ISSN 2959-409X

Anti-inflammatory response controlled by gamma wave

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Abstract:

It is now believed that the cause of Alzheimer's disease is the accumulation of amyloid-Bata, which is caused by a variety of factors, such as neuroinflammation. So in this study, the researchers will study the changes of microglia from M1 to M2 by changing the frequency of gamma wave. If microglia change from M1 to M2, that means it changes from pro-inflammatory to anti-inflammatory.

Keywords: gamma wave; microglia; Alzheimer's disease; Anti-inflammatory Response.

1. Introduction

Alzheimer's disease, which is named in honor of the German psychiatrist Alois Alzheimer, represents the most prevalent form of dementia. It is characterized as a gradual, progressive neurological deterioration marked by the presence of neuritic plaques and neurofibrillary tangles [1]. There are many hypotheses about the cause of Alzheimer's disease. Some say it's due to amyloid beta deposits, others to neuronal tangles, and still others to neuroinflammation. Neuritic plaques, which are extracellular and consist of amyloid beta (Aβ) peptides, and neurofibrillary tangles, which are intracellular and comprised of phosphorylated tau proteins, are the defining pathological features of Alzheimer's disease (AD). The individual neurotoxic effects of these proteins have been the subject of extensive research within the field of AD. Despite this, targeted treatments aimed solely at Aβ or tau have not resulted in significant therapeutic advancements. [3]. And through the use of TAM treatment reduce the content of Bace - 1 in the treatment of Alzheimer's disease have a certain effect it can improve memory ability of patients [3]. This may be because amyloid beta deposition is not a single cause. researcher found that gamma waves at different frequencies had an effect on Bace-1. Alterations in gamma-band activity (ranging from 20 to 50 Hz) have been noted across a variety of neurological conditions. Yet, the precise connection between gamma oscillations and the cellular underpinnings of these disorders remains elusive. In this study, the researchers demonstrate a diminution in gamma oscillations that are driven by behavior prior to the emergence of amyloid plaques or cognitive deterioration in a murine model simulating Alzheimer's disease (AD). By employing optogenetic stimulation of fast-spiking parvalbumin-expressing (FS-PV) interneurons at a frequency of 40 Hz, but not at other frequencies, the researchers were able to decrease the quantities of amyloid-β (Aβ) peptides, specifically the Aβ1-40 and Aβ1-42 variants. Examination of gene expression patterns indicated an upregulation of genes linked to the morphological alteration of microglia, and histological studies corroborated an increase in the colocalization of microglia with Aβ deposits. Following these findings, the researchers developed a non-invasive paradigm involving a 40 Hz flickering light that successfully lowered the levels of Aβ1-40 and Aβ1-42 in the visual cortex of mice before plaque deposition and alleviated the associated cognitive impairments. [2]. So researcher set out to find out the effect of gamma wave on neuroinflammation. Researcher investigated the effect of gamma wave on neuroinflammation by studying the content of M1 and M2 under 40Hz gamma wave, and thus to find a new method for the treatment of AD. In our experiments, researcher will use 5xFAD mice and WT wake-wake control tests, researcher will use Visual stimulation protocol and Transcranial alternating current stimulation to adjust the frequency of gamma wave [4].

2. Methods

2.1 Visual stimulation protocols

Using visual stimulation protocols to control gamma wave frequency typically involves the following steps. First is understanding Gamma Waves. Gamma waves are neural oscillations in the brain, ranging approximately from 30 Hz to 100 Hz. They are associated with cognitive functions such as memory, attention, and perception. Second is choosing a Visual Stimulation Protocol. Use some approaches to visual stimulation that can influence gamma wave activity. First is frequency Following Response (FFR): This involves presenting visual stimuli (such as

flickering lights) at specific frequencies to entrain brainwaves to that frequency. For gamma waves, researcher would typically use frequencies in the gamma range (e.g., 40 Hz to 100 Hz). [6]

2.2 Patterned visual stimulation

Second is patterned visual stimulation. Using specific patterns or sequences of visual stimuli can also modulate gamma waves. These can be simple patterns like checkerboards or more complex geometric designs. Third is color and Intensity Variations: Experimenting with different colors and intensities of visual stimuli can also affect neural oscillations, including gamma waves. Next is implementing the Protocol. Set up a controlled environment where the visual stimuli can be presented to the participant. Ensure that the stimuli are presented consistently and accurately. Depending on researcher's equipment and setup, researcher may use a computer screen, LED lights, or other visual devices to present the stimuli. And then measuring Gamma Waves. Use electroencephalography (EEG) or magnetoencephalography (MEG) to measure brain activity in real-time. These techniques can detect changes in gamma wave frequency and amplitude. Analyzing Results. Record and analyze the EEG/MEG data to see how the visual stimulation protocol affects gamma waves. Look for changes in the power spectrum or coherence at gamma frequencies during and after stimulation. Iterative Adjustment. Based on researcher's initial results, adjust the parameters of researcher's visual stimulation protocol (such as frequency, intensity, duration) to optimize the modulation of gamma waves. Transcranial Alternating Current Stimulation (tACS) is a non-invasive brain stimulation technique that involves applying a small electric current to the scalp to modulate neuronal activity. Electrode placement is crucial for targeting specific brain regions. Gamma waves are often associated with cortical regions. EEG studies have shown that gamma oscillations can be influenced by stimulating specific areas of the cortex. Typically, electrodes are placed over the scalp corresponding to the brain region researcher want to stimulate. Place the electrodes on the scalp according to the device instructions and the targeted brain region. Set the device to deliver alternating current at the desired gamma frequency (e.g., 40 Hz). Start with a low intensity and gradually increase it to a level that is comfortable and within safety guidelines [5].

2.3 Immunofluorescence

Researcher use immunofluorescence and FCM flow cytometry to detection. Frist is immunofluorescence. Prepare the cell culture or tissue samples on glass slides or coverslips. Fix the cells or tissue with a suitable fixative (e.g., paraformaldehyde) to preserve the antigen structure. Next permeabilization and Blocking. Permeabilize the cells with a permeabilization buffer (if necessary) to allow antibodies to penetrate into the cells. Block non-specific binding sites by incubating the samples in a blocking buffer (e.g., BSA or serum from the species of secondary antibody). Next primary Antibody Incubation. Incubate the samples with primary antibodies specific to M1 markers (e.g., CD86) and M2 markers (e.g., CD206) separately. This step allows the primaryantibodies To bind to their respective targets (M1 or M2 macrophages).Dilute the primary antibodies according to the manufacturer's instructions and incubate for the appropriate time and temperature.

And then washi it.Wash the samples several times with PBS or another appropriate buffer to remove unbound primary antibodies.Then is secondary Antibody Incubation.

Incubate the samples with secondary antibodies conjugated to fluorophores (e.g., anti-rabbit FITC for M1, anti-mouse Alexa Fluor 594 for M2) that specifically recognize the host species of the primary antibodies.Dilute the secondary antibodies as recommended and incubate for the appropriate time and temperature to allow binding to the primary antibodies.Washing and Mounting agane. Wash the samples thoroughly to remove unbound secondary antibodies. Optionally, stain nuclei with DAPI or another nuclear stain if desired.Mount the samples using an appropriate mounting medium to preserve fluorescence and prevent photobleaching. And next imaging and Analysis it. Visualize the samples using a fluorescence microscope equipped with filters suitable for the fluorophores used.Capture images of the fluorescence signals specific to M1 (e.g., FITC) and M2 (e.g., Alexa Fluor 594) markers.Analyze the distribution and intensity of fluorescence signals to determine the presence and localization of M1 and M2 macrophage populations in the sam1. [7]

2.4 FCM flow cytometry

Useing FCM flow cytometry. First is sample Preparation. Isolation of Macrophages: Isolate macrophages from the sample using appropriate techniques (e.g., from tissue, cell culture, or peripheral blood mononuclear cells). [8] If necessary, stimulate the macrophages to polarize them into M1 or M2 phenotypes using specific stimuli. Common stimuli include lipopolysaccharide (LPS) and interferon-gamma (IFN-γ) for M1 polarization, and interleukin-4 (IL-4) or IL-13 for M2 polarization. Second is surface Marker Staining. Select Markers. Identify specific surface markers that are characteristic of M1 and M2 macrophage phenotypes.

M1 Macrophages: CD86, CD80, CD40, MHC class II (HLA-DR in humans), etc. M2 Macrophages: CD206 (mannose receptor), CD163, CD200R, etc. And then is Flow Cytometry Staining Protocol. Single Staining: Pre-

pare single-color staining tubes for each antibody used. Use appropriate isotype controls for each antibody to control for non-specific binding. Multiple Staining: Alternatively, use a panel of antibodies conjugated to different fluorophores for multiparameter analysis.

And then is data acquisition. Instrument Setup: Set up the flow cytometer according to the manufacturer's instructions. Optimize voltage settings and compensation using appropriate controls. Acquisition: Run the samples through the flow cytometer to collect data on fluorescence intensity for each marker.

At the list is data analysis. Gating: Gate the data to distinguish macrophages from other cells based on forward scatter (FSC) and side scatter (SSC) properties. Population Analysis: Analyze the expression levels of the chosen surface markers to distinguish between M1 and M2 macrophage populations. Statistical Analysis: Use appropriate statistical tests to determine the significance of differences observed between M1 and M2 macrophage populations.[9]

3. Results

In visual stimulation protocols to find that in 40 Hz of gamma wave can change the microglia from M1into M2, from pro-inflammatory to anti-inflammatory. patterned visual stimulation has the same result, which improve the result. Immunofluorescence to find the samples with primary antibodies specific to M1 markers (e.g., CD86) and M2 markers (e.g., CD206). FCM flow cytometry to detacted the number of change in microglia's M1 and M2, which find that most of M1 change into M2.

4. Discussion

Research has some strengths in this study. The first is that researcher used a different test, which makes our results more accurate. Secondly researcher should pass our hypothesis, confirmed the M1 will transform under 40 Hz hello M2 from converting proinflammatory anti-inflammatory, it can be a treatment for Alzheimer's disease in a new direction. But there are drawbacks to our experiment. The first is that there are some limitations in the model researcher used; researcher found the effects of gamma wave on M1 and M2 and did not explore changes in BACE-1, which may also be the focus of future research. Researcher believe that our study may open a new way to treat Alzheimer's disease, but other factors should not be ignored.

5. Conclusion

By comparing the fluorescence detection images under different Hz gamma wave, it was found that gamma wave at 40Hz would cause more M1 to convert to M2. This suggests that gamma wave at 40Hz can effectively block the generation of neuroinflammation and thus reduce amino-bata deposition Reduce the risk of Alzheimer's disease.

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