Sleep wake-cycle disruptions in an animal model of temporal lobe epilepsy

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Introduction: The main goal of this work was to investigate - using *in vivo* electrophysiology - the sleep-wake cycle (SWC) architecture of Wistar rats submitted to the lithium-pilocarpine animal model of temporal lobe epilepsy [1]. Recurrent and spontaneous seizures generated over time in this model are important clues to evaluate both the establishment of epileptic process and SWC quality [2]. Although electrophysiological tracings are valuable approaches to detect sleep abnormalities and to allow differential diagnosis from epilepsy patients, long-term recordings may be very difficult to understand jeopardizing interpretation. To approach this issue, in this work, we used spectral state space maps developed elsewhere [3].

Materials and Methods: Animals in the PILO group (submitted to lithium-pilocarpine protocol) were video monitored and recorded for 9 days consecutively and received diazepam (DZP) injection from days 4 to 6. A second animal group (CTRLPILO) underwent the very same experimental protocol of PILO animals, but receiving vehicle instead of pilocarpine. State space maps were implemented to daily track forebrain dynamics by plotting its spectral content in a two dimensional space in which each axis represents the smoothed principal components of ratios of different frequency bands [3]. The following deriving parameters were assessed: general aspect with cluster relative positions, automatic detection of clusters, stage proportion, area and position of clusters.

Results: Animals of the PILO group showed a baseline decrease of REM stage proportion during non-DZP days, with some recovery when DZP was applied. REM cluster area was also decreased during non-DZP days with partial recovery during days of DZP application. Finally, REM cluster was displaced towards the wake cluster in non-DZP days, with partial recovery in DZP days.

Discussion: Our results show that pilocarpine associated with lithium induces disturbances in SWC dynamics of Wistar rats, corroborating previous electrophysiological studies [4]. During the recovery process after the convulsant insult has been applied, consolidation of aberrant hyperexcitable neuronal connections takes place, which results in recurrent and spontaneous seizures [5]. Both epileptic seizures and functional/structural changes themselves may cause disruptions in the normal SWC architecture. Our results also showed REM sleep recovery during DPZ application to levels similar to those of the control group. Notwithstanding neuropharmacology of DZP in Wistar rats remain unclear, it has proven effective in stopping or attenuating epileptic seizures [6]. Moreover, due to its hypnotic effect [7], DZP has also been widely applied to improve sleep quality under pathological conditions. This suggests that functional and structural mechanisms responsible for restoring normal forebrain dynamics are not completely suppressed in animals early on lithium-pilocarpine administration. Finally, the state space technique allowed us to identify a position shift of the REM stage within the map. This finding shows us that even though the frequency spectrum has not changed visibly, slight changes in spectral signatures may relate to a pathological sleep pattern.

Conclusion: Our results show that the animal model of temporal lobe epilepsy displayed altered SWC and that pharmacological treatment with DZP may have some ameliorating effect.

References: [1] 10.1016/0014-4886(86)90045-2; [2] 10.1097/00004691-200103000-00003;
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