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Journal Name:	<u>Journal of Advances in Medical and Pharmaceutical Sciences</u>
Manuscript Number:	Ms_JAMPS_29783
Title of the Manuscript:	Enhanced Cognitive Function in Higher Education: A colour stimuli ERP Study
Type of the Article	Original Research Article

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This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
<u>Compulsory</u> REVISION comments	PLEASE, SEE BELOW COMPULSORY REVISION COMMENTS In the present investigation, the authors tested reaction time (RT) and event related potential (ERP) in response to color stimuli in a sample selected according to the educational level and show the higher educational level is found, the shorter RT is found, and also the higher amplitude and longer latency of N200 and P300 ERP are found. While I am positive with regard to the goal of the study, there are drawbacks and flaws in the paper. I read it with interest, but I have many concerns. I have found myself with some remarks after reading the paper. I will outline in more detail below. First of all, there are many grammatical errors in the manuscript. Often English is not very good. Many sentences must be re-written. The abstract is not clear and all the manuscript is also not clear. In general, I recommend to be more clear in the explanations. Often I had to read it several times before understanding it. Relations between sentences are often incoherent. Unfortunately, it is quite difficult for me to find a clear logic in many part of this paper. Please, the authors must put their ideas together in an orderly form.	English was edited for the whole manuscript. And also title changed to 'Education level is associated with specific N200 and P300 profiles reflecting higher cognitive functioning', which reflected the results of this manuscript.

	Concerning Abstract: Background does not mention Reaction Time (RT), but mentions ERP. In fact, I'm not sure both RT and ERP are parts of this section. Method is not clearly explained. For instance, "Participants were asked to press" is part of RT, but not of ERP. As described, it seems it is part of RT and ERP. Results are also not clearly explained. In fact, they are very confusing. You must read it several times. As written, conclusions cannot be inferred from the results. The conclusions in the abstract are not based on the present findings. Based on the present findings you cannot say anything about neurological functional connectivity. Major concerns: 1. Methods: The design seems acceptable. However, 1.1. Population is not described in terms of females/males, years-old with standard deviation. Please add it. 1.2. Nothing is said about Reaction time. I consider something similar to what follows should be included: "For our purpose, we deal with the RT obtained as "decision time". The experimental task used to study the investigated question does not require a subject to make a correct versus incorrect response as usual". Possibly, 2.3 heading should be : "RT and ERP stimuli and recording". 1.3. In this section or another the authors should	Abstract was written with the points of reviewer. Please see abstract. Page 2. 1.1. Added in page 6 in 'study population'. 1.2. Added about reaction time in last line page 7 and first line page 8. 2.4 heading changed to 'RT and ERP stimuli and recording' in page 7. See amendments in page 4.
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	describe the characteristics of ERP. For instance, in contrast to the excellent anatomical resolution of brain imaging techniques (3–4 mm for fMRI) that allow the visualization of the brain network involved in a certain task, electrophysiological tools, and more precisely, cognitive ERPs with a fine temporal resolution (on the order of milliseconds) allow us to observe the various electrophysiological components representing the cognitive stages utilized to achieve performance. Thus, decreased amplitude and/or delayed latency compared to normal values can be interpreted as a cognitive deficit. This finding can be interpreted taking into account cerebral areas where ERP is recorded. (Rugg MD, Coles MGH. <i>Electrophysiology of Mind. Event-Related Brain Potentials and Cognition</i>. Oxford: Oxford University Press, Oxford Psychology Series; 1995.) 2. Results: 2.1 ANOVA in 3.1 “Reaction times (RTs) analysis “ should be expressed according to the standard practice, that is, something like “ $F(2,27) = 4.467$, $p = .021$”. The same across all the text. 3. Introduction: 3.1. First, argument is focused on justification for investigating color processing as an indicator of cognitive processing in relationship with education level. I consider the argument should be expressed as previously mentioned, that is, “color processing”, “cognitive processing” , and any result will be “associated with educational level”. Any expression conveying cause-effect relationship is	2.1 Corrected. 3.1 Rearranged and corrected. See in 'Introduction'. 3.2. The corrections about ERP were added in 'Introduction', see page 4 and 5. Explanation about ERP functioning was added in 2.3 section page 7, 1st para after '2.2 study population'. 3.3 See in 'Introduction'.
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	not appropriate. 3.2. Then, the Introduction is devoted to explain the instrument o measure, particularly, ERP. I consider any explanation of the instrument functioning should be included in Methods after 2.2 Study population. Here the authors should focus on the ERP findings reported by the literature to support or explain the present research question. I means, the relationship between ERP and cognitive function. This section is appropriate to affirm that various cognitive stages of the information-processing stream (N200, P300, and so on) can be differentiated (N200, P300, and so on), and the recorded ERP components may be considered as biological markers of level of functionality. 3.3. The main points of this section should be devoted to explain the relationship between ERP and cognitive function, focusing on decision-making. Later, in Discussion section the authors can conclude their event-related potential (ERP)-based cognitive assessment experiment proved that faster decision-making is associated with higher educational level. This conclusion can be directly inferred from their experiment. 3.4. Among the relationships between ERP and cognition, the main idea is that all areas of cognition, such as perception, attention, selective attention, attention switching, resistance to distractive interference and memory, executive function linked to problem-solving, planning, and decision-making, are known to be associated with ERP profiles. Cognitive ERPs allow the assessment of the different stages used in the information processing stream during performance of a task. Every cognitive function is associated	3.4 Amendments were added in 'Introduction'. 3.5 We added about RT in page 4, 1st para. 3.6. Please see page 6 for the aim. 4. 4.1 Added in page 10.
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	with various cognitive stages. Each of the serial cognitive stages is implemented within separate neural processes in order to achieve normal function (Haxby JV, Hoffman EA, Gobbini MI. The distributed human neural system for face perception. Trends Cogn Sci. 2000;4(6): 223–233.). Indirectly, the noninvasive evaluation of ERP conveys information on functional connections between brain areas, and provides a tool to investigate cortical activity (Lioumis P, Kicic´ D, Savolainen P, Mäkelä JP, Kähkönen S. Reproducibility of TMS-Evoked EEG responses. Hum Brain Mapp. 2009;30(4):1387–1396). Therefore, any comment on brain areas or connectivity should be expressed in terms of hypothesis. 3.5. Nothing is said about RT (reaction time). At least, it should be explained something like “ RT was used as a marker of cognitive processing speed”. 3.6. The aim of the study should be something similar to “... to investigate color processing as an indicator of cognitive processing in relationship with educational level by using RT and ERP”. 4. Discussion: 4.1 In my opinion, it must be focused on their event-related potential (ERP)-based cognitive assessment experiment proved that faster decision-making is associated with higher educational level. 4.2 The authors may support their findings by citing studies. The P300 has been identified as one of the markers for response inhibition (Smith JL, Johnstone SJ, Barry RJ. Effects of pre-stimulus processing on subsequent events in a warned	4.2 We added this information in Page 5. 4.3 Added in page 5.
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	Go/NoGo paradigm: response preparation, execution and inhibition. Int J Psychophysiol. 2006;61(2): 121–133) which involves the activation of the executive system of the frontal lobes (Kaiser S, Unger J, Kiefer M, Markela J, Mundt C, Weisbrod M. Executive control deficit in depression: event-related potentials in a Go/Nogo task. Psychiatry Res. 2003;122(3):169–184). The neural basis for this executive system is believed to be a distributed circuitry, which involves the following: the prefrontal areas and anterior cingulate gyrus (Posner MI, DiGirolamo GJ. Executive attention: conflict, target detection and cognitive control. In: Parasuraman R, editor. The Attentive Brain. Cambridge: MIT Press; 1998:401–423), the orbitofrontal cortex (Fuster JM. The Prefrontal Cortex: Anatomy, Physiology and Neuropsychology of the Frontal Lobe. 2nd ed. New York: Raven Press; 1989), the ventral frontal regions (Brown GG, Kindermann SS, Siegle GJ, Granholm E, Wong EC, Buxton RB. Brain activation and pupil response during covert performance of the Stroop Color Word task. J Int Neuropsychol Soc. 1999;5(4):308–319), the parietal, dorsal, and ventral prefrontal regions (Watanabe J, Sugiura M, Sato K, et al. The human prefrontal and parietal association cortices are involved in NO-GO performances: an event related fMRI study. Neuroimage. 2002;17(3):1207–1216). 4.3 Here, the authors may describe, for instance, that P300 deficit has been reported in many disorders (quote or quotes), but there is also abundance of literature reporting other ERP components such as mismatch negativity, sensory P50, N400 linked to language semantic processes , and so on (Campanella S, Petit G, Maurage P, Kornreich C,	4.4 Please see conclusion in page 12. 4.5 Limitation was added in page 12. 4.6 Please see page 12.
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	Verbanck P, Noël X. Chronic alcoholism: insights from neurophysiology. <i>Neurophysiol Clin.</i> 2009;39(4–5):191–207; Campanella S, Guerit JM. How clinical neurophysiology may contribute to the understanding of a psychiatric disease such as schizophrenia. <i>Neurophysiol Clin.</i> 2009;39(1):31–39). 4.4 I am not convinced of the scientific reliability and validity of the conclusions that have been inferred from the results. it is not clear what the authors can say about cognitive processing based on the present results. In the present study the authors did not examine brain ERP correlates of color processing. It is not clear what they can really say about the activation in the neurological networks based on their ERP findings. Please only focus on research question, which you can really answer with your design. 4.5 Limitations of the study are not described. This is a crucial point. Obviously, ERPs suffer from some limitations. Their spatial resolution is very weak and parameters of ERPs (latency and amplitude) are subject to large inter-individual differences (Rugg MD, Coles MGH. <i>Electrophysiology of Mind. Event-Related Brain Potentials and Cognition.</i> Oxford: Oxford University Press, Oxford Psychology Series; 1995). Also, it has been suggested that the analysis of an electrophysiological components may provide greater diagnostic power than any single endophenotype alone, showing information on the characteristics of the different groups. In particular, it has been highlighted the heterogeneity of electrophysiological features among the groups and the combined analysis could serve to minimize the impact of such heterogeneity (Calkins ME,	4.7 Please see in 'Introduction'.
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	Iacono WG. Eye movement dysfunction in schizophrenia: a heritable characteristic for enhancing phenotype definition. Am J Med Genet. 2000;97(1):72–76.)(Price GW, Michie PT, Johnston J, et al. A multivariate electrophysiological endophenotype, from a unitary cohort, shows greater research utility than any single feature in the Western Australian family study of schizophrenia. Biol Psychiatry. 2006;60(1):1–10.) 4.6 Within limitations, it is convenient to add something like “larger sample of participants might be more reliable to generalize the results to a larger population”. 4.7 ERP analysis is non-invasive, painless, and cheap to investigate this question and, somehow, this should be put into the text as an advantage in order to promote new investigations.	
<u>Minor</u> REVISION comments	NO COMMENT	
<u>Optional/General</u> comments	NO COMMENT	