P300 auditory wave image and its relation to cognitive function in subjects with marijuana addiction: a cross-sectional study in Cipinang and Pondok Bambu Penitentiary, Jakarta

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Abstract. Subjects with marijuana addiction tend to have cognitive function impairment. Auditory P300 wave, a potential objective tool in examining cognitive function, can assess cognitive function in the auditory pathway to the cortex. Cognitive function impairment can be assessed by prolonged latency and decreased amplitude. The present cross-sectional study was conducted between June and August 2012 involving 68 subjects with marijuana addiction. Cognitive function was assessed using Rey Auditory Verbal Learning Test. Subjects were assessed with an auditory P300 wave examination using both latency and amplitude. Forty subjects had cognitive function impairment; eight had abnormal P300 latency, whereas 60 (88.2%) had decreased amplitudes. There was significant correlation between P300 amplitude and cognitive function, but not between P300 latency and cognitive function. Marijuana can impair cognitive function, especially related to attention and memory deficit indicated by a decreasing P300 amplitude. However, P300 latency did not indicate a cognitive function impairment-related abnormality, which could have arisen from an improper range application developed with reference to American subjects. Overall, the results confirmed that cognitive function impairment due to marijuana addiction can be objectively revealed by decreasing P300 amplitudes. Further studies are needed to confirm appropriate range application in both adult and pediatric Indonesian populations.

1. Introduction
Auditory evoked response (AER) is activity in the auditory system that involves the ear, auditory nerves, and auditory regions in the brain, produced or stimulated by sounds (acoustic stimuli). The acoustic stimuli initiating AER could be clicks (short and sharp sounds), pure melody, or speech sounds. The category of AER is represented on the basis of the shape of the wave, which could be in the form of an early latency response, auditory middle latency response (AMLR), or auditory late response (ALR) [1].

The ELR consists of electrocochleography (ECochG) and auditory brainstem response (ABR). ECochG occurs between 1.5 and 2 millisecond after the acoustic stimuli is given, whereas the ABR occurs between 5 and 6 millisecond after acoustic stimuli. The AMLR occurs between 15 and
50 millisecond, after the ABR and before the ALR. The ALR consists of the P300 auditory response and mismatch negativity response and occurs in the range of 50–500 millisecond after acoustic stimuli. The P300 auditory wave occurs at the 300th millisecond as the main wave with an amplitude >5 µvolt following oddball auditory stimuli [1-3].

P300 auditory wave action potential is an objective image that provides information on neurophysiological changes or cognitive processes including attention, memory function, and perception, and was identified during the 1960s. This action potential originates from brain activity in the central nervous system. The response emerges in the nerve path from the midbrain, thalamus, and cortex, which are capable of providing information regarding auditory process at a higher level and generating comprehension, process, and integration of auditory signals leading to information regarding attention, comprehension, and behavioral control to the auditory signal at the cortex cerebri level [2-7].

P300 auditory wave action potential is recorded conventionally, using an oddball paradigm. The first stimuli, also known as standard stimuli, appear often (80%), regularly, are predictable, and are not the target signal. The second stimuli, also known as target stimuli, appear rarely (20%), irregularly, unpredictably, and are the target signal. The appearance of the P300 auditory wave depends on the ability to detect the difference between standard and target stimuli, which is affected by cognitive processes; therefore, this it is known as “cognitive evoked response”. The cognitive process can be differentiated on the basis of sound characteristics, the auditory temporal process, attention, and memory. The region of the brain that contributes to the P300 wave is a subcortical structure (hippocampus and the central region involving the limbic system and thalamus), an auditory region in the cortex and frontal lobe [2].

The P300 auditory test is an examination that helps assess cognitive function in terms of attention and memory. Several studies have reported that the latency in the P300 auditory test is systematically prolonged when cognitive function is damaged. In adults, situations that can damage cognitive functions include drug use, dementia, neurological disorders, mental disorders, trauma to the head, Parkinson's disease, alcoholism, cerebrovascular damage, brain tumors, schizophrenia, and Alzheimer's disease. In children, it is found in cases such as delayed speech, attention deficit hyperactivity disorder (ADHD), autism, auditory processing disorder, Down's syndrome, and difficulty studying. This shows that the P300 auditory test can be used clinically for cognitive function detection [8,9].

One of the drugs that can damage cognitive function is marijuana. The marijuana plant, Cannabis sativa, popularly known as weed, contains the alkaloid 9-tetrahydrocannabinol (Δ²-THC) alkaloid. Marijuana heightens sensory sensitivity including auditory sensation and causes cognitive function damage mainly in terms of memory and attention function, psychomotor characteristic damage, and psychotic reactions. Several studies show that there is cognitive damage to memory and attention during acute effects of marijuana use, which continue even after the subject no longer uses the drug [10-19].

There have been studies addressing the effect of marijuana on auditory functions that have been conducted since the 1960s. These studies show that marijuana can damage auditory signal processes. Roth et al. as quoted by Mulheran [11], stated that there is significantly decreased latency (>100 millisecond) in AER after inhaling 10 mg of marijuana. Ehlers et al. [20] studied the relationship of event-related potential components on marijuana addiction and other drugs in adult Indians and found prolonged P300 auditory wave latency. Roth et al. as quoted by Kouri [4], reported that using marijuana for a long period of time can decrease P300 auditory amplitude but not P300 auditory latency. Prolonged P300 latency caused by marijuana corresponds to delayed activity in the attention pathway when responding to stimuli, which is related to memory functions and renewing memory functions [20].

The present study was performed on adults because a homogenous population was needed in whom cognitive function disorder caused by marijuana addiction was suspected. Such a population is often found in penitentiaries. Subsequently, the P300 examination is expected to be conducted in children.
with delayed speech who often visit the otorhinolaryngology poly in Cipto Mangunkusumo Hospital community. There were 65 cases of delayed speech with normal peripheral hearing function in the polyclinic in the period of January 2009–December 2010. The cases increased to 145 during January 2010–December 2011. In patients with delayed speech, the otoacoustic emission and brainstem response auditory (BERA) examination results were normal, who were then referred to the pediatric neurology division to assess the possibility of ADHD, acoustic spectrum, or acoustic behavior disorders. This indicates that the P300 examination is required in children aged 7 years or older with delayed speech, with the expectation that at this age, children would comply with orders. This must be done to detect further disorders in the auditory system and higher levels until cortex cerebri. Because there was no experience using the P300 examination in children in the otorhinolaryngology department at Cipto Mangunkusumo Hospital, the present study was done on adults suspected to have cognitive disorders caused by marijuana addiction. Future studies will involve collaboration with fields such as psychiatry and pediatrics at the Cipto Mangunkusumo Hospital for cognitive function examination in psychotropic patients, drug users, and children and adults with cognitive function disorders.

2. Methods
The present study was a cross-sectional study aimed at evaluating latency and P300 auditory wave amplitude based on cognitive function in subjects with marijuana addiction. The study protocol had been approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Indonesia-Cipto Mangunkusumo Hospital. The study was conducted in the Cipinang and Pondok Bambu penitentiary. Data were collected during June–August 2012. The population of the study was inmates aged 18–40 years in the Cipinang and Pondok Bambu penitentiary with marijuana addiction. The subjects met the inclusion and exclusion criteria. The inclusion criteria were (1) men and women (18–40 years old) with marijuana addiction or with marijuana addiction history, (2) an education level of at least junior high school, (3) marijuana use >72 h prior, (4) urine test negative for marijuana, (5) understanding and following instructions, (6) normal threshold in an audiometric hearing examination, and (7) consent to be examined using the P300 test by signing an agreement letter. The exclusion criteria were (1) subjects with fluid leaking out of their ears or those who have undergone ear surgery, (2) subjects with cognitive function disorder caused by other factors (stroke or severe head trauma history), (3) subjects with severe mental disorder history, and (4) subjects with mental retardation. Further, subjects who declined participation during the study and those who could not follow the study procedures until completion were considered dropouts.

Numerical scale data were represented as mean and standard deviation if the data were normally distributed. Otherwise, it was represented as median, with minimum and maximum values. Categorical scale data were represented as distribution of frequency (n, %). Chi-square (Fisher) test was used to compare the proportions of P300 wave abnormality and cognitive function disorder among the subjects.

3. Results
3.1. Characteristics of the subjects
The study was a cross-sectional study aimed at evaluating P300 auditory wave amplitude and latency and their relationship to cognitive function. The subjects were adult inmates with marijuana addiction at the Cipinang Penitentiary, Jakarta; the study was extended to the Pondok Bambu Penitentiary, Jakarta, so that the subjects could include both genders. The subjects were enrolled from June to August 2012 as shown in the diagram below. Among the final 68 subjects included, interviews were performed by researchers using a questionnaire, followed by ear examination, urinary examination, pure melody audiometry examination, and P300 auditory examination. Subjects who were addicted to marijuana or had marijuana addiction and did not have other cognitive function disorders caused by other factors such as stroke or severe head trauma were selected through interview with a questionnaire and a urine test. The Rey Auditory Verbal Learning Test (RAVLT) using a
questionnaire was delayed for subjects with marijuana-positive urine until the subjects were free of marijuana for 3 days, which was confirmed with a urine test. Then, the P300 examination was conducted, and the results were analyzed.

The subject characteristics are shown in Table 1. The study involved 68 subjects who had marijuana addiction; 72.1% were men, and 27.9% were women. The most common age range was aged 24–29 years, represented by 23 subjects (33.8%). Several of the subjects were high school graduates with freelance occupations. There were 47 subjects (69.1%) who had used marijuana for more than 2 years.

| Variable                        | n   | %     |
|---------------------------------|-----|-------|
| Gender                          |     |       |
| Men                             | 49  | 72.10 |
| Women                           | 19  | 27.90 |
| Age                             |     |       |
| 18–23 y                         | 21  | 30.90 |
| 24–29 y                         | 23  | 33.80 |
| 30–35 y                         | 12  | 17.60 |
| 36–40 y                         | 12  | 17.60 |
| Education                       |     |       |
| Bachelor degree                 | 12  | 17.60 |
| High school graduate            | 41  | 60.30 |
| Junior high school graduate     | 15  | 22.10 |
| Occupation                      |     |       |
| Student                         | 8   | 11.80 |
| College student                 | 5   | 7.40  |
| Housewife                       | 8   | 11.80 |
| Freelance                       | 21  | 30.90 |
| Employee                        | 20  | 29.40 |
| Unemployed                      | 6   | 8.80  |
| Duration of use                 |     |       |
| 1 month                         | 1   | 1.50  |
| 6 months                        | 6   | 8.80  |
| 1–2 years                       | 14  | 20.60 |
| > 2 years                       | 47  | 69.10 |

The data were categorized on the basis of cognitive function damage suggested by the RAVLT examination using a questionnaire in the subjects with marijuana addiction, and 40 subjects (58.8%) were found to have impaired cognitive function, and 28 subjects (41.2%) were found to have normal cognitive function. The 30–35 and 36–40 age groups were merged during statistical analysis because the number of subjects in each group was only 12. The results show an insignificant relationship between cognitive function and age, as seen in Table 2. In terms of education level, the bachelor's degree group and the high school graduate group were merged into a higher education group, whereas the junior high school graduate group was considered as a lower education group. Statistical analysis showed a significant relationship between cognitive function and education level. Of the subjects, 49.1% in the lower education group suffered impaired cognitive function. Table 2 shows a significant relationship between cognitive function and the duration of marijuana use. The groups with 1 month, 6 months, and 1–2 years duration of use were merged during statistical analysis into a <2 years group,
because the number of subjects in each group was rather small, with one subject in the 1 month group, six subjects in the 6 months group, and 14 subjects in the 1 year group. Of the subjects who had used marijuana for more than 2 years, 72.3% suffered impaired cognitive function. In contrast, 71.4% of the subjects who had used marijuana for less than 2 years had no impairment in cognitive function.

Table 2. The relationship between cognitive function and subject characteristics.

| Variable            | Cognitive function | p     |
|---------------------|--------------------|-------|
|                     | Normal            | Damaged |       |
|                     | n     | %    | n     | %    |       |
| Age                 |                   |       |       |       |       |
| 18–23 y             | 9     | 42.80 | 12    | 57.20 |       |
| 24–29 y             | 9     | 39.10 | 14    | 60.90 |       |
| 30–35 y            * | 6     | 50    | 6     | 50    | 0.944 |
| 36–40 y            * | 4     | 33.33 | 8     | 66.67 |       |
| Education           |                   |       |       |       |       |
| Bachelor degree     | 6     | 50    | 6     | 50    |       |
| High school graduate| 21    | 51.22 | 20    | 48.78 | 0.002 |
| Junior high school graduate | 1 | 6.70 | 14 | 93.30 |       |
| Duration of use     |                   |       |       |       |       |
| < 2 years           | 15    | 71.4  | 6     | 28.6  | 0.001 |
| ≥ 2 years           | 13    | 27.6  | 34    | 72.3  |       |

Kolmogorov–Smirnov test
*Merged during analysis

3.2. P300 wave latency
The P300 wave latency was normal in 60 subjects (88.23%), shortened in 4 subjects (5.88%), and lengthened in 4 subjects (5.88%) as shown in Table 3. Table 4 shows that there were 40 subjects who suffered cognitive function damage. There were 3 subjects (7.5%) who had lengthened P300 wave latency, 4 subjects (10%) with shortened P300 wave latency, and 33 subjects (82.5%) were normal. Latency was not significantly different on the basis of impaired and unimpaired cognitive function. The duration of marijuana use did not show a significant relationship with P300 latency. Table 5 shows the relationship between P300 wave latency and age, and there was no significant relationship between the variables. The lengthened and shortened latency were regrouped during statistical analysis into abnormal latency, because the number of subjects in each group was small at four subjects in each group.

Table 3. P300 auditory wave latency in subjects with marijuana addiction.

| Variable | n | %   |
|----------|---|-----|
| Latency  |   |     |
| Normal   | 60 | 88.23 |
| Shortened | 4 | 5.88 |
| Lengthened | 4 | 5.88 |
Table 4. The relationship of P300 wave latency with cognitive function damage and duration of use.

| Variable                  | P300 wave latency |       |       | p     |
|---------------------------|-------------------|-------|-------|-------|
|                           | Normal            | Shortened | Lengthened |     |
|                           | n     | %   | n     | %   | n     | %   |
| Cognitive function        |                  |        |        |       |       |       |
| Unimpaired                | 27    | 96.40 | -     | -    | 1     | 3.60 |
| Impaired                  | 33    | 82.50 | 4     | 10   | 3     | 7.50 |
| Duration of use           |                  |        |        |       |       |       |
| <2 years                  | 19    | 90.40 | 1     | 4.80 | 1     | 4.80 |
| ≥2 years                  | 41    | 87.20 | 3     | 6.40 | 3     | 6.40 |

Kolmogorov–Smirnov test

Table 5. The relationship between P300 wave latency and age.

| Variable | P300 wave latency |       |       | p     |
|----------|-------------------|-------|-------|-------|
|          | Normal            | Abnormal |       |       |
|          | n     | %   | n     | %   |       |       |
| Age      |                  |        |        |       |       |       |
| 18–23 y  | 18    | 85.70 | 3     | 14.30|
| 24–29 y  | 20    | 86.90 | 3     | 13.10|
| 30–35 y* | 10    | 83.33 | 2     | 16.67|
| 36–40 y* | 12    | 100   | -     | -    |

Kolmogorov–Smirnov test *Merged during analysis

3.3. P300 wave amplitude

P300 wave amplitude decreased in 60 subjects (88.23%), as shown in Table 6. In subjects who suffered impaired cognitive function, there was a decrease in P300 wave amplitude in 40 subjects (100%), as shown in Table 7. There was a significant relationship between P300 wave amplitude and cognitive function \( p < 0.001 \). P300 wave amplitude and age did not show a significant relationship, as shown in Table 7. The relationship between P300 wave amplitude and duration of marijuana was significant \( p < 0.001 \).

Table 6. P300 auditory wave amplitude in subjects with marijuana addiction.

| Variable | n | %   |
|----------|---|-----|
| Amplitude|   |     |
| -        |   |     |
| Normal   | 8 | 11.76|
| Decreased| 60| 88.23|
| Increased| - | -    |
Table 7. The relationship of P300 auditory wave amplitude with cognitive function damage and subject characteristics.

| Variable                | P300 wave amplitude | n   | %    | n   | %    | p    |
|------------------------|---------------------|-----|------|-----|------|------|
|                        |                     |     |      |     |      |      |
| Cognitive function     |                     |     |      |     |      |      |
| Normal                 | -                   | 8   | 28.60| 20  | 71.40| <0.001* |
| Damaged                | -                   | -   | -    | 40  | 100  |      |
| Age                    |                     |     |      |     |      |      |
| 18–23 y                | -                   | 4   | 19.10| 17  | 80.90|      |
| 24–29 y***             | 3                   | 13.10| 20  | 86.90| 0.686** |
| 30–35 y                | 1                   | 8.33 | 11  | 91.67|      |
| 36–40 y***             | -                   | -   | -    | 12  | 100  |      |
| Duration of use        |                     |     |      |     |      |      |
| < 2 years              | 8                   | 38.10| 13  | 61.90| <0.001* |
| ≥2 years               | -                   | -   | -    | 47  | 100  |      |

*Fisher test
**Kolmogorov–Smirnov test
***Merged during analysis

4. Discussion
This was a cross-sectional study aimed at evaluating P300 auditory wave latency and amplitude and its relationship with cognitive function in subjects with marijuana addiction. The subjects with marijuana addiction were selected on the basis of the questionnaire Mini ICD-10. The study was conducted for 3 months, from June to August 2012. Anamnesis, questionnaire filling, urine test, ear examination, pure melody audiometry examination, P300, and RAVLT were done using the questionnaire.

4.1. Characteristics of the subjects with marijuana addiction
Subjects with marijuana addiction in this study involved 49 men (72.1%) and 19 women (27.9%). Statistical analysis showed a p value of <0.001, indicating that subject distribution based on gender was not normal. However, this is consistent with a study by Wagner and Anthony, which is cited by Schepis TS, stating that men tend to use marijuana more than women [21]. In addition, Nakamura also reported that marijuana addiction was more common in men than in women [22].

In this study, marijuana was chosen because there are several marijuana use instances in Indonesia, as reported by the Indonesian National Narcotics Agency based on drug evidence obtained during 2008–2010 in Indonesia, which included 96.8% marijuana, 1.56% ecstasy pills, 1.54% shabu, and 0.06% heroin [23]. The age of the subjects in the present study was 18 years and above, which is consistent with epidemiology data in developed countries showing that marijuana use begins at 18 years of age [24]. A survey reported that illegal drug users in Indonesia in 2008 consist of 86% high school students [25]. The most common age range of the subjects in the present study was 24–29 years old, represented by 23 subjects (33.8%). The majority were high school graduates with 41 subjects (60.3%), followed by junior high school and college students. This is similar to that reported by the Indonesian National Narcotics Agency in 2010–2011, with marijuana addiction being mostly found at the high school level [23].

In terms of occupation, marijuana addiction was found mainly in freelancers represented by 21 subjects (30.9%), followed by employees, students, housewives, unemployed individuals, and college students. This is consistent with a report about drug misuse by the Indonesian National Narcotics Agency, which stated that that most drug users were employees, unemployed people, laborers,
students, from police, civil servants, and college students [23]. There were 47 subjects (69.1%) in the present study with more than a 2 year duration of marijuana use and 21 subjects (30.9%) with less than a 2 year duration of use.

4.2. Cognitive function damage in subjects with marijuana addiction

The subjects went through a cognitive function examination with the RAVLT using a questionnaire. This test assessed two processes, learning and memory, because learning requires memory. The normal RAVLT score in the first trial was 5–10; in the second trial, 6–12; in the third, 8–14; and in the RAVLT recall, 5–13. If the RAVLT score was out of normal score range, the subject was considered to have impaired cognitive function.

There were 28 subjects (41.2%) who had unimpaired cognitive function, and there were 40 subjects (58.8%) who had impaired cognitive function where subjects were not able to recall the words given to them or remember them for a longer period. Solowij, as quoted by Roser, stated that cognitive function worsens in terms of attention and memory during acute marijuana usage and in marijuana addiction, even though subjects stop using it [12]. The effect of addiction is impairment in memory, learning, working, and attention. Further, consuming marijuana can decrease motor abilities, verbal expression, counting abilities, and time perception. Jager reported that a study on the long-term effect of marijuana use on cognitive function failed to show a disorder although there was evidence that cognitive function was impaired, especially in terms of memory and attention [26].

Subjects examined with the RAVLT using a questionnaire were confirmed to have not been using marijuana at least 3 days before the study, to rule out the pharmacologic effect of marijuana on the result. The selection method using a one-time negative urine drug test objectively proved that the subjects did not have marijuana in their bodies, as they stated.

Slow completion of procedures is probably caused by decreased cognitive function because of aging. Cognitive function in marijuana users indicates a quicker aging process compared with that in subjects who do not use marijuana at the same age. However, evidence of the effect of marijuana on decreased cognitive function is still arguable. The decrease in cognitive function was found to be far lower in marijuana users than those of older age. Young marijuana users do not have cognitive function impairment probably because they have sufficient cognitive ability to overcome cognitive function impairment caused by marijuana [27].

Almost all the 44 subjects were in two age groups (18–23 and 24–29 years). This shows that the subjects with marijuana addiction were sufficiently young and still had enough cognitive ability to overcome impairment caused by marijuana. However, 60.9% of the subjects in the 24–29 years age group had impaired cognitive function. There was no significant relationship found between cognitive function and age (\( p = 0.944 \)). However, a trend of impaired cognitive function with age has been reported. However, the age range in the reported study was 28–88 years with normal distribution. In the present study, most of the subjects were young (33.8%) with an age range of 24–29 years and 30.9% were in the age range of 18–23 years with abnormal data distribution. The narrow range of age, abnormal data distribution, and cognitive ability in young marijuana users may explain why the relationship between age and cognitive function was not statistically significant. This present study, found that 93.3% of the subjects with impaired cognitive function were at a lower education level. The relationship between cognitive function and education level showed a \( p \) value of 0.002, indicating a significant relationship between cognitive function and education level.

There have been no reports stating the relationship between cognitive function and duration of marijuana use. Our results showed a \( p \) value of 0.001, indicating a significant relationship between impaired cognitive function and duration of use of >2 years. More studies are needed to confirm this finding.

4.3. \( P_{300} \) auditory wave latency image

The normal \( P_{300} \) auditory wave latency was normal in 60 subjects (88.23%). The \( P_{300} \) wave latency shows the speed of stimuli sorting, which translated to the time needed to process stimuli before a
response [2]. According to Ehlers, the P300 wave latency increases because of marijuana exposure, and we found lengthened P300 wave latency in four subjects (5.9%) [20].

The relationship between P300 latency and cognitive function was not found to be significant using the Kolmogorov–Smirnov test (p = 0.565). However, there were seven subjects (17.5%) with impaired cognitive function who had abnormal latency. This must be studied further, to determine whether the cutoff used for the normal score was suitable for Indonesian adults.

There have been no reports stating the relationship between P300 wave latency and duration of marijuana use. We found a p value of 0.124, indicating no significant relationship between P300 wave latency and duration of marijuana use. Further studies are needed to confirm this finding.

In contrast to a study conducted by Teddy who found that there was lengthened P300 wave latency with age, in the present study, the relationship between P300 wave latency and age showed a p value of 0.310, indicating no significant relationship between them [22]. This could have been due to the uneven distribution of subject age.

There were four subjects (5.88%) who had shortened P300 wave latency and four subjects (5.88%) who had lengthened latency. Among these, the amplitude decreased. In four subjects with lengthened latency, there was only one who did not have impaired cognitive function. In four subjects with shortened latency who also had impaired cognitive function, one had a bachelor's degree, two were high school graduates, and another was a junior high school graduate. Intelligent quotient (IQ) was not tested, and the effect of IQ on the shortened P300 wave latency in the four subjects is not clear. Hall [2] explained that P300 wave latency could shorten because of several factors including faster information processing and stimuli-categorizing process. However, no reports explain the relationship between shortened P300 wave latency and marijuana addiction.

4.4. P300 auditory wave amplitude image

The P300 wave amplitude decreased by 88.23%. Roser performed a study to assess the effect of marijuana on P300 wave amplitude [12]. Marijuana could impact attention and memory impairment, and the amplitude was found to be significantly decreased. The relationship between P300 wave amplitude and cognitive function showed a p value of <0.001. There was thus a significant relationship between P300 wave amplitude and cognitive function. The decreased amplitude was followed by impaired cognitive function. Ranganathan stated that marijuana could decrease immediate cognitive ability and delayed free recall [28].

Bennet reported that there was decreased P300 wave amplitude with aging. Aging could increase attention function maturation and could affect the speed of motor reactions in the P300 examination [23]. But the change in P300 wave amplitude score based on age was not consistent. This is in contrast with results of the present study, in which the association between P300 wave amplitude and age showed a p value of 0.686 when analyzed with the Kolmogorov–Smirnov test. The P300 wave amplitude showed an abnormal score in 23 subjects (95.8%) in the age group of 30–40 years, 20 subjects (86.9%) in the age group of 24–29 years, and 17 subjects (80.9%) in the age group of 18–23 years. There was no significant relationship between P300 wave amplitude and age. However, the trend of the result showed that 95.8% of the age group of 30–40 years had decreased amplitude, which is in agreement with some previous reports.

There have been no reports stating the relationship between P300 wave amplitude and duration of marijuana use. In the present study, there were 47 subjects (100%) who had decreased amplitude with duration of use above 2 years (p < 0.001). This indicates a significant relationship between P300 wave amplitude and duration of marijuana use. Further studies are needed to confirm this finding.

Eight subjects (11.76%) had a normal P300 wave amplitude. Among these, the latency was normal, and they did not have cognitive function impairment. Seven of the subjects used 1–3 rolls per use. Four subjects had used marijuana 1–3 times, and the other four had used it 4–10 times. This indicates that in these eight subjects, there was no cognitive function impairment or changes in the P300 wave. Further studies are needed to clarify the dosage used by the subjects with marijuana addiction and its effects.
4.5. Limitations in this study
This study had the following limitations. The gender characteristics were not normally distributed, and there was inconsistency between the number of men and women. The number of female subjects who used marijuana was lesser than such male subjects. Therefore, it was challenging to reach conclusions on the basis of gender. In other words, the findings may not be applicable in the general population.

One of the requirements used for subject sorting was a urine examination negative for marijuana. Most of the subjects were uncertain of undergoing this test. This was understandable, because many of them were fearful of legal sanctions that could increase the punishment period. This could be overcome by the researchers seeking cooperation with the penitentiary officers and giving detailed and clear information to the subjects so that they understood the aim of the study and agreed to follow the procedures until the study was completed. During anamnesis, several of the subjects were found to have a marijuana use history, but only few of them had marijuana addiction. Subjects with a positive urine test were asked not to use marijuana for 3 days before they went through the second urine test. There were several subjects who did not complete the study. The researchers provided information again to emphasize that the result of the urine test would not affect their punishment period. The process to recall the subjects to complete the study was also an obstacle because many of them did not agree to be involved in the study anymore.

The research procedures were in the form of anamnesis, questionnaire filling, urine examination, audiometric test, P300, and RAVLT using a questionnaire. The process took a long time, and several of the subjects were impatient. This could be overcome by calling the subject for only a single visit. The relationship between cognitive function and P300 wave latency could not be verified. The conclusions of this study thus provide a basis for further studies.

5. Conclusions
Marijuana was found to impair cognitive function, especially in terms of attention and memory as indicated by decreased P300 wave amplitude. However, P300 wave latency was not found to indicate cognitive function impairment. This limitation was caused by the P300 wave latency range, which was developed with reference to American subjects. The results of our study support the assessment of cognitive function using decreased P300 wave amplitude. Further studies are needed to identify the optimal P300 wave latency range to be used for Indonesian children and adult populations.

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