Research Article

Substance Misuse Decreases Heart Rate Variability

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There are few biomarkers to reflect the physiological conditions for substance misuse. In this study, autonomic nervous and cardiovascular parameters were measured for participants in deferred prosecution programs. The goal of this study is to develop significant biomarkers of the above subjects and enhance their motivation to join further substance misuse disorder treatment program. This study recruited 34 participants with a mean age of 35.1 years. The participants spent approximately five minutes filling in the basic information form and another five minutes filling in the Pittsburgh Sleep Quality Index (PSQI). Blood pressure, heart rate, and heart rate variability data were also measured. Their sleep quality was measured by the Pittsburgh Sleep Quality Inventory (PSQI) with an average score of 8.6 and average systolic and diastolic pressure measured of 116.1 (standard deviation (SD) = 13.7) and 77.9 mmHg (SD = 8.1) during resting, respectively. Average heartbeat rates are 90.4 beats per minute (SD = 17.0); and average low-frequency power ratio is 56.4% (SD = 19.8%). Of the participants, 35% exhibited a low-frequency power rate below 30% and above 70%. The average biological HRV age of the participants was 46.0 years (SD = 22.9), which was significantly older than their average actual age ($p = 0.002^{**}$). The biological HRV age of the participants is 10 years older than their own actual age, and it effectively reflects the physiological conditions of participants in deferred prosecution programs. These physiological parameters, especially the biological HRV age, can be used in future treatment for substance use disorder counseling programs to increase the illness insight of program participants and increase their motivation to join further substance misuse disorder treatment program.

1. Introduction

Currently, substance misuse is a major problem in Taiwan. Over 50% of prison sentences in Taiwan are given for substance misuse-related reasons. Substance misuse causes users to exhibit compulsive behaviors. The negative influences of substance misuse in users include adverse drug reactions, overdoses, and an increased risk of developing infectious diseases, which may then influence the user's family, work, life, and even their residential community. According to the World Drug Report proposed by the United Nations Office on Drugs and Crime, in 2014, approximately 250 million people worldwide between the ages of 15 and 64 years had used at least one type of illegal drug. It is estimated that

of these, 29 million individuals who misuse substances were diagnosed with substance use disorder. The Global Burden of Disease Study reports indicate that in 2013, opioids, cocaine, amphetamine, and marijuana caused the loss of approximately 12 million lives [1]. Since the United Nations proposed the Single Convention on Narcotic Drugs in 1961, government agencies around the world have started viewing individuals who misuse substances as patients rather than criminals. Therefore, professional medical personnel should provide diagnosis, education, aftercare, rehabilitation, and social integration services to reduce drug-related hazards. Drugs are still a crucial concern worldwide. The 2030 Agenda for Sustainable Development proposed by the United Nations also features clear goals on drug problems, with a key goal being to "strengthen the prevention and treatment of substance abuse, including narcotic drug abuse and harmful use of alcohol" [2].

Studies have shown that substance misuse elicits numerous adverse effects on the brain [3], autonomic nervous system [4], cardiovascular function [5], and sleep quality of individuals [6]. In terms of the autonomic nervous system, substance misuse exhibits numerous significant differences in physiological parameters compared with nonusers [7, 8]. The prevalence of sinus bradycardia is higher among patients that are dependent on cocaine than in the general population [9]. Additionally, Professor Henry from the University of California, San Diego, discovered that methamphetamine damaged users' autonomic nervous system. In the study of [10], 17 participants who were dependent on methamphetamine and 21 participants who did not use any illicit drugs (the control group) were requested to rest for 5 min. While the participants rested, the researchers measured the changes in their autonomic nervous activities, revealing that participants who were dependent on methamphetamine exhibited significantly lower heart rate variability (HRV), parasympathetic nervous activity, and heart rate complexity. Related studies have also revealed that drug usage severely influences sleep quality [11].

Treatment for substance use disorders is a complex process. By improving the illness insight of substance misuse, their motivation to undergo substance use disorder treatment can be increased. In the process of counseling persons with active addictions, it was revealed that such persons were often unaware of substance misuse hazards and perceived substance misuse as an individual right that does not influence others. Therefore, the effects of typical substance use disorder hazard workshops are limited. Furthermore, as patients who are heavily substance misusers and already have a poor health status as a consequence of substance misuse, it is difficult for them to improve their health condition. By improving the illness insight of individuals who misuse substances, the motivation of such individuals to undergo substance use disorder treatment can be increased, effectively reducing the number of people that will face criminal penalties resulting from further substance misuse. According to Paragraph 3, Article 24 of the Narcotics Hazard Prevention Act amended by the Executive Yuan in 2008, regulations governing treatment for substance use disorder drug and treatment completion confirmation standards were established and announced. According to this act, the prosecution of category one and category two individuals who misuse substances is deferred, allowing the individual to first undergo substance use disorder treatment. According to statistics released by the Ministry of Justice, of all substance misuse-related crimes investigated by the Prosecutors' Offices of Taiwan that resulted in prosecution or deferred prosecution, the proportion of cases in which prosecution was deferred to allow the completion of substance use disorder treatment increased from 0.4% in 2006 to 15.3% in 2011. Studies have also indicated that imprisonment and criminal punishment do not help people addicted to cocaine; rather, the only methods that help such people are behavioral treatment and assistance in developing more desirable habits to replace substance misuse [12]. Studies in Taiwan have shown that individuals who misuse substances in deferred prosecution programs have lower levels of substance abuse and drug dependency compared with those undergoing compulsory drug treatment. Through the comprehensive use of different resources to provide early treatment for individuals who misuse substances in the deferred prosecution stage, substance misuse can be eliminated, thus preventing individuals from becoming heavy substance misusers. The reason is because most individuals who misuse substances are in their maturity stage and have adequate education and knowledge levels; they are pivotal to the economic productivity of Taiwan [13].

This study focused on deferred prosecution of individuals who misuse substances from the Probation Office of the Taipei District Prosecutors' Office. Using physiological measurement instruments, this study tested the autonomic nervous system and cardiovascular conditions of participants. This study was aimed at identifying physiological parameters that effectively demonstrate the physiological conditions of individuals granted deferred prosecution. Previous studies showed that some physiological parameters, such as heart rate variability (HRV), were related to drug dependence and substance use disorder [14]. For methamphetamine dependence subjects, there were significant reductions in HRV [10], also for smokers [15, 16]. Some studies even treated HRV biofeedback as an accessible, cost-effective intervention for substance abuse disorder [16, 17]. Resting heart rate variability is also a potential biomarker of symptom severity of substance misuse in the study of the subjects [18]. These revealed parameters can be applied in future substance use disorder treatment-related counseling sessions and workshops to increase the illness insight of those heavily involved in substance misuse, further increasing the efficacy of substance use disorder treatments.

2. Materials and Methods

2.1. Subject Information. This study recruited participants for whom prosecution related to substance misuse was deferred to allow them to complete substance use disorder treatment. The data collection period was between September 2017 and November 2017. After participants agreed to take part, questionnaires and physiological measurements
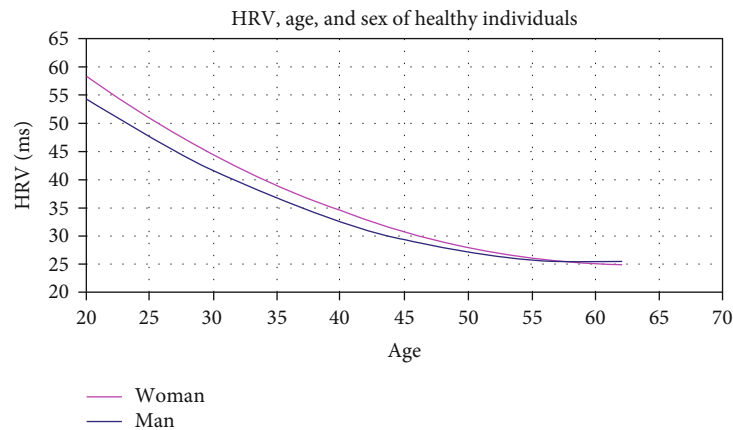
FIGURE 1: Relationship between HRV and the age of healthy people [19]. It is reproduced from that article in the below format: Table # is reproduced from Yi-Jung Lai et al. 2020 to proceed further.

TABLE 1: Definitions of the physiological parameters and their physiological relevance [25].

Name	Definitions and physiological relevance
Systolic blood pressure (SYS)	The blood pressure when the heart contracts to pump blood to the body, with a normal value ranging between 90 and 140
Diastolic blood pressure (DIA)	The blood pressure when the heart rests between beats, with a normal value ranging between 50 and 90
Pulse pressure	The gap between SYS and DIA, with a normal value being 30–50 mmHg
Number of heartbeats per minute (HR)	The average number of times the heart beats per min within 5 min
Number of occurrences of arrhythmia	Number of occurrences of arrhythmia within 5 min. If the value is >20, the participants should undergo a physical examination to understand the causes of the arrhythmia
Activity of the autonomic nervous system (HRV)	The variation in the time interval between heartbeats
LF power of the autonomic nerve system (LF)	Spectral power of LF R–R interval (0.04–0.15 Hz), which is related to the activity of parasympathetic nerves
HF power of the autonomic nerve system (HF)	Spectral power of HF R–R interval (0.15–0.4 Hz), which is related to the activity of parasympathetic nerves
LF power ratio of the autonomic nerve system (LF%)	Spectral power ratio of LF R–R interval. LF% = LF/(LF + HF). The normal range is 30%–70%
Age of the autonomic nervous system activity (HRV age)	The age that the HRV data norm corresponds to. HRV decreases as age increases [19] (Figure 1)

were conducted. The participants spent approximately 5 minutes filling in the basic information form and another 5 minutes filling in the Pittsburgh Sleep Quality Index (PSQI). The PSQI is a questionnaire that measures the overall sleep quality of an individual with scores ranging from 0 to 21; participants with scores equal to or lower than 5 demonstrate favorable sleep quality. In this study, the participants filled in the PSQI form according to their sleep quality in the previous month. This study used a noninvasive blood pressure meter, namely, the ANSWatch (Department of Health medical device product registration number: 001525; FDA approved number, K123130), to conduct measurements on the blood pressure, heart rate, heart rate variability (HRV), and blood pressure waveform of participants. Using the measured data as physiological condition indicators, the researchers conducted measurements for 7 minutes. During the measurement, the participants were requested to

gently close their eyes, place their arms horizontally against the table surface, and maintain a relaxed sitting posture. The Institutional Review Board of the China Medical University & Hospital Research Ethics Center approved this study on 2017/08/24 (approval number CRREC-105-099).

2.2. Cardiovascular Parameters. The physiological parameters collected in this study were related to heartbeat, blood pressure, and HRV. Parameters related to blood pressure included systolic, diastolic, and pulse pressure. This study measured the heart rate (beats per minute) of each participant. The autonomic nervous parameters were HRV, low-frequency power (LF), high-frequency power (HF), low-frequency power ratio (LF%), high-frequency power ratio (HF%), and biological HRV age. HRV was decreasing as age increased, as shown in Figure 1. There are some other cardiovascular parameters [20] [21]. Because the
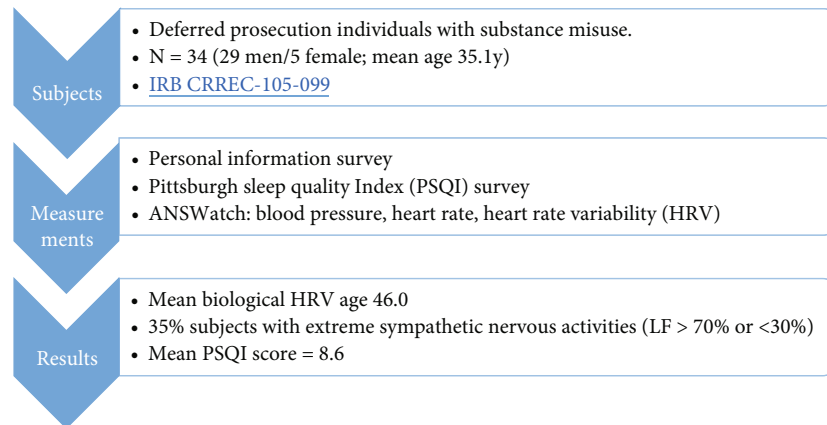
FIGURE 2: Experiment flowchart and major results.

TABLE 2: Basic information of participants.

Participants	Forty participants were recruited, with 34 providing effective data. Of these 34 participants, five were women. Additionally, six participants who had 20 irregular heartbeats within 5 minutes were excluded
Age	Mean: 35.1 (standard deviation 10.8) (minimum: 20; maximum 58)
Education level	The education level of 11 participants was university, college, or above ($N = 11$); the education level of 23 participants was high school or below ($N = 23$)
PSQI	8.6 (3.7)

TABLE 3: Distribution ratio of the drugs that the participants claimed to have used (multiple selections are accepted).

Amphetamine	MDMA	Marijuana	Ketamine	Nitrous oxide	Heroin	Others
67.6%	32.4%	29.4%	26.5%	5.9%	5.9%	5.9%

moderation of the vagus nerve primarily determines changes in the cardiac cycle, the constant interactions between the vagus and sympathetic nerves also influence the vagus nerves of those with substance abuse disorder [10]. Therefore, this study measured the HRV of participants for use as a critical physiological indicator. Table 1 shows the parameters and their corresponding physiological meanings used in this study.

2.3. Statistics

2.3.1. Descriptive Statistics. These statistics relate to the drug history of the participant, their demographic characteristics, and the number of cardiovascular vessels they have. The mean, standard deviation, and distribution ratio of the aforementioned factors were calculated. Additionally, the frequency distribution of participants that exhibited LF power ratio greater than 70%, between 30% and 70%, and less than 30% was also calculated. The data were presented using mean and standard deviation.

2.3.2. Inferential Statistics. The HRV and biological HRV age parameters were referenced from the actual age of the participants. The participants were divided into 10-year age groups. This study calculated the mean and standard deviation of participants' actual age and their corresponding biological HRV age. A paired sample t-test was subsequently

TABLE 4: Participants' cardiovascular data distribution. Data is represented as mean (std).

Parameter	Mean (standard deviation)
Systolic pressure	116.1 (13.7)
Diastolic pressure	77.9 (8.1)
Pulse pressure	38.3 (8.9)
Heartbeats per minute	90.4 (17.0)
HRV	34.6 (16.6)
LF	342.8 (305.3)
HF	295.4 (412.4)
LF%	56.4% (19.8%)
HF%	43.6% (19.8%)

employed to compare the statistical differences between the participants' actual age and their corresponding biological HRV age. For this test, a p value of 0.05 determined statistical significance.

The complete flowchart of this study is illustrated in Figure 2.

3. Results

Table 2 displays the basic information of the participants. After six participants who had over 20 irregular heartbeats

TABLE 5: Low-frequency power ratio distribution (sympathetic nervous activities).

LF%	<30%	30%-70%	>70%
Number of participants/all subjects	$N = 3/34$	$N = 22/34$	$N = 9/34$

TABLE 6: Age distribution of participants' ages and their biological HRV ages. p value is the t-test result between participant real age and their biological HRV age. Data is represented as mean (std).

	ALL $N = 34$	20~<30 $N = 14$	30~<40 $N = 10$	40~<60 $N = 10$
Participant real age	35.1 (10.8)	24.6 (3.1)	36.5 (2.3)	48.3 (6.5)
Biological HRV age	46.0 (22.9)	34.5 (18.2)	47.4 (28.3)	60.7 (14.3)
p value	0.002**	0.043*	0.114	0.028*

within 5 minutes were excluded, the data of the remaining 34 participants were employed in the statistical analysis stage. The mean age of the participants was 35.1, 11 participants exhibited education levels of university, college, or above, and the average PSQI score was 8.6. Table 3 displays the distribution ratio of the drugs that the participants had claimed to have used. According to the table, amphetamine was the most commonly used drug, with 67.6% of the drug-using participants stating that they had used this drug. Methylenedioxymethamphetamine (MDMA), marijuana, and ketamine were other commonly used drugs.

Table 4 shows the distribution of the participants' cardiovascular data. The means of the systolic, diastolic, and pulse pressure are all in the normal range. The participants exhibited a mean of 90 heartbeats per minute, which is slightly higher than the normal range. Participants demonstrated an LF power ratio of 56%, which is also in the normal range. This indicates that during the deferred prosecution period, under normal routines, the participants did not have abnormal cardiovascular activity. Table 5 shows the distribution of the LF power ratio; three participants exhibited an LF% lower than 30%, whereas nine participants demonstrated an LF% higher than 70%. Participants that had an LF% greater than 70% and less than 30% exhibited excessive and insufficient sympathetic nerve activity, respectively. The combined proportion of both types of participants comprised 35% of all participants (12/34 = 35%), indicating that over one-third of the participants exhibit sympathetic nerve activity outside the normal range. Table 6 shows the participants' distributions in terms of their actual age, their corresponding biological HRV age, and the differences between each age group. The mean age of the participants was 35.1 years old, and the mean biological HRV age was 46.0 years old. This shows that the biological HRV age of participants was 10 years older than their actual age ($p = 0.002$**). Furthermore, 20–30-year and 40–60-year age groups exhibited differences between their biological HRV age and actual age, with their HRV age higher than their actual age.

4. Discussion

Current substance misuse prevention strategies have begun focusing on the prevention of and withdrawal from sub-stance use among light users. By increasing substance light users' illness insight and crime awareness, their self-motivation to accept substance misuse treatment can be heightened, thereby increasing the recovery rate from substance use. Thus, potential psychological and physiological damage to substance misuse individuals and adverse influences on society caused by heavy substance misuse users can be reduced. Deferred prosecution for treatment is aimed at reducing the reliance of light substance use on controlled drugs and helping them return to normal life. Additionally, the data of this study demonstrates that the health conditions of light substance users are similar to those of healthy nonusers; the cardiovascular performance and sleep condition of light substance users did not differ substantially from standard levels, highlighting the difficulty of increasing the illness insight of light substance users.

This study revealed that the biological HRV age reflected the physiological condition of participants in the deferred prosecution program; the average biological HRV age of light drug users was 10 years older than that of healthy nonusers of the same age. Biological HRV age is a parameter that changes according to physiological health conditions. For example, if a person is sick or unhealthy, their biological HRV age will increase. On the average, a person has a lower HRV as they grow older; therefore, HRV is an effective indicator for observing the aging of the human body. Because the inspection of HRV involves noninvasive methods, those with substance use disorders could conduct self-assessments in their home environment [22]. HRV has been used as a biomarker for severe substance use disorder [18] and also as a useful biomarker for other addictions, such as video game addiction [23] and alcohol addiction. According to the results of this study, the biological HRV age may be more sensitive than traditional HRV parameters, such as LF and HF, to be a biomarker on addiction subjects.

In the future, HRV analysis has potential applications in deferred prosecution cases and substance misuse individuals with mild substance abuse disorder, especially with e-healthcare monitoring [24]. Further verification of different subject's condition is required. For example, changes in the biological HRV age of heavy substance misuse individuals before and after participating in courses of treatment for substance use disorders should be further examined and

discussed. The limitation of this study is the sample size. There were only 40 subjects who agreed to participate in this study. Those subjects were individuals who misuse substances and were under deferred prosecution from the Probation Office of the Taipei District Prosecutors' Office. The agreement of both the District Prosecutors' Office and subjects to participate the study is tough task.

5. Conclusions

This study analysed the distribution of cardiovascular-related physiological parameters of individuals who misuse substances as well as in deferred prosecution programs. Results revealed that the biological HRV age of participants in deferred prosecution programs was on the average 10 years older than their actual age. This study confirmed that the results of the HRV analysis would be beneficial to increase the illness insight of participants undergoing deferred prosecution, further increasing the efficiency of future treatment for substance use disorders.

Data Availability

Data is not to be publicly available due to the protection of subjects.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Li-Wei Chou is the first author.

Acknowledgments

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