

# **Tenth London International Cough Symposium 2018**

## **Course Programme**

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## **Acetylcholine downregulates the cough reflex in the caudal nucleus tractus solitarii of the rabbit**

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Cough is one of the most important defensive reflex brought into action by actually or potentially damaging events applied to the airways. Peripheral and central mechanisms underlying nociception and cough share similar features and neuroactive agents involved in the central control of pain sensation and associated reflex responses may play a role also in the modulation of the cough reflex. Cholinergic transmission affects the perception of pain via both nicotinic and muscarinic receptors.

The caudal nucleus tractus solitarii (cNTS) has been shown to be a strategic site for the cough reflex regulation by both excitatory and inhibitory neurotransmitters. Acetylcholine (ACh) is widely distributed in the region of the NTS. However, no information is available on the role played by ACh in the modulation of the cough reflex within this medullary region. We addressed this issue making use of bilateral microinjections (30-50 nl) of 10 mM ACh combined with 5 mM physostigmine as well as of 10 mM mecamlamine or 10 mM scopolamine into the caudal NTS of pentobarbital sodium-anesthetized, spontaneously breathing rabbits. Microinjections of ACh/physostigmine elicited transient increases in respiratory frequency accompanied by decreases or even the complete suppression of expiratory activity. More interestingly, they caused depressant effects on the cough reflex induced by mechanical and chemical (citric acid inhalation) stimulation of the tracheobronchial tree. Downregulation of cough reflex responses was prevented by scopolamine, but not by mecamlamine. ACh-induced depressant effects were mimicked by microinjections of 1 mM muscarine, but not by 1 mM nicotine, thus confirming the involvement of muscarinic receptors in the downregulation of cough responses.

The results show for the first time that ACh exerts an inhibitory modulation of the cough reflex through muscarinic receptors within the caudal NTS. They also may provide hints for novel antitussive approaches.

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