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Research Report

The densities of calbindin and parvalbumin, but not calretinin neurons, are sexually dimorphic in the amygdala of the guinea pig

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ABSTRACT

In the amygdala, the calcium-binding proteins (calbindin, parvalbumin or calretinin) are useful markers of specific subpopulations of γ-aminobutyric acid (GABA) containing neurons. In the rat and monkey they together mark the vast majority of GABA-containing neurons in this brain region. As GABA involvement in the control of various behaviors in a sex-specific manner and sexual dimorphism of the GABAergic system itself were recently proven, the question is how much dimorphic may be various subpopulations of this system. Thus, the present study investigates for the first time the presence/absence of sexual dimorphism among neurons expressing calbindin (CB), parvalbumin (PV) and calretinin (CR) which form in the amygdala main subsets of GABAergic system. The results show that in the amygdala of the guinea pig the densities of CB and/or PV expressing neurons are sexually dimorphic with the female>male pattern of sex differences in the basolateral amygdala. In the medial and cortical amygdala respectively CB and PV values are also sexually dimorphic, favoring males. The densities of CR expressing neurons are in the amygdala of the guinea pig sexually isomorphic. In conclusion, the results of the present study provide an evidence that in the amygdala of the guinea pig the densities of neurons expressing CB and/or PV are sexually dimorphic what supports the idea that GABA participates in the mediation of sexually dimorphic functions, controlled by this brain area.

1. Introduction

The amygdala is a set of nuclei and cortical regions located within the temporal lobe. It is known to be involved in several important aspects of emotion including the appreciation of affectively significant stimuli, the formation of stimulus-reward associations, the generation of emotional behavior and the formation and retrieval of emotional memories, particularly those related to fear and anxiety (Adolphs et al., 1994; LeDoux, 2000; Sah et al., 2003; Pape and Pare, 2010)·

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Moreover, many studies indicate that this part of the brain is also strongly involved in the integrative circuitry mediating pheromonal and reproductive functions (Baum, 2009; Kevetter and Winans, 1981; Martel and Baum, 2009; Morris et al., 2008; Segovia et al., 2006) as well as various aspects of its anatomy and physiology seem to be sexually dimorphic (Hamann, 2005; Fagergren and Hurd, 1999; King et al., 1999; Morris et al., 2008; Rollins and King, 2000; Równiak, 2013; Segovia et al., 2006; Swaab et al., 2003).

An important role in the sexually dimorphic functions mediated by the amygdala and other brain structures may be played by cells which contain γ-aminobutyric acid (GABA). For example, it has become evident that GABA is involved in steroid induced negative feedback control of luteinizing hormone-releasing hormone (Grattan and Selmanoff, 1993) and plays a critical role in the modulation of gonadotropin and prolactin release from the pituitary gland (Lieb et al., 1994; Moguilevsky et al., 1991, 1992). GABA participates in the neural circuitry controlling lordosis behavior by exerting dual effects, i.e. facilitation of lordosis through acting in the medial hypothalamus and the midbrain central grey and inhibition of lordosis through actions in the preoptic area (McCarthy et al., 1991a, 1991b). Maternal behavior is also connected with the functioning of the GABAergic system. An implication of GABAA-benzodiazepine receptor complex in the development of maternal behavior in female rats has been described (Del Cerro et al., 1995). GABA inhibitory mechanisms also regulate male sexual behaviors. Likewise, corticosterone mediates the stress-induced inhibition of male sexual behavior through the GABAergic system (Boyd and Moore, 1990; Naumenko and Serova, 1990). Finally, it is worth mentioning that in the amygdala and various other brain structures GABAergic populations are sexually dimorphic (Stefanova, 1998; Stefanova et al., 1997a; Yahr, 2011).

The amygdala has a large population of GABAergic neurons (Pitkänen and Amaral, 1994). It is known that in the majority of them, GABA coexists with different calcium-binding proteins

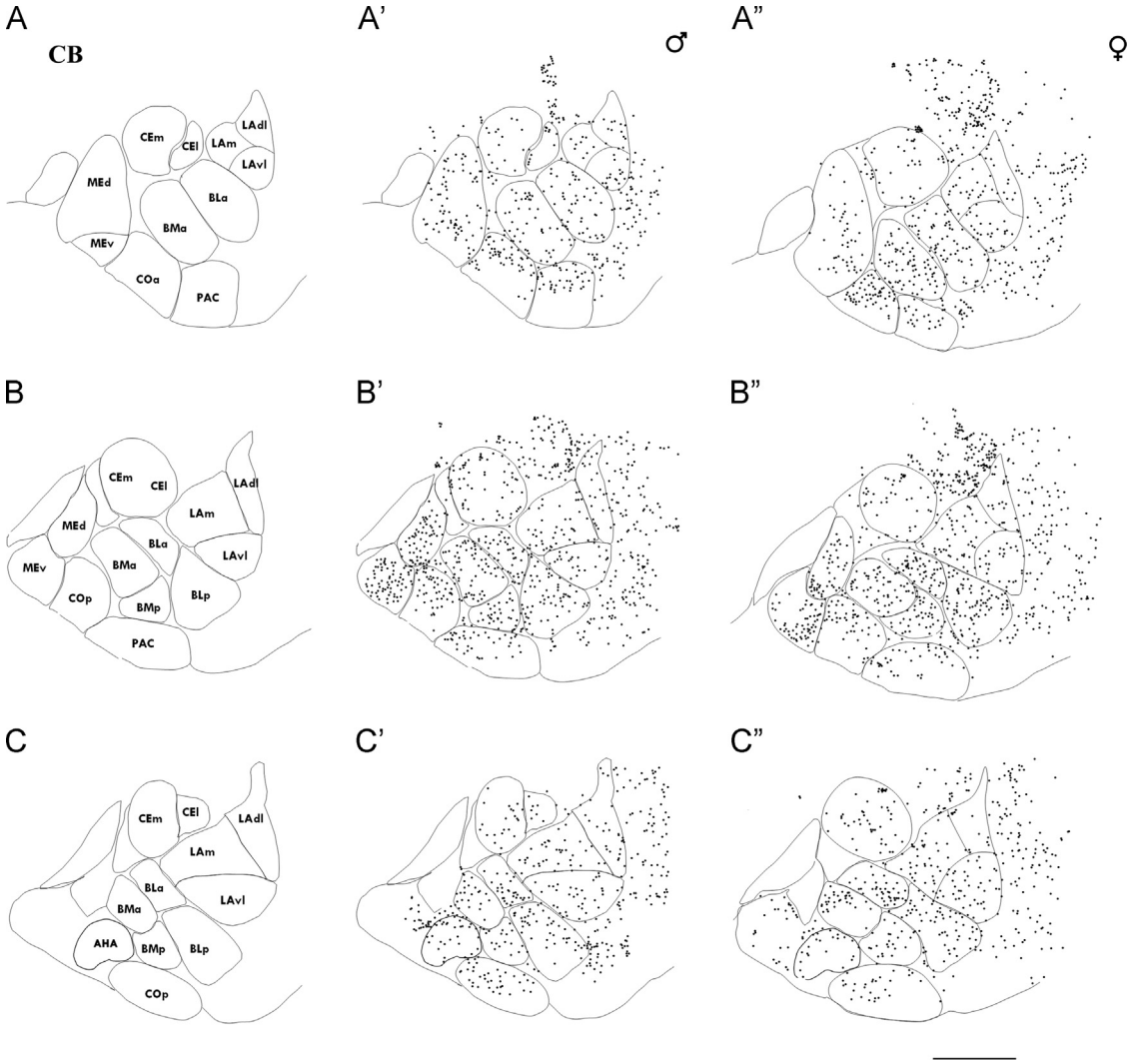

Fig. 1 – Computer-generated plots illustrating the distribution of CB+ neurons in the various nuclei and cortical regions of the guinea pig amygdala in the male (A′, B′, C′) and female (A″, B″, C″) subjects. Each dot represents one immunostained neuron. Three coronal levels are presented (A′, A″ are the most rostral and C′, C″ are the most caudal). Note the differences in the density of neurons between male and female subjects, between various nuclei on the section and between the sections from the single nucleus. Scale bar=2000 μm in C″ (applies to all sections).