



# HYPOTHALAMIC NEWSLETTER

Welcome to this edition's Hypothalamic Newsletter! We will be discussing how music impacts the brain, the dangers of drugs, and Alzheimers disease.

## Long-term Cocaine Use is Shown to Trigger Anatomical Changes in the Brain

Have you ever thought of how the use of cocaine long-term can impact brain anatomy? Could this explain why repeated drug use can occur? A recent study by Jedema and colleagues revealed specific regions of the brain that are impacted with long-term use of cocaine. They assessed the anatomy of rhesus macaques before and after 12 months of cocaine use using a magnetic resonance imaging (MRI) machine, as well as their inhibitory control and visual working memory using neurocognitive assessments and tests.

## The Macaques Study

Excitingly, the study by Jedema and colleagues revealed that macaques who used cocaine long-term (i.e. 12 months) had lower gray matter density in the temporal cortex, amygdala, orbitofrontal cortex, and insula regions of the brain. Reduction in gray matter density in these regions was significantly correlated with cognitive impairments. Most importantly, previous research revealed that the insula is responsible for detecting and sending interoceptive cues to the cingulate cortex. Interoceptive cues refer to messages about the internal state of the body. One of the primary functions of the insula is to process sensory stimuli.

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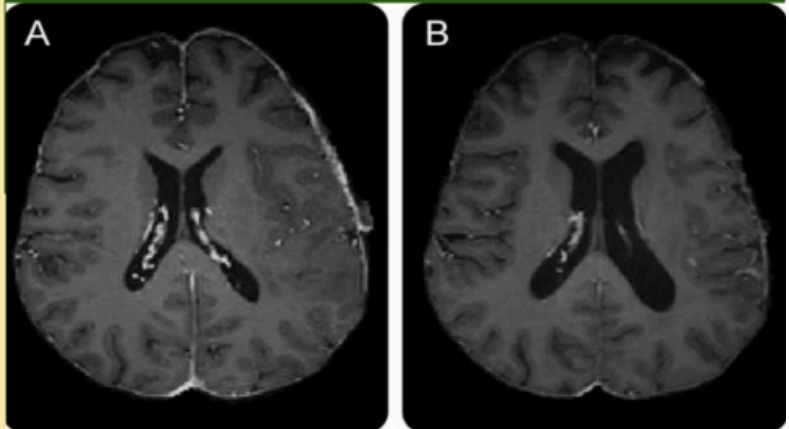
## The Macaques Study Continued

With less grey matter density in the insula, as triggered with long-term use of cocaine, individuals abnormally face stronger sensitivity to interoceptive messages. This can be hazardous because these individuals will likely then experience heightened levels of pain compared to healthy individuals not using cocaine long-term. To cope with increased sensitivity to pain, they may turn to cocaine or other harmful substances.

Additionally, even after 2 years of abstinence, the macaques who used cocaine long-term continued to have reduced grey matter density in the previously mentioned brain regions.

Therefore, it is suggested that long-term use of cocaine can impact the brain for over 2 years, even if individuals abstain. This could mean that individuals who use cocaine long-term have an increased vulnerability to relapse, even if they have been abstaining for at least 2 years, and this can be explained by lasting changes in brain anatomy following long-term use.

## A study discovers a gene signature for plaque eating Microglia in Alzheimers.



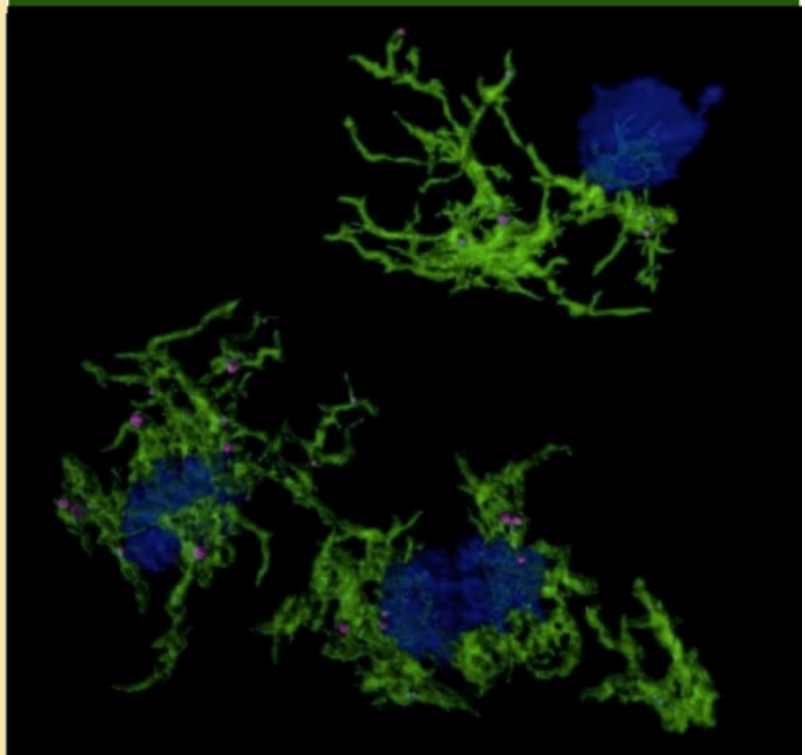
Have you ever heard of Alzheimer's disease? If you have, you probably know that Alzheimer's disease is a type of dementia that affects thinking and behavior. Currently, Alzheimer's has no cure and is the leading cause of death in the elderly. Scientists have been researching to understand Alzheimer's further and hopefully find a cure for the disease. A team of scientists from Duke-NUS Medical School and Monash University conducted a study on Alzheimer's. The research team found gene expression signatures on microglia related to amyloid plaque phagocytosis. Amyloid plaque phagocytosis deals with the  $A\beta$  protein in the brain. Amyloid- $\beta$  peptides are the main ingredient in the mass of decaying nerve terminals around an amyloid core.  $A\beta$  peptides usually are 40 to 42 amino acids long and are produced from an amyloid precursor protein (APP).

The largest brain of any animal is that of the sperm whale.

### A gene signature for plague eating Microglia in Alzheimers continued.

According to Enrico Petretto, an associate professor from Duke-NUS's Cardiovascular and Metabolic Disorders Programme, the study's main goal was to understand the difference between the microglia that were consuming the A $\beta$  proteins and those who weren't. The study achieved this by using a stain, specifically methoxy-XO4. Methoxy - XO4 is a permeable fluorescent amyloid  $\beta$  marker. Methoxy - XO4 binds to amyloid accumulation in post-mortem AD brain sections. Observations made of post-mortem AD brains reveal particular neuropathological changes. These changes include the loss of neurons and synapses in the cortical and subcortical regions of the brain.

The Duke-NUS and Monash study used Methoxy-XO4 in preclinical models of Alzheimer's, and then the team exclaimed and identified the gene expressions on the stained microglia. Furthermore, the study revealed that the microglia that did not ingest the amyloid plaque had similar gene expression patterns to aged microglia. Aged microglia are known to be a significant factor in Alzheimer's pathogenesis. The microglia that did ingest the Alzheimer's amyloid plaques developed a unique gene expression pattern. The credit for this change can be given to a gene called HIF1A. HIF1A, hypoxia-inducible factor 1 subunit alpha, is a protein-coding gene. Further research has to be done before scientists fully understand the relationship between HIF1A and cognitive decline in Alzheimer's disease.



## The Effects of Classical and Heavy Metal Music on the Brain

Are you a metal head? Or maybe you prefer a more relaxing piano sonata? Studies show that different forms of music can in fact affect your brain in different ways. The Department of Neurology in The Medical University of Bialystok, Poland, carried out a study involving 33 healthy students to investigate this concept. On the first day, the students were presented with a sample of classical music; Mozart's Sonata for Two Pianos in D Major for 8 minutes. On the second day, they were presented with heavy metal music; Black Sabbath's "Fear of the Dark" for 7 minutes. The participants wore headphones and were in a silent room, told to focus completely on the music as an EEG (electroencephalogram) took measurements of brain activity, particularly in the temporal lobes, responsible for long term memory. Alongside brain activity, blood pressure and heart rate were also monitored. As a result of the experiment, on average there was no significant shift in the blood pressure or heart rate in the students.

However, there was a notable shift in brain activity. The alpha rhythm is a measure of brain activity in oscillations, varying on average from 7 to 13 hertz. They play a large role in the cognitive functioning of the brain. They are significant for memory, attention, and perception. During the study, the alpha rhythm was measured in waves, and the amplitude was measured. When comparing the amplitude before and after listening to classical music, there is a decrease from 12.75  $\mu\text{V}$  to 11.47  $\mu\text{V}$ . Otherwise, there were no significant changes throughout the process. Thus as a result of the study, it is seen that classical music is unique with its effect on brain activity. Listening to it lowers the alpha rhythm of the brain. Not very much is known at present about the interpretations of these waves, thus the implications of these results are somewhat up to interpretation. Perhaps it is evidence that classical music is relaxing to the brain? Perhaps it is even more distracting than heavy metal music, and lowers the brain's ability to cognate slightly? The brain is a very fascinating mechanism, and there is still lots we have to discover about how it truly works, and what results such as this truly are telling us about our minds.

