A convergent and essential interneuron pathway for Mauthner-cell-mediated escapes

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The Mauthner cell (M-cell) is a command-like neuron in teleost fish whose firing in response to aversive stimuli is correlated with short-latency escapes [1-3]. M-cells have been proposed as evolutionary ancestors of startle response neurons of the mammalian reticular formation [4], and studies of this circuit have uncovered important principles in neurobiology that generalize to more complex vertebrate models [3]. The main excitatory input was thought to originate from multisensory afferents synapsing directly onto the M-cell dendrites [3]. Here, we describe an additional, convergent pathway that is essential for the M-cell-mediated startle behavior in larval zebrafish. It is composed of excitatory interneurons called spiral fiber neurons, which project to the M-cell axon hillock. By inăvivo calcium imaging, we found that spiral fiber neurons are active in response to aversive stimuli capable of eliciting escapes. Like M-cell ablations, bilateral ablations of spiral fiber neurons largely eliminate short-latency escapes. Unilateral spiral fiber neuron ablations shift the directionality of escapes and indicate that spiral fiber neurons excite the M-cell in a lateralized manner. Their optogenetic activation increases the probability of short-latency escapes, supporting the notion that spiral fiber neurons help activate M-cell-mediated startle behavior. These results reveal that spiral fiber neurons are essential for the function of the M-cell in response to sensory cues and suggest that convergent excitatory inputs that differ in their input location and timing ensure reliable activation of the M-cell, a feedforward excitatory motif that may extend to other neural circuits.
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