

## ○1E1-5 Different functional roles of M2 and M3 receptors in gastric contraction induced by carbachol and nerve stimulation

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Roles of muscarinic receptors in regulation of mouse gastric contractility were examined using mice genetically lacking M2 and/or M3 receptors. Carbachol (CCh) produced contraction of antral and fundus strips from M2KO and M3KO mice but not in those from M2/M3KO mice. A comparison of dose-response curves with those of wild type (WT) mice showed a decrease in pEC50 (M2KO) or amplitude of contraction (M3KO). The tonic phase of CCh-induced contraction was decreased only in M3KO mice. Electrical field stimulation (EFS) elicited frequency-dependent contraction in physostigmine and L-NAME-treated gastric strips of M2KO and M3KO mice, but the cholinergic contractions significantly decreased. In the M2/M3KO mice, cholinergic contractions by EFS were abolished but non-cholinergic contractions were more marked than those of WT. Gastric emptying in WT mice and that in M2/M3KO mice was comparable. The results indicate that M2 and M3 receptors but not other subtypes mediate cholinergic contraction in mouse stomach. But their contribution to dose-response relationship is different. Although cholinergic contractions were impaired in the KO mice, gastric emptying was normal, probably due to compensation of non-cholinergic pathway.