How halting controls walking: Using connectome informed models and experiments to uncover fundamental neural circuit mechanisms for locomotor control in a Drosophila model system.

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Walking is a complex motor program involving coordinated activity across the brain and the spinal cord. Halting at the correct time in an appropriate manner is a critical but often overlooked component of walking control. It is unclear how halting is implemented by overriding the distributed walking state neural activity. We elucidate two fundamental mechanisms by which Drosophila implement halting. The first mechanism relies on GABAergic neurons ("walkOFF" neurons) that inhibit specific descending walking commands in the brain, while the second mechanism relies on excitatory cholinergic neurons in the nerve cord ("break" neurons) that lead to an active arrest of stepping movements. Using connectome informed models and functional studies, we show that two types of "walkOFF" neurons inhibit distinct populations of walking promoting neurons leading to different halting phenotypes. The "break" neurons on the other hand, override all walking commands by actively increasing the resistance reflex at the leg joints leading to an arrest of leg movements in the stance phase. While the "walkOFF" neurons are required for halting during tasks like feeding and egg-laying, the "break" neurons are essential for spontaneous stopping that shapes the episodic nature of locomotor bouts. Thus, this work uncovers the neural circuits underlying two distinct mechanisms to bring about context dependent halting of the walking state.