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LACK OF EFFECT OF 6 g INOSITOL TREATMENT ON POST-ECT COGNITIVE FUNCTION IN HUMANS

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Summary—Cholinergic agonists have been reported to ameliorate ECT-induced memory impairment. Inositol metabolism is involved in the second messenger system for several muscarinic cholinergic receptors. Inositol 6 g daily was given in a cross-over double-blind manner for 5 days before the 5th or 6th ECT in a series of patients. No effect was found on post-ECT cognitive impairment.

Introduction

ECT-induced memory impairment may be pharmacologically reversible, and possible drug treatments have been recently reviewed (Khan et al., 1993; Krueger et al., 1992). We have studied vasopressin in ECT-induced memory impairment with negative results (Lerer et al., 1983); naloxone with negative results (Levine et al., 1990); and physostigmine with positive results (Levine et al., 1987). Some theories of ECT-induced memory deficits postulate a cholinergic deficit reversible with physostigmine (Levine et al., 1987), and several muscarinic cholinergic receptors are linked to phosphatidylinositol (PI) as a second messenger. Therefore we hypothesized that exogenous inositol might enhance cholinergic function and reverse ECT-induced memory impairment. When given in doses of 12 g daily, inositol treatment raises human CSF inositol by 70% (Levine et al., 1993). Since there are no previous studies of possible interaction of ECT and inositol, a lower dose of inositol was chosen for study with ECT for safety reasons. We studied the effect of 6 g inositol daily on cognitive effects of ECT in humans.

Subjects: The protocol was approved by the Human Subjects Committee and the Ministry of Health. All patients gave written informed consent. There were 15 subjects including ten females and five males, with a mean age of 49 (range 27–72). Patients were treated with ECT for a variety of indications including DSM-IIIR major depressive disorder (eight patients) schizoaffective disorder depressed (two patients) and neuroleptic non-responsive schizophrenia (five patients). Patients were free of psychotropic medication for at least 7 days before beginning ECT treatment.

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Cognitive function tests were as in Levine et al. (1987) and Levine et al. (1990), and included orientation (place, date, date of birth, country of birth and the name of the hospital and of the treating physician) digit repetition, pictures recall test (a set of 12 pictures of daily occurrences presented to the subjects simultaneously, after which they were withdrawn and the subjects were requested to describe them), story repetition (recall of a story consisting of 20 sentences) and categorization (to list as many objects as they could belonging to each of three categories within 60 s). For story repetition and picture recall tests, three different versions were used, each for a different time point. The different versions were the same used in previous studies (Levine et al., 1987, 1990).

ECT was administered twice weekly, except as below. One hour prior to each ECT treatment all subjects received 1 mg of atropine i.m. and ECT was given by means of a MECTA-SR1 apparatus with bitemporal electrode placement. Anaesthesia was induced by methohexital (1.0 mg/kg) and succinylcholine (0.5 mg/kg), followed by oxygenation (100% oxygen by mask for several seconds). Seizure duration was monitored centrally by the MECTA single channel EEG monitor without a cuff method. A constant current bi-directional, brief pulse square wave stimulus was used. A method of limits procedure was used to determine seizure threshold (Malitz et al., 1982). ECT was given at 20% above threshold, and seizure length was at least 25 s.

The fifth and sixth ECT were each given 6 days after the previous ECT treatment. *Myo*-inositol or dextrose placebo was given for 5 days before the fifth or sixth ECT. The study design was controlled, cross-over double-blind. *Myo*-inositol (Sigma) was given in powder, dissolved in juice, 3 g AM and 3 g PM; placebo was dextrose powder dissolved in juice. Seven patients received inositol first and then placebo, and eight patients vice versa. Cognitive function tests were administered after the fifth ECT and after the sixth ECT. Each of the time cognitive function tests was administered at 20, 60 and 90 min following ECT.

Mean length of seizure was 40.3 ± 13 s for the inositol phase and 40.5 ± 12 s for the placebo phase. The Hamilton Depression Scale (HDS) for depressed patients and BPRS for schizoaffective and schizophrenic patients were administered 24 h following the fifth and sixth ECTs. No differences were found for the inositol versus placebo phases of the study.

Results

Table 1 shows the clinical results at 20 min, 60 min and 90 min after ECT. There were no significant effects of inositol treatment on any of the measures. Forgetting scores (Squire, 1977) calculated for 20–60 min and 60–90 min also showed no significant effect of inositol treatment.

Analysis of data by age (above and below 60), diagnosis and gender showed no difference between placebo or inositol treatments in any subgroup.

Discussion

These results agree with animal results suggesting that inositol depletion is not involved in ECS effects (Patishi et al., in press). Our basic study design was the "preventive model" as defined by Khan et al. (1993), with inositol being given for 5 days before the test ECT.

Table 1
Lack of Effect of Inositol on ECT-induced Cognitive Dysfunction

	20 min		60 min		90 min	
	Placebo	Inositol	Placebo	Inositol	Placebo	Inositol
Orientation	10.20±2.3	10.87±2.8	10.60±1.8	11.27±1.7	10.67±2.0	11.33±1.3
Digital repetition	88.40±39.9	96.67±28.8	97.60±28.3	99.07±29.2	95.60±26.8	97.87±26.7
Story repetition	6.47±5.7	6.53±5.80	9.00±6.3	9.33±6.8	11.66±6.8	12.13±7.1
Visual test	11.73±4.5	11.33±5.60	15.33±3.1	14.07±4.1	17.07±3.5	16.93±3.3
Categorization	7.93±3.3	7.73±2.96	7.67±3.1	5.73±2.7	8.47±2.4	7.67±2.1
Story forgetting score			4.40±4.8	5.07±5.7	2.20±3.7	2.60±4.0
Visual memory forgetting score			4.87±3.1	4.80±5.5	2.80±2.0	2.60±3.9

However, our study has several methodological drawbacks: (1) a low dose of 6 g daily of inositol was used; (2) patients were tested in the hours following the seizure, and the phenomenon studied may have been post-ictal and not true ECT-induced cognitive impairment; (3) patients were not restricted to those developing a specific ECT-induced syndrome of memory impairment; (4) inositol effects may be short-lived, and the last dose of inositol was given the night before testing; and (5) the fifth and sixth ECT treatments were widely spaced and cognitive impairment may thus have been minimized.

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