Study on Sleep Evaluation by Topography Mapping in Normal Volunteers and Aged Patients with Sleep and Cerebrovascular Disorders Following Administration of Zopiclone

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Abstract

The effects of sleeping pills are usually evaluated by interpretation of sleep polysograms but this takes much effort and time. We continuously took electroencephalograms of normal volunteers and aged patients with sleep and cerebrovascular disorders during sleep. After high-speed Fourier transformation, we divided the recordings at all electrodes into six bands, and prepared topography maps from the equivalent potential of each band. We examined if we could evaluate the effects of sleeping pills using topography maps at each stage of sleep. The equivalent potential height of each band during sleep was measured and displayed on a color scale at the same time as spectra for all six electrodes on the topography map. Changes in sleep with passage of time as shown by the trend graph drawn by CSA for the four electrodes (C3, C4, O1, and O2) were observed. As a result, the sleep-inducing effects of Zopiclone in normal volunteers and aged patients with cerebrovascular disorders could be evaluated using topography maps at each stage of sleep using maps made by color scale displays of equivalent potential in each band and spectra of the six electrodes as well as by polosography. Changes in sleep with passage of time could be observed on the trend graph. Normal volunteers given Zopiclone showed that equivalent potentials of δ and θ bands were higher at ST3 and ST4. Aged patients with cerebrovascular disorders showed that equivalent potentials tended to be low.

Predicting Patterns of Clozapine Response in a Group of Chronic State Hospital Schizophrenics

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Reports estimate that 30-60% of treatment refractory schizophrenics show at least a 20% decrease in BPRS when treated with clozapine . We assessed 14 schizophrenics refractory to traditional neuroleptics with MRI to determine whether brain morphology predicts the pattern of clinical response to clozapine after 2, 6 and 12 weeks. Baseline assessment revealed this sample of severely impaired schizophrenics (mean BPRS total=63, SD=10; mean preclozapine standard neuroleptic dose=2009 CPZ mg equiv./day and mean 12 week cloz dose=644 mg/day), relative to healthy controls, had reductions of cortical gray matter volume (mean head size- and age-corrected z-score= -1.55) and increases in cortical sulcal (mean z=.653) and ventricular CSF volume (mean z= 1.50) ; those patients with the highest BPRS total (BPRS tot) and positive symptoms (BPRS pos) tended to have less cortical gray matter volume in the frontal and temporal but not parietal regions ($p \leq .05$), while patients with more negative symptoms (BPRS neg) tended to have *smaller* lateral ventricular volumes ($p \leq .05$). Significant improvement occurred in BPRS pos at 6 weeks ($p \leq .05$) and in BPRS tot at 12 weeks ($p < .05$); paired t-tests for all other BPRS change scores were n.s.. A lower than expected % of subjects achieved a 20% improvement at each time period (0 % at 2 wks, 7 % at 6wks and 14 % at 12 weeks). A cluster analysis of BPRS tot change scores across time periods revealed 3 distinct response patterns: early responders (ER; n=5) improved by 2 weeks, delayed responders (DR, n=5) improved by 6 weeks, and non-responders (NR; n=4) did not improve after 12 weeks. To determine whether these response patterns could be predicted from baseline brain morphology and clinical status, the three groups were compared using non-parametric tests. The ER had significantly less cortical gray matter volume in anterior and temporal regions and more third ventricular CSF volume than either the DR or NR., but DR and NR did not significantly differ. The NR had significantly lower baseline BPRS pos and BPRS tot scores than the DR and the ER; the latter two groups did not statistically differ. In conclusion, the ER had the greatest brain volume deficits and the most severe clinical symptoms at baseline, whereas the NR showed the opposite pattern; the DR showed a mixed pattern, with smaller brain volume deficits but more severe symptoms.

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Angiotensin II Inhibits Inducible Nitric Oxide Formation in Rat Astroglial Cultures.

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Exposure of adult rat astroglial cultures to lipopolysaccharide (LPS) stimulated the formation of nitric oxide as evidenced by a time-dependent increase in NO_2 accumulation after 24 hrs of exposure. Simultaneous addition of angiotensin II (Ang II) with LPS was found to inhibit induction of nitric oxide formation in a dose dependent manner (IC50-1nM). This inhibitory effect was blocked by an Ang II type 1 receptor antagonist losartan but not by the Ang II type 2 receptor antagonist PD123177. Cell pretreatment with Ang II or the simultaneous addition of Ang II with LPS was required for maximal inhibition of NO_2 formation. To determine if LPS and Ang II were acting to alter iNOS gene expression and protein, groups of cells were treated with LPS or LPS+Ang II (100nM). Northern and Western blot analyses indicated that Ang II decreases LPS induced iNOS mRNA and protein levels. Down regulation of protein kinase C by 24 hr pretreatment with PMA abolishes the inhibitory effect of Ang II. Cytokine induction of iNOS with interleukin 1β, tumor necrosis factor-α, and interferon-γ (IFN) is not inhibited by Ang II. Also, the inhibitory effect of Ang II on LPS induction of NO is consistently abolished in the presence of IFN. These results suggest that endotoxin and cytokine induction of iNOS act through different messenger pathways. These results indicate that Ang II has a potentially important role in the intracerebral modulation of endotoxin induced inflammation. Grant support by NIH grant NS-19441, NIAAA AA00127 and an Alcohol Beverage Medical Research Foundation grant.

A double-blind study of paroxetine and maprotiline in major depression.

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A double-blind comparison of paroxetine and maprotiline was undertaken involving both out and in patients presenting with DSMIIIR major depression who achieved a minimum score of 18 points on the 21-item Hamilton Depression Rating Scale (HAMD) at baseline. After a 7 day placebo washout period, patients were randomly allocated to receive paroxetine 20-40mg/d or maprotiline 50-150mg/d, the dose being titrated according to clinical response. Assessments conducted at baseline (day 0) and at the end of weeks 1,3 and 6 included the 21-item HAMD, the Montgomery-Asberg Depression Rating Scale (MADRS) and the CGI. Adverse events were elicited via non-leading questioning. 131 patients (65 paroxetine and 66 maprotiline) were evaluable on an intent to treat basis. The two groups were demographically well matched and demonstrated comparable antidepressant response as evidenced by HAMD MADRS and CGI scores; Adverse events were reported by 57% paroxetine and 67% maprotiline treated patients. Anticholinergic events, were reported by 19% paroxetine and 41% maprotiline treated patients ($p=0.007$). Twelve patients (6 paroxetine, 6 maprotiline) were withdrawn from the study due to adverse events. This study further confirms the efficacy of paroxetine in the treatment of major depression. Significantly more anticholinergic events were reported for maprotiline suggesting a tolerability advantage for paroxetine.