Changes in Brain Wave Amplitude Due to Methadone Administration based P300 Similar Stimuli

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Abstract: Drug use in Indonesia tends to be increasingly out of control where the number of users continues to increase every year. The dangers of drugs can cause various adverse effects, including psychotic behavior, convulsions, and even death due to overdose. The most dominant part disturbed by drugs is the frontal lobe of the brain, one effect is the reduced concentration of the user. To minimize this addiction, therapy with methadone (a synthetic drug to replace opioid drugs) is used. In this paper, an experiment with therapeutic patients to detect changes in brain wave amplitude due to methadone administration was carried out. EEG data recording of each subject is done using an EEG system with 19 channels. To stimulate the change in amplitude, each subject is given a stimulus that is by displaying several random images on a monitor. Each of them consists of 4 images similar to drugs referred to as non-targets and 1 image of drugs called targets. In one session all images will be displayed randomly for 10 turns (a total of 20 seconds). To minimize interference or artefacts on the recording, the data is filtered by bandpass (0.5-70 Hz) and wavelet, respectively. From this experiment it was found that significant changes in brain wave amplitude after methadone intake were obtained. These results indicate that the use of methadone is very influential on brain wave activity. The decrease is part of the reduced level of desire to consume drugs.

1 INTRODUCTION

Drugs are substances that, if injected into the human body, whether orally or taken, inhaled, or injected, can change a person's thoughts, moods or feelings, and behaviour [1-4]. Drugs can cause physical and psychological dependence (addiction). The abuse of narcotics and illegal drugs among the younger generation is increasing now. The rise of deviant behavior of the young generation can endanger the survival of this nation in the future. Because youth, as a generation that is expected to be the successor to the nation, are becoming increasingly vulnerable to being devastated by nerve-damaging addictive substances. So that the young man cannot think clearly. As a result, the hopeful and intelligent generation of the nation will remain only memories [5-8]. The target of the spread of this drug is young people or adolescents. If averaged, the target age of this drug is the age of students, which ranges from age 11 to 24 years. This indicates that the dangers of drugs at any time can target our students anytime. Narcotics come from three types of plants, namely opium, cannabis, and coca. Drug dependence can be interpreted as a condition that drives a person to consume drugs repeatedly or continuously. If he does not do so, he feels addicted (craving) which causes discomfort and even a very painful feeling to the body [9-10]. Narcotics are substances or medicines that come from plants or not plants, both synthetic and semi-synthetic which can cause a decrease or change in consciousness, loss of pain and can cause dependence (Law No. 35 of 2009). Psychotropic substances are substances or drugs, both natural and synthetic not narcotics, which have psychoactive properties through selective influences on the central nervous system that cause changes in mental activity and behavior. Psychotropic substances are substances or drugs, both natural and synthetic not narcotics, which have psychoactive properties through selective influences on the central nervous

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system that cause changes in mental activity and behaviour[11-12].

In an effort to minimize the symptoms of drug addiction, there are several ways commonly done one of which is methadone therapy. Methadone is a type of drug that is also a synthetic opioid drug. however, this drug can be used to prevent symptoms of craving and the most important of these drugs is to have a longer life time which is around 22 hours. This time is different from the time possessed by drugs in general, which is around 3-4 hours. So far, methadone is quite effective against stopping use of opioid users, such as heroin, morphine, and cocein. [9-15]. To identify metadhone's reaction to changes in brain activity, an experiment involving several subjects with a recording device using EEG was conducted [11, 12, 16-17]. Even Related Potential (ERP) is one of the types of signals that can be recorded from the brain in the EEG. Sinal is data that reflects neural bio-electric activity associated with providing stimulus. ERP component consists of several components, one of which is a positive component named P1, P2, P3, or according to the latency period (P50, P100, P300) [16-22]. Each component reflects the activation of each neuron. The ERP signals are very sensitive to the given stimulus, but psychological factors can also affect the signal performance [20-22]. The P300 component is a wave that can detect the brain's implusivity when given a certain stimulus. In this study, the P300 signal was used to detect the effect of methadone administration on brain implusivity in drug addicted patients [16, 18, 23].

EEG-P300 signal is the type of ERP component chosen to recognize patterns of brain activity due to drugs in this study. P300 terminology is obtained from the positive wave polarity at 300 milliseconds after the stimulus is given. P300 depends on the duration of the stimulus process but does not depend on the process of selecting and implementing responses. The P300 component is more likely to reflect the cognitive process of processing stimulus information [24]. Based on the shape and characteristics of the P300 components, the features used for identification are the maximum amplitude and and the frequency. Latency is the time it takes for the brain to respond to stimuli. In the simple task of auditing discrimination the latent period is around 300 milliseconds, whereas in the complex decision making process the latent period can reach 400-800 milliseconds [24, 25].

Research and experiments with proposed experimental patterns and using brain signal recording to observe changes in brain activity for methadone administration are still rarely performed. In addition to the much lower cost, experiments using EEG have several advantages such as portable, non-invasive, and more flexible to be developed both from software and integration with other hardware. Another thing that encourages the implementation of this activity is that researchers are more flexible in conducting observations from various points of view as well as bases in choosing an algorithm that is suitable for the signal character. Furthermore, this trial was specifically designed based on the needs and complaints and constraints faced by psychiatric doctors in hospitals.

2 METHOD

Methadone therapy is expected to reduce drug use, risk behavior, crime, and increase productivity, and get family support for narcotics users. In the experiment, we worked with 8 male respondents aged 20-40 years who were addicted to drugs and were undergoing the methadone rehabilitation at Hasan Sadikin Hospital, Bandung, Indonesia. Data collection was carried out for 3 days. Respondents were controlled so as not to consume methadone and other substances before data collection. For data processing, 7 channel electrodes were used in the frontal section (Fp-1, Fp-2, F7, F3, Fz, F4, F8) according to the 10-20 system.

At the time of recording, subjects were given stumulus in the form of images collection consist of 4 nontarget images and 1 target images stimulus, respectively. All stimuli images are randomly flasshed about 300 milliseconds with pauses of each 100 millisecon (Fig. 1). This collection of images is displayed with random stimulus arrangements about 10 times or for 20 seconds. EEG data recording is done before and after 1 hour the subject consume the methadone.

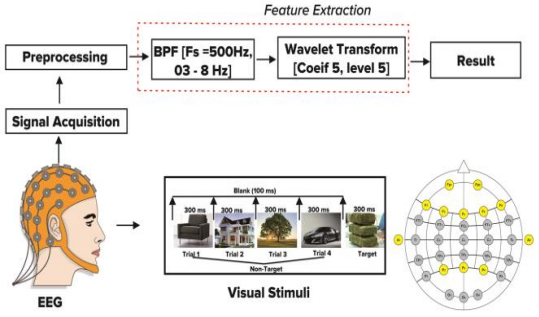

Fig. 1. The used Stimulus in the Experiment.

3 RESULTS AND DISCUSSIONS

The process of selecting different images aims to make it easier for subjects to distinguish targets and non-targets (Adjusted with the subject's condition as a drug user). Assumption that subjects who are familiar with and addicted to drugs will give a different response when given a target image stimulation than non-target stimulation both in terms of amplitude and latency of the EEG-P300 component. Observation of differences in the components of EEG-P300 before and 1 hour after the subject consume the methadone. The P300 component when viewing target images will provide higher amplitude with faster latency than non-target. Subjects who have not been given methadone have a higher level of interest in methadone (craving), consequently the amplitude after consuming methadone must be lower with slower latency. Subjects are in a state of craving if given a drug stimulus will respond more quickly and be expressed by a smaller (faster) latency. The decrease in amplitude value is also supported by the influence of methadone which tends to make the subject sleepy where theta waves increase and beta waves decrease. The filtered and extracted EEG signals (subject 6) (a) before and (b) after methadone intake are given in Fig. 3.

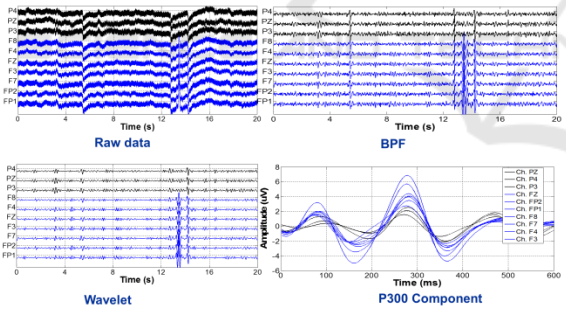

Fig. 3 Filtered EEG Signals (a) Before and (b) After Methadone Intake.

In Fig. 4 clearly visible the changes in the regularity of the extracted signal pattern after consuming methadone. The regularity of the signals between these channels is a representation of the calmness and comfort of the subject. This indication shows that the effect of methadone consumption can be significantly seen in brain activity within a 1 hour period of drug use.

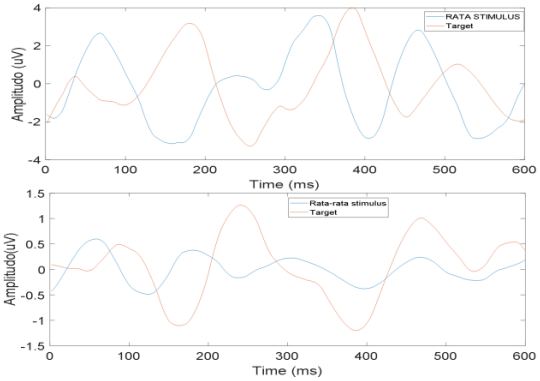

Fig. 4 Extracted EEG Signals using wavelet method: (a) before, and (b) after Methadone Intake

After processing the data, comparison of subjects' responses to target and non-target image stimuli can be seen by comparing the results of the average amplitude and latency of all subjects in Table 1. In general (both before and after consuming methadone) the results of amplitude due to target stimulus tend to produce higher amplitude and slower latency for non-targets. Before consuming methadone, subjects 3 and 6 had lower amplitudes towards nontarget. Similar results were also found after consuming methadone in which subjects, 3, 6, and 7 had lower amplitudes towards nontarget. This is due to the type of drug consumed by the subject which is very varied which causes methadone therapy to be less effective in the subject. In addition, the dose of methadone used during methadone therapy does not decrease and remains high, which is likely due to the efforts of subjects who are old enough so that the process of new neuron growth is much slower. Another possibility is that subjects 3, 6, and 7 showed positive urine test results using benzo during experiments. The use of benzo will certainly strengthen each other against the use of methadone which causes the subject to be sleepy. This result is in accordance with the decrease in amplitude and tends to increase the latency value.

Except for subjects 4 and 8, a decrease in the amplitude of the EEG-P300 signal was found after being given methadone. A decrease in amplitude indicates a decrease in the respondent's desire to consume drugs or a reduced level of subject concentration. Meanwhile, faster latency after using methadone indicates an increase in respondents' awareness after using methadone. In subjects 4 and 8, the amplitude and latency after being given methadone have a higher value compared to before using methadone. This difference occurred because it was suspected that subjects 4 and 8 did not take methadone treatment regularly, and they were more likely to take other drugs than methadone during the

treatment period. This can be proven from the dose of methadone given at the time of the study was almost the same as the highest dose of the subject even though the subjects had been undergoing methadone therapy for 2 and 6 years, respectively. A similar dose of methadone is thought to be not strong enough and does not work optimally to reduce craving on the subject. In addition, there are benzo levels and a history of amphetamine use which can cause methadone not to function optimally in decreasing drug use.

Table 1. Amplitude dan Latency of all subject before and after methadone intake (Target and nontarget)

Subject	Target Stimulant				Non-Target Stimulant			
	Pre-Methadone		Post-Methadone		Pre-Methadone		Post-Methadone	
	Amplitude (uV)	Latency (ms)	Amplitude (uV)	Latency (ms)	Amplitude (uV)	Latency (ms)	Amplitude (uV)	Latency (ms)
Subject 1	314.8755	286	162.9096	526	26.4366	562	8.2277	600
Subject 2	39.7248	386	34.6898	2	19.0109	86	2.5528	486
Subject 3	38.7495	76	11.8405	576	50.1381	236	14.9654	600
Subject 4	8.7280	174	10.4094	558	3.7651	324	2.5209	196
Subject 5	14.4102	424	4.3683	134	2.1886	552	0.3239	304
Subject 6	2.6643	218	2.6840	600	6.4819	134	19.6049	560
Subject 7	6.4835	590	1.9905	322	3.8031	372	3.0156	542
Subject 8	16.5735	600	28.1349	194	10.3552	280	5.8296	278

All data is then grouped by target, non-target, both before and after consuming methadone, then averaged, so that the graph in Fig.5. y-axis indicates amplitude in microvolts and x-axis indicates latency in milliseconds. Subject data 1 in Table 1 has a very high amplitude value, so it is not included in the average data processing. The data anomaly is likely to occur because of the influence of the environment during the data collection process.

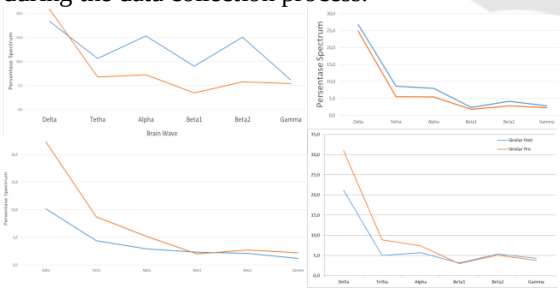

Fig. 5. Comparison of EEG-P300 Amplitude and Latency before and after Methadone Intake.

From the experimental results, the pre-methadone signal obtained in the target image has slightly lower amplitude than post-methadone, and has shorter latency. A decrease in amplitude after a subject consumes methadone indicates a decrease in the subject's desire to consume drugs. The reduced latency in post-methadone indicates the higher level of concentration or awareness of the subject which is characterized by the faster subject responding to an impulse. This majority statement is consistent with the initial assumption that the amplitude tends to decrease after consuming methadone with latency which tends to be slower. The inaccuracy of the results obtained can occur because post-methadone data retrieval is done 1 hour after the subject drinks methadone, while methadone only reacts optimally to the brain after more than 3 hours. This allows the implantivity response to the target image to be lower than at 1 hour after the subject took methadone. Drug abuse that is not controlled slowly will have a negative impact on thoughts, behavior, and social relations. However, permanent effects will occur on the body that can slowly destroy the system and function of the brain which culminates in permanent disability or even death.

4 CONCLUSIONS

Methadone intake by the drug rehabilitation patients causes a decrease in the brain's implusivity to given stimuli which indicates a decrease in the level of desire for drugs after being given methadone. The main results of the present analysis indicated that the subjects have a longer P300 latency and a lower P300 amplitude after consuming methadone. This study revealed that drug patients have abnormalities in the P300 component, which may reflect deficits in cognitive function.

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