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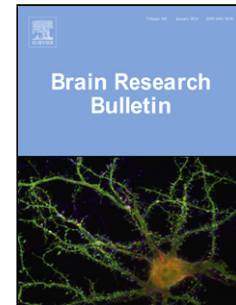
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<AT>Enteric glia regulate gut motility in health and disease

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<ABS-HEAD>Highlights ► The enteric nervous system (ENS) is the largest assembly of neurons and glia outside the central nervous system ► The ENS resides within the wall of the digestive tract and regulates local gut reflexes involved in gastrointestinal motility, blood flow and fluid transport ► Enteric glial cells are necessary and sufficient to modulate neuronal reflex circuits controlling gut motility ► Enteric glia respond to various neurotransmitters via increase in intracellular calcium and release of neuroactive substances, such as ATP through Cx43 hemichannels or Ca<sup>2+</sup>-dependent exocytosis ► Enteric glial cells are actively involved in gut motility disorders and regulation of inflammation

## <ABS-HEAD>Abstract

<ABS-P>The enteric nervous system, often referred to as the second brain, is the largest assembly of neurons and glia outside the central nervous system. The enteric nervous system resides within the wall of the digestive tract and regulates local gut reflexes involved in gastrointestinal motility, blood flow and fluid transport; all these functions can be accomplished in the absence of the extrinsic innervation from the central nervous system. It is neurons and their circuitry within the enteric nervous system that govern the gut reflexes. However, it is becoming clear that enteric glial cells are also actively involved in this process through the bidirectional signaling with neurons and other cells in the gut wall. We synthesize the recently discovered modulatory roles of enteric gliotransmission in gut motility and provide our perspective for future lines of research.

<KWD>Keywords: bidirectional purinergic signaling; enteric glial cells; enteric neurons;

enteric nervous system; gliotransmission

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