



Antiepileptic activity of delta sleep-inducing peptide and its analogue in metaphit-provoked seizures in rats

Olivera P. Stanojlović^{a,*}, Dragana P. Živanović^a,
Slobodan D. Mirković^a, Inessa I. Mikhaleva^b

^a Department of Physiology, School of Medicine, University of Belgrade, 11000 Belgrade, Višegradska 26/II, Serbia

^b Shemyakin Institute of Bioorganic Chemistry, Russian Academy of Sciences, Moscow, Russia

KEYWORDS

Metaphit;
Audiogenic epilepsy;
Delta sleep-inducing peptide;
Analogue;
EEG;
Power spectra

Summary

Problem: Previous studies have shown that humoral, endogenous and somnogenic, delta sleep-inducing peptide (DSIP) has influence on insomnia, pain, adaptation to stress, epilepsy, etc. We investigated the potential of DSIP and its analogue DSIP₋₁₂ (a nonapeptide with alanine in position 2 of DSIP molecule substituted by β-alanine) to antagonize metaphit (1-[1(3-isothiocyanatophenyl)-cyclohexyl]piperidine) induced generalized, reflex audiogenic seizures in adult male Wistar albino rats.

Methods: The rats divided in four groups received (i.p.): saline; metaphit; metaphit + DSIP; and metaphit + DSIP₋₁₂, respectively. Metaphit-treated animals displaying seizure in eight previous tests received DSIP or DSIP₋₁₂ and afterwards audiogenic stimuli were applied at hourly intervals for the next 30 h. The animals were exposed to sound stimulation 60 min after metaphit administration and further on at hourly intervals. Incidence and severity of seizures were behaviorally analyzed. Selected EEGs and power spectra were recorded and analyzed.

Results and conclusions: Metaphit led to hypersynchronous epileptiform activity (polyspikes and spike-wave complexes) and increased power spectra 0.5–30 h after the treatment. Severity of metaphit seizures increased with time to reach the peak 7–12 h after injection. DSIP and DSIP₋₁₂ significantly (^{*}*P* < 0.05 and ^{**}*P* < 0.01) increased in δ and θ frequency bands and decreased the incidence, mean seizure grade and duration of metaphit convulsions. The results suggest that DSIP and DSIP₋₁₂ may be considered as potential antiepileptics in the animal model, DSIP₋₁₂ being more efficient than DSIP.

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Introduction

Audiogenic seizures, representing a generalized form of the reflex epilepsy, express typical signs

* Corresponding author. Tel.: +381 11 3611945;

fax: +381 11 3611945.

E-mail address: maxol@eunet.yu (O.P. Stanojlović).

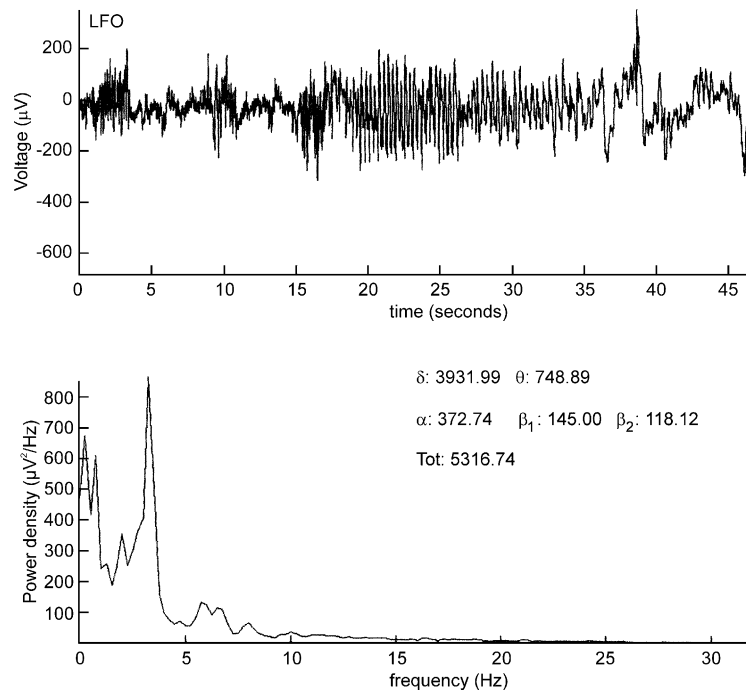


Figure 1 The evolution of EEG changes in one particular metaphit-treated animal (10 mg/kg, i.p.). Spiking of large amplitude and high frequency and their progression into multiple spikes (upper tracings). Power spectra of the corresponding EEG activity started to increase (bottom). Numbers in the lower parts of the figure refer to the absolute power (μV^2) of the δ , θ , α , β_1 , β_2 , bands and of the total (Tot) spectra. LFO: left frontooccipital cortex.

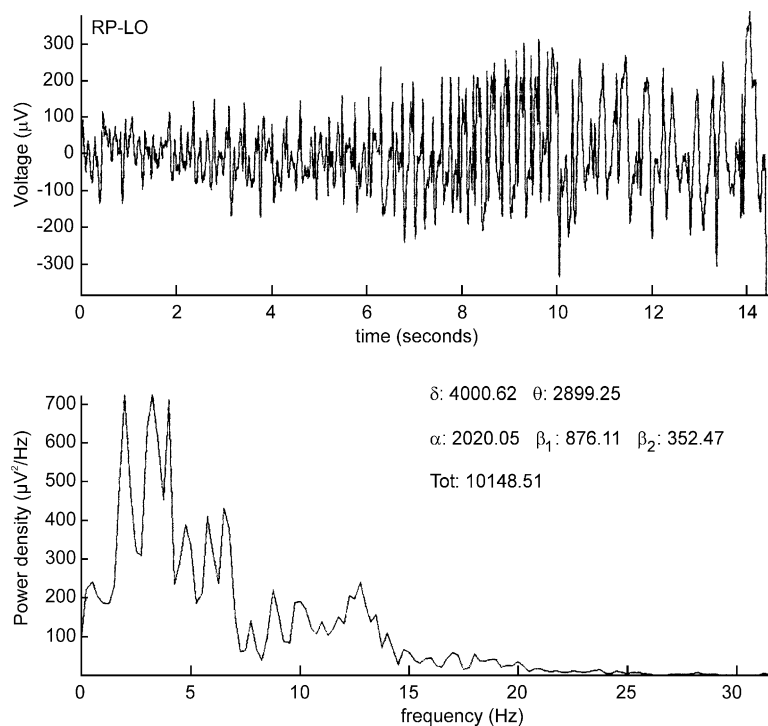


Figure 2 Examples of EEG recording and power spectra following metaphit administration with behavioral seizure grade 3. A high amplitude, low frequency synchronized spiking activity (1–4 Hz) was not terminated with sound offset. Power spectra started to increase with fast tendency in the course of metaphit epilepsy. For the details see caption to Fig. 1. RP-LO: right parietal-left occipital cortex.

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