# PACIFIC JOURNAL OF MEDICAL SCIENCES

## {Formerly: Medical Sciences Bulletin}

## ISSN: 2072 – 1625

**Pac. J. Med. Sci. (PJMS)**

## URINARY LEVELS OF PHENYLETHYLAMINE PREDICT MOOD, COMPREHENSION AND ACADEMIC PERFORMANCE IN HEALTHY UNDERGRADUATES

**ADESOLA A. ONIYIDE[1]\*, KEHINDE S. OLANIYI[1]\*, CHRISTOPHER O. AKINTAYO[1], TOLUWANI B. AGUNBIADE[2], RICHARD D. AGBANA[3], ADESOLA ALADEKUGBE[1], OLAMIDE D. AWONOWO[1], TOSIN A. AGBESANWA[4] AND OLUROTIMI J. SANYA[1]**

1. Department of Physiology, College of Medicine and Health Sciences, Afe Babalola University, Ado-Ekiti, Nigeria.
2. Department of Medical Microbiology and Parasitology, College of Medicine and Health Sciences, Afe Babalola University, Ado-Ekiti, Nigeria.
3. Department of Community Health, College of Medicine and Health Sciences, Afe Babalola University, Ado-Ekiti, Nigeria.
4. Department of Family Medicine, Ekiti State University Teaching Hospital, Ado-Ekiti, Nigeria.

Running title: *PEA marks depressive-like behaviors*

*Corresponding authors: adesolaoniyide2000@gmail.com, and kennethnitty2010@gmail.com;ORCID iD: 0000-0002-8229-9688

# URINARY LEVELS OF PHENYLETHYLAMINE PREDICT MOOD, COMPREHENSION AND ACADEMIC PERFORMANCE IN HEALTHY UNDERGRADUATES

**ADESOLA A. ONIYIDE[1]\*, KEHINDE S. OLANIYI[1]\*, CHRISTOPHER O. AKINTAYO[1], TOLUWANI B. AGUNBIADE[2], RICHARD D. AGBANA[3], ADESOLA ALADEKUGBE[1], OLAMIDE D. AWONOWO[1], TOSIN A. AGBESANWA[4] AND OLUROTIMI J. SANYA[1]**

5. Department of Physiology, College of Medicine and Health Sciences, Afe Babalola University, Ado-Ekiti, Nigeria.
6. Department of Medical Microbiology and Parasitology, College of Medicine and Health Sciences, Afe Babalola University, Ado-Ekiti, Nigeria.
7. Department of Community Health, College of Medicine and Health Sciences, Afe Babalola University, Ado-Ekiti, Nigeria.
8. Department of Family Medicine, Ekiti State University Teaching Hospital, Ado-Ekiti, Nigeria.

Running title: *PEA marks depressive-like behaviors*

*Corresponding authors: adesolaoniyide2000@gmail.com, and kennethnitty2010@gmail.com;ORCID iD: 0000-0002-8229-9688

**ABSTRACTS**:
Phenylethylamine (PEA) is a neuromodulator that plays a crucial role in neuronal homeostasis. However, it is unknown whether the concentration of PEA can predict mood, comprehension and academic performance of undergraduate students. The study investigated the correlation of urine PEA, and mood, comprehension and academic performance of undergraduates. One hundred and sixty healthy volunteers were randomly selected from undergraduates of Afe Babalola University. These individuals were recruited and informed of what they should expect during the study and informed consent was obtained. Questionnaires were administered to gather volunteers' biodata, socio-demographic background, mood and academic performance. Comprehension test was administered with result recorded and urine sample was collected for PEA estimation. Our results showed that urine PEA levels were significantly reduced in subjects with low mood, poor comprehension test score and poor academic performance. The present study demonstrates that weak academic performance, poor comprehension and low mood in healthy subjects are associated with reduced urine PEA.

**Keywords**: Academic, Comprehension, Mood, Neuromodulator, Performance, Phenethylamine.

## INTRODUCTION:

Phenylethylamine (PEA), known as β-Phenylethylamine (β-PEA) and 2-phenylethan-1-amine, is a naturally occurring organic compound, which can also be synthesized and used as supplements [1]. Phenylethylamine is a monoamine alkaloid present in trace amount in the central nervous system (CNS). It plays an important role in neural homeostasis as a neuromodulator and, to a lesser extent, a neurotransmitter in the CNS [2]. It is synthesized from the amino acid L-phenylalanine by decarboxylation catalyzed by Aromatic L-amino acid decarboxylase.

PEA can also be found in many other organisms and foods, such as chocolate, especially after microbial fermentation [3]. Phenethylamine has been sold as dietary supplement in attempt to treat mood instability and to achieve weight loss [4]. However, in orally ingested PEA, a significant amount is metabolized in the small intestine by Monoamine oxidase B (MAO-B) and then by aldehyde dehydrogenase, which converts it to phenylacetic acid [5], and for significant concentrations to reach the brain, the dosage must be higher than for other methods of administration [6]. Phenethylamine has earlier been used as a biomarker for some neurological disorders such as bipolar disorder which is associated with elevated plasma level of PEA [7]. Urine PEA was observed to be low in patients with autism, attention deficit hypersensitive disorder (ADHD) depression, and attention deficits [8, 9]. However, it is not known if urine level of PEA in healthy undergraduates is related to their academic performance, comprehension and mood. The present study aimed at investigating the relationship of urine PEA levels with academic performance, comprehension and mood in undergraduate students.

## METHODOLOGY:

One hundred and Sixty (160) healthy volunteers randomly selected from undergraduate students of Afe Babalola University were used in this study. These individuals were informed on what they need to do during the study and informed consent was obtained thereafter. They were screened and certified healthy by the school health center before recruited for the study. The study design was a cross-section descriptive study. Subjects were asked to sit comfortably on a chair inside the physiology laboratory of Afe Babalola University which is at a comfortable room temperature, and provides a quiet and neutral environment with no distraction. Interactions between participants and investigators were limited to those necessary for collecting data.

Comprehension was assessed with the participants using a reading task extracted from International English Language Testing System (IELTS) [10]. It involves reading a passage within a given time and answering of the follow up questions. Test scores were recorded against their cumulative grade point average

(CGPA) which is a measure of academic performance graded on the scale of 1 to 5 [10]. Mood assessment was done using self-report 1 to 10 mood rating scale where participants will rate their mood by giving score from 1 to 10 with 1 indicating extremely sad and 10 indicating very happy as previously described [11]. All the 160 participants were separated into two groups, mood score 1 to 5 and mood score 6 to 10. The point mood score was recorded against urinary level of PEA.

Determination of urine Phenylethylamine:

Point urine samples were collected via aseptic procedure and immediately stored in the refrigerator for the determination of PEA. Urine level of PEA was determined with an Enzyme-linked Immunosorbent Assay ELISA kit (Fortress Diagnostic, Antrim, United Kingdom) with high sensitivity and specificity for detection of PEA, and no significant cross-reactivity or interference between PEA and analogues. This assay used the competitive inhibition enzyme immunoassay technique. A monoclonal antibody specific to phenylethylamine has been pre-coated onto a microplate. A competitive inhibition reaction was launched between biotin labeled phenylethylamine and unlabeled phenylethylamine (Standards or samples) with the pre-coated antibody specific to phenylethylamine. After incubation the unbound conjugate was washed off. Then, avidin conjugated to Horseradish Peroxidase (HRP) was added to each microplate well and incubated. The amount of bound HRP conjugate

is reverse proportional to the concentration of β-endorphin in the sample. After addition of the substrate solution, the intensity of color developed is reversely proportional to the concentration of PEA in the sample.

This study was approved by the Ethical Review Committee of Afe Babalola University, Ado Ekiti, Ekiti State, Nigeria and consent was provided by each participant.

One hundred and sixty apparently healthy students, within the age bracket of 15 – 25 years, in Afe Babalola University were recruited for the study. The study was carried out in the physiology laboratory of the school.

All data were analyzed using Graph pad prism 5 and expressed as the Mean ± S.E.M. Data were analyzed using Kruskal-Wallis test for analysis of non-parametric data followed by Dunn's post hoc test. The level of significance was considered at p<0.05

**RESULTS**:

The socio-demographic variables of the participants are presented in Table 1.

Undergraduate comprehension score correlates with cumulative grade point average (CGPA):

The students with CGPA of 4.40 ± 0.09 had over 75% score in comprehension test while those with 3.19 ± 0.09 and 2.80 ± 0.08 had 50 - 75% and less than 50% scores respectively as shown in table 2.

Reading habit enhances academic performance:

Participants that read average of 3 - 4 books per month and greater than 5 books per month had higher CGPA compared with participants that read only 1 - 2 books per month as shown in table 3.

Comprehension correlates with urine phenylethylamine concentration in healthy undergraduates:

The urine PEA concentration of undergraduates with >75% comprehension score is significantly higher than undergraduates with 50-75% and <50%. Likewise, undergraduates with 50-75% comprehension score has higher urine PEA concentration than those with <50% comprehension score as shown in table 4.

Mood score corresponds with urine phenylethylamine concentration in healthy undergraduates:

The urine concentration of PEA in undergraduates with high mood score was significantly higher than undergraduates with low mood score as shown in table 5.

Thought affects urine phenylethylamine concentration:

The level of urine PEA was significantly higher in undergraduates with dominant positive emotion compared with those with dominant negative emotion as shown in table 6.

**Table 1: socio-demographic variables**

| Parameters | Percent (n) |
|---|---|
| Age group | |
| 16-17 | 21.9 (35) |
| 18-19 | 33.1 (53) |
| 20-21 | 31.9 (51) |
| >22 | 13.1 (21) |
| Gender | |
| Male | 25 (40) |
| Female | 75 (120) |
| Departments | |
| Medicine | 20 (32) |
| Physiology | 15 (24) |
| Anatomy | 28.1 (45) |
| Others | 36.9 (59) |

**Table 2: Cumulative grade point average (CGPA) and comprehension test (CT) in healthy undergraduates**

| Comprehension test (%) | CGPA |
|---|---|
| < 50 | 2.80 ± 0.08 |
| 50 – 75 | 3.19 ± 0.09 |
| >75 | 4.40 ± 0.09*# |

(n=47 for CT<50; n=60 for CT 50-75; n=53 for CT>70). Data were analyzed using Kruskal-Wallis test for analysis of non-parametric data followed by Dunn's post hoc test ($p < 0.05$ vs. <50; #$p < 0.05$ vs. 50-75).

**Table 3: Cumulative grade point average (CGPA) and average number of other books read per month in healthy undergraduates**

| Average number of books | CGPA |
|---|---|
| 1 – 2 | 2.67 ± 0.09 |
| 3 – 4 | 3.43 ± 0.06* |
| >5 | 3.73 ± 0.08* |

Data are expressed as mean ± S.E.M. (n=54 read 1-2; n=51 read 3-4; n=55 read >5).

**Table 4: Comprehension Test (CT) score and urine Phenylethylamine (PEA) concentration in healthy undergraduates**:

| Comprehension test (%) | PEA (ng/mL) |
|---|---|
| <50 | 32.79 ± 1.74 |
| 50 – 75 | 38.98 ± 1.67*S |
| >75 | 55.53 ± 2.30*# |

(n=52 for CT<50; n=53 for CT 50-75; n=55 for CT>70). Data were analyzed using Kruskal-Wallis test for analysis of non-parametric data followed by Dunn's post hoc test ($p < 0.05$ vs. <50; #$p < 0.05$ vs. 50-75).

**Table 5: Mood score and urine Phenethylamine (PEA) concentration in healthy undergraduates**

| Mood score | Urine PEA (ng/mL) |
|---|---|
| 1 – 5 | 41.27 ± 1.58 |
| 6 – 10 | 55.36 ± 1.59* |

(n=52 for 1-5 mood score; n=108 for 6-10 mood score).

**Table 6: Thought and urine Phenylethylamine (PEA) concentration in healthy undergraduates**

| Mood score | Urine PEA (ng/mL) |
|---|---|
| Negative | 51.59 ± 3.37 |
| Positive | 66.10 ± 1.48* |

(n=43 for negative thought; n=117 for positive thought).

## DISCUSSION:

The present study has demonstrated the relationship between urine PEA concentration and academic performance, comprehension and mood. Our results showed that undergraduate students (n=53) with highest CGPA (4.40±0.09) had comprehension score >75% compared with those that had CGPA of 3.19±0.09 (n=60) and 2.80±0.08 (n=47) with corresponding comprehension scores of 50-70% and <50% respectively. This confirm the importance of the ability to comprehend in academic performance and this finding is consistent with the result of previous study by Kerstjens and Nevel, which showed positive correlation between International English Language Testing system (IELTS) test score and academic performance [10]. Therefore, the ability to solve problem form an integral part of cognition as previously reported [12]. However, cognition entails more than the ability to comprehend and solve problems [13]. In addition, the prediction of associated factor with academic performance has been an interesting study in cognitive neuroscience research [14].

Several factors including reading habit, thinking strategies and stress have been shown to influence working memory, learning and cognition [15, 16]. In the present study, it was observed that reading habit affects academic performance as shown in table 3 where participants that read average of 3-4 other books (books that are different from their lecture notes) per month and greater than 5 books per month

had higher CGPA compared with participants that read only 1-2 books per month. Crucially, the present result showed significant increase in the level of urine PEA in participants with 50-75% and >75% comprehension score compared with those that have <50% comprehension score. The urine PEA concentration was also higher in participant with >75% comprehension score compared with those that have 50-75% comprehension score. This is similar to previous studies that demonstrated association between PEA and attention deficit [8]. The finding of the present study therefore suggests that urine PEA in healthy individuals may predict academic performance.

Besides, the results of the present study revealed that urine PEA concentration was significantly higher in participants with predominant positive emotion (positive thought) compared with those that expressed negative emotion (negative thought). Therefore, this observation corroborated previous work that documented an association between low PEA and depression [9]. By extension the present finding showed higher level of urine PEA in participants with high mood (6-10) compared with low mood (1-5), suggesting the diagnostic potential of urine PEA in individual with depressive-like behaviors.

## CONCLUSION:

The present study demonstrates that poor academic performance, poor comprehension and low mood in healthy subjects are

accompanied by reduced urine phenylethylamine. Therefore, urine phenylethylamine could be a useful biomarker for determination of depressive-like behaviors.

## REFERENCES:

1. Gilbert D, Cooper SJ, β-Phenylethylamine-,d-amphetamine-and l-amphetamine-induced place preference conditioning in rats. European Journal of Pharmacology 1983;95(3-4):311-4.

2. Oanca G, Stare J, Vianello R, Mavri J, Multiscale simulation of monoamine oxidase catalyzed decomposition of phenylethylamine analogs. European Journal of Pharmacology 2017;817:46-50.

3. Gammone M, Vicentini A, Riccioni G, De Girolamo M, D'Aulerio A, D'Orazio N. Food-Related Atrial Fibrillation? The Potential Role of Biogenic Amines in "Nutri-Arrhythmias." Genesis Reports 2019; 2(1):1.

4. Seo JW, Choi MJ, Li ZH, Lee YE, Ryu IS, Yoo SS. The reinforcing effects of beta-phenylethylamine (PEA) in rodents. In 日本毒性学会学術年会 第 44 回日本毒性学会学術年会 2017; 259: 日本毒性学会.

5. Ha TJ, Lee MH, Seo WD, Baek IY, Kang JE, Lee JH, Changes occurring in nutritional components (phytochemicals and free amino acid) of raw and sprouted seeds of white and black sesame (Sesamum indicum L.) and screening of their antioxidant activities. Food Science and Biotechnology 2017;26(1):71-8.

6. Overduin J, Guérin-Deremaux L, Wils D, Lambers TT, NUTRALYS® pea protein: characterization of in vitro gastric digestion and in vivo gastrointestinal peptide responses relevant to satiety. Food Nutrition Research; 59(1):25622.

7. Allison JK, Amtmann GA, Steele JB, inventors; Power Supplements LLC, Synergistic nutraceutical beverage formulations providing enhanced thermogenesis, mental clarity, and stamina while minimizing adrenaline and dopamine concentration perturbations associated with withdrawal. United States patent application US 15/653,869. 2018.

8. Kusaga A, Yamashita Y, Koeda T, Hiratani M, Kaneko M, Yamada S, Matsuishi T, Increased urine phenylethylamine after methylphenidate treatment in children with ADHD. Annals of Neurology 2002;52(3):372-4.

9. Faraone SV, Bonvicini C, Scassellati C, Biomarkers in the diagnosis of ADHD–promising directions. Current Psychiatry Reports 2014;16(11):497.

10. Kerstjens M, Nery C, Predictive validity in the IELTS test: A study of the relationship between IELTS scores and students' subsequent academic performance. IELTS Research Reports 2000;3:85-108.

11. Salovey P, Mayer JD, Goldman SL, Turvey C, and Palfai TP, Emotional attention, clarity, and repair: exploring emotional intelligence using the Trait Meta-Mood Scale. In J. W. Pennebaker (Ed), Emotion, Disclosure, and Health 1995;125-154.

12. Schmitt DP, Allik J, Simultaneous administration of the Rosenberg Self-Esteem Scale in 53 nations: exploring the universal and culture-specific features of global self-esteem. Journal of Personality and Social Psychology 2005;89(4):623.

13. Batson CD, Brady RA, Peters BT, Ploutz-Snyder RJ, Mulavara AP, Cohen HS, Bloomberg JJ, Gait training improves performance in healthy adults exposed to novel sensory discordant conditions. Experi brain research 2011;209(4):515-24.

14. Blum AM, Deficit or Difference? Assessing Narrative Comprehension in Autistic and Typically Developing Individuals: Comic vs. Text. University of California, Berkeley; 2019.

15. Colomé À, Rodríguez-Ferreiro J, Tubau E, Too worried to judge: on the role of perceived severity in medical decision-making. Frontiers in Psychology 2018;9:1906.

16. Alexander ES, Onwuegbuzie AJ. Academic procrastination and the role of hope as a coping strategy. Personality and individual differences 2007;42(7):1301-10.