Physiology and Pharmacology 29 (2025) 54-62
Experimental Research Article

Evaluation of the cardiovascular effect of GABAB receptor of the Pedunculopontine tegmental nucleus (PPT) in anesthetized rats

Mohammad Naser Shafei[1, 3], Hossein Pasandi[2], Vida Alikhani[2*]

1. Applied Biomedical Research center, Mashhad University of Medical Science, Mashhad, Iran
2. Department of Physiology, Medicine School, Gonanbad University of Medical Science, Gonabad, Iran
3. Division of Neurocognitive Sciences, Psychiatry and Behavioral Sciences Research Center, Mashhad University of Medical Science, Mashhad, Iran

ABSTRACT

Introduction: The cardiovascular effect of the pedunculopontine tegmental nucleus (PPT), a mesencephalic area, has been evaluated. Due to the presence of the GABAB receptor of GABAergic system in the PPT, this study has investigated the possible cardiovascular effect of this receptor in the PPT and has compared it with GABAA.

Methods: Rats randomly were divided into control, two doses of 0.5 and 1 nmol of Baclofen (GABAB receptor agonist), 0.5 and 1 nmol, of Phaclofen (GABAB receptor antagonist) and two doses of 0.1 and 0.2 nmol of Bicuculline (BMI, GABAA receptor antagonist) and co-injection of Phaclofen (1nmol)+ Bicuculline (0.2 nmol) groups. After anesthesia, a heparinized polyethylene catheter was placed in the femoral artery and was connected to a pressure transducer cardiovascular response was recorded by a Power lab device. Then the systolic blood pressure (SBP), mean arterial pressure (MAP) and heart rate (HR) were continuously recorded. The injection of drugs into the PPT was done stereotaxically. Cardiovascular changes (Δ,difference between pre and post-injection) induced by drug were calculated and analyzed.

Results: Injection of both doses of Baclofen and Phaclofen did not induce significant changes in MAP, SBP, and HR. Injection of both doses of BMI significantly increased ΔMAP, ΔSBP, and ΔHR than control group. Injection of Phaclofen (1nmol) and BMI (0.2 nmol) could increase ΔMAP, ΔSBP, and ΔHR that was non-significant than Phaclofen alone.

Conclusion: We found that GABAB receptors of the PPT were not involved in cardiovascular activity and this effect was mainly mediated through GABAA receptors.

Keywords:
Mean arterial pressure
Heart rate
Pedunculopontine tegmental nucleus
GABA
Bicuculine

Introduction

The pedunculopontine nucleus (PPT) is located in the upper part of the brainstem, near the superior cerebellar peduncle (Martinez-Gonzalez et al., 2011). It has an irregular shape and is composed of two parts: a rostral part and a caudal part (Martinez-Gonzalez et al., 2011). Glu-

* Corresponding author: Vida Alikhani, Alikhaniv4013@mums.ac.ir
Received 23 December 2023; Revised from 12 May 2024; Accepted 15 June 2024
Citation: Shafei M.N., Pasandi H, Alikhani V. Evaluation of the cardiovascular effect of GABAB receptor of the Pedunculopontine tegmental nucleus (PPT) in anesthetized rats. Physiology and Pharmacology 2025; 29: 54-62. http://dx.doi.org/10.61186/phypha.29.1.54

tamatergic, GABAergic, and cholinergic neurons have been identified within this nucleus. The distribution of these neurons within the PPT varies, with GABAergic neurons exhibiting the highest density in the rostral PPT, which gradually decreases towards the caudal part. Glutamatergic and cholinergic neurons, on the other hand, have the highest density in the caudal PPT (Benarroch 2013; Mena-Segovia et al., 2009). Studies have demonstrated that the PPT is one of the regions with cholinergic outputs and projects to the lateral ventral medulla (Yasui et al., 1990). The Rostral ventrolateral medulla (RVLM) is one of the most important axons that provide innervation to other brain regions. They send efferent signals and projections to other brainstem nuclei and lower brain regions, while also receiving afferent signals from other brain regions (Wang and Morales 2009). The PPT is involved in various functions, including arousal, regulation of REM sleep, movement control, modulation of sensory responses, learning, memory, and regulation of cardiovascular and respiratory activities (Alderson et al., 2008; Winn 2008).

GABA is a non-protein amino acid present in body fluids. In the brain, it is synthesized through the GABA shunt metabolic pathway. GABA is produced in mitochondria through the decarboxylation of glutamate by the enzyme glutamate decarboxylase (GAD) in the tricarboxylic acid cycle and stored in the cytoplasmic terminals of GABAergic neurons. GABA has three types of receptors: A, B, and C. $GABA_A$ and $GABA_C$ receptors are ionotropic, while $GABA_B$ receptors are metabotropic. $GABA_A$ receptor is associated with chloride channels and its activation leads to the influx of chloride ions, hyperpolarizing the membrane potential and exerting inhibitory effects on neurons. The $GABA_A$ receptor has binding sites for benzodiazepines, barbiturates, picrotoxin, muscimol (a $GABA_A$ agonist), and bicuculline (a $GABA_A$ antagonist) (Bormann 2000).

The $GABA_B$ receptor functions by opening potassium channels and inhibiting calcium channels. The Baclofen is an agonist and phaclofen is an antagonist of $GABA_B$ receptor. The $GABA_C$ receptor, similar to $GABA_A$, has gated chloride channels and is insensitive to bicuculline, benzodiazepines, and anesthetics (Dutar and Nicoll 1988; Li and Pan 2010).

We hypothesize that activation of the GABA-B receptor in the PPT will modulate cardiovascular activity in anesthetized rats, potentially through interactions with key brain regions involved in cardiovascular regulations, such as the rostral ventrolateral medulla (RVLM Our objectives are to examine the effects of GABA-B receptor activation on cardiovascular parameters—such as heart rate, blood pressure, and other cardiovascular parameters. We aim to clarify the interactions between the PPT and cardiovascular centers, particularly the RVLM, to detail the neural pathways responsible for these cardiovascular responses. Additionally, we seek to characterize the role of GABAergic neurons within the PPT in regulating cardiovascular function and to explore the potential therapeutic implications of targeting this pathway for treating cardiovascular disorders. Considering the involvement of the PPT in regulating cardiovascular activity and its connection with brain cardiovascular areas (i.e RVLM), as well as the presence of GABAergic neurons in the PPT, this study evaluates the possible role of $GABA_B$ receptor of the GABAergic system in the PPT on cardiovascular function in anesthetized rats.

Material and Methods

Forty-two male Wistar rats with an average weight of 250-300 g were used and housed in a constant condition. The animals had no restrictions on food and water intake and were maintained under a 12-hour light/dark cycle, the room temperature was maintained at around 25°C. The University Ethics Committee of Mashhad University of Medical Sciences approved the experimental procedure with the ethical code: IR.MUMS.REC.1394.159. At the beginning of the experiment, the animals were weighed and anesthetized with a dose of 1.2-1.4 g/kg of urethane, administered intraperitoneally (Alderson et al., 2008).

After anesthesia, the femoral artery was cannulated by a polyethylene catheter (PE=50) filled with saline-heparin solution. The catheter was then connected to a PowerLab system via a blood pressure transducer. Cardiovascular parameters including systolic blood pressure (SBP), Mean arterial blood pressure (MAP), and heart rate (HR) were continuously recorded using a Lab Chart computer program.

For injection of drugs, the animal was placed in a stereotaxic apparatus and the head was fixed. A longitudinal incision was made on the head and the PPT's coordination was determined according to the Paxinos and Watson rat brain atlas (AP: 7.6–8.5 mm, L: 1.7-2.2

and H: 5.5–6.2 mm). Then, a hole about 2 mm in diameter was drilled into the skull and adjusted above the PPT. Drugs were microinjected into the PPT through a micropipette inserted into the PPT and connected to a manual pump. The injection volume for all experiments was 150-100 nl.

Urethane (Sigma, USA), baclofen (a selective $GABA_B$ agonist, Sigma), phaclofen (a selective $GABA_B$ antagonist, Sigma) bicuculline methiodide (BMI, a competitive $GABA_A$ antagonist, Sigma). All drugs were dissolved in saline except phaclofen which was dissolved in HCL 0.1 N, then the PH augmented above seven by adding NaOH.

Animals were randomly divided into nine groups: (n=6)

Group 1 (Control): In this group, saline was microinjected into the PPT.

Groups 2 and 3: BMI (a competitive antagonist of $GABA_A$ receptor) was injected into the PPT at doses of 0.1 and 0.2 nmol.

Group 4 and 5: baclofen (a selective $GABA_B$ receptor agonist) was injected into the PPT at doses of 0.5 and 1 nmol.

Group 6 and 7: phaclofen (a selective $GABA_B$ receptor antagonist) was injected into the PPT at doses of 0.5 and 1 nmol.

In all groups, continuous recordings of MAP, SBP, and HR were obtained 5 min before and 30 min after injection.

The brains were first extracted from the skulls, which were then soaked in 10% formalin for a day to fix the tissue. Next, a vibratome was used to cut the brains into thin slices measuring 60 microns. These slices were then viewed under a light microscope to confirm that the injections had been accurately placed, as per the Paxinos and Watson atlas (Shafei et al., 2012).

Data analysis and statistical tests

The results are expressed as mean and standard error (mean ± SEM). Changes (Δ difference between pre and post of injection drugs) MAP, SBP, and HR several times were calculated and analyzed. The repeated measure ANOVA with Tukey's *post-hoc* test was used for analyzing changes in all parameters several times. $P<0.05$ was used for indication of statistical significance.

Results

The effect of injection of saline into the PPT on cardiovascular responses

MAP, SBP, and HR before and after saline injection were recorded. The results showed that the cardiovascular responses before saline injection were 110.24±2.27 mmHg, 120±4.36 mmHg, and 340±13.49 beats/min for MAP, SBP, and HR, respectively. After the saline injection, the maximum responses for MAP, SBP, and HR were 116 ± 3.37 mm Hg, 360 ± 11.61 beats/min, and 122 ± 3.51 mm Hg. There was no significant difference in cardiovascular parameters between pre and post-injection.

Effects of injection of BMI on cardiovascular responses into the PPT

Injection of BMI with doses of 0.1 and 0.2 nmol increased ΔMAP, ΔSBP and ΔHR. As it is shown in Figure 1, both doses of BMI (0.1 and 0.2 nmol) significantly increased ΔMAP and ΔSBP and ΔHR ($P<0.05$ to $P<0.001$, repeated measure ANOVA, n=6). A comparison of the effects of two different doses showed that the effect of higher dose (0.2 nmol) is greater than lower dose 0. 1 nmol) and this effect in the ΔMAP and ΔHR were significant ($P<0.05$, Figure 1, repeated measure ANOVA, n=6).

The effect of baclofen injection into the PPT on cardiovascular responses

Two doses of 0.5 and 1 nmol of baclofen were evaluated in two separate groups. At first, the MAP, SBP, and HR were measured, and after injection of two doses of baclofen, the changes (Δ) of these parameters were measured. Injection of baclofen with doses of 0.5 and 1 nmol did not cause significant changes in ΔMAP. Injection of baclofen at both doses caused an increase in ΔHR, which does not show a significant difference compared to the control group (Figure 2).

The effect of injection of phaclofen on cardiovascular responses in PPT

Two doses of 0.5 and 1 nmol of phaclofen were studied in two separate groups. First, the baseline values of MAP, SBP, and HR were measured, and after the injection of two doses of phaclofen into the PPT, the changes (Δ) of these parameters were measured. phaclofen at doses of 0.5 and 1 nmol increased ΔMAP, ΔSBP, and

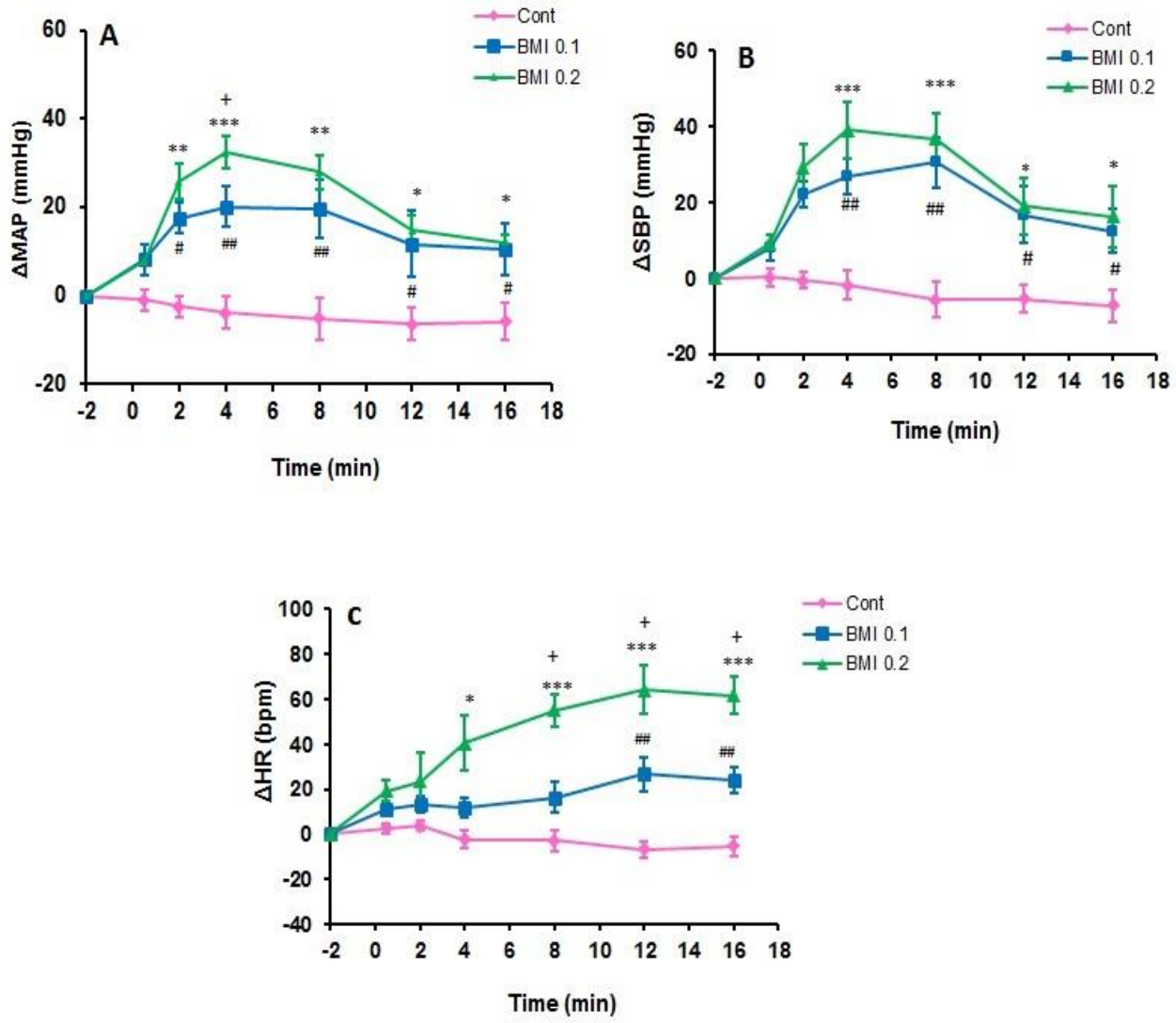

FIGURE 1. Comparing the cardiovascular effects of two doses of BMI (0.1 and 0.2 nmol) microinjected into the PPT than the control group. The time course of mean changes in MAP (A), SBP (B) and HR (C) are shown. (n=6).
Both doses of BMI, significantly increased ΔMAP, ΔSBP and ΔHR and the effect of 0.2 nmol is greater than 0. 1 nmol in the ΔMAP and ΔHR.
P<0.01: Comparison dose 0.1 nmol BMI with the control
* P<0.05; *** P<0.001: Comparison dose 0.2 nmol BMI with the control
+ P<0.05: Comparison dose 0.2 nmol with dose 0.1 nmol
MAP: Mean arterial blood pressure, SBP: systolic blood pressure, HR: heart rate

ΔHR, which was not significant compared to the control group (Figure 3).

Comparing the cardiovascular effects of the injection of BMI and phaclofen into the PPT

In this experiment, the highest dose of phaclofen was compared with the highest dose of BMI. These changes are shown in Figure 4. As has been shown, injection of BMI (0.2 nmol) resulted in an increase in ΔMAP and ΔSBP, which varied at different time points. Two minutes after BMI injection, ΔMAP and ΔSBP significantly increased compared to injection of Phocalofen (P<0.05), and reached its maximum increase between minutes 4 and 8 (P<0.01). Although the ΔMAP and ΔSBP decreased afterward, at minute 12, the pressure resulting from BMI injection was still significantly higher than that resulting from Phocalofen injection (P<0.05).

ΔHR also increased following the injection of BMI, with a significant difference from the phaclofen at minute 12 (P<0.05) and minute 16 (P<0.01).

Discussion

In the present study, the cardiovascular role of the phaclofen (a $GABA_B$ receptor antagonist) and baclofen (a

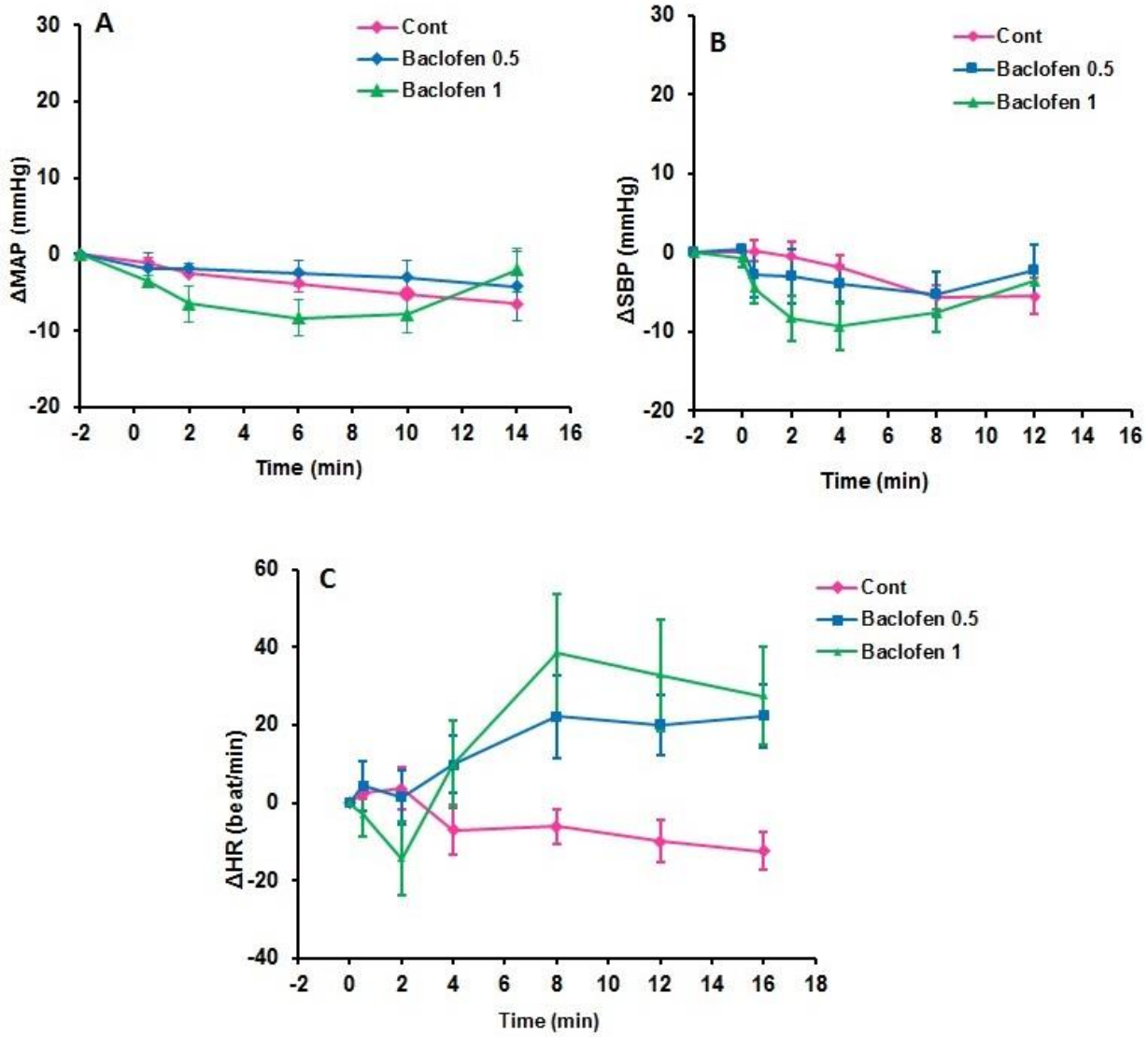

FIGURE 2. Comparing the cardiovascular effects of injection of two doses of 0.5 and 1 nmol of baclofen into the PPT compared to the control group.
Both doses baclofen did not change significantly in CV parameters.
The time course of average changes in MAP (A), SBP (B) and HR (C) are shown in the figure. (n = 6)
MAP: Mean arterial blood pressure, SBP: systolic blood pressure, HR: heart rate

$GABA_B$ receptor agonist) of the PPT have been investigated. Then these parameters were compared with BMI (a $GABA_A$ receptor antagonist). Results indicated that the $GABA_B$ receptor of this nucleus did not important effect on cardiovascular parameters and most of this effect mediated by $GABA_A$ receptor. This effect is in line with our previous results that indicate BMI increased cardiovascular parameters.

GABA is one of the most important inhibitory neurotransmitters in the central nervous system, which has multiple effects on the brain. One of its most important effects is the regulation of the activity of the central cardiovascular system (Alves et al., 2016; Avanzino et al., 1994; Callera et al., 1999). In the current study, injection of BMI increased SBP and HR confirming the inhibitory effect of the $GABA_A$ receptor of the PPT on cardiovascular responses. In line with our findings, several studies have shown that GABA has the same effect in other nuclei. For example, it has been shown that the injection of BMI in the PVN increases SBP and HR (Faber et al., 2023; Turossi Amorim et al., 2019). Also, Nasimi *et al.* showed that BMI increases SBP in the diagonal band of Broca. In the amygdala and RVLM, a GABA inhibitory effect has also been observed, which that mediated via $GABA_A$ receptor (Nasimi and Hatam 2005).

In our study, injection of baclofen did not affect car-

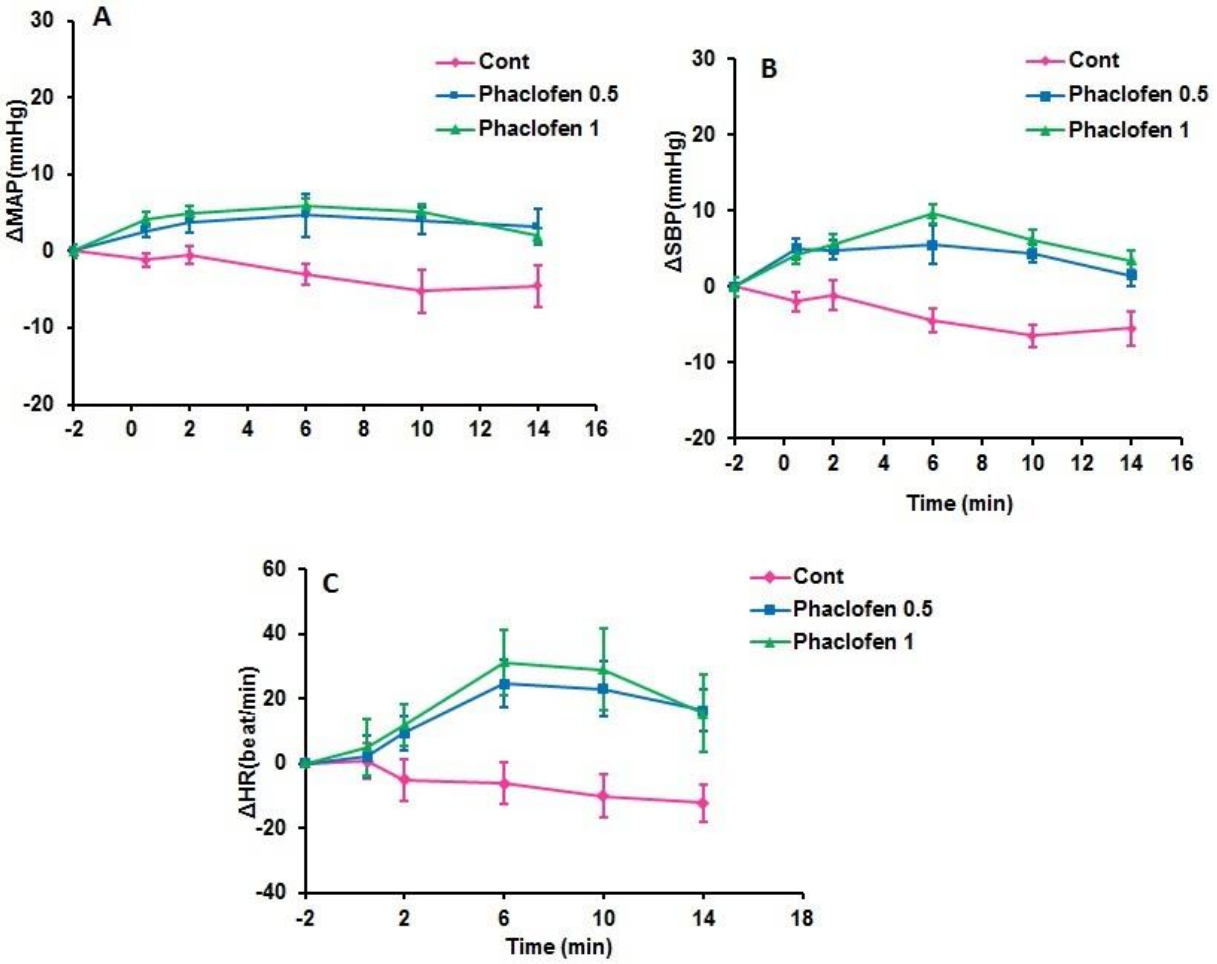

FIGURE 3. Comparing the cardiovascular effects of injection of two doses of 0.5 and 1 nmol of phaclofen in PPT compared to the control group.
Phaclofen at both doses did not increase CV parameters, significantly.
The time course of average changes in MAP (A), SBP (B) and HR (C) are shown in the figure. (n=6)
MAP: Mean arterial blood pressure, SBP: systolic blood pressure, HR: heart rate

diovascular responses. These results showed that the cardiovascular effects of the GABAergic system of the PPT are conducted through the $GABA_A$ receptors, while the cardiovascular effect of the $GABA_B$ receptor was not observed in our study. However, the presence of $GABA_B$ receptors in the PPT cannot be ignored. As our study was conducted in basic conditions and without any intervention, it is possible that the $GABA_A$ receptor is active in normal conditions and the $GABA_B$ receptor has no effect on cardiovascular activity in normal conditions.

Studies have shown that most of the GABAergic neurons are located in the rostral part of the PPT, and this area is connected with different areas of the brain such as the hypothalamus, basal ganglia, RVLM (Martinez-Gonzalez et al., 2012; Rosborough 2014). For example, Ford *et al.* showed that there are projections from the rostral part of the PPT to the lateral hypothalamus (Ford et al., 1995).

The mechanism of action of $GABA_A$ receptors is through the ion channels and the entry of CL^-, while the effects of $GABA_B$ receptors are mediated by the activation of K^+ efflux and the activation of cell signaling pathways. Therefore, the mechanism of action of $GABA_B$ receptors has a longer duration compared to $GABA_A$ receptors (Bormann 2000; Dutar and Nicoll 1988; Li and Pan 2010). It has been shown that $GABA_B$ receptors are G protein-coupled receptors that mediate slow and prolonged inhibitory action, via activation of Gαi/o-type proteins. $GABA_B$ receptors mediate their inhibitory action by activating inwardly rectifying K^+ channels, inactivating voltage-gated Ca^{2+} channels, and

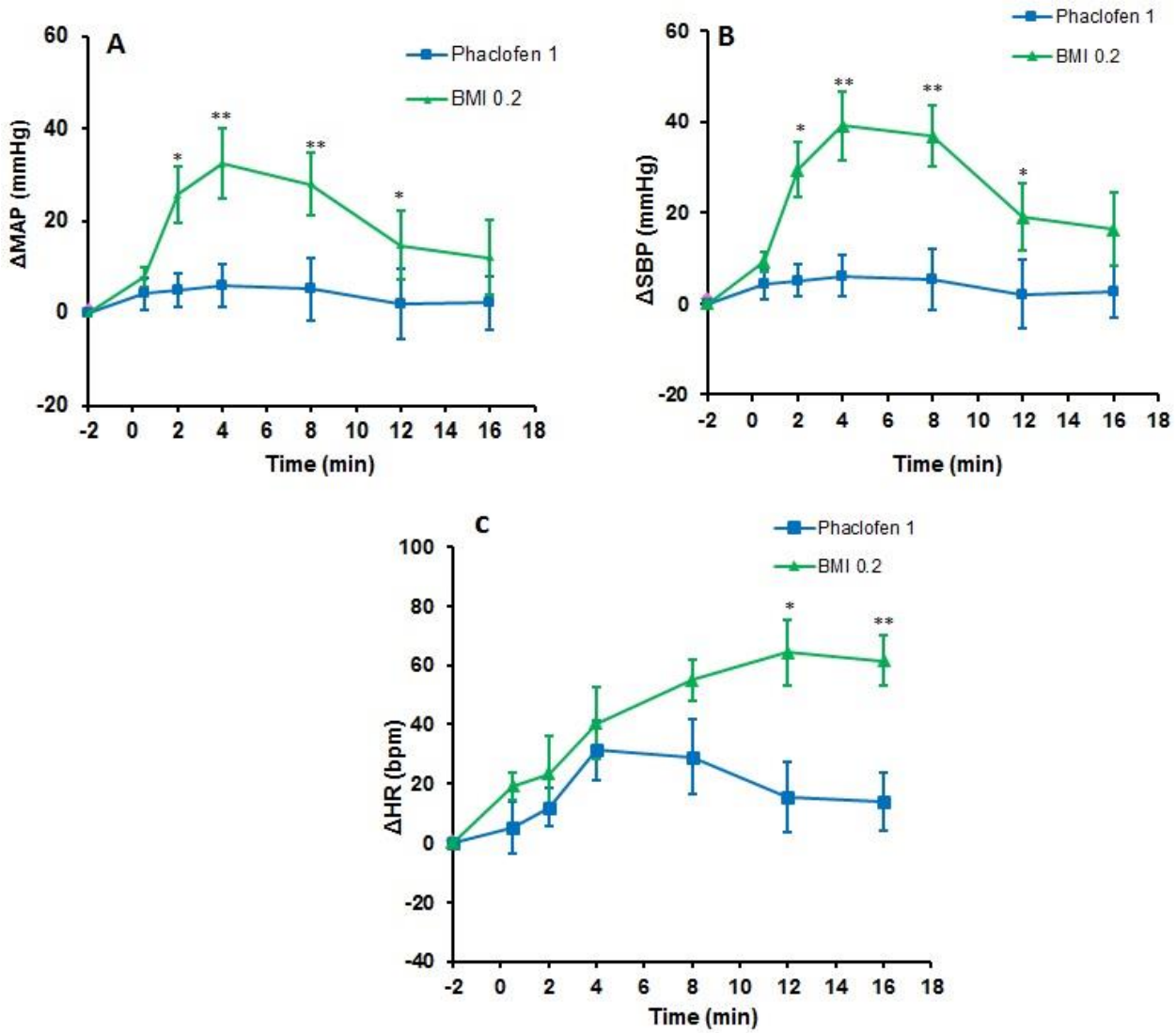

FIGURE 4. Comparing the cardiovascular effects of injection of BMI and phaclofen in the PPT
The time course of mean changes in MAP (A), SBP (B) and HR (C) are shown. (n=6)
Injection of 0.2 nmol BMI resulted in a significant increase in CV parameters, at different time points.
* $P<0.05$; ** $P<0.01$: Compared to phaclofen
MAP: Mean arterial blood pressure, SBP: systolic blood pressure, HR: heart rate

inhibiting adenylate cyclase (Miho 2018). As we have only studied the short-term effects of GABA, it appears that $GABA_B$ receptors were not activated in this study. However, the role of $GABA_B$ receptors has been identified more in stress, pain, and anxiety. Therefore, it seems that the role of this receptor in cardiovascular regulation is less than $GABA_A$. In line with our results, in another study, the role of $GABA_A$ and $GABA_B$ receptors in the NTS and its effects on the cardiovascular system were investigated. They showed that the injection of muscimol into the NTS increased MAP and decreased the effects of HR, while the injection of baclofen increased SBP without affecting HR. Based on this research, they showed that activation of $GABA_A$ receptors in the NTS reduces the effects of HR, while activation of $GABA_B$ receptors causes a decrease in pressor responses (Callera et al., 1999). Similar to our findings, in another study the cardiovascular role of GABAergic in Bed nucleus of the stria terminalis (BST) was investigated. Its results showed that blockade of the $GABA_A$ receptor increases SBP and HR, but phaclofen as a $GABA_B$ antagonist does not affect SBP and HR. As a result, the role of GABA in BST is mediated by the $GABA_A$ receptor and $GABA_B$ receptor does not play much role (Hatam and Ganjkhani 2012). Also, this study showed that the decrease in HR caused by GABA is done by inhibiting

sympathetic input to the heart, and GABA also reduces SBP by inhibiting the release of vasopressin (Hatam and Ganjkhani 2012). In another study, the role of GABA in the Ventral tegmental area (VTA) in the baroreflex pathway was evaluated. According to this study, about 20-30% of VTA neurons are GABAergic, which may play a role in the baroreflex system. They showed that the injection of BMI into the VTA caused a significant decrease in blood pressure. Which indicates the weakening of baroreflexes. Also, injection of baclofen caused a moderate weakening of baroreflex and phaclofen did not cause obvious effects. As a result, they suggested that $GABA_A$ receptors in the VTA cause a large decrease, and $GABA_B$ receptors in the VTA cause a moderate decrease in baroreceptor reflexes (Hatam et al., 2015). In another research conducted on the cardiovascular effects of GABA receptors in the VTA, it was found that the Muscimol in the VTA does not have a significant effect on MAP and HR, but the BMI caused a significant increase in MAP and HR, while the injection of baclofen and phaclofen in the VTA, had no effect on MAP and HR. So, this effect is exerted by $GABA_A$ receptors. In a study, the cardiovascular effects of two $GABA_B$ agonists and antagonists in the RVLM were investigated. Bilateral injection of $GABA_B$ agonists caused an increase in MAP and HR, these effects disappeared after baclofen injection into the RVLM. This study showed that there was an inhibitory mechanism in the RVLM on cardiovascular responses mediated by $GABA_B$ receptors (Avanzino et al., 1994).

Conclusion

This research offers novel insights into a comprehensive evaluation of $GABA_B$ receptors in PPT involved in cardiovascular regulation, highlighting the role of GABAergic neurons and interactions with brain cardiovascular areas. As the blockade $GABA_B$ receptors in the PPT by phaclofen injection, did not change the cardiovascular responses but increased by BMI, we proposed that GABA argic cardiovascular effects of the PPT are inhibitory and mainly are mediated by the $GABA_A$ receptor.

Acknowledgments

We would like to thank Mashhad University of Medical Science for their financial support.

Conflicts of interest

The authors have no conflicts of interest.

References

Alderson H L, Latimer M P, Winn P. A functional dissociation of the anterior and posterior pedunculopontine tegmental nucleus: excitotoxic lesions have differential effects on locomotion and the response to nicotine. Brain Structure and Function 2008; 213: 247-253. https://doi.org/10.1007/s00429-008-0174-4

Alves T B, Totola L T, Takakura A C, Colombari E, Moreira T S. GABA mechanisms of the nucleus of the solitary tract regulates the cardiovascular and sympathetic effects of moxonidine. Autonomic Neuroscience 2016; 194: 1-7. https://doi.org/10.1016/j.autneu.2015.11.001

Avanzino G L, Ruggeri P, Blanchi D, Cogo C E, Ermirio R, Weaver L C. GABAB receptor-mediated mechanisms in the RVLM studied by microinjections of two GABAB receptor antagonists. American Journal of Physiology-Heart and Circulatory Physiology 1994; 266: H1722-H1728. https://doi.org/10.1152/ajpheart.1994.266.5.H1722

Benarroch E E. Pedunculopontine nucleus: functional organization and clinical implications. Neurology 2013; 80: 1148-1155. https://doi.org/10.1212/WNL.0b013e3182886a76

Bormann J. The 'ABC' of GABA receptors. Trends in pharmacological sciences 2000; 21: 16-19. https://doi.org/10.1016/S0165-6147(99)01413-3

Callera J C, Bonagamba L G, Nosjean A, Laguzzi R, Machado B H. Activation of GABAA but not GABAB receptors in the NTSblocked bradycardia of chemoreflex in awake rats. American Journal of Physiology-Heart and Circulatory Physiology 1999; 276: H1902-H1910. https://doi.org/10.1152/ajpheart.1999.276.6.H1902

Dutar P, Nicoll R. A physiological role for GABAB receptors in the central nervous system. Nature 1988; 332: 156-158. https://doi.org/10.1038/332156a0

Faber J, Milanez M I, Simões C S, Campos R R. Frequency-coded patterns of sympathetic vasomotor activity are differentially evoked by the paraventricular nucleus of the hypothalamus in the Goldblatt hypertension model. Frontiers in Cellular Neuroscience 2023; 17: 1176634. https://doi.org/10.3389/fncel.2023.1176634

Ford B, Holmes C J, Mainville L, Jones B E. GABAergic neurons in the rat pontomesencephalic tegmentum: codistribution with cholinergic and other tegmental neurons projecting to the posterior lateral hypothalamus. Journal of Comparative Neurology 1995; 363: 177-196. https://doi.

org/10.1002/cne.903630203

Hatam M, Ganjkhani M. Effect of GABAA receptors in the rostral ventrolateral medulla on cardiovascular response to the activation of the bed nucleus of the stria terminalis in female ovariectomized rats. Iranian Journal of Medical Sciences 2012; 37: 242.

Hatam M, Rasoulpanah M, Nasimi A. GABA modulates baroreflex in the ventral tegmental area in rat. Synapse 2015; 69: 592-599. https://doi.org/10.1002/syn.21863

Li D-P, Pan H-L. Role of GABAB receptors in autonomic control of systemic blood pressure. Advances in Pharmacology 2010; 58: 257-286. https://doi.org/10.1016/S1054-3589(10)58011-6

Martinez-Gonzalez C, Bolam J P, Mena-Segovia J. Topographical organization of the pedunculopontine nucleus. Frontiers in neuroanatomy 2011; 5: 22. https://doi.org/10.3389/fnana.2011.00022

Martinez-Gonzalez C, Wang H L, Micklem B R, Bolam J P, Mena-Segovia J. Subpopulations of cholinergic, GABAergic and glutamatergic neurons in the pedunculopontine nucleus contain calcium-binding proteins and are heterogeneously distributed. European Journal of Neuroscience 2012; 35: 723-734. https://doi.org/10.1111/j.1460-9568.2012.08002.x

Mena-Segovia J, Micklem B, Nair-Roberts R, Ungless M, Bolam J. GABAergic neuron distribution in the pedunculopontine nucleus defines functional subterritories. Journal of Comparative Neurology 2009; 515: 397-408. https://doi.org/10.1002/cne.22065

Miho T. Diversity of structure and function of GABA [B] receptors: a complexity of GABA [B]-mediated signaling. Proceedings of the Japan Academy. Ser. B: Physical and Biological Sciences 2018; 94: 390-411. https://doi.org/10.2183/pjab.94.026

Nasimi A, Hatam M. GABA and glutamate receptors in the horizontal limb of diagonal band of Broca (hDB): effects on cardiovascular regulation. Experimental brain research 2005; 167: 268-275. https://doi.org/10.1007/s00221-005-0035-9

Rosborough K. Understanding the role of cholinergic tone in the pedunculopontine tegmental nucleus: The University of Western Ontario (Canada), 2014.

Shafei M N, Nasimi A, Alaei H, Pourshanazari A A, Hosseini M. Role of cuneiform nucleus in regulation of sympathetic vasomotor tone in rats. Pathophysiology 2012; 19: 151-155. https://doi.org/10.1016/j.pathophys.2011.11.001

Turossi Amorim E D, de Jager L, Martins A B, Rodrigues A T, Cruz Lucchetti B F, Ariza D, et al. Glutamate and GABA neurotransmission are increased in paraventricular nucleus of hypothalamus in rats induced to 6-OHDA parkinsonism: Involvement of nNOS. Acta Physiologica 2019; 226: e13264. https://doi.org/10.1111/apha.13264

Wang H L, Morales M. Pedunculopontine and laterodorsal tegmental nuclei contain distinct populations of cholinergic, glutamatergic and GABAergic neurons in the rat. European Journal of Neuroscience 2009; 29: 340-358. https://doi.org/10.1111/j.1460-9568.2008.06576.x

Winn P. Experimental studies of pedunculopontine functions: are they motor, sensory or integrative? Parkinsonism & related disorders 2008; 14: S194-S198. https://doi.org/10.1016/j.parkreldis.2008.04.030

Yasui Y, Cechetto D F, Saper C B. Evidence for a cholinergic projection from the pedunculopontine tegmental nucleus to the rostral ventrolateral medulla in the rat. Brain research 1990; 517: 19-24. https://doi.org/10.1016/0006-8993(90)91002-X