POSTNATAL DEVELOPMENTAL CHANGES IN ENTERIC DOPAMINERGIC SYSTEM

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The postnatal period is a key period of life, characterized by the maturation of various organs and in particular of the gut. Currently, we have a poor understanding of the development of neurological and endocrine factors that control intestinal motility. Such knowledge can provide indications about the potency, efficacy, or therapeutic range of a drug in premature infants. Dopaminegic antagonists are often used as prokinetic drugs to treat impaired GI propulsion, although the role of the enteric dopaminergic system in the control of intestinal motility in neonatal *vs* adult has not been adequately addressed. In this view the aim of this study, was to examine, the functionality of the dopaminergic systems in the regulation of duodenal contractility in neonatal *vs* adult, using a murine animal model. Transcripts for all dopaminergic receptors (D1-like family, D1 and D5 receptors, and D2-like family, D2, D3, and D4 receptors) can be detected in mouse gut at each age. Mechanical responses to dopamine (DA) were examined *in vitro* in duodenal longitudinal muscle from postnatal and adult mice as changes in isometric tension. In neonatal duodenum, DA evoked a TTX-insensitive muscular contraction, reduced by SCH 23390, D1-like receptor antagonist, but not by domperidone, D2-like receptor antagonist, and mimicked by a D1 receptor agonist. The contractile response to DA decreased in intensity with age and in adults, in its place, a distinct TTX-insensitive muscular relaxation was detected. Inhibitory response to DA was mimicked by D1 or D2 receptor agonists and reduced by domperidone, and, to a lesser extent, by SCH 23390. In neonatal mice the excitatory responses mediated by D1 receptor activation were antagonized by U-73122, phospholipase C (PLC) inhibitor, whilst in adults the inhibitory effects were blocked by DDA, adenylyl cyclase inhibitor. In mouse gut, dopaminergic transmission undergoes to postnatal change in the pattern of receptor functionality. In postnatal period, DA leads to muscular contraction exclusively via D1-like receptors, likely D5 receptors, linked to activation of PLC. In adults, DA is able to relax duodenum recruiting D2 receptors and shifting the effects mediated by D1-like receptors, likely D1 receptors, activating cAMP pathway.