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Research Report

Seizure activity affects neuroglial Kv1 channel immunoreactivities in the gerbil hippocampus

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ABSTRACT

In order to confirm the species-specific distribution of voltage-gated K^+ (Kv) channels and the definitive relationship between their immunoreactivities and seizure activity, we investigated Kv1 channel immunoreactivities in the hippocampus of seizure resistant (SR) and seizure sensitive (SS) gerbils. There was distinct difference of the Kv1 channel subtypes immunoreactivity in the hippocampi in both SR and SS gerbils. Kv1.1, Kv1.2, Kv1.3, Kv1.4, and Kv1.6 immunoreactivities in the SS gerbil hippocampus were lower than that in the SR gerbil hippocampus. However, Kv1 immunoreactivities were obviously presented in astrocyte within the stratum radiatum of the CA1 region of pre-seizure SS gerbil hippocampus. Following seizure-onset, Kv1 immunoreactivities (except Kv1.5) were markedly elevated, whereas their immunoreactivites in astrocytes were down-regulated. Therefore, the present study demonstrates that seizure activity may distinctly affect neuroglial Kv1 immunoreactivities in the gerbil hippocampus.

1. Introduction

Voltage-gated K^+ (Kv) channel activation following an action potential is a major regulatory influence in determining the degree of repolarization and the repetitive neuronal firing (Hille, 1992). In mammals, Kv channels are divided into four subfamilies (Kv1–Kv4), which differ in terms of their primary structures, biophysical properties, and subcellular localization (Chandy and Gutman, 1993).

Epilepsy is a chronic condition characterized by the presence of spontaneous episodes of abnormal neuronal discharges (Margerison and Corsellis, 1966; Wittner et al., 2001), and it is likely that Kv channels are potential mediators of the pathogenesis of epilepsy (Wickenden, 2002). Of these Kv channels, Kv1 (Shaker) subfamily contributes to differences in the seizure susceptibilities of brain areas (Madeja et al., 1997). Indeed, mutations or down-regulations of Kv1 channels lead to a variety of symptoms indicative of excessive neuronal excitability including epilepsy (Browne et al., 1994; Zuberi et al., 1999; Tsaur et al., 1992).

Mongolian gerbil provides an opportunity for investigators to identify neurological factors that correlate with seizure behavior since seizure activity in this animal begins at ~2 months old. Mongolian gerbil exhibits seizure activity in response to a variety of stimuli without the neuronal degeneration associated with the use of neurotoxins like kainate. In addition, this model allows epileptic and non-epileptic animals to be directly compared, which allows differences in brain anatomy and electrophysiology differences correlated with seizure behavior to be identified (Buchhalter, 1993; Peterson and Ribak, 1987; Kang et al., 2003a,b,c,d,e, 2005; Loskota et al., 1974a; Paul et al., 1981). Moreover, the seizure activity in this animal model has been linked to the functional alteration of various ion channels/

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transporters (Kang et al., 2003a,b,c,d,e, 2004a,b; 2005; Kim et al., 2005; also see review, Buckmaster, 2005). Although the localization of Kv1 channel immunoreactivity in the gerbil hippocampus is likely to be species-specific (Park et al., 2001), it is not known whether Kv1 channel immunoreactivity differs in seizure resistant (SR) and seizure sensitive (SS) gerbils. Thus, the possibility cannot be excluded that spatio-temporal alterations in Kv1 subfamily expression in the gerbil hippocampus may be the results of seizure activity. Therefore, in the present study, we investigated Kv1 subfamily channel immunoreactivities in the gerbil hippocampus following spontaneous seizures to confirm the

Table 1 – Summary of the distributions of Kv1 channels in the rodent hippocampus

Subunit	Species (strain)	Regions								References
		SP	SR	SO	SL	SLM	GL	ML	HR	
Kv1.1	Rat	+++, IN	+++	+++	+++	–	ND	+++	ND	Rhodes et al. (1997)
		–	+++	+++	+++	–	–	+++	–	Monaghan et al. (2001)
		++, CA1* +++, CA3*					+++*			
		ND	ND	ND	+++	ND	+++	+++	+++	Veh et al. (1995)
	Mouse	–	+++	+++	+++	–	–	+++	+++, IN	Wang et al. (1994)
		+++*					+++*		+++*	
		+	+	+	ND	ND	+	+	ND	Grosse et al. (2000)
	Gerbil	++, CA1 +++, CA3	++	++	ND	ND	+++	–	ND	Park et al. (2001)
	SR	+, CA1 ++, CA3	+	+	–	–	+++	+	++, IN	The present study
	SS	–, CA1 ++, CA3	+	+	–	–	+	+	+, IN	The present study
Kv1.2	Rat	++, IN	–	–	–	++	+	+++	–	Rhodes et al. (1995)
		ND	ND	ND	–	++	ND	+++	ND	Rhodes et al. (1997)
		– +++*	+	+	–	+++	– +++*	+++	–	Monaghan et al. (2001)
		ND	ND	ND	+	ND	ND	+++	+	Veh et al. (1995)
		+++, D +++*	–	–	–	+++	– +*	+++	+++, D +++*	Sheng et al. (1994)
	Mouse	– +++*	–	–	–	++	– +++*	+++	– +++*	Wang et al. (1994)
		–	+	+	ND	ND	–	+	ND	Grosse et al. (2000)
	Gerbil	+	ND	ND	ND	ND	+	+++	+++, IN	Park et al. (2001)
	SR	++ +++ IN	++	–	–	++	–	++	+++	The present study
	SS	– +++, IN	++	–	–	++	–	++	+++, IN	The present study
Kv1.3	Rat	ND	ND	ND	+++	ND	ND	ND	+++	Veh et al. (1995)
	Mouse	+++	+	–	–	ND	+++	ND	ND	Grosse et al. (2000)
	Gerbil	–	ND	ND	ND	ND	–	–	ND	Park et al. (2001)
	SR	+++ ++, IN	–	–	–	–	–	–	+++, IN	The present study
	SS	+ ++, IN	–	–	–	–	–	–	++, IN	The present study
Kv1.4	Rat	++, IN	–	–	+++	++	+	+++	–	Rhodes et al. (1995)
		+++, IN	++	++	+++	++	ND	+++	ND	Rhodes et al. (1997)
		– +++*	++	++	++	++	– +++*	++	–	Monaghan et al. (2001)
		– +++*	+	+	+++	++	– +++*	+++	+++ +++*	Sheng et al. (1992)
		+	+++, CA1 +, CA3	+++, CA1 +, CA3	++	+++, CA1 +, CA3	++	+	+++	Lujan et al. (2003)
		–	–	–	+++	ND	–	+++	+++	Maletic-Savatic et al. (1995)
		–	+	+	+++	++	–	+++	+++	Cooper et al. (1998)
		ND	ND	ND	+++	ND	+	+++	+	Veh et al. (1995)
	Mouse	–	+	–	+++	ND	–	++	ND	Grosse et al. (2000)
	Gerbil	+++	ND	ND	ND	ND	+++	–	+++	Park et al. (2001)
	SR	++	++	++	+++	++	++	+	++	The present study
	SS	–	++	++	+++	++	+	+	–	The present study
Kv1.5	Rat	+++	+++, IN	+++, IN	–	ND	+++	–	+++, IN	Maletic-Savatic et al. (1995)
	Mouse	–	+	–	ND	ND	–	–	ND	Grosse et al. (2000)
	Gerbil	–	++	++	ND	ND	–	++	ND	Park et al. (2001)
	SR	–	+	+	+	+	–	+++	–	The present study
	SS	–	+	+	+	+	–	+++	–	The present study
Kv1.6	Rat	+++, IN	+++, IN	+++, IN	ND	ND	ND	+++	ND	Rhodes et al. (1997)
		ND	ND	ND	+++	ND	+++	+++	+++	Veh et al. (1995)
	Mouse	–	+	+	ND	ND	–	+	ND	Grosse et al. (2000)
	Gerbil	+++	ND	ND	ND	ND	+++	–	+++	Park et al. (2001)
	SR	++	–	–	–	–	+	–	++	The present study
	SS	–	–	–	–	–	–	–	–	The present study

–, absent; +, weak; ++, moderate; +++, strong; ND, non-description; IN, interneurons; * mRNA expression; D, proximal dendrites.