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Impact of insulin signaling and proteasomal activity on physiological output of a neuronal circuit in aging *D. melanogaster*

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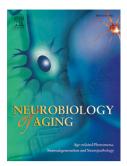
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ACCEPTED MANUSCRIPT

1 2	Impact of insulin signaling and proteasomal activity on physiological output of a neuronal circuit in aging <i>D. melanogaster</i>
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17	Abstract
18 19 20 21 22	The insulin family of growth factors plays an important role in development and function of the nervous system. Reduced insulin and insulin-growth-factor signalling (IIS), however, can improve symptoms of neurodegenerative diseases in laboratory model organisms and protect against age-associated decline in neuronal function. Recently, we showed that chronic, moderately lowered IIS rescues age-related
23 24 25	decline in neurotransmission through the <i>Drosophila</i> Giant Fiber escape response circuit (Augustin et al., 2017). Here, we expand our initial findings by demonstrating that reduced functional output in the GFS of aging flies can be prevented by
26 27 28 29	increasing proteasomal activity within the circuit. Manipulations of IIS in neurons can also affect longevity, underscoring the relevance of the nervous system for aging.
30	
31 32	1. Introduction
33	Aging neural circuits undergo morphological and functional changes that underlie
34	different types of behavioral impairment (Hof and Morrison, 2004). In humans,
35	circuit-level changes during normal, non-pathological aging affect gustatory function

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