

## ROLE OF NORADRENERGIC SYSTEM IN THE MECHANISM OF ACTION OF ENDOGENOUS NEUROTOXIN 1,2,3,4-TETRAHYDROISOQUINOLINE: BIOCHEMICAL AND FUNCTIONAL STUDIES

*Jerzy Michaluk*<sup>1</sup>, *Anna Krygowska-Wajs*<sup>2</sup>, *Beata Karolewicz*<sup>1</sup>,  
*Lucyna Antkiewicz-Michaluk*<sup>1#</sup>

<sup>1</sup>Institute of Pharmacology, Polish Academy of Sciences, Smętna 12, PL 31-343 Kraków, Poland

<sup>2</sup>Clinic of Neurology, Jagiellonian University, Collegium Medicum, Botaniczna 3, PL 31-503 Kraków, Poland

*Role of noradrenergic system in the mechanism of action of endogenous neurotoxin 1,2,3,4-tetrahydroisoquinoline: biochemical and functional studies.* J. MICHALUK, A. KRYGOWSKA-WAJS, B. KAROLEWICZ, L. ANTKIEWICZ-MICHALUK. *Pol. J. Pharmacol.*, 2002, 54, 19–25.

It is well recognized that 1,2,3,4-tetrahydroisoquinoline (TIQ) is a substance capable of inducing in animals a syndrome, regarded as an animal model of Parkinson's disease. This study was designed to evaluate the effect of the endogenous neurotoxin TIQ on the brain noradrenaline (NA) metabolism in mice and on an arterial blood pressure in rats. It was shown for the first time that TIQ significantly increased NA metabolism, induced NA release and raised the level of its final metabolite, 3-methoxy-4-hydroxyphenylglycol (MHPG), in mouse brain. The comparative biochemical studies using specific agonist (clonidine) and antagonist (yohimbine) of  $\alpha_2$ -adrenergic receptors ligands have shown that observed biochemical effects were similar to those produced by  $\alpha_2$ -adrenergic antagonist, yohimbine. In functional studies, the systolic and diastolic blood pressure was measured using a non-invasive blood pressure transducer. Both acute and multiple treatment with TIQ produced a strong hypotensive effect, having decreased both systolic and diastolic blood pressure in rats. Development of tolerance to the hypotensive effect was observed after multiple treatment with TIQ. The data coming from these experimental studies apparently suggest an important role of the noradrenergic system in the mechanism of action of endogenous compounds from TIQ group. The results may also support the hypothesis assuming a causal relationship between noradrenergic denervation, activity of the nigrostriatal dopamine system, and some clinical manifestation of Parkinson's disease.

**Key words:** 1,2,3,4-tetrahydroisoquinoline, endogenous neurotoxin, noradrenaline metabolism, mouse brain, arterial blood pressure in rats

---

<sup>#</sup> *correspondence*; e-mail: antkiew@if-pan.krakow.pl