DISSERTATION ABSTRACT

Turesson, Jenny (2006). **Oxygen chemoreflexes in fish –With emphasis on glutamatergic control mechanisms in the medulla.** Department of Zoology, Zoophysiology, Göteborg University, Box 463, SE-405 30 Göteborg, Sweden

The main objective of this thesis was to establish central control mechanisms important for eliciting oxygen chemoreflexes in fish. Previous cardiorespiratory reflex studies in fish have only focused on describing mechanisms in sensory and motor pathways activated during oxygen chemoreception. In the present work however, emphasis was placed on gaining information on the central control of these systems via the excitatory amino acid glutamate.

Oxygen chemoreflexes were elicited by hypoxia and/or sodium cyanide (NaCN) in three different species of fish (shorthorn sculpin, *Myoxocephalus scorpius*; channel catfish, *Ictalurus punctatus*; zebrafish, *Danio rerio*). Pharmacological tools were applied either systemically or centrally to manipulate putative involvement of the central ionotropic receptors (N-Methyl-D-Aspartate (NMDA), α-Amino-3-OH-5-Methyl-4-isoxazole-Propionic-Acid (AMPA), kainate). The nerve tracer Fast blue was injected into the *ganglion nodosum* to reveal the location of the first relay station (vagal sensory column) of vagal oxygen chemoreceptor signals in the shorthorn sculpin. Antibodies directed toward glutamate and subunits of NMDA and AMPA ion channels were employed to establish their presence in the vagal sensory area of both channel catfish and the shorthorn sculpin. Zebrafish larvae were used to study the ontogeny of the oxygen chemoreflex and its glutamatergic component, together with Western blot protocols to establish the ontogenetic appearance of NMDA and AMPA receptors during zebrafish development.

The results herein together with information from previous teleost literature, describe a very complex picture of teleost oxygen chemoreflex control. It appears that the different modalities of the cardiorespiratory reflexes such as heart rate, blood pressure, ventilation frequency and amplitude arise from input of different groups of oxygen receptors. Furthermore, glutamate microinjected centrally into different portions of the vagal sensory column showed that each reflex modality seemed to have a designated area for the integration of the oxygen receptor signals. In addition, hypoxic stimuli before and after application of pharmacological agents either into the blood or microinjected into the medulla, revealed that each respiratory reflex modality was functioning through a specific glutamate receptor type. Consequently, the increase in ventilatory frequency was dependent on functional NMDA receptors, while the increase in amplitude appeared to be kainate receptor dependent. AMPA receptors on the other hand are involved in both ventilatory reflex components. Westen blot protocols displayed a maturation of the NMDA receptor channel during development, which confirm the finding of a late (13 days post fertilization) NMDA dependent component of the oxygen receptor activated increase in ventilatory frequency in zebrafish larvae.

Taken together, this thesis establishes glutamate and its ionotropic receptors in the central integration of oxygen receptor signals in fish. It adds to the complex picture of oxygen chemoreflex activation in fish that involves several oxygen receptor populations, by identifying different central projection areas and specific glutamate receptor types for each reflex modality.

Keywords: Chemoreceptors, hypoxia, cardiorespiratory, NTS, nGV, vagus, glutamate, NMDA receptors, AMPA receptors, kainate receptors, ontogeny, teleost.

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