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Brief Report

Principal component analysis on the effect of early morning awakening in major depressive disorder

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Abstract

Sleep disturbance is one of the most prevalent symptoms associated with Major Depressive Disorder (MDD). A recent article (Wu et al., 2022, *Journal of Multiscale Neuroscience* **1**, 133-139) explored the significant relationship between early morning awakening (EMA), a type of sleep disturbance, and recovery in MDD patients. In the paper, the authors examined the relationship between EMA and the treatment of MDD with twelve neuropsychological parameters. The authors employed two univariate statistical techniques, students' t-test and ANOVA, to analyze their data. While their analysis derived a meaningful conclusion that EMA may result in a statistically and clinically significant delay in recovery, we found that a multivariate statistical technique, principal component analysis (PCA), extracted additional quantitative information from their study. In this paper, we present quantitative features in the interaction between EMA and the treatment of MDD obtained from PCA.

Keywords: Sleep disturbance; early morning awakening; major depressive disorder; cognition; psychiatry; principal component analysis

1.Introduction

Major depressive disorder (MDD) is a convoluted illness affected by environmental, neurological, social, and genetic factors (Chiriţă et al., 2015). Of all the symptoms associated with MDD, sleep disturbance is the most prevalent (Murphy & Peterson, 2015). In a recent article published in *Journal of Multiscale Neuroscience*, Wu et al. presented their findings on the effect of early morning awakening (EMA), a type of sleep disturbance, in treating patients with MDD (Wu et al., 2022). By using the Hamilton Depression Scale (HAMD), Hamilton Anxiety Scale (HAMA), and Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) scores, the authors of the study examined the relationship between EMA and recovery in MDD patients (Wu et al., 2022).

In the article (Wu et al., 2022), twelve variables (**Table 1**) were measured in EMA and non-EMA patients at two time points: baseline, and after four weeks of treatment with escitalopram, which is an antidepressant that is commonly prescribed due to its highly beneficial effects on depressive disorder symptoms and increased tolerance in patients (Waugh & Goa, 2003; Llorca & Fernandez, 2007). While Wu and colleagues found that EMA had a significant effect on depression and anxiety scores, as well as a nonsignificant effect on cognitive scores (Wu et al., 2022), no comprehensive analysis considering all of the variables was performed. In assessing these neuropsychological scores (**Table 1**) collectively, we found that further quantitative information can be obtained from the scores via principal component analysis (PCA).

Variable Identification	Description
1	HAMD score (Hamilton Depression Scale)
2	HAMA score (Hamilton Anxiety Scale)
3	Immediate memory (Learning)
4	Immediate memory (Story Memory)
5	Visuospatial Construction
6	Language
7	Attention (Digit span)
8	Attention (Coding)
9	Delayed memory (List Recall)
10	Delayed memory (List Recognition)
11	Delayed memory (Story Recall)
12	Delayed memory (Figure Recall)

Table 1: Variables used in Principal Component Analysis.

Source: Wu et al. (2022).

PCA is a multivariate statistical technique that can reduce the dimensionality of a complex data set into a small set of uncorrelated elements and graphically presents the relationships between the variables and observations (Fowler et al., 1998; Jolliffe & Cadima, 2016). It has been widely used in biological sciences (Simmons-Boyce et al., 2009; Kang & Patterson, 2011). In this article, we will report our analysis of the data presented in the original paper (Wu et al., 2022) by using PCA to characterize systemic features in the effect of EMA on the treatment of MDD.

While the procedure of PCA is well established (Gwet, 2020), the following briefly describes our procedure: The numerical values of the twelve variables (**Table 1**) were subjected to PCA without manual centering of data, since the statistical software employed in our analysis, SigmaPlot (Version 15, Inpixon, Palo Alto, CA) can automatically achieve it. In the analysis, a covariance matrix was used because all measurements have the same unit and similar variations, and Mardia's method was used for outlier detection.

2. Results

Our PCA results are presented in **Figure 1**. PCA successfully reduced the dimensionality from twelve to two, as the first two principal components explain 99.4% of the total variability in the data. This allows simpler visual and numerical examination of the interrelation between the observations (groups) because they can be displayed on a two-dimensional score plot (**Figure 1a**). The score plot indicates that the first principal component (PC1) depicts the effect of the treatment with escitalopram for four weeks in both EMA and non-EMA groups. The second principal component (PC2) illustrates the effect of EMA on treatment with escitalopram. Therefore, each PC successfully captures the factors studied in the original paper.

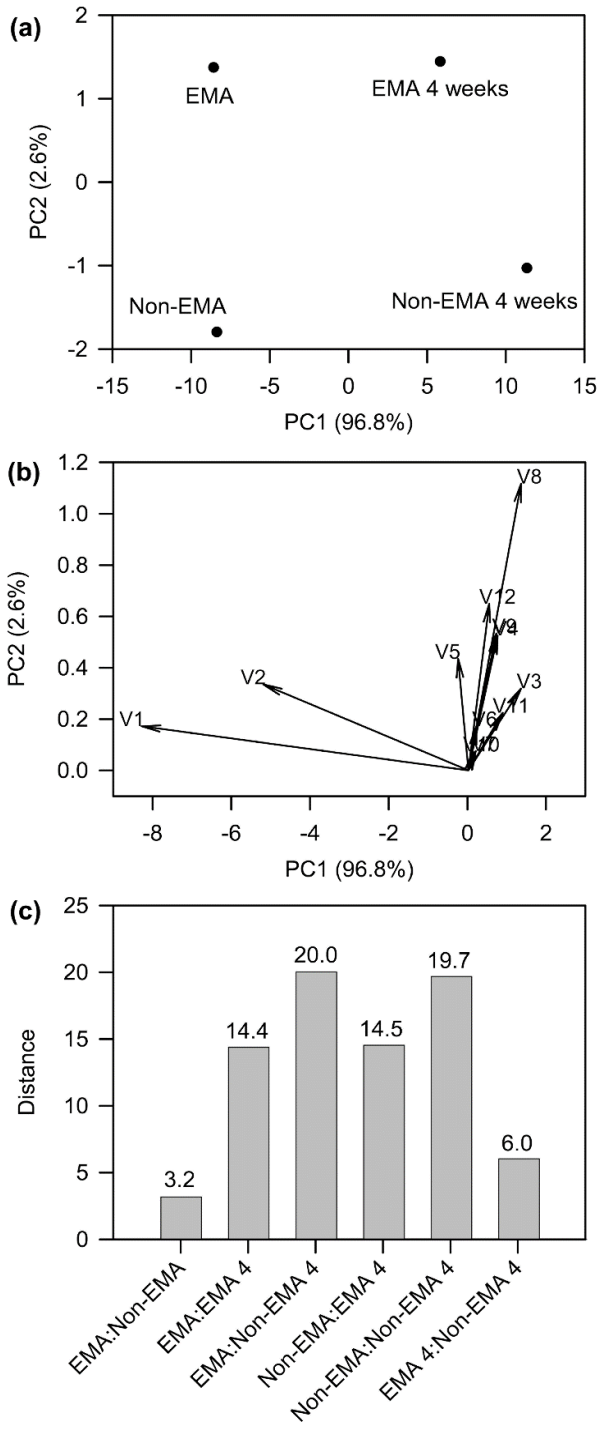

Figure 1. PCA results of the twelve neuropsychological variables for the four observations. (a) Score plot of the four observations. (b) PCA loadings plot of the twelve variables. (c) Distances between each group in the score plot. Numerical values in the score and loadings plot are available in the Appendix.

2.1 Neuropsychological Score

The next question is the magnitude of contribution by each variable (neuropsychological score) to PC1 and PC2. This can be answered from the loadings plot (**Figure 1b**), which quantitatively shows the contributions of the twelve variables to each PC. For PC1, V1 (HAMD score) and V2 (HAMA score) are major contributors to the principal component, showing a noticeable negative correlation with the treatment while all other variables show much smaller contributions to PC1. This is consistent with the interpretation in the original paper (Wu et al., 2022). In the case of PC2, V8 (Attention (Coding)) is the primary determinant.

2.2 Treatment Efficacy

The last question, which is the main topic of this present paper, is how treatment efficacy compares between pre-treatment and post-treatment groups. This can be answered with the distance plot (**Figure 1c**), which shows neuropsychological distances between each group in the score plot (**Figure 1a**). According to our analysis, the distance between the pre-treatment and post-treatment non-EMA groups, which is 19.7 (**Figure 1c**), is larger than the distance between the pre-treatment and post-treatment EMA groups, which is 14.4 (**Figure 1c**). This implies that treatment is more effective in non-EMA groups than EMA groups. In addition, the distance between EMA and Non-EMA increases from 3.2 to 6 (**Figure 1c**) after four weeks of treatment, further quantitatively demonstrating the difference in the effectiveness of escitalopram in the treatment of MDD between two groups, EMA and non-EMA. Without using PCA, this assessment would not have been possible.

3. Conclusion

In summary, our PCA successfully reduced the high dimensionality of data in the original paper (Wu et al., 2022) from twelve to two without losing much information. Our analysis quantitatively illustrates that treatment with escitalopram is more effective in non-

EMA groups than in EMA groups. Our PCA analysis shown in this paper may provide important information for future research on major depressive disorders.

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Conflict of Interest Statement

The authors declare no conflict of interest.

Appendix

Numerical values in the score plot (**Figure 1a**).

Observation	PC1	PC2
Non-EMA	-8.4061	-1.7949
EMA	-8.613	1.3756
Non-EMA 4 weeks	11.2598	-1.0282
EMA 4 weeks	5.7595	1.4475

Numerical values in the loadings plot (**Figure 1b**).

Variable	PC1	PC2
V1	-8.29	0.172
V2	-5.201	0.336
V3	1.337	0.32
V4	0.742	0.525
V5	-0.261	0.435
V6	0.2	0.172
V7	0.184	0.0755
V8	1.337	1.117
V9	0.708	0.534
V10	0.119	0.0734
V11	0.871	0.225
V12	0.528	0.65

References

Chiriță, A. L., Gheorman, V., Bondari, D. & Rogoveanu, I. (2015) Current understanding of the neurobiology of major depressive disorder. *Romanian Journal of Morphology and Embryology* **56** (Supplement 2), 651–658.

Fowler, J., Cohen, L. & Jarvis, P. (1998) *Practical Statistics for Field Biology*. England. John Wiley & Sons.

Gwet, K. L. (2020) Beginner's Guide to Principal Components: Applications with Microsoft Excel. Maryland: AgreeStat Analytics.

Jolliffe, I. T. & Cadima, J. (2016) Principal component analysis: a review and recent developments. *Philosophical Transactions of the Royal Society A,* **374**, 20150202.

Kang, J. & Patterson, A. K. (2011) Principal component analysis of mRNA levels of genes related to inflammation and fibrosis in rats treated with TNBS or glutamine. *Inflammatory Bowel Diseases*, **17**, 1630–1631.

Llorca, P. M. & Fernandez, J. L. (2007) Escitalopram in the treatment of major depressive disorder: clinical efficacy, tolerability and cost-effectiveness vs. venlafaxine extended-release formulation. *International Journal of Clinical Practice* **61**, 702–710.

Murphy, M. J. & Peterson, M. J. (2015) Sleep disturbances in depression. *Sleep Medicine Clinics* **10**, 17–23.

Simmons-Boyce, J. L., Purcell, S. L., Nelson, C. M. & MacKinnon, S. L. (2009) Dietary Ascophyllum nodosum increases urinary excretion of tricarboxylic acid cycle intermediates in male Sprague-Dawley rats. *The Journal of Nutrition* **139**, 1487–1494.

Waugh, J. & Goa, K. L. (2003) Escitalopram: a review of its use in the management of major depressive and anxiety disorders. *CNS Drugs* **17**, 343–362.

Wu, X., Ding, L., Chen, N. & Gao, L. (2022) Effect of early morning awakening in major depressive disorder. *Journal of Multiscale Neuroscience* **1**, 133-139**.**