Brain Mapping of drug addiction in withdrawal condition based P300 Signals

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Abstract. Drug abuse for a long time will slowly cause changes in brain structure and performance. These changes tend to occur in the front of the brain which is directly interfere the concentration and the decision-making process. In this study an experiment involving 10 drug users was performed. The process of recording data with EEG system is conducted during craving condition and 1 hour after taking methadone. From brain mapping results obtained that brain activity tend to occur in the upper layer of the brain during craving conditions and tend to be in the midle layer of the brain after one hour of taking methadone.

1. Introduction
The current sense of health becomes wider and more dynamic. This means that a person's health can not only be measured from the physical, mental, and social aspects, but also can be measured from his productivity. For someone who has not or does not work anymore, productive can be interpreted socially. Lately, drug abuse is something we're used to seeing around us. They do not know what negative impact they get after abusing the drug, which is in their minds is only a moment's pleasure. Increased drug abuse in Indonesia with social and economic impacts is increasingly alarming. Although in medicine most of the class of nakotics, psychotropic, and other adictivesubsstance beneficial for the treatment, but if in wrong use will result very harm to individual and society especially young generation. No one has ever been trained and prepared to be a parent, and it is not easy to be a parent especially to be an ideal parent. It is difficult to find early evidence in a drug user, usually a user will be detected after reaching the addiction level. Moreover, until now there is no tool that can be used to detect early abuse of drugs.

The influence of drugs on the brainworks: drugs can change the atmosphere of feelings, the ways of thinking, an awareness and behavior of users. That is why narcotics are called psychoactive substances. There are several kinds of effects of drugs on the brain, such as inhibiting the brain work called depreasnsia (decrease awareness for drowsiness) such as opioid group (opiate, morphine, heroin, pethidine) and sedatives (sedativa and hypnotics). The drugs also affects the brain which responsible for the life feelings called the limbus systemas the center of pleasure in the brain. The drugs can also stimulate the brain works so-called stimulants that cause the user in fresh and enthusiasm, more confidence, and become familiar with others. However, this can cause the user can not sleep, anxiety, heart pounding in faster andincreases of blood pressure. Examples are
amphetamines, ecstasy, methamphetamine, cocaine, and nicotine contained in tobacco. Everything related to the drugs are directly connected to the brain activities. Therefore, by measuring the brain activity with electroencephalography (EEG) equipment, the information of the drugs user can be identified.

EEG equipment is now becoming more accessible in the general market, allowing a variety of research related to brain activity easier and wider. The acquired and processed of the brain signals which communicated with external devices is called brain-computer interface (BCI). The brain signal activity used in BCI can be measured using invasive or noninvasive techniques. The BCI based EEG equipment is one of the noninvasive techniques and it is not only used by patients but also by healthy users with various applications [1-7]. Over the last few decades, EEG activities have been widely used to study the brain cognitive dysfunction and neurobiological alterations among drug addicts [8]. In addition to EEG spectral analysis to examine the effects of drug abuser on brain functionality (Davydov and Polunina, 2004; Franken et al., 2004; Polunina and Davydov, 2006; Fingelkurts et al., 2009) [9-12], brain event-related potential (ERP) components were evaluated as a reliable approach to study cognitive abilities related to information processing, selective attention, and memory updating of addicts [8]. Among various ERP components, measuring the amplitude and latency of mismatch negativity, P300, and P600 components in standard condition has attracted special attention in ERP evaluation among addicts [2,13,14]. Additionally, examining cognitive responses to drug-related stimuli showed promising results in providing better understanding of brain functional alterations during withdrawal and abstinence periods associated with addiction traits such as craving and anhedonia [15-16]. For this purpose, various types of ERP paradigms have been designed to probe subjects’ evoked cognitive responses using deviant, affective, and drug-related stimuli [8]. P300 is associated with selective attention, memory renewal, motivation, stimulus significance, activation of inhibitory processes [17-19] and has been investigated among opioid dependents [15, 16, 20-24].

In this paper, an application of signal processing before the brain mapping is proposed. Brain mapping has opened important perspectives for the neurophysiological evaluation of drug abuser, for the discrimination of drug effects on the brain and for the study of the relationship between the brain and behavior. All involved subjects received total brain map analysis. This study demonstrated that there are increased brain disturbances in substance abusers and dependents which can be identified and measured using the EEG tools. These disturbances are not found in as great a number of non-drug abusers with similar psychiatric problems. The drug abusing subjects had the greatest number of total brain abnormalities. Moreover, increasing abnormalities were observed in the more severe drug abuser or dependents compared to the normal controls.

2. Experiment Method

An electroencephalogram is a test that measures and records the electrical activity of the subject brain. Special sensors are attached to their head and hooked by wires to a computer. The computer records the brain's electrical activity on the screen. In the experiment, 10 male rehabilitation subjects were hired from Hasan Sadikin General Hospital (HSGH) of Bandung-Indonesia. Before the experiment, all subject were interviewed by the medical doctor according to their personal data and time period information of the drug abuse. Then the subject completed the questionnaires. Also, urine tests were performed on all subjects. During the experimental period it has been determined that no subjects are taking prescription. The experiment was supported by the Ethical clearance from RSHS Committee to make sure that the conducted experiment was based on the clinical ethic. Moreover, all subject were provided by written informed consent and rewarded with IDR 150.000 for transport compensation.

Participants (i.e., has been informed about the entire experiment procedure) were requested to contribute in an experiment of the EEG signals record of the brain activities. The experiment consist of three session which are before, ten minutes and one hours after methadone consumption, respectively. The EEG technologist will attach several flat metal discs (electrodes) to different places on the head, using a sticky paste to keep contact between the electrodes and the scalp. During the experiment, the electrodes impedance was retained under 5 KΩ such that a high-quality of the EEG
data is obtained. After preparation, each subject were sitting relaxed on a chair while concentrate to the flashed stimuli on the monitor. They were asked to count how many time the drug picture was appear. The sequence appearance of the flashed picture (shown in Fig. 1) were randomly displayed at the separate but sequential experiment. In this paper, we are only considering the channels of Fp1, Fp2, F7, F3, Fz, F4, F8, P3, and P4. The recorded EEG signals were amplified and preprocessed with embedded softwares on WinEEG system with sampling rate about 500 Hz. The experiment process is shown in Fig. 2. The stimuli was run on a different computer with the EEG machine was attached to record and save the data.

![Flashed similar stimuli with (e) as a target](image1.jpg)

**Figure 1.** Flashed similar stimuli with (e) as a target [11].

![Experiment setup](image2.jpg)

**Figure 2.** Experiment setup.
3. Results and Discussions

Raw data is the result of recording EEG signals that have not experienced signal processing or still contain noise and artifact. It is characterized by an irregular waveform signal. Raw data of EEG signals for subject 6 can be seen in Fig. 3. The raw data of EEG signal is filtered using bandpass filter with frequency range 0.5 Hz to 30 Hz because in EEG signal research, the frequency with information is in the range of 0.5 Hz – 30 Hz. So the signal that is outside the frequency will be categorized as an artifact or noise. The bandpass filter results in the EEG signal shown in Fig. 4. Figs. 5-7 show the extracted P300 signals using wavelet method which are Fig. 6 and Fig. 7 indicated the average P300 signals from Fig. 5.

To analyze the P300 features extracted during the paradigm experiment, data were fitted into a repeated model while tasks and features (amplitude/latency) were chosen as within-subjects factors. Results showed that the P300 amplitude of each subject before was lower compared with after taking methadone, while their latency was longer. Results also indicated that task type had a significant effect on between target and non-target differences of P300 amplitude, and the after treatment analysis confirmed the higher P300 amplitude compared with non-target.

The maximum amplitude of about 4 micro volts when craving condition tends to be higher when compared with the amplitude after one hour of drinking methadone which is about 1.25 micro volts. The high amplitude of the target is also followed by high amplitude of the non-target, which means that the brain activity is much higher overall and tended to not focus. The differences can be seen in the post-drinking methadone (Fig. 7(b)) where the target amplitude is significantly higher than non-target.

The high amplitude of the target is triggered by the flashed image of the drug, while the high non-target is suspected to be triggered by the craving condition. Latency also looks significantly different before and after taking methadone i.e. each about 390 ms and 240 ms. This difference can be interpreted as a change in the condition of the subject body including brain as a whole that is subject conditions become more comfortable after taking the drug. Moreover, subjects tend to be more focused and especially more responsive to stimuli inputs. The difference between these two features seems to be sufficient to describe the effect of drugs on brain activity.

Fig. 8 shows brain activity maps which obtained from the P300 signal from two of the 10 methadone subjects when before taking the drug or methadone (craving condition) and after one hour of taking the drug. Red color indicates more dominant the brain activity than other areas. The first that can be seen from Fig. 8 is that in the craving condition the brain activity tends to spread rather than after taking the drug (more active in the frontal lobe area). The spread of brain activity occurs in subject 1 which is the second line of the condition after taking the drug. These area is an occipital lobe and the increase in activity is thought to be due to visual effects of the stimuli. For both subjects, changes in brain activity in the frontal lobe appear to change from the outer layer to the deeper layers. This pattern of change is most clearly seen in subject 1 i.e., the second line craving condition and the second line after taking the drug.

Similar to the P300 signal occurs in the brain map of the beta wave before and after taking the drug, the concentration of brain activity occurs in the second row for each subject. The brain activity at 10 minutes after taking the drug is not significantly change compared with craving conditions. It can be concluded that the drug is very decisive to the dynamics changes of the brain activity. The Reasons why the results may not be helpful include moving during experiment, taking some medicines, drinking coffee, tea, or other foods that contain caffeine before the test, being unconscious from severe drug poisoning. The EEG records changes in the brain waves that may not be in just one area of the brain. A problem affecting the entire brain such as drug intoxication or metabolic disorders that change the chemical balance in the body, including the brain may cause these kinds of changes.
Figure 3. Raw data.

Figure 4. Filtered signals using Bandpass Filter method.

Figure 5. The extracted signals using wavelet method.
Figure 6. Extracted P300 signals (target) for each considered channels: (a) before and (b) after taking methadone.
Figure 7. The Average Extracted P300 signals (target and nontarget): (a) before and (b) after taking methadone.

Figure 8. 3D Brain Mapping of the brain activities of two subjects before and after taking methadone.

4. Conclusions

The comparison effect of the drug abuse to the brain activities before (craving condition) and after taking the drug or methadone is provided. It is obtained that the maximum average amplitudes is highly higher in craving condition than after taking the drug. The abnormality of the brain activity in the craving condition is highly related with the drug abuse. The drug abusing subjects had the greatest number of total brain abnormalities. Moreover, increasing abnormalities were observed in the more severe drug abuser or dependents compared to the normal controls.

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