·基础研究·

EEG Characteristics in Frequency Domain in Synaptic Dysfunction Rat Model*

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ABSTRACT: EEG characteristics in frequency domain were investigated in the frontal lobe, occipital lobe and hippocampus, i.e. cognition - related cortex of synaptic dysfunction model rat, providing electrophysiological basis for further study on plastic extent and nerve regeneration of the damaged neurons. Synaptic dysfunction model was made via microinjecting β - amyloid protein1 - 40 (Aβ1 - 40) into hippocampal CA1 area of rat. Morris water maze behavioral test was performed to evaluate the learning and memory function of model group. Then EEG in the above areas for two groups were recorded. The spectrum for two groups was performed and the characteristics in frequency domain were analyzed. The results showed: (1) The average escape latency in 3rd, 4th, 5th and 6th training times of model group are higher than those of normal. The average escape latency of normal group in 5th training time decreased more markedly than that in 2nd training time, while that of model group in 7th training time decreased more remarkably than that in 2nd training time ($P < 0.05$). Without platform, the platform quadrant time percentage of model group was lower than the control ($P < 0.05$). (2) Alpha rhythm in EEG of model rat was slowing down; alpha - band power decreased with peek frequency left shifted nearly 2Hz. And the power of delta - band and theta - band in frontal lobe, occipital and hippocampus all increased with different extent. The synaptic dysfunction model rats were made successfully by microinjecting Aβ1 - 40 method. The model rats show the decreased learning and memory dysfunction. EEG frequency spectrum features in model rat show slower alpha rhythm with power amplitude lower or loss, slow waves (delta and theta wave) increasing with higher power amplitude. These can be consistent with the EEG of Alzheimer's disease patients, which can provide electrophysiological basis for further plasticity and nerve regeneration study on the impaired cortex with synaptic dysfunction.

Key words: Rat model; EEG; Characteristics in frequency domain; Synaptic dysfunction

Introduction

Surface electroencephalogram (EEG) is the integrated electrical signals synchronized of postsynaptic potentials across large populations of cortical neurons, which could at some extent reflect the variation of cortical excitability. The EEG power spectrum analysis can reflect the amplitude and distribution state of each EEG frequency bands, directly revealing some state of brain function.

The cortex (frontal lobe, occipital lobe and temporal area including hippocampus) are involved in the storage of different kinds of memory in different task[1,2]. So the EEG frequency spectrum distributions of above areas were investigated here after microinjecting $A\beta_{1-40}$, to evaluate the variation of EEG frequency spectrum features in the cognition - related cortex, which could afford electrophysiological basis for further study of plastic extent and nerve regeneration of the damaged neurons.

Materials and methods

Materials

$A\beta_{1-40}$ was bought from Sigma Company. A total of 30 healthy national second SD rats, aged 6 months and weighing 260 - 310g, are chosen of either sex. The rats were randomly divided into the model group and control group.

Methods

Animal model making: β - amyloid $protein_{1-40}$ ($A\beta_{1-40}$) was dissolved in NS to 10g/l and incubated a week continuously in the 37℃ incubator. After anaesthetized with 10% chloral hydrate (0.3g/Kg i.p.), rats were fixed on the Stereotaxic instruments. Then 7μg $A\beta_{1-40}$ per rat was microinjected into unilateral hippocampal CA1 area of rat in 10 min, with needle leaving 5 min.

Investigating the learning and memory function: Morris water maze behavioral test was used including 5 - day place navigation with static platform randomly placed in one quadrant and spatial probe test without platform.

Recording the EEG of the related cortex: Rats were anaesthetized and fixed with the above methods. The frontal lobe, the occipital lobe and the hippocampus, which are related with cognition, were chosen to record EEG. Recording electrode was made of stainless steel needle electrode, 0.5mm in diameter. Reference electrode was inserted homolaterally under the cranium in front of the Bregma point. One electrode was stirred into rat - tail as ground electrode. Sampling rats was 200Hz, and the signals were recorded directly into computer via Powerlab /8SP bioelectric amplified recorder.

EEG power spectrum analysis: Welch periodogram method was used to analyze the EEG power spectrum; Fast Fourier transformation (FFT) was applied to get the power of each EEG frequency band per 6 seconds (2/3 overlapped). The frequency range of EEG are δ wave in

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0.5 – 3.5Hz, θ wave in 4 – 7Hz, α wave in 8 – 13Hz, β wave in 14 – 25Hz, according to Walter method.

Statistic analysis: The average escape latency for both group were compared. And then power variation, the peek frequency of α – band, δ – band, and θ – band in EEG of the three areas were compared respectively in two groups.

The data was shown as Mean ± SD. The two – group t – test was used to analyze data.

RESULTS

The Morris water maze behavioral test and pathology

The average escape latency in 3rd, 4th, 5th and 6th training times of model group are higher than that of normal (Fig.1). The average escape latency in 2nd training time of the normal group prolonged more markedly than that in 5th training time ($P < 0.05$, $\alpha = 0.05$), while the average escape latency in 2nd training time of the model group prolonged more markedly than that in 7th training time ($P < 0.05$, $\alpha = 0.05$). This indicated that learning and memory of the platform place in the model group is much slower than that in the normal rats. Secondly, without platform, the platform quadrant time percentage in model group was lower than that in the control group ($P < 0.05$, $\alpha = 0.05$), which is shown in Tab.1.

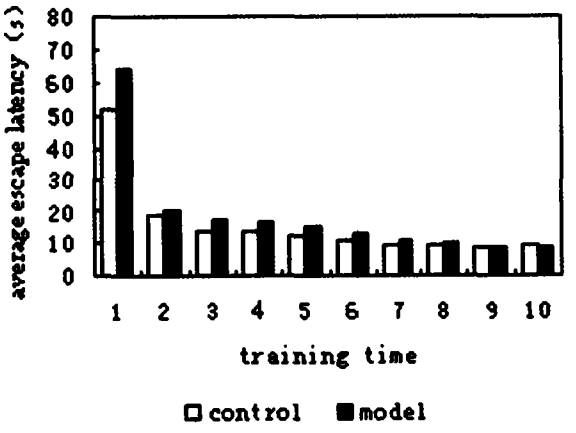

Fig.1 the comparison of the average escape latency for both groups in place navigation

图 1 · 两组定位航行实验中平均逃避潜伏期的比较

Table 1 The platform quadrant time percentage comparison of both groups in space probe test

表 1 两组空间探索实验中平台象限时间百分比的比较

Test subject	Control	Model
The platform quadrant time percentage	42.10 ± 5.81	36.40 ± 3.48#

#: $P < 0.05$, $\alpha = 0.05$.

The EEG power spectrum of two groups

Based on the results of the Morris water maze behavioral test, both of the two groups were chosen to analyze the EEG power spectrum. EEG and corresponding power spectrums of the frontal lobe, occipital lobe and hippocampus in normal rat are respectively shown in Fig.2, Fig.3, and Fig.4. EEG of normal rat was that α rhythm is main rhythm with sporadic δ and θ wave; peek power is at δ and θ frequency range.

Fig.5, Fig.6, and Fig.7 respectively showed the EEG and corresponding power spectrum of frontal lobe, occipital lobe and hippocampus in the rats of model group. Contrasting with normal rat EEG and power spectrum, the synaptic dysfunction model rat presented the EEG and power spectrum as follows: alpha rhythm was slowing down, the delta and theta waves in frontal and occipital lobes and hippocampus appeared more often. The alpha – band power remarkably decreased in occipital lobe and hippocampus with peek frequency left shifted about 2Hz. What's more, the power of delta – band and theta – band in frontal lobe, occipital lobe and hippocampus all increased highly.

DISCUSSION

Both the learning and memory function of model group reduce more markedly than that of normal group. The EEG frequency spectrum features in synaptic malfunction model group appear at some extent consistent with the EEG characteristics of Alzheimer's disease (AD)[3]: Slow waves (δ wave and θ wave) increased with higher power amplitude, α rhythm (frequency depressing) slowed with power amplitude lower or loss. Thus when the synaptic function fails in hippocampus and association cortical areas, it could provide the electrophysiological basis for further nerve regeneration study on the frontal cortex with synaptic malfunction. The neurotoxicity effect of β – amyloid protein is densely studied currently with or without aggregation, proved in vivo and in vitro[4,5]. Aggregated $A\beta_{1-40}$ microinjected into hippocampal CA1 area in some extent mimicked Alzheimer's disease with reduced cognitive function and abnormal AD – like EEG.

Possible reasons for such result are as follows: Aggregated $A\beta_{1-40}$ generates neurotoxicity by activating astrocyte to induce inflammatory reaction, and increasing intracellular calcium concentration to cut down membrane action etc[6]. Such neurotoxicity leads to neuron apoptosis, the reduction of normal neurons, and the impairments of synaptic transmission function. The abnormal EEG is thought to be associated with functional disconnections among cortical areas resulting from death of cortical neurons, axonal pathology, etc[3]. What's more, the cholinergic atrophy associated with monoaminergic deficits could produce the impairments of learning and memory function, and abnormal EEG[7]. While recently reported, cholinergic – serotonergic imbalance in frontal and temporal cortex also played an important role in the cognitive symptom[8].

However, widespread neuritic dystrophy is supposed to be characterization of the neocortex in AD. Lower concentration fibril Aβ was found to generate neuronal dystrophy significantly earlier than Aβ neurotoxicity[9], which suggested that disordered plastic changes and loss of synaptic integrity induced by fibril Aβ may play a significant role in the development of AD pathology. However, the underlying mechanisms involved are unknown, and need further research.

In a word, the results of Morris water maze behavioral test and EEG power spectrum suggest cognitive function of frontal lobe, occipital lobe and hippocampus in synaptic function failure rat model was decreased. Such EEG power appearance may provide the electrophysiological basis for further nerve regeneration study on the auditory cortex when the synaptic function fails.

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突触功能障碍大鼠模型EEG频域特征*

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摘要:本文旨在探讨突触功能障碍大鼠模型在额叶、颞叶和海马这些与认知功能有关的脑区EEG频域特征。先用海马CA1区$A\beta_{1-40}$微量注射法制备突触功能障碍模型,用Morris水迷宫行为学测试系统检测其学习记忆能力;然后记录上述脑区的EEG并做频谱分析。结果显示:(1)模型组在第3、4、5、6训练时间段的平均逃避潜伏期较正常组明显延长,和第2训练时间段的相比较,正常组第5训练时间段平均逃避潜伏期明显缩短,模型组到第7训练时间段平均逃避潜伏期开始明显缩短($P<0.05$);撤去平台后,模型组在原平台所在象限的时间百分比明显降低($P<0.05$)。(2)模型组的EEG表现为α节律慢化,功率下降,其主峰频率左移2Hz,并且额叶、颞叶和海马的δ波和θ波功率不同程度地增高。由此Aβ1-40微量注射法成功制备了突触功能障碍大鼠模型。该模型大鼠的学习记忆能力降低,其频谱特征表现为α节律慢化,功率下降或消失,慢波(δ波和θ波)活动增多,功率不同程度地增高。这些与阿尔茨海默病(Alzheimer's disease,AD)的EEG一致,可为以后对突触功能障碍时受累皮层进行深入的可塑性和神经再生的研究提供电生理基础。

关键词:大鼠模型;EEG;频域特征;突触功能障碍

中图分类号:R338.1 **文献标识码**:A

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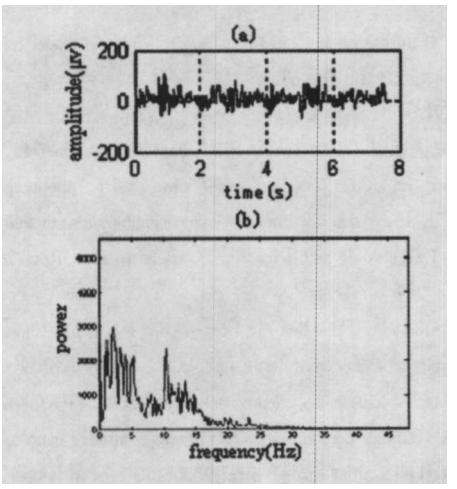

Fig.2 EEG and power spectrum of frontal lobe in normal rat
(a) is EEG, (b) is the corresponding power spectrum
图 2 正常大鼠额叶脑电图和相应功率谱图
(a)是脑电图，(b)是相应功率谱图

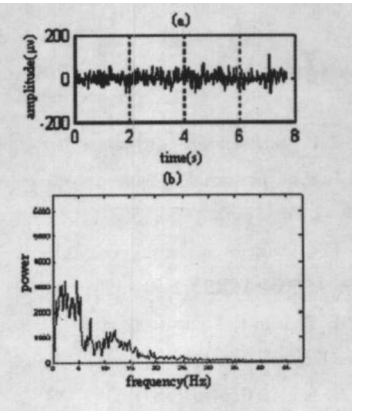

Fig.3 EEG and power spectrum of occipital lobe in normal rat
(a) is EEG; (b) is the corresponding power spectrum
图 3 正常大鼠枕叶脑电图和相应功率谱图
(a)是脑电图，(b)是相应功率谱图

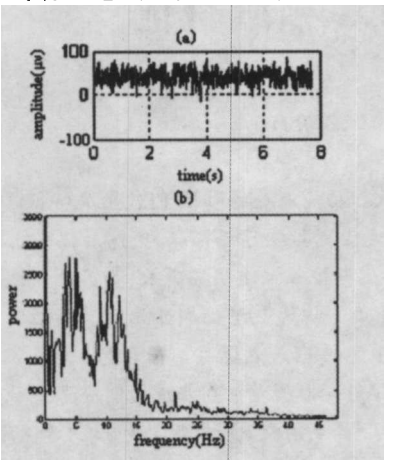

Fig.4 EEG and power spectrum of hippocampus in normal rat
(a) is EEG; (b) is the corresponding power spectrum
图 4 正常大鼠海马的脑电图和相应功率谱图。
(a) 是脑电图 (b)相应功率谱图

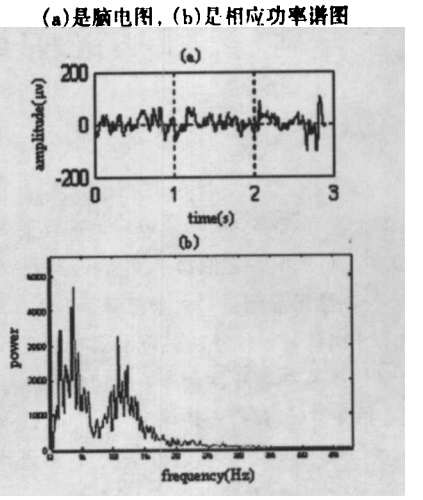

Fig.5 EEG and power spectrum of frontal lobe in model rat
(a) is EEG; (b) is the corresponding power spectrum
图 5 模型大鼠额叶脑电图和相应功率谱图
(a)是脑电图，(b)是相应功率谱图

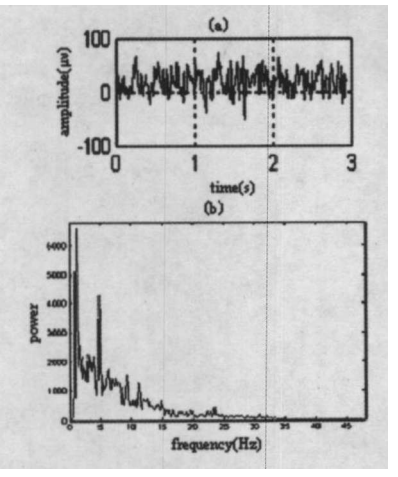

Fig.6 EEG and power spectrum of occipital lobe in model rat
(a) is EEG; (b) is the corresponding power spectrum
图 6 模型大鼠枕叶脑电图和功率谱图
(a)是脑电图，(b)是相应功率谱图

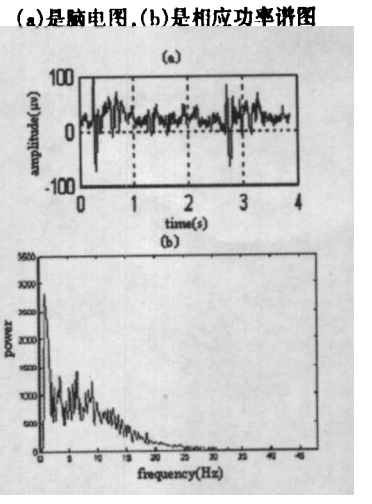

Fig.7 EEG and power spectrum in hippocampus of model rat
(a) is EEG; (b) is the corresponding power spectrum
图 7 模型大鼠脑电图和相应功率谱图。
(a)是脑电图，(b)是相应功率谱图