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Synchronized gamma oscillations (30–50 Hz) in the amygdalo-hippocampal network in relation with seizure propagation and severity

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ABSTRACT

In this study, we demonstrate that gamma oscillations (30–50 Hz) recorded in the local field potentials (LFP) of the hippocampus are a marker of temporal lobe seizure propagation and that the level of LFP synchrony in the amygdalo-hippocampal network, during these oscillations, is related to the severity of seizures. Sprague–Dawley rats were given a single systemic dose of kainic acid (KA; 6 mg/kg, i.p.) and local field potential activity (1–475 Hz) of the dorsal hippocampus, the amygdala and the neocortex was recorded. Of 135 ictal discharges, 55 (40.7%) involved both limbic structures. We demonstrated that 78.2% of seizures involving both the hippocampus and amygdala showed hippocampal gamma oscillations. Seizure duration was also significantly correlated with the frequency of hippocampal gamma oscillations ($r^2 = 0.31$, $p < 0.01$) and LFP synchrony in the amygdalo-hippocampal network ($r^2 = 0.21$, $p < 0.05$). These results suggest that gamma oscillations in the amygdalo-hippocampal network could facilitate long-range synchrony and participate in the propagation of seizures.

Introduction

Mesial temporal lobe epilepsy (MTLE) represents the most common form of refractory epilepsy. Due to several evidences linking the hippocampus and parahippocampal regions to seizures, these regions appear to be key structures involved in epilepsy (Sharma et al., 2007; Zhang et al., 2002). Indeed, several studies have shown that MTLE is often related to histopathological lesions of the hippocampus, that include neuronal loss in the CA1 and CA3 regions, and mossy fiber sprouting in the inner molecular layer of the dentate gyrus (Falconer et al., 1964; Guimarães et al., 2007; Keller and Roberts, 2008; Quigg et al., 1997; Sutula and Roberts, 2007; Xu et al., 2007). In animal models of MTLE, results have shown that chemically-induced seizures lead to electroencephalographic abnormalities and abnormal neuronal reorganization in the hippocampus similar to those observed in epileptic patients in post-mortem studies (Ben-Ari, 1985; Bouilleret et al., 1999; Nadler, 1981).

Functional alterations of extrahippocampal structures of the mesial temporal lobe such as the amygdala, are also believed to be involved in epileptiform brain activity (Aroniadou-Anderjaska et al., 2008). Although the correlation between changes recorded in the amygdala and the occurrence of seizures is less clear than for the hippocampus, neuronal loss and gliosis of this region are sometimes observed in patients with temporal lobe epilepsy (Bernasconi et al., 2005; Yilmazer-Hanke et al., 2000). Moreover, animal studies have shown that the amygdala is very susceptible to kindling, following repeated electrical stimulation (Blumenfeld et al., 2007; Goddard 1967; Goddard et al., 1969, McNamara, 1984; McIntyre et al., 2002; Morimoto et al., 2004). Finally, in patients with refractory epilepsy, amygdalectomy alone has been considered as an effective method to control seizures (Feindel and Rasmussen, 1991; Jooma et al., 1995; Paglioli et al., 2006; Wieser, 2000).

Although seizure onset zones have not been clearly identified, there is evidence that suggests that the amygalo-hippocampal complex is primarily involved in human and animal models of MTLE (Bertram, 2008; McIntyre and Gilby, 2008). From a physiological perspective, studies have shown that such regions are characterized by synchronous oscillations at seizure onset, in the low and high frequency bands (Bartolomei et al., 1999, 2004; Bettus et al., 2008; Gotman and Levtova,

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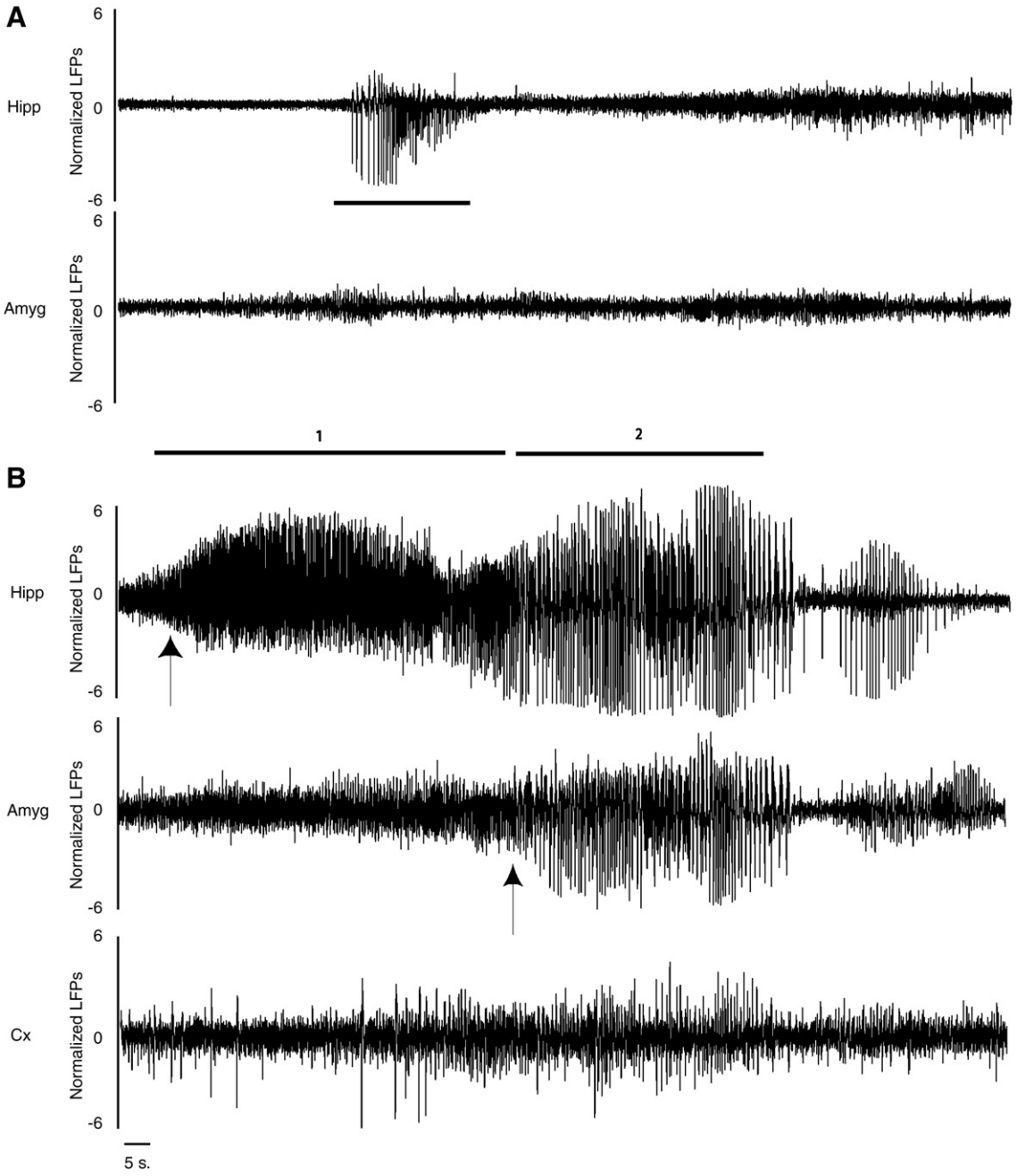
A
Hipp
Amyg
Normalized LFPs
6
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-6
1
2
B
Hipp
Amyg
Cx
Normalized LFPs
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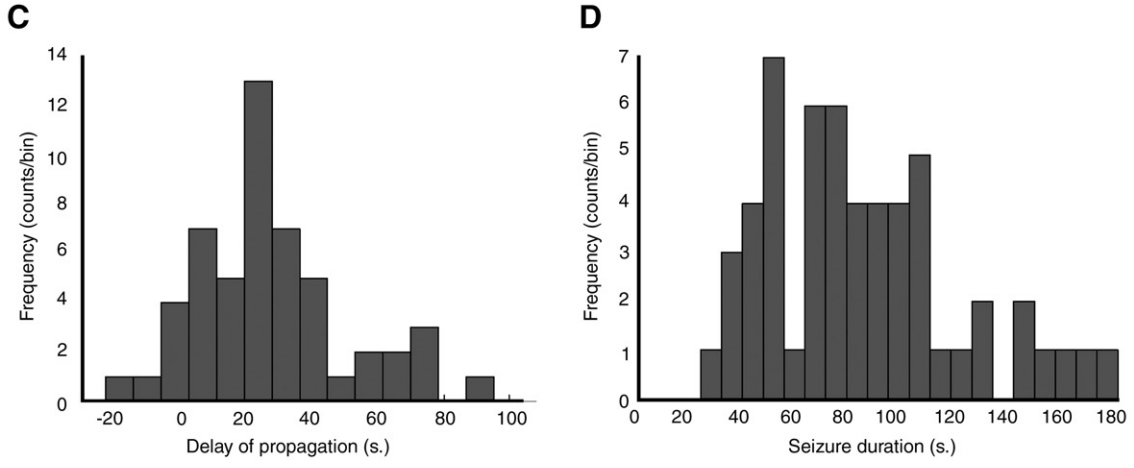
C
Frequency (counts/bin)
Delay of propagation (s.)
D
Frequency (counts/bin)
Seizure duration (s.)