Perfusion MRI changes during status epilepticus in the rat pilocarpine model

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Introduction

There is a known relationship between convulsive status epilepticus (SE) and hippocampal injury, although the precise causes of hippocampal vulnerability remain uncertain[1]. Potential mechanisms of injury include excitotoxicity and ischaemia[1]. It is hypothesised that during the early phase of seizures, CBF increases in the cortex to meet energy demand, but it remains uncertain whether similar changes occur in the hippocampus[2]. Perfusion MRI was performed to test the hypothesis that hippocampal blood flow does not increase as much as cortical blood flow during the course of SE; this would be consistent with an ischaemic contribution to hippocampal injury.

Methods

Ten adult Sprague-Dawley rats were anaesthetised with fentanyl/medetomidine, and placed on a specially modified animal holder to reduce the effects of seizures-associated motion. Methylscopolamine i.p. (1mg/kg) was given to reduce mortality. Either pilocarpine (375mg/kg) (n=7) for induction of SE or saline (n=3) was administered. Diazepam (10mg/kg) was administered i.p. 90 min after the onset of SE. Coronal images were obtained approximately 4.3mm from bregma on a 2.35T horizontal bore SMIS system. Perfusion imaging was performed contiguously for up to 3 hours. For CBF maps, a continuous arterial spin labelling sequence was used with T_1 fits using 8 different TI times with 22 averages. A low average acquisition, consisting of 22 averages, was used so that scans affected by motion could be identified and removed. Five periods were investigated: baseline, after the injection of pilocarpine, early SE, late SE, and post-diazepam. A repeated measures (degrees of freedom-adjusted mixed-model) ANOVA with contrasts to the baseline and the hippocampus was used for statistical analysis. Main effects were: Treatment (Saline, Pilocarpine); Time (Baseline, Pilocarpine, Early SE, Late SE, Diazepam); Anatomy (Hippocampus, Cortex)

Results

Figures 1 and 2 show the perfusion changes during SE. Significant differences were found between the hippocampus and the cortex in experimental but not in control animals ($F = 14.73$, $p = 0.005$). When compared to baseline, there was a significant difference between hippocampal and cortical blood flow in the experimental animals, compared to control animals, after injection of pilocarpine ($F = 9.45$, $p = 0.014$) and in the first 30 minutes of SE ($F = 6.87$, $p = 0.031$). No significant differences were observed for the late SE period ($F = 1.76$, $p = 0.221$) or following diazepam injection ($F = 0.162$, $p = 0.698$).

Discussion and Conclusion

These data indicate that there are differences in regional CBF responses to pilocarpine-induced SE in the cortex and the hippocampus. Seizure activity in combination with increases in glucose and O_2 utilisation have been reported in the cortex and the hippocampus during SE, and demonstrate higher energy requirements during SE[3,4]. In this study increases in cortical CBF were observed during the early stages of SE, only a limited CBF change was observed in the hippocampus. The subsequent lack of difference between the two regions during the later stages of SE may reflect the hypothesised local failure of the vascular system due to persistent seizure activity[1,5]. Taken together, these data support the hypothesis that relative ischaemia in the hippocampus during SE may underlie its selective vulnerability to seizure activity.

References

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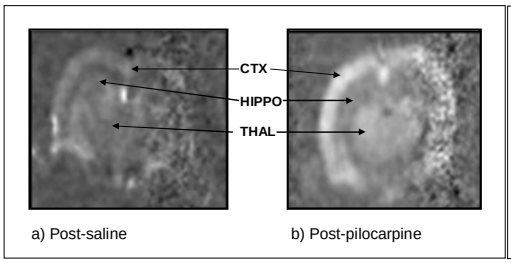

Figure 1. *Perfusion-weighted images post-injection from a) a saline-injected animal and b) a pilocarpine-injected animal.*

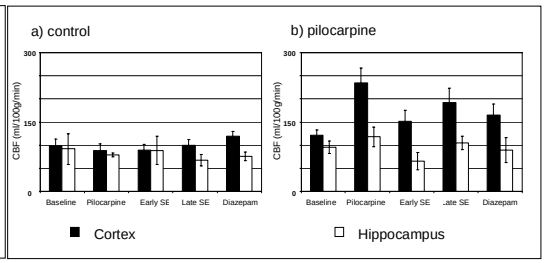

Figure 2. *Mean (sem) CBF measurements over the course of SE in the cortex and the hippocampus in a) saline-injected controls (n=3) and b) pilocarpine-injected animals (n=7)*