Brain Research Bulletin 96 (2013) 10–18

Contents lists available at SciVerse ScienceDirect

Brain Research Bulletin

journal homepage: www.elsevier.com/locate/brainresbull

Research report

Hippocampal theta rhythm induced by rostral pontine nucleus stimulation in the conditions of pedunculopontine tegmental nucleus inactivation

Paweł Matulewicz, Magda Kuśmierczak, Jolanta Orzeł-Gryglewska, Edyta Jurkowlaniec*

Department of Animal and Human Physiology, University of Gdańsk, Wita Stwosza 59 St., 80-308 Gdańsk, Poland

ARTICLE INFO

Article history:
Received 28 January 2013
Received in revised form 12 April 2013
Accepted 14 April 2013
Available online 28 April 2013

Keywords:
Theta
PPN
RPO
Carbachol
Electrical stimulation

ABSTRACT

Theta rhythm in rat hippocampus occurs during cortical activation in different forms of waking as well as during paradoxical phase of sleep. The multi-level regulatory system of theta, based mainly on cholinergic transmission, includes structures from the forebrain to the medulla. Among them the most important are two reticular nuclei: the pedunculopontine tegmental nucleus (PPN) and rostral pontine tegmental nucleus (RPO). Functional relations between these two nuclei are still unidentified. It is known that cholinergic stimulation of these nuclei with carbachol leads to induction of theta in the hippocampus. Electrical stimulation has the same effect but only when applied to the RPO. In our experiments, performed on urethanized rats, each of these two methods was applied to the RPO with the PPN being inactivated in the contralateral hemisphere. We found that inactivation of the PPN does not suppress theta induced with carbachol microinjection into the RPO, but completely blocks theta induction with electrical stimulation of the RPO. The results suggest the important role of the PPN in theta rhythm generation from brainstem level, depending on the method of theta rhythm induction, i.e. cholinergic or electric stimulation of the RPO.

© 2013 Elsevier Inc. All rights reserved.

1. Introduction

Theta rhythm is a slow, synchronized EEG activity with a frequency of 4–8 Hz and amplitude of 20–60 μV in humans (Niedermeyer and Lopes da Silva, 2005; Walter and Dovey, 1944). In rodents, which are used as the animal model in studies of the rhythm, theta waves are recorded with deep, hippocampal electrodes and their frequency range from 3 to 12 Hz depending on physiological conditions. The amplitude can reach a value of up to 2000 μV (Bland, 1986). Due to larger frequency range than in humans, this type of signal in rats was initially described as rhythmic slow activity (RSA) (Vanderwolf, 1988; Vanderwolf and Robinson, 1981), while now the term theta rhythm (Bland and Oddie, 2001; Kavanau, 1998; Vertes and Kocsis, 1997) is commonly used. Theta is always present during states of increased activation of the cortex, i.e. waking and paradoxical sleep phase (Jones, 1998). Theta is parallel to cortical high-frequency beta and gamma rhythms (Leung, 1998; Maloney et al., 1997; Steriade, 1998), which are indicators of this cortical activation. The source of the theta rhythm are deep cortical structures: the hippocampus in animals and presumably anterior part of the cingulate cortex in humans (Nishida et al., 2004). Theta presence has been demonstrated in humans during cognitive (Basar et al., 2000; Burgess and Gruzelier, 1997) and memory processes (Basar et al., 2001; Klimesch, 1999; Wiebe and Staubli, 2001; for review see Battaglia et al., 2011). Theta waves are considered to play a primary role in the memory traces formation, by taking part in long-term synaptic reinforcement (LTP, long-term potentiation) (Abel and Kandel, 1998; Eichenbaum et al., 1992). It is believed that theta plays a vital role in sensorimotor integration (Bland and Oddie, 2001; Caplan et al., 2003; Cruikshank et al., 2012), as well as spatial orientation (Caplan et al., 2003; O'Keefe and Recce, 1993; Skaggs and McNaughton, 1996). Theta rhythm may be associated with synchronization of functional neuronal assemblies, and even groups of brain structures (Basar et al., 2001; Steriade, 1998). On the other hand, the increase in signal power in the theta frequency can be considered as a physiological marker of neurodegenerative processes, such as Alzheimer's disease (Montez et al., 2009; Prichep et al., 2006; Roh et al., 2011; Van der Hiele et al., 2007) or epilepsy (Beleza et al., 2009; Clemens, 2004; Clemens et al., 2010). Theta relationship with such altered states of central activation remains the cause of the continuous interest of researchers and encourages them to use animal models of this rhythm.

In animals, theta rhythm occurs during interaction between neurons of the medial septum, diagonal bundle of Broca and the hippocampus (Vertes et al., 2004). Many other structures are

* Corresponding author. Tel.: +48 58 523 61 20; fax: +48 58 523 61 21.
E-mail address: edyta.jurkowlaniec@biol.ug.edu.pl (E. Jurkowlaniec).

0361-9230/$ – see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.brainresbull.2013.04.005

involved in the regulation of the rhythm: the limbic cortex (entorhinal and cingulate), basal nuclei, hypothalamus (mammillary body), pontine nuclei: pedunculopontine tegmental nucleus (PPN) and rostral pontine tegmental nucleus (RPO) and the gigantocellular nucleus of the medulla oblongata. These structures form the "theta rhythm synchronization system" described by Bland and Oddie (1998). Our research indicates that this system can also include the midbrain ventral tegmental field (VTA) (Jurkowlaniec et al., 2003; Orzeł-Gryglewska et al., 2006, 2007, 2010, 2012). A characteristic feature of the structures belonging to this system remains that theta rhythm can be induced by their electrical stimulation or through direct microinjection of acetylcholine analog – carbachol, or other pharmacological agents.

Theta rhythm can be recorded through chronically implanted electrodes in the hippocampus in freely moving animals. This method can be regarded as tedious as it requires waiting for the spontaneous appearance of the rhythm during waking (exploratory reactions with high-frequency theta, i.e. 6–13 Hz), freezing (in anticipation of a stimulus) or during paradoxical sleep phase (low-frequency theta, 3–6 Hz). The urethanized animal model, usually a cat or a rat, is also used. Urethane anesthesia does not block the occurrence of hippocampal theta rhythm and if the anesthesia is not too deep, the rhythm can occur spontaneously (such a model was used in the studies by Bland et al., 1995, 1994; Bocian et al., 2009; Gołębiewski et al., 1999). Theta can be induced also by intracerebral microinjection of carbachol into specific brain structures. The method of carbachol-induced theta has been widely discussed in the work of Kubin (2001). In deep urethane anesthesia (where spontaneous episodes of theta rhythm do not occur) the rhythm can be elicited using electrical stimulation as well as sensory stimulation, the so-called tail-pinch method (Bland et al., 1995, 1994; Hanada et al., 1999; Kirk and McNaughton, 1991; Nunez et al., 2002, 1991; Vertes and Kocsis, 1997; Yoder and Pang, 2005), and these methods are also often used in our laboratory (Kroplewski et al., 2010; Leszkowicz et al., 2007; Leszkowicz and Trojniar, 2005; Matulewicz et al., 2010; Nowacka et al., 2002), including the current work. The present study aimed at examining whether blockade of the PPN would affect the possibility of theta rhythm generation by the RPO. Despite many years of research, functional interrelations between these two reticular nuclei in the regulation of theta rhythm are still not definitively characterized. Many authors have attributed a critical role in regulating the theta rhythm to the second of these nuclei, the RPO. For example Nunez et al. (1991), having observed increase in cell discharges in this nucleus during sensory-induced and spontaneous episodes of theta rhythm after local injection of carbachol, suggested that the RPO is essential for the regulation of hippocampal oscillatory activity. Also Vertes (1981), Vertes et al. (1993) considers the RPO to play a particular role in theta regulation because its electrical stimulation induces theta rhythm at the lowest threshold, and after the RPO cholinergic stimulation theta rhythm appears with relatively short latency compared to stimulation of other nuclei (PPN or reticular tegmental nucleus, RTG). Hanada et al. (1999) argue that most of the cells classified as theta-on (with a maximum activity during theta rhythm) is located precisely in the RPO. In many models electric stimulation of the RPO is a standard method for obtaining hippocampal theta rhythm (Bland and Oddie, 1998; Kirk and McNaughton, 1991; Vertes and Kocsis, 1997). It is interesting that damage to the structure either does not affect characteristics of theta rhythm, or the effect is negligible (Faris and Sainsbury, 1990). Horner and Kubin (1999), when inducing theta rhythm with carbachol microinjection into the RPO, showed that in this nucleus there are also ineffective places from which theta cannot be elicited. Nunez et al. (1991) estimate that about 30% of RPO neurons reduce their activity during electrically induced theta rhythm.

As shown by Vertes et al. (1993), increased cholinergic transmission within the PPN produces theta rhythm in the hippocampus. However, the authors believe that the place of the PPN in the regulation of theta rhythm is rather subordinate to the RPO, which is indicated by longer latency of theta after direct injection of cholinomimetics to the PPN. In contrast, Kinney et al. (1998) tend to support the primary role of the PPN in theta elicitation. Moreover, also studies conducted in our laboratory indicate the importance of the PPN: blockade of its activity with direct injection of procaine suppresses theta rhythm (Nowacka et al., 2002).

The aim of the present study was to evaluate the effect of inactivation of the PPN by lidocaine or procaine on hippocampal theta rhythm induced with carbachol injection or electrical stimulation of the RPO.

2. Results

2.1. Hippocampal EEG pattern after carbachol injected into the RPO followed by lidocaine injection into the PPN

After carbachol microinjections into the RPO, large irregular slow activity (LIA) present in hippocampal EEG during control conditions was replaced by rhythmical slow activity (RSA, theta rhythm) in both hippocampi. Mean latency of theta episodes calculated for 5 rats was 4.7 ± 2.0 min (mean ± SEM) and in two rats theta rhythm began during the injection; the rhythm lasted between 38.3 and 74.1 min, with mean duration of 58.4 ± 6.7 min. Administration of lidocaine into the PPN did not diminish or suppress theta rhythm produced by intra-RPO carbachol injection.

Fig. 1A presents samples of hippocampal EEG recording and the corresponding power spectra from a representative rat: in pre-injection conditions theta rhythm was evoked by sensory stimulation (tail pinch), and when carbachol was administered theta appeared almost immediately after this injection and lasted for 69.0 min in this case (which is one of the longest time lengths for theta duration in these experiments). This theta episode was unaffected by lidocaine injection into the PPN and when it ended, LIA reappeared in EEG.

Fig. 2A shows power distribution in 1-Hz bands (mean values) after carbachol and subsequent lidocaine injection in comparison to carbachol alone. Dominating peaks of signal power occurred at theta frequency band in both conditions, with maximum values at 4–5 Hz and they showed similar magnitude (around 750 and 650% of baseline for carbachol followed by lidocaine and carbachol alone respectively).

Possible differences between carbachol and lidocaine effect in comparison to the administration of carbachol alone were statistically analyzed in five of 3-Hz frequency bands, at the range of 0.6–15 Hz (Fig. 2B) with the use of Student's *t*-test for independent samples. One-way ANOVA comparison with post hoc Tukey's test (results of comparisons not shown in the Figures) revealed significant ($p \leq 0.05$) increase of signal power in the theta frequency band (3–6 Hz) in comparison to control conditions (before drugs administration) with no statistically significant differences between carbachol and lidocaine or carbachol alone effect in theta ($388.6 \pm 44.3\%$ and $336.1 \pm 34.3\%$ respectively) or in 6–9 Hz frequency band ($10.5 \pm 8.5\%$ and $10.9 \pm 6.8\%$ respectively). In the delta frequency band (0–3 Hz) there was a clear decrease of signal power after drugs injections compared to control conditions (one-way ANOVA, $p \leq 0.05$), similar in both carbachol and lidocaine and carbachol effects ($-62.1 \pm 4.1\%$ and $-43.2 \pm 6.1\%$ respectively), but statistically significantly higher in the conditions of carbachol followed by lidocaine ($p \leq 0.01$). In the 9–12 Hz and 12–15 Hz frequency bands Student's *t*-test for independent samples revealed statistically significant differences

Download English Version:

https://daneshyari.com/en/article/4318948

Download Persian Version:

https://daneshyari.com/article/4318948

Daneshyari.com