

The Effects of Vinpocetine on the Psychomotor Performances: Randomized clinical trial, single blind random clinical study.

Hayder Al-Kuraishy^{*}, Salahalduin Al-Windy^{**} and Ali I. Algareeb^{***}

^{*} College of Medicine, Al-Mustansyria University.

^{**} Department of Biology, College of Science, Baghdad University.

^{***} College of Medicine, Al-Mustansyria University.

Abstract

Psychomotor performance parameters reflects the psychomotor and cognitive function in human being, 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 CFF or descending CFF.

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 done.

The results of this study showed significant effects ($p < 0.05$) of this drug on TRT, RRT and descending CFF but insignificant effect on ($p > 0.05$) movement reaction time (MRT) and ascending CFF.

These consequences indicate a positive effect of vinpocetine on central nervous system but not on the peripheral nervous system.

Introduction

The psychomotor performances can be tested by measuring the main components of psychomotor performance which include, 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, 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 response which may be simple or complex reaction time^[3].

Miller and Law (2001) determined that the reaction time for motor perception and response was the same in all types of reaction time^[4], 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 interpret the signal input^[5]. The psychomotor performance affected by many factors, these are:

- Major factors: which related to the recognition, choice, number, type and stimuli intensity?

- Associated factors: which includes the secondary factors like age, gender, fatigue and distraction from stimuli.

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 from flickering to steady state^[7].

Vinpocetine (vinpocetine – ethyl apovincamate) was synthesized in the late 1960 from alkaloid vincamine, it extracted from the Periwinkle plant (vinca minor)^[8].

Vinpocetine emerge to have several different mechanisms of action that consent to 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 attenuation 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 linked to blocking property on the excitotoxicity effects of glutamate, aspartate, and partially related to phosphodiesterase enzyme inhibition which increase cerebral blood flow and decrease platelet aggregation^[10].

So this study is designed to explore the effects of vinpocetine on the psychomotor performance in human, utilizing Leeds psychometric tester device, and how vinpocetine affect the normal human cognitive function.

Subjects and methods

This study was carried in department of pharmacology, college of medicine, Al-Mustansiriya University, Baghdad Iraq during 2009.

The subjects of this study were medical college students, 10 volunteers, all of them were males, they accepted to enroll and complete this single blind random clinical study.

The psychometric tests were performed before oral administration of 5mg vinpocetine tablets and after 2 – 3 hrs the psychometric test was done.

The subject was asked to sit in front of instrument screen in a state of mental and physical lessening. 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).

Statistical Analysis

The results are expressed as number, mean \pm SD. The data were analyzed by using paired t-test, taking *P* value \leq 0.05 as lowest limit of significance.

Results

Table (1) shows the characteristics of this study.

Table (1):
The characteristics of the study.

Number		10
Gender		Male
Age (years)	Lower limit	20
	Upper limit	21
Range		1
Mean \pm SD		20.2 \pm 0.41

Table (2) shows the effects of single oral dose of vinpocetine on the psychomotor parameters.

Table (2):
Assessment of psychomotor parameters.

Variable	Mean \pm SD before (M. Sec.)	Mean \pm SD after (M. Sec.)	P	t
TRT	635.80 \pm 114.57	528.90 \pm 69.84	0.004*	3.788
RRT	424.60 \pm 103.79	347.80 \pm 52.035	0.023*	2.731
MRT	211.50 \pm 48.196	189.20 \pm 31.304	0.064	2.107
ACFF	54.626 \pm 82.713	26.6509 \pm 1.568	0.310	1.077
DCFF	26.1309 \pm 2.068	30.10 \pm 2.751	0.002*	- 4.161

*significant effects.

There is significant effects of vinpocetine on TRT and RRT when $P \leq$ 0.05 but insignificant effect on MRT.

Moreover; the vinpocetine produces significant effect on the descending CFF but insignificant effects on the ascending CFF.

The paired samples test reflects the dose of vinpocetine (Table (3)). comparative effects before and after single oral

Table (3):
Paired sample test shows the paired differences.

Variables (Before – after)	Paired differences						
	Mean	S.D.	S.E.	95% confidence interval		t	d.f.
				<i>lower</i>	<i>upper</i>		
TRT	106.900	89.251	28.223	43.0531	170.746	3.788	9
RRT	76.800	88.932	28.123	13.181	140.418	2.731	9
MRT	30.100	46.965	14.851	-2.297	64.897	2.107	9
ACFF	27.976	82.165	25.982	-30.801	86.753	1.077	9
DCFF	- 3.969	3.0166	0.953	-6.127	-1.811	-4.161	9

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 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 ages.

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 2005 study which showed that the small sample size in psychometric testing is a causative factor for non-significant effect of vinpocetine [13].

Vinpocetine was introduced in clinical practice for the conduct of cerebrovascular disorders and associated symptoms. Untimely experiments with vinpocetine indicated five main pharmacological and biochemical actions [14].

- Selective improvement of brain circulation and oxygen utilization without significant modification in parameters of systemic circulation.
- Increased broadmindedness of brain toward hypoxia and ischemia.
- Anti-convulsant activity.
- Inhibitory effect on phosphodiesterase type I.

- Improvement of rheological properties of the blood flow and inhibit thrombocyte aggregations.

Furthermore; vinpocetine block voltage gated Na^+ channels and block selected Ca^{2+} -calmodulin dependent cGMP leading to increase cGMP, also it inhibit adenosine uptake, all of these donated for neuroprotection effects of vinpocetine [15].

The significant effect 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 neurons followed by complete blockade of spiking activity at higher dose, this lead to upgrading of noradrenergic pathway and enhancing the cognitive function and psychomotor performance.

In deference 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, and to explain how vinpocetine presented the beneficial effect on psychomotor performance action, a briefly review on the neuron-pharmacology of psychomotor performance system 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 scheming both the cognitive and non-cognitive functions of vigilance and psychomotor functions^[19].

A meta-analysis of six randomized, controlled trial involving 731 patients with degenerative senile cerebral dysfunction showed that vinpocetine was extremely effective in the treatment of senile cerebral dysfunction, by means of numerous psychometric testing scale in addition to physical symptoms, the researcher were capable to show a exceedingly 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 kainite receptors, this discovery suggested that vinpocetine improve the cognitive through regulation of glutamate receptors^[21].

The pretreatment with vinpocetine on flunitrazepam induced impairment of memory, were studied in 8 normal volunteers.

Tests of critical flickering fusion threshold via 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].

Therefore; vinpocetine advance the psychomotor performance actions, chiefly the TRT and RRT and descending CFF this indicated that vinpocetine create central effects on neuron rather than peripheral effects through ion channel inhibition and blocking the cerebral excitotoxicity, this, *per se* explain the enhancement in the cognitive function after taken the vinpocetine drugs.

Conclusions

- Vinpocetine improve the psychomotor performance.
- Vinpocetine should be regarded as magic herb.
- Vinpocetine produce central rather than peripheral effect.

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.

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تأثير الفنبوستين على الأداء النفسي الحركي: الدراسة العشوائية، أعمى عشوائي واحدة دراسة سريرية.

الخلاصة

قياس الأداء الحركي النفسي ومؤشراته تعكس فعالية
المقدرة الذهنية والأداء الحركي النفسي، هذه المؤشرات تشمل

الوقت الانعكاسي الكامل، والوقت الانعكاسي الإدراكي،
والوقت الانعكاسي الحركي، وأيضاً معدل التذبذب الاندماجي
للضوء والذي يشمل الصاعد والنازل يعكس بصورة غير
مباشرة أداء القدرة الذهنية.

عقار الفنبوستين قُدم في هذه الدراسة كجرعة منفردة
٥ ملغم لبيان تأثيره على الأداء الحركي النفسي لعشرة
متطوعين ذكور، وكل شخص يتم تقييمه في مقياس الأداء
الحركي النفسي قبل وبعد اخذ هذا العقار. ولقد أظهرت هذه
الدراسة بأن هذا العقار له تأثير محفز على مؤشرات الأداء
الحركي النفسي، وبذلك نستخلص بأن عقار الفنبوستين له
تأثير محفز على الجهاز العصبي المركزي ولكن ليس على
الجهاز العصبي المحيطي لأنه يقلل الوقت الانعكاسي
الحركي.

