adjacent regions in one schizencephalic patient; another had normal $[^{11}\text{C}]\text{FMZ-}V_d$ in the thickened cortex itself but increases in all adjacent regions. Binding was reduced within focal cortical dysplasia but increased in adjacent cortex. $[^{11}\text{C}]\text{FMZ-}V_d$ was normal within one patient's polymicrogyric cortex but increased in one of six adjacent volumes of interest. The localization of abnormalities correlated with EEG and clinical data in cortical MCDs.

CONCLUSIONS: Flumazenil binding was decreased in some MCDs with increased grey-matter volume and in-

creased in some adjacent or overlying areas of normal-appearing cortex, suggesting functional abnormalities beyond magnetic resonance imaging (MRI)-detectable structural changes.

COMMENTARY

Benzodiazepine receptor imaging with [^{11}C]flumazenil (FMZ) has been used by several groups for the investigation of patients with suspected temporal lobe epilepsy. Although it is very sensitive to the presence of mesial temporal sclerosis, its clinical impact has been muted by the success of magnetic resonance imaging (MRI), as well as ictal single-photon emission computed tomography (SPECT) and fluorodeoxyglucose-positron emission tomography (FDG-PET). However, these techniques are much less helpful in patients with malformations of cortical development (MCDs), who, moreover, may have particularly severe epileptic syndromes and ictal-onset zones that are difficult to localize. Moreover, it has been suggested that poor surgical outcome may be due to the presence of functional abnormalities in cortex (adjacent to malformations) that appears normal on MR. Hammers et al. reported results of benzodiazepine (BZD)-receptor imaging in 10 patients. They performed a very careful partial-volume correction and comparison with normal data. The results showed a highly variable pattern of increases and decreases in FMZ binding, dependent in part on the extent and types of malformations, in both normal and abnormal cortex. The best correlations between PET and EEG data were found in patients with predominantly cortical dysplasia.

This study provides strong support for the hypothesis that functional abnormalities exist in “anatomically normal” regions in patients with MCD. However, their clinical implications are uncertain. Moreover, FMZ-PET remains a research procedure for this patient population.

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