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

Jerzy Michaluk¹, Anna Krygowska-Wajs², Beata Karolewicz¹,
Lucyna Antkiewicz-Michaluk¹#

¹Institute of Pharmacology, Polish Academy of Sciences, Smetna 12, PL 31-343 Kraków,
²Clinic of Neurology, Jagiellonian University, Collegium Medicum, Botniczna 3, PL 31-303 Kraków, Poland

Role of noradrenergic system in the mechanism of action of endogenous
neurotoxin 1,2,3,4-tetrahydroisoquinoline: biochemical and functional stu-

It is well recognized that 1,2,3,4-tetrahydroisoquinoline (TIQ) is a sub-
stance 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) metabo-
lism 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 re-
lease and raised the level of its final metabolite, 3-methoxy-4-hydroxy-
phenylglycol (MHPG), in mouse brain. The comparative biochemical studies
using specific agonist (clonidine) and antagonist (yohimbine) of α₂-adrener-
ge receptors ligands have shown that observed biochemical effects were
similar to those produced by α₂-adrenergic antagonist, yohimbine. In func-
tional 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 sys-
tolic and diastolic blood pressure in rats. Development of tolerance to the hy-
potensive 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 Par-
kinson’s disease.

Key words: 1,2,3,4-tetrahydroisoquinoline, endogenous neurotoxin, nor-
adrenaline metabolism, mouse brain, arterial blood pressure in rats

# correspondence; e-mail: antkiew@if-pan.krakow.pl