EEG Patterns Analysis of Methadone Patients with Closed Eyes Condition using Wilcoxon Test

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Abstract: This research was conducted to know the effect of methadone on brain waves before and after consuming methadone with closed eyes and relaxed body conditions. EEG signal recording will use 19 channels, which are placed using a 10-20 system. The raw data will be filtered using a bandpass filter (0.5 - 70 Hz), removal of artifacts using the Independent Component Analysis (ICA) method, and feature extraction using the Fast Fourier Transform method. Then a significant test will be carried out using the Wilcoxon test with a significance value (accuracy) of 95% or $p < 0.05$. The results were obtained, namely the effect of methadone on brain waves with an average number of participants that is 14 people on alpha waves. Furthermore, each wave occurs at a different recording stage.

1 INTRODUCTION

Methadone maintenance therapy is one of the stages of rehabilitation for opioid drug users, such as cocaine, heroin, marijuana, and others (Dewi, 2017). This therapy is done to help addicts reduce the habit of using needles (Kementerian Kesehatan RI, 2013). This is because the methadone given is like a syrup, so it must be consumed by mouth, not by injection. To determine the effect of methadone, it is still seen through changes in behaviour alone. This is not accurate enough, because not all patients follow the therapy properly and routinely. Several researchers have researched about EEG recording to determine the effect of methadone on patients during the rehabilitation process.

EEG has been use since 1929 (Simbolon, 2019). EEG is used to record the electrical activity in the brain with electrodes placed on the scalp (Sanei, 2007). Usually, an EEG is used to look for abnormalities in the brain, such as epilepsy. However, now, EEG can be used to see the effects of drug on the brain.

The electrical activity of the brain based on its frequency is divided into delta, theta, alpha, and gamma waves. Delta (δ) has a frequency range from 0.5-4 Hz and an amplitude of 20-200 μV. Delta waves are generated in a state of deep sleep, without dreams or what is commonly known as deep sleep. Theta (θ) has a frequency range of 4-8 Hz and an amplitude of 10 μV. Theta waves are generated during light or very drowsy sleep, trance, hypnosis, meditation. Alpha (α) has a frequency range from 8-13 Hz and an amplitude is normally below 50 μV. Alpha waves are generated in a state of relaxation or begin to rest, going to sleep, the transition between conscious and unconscious. Beta (β) has a frequency range from 13-30 Hz and an amplitude is normally below 30 μV. Beta waves are generated when you are thinking, focused. Gamma (γ) has a frequency range from 30-50 Hz. Gamma waves are generated when a person feels panic, fearful, and is in a state of full awareness. The brain wave pattern of normal people can be seen in Figure 1.

To determine the effect of methadone, several researchers conducted studies on theta, alpha, and beta waves (Jahja, 2019; Wang, 2014; Kusumandari, 2019; Gunawan, 2012; Uson, 2008). With the results are that the used of methadone affect those three brain waves. However, the data processing used was to see the trend of these three waves in methadone

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maintenance therapy patients with normal people. Besides that, some focus on the frontal part only

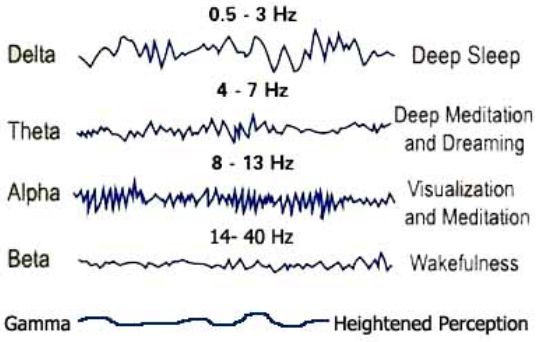

Figure 1: Brain wave pattern of normal people.

(Turnip, 2019; Turnip 2017). Based on this, this study will focus on 4 waves, namely delta, theta, alpha, and gamma to see the effect of methadone before and after consuming methadone. The stage after consuming methadone will be divided into 3 sessions, namely 10 minutes, 1 hour, and 3 hours after consuming methadone. From 3 sessions after consuming methadone, it will be compared with before consuming methadone. The recording process will be carried out with closed eyes and relaxed body condition. It aims to help doctors find out which brain waves have undergone significant changes to create the right treatment for other brain waves as well.

2 METHOD

2.1 Participants

Participants used 30 men aged 25-45 years and have a history of at least high school education. These participants will be divided into 2 groups, namely 19 participants for methadone rehabilitation patients and 11 participants as control participants. The methadone rehabilitation patient participants were TRM of RS Hasan Sadikin, Bandung. The criteria that a methadone patient participant must have is that it has been more than 6 months and its regular use, has been in a stabilized dose, which is above 60 mg, is a THD patient (take-home doses), does not use other types of drugs other than benzodiazepines for the last 1 month, and do not have serious physical illnesses, epilepsy, and organic mental disorders that can make communication difficult.

2.2 Experiment

The experiment is carried out in the UNPAD Faculty of Medicine treatment room, Bandung. Each participant in a methadone rehabilitation patient will undergo 2 recording stages, before and after consuming methadone. During the recording process, participants will be directed by the operator to be relaxed, eyes closed, and minimize any unexpected movements and eye blinks.

Experiments have been completed with ethical clearance. Before the experiment, each participant was required to take a urine test and fill out informed consent. Then the subjects were interviewed by medical team about the subject related with an abuse of drug. During the recording, the subject was asked to relax with closing eyes before, after 10 minutes, one hour, and after three hours of methadone intake. This time rule was chosen to identify the change of brain activity to the given doses of methadone. It is also predicted that after three hours, the craving has been stopped as the methadone has effectively functioning. The experiments were conducted in a room that has been conditioned from the noise and comfort with the subject. Then the subject is paired with a device in the form of an electro-cap on the head and also a belt tied to the chest of the subject such that the electro-cap is fit with the subject body. The EEG signals are recorded through 19 electrode channels, including Fp1, Fp2, F7, F3, F2, F4, F8, T3, C3, Cz, C4, T4, T5, P3, P2, P4, T6, O1, O2 (Fig. 1). The Cz (central part of the brain) is chosen as a reference. When electrodes are installed on the subject head, there will be a large impedance between the scalp and the electrode. Therefore, electrolyte liquid is needed which serves to minimize those impedance such that the current (brain activity) flows more easily. The used electrolyte liquid is electro-gel. Electrode

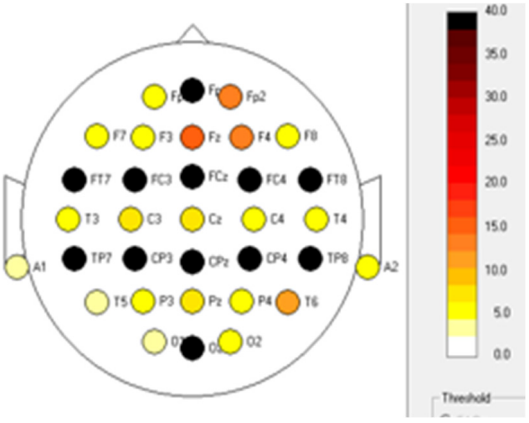

Figure 2: Position with impedance electrode.

impedance can be monitored in the WinEEG software before the signal recording process is started. The appearance of the impedance setting is shown in Fig. 2. The dark colour on the electrode indicator indicates a large impedance (inactive), while the bright colour indicates a low impedance. In this experiment, the impedance is retained under 5 KOhm such that a high-quality of the EEG data is obtained.

2.3 Pre Processing

The results of the recording of the EEG signal will be obtained in the form of raw data which will be followed by a filtering process using a Finite Impulse Response (FIR) with a bandpass filter (0.5-70 Hz) impulse response type and artifact removal using the Independent Component Analysis (ICA) method (Wang, 2014).

Independent Component Analysis (ICA) can be used to extract the signal source underlying a series of mixed signals being measured. In this study, the ICA method was used to separate the EEG signal from the overlapping artifacts on the electrodes attached to the scalp assuming statistically the signal source is independent.

EEG data is assumed to fit the following equation model:

$$x(t) = As(t)v(t) \quad (1)$$

Where, in equation (1) there are three parts, namely $x, s,$ and v, each of which is a vector of the signal source, the observed signal, and the noise that occurs at discrete time. $x(t) = [x_1(t), x_2(t), \ldots, x_m(t)]^T$is a linear mixture of sources. $N\ s(t) = [s_1(t), s_2(t), \ldots, s_m(t)]^T$, A is a mixed matrix with size MxN, and $v(t) = [v1(t), v2(t), \ldots, vM(t)]^T$is additional noise on the EEG sensor.

2.4 Feature Extraction

To get the characteristics of each wave, feature extraction will be carried out using the Fast Fourier Transform (FFT). Mathematically represented by equation (2), namely (Turnip, 2019):

$$s(f) = \int_{-\infty}^{\infty} s(t)e^{-j2\pi ft}dt \quad (2)$$

Whereas $s(f)$ is the frequency domain signal, $s(t)$ is the time domain signal, and $e^{-j2\pi ft}$ is a constant.

The signal processing scheme is given in the Figure. 3

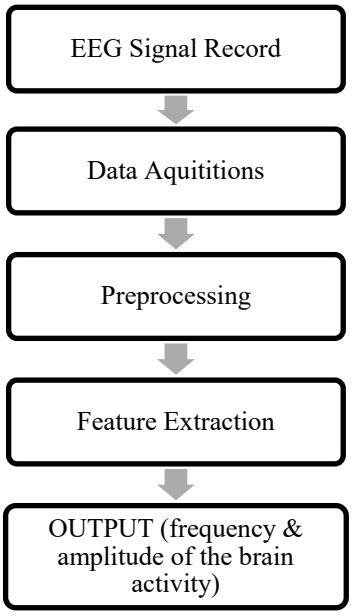

Figure 3: Signal processing scheme.

2.5 Wilcoxon Signed-rank Test

The Wilcoxon signed-rank test is the nonparametric test equivalent to the dependent t-test. As the Wilcoxon signed-rank test does not assume normality in the data, it can be used when this assumption has been violated and the use of the dependent t-test is inappropriate. It is used to compare two sets of scores that come from the same participants. This can occur when we wish to investigate any change in scores from one time point to another, or when individuals are subjected to more than one condition.

The Wilcoxon signed-rank test represented by equation (3):

$$W = \sum_{i=1}^{N_r}\left[sgn\left(x_{2,i} - x_{1,i}\right).R_i\right] \quad (3)$$

Whereas W is test statistic, N_r is sample size, sgn is sign function, $x_{1,i}, x_{2,i}$ is corresponding ranked pairs from two distribution, and R_i is rank i.

3 RESULT & ANALYSIS

The results of EEG recording on closed eyes can be seen in Figure 2. Raw data in Figure 2 will go through several stages of signal processing, namely from the filtering process, removal of artifacts, feature extraction, and up to data processing.

The effect of methadone use can be seen through changes in the amplitude value before and after

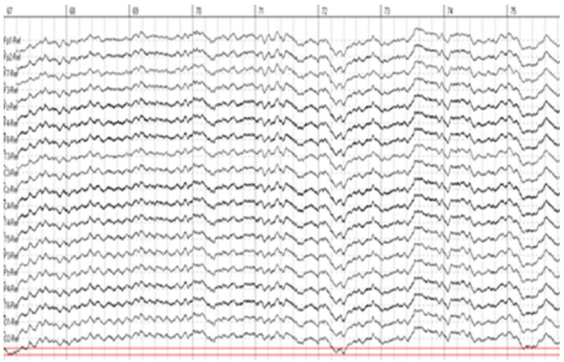

Figure 2: Raw data on closed eye.

consuming methadone. One way is to use the Wilcoxon test. Wilcoxon test is intended for data that are not normally distributed (Turnip, 2017). To determine the influence of methadone use, it can be seen from the Sig.2-tailed value. In this study, using the assumption of accuracy with a Sig. 2-tailed value <0.05 (p <0.05) which is equivalent to 95%. The sig.2-tailed value can be seen from before 10 minutes, before 1 hour after consuming methadone, and before 3 hours after consuming methadone.

Based on the results of recording with closed eyes, it can be seen that each wave has a different rate of change for each channel, as shown in Table 1.

Table 1: Recapitulation of the Wilcoxon test of 19 participants.

Channel	*Delta*		*Theta*		*Alpha*		*Gamma*	
	Sig.2-tailed	Number of participants	Sig.2-tailed	Number of participants	Sig.2-tailed	Number of participants	Sig.2-tailed	Number of participants
F_{p1}	-	-	-	-	-	-	0.019	5
F_{p2}	0.011	3	-	-	-	-	0.003	5
F_7	0.033	4	-	-	-	-	-	-
F_3	0.02	4	-	-	-	-	0.022	5
F_z	0.012	5	-	-	-	-	-	-
F_4	0.016	4	-	-	0.049	12	0.036	5
F_8	0.009	3	-	-	-	-	-	-
T_3	0.049	5	-	-	-	-	0.002	5
C_3	0.012	4	-	-	-	-	0.046	7
C_z	0.022	4	-	-	0.049	15	0.006	5
C_4	0.018	5	-	-	0.005	15	0.018	6
T_4	0.018	5	-	-	-	-	0.036	6
T_5	0.025	5	-	-	-	-	0.03	6
P_3	0.013	3	-	-	-	-	0.027	7
P_z	0.028	5	-	-	0.012	14	-	-
P_4	0.018	5	-	-	0.03	14	0.014	6
T_6	0.012	5	-	-	-	-	0.024	4
O_1	0.006	3	-	-	-	-	-	-
O_2	0.016	5	-	-	0.027	14	0.014	6
Average	-	4.24	-	-	-	14	-	5.57

In Table 1, it can be seen that, in the delta, almost all channels experienced significant changes with a p-value <0.05, with the mean change of participants at 4.24 people. This change occurred before taking methadone to 10 minutes after taking methadone. In the theta wave, there was no significant change in all channels and all recording stages. This is because all of them have a p value> 0.05. In alpha waves, several channels experience significant changes, namely on the F4, Cz, C4, Pz, P4, and O2 channels with an average number of participants who experience changes, namely 14 people. However, not all of these channels have undergone significant changes at the same stage. Channels F4 and Cz occurred before consuming methadone with 10 minutes after consuming methadone, while C4, Pz, P4, and O2 occurred before consuming methadone 1 hour after consuming methadone. This change in alpha waves occurs, because of the p-value <0.05. In gamma waves, almost all channels experienced significant changes and occurred at the same stage, namely before consuming methadone with 3 hours after consuming methadone with the average participant who experienced changes, namely 5.57 people. When compared with the average number of participants who experienced changes from before to after

consuming methadone, the effect of methadone was mostly felt in alpha waves although not in all channels.

4 CONCLUSIONS

Based on the average number of participants, it can be seen that there is an effect of methadone that is mostly felt by 14 participants on alpha waves. Besides, each wave occurs at a different recording stage.

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