

# Integrative Medicine – Acupuncture, Neurobiology and the Nitric Oxide Connection

By William R. Morris, OMD, Lac

## Nitric oxide (NO) Functions

Nitric oxide research seems to show that acupuncture modulates nitric oxide activity in the brainstem somatic sensory paths (nucleus gracilis), basal ganglia striatum, and the cerebral cortex, as well as the hippocampus. Nitric oxide is a messenger molecule with biological actions that range from signal transduction to cell killing. Nitric oxide accounts for tonic relaxation of all types of blood vessels and non-adrenergic and non-cholinergic relaxation of the gastrointestinal tract. Nitric oxide acts as a neurotransmitter in the central and peripheral nervous system, contributes to the antimicrobial activity of macrophages, decreases platelet aggregation, and is involved in hormone release.

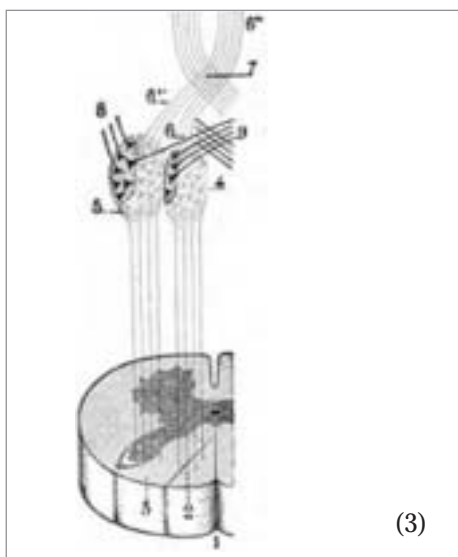
Current evidence indicates that, in the CNS, nitric oxide is produced enzymatically in postsynaptic structures in response to activation of excitatory amino acid receptors. It then diffuses out to act on neighboring cellular elements, probably presynaptic nerve endings and astrocyte processes. In several peripheral nerves, and quite possibly in parts of the CNS as well, nitric oxide might be formed presynaptically and thus act as a neurotransmitter(1).

Although the influence of NO on striatal neuronal activity remains to be thoroughly characterized, evidence has accumulated suggesting that NO signaling may mediate and/or regulate multiple aspects of striatal neurotransmission including the integration of convergent motor information within striatal networks. A major component of the cortical regulation of the nigrostriatal dopamine (DA) system is known to occur via activation of striatal efferent systems projecting to the substantia nigra through the intermediary role of striatal nitric oxide synthase (NOS). Striatal NO tone regulates the basal activity and responsiveness of DA neurons to cortical and striatal inputs. In addition striatal NO signaling may play an important role in the integration of information transmitted to basal ganglia

output centers via corticostriatal and striatal efferent pathways(2).

## Acupuncture modulates NO concentration

Increased concentrations of NO were found on the skin adjacent to meridians and acupoints relative to surrounding areas. The hypotensive and bradycardiac responses to EA ST36 are modified by influences of L-arginine-derived NO synthesis in the gracile nucleus. It appears that NO plays an important role in mediating the cardiovascular responses to electro-acupuncture ST36 through the gracile nucleus(3).



The work of Dr. Sheng-Xing Ma at the Harbor-UCLA Medical Center suggests that at least some acupuncture effects involve transmission of biological information by nitric oxide.(4) In addition, enhanced NO in the acupoints/meridians is generated from multiple resources including neuronal NOergic system, and NO might be associated with acupoint/meridian functions including low electric resistance. He recently reported that stimulation of hindlimb acupoints (LB 64, 65) resulted in increased synthesis of the signaling molecule nitric oxide at a specific location of the brain stem of rats.

Other studies demonstrate the activity of nitric oxide modulation through

acupuncture, needling Zusanli (ST 36) may modulate NOS activity in the hippocampus under diabetic conditions(5). In addition, Li et al investigated 42 people between the ages of age 55 and 70 were given the warm needling at Zusanli (ST 36), the results showed that IL-2 and NO contents increased significantly after the warm needling ( $P < 0.01$ )(6).

## Hippocampal Function Related to Nitric Oxide Synthase (NOS)

The hippocampus is a central processing area at which meet the sensory and associative cortex, Learning and memory are essential to an animal's ability to survive and thrive. In many species, including humans, a cortical structure known as the hippocampus is critical for the formation of long-term memory. Studies of long-term potentiation (LTP) in the hippocampus help to show how memories may be encoded and stored at the synaptic level. suggested that acupuncture treatment may modulate NOS activity in the hippocampus under diabetic conditions(5, 7). In addition, Kang et al showed that acupuncture modulates the expressions of NOS and c-Fos in the gerbil hippocampus post transient global ischemia(8).

The hippocampus matures postnatally, which means that the functions it serves are not available for some time after birth. According to Nadel, the role of the hippocampus is the core of a "spatial/cognitive mapping system." and involves possible relations between space and language(9). In infant rats, stressful experiences can impact postnatal hippocampal development as well as the later development of the hippocampus inrelation to unusual "fears and phobias". It is generally assumed that in the adult organism the hippocampus interacts with the neocortex during memory "consolidation" so as to enable information to be permanently stored in cortical sites(9-12).

Since the hippocampus has connections with the hypothalamus and other structures dealing with somatovisceral, emotional, and endocrine functions

where different parts of the brain combine to form a cognitive map, we can then understand the possibility of actual changes in all these areas, including the consolidation of pain memories.

---

## References

1. **Garthwaite, Department of Physiology UoL, UK.** Glutamate, nitric oxide and cell-cell signalling in the nervous system. *Trends Neurosci.* 1991;14(2):60-7.
2. **West AR, Grace AA.** Striatal Nitric Oxide Signaling Regulates the Neuronal Activity of Midbrain Dopamine Neurons In Vivo. *J Neurophysiol.* 2000;83(4):1796-1808.
3. **Chen S, Ma S-X.** Nitric Oxide in the Gracile Nucleus Mediates Depressor Response to Acupuncture (ST36). *J Neurophysiol.* 2003;90(2):780-785.
4. **Ma SX.** Enhanced nitric oxide concentrations and expression of nitric oxide synthase in acupuncture points/meridians. *J. Alt. Complement. Med.* 2003;9:207-15.
5. **Jang MH SM, Lim BV, Kim HB, Kim YP, Kim EH, Kim H, Shin MS, Kim SS, Kim CJ., Department of Physiology CoM, Kyung Hee University, Dongdaemoon-gu, Seoul, Korea.** Acupuncture increases nitric oxide synthase expression in hippocampus of streptozotocin-induced diabetic rats. *Am J Chin Med.* 2003;31(2):305-13.
6. **Li SJ, Tang J, Han JS.** [Tolerance to 5-HT and its implication in electro-acupuncture tolerance and morphine tolerance]. *Zhongguo Yao Li Xue Bao.* 1982;3(3):159-63.
7. **Mi-Hyeon Jang M-CS, Baek-Vin Lim, Hyun-Bae Kim, Young-Pyo Kim, Ee-Hwa Kim, Hong Kim, Mal-Soon Shin, Sung-Soo Kim, Chang-Ju Kim.** Acupuncture increases nitric oxide synthase expression in hippocampus of streptozotocin-induced diabetic rats. *American Journal of Chinese Medicine.* 2002.
8. **Kang J-E, Department of Acupuncture and Meridianology GSoE-WMS, Kyung Hee University, Yongin, Korea , Lee H-J, et al.** Acupuncture Modulates Expressions of Nitric Oxide Synthase and c-Fos in Hippocampus After Transient Global Ischemia in Gerbils. *The American Journal of Chinese Medicine.* 2003;Vol. 31(No. 4):581-590.
9. **Nadel L.** The psychobiology of spatial behavior: The hippocampal formation and spatial mapping. In: E. Alleva H-PL, L. Nadel, A. Fasolo and L. Ricceri, ed. *Behavioural brain research in naturalistic and semi-naturalistic settings: Possibilities and Perspectives.*: Kluwer Press; 1995.
10. **Nadel LaJ, W.J.** The role of the hippocampus in PTSD, panic and phobia. In: Kato N, ed. *Hippocampus: Functions and Clinical Relevance.* Amsterdam: Elsevier Science B.V.
11. **Nadel L.** Multiple memory systems: What and Why. In: Tulving DSaE, ed. *Memory Systems.* Cambridge, MA: MIT Press; 1994:pp. 39-63.
12. **O'Keefe JaN, L.** *The hippocampus as a cognitive map* Oxford: The Clarendon Press.; 1978.