Potential Effects of Vinpocetine on Psychomotor Performances and Cognitive Function Capability in Normal Healthy Volunteers: Randomized Clinical Trail

Corresponding Author:
Dr. Hayder M Alkuraishy,
Lecturer, Pharmacology, College of Medicine - Iraq

Submitting Author:
Dr. Hayder M Alkuraishy,
Lecturer, Pharmacology, College of Medicine - Iraq

Article ID: WMC003038
Article Type: Clinical Trials
Submitted on: 16-Feb-2012, 10:28:07 PM GMT  Published on: 17-Feb-2012, 12:28:22 PM GMT
Article URL: http://www.webmedcentral.com/article_view/3038
Subject Categories: CLINICAL TRIALS
Keywords: Psychomotor Performance, Cognitive Function, Vinpocetine, Movement reaction time, Total reaction time and flickering fusion frequency

How to cite the article: Alkuraishy H M. Potential Effects of Vinpocetine on Psychomotor Performances and Cognitive Function Capability in Normal Healthy Volunteers: Randomized Clinical Trail. WebmedCentral: Journal of clinical research and healthcare management 2012;3(2):WMC003038

Copyright: This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Journal of Clinical research and healthcare management is an associate journal of Webmedcentral.
Potential Effects of Vinpocetine on Psychomotor Performances and Cognitive Function Capability in Normal Healthy Volunteers: Randomized Clinical Trail

Author(s): Alkuraishy H M

Abstract

Parameters of psychomotor performance reflect the psychomotor performance and cognitive function, these parameters includes TRT (total reaction time), RRT (recognition reaction time) and MRT (movement reaction time), also critical flickering fusion frequency (CFFF) which either ascending ACFF or descending DCFF. Vinpocetine drug is introduced in this study as single oral dose of 5mg and ten males medically students enrolled in this study, each subject do psychometric testing and after 2-3 hours of vinpocetine taken, the psychometric testing also done. The results of this study showed significant effects of this drug on TRT, RRT and descending CFF but insignificant effect on movement reaction time (MRT) and ascending CFF. These results indicate positive effects of vinpocetine on central processing cognitive function and psychomotor performance abilities.

Introduction

The psychomotor performances can be experienced by measuring the main components of psychomotor performance which comprise, the total reaction time (TRT), recognition reaction time (RRT) and the movement reaction time (MRT)(1), also psychomotor performance can be measured by other methods like cancellation test and mental arithmetic and logical deduction test(2).

Human psychomotor performance reflects, the time a subject takes to react to a single or more stimuli, but there is only one correct response; depending on the reaction which may be simple or complex reaction time(3).

Miller and Law (2001) resolute that the reaction time for motor perception and response was the same in all types of reaction time, implying that the differences in the psychomotor performance are due to processing time, which is the time needed to recognize the meaning of sensation from memory to construe the signal input(4,5). The psychomotor performance affected by many factors, these are: Major factors (which related to the recognition, choice and number, type and stimuli intensity) and associated factors (which include the secondary factors like age, gender, fatigue, distraction).

Many drugs affect the psychomotor performances like nootropic agents, CNS stimulants and depressants by different ways depending on the neurotransmitter that was affected (6).

The critical flickering and fusion frequency (CFF) measure the cognitive functions and it either descending, measure the time needed for perception of light from steady to flickering state while, ascending measure the time needed for perception of light form flickering to steady state(7).

Vinpocetine (vinpocetine – ethyl apovincaminate) was synthesized in the late 1960 from alkaloid vincamine (8).

Vinpocetine emerge to have numerous dissimilar mechanisms of action that permit for its anti-oxidant, vasodilating, and neuroprotective actions.

It block voltage dependent Na+ channel at neuron so decrease the damage of reperfusion injury and may be beneficial in lessening the toxic effects of oxidative stress from anoxia, also it inhibit lipid peroxidation and effective scavenger of hydroxical radicals(9).

The neuroprotective effects of vinpocetine related to blocking effects on the excitotoxicity effects of glutamate and aspartate, and partly related to phosphodiestrase enzyme inhibition which increase cerebral blood flow and decrease platelet aggregation (10).

This study is planned to scrutinize the effects of vinpocetine on the psychomotor performance and cognitive function in Normal Healthy Volunteers.

Methods

This study was carried in department of pharmacology and medicine, college of medicine, Al-Mustansiriya University, Baghdad Iraq during 2011. The subjects of this study were medical college
students, 30 volunteers, all of them were males, they accepted to enroll and complete this single blind random clinical study. The psychometric tests were performed before and after 2 – 3 hours of oral administration of 5mg vinpocetine tablets. The subject was asked to sit in front of instrument screen in a state of mental and physical relaxation. Then he had to touch the button on the pad of instrument as side of his dominant hand, as soon as possible when the light is illuminated, this time represents total reaction time, the arithmetic mean of at least 5 readings was recorded. The instrument analyze the response into total reaction time (TRT) and recognition reaction time (RRT), while movement reaction time (MRT) is calculated by subtraction of TRT from RRT i.e. MRT = TRT – RRT. Assessment of critical flicker – fusion frequency (CFFF) by asking the subject to respond when the illuminated light change from steady to flicking (decreasing CFF) and from flicking to steady (ascending CCF). The results are expressed as number, mean ± SD. The data were analyzed by using paired T-test, taking P value ? 0.05 as lowest limit of significance.

Results

Table (I): Shows the characteristics of this study. There is significant effects of vinpocetine on TRT and RRT P ? 0.05 but insignificant effect on MRT P ?0.05. Also the vinpocetine produces significant effect on the descending CFF but insignificant effects on the ascending CFF. The paired samples test reflects the comparative effects before and after single oral dose of vinpocetine (table III).

Discussion

This study showed that vinpocetine improves the psychomotor performance regardless of intra-individual and inter-individual variations of psychomotor performance testing and its components. The Arcelin and Brisswalter 1999 reported 13.3% inter-individual variations and 7.2% for intra-individual variations. Psychomotor performances and cognitive function are deteriorated with aging (12), therefore, aging factor is missed in this study because all subjects enrolled in this study were of young age. The non-significant effects of vinpocetine on the movement reaction time and the ascending CFF were due to small sample size, this supported by Portin study which showed that the small sample size in psychometric testing is a contributing factor for non-significant effect of vinpocetine(13). Vinpocetine was introduced in clinical observe for the management of cerebrovascular disorders and related symptoms and early experiments with vinpocetine indicated five main pharmacological and biochemical actions (14):

* Selective enhancement of brain circulation and oxygen utilization without significant alteration in parameters of systemic circulation.
* Increased tolerance of brain toward hypoxia and ischemia.
* Anti-convulsant activity.
* Inhibitory effect on phosphodiesterase type I.
* Improvement of rheological properties of the blood and inhibit thrombocyte aggregation.

Moreover, vinpocetine block voltage gated Na+ channels and block selectively Ca+ -calmodulin dependent cGMP leading to ? cGMP, also it inhibit adenosine uptake, all of these contribute for neuroprotection effect of vinpocetine(15). The noteworthy consequence of vinpocetine on TRT, RRT may be due to activation of noradrenergic neurons, this supported by Gaal 2006 study that showed vinpocetine produce a significant and dose dependent increase in the firing rate of locus coeruleus neuron followed by complete blockade of spiking activity at higher dose, this lead to improvement of noradrenergic pathway and enhancing the cognitive function and psychomotor performance.(16) In respect to critical flickering fusion frequency (CFFF) the threshold for fusion is better in female than male but male have good flickering, therefore all visual perceptions parameters are faster in females(17), so females excluded from this study. The brain pathway for ascending (fusion) CFF is highly differ from descending (flickering) CFF pathway, the flickering neurotransmitter is mainly noradrenalin while the neurotransmitter for fusion is mainly dopamine and serotonin(18), this explain the significant effect of vinpocetine on flickering CFF and insignificant effect on the ascending CFF in our study. Therefore, vinpocetine significantly improved psychomotor performance and cognitive function, to explain how vinpocetine offered the beneficial effect on vigilance, a briefly review on the neuropharmacology of psychomotor performance system should be done. The neuronal system controlled the psychomotor performances centered on the prefrontal cortex, cingulate and striatum, the basal forebrain bundle.
plays a role in controlling both the cognitive and non-cognitive functions of vigilance (19). A meta-analysis of six randomized, controlled trials involving 731 patients with degenerative senile cerebral dysfunction showed that vinpocetine was highly effective in the treatment of senile cerebral dysfunction, using several psychometric testing scale in addition to physical symptoms, the researcher were able to show a highly significant effect of vinpocetine on both cognitive and motor function (20). Add to this, vinpocetine preferentially antagonizes quisqualate / AMPA receptor responses, this examined in brain rats, the vinpocetine reduce efflux of dopamine and acetylcholine evoked by glutamate, quisqualate and NMDA receptor but not by kainate, this finding suggested that vinpocetine improve the cognitive through regulation of glutamate receptor (21).

Tests of critical flickering fusion threshold, a Sternberg memory scanning task, along with subjective rating of drugs action were used. Drugs effect were found to be modest this explain the improvement in short term memory process (22). Vinpocetine requisite to neuroreceptors has newly been characterized using standard broadcast methodology. The study established relatively high affinity of vinpocetine to sodium and potassium channel receptors, adrenergic a receptors, peripheral GABA-Abenzodiazepine receptors and dopamine, whereas attraction to other receptor systems was low. Even though the concentration of nicotinic acetylcholine receptors is so high in the thalamus that they characteristically distinguish this region. (23) Increases in neuronal levels of DOPAC, a metabolic breakdown product of dopamine, have been revealed to occur in striatal isolated nerve endings as a result of revelation to vinpocetine. Such an effect is reliable with the biogenic pharmacology of reserpine, a structural relation of vinpocetine, which depletes catecholamine levels and may cause depression as a side-effect of the cardiovascular and anti-psychotic effects.(24,25)

Entertainingly, the thalamus and the putamen have shown the maximum increases in brain blood flow after a 2-week of vinpocetine treatment in the human brain. These observations on brain metabolism are reliable with the observation that the relatively high uptake of vinpocetine in specific brain regions strength exclusively be related to the drug action of vinpocetine. (26,27,28). Vinpocetine also inhibits the voltage-dependent Na+ -channels, so caring the existing neurons from further demolition after ischemic hurt (29). Vinpocetine may also interrelate with glutamate receptors and protects cells alongside the cytotoxic consequence of glutamate. In adding together to enzymatic and receptor-related effects, vinpocetine can act directly as an antioxidant and protect effects of regional and global hypoxia. These studies maintain the hypothesis that vinpocetine is a centrally acting compound. On the other hand, it has also been recommended that vinpocetine has an outcome on regional cerebral blood flow and this achieve does not necessarily imitate a alter in neurotransmission neuronal activity. In a consequent study, vinpocetine, administered by repeated intravenous injection during a 2-week treatment regime, increased regional cerebral blood flow and glucose metabolism predominantly in the thalamus, basal ganglia and occipital cortex (30). Furthermore the beneficial rheological effects of high-dose parenteral vinpocetine (partially caused by hemodilution) observed previously, and also necessitate its long-term oral admission to preserve the favorable rheological changes. (31)

Although, the regional changes in cerebral blood flow after vinpocetine infusion, as compared to that obtained after placebo infusion, point to that vinpocetine treatment results in a regional redistribution of cerebral blood flow, the blood flow increases are the maximum in the thalamus, the basal ganglia, and the brain stem. The regional uptake of vinpocetine was the premier in these structures, indicating a correlation between the drug’s pharmacological and physiological effects, as well (32,33,34) Therefore, vinpocetine advance the psychomotor performance functions mainly the TRT and RRT and descending CFF this indicated that vinpocetine produce central effects on neuron rather than peripheral effects through ion channel inhibition and blocking the cerebral excitotoxicity, this, per se the improvement in the cognitive function after taken the vinpocetine.

**Conclusion(s)**

Vinpocetine improve the psychomotor performance and cognitive function.

**Recommendations**

- Study the effect of vinpocetine on nitric oxide peroxynitrate action.
- Detect the final common pathway for vinpocetine action.
- Long term therapy to detect the potential side effects.
References

30. Tretter L, Adam-vizi V. The neuroprotective drug vinpocetine prevents veratridine-induced [Na+] and [Ca2+] rise in synaptosomes. Neuroreport


Illustrations

Illustration 1

Table 1: The characteristics of the study.

<table>
<thead>
<tr>
<th>Number</th>
<th>30</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td>Male</td>
</tr>
<tr>
<td><strong>Age (year)</strong></td>
<td></td>
</tr>
<tr>
<td>Lower limit</td>
<td>20</td>
</tr>
<tr>
<td>Upper limit</td>
<td>21</td>
</tr>
<tr>
<td><strong>Range</strong></td>
<td>1</td>
</tr>
<tr>
<td><strong>Mean ± SD</strong></td>
<td>20.2 ± 0.41</td>
</tr>
<tr>
<td><strong>Smoking</strong></td>
<td>None</td>
</tr>
<tr>
<td><strong>Medications</strong></td>
<td>None</td>
</tr>
<tr>
<td><strong>Time</strong></td>
<td>9-11a.m</td>
</tr>
</tbody>
</table>
Illustration 2

Table 2: Assessment of psychomotor parameters.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD before (M. Sec.)</th>
<th>Mean ± SD after (M. Sec.)</th>
<th>P</th>
<th>t</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRT</td>
<td>635.80 ±114.57</td>
<td>528.90 ±69.84</td>
<td>0.004*</td>
<td>3.788</td>
</tr>
<tr>
<td>RRT</td>
<td>424.60 ±103.79</td>
<td>347.80 ±52.035</td>
<td>0.023*</td>
<td>2.731</td>
</tr>
<tr>
<td>MRT</td>
<td>220.50 ±48.196</td>
<td>189.20 ±31.304</td>
<td>0.064</td>
<td>2.107</td>
</tr>
<tr>
<td>ACFF</td>
<td>54.626 ±82.713</td>
<td>26.6509 ±1.568</td>
<td>0.310</td>
<td>1.077</td>
</tr>
<tr>
<td>DCFF</td>
<td>26.1309 ±2.068</td>
<td>30.10 ±2.751</td>
<td>0.002*</td>
<td>-4.161</td>
</tr>
</tbody>
</table>
Illustration 3

Table 3: Paired differences in psychomotor performances parameters before and after vinpocetine.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean</th>
<th>S.D.</th>
<th>S.E.</th>
<th>95% confidence interval</th>
<th>t</th>
<th>d.f.</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRT</td>
<td>106.900</td>
<td>89.251</td>
<td>28.223</td>
<td>43.0531</td>
<td>170.746</td>
<td>3.788</td>
</tr>
<tr>
<td>RRT</td>
<td>76.800</td>
<td>88.932</td>
<td>28.123</td>
<td>13.181</td>
<td>140.418</td>
<td>2.731</td>
</tr>
<tr>
<td>MRT</td>
<td>31.300</td>
<td>46.965</td>
<td>14.851</td>
<td>-2.297</td>
<td>64.897</td>
<td>2.107</td>
</tr>
<tr>
<td>ACFF</td>
<td>27.976</td>
<td>82.165</td>
<td>25.982</td>
<td>-30.801</td>
<td>86.753</td>
<td>1.077</td>
</tr>
<tr>
<td>DCFF</td>
<td>-3.969</td>
<td>3.0166</td>
<td>0.953</td>
<td>-6.127</td>
<td>-1.811</td>
<td>4.161</td>
</tr>
</tbody>
</table>
Disclaimer

This article has been downloaded from Journal of Clinical research and healthcare management an associated journal of WebmedCentral. Authors must ensure that they obtain all the necessary permissions before submitting any information that requires obtaining a consent or approval from a third party. Authors should also ensure not to submit any information which they do not have the copyright of or of which they have transferred the copyrights to a third party. Contents on Journal of Clinical research and healthcare management are purely for biomedical researchers and scientists. They are not meant to cater to the needs of an individual patient. The web portal or any content(s) therein is neither designed to support, nor replace, the relationship that exists between a patient/site visitor and his/her physician. Your use of the Journal of Clinical research and healthcare management site and its contents is entirely at your own risk. We do not take any responsibility for any harm that you may suffer or inflict on a third person by following the contents of this website.