EXPERIMENTAL RESEARCH ON FORECASTING INDEX OF BIOLOGICAL IMAGE AEROBIC EXERCISE ANALYSIS OF ARTIFICIAL NEURAL NETWORK

ORIGINAL ARTICLE
ARTIGO ORIGINAL
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PESQUISA EXPERIMENTAL SOBRE ÍNDICE DE PREVISÃO DE IMAGEM BIOLÓGICA ANÁLISE DE EXERCÍCIO AERÓBIO DE REDE NEURAL ARTIFICIAL

INVESTIGACIÓN EXPERIMENTAL SOBRE ÍNDICE DE PRONÓSTICO DE IMÁGENES BIOLÓGICAS ANÁLISIS DE EJERCICIO AERÓBICO DE REDES NEURONALES ARTIFICIALES

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ABSTRACT

Objective: The paper uses artificial neural network images to explore the effects of aerobic exercise on the gamma rhythm of theta period in the awake hippocampal CA1 area of APP/PS1/tau mice and the low-frequency gamma rhythm of the sleep state hippocampal CA1 area SWR period. Methods: Clean grade 6-month-old APP/PS1/tau mice were randomly divided into quiet group (AS) and exercise group (AE), C57BL/6J control group mice were randomly divided into quiet group (CS) and exercise group (CE). The AE group and the CE group performed 12-week treadmill exercise, 5d/week, 60min/d, the first 10min exercise load was 12m/min, the last 50min was 15m/min treadmill slope was 0°. Eight-arm maze detection of behavioral changes in mice; multi-channel in vivo recording technology to record the electrical signals of the awake state and sleep state in the hippocampal CA1 area, MATLAB extracts the awake state theta period and sleep state SWR period, multi-window spectrum estimation method Perform time-frequency analysis and power spectral density analysis. Results: 12 weeks of aerobic exercise can significantly improve the working memory and reference memory of the AS group, increase the gamma energy in theta period of the awake hippocampus CA1 area and the low-frequency gamma energy in the sleep state CA1 area SWR period. Conclusions: Aerobic exercise can improve the neural network state of the AD model and increase the gamma energy in theta period of the hippocampus CA1 area, and the low-frequency gamma energy in the SWR period is one of the neural network mechanisms for its overall behavioral improvement. ***Level of evidence II; Therapeutic studies - investigation of treatment results.***

Keywords: Neural networks, computer; Exercise; Diagnostic imaging.

RESUMO

Objetivo: o artigo usa imagens de redes neurais artificiais para explorar os efeitos do exercício aeróbio no ritmo gama do período teta na área CA1 do hipocampo desperto de camundongos APP/PS1/tau e o ritmo gama de baixa frequência da área CA1 do hipocampo do estado de sono Período SWR. Métodos: Camundongos APP/PS1/tau de grau limpo de 6 meses de idade foram divididos aleatoriamente em grupo quieto (AS) e grupo de exercício (AE), os camundongos do grupo controle C57BL/6J foram divididos aleatoriamente em grupo quieto (CS) e grupo de exercício (CE). O grupo AE e o grupo CE realizaram 12 semanas de exercício em esteira, 5d/semana, 60min/d, a primeira carga de exercício de 10min foi de 12m/min, a última de 50min foi de 15m/min e a inclinação da esteira foi de 0 °. Detecção de labirinto de oito braços de mudanças comportamentais em camundongos; tecnologia de gravação in vivo multicanal para registrar os sinais elétricos do estado de vigília e do estado de sono na área CA1 do hipocampo, MATLAB extrai o período de tempo teta do estado de vigília e o período de tempo SWR do estado de sono, método de estimativa de espectro de múltiplas janelas. e análise de densidade espectral de potência. Resultados: 12 semanas de exercícios aeróbicos podem melhorar significativamente a memória de trabalho e a memória de referência do grupo AS, aumentar a energia gama no período teta da área CA1 do hipocampo acordado e a energia gama de baixa frequência na área CA1 do estado de sono período SWR. Conclusões: O exercício aeróbico pode melhorar o estado da rede neural do modelo AD e aumentar a energia gama no período teta da área CA1 do hipocampo e a energia gama de baixa frequência no período SWR é um dos mecanismos da rede neural para seu comportamento geral. ***Nível de evidência II; Estudos terapêuticos- investigação dos resultados do tratamento.***

Descritores: *Redes neurais de computação; Exercício físico; Diagnóstico por imagem.*

RESUMEN

Objetivo: El artículo utiliza imágenes de redes neuronales artificiales para explorar los efectos del ejercicio aeróbico en el ritmo gamma del período theta en el área CA1 del hipocampo despierto de ratones APP/PS1/tau y el ritmo gamma de baja frecuencia del área CA1 del hipocampo en estado de sueño. Período de ROE. Métodos: Se dividieron aleatoriamente ratones APP/PS1/tau de 6 meses de edad de grado limpio en grupo tranquilo (AS) y grupo *de ejercicio (AE), los ratones del grupo de control C57BL/6J se dividieron aleatoriamente en grupo tranquilo (CS) y grupo de ejercicio (CE). El grupo de EA y el grupo de EC realizaron 12 semanas de ejercicio en cinta rodante, 5 días a la semana, 60 min/d, la primera carga de ejercicio de 10 min fue de 12 m/min, los últimos 50 min fueron de 15 m/min y la pendiente de la cinta fue de 0 °. Detección en laberinto de ocho brazos de cambios de comportamiento en ratones; tecnología de grabación in vivo multicanal para registrar las señales eléctricas del estado despierto y del estado de sueño en el área CA1 del hipocampo, MATLAB extrae el período de tiempo theta del estado despierto y el período de tiempo de SWR del estado de suspensión, método de estimación de espectro de múltiples ventanas Realizar análisis de tiempo-frecuencia y análisis de densidad espectral de potencia. Resultados: 12 semanas de ejercicio aeróbico pueden mejorar significativamente la memoria de trabajo y la memoria de referencia del grupo AS, aumentar la energía gamma en el período theta del área CA1 del hipocampo despierto y la energía gamma de baja frecuencia en el período SWR del área CA1 del estado de sueño. Conclusiones: El ejercicio aeróbico puede mejorar el estado de la red neuronal del modelo AD y aumentar la energía gamma en el período theta del área del hipocampo CA1 y la energía gamma de baja frecuencia en el período SWR es uno de los mecanismos de la red neuronal para su comportamiento general.* ***Nivel de evidencia II; Estudios terapéuticos- investigación de los resultados del tratamiento.***

Descriptores: *Redes neurales de la computación; Ejercicio físico; Diagnóstico por Imagen.*

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INTRODUCTION

The neural system is accompanied by changes in the complex electrical activities of neurons in the high-level cognitive process. The simultaneous release of a large number of neurons can cause regular changes in the local field post-synaptic potential, thereby forming neural network oscillations. Regular neural network oscillations are an important part of brain function. Gamma oscillation is the resonance of local field potential (LFP) at 30-80 Hz caused by the activation of a local loop composed of excitatory neurons and fast inhibitory neurons. Gamma oscillation is the basis of advanced cognitive function of the brain, and participates in the adjustment of cognitive functions such as perception, attention, learning and memory. Studies have found that the gamma activity of AD patients is reduced, and the hippocampus cells of AD 5xFAD model mice the increase of β-amyloid peptide (Aβ) content is accompanied by a decrease in the gamma power of SWR, and the modulation depth of gamma to neuron discharge decreases. Studies have shown that aerobic exercise can reduce Aβ deposition and tau protein hyperphosphorylation in the early (6-month-old) and advanced (9-month-old) AD models, reduce synaptic loss, increase synaptic plasticity, and improve cognitive function. While improving the pathological characteristics of AD, can it improve the gamma rhythm that is closely related to cognitive function, and provide neuro-physiological mechanisms of cell function for aerobic exercise to improve the behavior of the AD model.[1]

METHODS

Experimental animals and training programs

Twenty six-month-old APP/PS1/tau three transgenic AD model mice were randomly divided into a quiet group (AS) and an exercise group (AE), 10 mice in each group, and C57BL/6J mice of the same month age were used as a control group, randomly divided For the quiet group (CS) and the exercise group (CE), 10 animals in each group. The experimental mice were bred in the animal room of a scientific research center of a university. The environment was a 12-hour light-dark cycle, the temperature was (22±2) °C, and the humidity was 45%-55%.

During the experiment, strictly follow the "Articles of the Experimental Animal Management Committee" and "Articles of the Experimental Animal Ethics Committee" of a university. Before the formal training, the mice in the AE group and the CE group were trained for 3 days, specifically 30 min/d, the exercise load was 10 m/min, and the slope was 0°. The formal training program is: 60min/d, 5d/week, exercise load is 12m/min in the first 10min, exercise load is 15m/min in the latter 50min, and exercise is 12 weeks. The mice in the CS group and the AS group were free to eat every day. At the end of exercise intervention, the selected data were the 9-month-old AD model and the corresponding normal-month control group.

Behavioral test

The behavioral test used an eight-arm labyrinth experiment. The diet was restricted throughout the experiment, keeping its weight at 80% to 85% of the normal mice. The experimental process includes a 3d adaptation process and a 10d test process. Adaptation process: Put the same amount of chocolate prey on the ends of the 8 arms of the maze, place the mouse in the maze and let it explore for 10 minutes freely. Test procedure: Set arms 1, 2, 5, and 7 as target arms, place bait only at the end of the target arm, close each arm door of the maze, place the mouse in the central area of the maze, and open the arm door after 10s Video capture. Mice searched for food in the maze and ingested food. When the mice walked through all the target arms, the experiment was stopped. The observation index is the number of working memory errors, that is, the number of times the animal enters the arm that has already eaten the bait in the same training; refer to the number of memory errors, that is, the number of times the animal enters the arm that has not put the bait.

Multi-channel electrode embedding

5% chloral hydrate was anesthetized by intraperitoneal injection at a body weight of 300 mg/kg Determine the coordinates of the target brain area according to the stereotaxic map of the mouse brain, grind the skull with a dental drill under the microscope, use the needle of the syringe to pierce the dura mater, implant the microwire array electrode under the dissecting microscope, seal the exposed tissue of the brain tissue with basilica, dental Cement fixed.Relevant experimental records were made 7 days after the operation. After recording, burn the recording site with a current of 10μA for 30s, then perform perfusion, brain extraction, post-fixation, dehydration, embedding, sectioning (40μm), and Nissl staining for histological positioning to exclude electrodes that are not within the target range Mice are not counted in subsequent data analysis.

Multi-channel EEG signal recording and data analysis

Field potential responds to the local excitability of the neural network, which is the sum of the excitability and inhibitory post-synaptic potential near the electrode tip, showing slow potential characteristics. When the envelope amplitude is greater than 4 standard deviations of the average value or more, and when the continuous time is greater than 15ms, it is defined as the SWR period (Figure 1).

Data processing and analysis

In the standard BP algorithm, let k be the number of iterations, then the weights and thresholds of each layer are corrected according to the following formula

$$x(k+1)=x(k)-\alpha g(k) \qquad (1)$$

In the formula: x(k) is the connection weight vector or threshold vector between levels in the kth iteration. $g(k)=\frac{\partial E(k)}{\partial x(k)}$ is the gradient vector of the output error of the neural network of the kth iteration to each weight or threshold. The negative sign indicates the reverse direction of the gradient, that is, the direction of the gradient's speed decrease. Taking the two-layer BP network as an example, when there is only one input sample, there is

$$E(k)=E[e^2(k)]\approx\frac{1}{s^2}\sum_{i=1}^{s^2}[t_i^2-a_i^2(k)]^2 \qquad (2)$$

$$\begin{aligned}a_i^2(k)&=f^2\{\sum_{j=1}^{s^2}[\omega_{i,j}^2(k)a_i^1(k)+b_i^2(k)]\}\\&=f^2\{\sum_{j=1}^{s^2}[\omega_{i,j}^2(k)f^1(\sum_{j=1}^{s^1}(i\omega_i^1(k)p_i+ib_i^1(k)))+b_i^2(k)]\}\end{aligned} \qquad (3)$$

Its essence is to change the learning rate η to improve network performance, and the iterative relationship of its network connection weight is changed from traditional BP algorithm to

$$\begin{aligned}\Delta w(t+1)&=\eta\frac{\partial E}{\partial w}\\ \Delta w(t+1)&=\eta\frac{\partial E}{\partial w}+\alpha\Delta w(t)\end{aligned} \qquad (4)$$

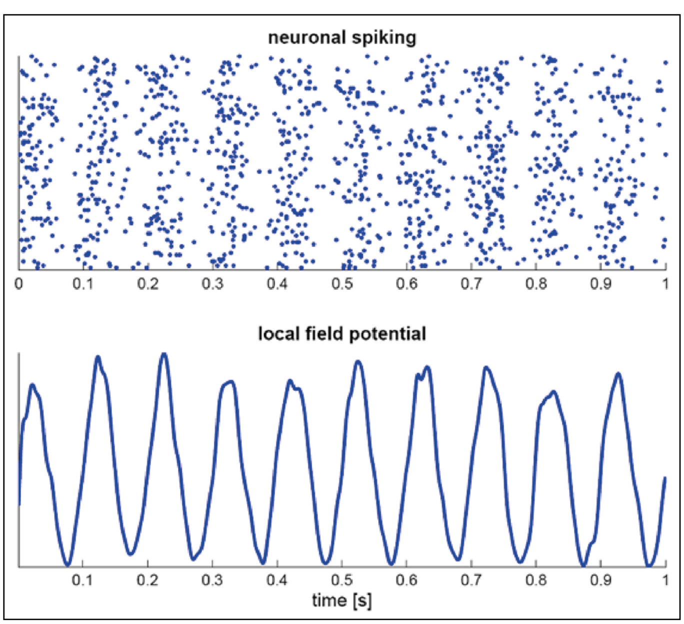

Figure 1. Field potential waveforms in different frequency bands.

Among them, momentum term $\alpha\Delta w(t)+\alpha[\ w(t)-w(t-1)])$. α is the momentum factor, $0<\alpha<1$. The role of the momentum term is to memorize the direction of change of the connection weight at the previous moment (that is, the value of the change), so that a larger learning rate coefficient η can be used to increase the learning speed. The additional momentum term uses its "inertial effect" to suppress the oscillations that may occur during network training, which plays a role in buffering and smoothing. In addition, the additional momentum term is also beneficial to break away from the flat area. If the training of the network has entered the flat area of the error surface, the error will change very little, so $\Delta w(t+1)$ is approximately $\Delta w(t)$, and the average $\Delta w(t)$ will become

$$\Delta w=\frac{-\eta}{1-\alpha}(\partial E/\partial w) \qquad (5)$$

RESULTS

Behavioral experiment results

Effects of aerobic exercise on working memory of 8-arm maze in 9-month-old APP/PS1/tau mice

Working memory is the ability to temporarily process and store information, reflecting short-term memory ability. The number of working memory errors in mice of each group at 9 months of age (Figure 2) is a trend of decreasing working memory errors as the number of test days increases.

Effects of aerobic exercise on the reference memory of eight--arm maze in 9-month-old APP/PS1/tau mice

In this study, the reference memory test is the ability of the animal to find the bait correctly according to the reference object, which reflects the long-term memory ability. With the increase of test days, the number of reference memory errors in each group showed a downward trend (Figure 3).

The effect of aerobic exercise on the gamma energy of theta period in hippocampal CA1 area of 9-month-old mice during waking exploration

The time-frequency graph and PSD graph of theta period in the hippocampus CA1 area of each group of mice are shown in Figures 4 to 5, and the normalized gamma energy is shown in Figure 6. The gamma energy of theta in the CS group was 0.51±0.02, the CE group was 0.53±0.03, the AS group was 0.33±0.05, and the AE group was 0.50±0.06. Two-factor analysis of variance showed that the interaction item of genotype and exercise was statistically significant, that is, F(1,412)=290.164,

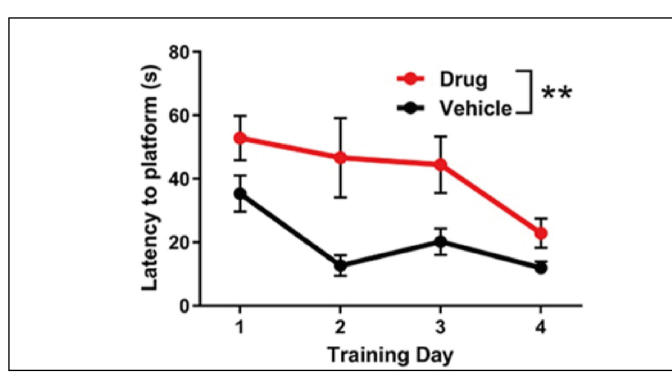

Figure 2. Effect of aerobic exercise on the number of working memory errors in the eight-arm maze of mice.

P=0.000, partial η2=0.413, suggesting that genotype and exercise have no effect on theta period There is an interaction between the effects of gamma energy. The effect between the AD model and the control group was statistically significant, and the difference was very significant, that is, F(1,412)=669.433, P=0.000, partial η2=0.619; the effect between the exercise model and the quiet control subject was also statistical Meaning, the difference is very significant, that is, F(1,412)=557.774, P=0.000, partial η2=0.575. The results of pairwise comparison showed that the gamma energy of the AS group was lower than that of the CS, and the difference was statistically significant (P=0.000<0.01). The CS group was significantly lower than the CE group (P=0.000<0.01). The AE group was larger than the AS group and had a very Significant difference (P=0.000<0.01). This shows that when 9-month-old APP/PS1/tau mice explore freely, the gamma energy of hippocampal CA1 area during theta period decreases significantly, while 12-week aerobic exercise effectively improves the APP/PS1/tau mouse hippocampus CA1 area during theta oscillation period. Gamma energy and exercise also have a positive effect on the normal control group.

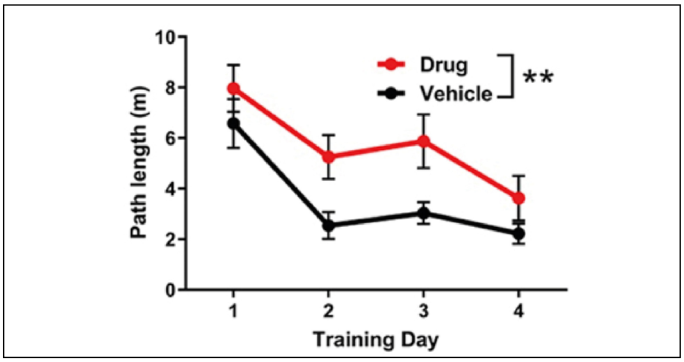

Figure 3. Effects of aerobic exercise on the number of reference memory errors in the eight-arm maze experiment in mice.

DISCUSSION

In the pathogenesis of neurodegenerative disease AD, although the early clinical symptoms are not typical, the progressive damage of plot memory and spatial memory is its common feature. APP/PS1/tau mice contain mutant PS1M146V, APPswe and tauP301L pathogenic genes, also known as 3xTg mice, which can simulate the age-dependent Aβ deposition, synaptic function defects, neuronal fiber tangles and other typical pathological changes in AD It is an ideal transgenic animal model for AD research in recent years. In this model, intracellular Aβ appeared in the neocortex at 3 to 4 months old; extracellular amyloid plaques appeared in the 4/5 layer of the frontal lobe at 6 months old; intracellular Aβ and synaptic dysfunction appeared in the hippocampal CA1 area; hippocampus at 9 months old A small amount of extracellular amyloid plaques appeared; a large number of extracellular amyloid plaques appeared in the hippocampus at 12 months of age, and a large number of tau immune responses.[4]

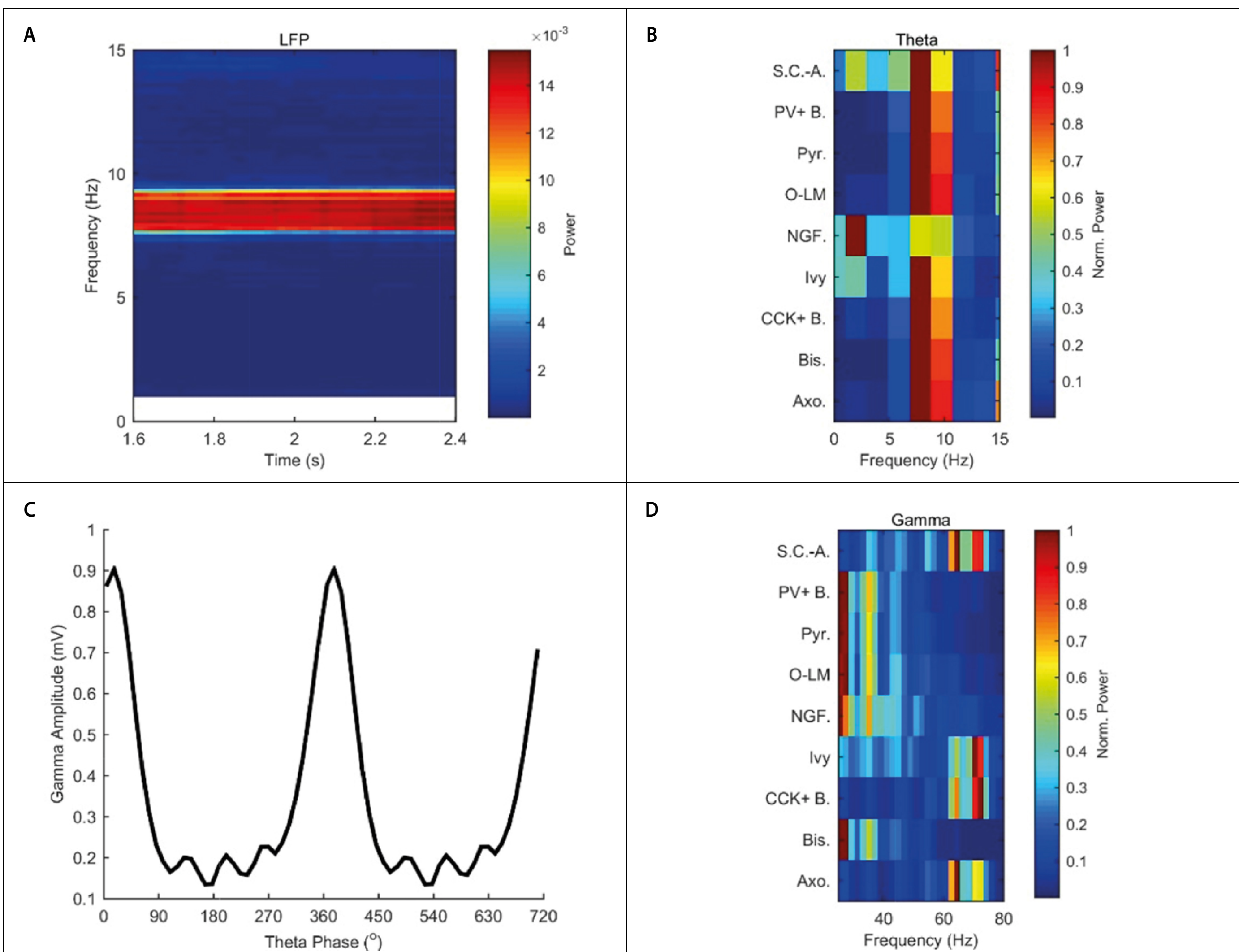

Figure 4. Time-frequency map of mice in theta period of hippocampus CA1 area during theta period;

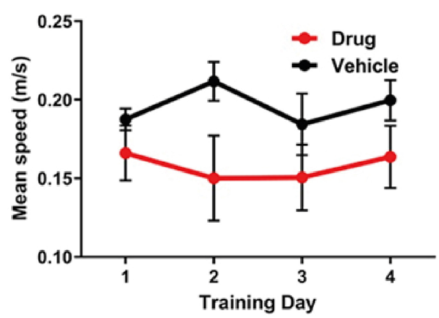

Figure 5. The PSD time-frequency diagram of the theta period standardized.

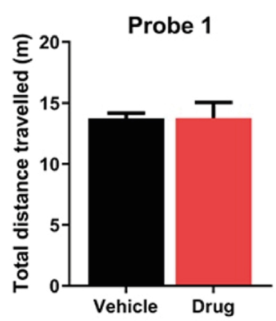

Figure 6. Normalized gamma energy in theta period.

The SWR is a unique oscillation of the hippocampus and the structures near the hippocampus.Eliminating the SWR of rat hippocampus through electrical stimulation will interfere with the extraction of spatial memory information, and the coupling of low-frequency gamma rhythms in the CA3 and CA1 areas of the hippocampus during SWR is conducive to the extraction/reading of memory. Combined with the study, it was found that before the senile plaque deposition in the 3-month-old AD model, applying optogenetic methods to activate the intermediate neurons in the hippocampal CA1 region at the gamma frequency band 40Hz can reduce the content of its Aβ1-40 and Aβ1-42 peptides, and exercise intervention can reduce June Extracellular deposition of hippocampal Aβ in the age-old AD model. The above results suggest that exercise intervention reduces the Aβ content of the AD model and enhances the progression of AD disease in the 9-month-old APP/PS1/tau mice in the wakeful exploration state of the hippocampus and sleep period. Gamma oscillation activity, which in turn improves its spatial learning and memory ability.[5]

It has been found that 7-month-old 3xTg mice have cortical cortex [3H]-flunitrazepam and GABAA receptor affinity constants increased, and 6 months of free wheel movement can increase the function of the GABAergic system. Whether long-term aerobic exercise improves the function of PV-positive neurons by increasing the number of PV-positive neurons in the AD model hippocampus or increasing the Nav1.1 level remains to be further studied.

CONCLUSION

month-old APP/PS1/tau mice have abnormal neural networks in the gamma band of the hippocampal CA1 area. Long-term aerobic exercise can improve the state of the AD neural network. Increasing the gamma energy in theta period and the low-frequency gamma energy in the SWR period are the overall behavioral improvements. One of the neural network mechanisms.

The author declare no potential conflict of interest related to this article

AUTHORS' CONTRIBUTIONS: Min Lin analyzed and explained the use of artificial neural network images to study the effects of aerobic exercise on the gamma rhythm of the theta cycle in the CA1 area of the waking hippocampus of APP / PS1 / tau mice and the low frequency gamma rhythm of the SWR cycle in the hippocampus CA1 area of the sleep state.

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