Auricular acupuncture for sleep quality in participants with mental and behavioral disorders due to prior multiple drug use: a retrospective consecutive case series

Yuri Gimelfarb, Eran Goldstien
AMHC administration, affiliated with the Sackler Faculty of Medicine of Tel Aviv University, Bat Yam, Israel

Background: Poor sleep quality is associated with psychoactive substance abuse/addiction/withdrawal. Auricular acupuncture (AA) is a nonpharmacological method used for the treatment of sleep disturbances. This study aimed to examine the quality of sleep before and after AA in participants with mental and behavioral disorders due to prior multiple drug use in the therapeutic community.

Methods: This was a consecutive case series of 27 participants (25 male [92.6%]). The median age was 35.0 years (interquartile range [IQR], 29.0–37.2 years), methadone/buprenorphine were not used, and the participants were treated with AA (median number of treatments, 15.0 [IQR, 12.0–18.0]) during a median period of 51.0 days (IQR, 49.0–51.0 days) according to the National Acupuncture Detoxification Association (NADA)–Acudetox protocol. Sleep quality was determined using the Pittsburgh Sleep Quality Index (PSQI), a self-rated questionnaire that assesses sleep quality and disturbances over a 1-month interval.

Results: The global PSQI score dropped (indicating better sleep quality) by a median of 3.0 points (IQR, 0.0–8.0 points) after treatment. In the multivariate logistic regression analysis, with an increase in global PSQI score during AA by 1 point, there was a 0.73-fold reduction in the risk of poor sleep quality post-AA (adjusted odds ratio, 0.73; 95% confidence interval, 0.52–1.01; $p < 0.055$; Nagelkerke’s $R^2 = 0.66$).

Conclusion: The results revealed a positive effect of AA (by the NADA-Acudetox protocol) on sleep quality (as measured by PSQI) among participants in a treatment center with mental and behavioral disorders due to multiple drug use.

Keywords: Ear acupuncture; Logistic models; Sleep quality; Therapeutic community

Introduction

Sleep is an active phenomenon, cyclical from a biological point of view and essential for the survival of the human race. Sleep disorders are commonly found among substance abusers, including alcohol [1], stimulants (amphetamines, cocaine, and caffeine), and opiates. Sleep disorders are common during both active substance use and detoxification [2]. In addition, there are no differences in sleep quality among mildly, moderately, and severely dependent drinkers [1].

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Corresponding author: Yuri Gimelfarb, MPH
AMHC administration, affiliated with the Sackler Faculty of Medicine of Tel Aviv University, 15 KK"L Street, Bat Yam 5943602, Israel
Tel: +972-3-555-2749 • Fax: +972-3-555-2787 • E-mail: Ystatist@gmail.com
Eran Goldstien's current affiliation is Amal Group-Health Care Service, Holon, Israel.

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Both sleep disturbance and substance use disorders have been associated with negative outcomes, including decreased health-related quality of life [3], motor vehicle accidents [4], and suicide [6].

Therefore, promoting clinical care for patients with sleep disturbances and substance use disorders has the hypothetical effect of having a cascading positive impact on recovery from substance use disorders [6,7].

Nonpharmacological therapies to improve sleep in substance use disorders are attractive because they avoid adverse effects and the need for long-term pharmacological therapies. One nonpharmacological intervention for patients with substance use disorders is auricular acupuncture (AA). AA is an important component of traditional Chinese medicine. It has been accepted in China for thousands of years and is now used as an alternative and complementary medical therapy in Western countries. AA is one method by which specific points on the auricle are stimulated to treat various conditions [6,8,9].

Chen et al. [10] published a systematic review of six randomized controlled trials (RCTs) and papers written in Chinese or English. They concluded that AA intervention for insomnia produces better index rates of improvement and recovery than alternative interventions. AA also produces better rates of insomnia improvement and recovery than diazepam. Compared to control interventions, AA treatment is favored by increasing nocturnal sleep up to 6 hours, with subjects feeling sufficiently refreshed upon waking [10].

Lee et al. [11] published a systematic review of 10 RCTs performed in China, Korea, and the USA. The results suggested beneficial effects of AA on sleep efficiency compared with placebo [11]. Therefore, AA is often recommended as a treatment option for a wide spectrum of chronic conditions, such as sleep disturbances.

Very few studies have investigated sleep quality due to AA among patients with psychoactive substance use (Table 1). This imbalance was addressed in this study.

The objective of this study was to examine the quality of sleep before and after AA in participants with mental and behavioral disorders due to multiple drug use. The research hypothesis is that treatment with AA is associated with an improvement in the quality of sleep in this population.

Methods

Ethical statements: This study was approved by the Institutional Review Board (IRB) of AMHC (IRB No: 43Z), without requirement for informed consent because of the retrospective analysis of prospectively collected data.

1. Patients

To participate in the current study, male or female patients had to meet the following inclusion criteria: (1) age 18 years and older; (2) experienced mental and behavioral disorders due to psychoac-

### Table 1. Summary of studies with AA intervention on sleep quality, as evaluated by PSQI

| Study | Year | Study and duration | Participant | Intervention | Control | PSQI outcome |
|-------|------|--------------------|-------------|--------------|---------|--------------|
| Jiang et al. [33] | 2010 | Single-blinded, RCT, 4 weeks | People with insomnia | AA (n = 63) | AA on sham points (n = 62) | As compared to control population, AA improved the quantity and quality of sleep |
| Jiao et al. [34] | 2015 | A three-factor (3 needling protocols) and three-level experimental scheme, based on orthogonal method | Patients of insomnia differentiated as internal harassment of phlegm-heat syndrome (n = 54) | AA | Body acupuncture and abdominal acupuncture | AA, after body acupuncture, is the second best choice for insomnia |
| King et al. [35] | 2015 | A feasibility 3-week study | Veterans with post-traumatic stress disorder and sleep disturbance | Multimodal treatment +9 AA treatments (n = 12) | Multimodal treatment without AA (n = 8) | Differences between groups were found on sleep quality (p<0.003) and daytime dysfunction (p<0.004) components |
| Current study | 2022 | Consecutive case series study, median period of 7.3 weeks | Patients with mental and behavioral disorders due to multiple drug use in therapeutic community | AA according to NADA-Acudetox protocol (n = 27) | No | PSQI global score declined by median of 3.0 points (p<0.0001) |

AA, auricular acupuncture; PSQI, Pittsburgh Sleep Quality Index; RCT, randomized controlled trial; NADA, National Acupuncture Detoxification Association.
tive substance use (codes F10–F19) according to the International Classification of Diseases and Related Health Problems, 10th edition; (3) were in the therapeutic community Ramot Yehuda-Zoharim, Israel; (4) received AA as an integrated part of the comprehensive treatment in the community; and (5) were not treated with buprenorphine or methadone at that time. The exclusion criteria were severe metabolic or systemic disease and female participants who were pregnant or lactating.

We analyzed prospectively collected data [12,13] in a consecutive case series (level IV evidence).

2. Setting
This study was conducted in the therapeutic community Ramot Yehuda-Zoharim, Israel, which was established to treat and rehabilitate users and addicts in all areas of life, based on a broad range of different theories, treatment strategies, and methods, as well as various approaches to rehabilitation.

Each participant was interviewed by the center’s admission committee. Each potential participant was interviewed by a doctor, social worker, and the director of admissions. The admissions committee consisted of the staff of the therapeutic community. The admissions interviews consisted of three parts. In the medical section, the medical files of the patients, illnesses, and medications were reviewed by the physician. In the social part, a psychosocial interview was conducted by the social worker to gauge the level of personal psychosocial ability of each candidate, and the mental and social support factors that generally exist in his/her life. In the final administrative part, the laws that govern life in the community were explained.

The participants underwent extensive medical examinations and tests. Tests were performed to detect acquired immunodeficiency syndrome and tuberculosis, and a dental examination was performed to treat acute conditions as soon as possible.

The center’s principles are based on obtaining a maximum level of independence, as well as progress in changing behaviors and previous drug-based lifestyles. The center is a laboratory of preparation for return to life that is normative in the drug-free sense. The staff has a varied background from many professions and includes previous drug users. To prevent drug use, the use of drug substitutes or any other pharmacological substances is prohibited.

3. Outcome measure
The Pittsburgh Sleep Quality Index (PSQI) is a self-rated questionnaire that examines sleep quality retrospectively over a period of 1 month. Nineteen items are included in seven “component” scores: C1, subjective sleep quality; C2, sleep latency; C3, sleep duration; C4, habitual sleep efficiency; C5, sleep disturbances; C6, use of sleeping medication; and C7, daytime dysfunction. The questionnaire is easy to manage and can be completed within 5 minutes [14].

Each component score is weighted equally on a scale from 0 (no difficulty) to 3 (severe difficulty), with higher scores representing poorer sleep quality. The seven component scores are then summed to yield a global PSQI score, which has a range of 0 to 21; higher scores indicate worse sleep quality [14]. In previous studies, the internal consistency coefficient (as measured by Cronbach alpha) ranged from 0.72 [15-17] to 0.85 [14,16,18,19], indicating a high degree of internal consistency. Cronbach alpha was used to assess the consistency of results across items in the current test.

The internal consistency of the PSQI has not yet been investigated in populations with substance use. Nonetheless, for the Hebrew version of the PSQI, internal consistency was supported with Cronbach alpha scores from 0.52 to 0.70 in one study [17] and 0.63 in another [20].

Poor sleep quality was defined as a global score of > 5 on the PSQI [21-23], which has been determined to yield a diagnostic sensitivity of 89.6% [14] to 98.7% [19] and a specificity of 84.4% [19] to 86.5% [14] in identifying poor sleep quality vs. good sleep quality (PSQI of < 5).

4. Interventions
Participants were treated by acupuncturists (E.G.) according to the National Acupuncture Detoxification Association (NADA)-Acudetox protocol [6-8,24]. The protocol included the insertion of acupuncture needles into two auricles (after wiping them with alcohol). The needles were inserted at five points (sympathetic, kidney, Shen Men, liver, and lung), four to five times per week. They were left in place for 20 to 40 minutes during each treatment session. The sessions were conducted in a quiet place. Needle stimulation was performed by inserting sterilized ear acupuncture needles (type DB2, stainless steel, 15 x 0.18 mm; Dong Bang Acupuncture, Inc., Boryeong, Korea) to a depth of 1 to 3 mm at the appropriate points [9]. AA was the only treatment performed during the study period.

5. Measurement
The Hebrew version of the PSQI [17,20-22,25] was administered before the beginning of the AA process and within 72 hours after finishing the treatment process. A clinically significant effect was defined as a decrease of at least 1.93 for a beneficial effect and an increase of 2.9 or more for a negative effect [26].

6. Statistical analysis
Data were analyzed using IBM SPSS ver. 20.0 for Windows (IBM...
Categorical variables are presented as frequency tables and continuous variables as medians with interquartile ranges (IQRs). Nonparametric analysis was conducted.

Internal consistency analysis of the seven-component PSQI score items was conducted using Cronbach alpha \[27\]. The pre-post comparison of the total PSQI and all components was performed using the Wilcoxon signed-rank test.

Univariate and multivariate (while controlling for confounding variables) logistic regression analysis was performed (with odds ratios [ORs] and 95% confidence intervals [CIs]) to establish predictors of post-AA poor sleep quality (PSQI of > 5) vs. good sleep quality (PSQI of < 5). Variables that were significant at the \(p < 0.10\) level in the univariate logistic regression analysis were included in the multivariate logistic regression model with post-AA sleep quality as the dependent dichotomous variable (PSQI of > 5, and others) to enable evaluation of predictive performance after controlling for other variables \[28,29\].

The predictive performance of these parameters was also examined using receiver operating characteristic (ROC) curves. Differences between ROC curves were identified using nonparametric comparisons of the area under the curve (AUC) \[30-32\]. A \(p\)-value of < 0.05 was considered to be statistically significant.

**Results**

1. **Participants**

The sample was comprised of 27 participants. Of these participants, 25 (92.6%) were male and 14 (51.8%) were single. At the beginning of the study, the median age of the participants was 35.0 years (IQR, 29.0–37.2 years). The median length of stay (LOS) in the therapeutic community was 78.5 days (IQR, 22.0–142.0 days).

2. **Descriptive data**

1) Characteristics of substance use

All participants had mental and behavioral disorders due to multiple drug use. All reported drug use, while only eight participants (30.8%) reported alcohol use. The median age when they began drug use was 16.0 years (IQR, 14.0–19.0 years). The median number of previous withdrawal attempts was 2 (IQR, 1.0–4.8). In the past, participants had received treatment in one to three other residential facilities and were free from psychoactive substance use during a median period of 12 months (IQR, 1.0–30.0 months).

2) Auricular acupuncture treatment

Participants received a median of 15 treatment sessions (IQR, 12.0–18.0 sessions) in the current study. The median period of time for treatments was 51.0 days (IQR, 49.0–51.0 days). After the AA treatments, 16 participants (59.3%) reported a positive change in how they felt, and 11 participants (40.7%) reported that they felt no change.

3. **Outcome data**

1) Global Pittsburgh Sleep Quality Index at the beginning of follow-up

Cronbach alpha for the global PSQI at the beginning of the follow-up period was 0.53. The median global PSQI score was 9.0 (IQR, 7.0–13.0).

2) Global Pittsburgh Sleep Quality Index at the end of follow-up

Cronbach alpha for the global PSQI at the end of the follow-up period was 0.71. The median global PSQI score was 6.0 points (IQR, 2.0–7.0 points). At the end of the follow-up period, 14 participants (51.9%) reported poor post-AA sleep quality (PSQI of > 5).

3) Comparison between Pittsburgh Sleep Quality Index components and global scores pre- and post-auricular acupuncture

Comparisons between PSQI components and global scores during AA treatment are presented in Table 2 and Fig. 1. From the data presented in Table 2 and Fig. 1, it can be seen that there were statistically significant reductions in subjective sleep quality \((p < 0.002)\), sleep latency \((p < 0.011)\), habitual sleep efficiency \((p < 0.023)\), sleep disturbances \((p < 0.007)\), and daytime dysfunction \((p < 0.015)\) components, as well as in global score \((p < 0.0001)\). The global score dropped (indicating better sleep quality) by a median of 3.0 points (IQR, 0.0–8.0 points) post-AA treatment.

4. **Other analyses**

1) Univariate analysis of post-auricular acupuncture poor sleep-quality prediction

The results of the univariate logistic regression analysis are shown in Table 3. As shown in Table 3, younger age at first use \((p < 0.05)\), fewer withdrawal attempts \((p < 0.03)\), and little change in global PSQI score \((p < 0.02)\) were found to be significant predictors of poor post-AA sleep quality. The number of AA treatments was not found to be a predictor of poor sleep quality (OR, 0.85; 95% CI, 0.68–1.06; \(p < 0.15\)).

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2) Multivariate analysis of post-auricular acupuncture poor sleep-quality prediction

The results of the multivariate logistic regression model are presented in Table 4. Only variables that significantly predicted poor sleep quality in the univariate models were chosen for multivariate analysis. With an increase in the global PSQI score during AA by 1 point, there was a 0.73-fold reduction in the risk of poor sleep quality post-AA (OR, 0.73; 95% CI, 0.52–1.01; p < 0.055).

3) Feasibility of multivariate model for post-auricular acupuncture poor sleep-quality prediction

Statistical analysis of the multivariate logistic regression model (Table 4) revealed a statistically significant change from the basic

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**Table 2.** Comparison between Pittsburgh Sleep Quality Index components and global scores by Wilcoxon signed-rank test (n=27)

| Component                  | Pre-AA | Post-AA | Z   | p-value |
|----------------------------|--------|---------|-----|---------|
| C1-Subjective sleep quality| 1.0 (1.0–2.0) | 1.0 (0.0–1.0) | -3.1 | 0.002   |
| C2-Sleep latency           | 2.0 (1.0–3.0) | 1.0 (0.0–2.0) | -2.5 | 0.011   |
| C3-Sleep duration          | 1.0 (1.0–2.0) | 1.0 (0.0–1.0) | -1.7 | 0.090   |
| C4-Habitual sleep efficiency| 0.0 (0.0–2.0) | 0.0 (0.0–0.25) | -2.3 | 0.023   |
| C5-Sleep disturbances      | 1.0 (1.0–2.0) | 1.0 (1.0–2.0) | -2.7 | 0.007   |
| C6-Use of sleeping medication| 0.0 (0.0–0.0) | 0.0 (0.0–0.0) | -2.7 | 0.785   |
| C7-Daytime dysfunction     | 2.0 (1.0–3.0) | 1.0 (0.0–2.0) | -2.4 | 0.015   |
| Global score               | 9.0 (7.0–13.0) | 6.0 (2.0–7.0) | -3.5 | 0.0001  |

AA, auricular acupuncture; IQR, interquartile range.

**Table 3.** Summary of univariate logistic regression analysis revealing the possible factors predicting post-AA poor sleep quality (n=27)

| Variable                                      | OR (95% CI) | p-value |
|-----------------------------------------------|-------------|---------|
| Age (yr)                                      | 0.92 (0.81–1.03) | 0.15    |
| Sex, males vs. females                        | 1.08 (0.06–19.3) | 0.96    |
| LOS in Zoharim pre-AA (day)                   | 1.01 (0.99–1.02) | 0.17    |
| Previous treatments in therapeutic communities | 1.34 (0.40–4.56) | 0.63    |
| Previous treatments in Zoharim                | 2.20 (0.33–14.73) | 0.42    |
| Substance use, drugs with alcohol vs. drugs   | 1.67 (0.30–9.16) | 0.56    |
| Age at first substance use (yr)               | 0.76 (0.58–1.00) | 0.05    |
| Withdrawal attempts                           | 0.61 (0.39–0.96) | 0.03    |
| Duration of being free from psychoactive      | 0.99 (0.96–1.02) | 0.35    |
| substances                                    |             |         |
| Global PSQI score pre-AA (point)              | 1.04 (0.87–1.25) | 0.67    |
| AA treatment sessions                         | 0.85 (0.68–1.06) | 0.15    |
| Length of AA treatments (day)                 | 0.98 (0.92–1.05) | 0.56    |
| Global PSQI score change (point)              | 0.76 (0.60–0.96) | 0.02    |

AA, auricular acupuncture; OR, odds ratio; CI, confidence interval; LOS, length of stay; PSQI, Pittsburgh Sleep Quality Index.

**Table 4.** Summary of multivariate analysis revealing possible factors predicting post-auricular acupuncture poor sleep quality (n=27)

| Variable                                      | OR (95% CI) | p-value |
|-----------------------------------------------|-------------|---------|
| Age at first use (yr)                         | 0.76 (0.48–1.20) | 0.240   |
| Withdrawal attempts                           | 0.59 (0.30–1.15) | 0.120   |
| Global PSQI score change (point)              | 0.73 (0.52–1.01) | 0.055   |

OR, odds ratio; CI, confidence interval; PSQI, Pittsburgh Sleep Quality Index.

For the multivariate logistic regression model, Nagelkerke $R^2 = 0.66$; sensitivity = 92.3%; specificity = 81.8%; likelihood-ratio test = 16.35; degree of freedom (df) = 3; $p < 0.001$; Hosmer–Lemeshow test, $\chi^2 = 5.84$; df = 8; $p < 0.67$; area under the receiver operating characteristic curve = 0.90 (95% CI, 0.77–1.00), $p < 0.001$.
model (likelihood-ratio test, 16.35; degree of freedom [df] = 3; p < 0.001). The explained variation in the model was high at approximately 66% (Nagelkerke $R^2 = 0.66$). The Hosmer-Lemeshow goodness of fit test was not significant ($\chi^2 = 5.84; df = 8; p < 0.67$). The sensitivity and specificity of predicting post-AA poor sleep quality were 92.3% and 81.8%, respectively. The AUC-ROC of the model was 0.90 (95% CI, 0.77–1.00; p < 0.001), which was considered high discrimination.

4) Adverse events
No adverse events were observed during the follow-up period.

**Discussion**

This study examined changes in sleep quality due to AA among participants with mental and behavioral disorders due to multiple drug use treated in a therapeutic community. The findings point to a beneficial effect of AA on sleep quality, as measured by global PSQI scores, and allowed us to accept the study hypothesis that AA treatment is associated with an improvement in the quality of sleep in psychoactive substance users. The global score pre- and post-AA treatment dropped by a median of 3.0 points, indicating that AA was clinically effective in improving sleep quality [26]. Our findings are consistent with those of previous studies, not only of pre-post cohort studies [24] but also of RCTs [6,33] and other types of studies with control subpopulations [34,35].

In the meta-analysis, the effectiveness of AA was expressed using recovery from insomnia and improvement proportions, and the efficiency of AA (n = 338) was better than that of the alternative treatments (oral estazolam [n = 65], oral diazepam [n = 60], barbiturates [n = 60], and sham AA [n = 30]) in the control population (relative risk, 1.93; 95% CI, 1.40–2.66). When the effectiveness of AA was expressed using sleep time for more than 6 hours, the effectiveness of AA (n = 158) was better than that of the alternative interventions (oral estazolam [n = 65], oral diazepam [n = 30]) in the control population (relative risk, 2.64; 95% CI, 1.22–7.22) [10]. Another meta-analysis indicated that acupuncture and acupressure may help improve sleep-quality scores when compared to placebo (p < 0.006) or no treatment (p < 0.002) [36].

A variety of possible biophysiological explanations have been proposed to understand the effect of AA on sleep quality. In traditional Chinese medicine, the insertion of needles into points on the body or ears releases qi (“life energy”) blockage. Each of the five ear points in the NADA-Acudetox protocol has a specific role. The Shen Men (“Spirit Gate”, in Chinese) point calms the emotions, and the sympathetic point balances activity in the parasympathetic and sympathetic nervous systems and relaxes muscle tension. The lung, liver, and kidney points balance the functions of these organs. NADA-Acudetox treatment also affects the balance between yang and yin, two opposing factors that regulate functioning in living organisms in nature. NADA-Acudetox “tonifies yin,” meaning that yin elements such as softness, humidity, and darkness become stronger. This occurs at the expense of yang elements such as hardness, dryness, and lightness. Moreover, “empty fire” syndrome is treated, indicating that the feeling of inner emptiness typical of psychoactive substance misusers is replaced, during a period of treatment sessions, with a psychophysiological feeling ofsolidness and fullness [8].

The western approach to acupuncture effects on the human body originates from studies (on humans and animals) focusing on the release of neurotransmitters and inhibition of pain, as well as the identification of activated areas in the human brain. AA treatment evidently affects the parasympathetic component of the autonomic nervous system and its influence on reflexes in the cerebral cortex, hypothalamus, brainstem, and spine [8].

Moreover, previous studies have demonstrated that acupuncture increases endogenous opioid and nocturnal melatonin levels. The opioidergic system is theorized to have a somnogenic effect and may interact with melatonin to normalize the circadian cycle and promote sleep. These findings provide a possible physiological basis for how acupuncture affects sleep [11,29,37,38].

An additional possible explanation for the positive effect of AA treatment on sleep quality is staying in the therapeutic community after the withdrawal process and, as a result, being free from the influence of multiple substances. Another rationale is the acquired personal skills of participants to adopt a new life without multiple substances in the therapeutic community.

Participants with minimal changes in global PSQI scores were more likely to suffer from poor sleep quality than those with substantial changes. Analysis of this finding was not the aim of the current study, and there is currently no way to establish a cause-and-effect relationship between these variables.

This study has several limitations. First, this was a consecutive case series study, as has been published in previous studies, but not in controlled trials [12,13]. Therefore, one cannot exclude that the improvement in sleep quality was due to indwelling in the therapeutic community and not specifically because of the AA treatment process. To overcome this possible uncertainty, the expected effect of time spent in the therapeutic community on sleep quality was examined. The LOS in the therapeutic community was not found to be a predictor of sleep quality. Thus, it can be concluded that staying in a therapeutic community is unlikely to improve sleep quality among subjects with mental and behavioral disorders.
due to multiple drug use.

Second, the effect of AA on sleep quality was not examined after an equal number of AA treatments. To overcome this bias, we examined the expected effect of the number of AA treatments on sleep quality. The number of AA treatments was not found to be a predictor of sleep quality. From this, it can be concluded that cumulative exposure to AA-treatment processes only likely does not improve sleep quality in this subpopulation.

Third, middle- and/or long-term outcomes may be more meaningful and helpful in providing patients with mental and behavioral disorders due to multiple drug use.

Fourth, logistic regression models, based on small study populations, may have limited power. However, each of the parameters mentioned above in the multivariate model, alone and together, indicated that the multivariate logistic regression model was accurate for post-AA poor sleep quality prediction.

Finally, the participants in our study had mental and behavioral disorders due to multiple drug use. Because of the retrospective design of the study, there was no way to determine the different types of substances used pre-AA and, therefore, to establish the influence of each substance on changes in sleep quality.

With minimal utilization of high-cost equipment, AA can be included in integrated care for sleep-quality improvement. In our study, the results revealed a positive effect of AA (by the NADA-Acudetox protocol) on sleep quality (as measured by PSQI) among participants, who are in a therapeutic community, with mental and behavioral disorders due to multiple drug use. Future prospective designs need to be more specific in methodology, such as implementation, protocol selection, extension, and time of AA stimulation in participants exposed to different substances. We expect that this study will raise attention to this low-cost, safe interventional method and produce scientific evidence to support its application in populations with mental and behavioral disorders due to multiple drug use.

Notes

Conflicts of interest
No potential conflict of interest relevant to this article was reported.

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Author contributions
Conceptualization, Data curation: YG, EG; Formal analysis, Project administration, Supervision: EG; Methodology, Investigation, Software: YG; Writing-original draft: YG; Writing-review & editing: YG, EG.

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