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The Effect of Pyritinol Upon P300 Topography

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The time course of information processing and parts of cognitive functioning can be measured objectively by means of exogenous and endogenous evoked potentials. Reports by Morstyn et al. (1983), Maurer and Dierks (1987, 1988), and Maurer et al. (1988*a*) suggested that topographical P300 patterns may be promising in the evaluation of disturbed information processing in patients with dementia or psychoses and in patients receiving psychopharmacological treatment (Maurer et al. 1988*b*). Maurer et al. (1989) found an amplitude increase of P300 after physostigmine and a decrement after biperiden injection. Depth recordings have suggested that the P300 is generated in allocortical structures such as entorhinal cortex, amygdala, and hippocampal formation (Halgren et al., 1982). The aim of the present investigation was to find out whether pyritinol, suggested in some experiments to enhance cognitive activity, has an effect upon allocortical functioning measured by means of P300 maps.

Six healthy senior citizens of Würzburg (mean age = 70 years) participated in the investigation. The study was performed in a placebo-controlled, double-blind crossover design. P300 was recorded 15 min before and 90, 120, 180, and 220 min after a single oral dose of 600 mg pyritinol. The methodology has already been described by Maurer et al. (1989). For P300 generation the auditory paradigm was used (tone bursts of 50-ms duration, 10-ms rise and fall time, probability for target tones 1:5). Twenty electrodes were placed on the head according to the 10:20 system with an additional Oz electrode and mastoids as reference. EEG was recorded with an epoch length of 1024 ms, sampling rate of 250 Hz, and bandpass 0.1-70 Hz. EOG electrodes were used to prevent artifact contamination in the P300 map. Further data processing was performed on a Brain Atlas III (Bio-Logic Systems Corp.). For data evaluation, reference-independent measurements were used; for statistical comparison, the Mann-Whitney *U* test was used.

Before pyritinol administration, P300 amplitude did not differ significantly in the two groups (placebo: 14.5q3.5fV; pyritinol: 14.2q1.7fV; $p = 0.69$). After pyritinol medication, an amplitude increase was observed ($p = 0.036$; Fig. 1). A comparison between baseline and treatment conditions showed a significant amplitude increase for the pyritinol group and no significant change for the placebo group. No significant changes in localization of topography of mean maxima and minima occurred.

The influence of pyritinol upon EEG parameters in healthy volunteers is well documented (Künkel and Westphal, 1970). The results pointed to a vigilance-

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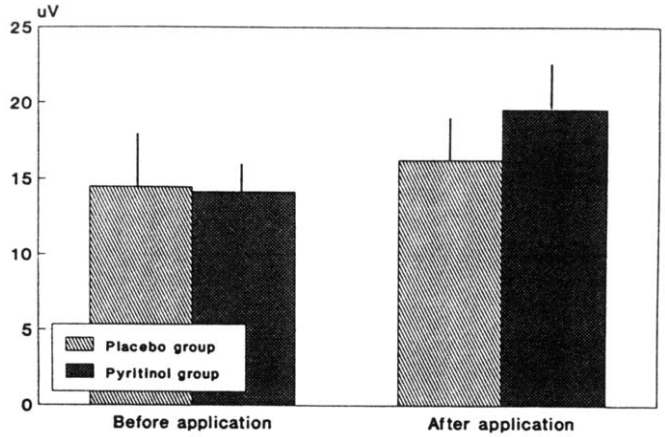
Fig. 1. Amplitudes of P300 before and after pyritinol administration



enhancing effect of the substance. An animal study of spontaneous and evoked electrical activity in the CNS in the cat following acute administration of pyritinol was published by Dolce (1970). Some of the observed changes were interpreted as resulting from an activation of the limbic system and the reticular formation. In stereotactic recordings done by Diemath (1966), evidence was obtained for a pyritinol-induced increase in excitability of structures located in the amygdala and in the gyrus cinguli, i.e., in the limbic system. Ihl et al. (1988) used topographic EEG mapping to study the effects of pyritinol on the electrical activity of the brain in patients with dementia of the Alzheimer's type. This is, to our knowledge, the first report concerning P300 amplitude and topography in elderly subjects treated with pyritinol. The interpretation of P300 amplitude augmentation after drug administration is identical to that given for physostigmine in the report by Maurer et al. (1989, this issue). Pyritinol activates the cholinergic acting cells in the basal nuclei of Meynert and in the medial septum and leads consecutively to a cholinergic reaction in allocortical structures such as entorhinal cortex and amygdala, resulting in an amplitude augmentation. Our data suggest that P300 amplitude and topography may be useful in assessing the influence of drugs on the cholinergic system and on the association cortices, whose structures and function are impaired in dementia of the Alzheimer's type.

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