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Research Paper

The effect of pain relievers on brain activity and human emotion

Neda Kaffash [a] , Fardad Farokhi [b]

[a] Department of Biomedical Engineering Science and Research Islamic Azad University Branch, Masters in Biomedical Engineering, Tehran, Iran

[b] Azad University Central Tehran Branch, Electrical Engineering, Facaulty Member Tehran, Iran

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Abstract

Acetaminophen oral (APAP) and non-steroidal anti-inflammatory drug (NSAID) are powerful medicines used to reduce and relief the pain. These painkillers used for mild to moderate pain relief but studies show that these pain killers affect both physical pain and social pain. The finding of a new scientific research noted that APAP and NSAID affect cognitive and affective processes. In this survey, we represent the effect of APAP and NSAID on human emotion (happiness, sadness, neutral) and behavior by using EEG brain signals. After that, we indicate the brain over activity and brain locations with Quantitative electroencephalography. At least we have statistical analysis with SPSS. As a result, APAP have a greater effect on emotions than NSAID.

Keywords: APAP, NSAID, EEG signal, painkiller, emotion.

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Introduction

APAP and NSAID are analgesic painkillers that are used for relief of mild to moderate pain. When people have physical pain, one of the common painkillers they use is APAP (the active ingredient in Tylenol). APAP is the most popular painkiller in USA. An estimated 23% of all US adults take APAP during an average week (Kaufman *et al.*, 2002). It is an effective pain reliever for physical ailments. (Kaufman, Kelly, Rosenberg, Anderson, & Mitchell, 2002).Moreover, both painkillers affected the spontaneous EEG. Although non-steroidal anti-inflammatory drugs (NSAIDs) are the most frequently used analgesics, their mode of action is still largely unknown. A research showed that some drugs (like opiate-based drugs, antidepressants, and APAP) reduce not only physical pain but also social pain (e.g., DeWall et al., 2010; Panksepp, 2004). APAP showed effects (relieve aches and pain) by inhibiting the enzymes COX-1 and COX-2, and is active in both the central and peripheral nervous systems. There is an idea that placebos reduce negative emotions like anxiety and fear [4].

In this paper, combining music stimuli along different dose of APAP and NSAID is used in order to detect changes in different brain lobes. We design a system , represent the effect of mention painkillers on human emotions (happiness, sadness and neutral mode). The control subjects in this study are a group of thirteen people, seven male and six female 18 to 30 years old. We used ANT eego mylab device to record EEG brain signals. The effectiveness of two painkillers is studied on emotional status of EEG brain signal.

The main achievements of our paper include : A new dataset of EEG signal is created, Audio music tracks are used to record EEG signal, In order to increase subject's response to the music, each participant bring their own and preferred audio music which is effective for happy and sad emotions stimulation. Two painkillers are selected that don't have major physiological side effects on participants. Moreover, QEEG is used to analyze the changes in the brain activity.

2. Pain

Pain is a sensation but isn't just a physical sensation. It is impressed by behavior, social factors and it can affect emotions and mentality.

Pain is often related to negative emotions such as fear and anxiety [3]. Pain experience activates a network called the pain matrix, including insular, cingulate, periaqueductal, and somatosensory areas (Peyron et al., 2000; Rain ville, 2002; Farrell et al., 2005; Salimi- Khorshidi et al., 2009), which several regions (especially insula and cingulate cortex) are also activated when observing pain delivered to others (Singer et al., 2004; Lamm et al., 2011).

3. Emotion

According to the book "Discovering Psychology" by Don Hockenbury and Sandra E. Hockenbury, ‘’an emotion is a complex psychological state that involves three distinct components: a subjective experience, a physiological response, and a behavioral or expressive response’’. Studies of the physiology of emotion focused on these autonomic nervous system responses, and role of the brain in emotions. Brain scans have shown that the amygdala (part of the limbic system) plays an important role in emotion and fear in particular. The amygdala itself has a structure that has been linked to memory and emotion. All emotions have a motor component. Even if we try to hide our feelings, there will be micro-momentary muscular activation. The anterior cingulate is located right next to the premotor area, which begins the process of forming an emotional expression in the body. The premotor area connects to the motor cortex above it, and then back to the specific muscles of expression. Sadness has been studied more than the other emotions because depression may last for a long time; the effects of antidepressants can be measured based on improved symptoms. APAP dulls the intensity of our feelings about others more than our feelings ourselves. Positron Emission.

Tomography (PET) scanning and functional MRI studies have shown that some emotions associated with different regions of limbic system. Happiness activates several areas of the brain, including the right frontal cortex, left amygdala, and the left insula. This activity involves connections between awareness (frontal cortex and insula) and the “feeling center” (amygdala) of the brain activity than other emotions. Sadness is associated with increased activity of the right occipital lobe, the left insula, the left thalamus the amygdala and the hippocampus. The hippocampus is strongly linked with memory, and it makes sense that awareness of certain memories is associated with feeling sad.

4. Materials and methods

4.1. Participants

We recruited 13 subjects (7women,6 men) in our experiment. All of them are healthy and right-handed and they had no reported history of brain diseases and had normal hearing sensitivity. Before test, subjects must have clean hair without any makeup on their hair and face. The subjects must fill the pretest. The pretest included personal information, history of brain diseases, public mood and had normal hearing power.

4.2. Proceture

EEG signals were recorded in a room with the same conditions (temperature and light) for all participants. They were instructed to open their eyes. Before the recording, the procedure was explained. They should have their own music. One of them was joyful and another one was unhappy music. We conducted three experiments in three days for our study. In the first experiment, subjects took placebo (400 mg sugar). In the second experiment, they received 1000 mg dose of APAP, after waiting 3 hours for the drug to take effect, each participant listened to three minutes audio music tracks for each emotional happiness and sadness topics. In the third experiment, they took 500 mg dose of NSAID. After listening to each audio track, participants

filled posttest and their rating range from 0 (low) to 5 (high) for their own emotional reaction to the audio music. EEG signals were recorded in 32 channels according to DEAP dataset.

4.3. EEG recording and analysis

EEG signals were recorded during the task using 32 channels (according to DEAP database placement). We used ANT eego my lab device to record EEG brain signals. The reference electrode is connected to the left ear lobe and the ground electrode is connected to the right ear lobe. The sampling rates of EEG signals were 250 Hz. For noise reduction, band pass filter with a pass band from 1.0 Hz to 40 Hz was used. EEGLAB was used to eliminate eye movements, blinks and muscle movements. Each music last for 3 min. The middle of music represents stable emotional state. Therefore, we removed the first 30s signal and the last 30s signal. The human emotion recognition system is shown in figure 1.

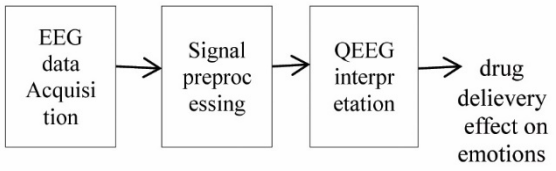


Fig 1: Drug effectiveness framework using EEG signals

5. Painkillers:Psychological Mechanisms of Action

When you take a pain reliever like ibuprofen, it keeps injured or damaged cells from making and releasing prostaglandin. When the cells don't release this chemical, it means that the brain won't get the pain message as quickly or clearly.

So your pain goes away or becomes less severe for as long as the cells aren't releasing the chemical. APAP works in the brain so you don't feel the pain. APAP reduces neural activity in the ACC and AI during social pain (De Wall *et al.*, 2010) and increase theta activity, with only little effect on other frequencies. In particular, the anterior insula (AIs) is engaged not only when experiencing disgusting /pleasing tastes, but also when viewing disgusted/pleased faces (Wicker et al., 2003; Jabbi et al., 2007). Furthermore, brain regions showing shared emotional activations such as AIs have been associated with many other functions beside pain, emotion, and empathy (Kurth et al., 2010).

5.2. Signs of Painkiller in this study

Changes in physical appearance that could indicate the use of painkillers include pupils that are dilated or constricted, changes in weight, and bloodshot or glazed eyes. With painkillers, people who are using them will most often seem very drowsy, or they could nod off without realizing it. Some general signs of painkiller intoxication and use may include: Drowsiness, Poor concentration, Memory problems, Constipation, Slower breathing rate, slower reactions and movements, Apathy, Mood swings, Depression. There are also a variety of lifestyle changes that may occur and indicate painkiller use. These can include: People who are using painkillers may have less money, or they may try to do things like stealing or illegal activities to get more money to pay for the drugs. There is a sense of preoccupation that almost always occurs when someone is using prescription painkillers or any other drug that they're using. They're more concerned with maintaining their addiction than other areas of their life, so their social interactions and work can start to suffer [7]. Individuals who are taking painkillers may exhibit angry outbursts or a general change in attitude. They may also appear anxious or as if they're keeping secrets or not being forthcoming. There can be an overall sense of irritability as well. It's not uncommon for people who are using prescription painkillers to become very aggressive toward individuals who try to talk to them about the drugs, or who they perceive as trying to control their actions.

6. QEEG interpretation

A QEEG brain map enables us to see unique pattern of mental strengths and weaknesses - areas of the brain where there is too little or too much activity, and areas that are not coordinating their activity the best they could so in this research, we want to represent and explain the area of brain activity before and after use of pain relievers. In the first QEEG comparison and interpretation in the mode (there is no pain killer) shows sad music track cause occipital lobes, and temporal lobe over activity, and happy music track cause frontal partial and occipital over activity. When we have Acetaminophen oral (APAP) the over activity in all n\brain lobes diminish deeply but non-steroidal anti-inflammatory drug (NSAID) not only has no meaning full impact on the over activity area but also worse the activity of occipital lobe.

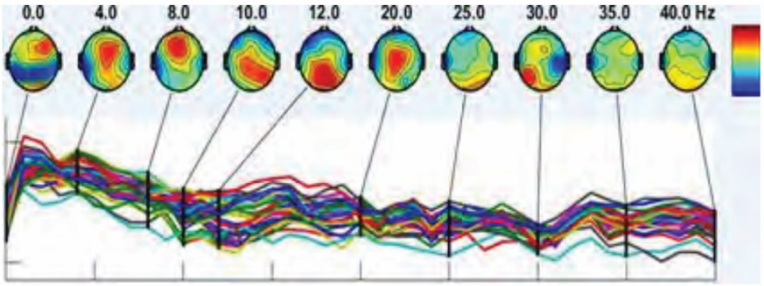


Fig 2: Brain overactivity in happiness with out using painkillers

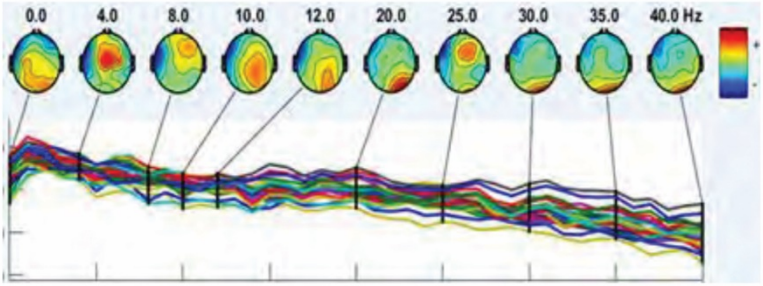


Fig 3: Brain over activity in happiness with using APAP

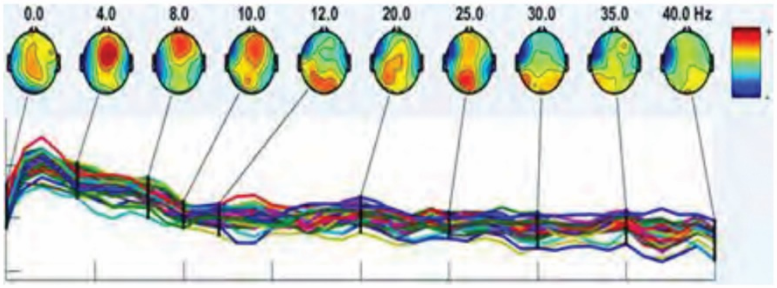


Fig 4: Brain over activity in happiness with using NSAID

4. Results

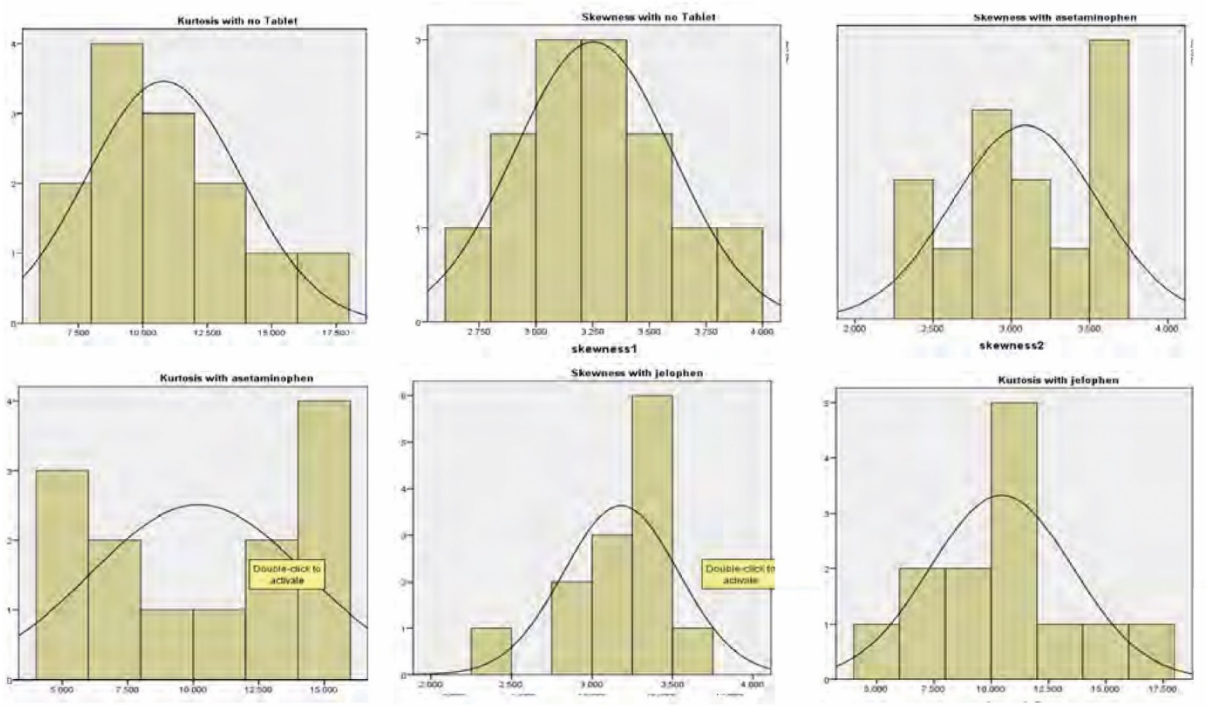
In this study, thirteen subjects were participated voluntarily. Each subject listened to two recorded audio music. After listening to each music, subjects had to fill posttest to label the music and score the music from 0 – 5. SPSS analysis showed that participants who took APAP evaluated extreme stimuli (mean skewness =3.09, mean kurtosis= 10.2) than those who took NSAID (mean skewness =3.18, mean kurtosis= 10.44). Before they took pain killers(mean skewness = 3.25, mean kurtosis= 10.81). After that, Spearman correlation coefficient was calculated. First the correlation was computed between participants who took APAP and those didn't take it. The relevance between two states was positive and they had correlation with each other (P=0, n=320, r=45%). But the correlation was somewhat different between subjects who took NSAID and those didn't take it. (P=0, n=320, r=50%). Normal distribution diagram of sadness with and without using painkillers were shown in figure 5.

We used QEEG to represent the effect of APAP and NSAID on emotions. With no painkillers, we have over activity in alpha band and when subjects use APAP, we have over activity in Beta band and NSAID doesn't have any impressive brain activity. According to the recent studies, we proposed a method that represented the effect of painkillers on emotions. The results show that we have less emotion recognition in subjects take APAP than those who take NSAID. In other words, diagnose different types of emotion in APAP is harder than NSAID. It means that APAP is more effective on social pain than NSAID. Because APAP affect on brain and synapses but NSAID has a tremendous effects on muscle and Na^+, K^+ channels. So APAP is more effective on emotions. As a result, Painkillers not only cause physical symptoms. They're also responsible for a variety of mental, emotional and psychological symptoms.

6. Conclusion

To sum up, this study in healthy volunteers indicates a central analgesic action for the NSAID and APAP. We represented that painkillers reduced both physical pain and emotional pain. It means that participants who took the painkillers had a weaker emotional response than those who had taken a placebo .Based on a survey, APAP (main ingredient of Tylenol) could reduce emotions in human but another research showed that APAP reduced positive emotions.

Fig 5: a. Normal distribution diagram of sadness without taking pain killers(kurtosis), b. Normal distribution diagram of sadness without taking pain killers(skewness), c. Normal distribution diagram of sadness using APAP(skewness), d. Normal distribution diagram of sadness using APAP(kurtosis), e. Normal distribution diagram of sadness using NSAID (skewness), f. Normal distribution diagram of sadness using NSAID(kurtosis).



The results of [5] and [6] show the effect of painkillers on subject emotions. We used QEEG to show the results of pain relievers. One more point is that, we survey the post test scores that participants have filled them. They showed that subjects gave lower scores after taking pain relievers.

The main purpose of this research is that use of some pain relievers can lead to both short- and long-term changes in the brain, which can lead to mental health issues including depression, anxiety, aggression and other problems. These pain relievers may have destructive effect on the emotion of people who have mental disorders. For example, those who have depression and take pain relievers for their treatments, these painkillers may put them on higher risk of depression because these

pain relievers reduce their social and emotional pain too and they may affect their emotions. It is so important and vital to take first important step today and reach out to someone who can help you move towards a fuller and healthier life.

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