DISSERTATION ABSTRACT

Holmberg, Anna (2006). **Ontogeny of gut motility and the enteric nervous system in *Danio rerio* and *Xenopus laevis*.** Department of Zoophysiology, Göteborg University, Box 463, 405 30 Göteborg, Sweden.

Using a combination of immunohistochemistry and video microscopy, the development of gut motility and its control were studied in zebrafish, *Danio rerio,* and African clawed frog, *Xenopus laevis*. Of special interest was to elucidate whether the control system of the gut is first activated by the presence of food or is functioning before first feeding. The appearance of gut neurons (marked by antibodies against acetylated tubulin, human neuronal protein C/D (Hu), and HNK-1), the neurotransmitters PACAP and NKA/SP, and the enzyme NOS were mapped in both zebrafish and *Xenopus*. In agreement with earlier studies, enteric neurons were detected in the majority of the intestine well before the onset of exogenous feeding in both zebrafish and *Xenopus*. However, the present study showed that (Hu positive) neurons are not established in the most anterior part of the intestinal bulb until around 13 dpf in zebrafish. PACAP, NKA and NOS were found in gut neurons prior to the stage of first feeding in both zebrafish and *Xenopus*. However, even if structural neurons are present they might not release their neurotransmitters, receptors may not be expressed or fully functional or contractile mechanisms of the smooth muscle might not respond until after onset of exogenous feeding. Therefore, the ontogeny of gut motility and its control was studied in live anaesthetised specimen of zebrafish by using video microscopy in combination with image analysis to monitor the frequency of gut contractions. From the first stage investigated (3 dpf, days post fertilisation) erratic local spontaneous contractions were distinguished in the intestine. In older embryos and larvae (4-7 dpf) coordinated spontaneous anterograde, retrograde, and short rectal contractions waves were present. The frequency of anterograde contraction waves was controlled by endogenous acetylcholine and nitric oxide (NO) from 4 dpf i.e. before the first feeding, while retrograde contraction waves were affected by endogenous NO one day later. The parallel development of neurons and a regular controlled motility pattern may indicate that the enteric nervous system can control/modulate the intestinal motility before the onset of feeding, at least in the middle intestine. The involvement of neurons was shown by application of tetrodotoxin (TTX), which reduced the length and frequency of anterograde contraction waves at 7 dpf, but did not affect anterograde or retrograde activity at 4 dpf. Taken together, these findings show the presence of organized gut motility before onset of exogenous feeding, but that this activity is not under neuronal, at least not TTX-sensitive, control until 7 dpf.

Keyword: neurotransmitters, development, intestine, zebrafish, African clawed frog, teleost, amphibian, NKA, PACAP, NOS, acetylcholine

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