Seizure (2006) **15**, 509—519

ELSEVIER

SEIZURE

www.elsevier.com/locate/yseiz

Electroencephalographic characterization of scopolamine-induced convulsions in fasted mice after food intake

Asiye Nurten [a,*], **Ilknur Ozen** [a], **Sacit Karamursel** [a,b], **Ihsan Kara** [a]

[a] *Istanbul University, Institute for Experimental Medical Research, Department of Neuroscience, 34280, Istanbul, Turkey*
[b] *Istanbul University, Istanbul Medical Faculty, Department of Physiology, Istanbul 34390, Turkey*

Received 28 November 2005; received in revised form 24 May 2006; accepted 12 June 2006

KEYWORDS
Scopolamine;
Fasting;
Convulsion;
EEG;
Mice;
Food

Summary The present study was conducted to evaluate scopolamine-induced convulsions in fasted mice after food intake effects on the cortical electroencephalogram (EEG). Continuous EEG recordings were taken with Neuroscan for 10 min in freely moving mice with six chronic cortical electrode implants. Animals were weighed and deprived of food for 48 h. EEG recordings were taken at the 24th and 48th hour after their food deprivations. Later, all animals were treated with saline or scopolamine of 3 mg/kg i.p. and EEG recordings were repeated for 10 min. Twenty minutes later, they were given food pellets and were allowed to eat ad libitum. All animals were observed for 60 min to determine the incidence and onset of convulsions and EEG recordings were taken simultaneously. The present results demonstrate that food deprivation causes differences in EEG in the elapsed time. The changes in EEG induced after food deprivation become different with scopolamine administration. In scopolamine treatment group, eating caused a series of high-voltage polyspikes and synchronized spikes with a predominant frequency in the 1—3 Hz range and fast activity that represents a typical epileptiform manifestation. It was concluded that the EEG properties and the behavioral patterns of these convulsions are in accordance with each other.

Introduction

During the training sessions of the experiments investigating the effects of scopolamine on memory and learning processes in mice, we observed that some of the fasted animals exhibited seizures soon after finding and starting to eat the food pellet in the maze. Then, we described that mice treated with scopolamine after fasting for 48 h have developed clonic convulsions soon after allowed to eat ad libitum.[1—4] The additive effect of scopolamine treatment and access to food is essential in the induction of convulsions.[5] Interestingly, scopolamine reverses convulsions elicited by the anticholinesterase compound

* Corresponding author. Tel.: +90 212 414 20 00x33355; fax: +90 212 532 41 71.
E-mail address: nurtena@istanbul.edu.tr (A. Nurten).

1059-1311/$ — see front matter
doi:10.1016/j.seizure.2006.06.006

soman,[6] and muscarinic agonists carbachol,[7] and pilocarpine.[8] It is suggested that scopolamine, as a muscarinic antagonist, blocks postsynaptic muscarinic receptors and produces its anticonvulsive activity via reducing cholinergic transmission. On the other hand, it is shown that the topical administration of scopolamine to the cerebral cortex in high concentrations induces the convulsive activity in electrocorticogram.[9] It is well documented that scopolamine, acting at the presynaptic muscarinic receptors on the cholinergic synapses, also enhances acetylcholine release.[10,11] Thereby, cholinergic hyperactivity due to increased transmission at the cholinergic synapses may lead to convulsions in scopolamine pretreated fasted animals. Also, scopolamine-induced glutamatergic hyperactivity may cause these convulsions, since scopolamine may enhance glutamatergic transmission via antagonizing the presynaptic cholinergic inhibition on glutamate release.[12,13] Changes in [^{3}H] glutamate binding induced by fasting and reversal by scopolamine treatment and food intake have been evaluated as glutamatergic contributions to the underlying mechanism(s) of these convulsions.[3] Previous findings also showed that noncompetitive *N*-methyl-D-aspartate (NMDA) antagonist MK-801,[1] alpha-2 agonists clonidine and tizanidine[2] and dopaminergic antagonists chlorpromazine and haloperidol[3] suppressed these convulsions.

The effects of anticonvulsant drugs on convulsions are also evaluated and it is found that convulsions do not respond to most of the conventional anticonvulsant drugs except valproat, gabapentin and diazepam that markedly reduce the incidence of scopolamine-induced convulsions.[4]

Hypoglycaemia is one of the metabolic derangements that cause convulsions.[14] Previous findings showed that a moderate degree of hypoglycaemia occurs in fasted mice after 48 h of food deprivation and plasma glucose levels increase to fed levels after refeeding for 5—10 min.[3,15,16] Although food intake increases plasma glucose levels immediately near to fed levels in 5 min, plasma glucose concentrations sustain at the same levels after refeeding in scopolamine treated animals. However, hypoglycaemia present in saline or scopolamine treated animals does not cause convulsions in those animals.[3] It was shown in the previous experiments that, while the plasma glucose is at normoglycaemic level, a decrease in the cerebral glucose level could cause convulsions. In glucose transporter type1 (GLUT-1) deficiency[17] where the plasma glucose is at normoglycaemic level while cerebrospinal fluid glucose is at low levels, seizure frequency and intensity increase after fasting for a few hours, predominantly in the morning, before breakfast and rapidly improve after intake of sweets.[18]

The electroencephalographic patterns during scopolamine-induced convulsions in fasted mice after food intake were not described yet. In view of the facts mentioned above, the present study was conducted to evaluate scopolamine-induced convulsions in fasted mice after food intake effects on the cortical electroencephalogram.

Materials and methods

Animals

Inbred albino Balb/C male mice weighing 25—30 g were used. They were housed under standard laboratory conditions for at least 1 week prior to experimentation and were allowed to free access to both food and water. All animal studies carefully conformed to the guidelines outlined in *Interdisciplinary Principles and Guidelines for the Use of Animals in Research and Education* from the New York Academy of Sciences.

Electrode implantation

Animals were anesthetized with thiopental (50 mg/kg i.p.) and positioned in a stereotaxic apparatus. The EEG electrodes were constructed from insulated stainless steel wire (200 μm diameter) with insulation removed at the end to form the contact. Six holes were drilled through the skull, and electrodes were positioned to contact the dura of the frontal, parietal and occipital regions of the cerebrum. A reference electrode was placed above the cerebellum. Electrodes were fixed on the skull with dental acrylic cement. Third-generation cephalosporins seftriakson (75 mg/kg, i.m.) was given single dose as an antibiotic agent after the surgery.

Recording of EEG

Eight days after operation, the experiment was performed in freely moving mice that lived in a Plexiglas recording cage. Animals were placed with their recording cage in a Faraday cage and continuous EEG recordings were taken for 10 min with Neuroscan (SynAmps Model 5083, USA). The behavior of the animals during the EEG recording session was observed. For each animal, a control EEG sample was recorded before the experiment began and was used as a baseline value to compare all subsequent EEG recordings for that animal.

EEG signals were recorded with a band pass of 0.30—70 Hz digitally with a sampling frequency of 1000 Hz. After giving foods, EEG was recorded for 60 min, properties of EEG were specified and power