

朱寰 孙梦实 李小龙 2022 2 24

A brief Introduction of Locomotion









What is **Locomotion**?

- Any of a variety of methods that animals use to move from one place to another.
- Including self-propelled locomotion, e.g., running, swimming, jumping, and passive locomotion, e.g., sailing (some jelly fish), rolling (some beetles and spiders)
- There are some reasons for animal to move, such as to find food, a mate, a suitable environment, or to evade predators.





Topic

General Overview & The locomotion circuits The locomotion inducers The locomotion neurotransmitters

General Overview & The Locomotion Circuits

Parameters

A **Female** *Drosophila*'s:

- Maximum walking speed is 4.2cm/s
- Continuous straight walking speed is about 1.5cm/s
- Duration of single step ranges from 60ms to 150ms in continuous straight walks
- Step rate is from 6.7 to 16.5 step/s in continuous straight walks

(Strauss R, Heisenberg M, 1990)





Alternating tripod gait of walking desert ants.



Two examples of leg coordination during straight walk obtained from the same individual. (Strauss R, Heisenberg M, 1990)

Mushroom body for locomotion



Head of (B) a CS male and (D) a CS male with MB ablated by HU (hydroxyurea, 硫酸羟脲)





Single flies with **clipped wings** were confined to an elevated **circular** disk (8.5 cm in diameter) surrounded by a water-filled moat between two opposing and inaccessible landmarks



MB Ablation by **HU**



Brain structure volume from brain of HU ablated fly and control.

(de Belle JS, Heisenberg M. 1994)



Head of (A) a *Berlin* male and (C) a *Berlin* male with MB ablated by HU (hydroxyurea, 硫酸羟脲), (B)(D) is same as (A)(C) but is from CS.





Anatomy and **Orientation** are Not Influenced by HU ablation



External anatomy was not influenced by genotype or HU treatment.

All groups of flies demonstrated comparable patterns of landmark orientation



...But Activity is Damaged



Mean percent of time flies were actively walking during 15 minutes in Buridan's paradigm.







Larva Circuit in locomotion



Refinery of backward crawling neuron



After a screening of 75 sparse expressing *Gal4* lines, TrpA1 activation R53F07 induces backward crawling.

> (Clark MQ, McCumsey SJ, Lopez-Darwin S, Heckscher ES, Doe CQ, 2016)



3 lines that induce backward crawling once activated are identified by cross section.



Stochastic Refinery of MDN by *heatshock*

A Split2-gal4, hs-FLP, UAS-FRT-stop-FRT-Chrimson:GFP heat shock larvae to induce stochastic Chrimson expression within Split2 pattern Behavior screen larvae for light-induced backward locomotion Stain backward crawling larvae to identify Chrimson+ neurons







Annotation of MDN by TEM Reconstruction and find its **Descending Neurons**







MDN induces backward crawling via **Descending Neurons**













Central Complex in locomotion

Behavior video data Collection, Tracking and Quantification of Behavior



A frame of collected video. Each video consisted of ~30,000 1024x1024 pixel frames of ~10 male and ~10 female flies.



An example of automatic behavior classification results. Color indicates that the classifier predicted that the behavior was occurring.

Behavioral Effects of neural activation and Anatomical Expression of Gal4 lines



Table of behavioral effects of neural activation for all 2,205 GAL4 lines assayed.



Central Complex activation is walk-increasing



Cross-section of the walk-increasing regions all points to ring neurons.





...Some other behavior





Ventral Nerve Cord in locomotion







The high-throughput serial-section transmission electron microscopy (TEM) pipeline built around GridTape.

Reconstruction of VNC and **Classification** of neurons



Reconstruction of motor neuron(A) and sensory neurons(B).



Reconstruction of all front leg motor neurons.

Connection between **bCS** and **MN bundles**, fast tibia flexor MN is a major target





The Locomotion Inducers

Metabolism influences locomotor behaviors:

temperature

disease model





short-term various stimuli, SVS

Gut microbial factor

LETTER

A gut microbial factor modulates locomotor behaviour in *Drosophila*

Catherine E. Schretter¹*, Jost Vielmetter², Imre Bartos³, Zsuzsa Marka³, Szabolcs Marka³, Sulabha Argade⁴ & Sarkis K. Mazmanian¹*

https://doi.org/10.1038/s41586-018-0634-9

2018





CFS: cell-free supernatant (CFS) collected from bacterial cultures HK: heat-killed bacteria





a







Xylose isomerase

(Xi)



Proceedings of the National Academy of Sciences of the United States of America

Octopamine mediates starvation-induced hyperactivity in adult *Drosophila*

Zhe Yang (杨哲)^{a,1}, Yue Yu (于悦)^{a,1}, Vivian Zhang (张维嘉)^{b,1}, Yinjun Tian (田引军)^a, Wei Qi (祁伟)^{a,c}, and Liming Wang (王立铭)^{a,2}

^aLife Sciences Institute, Zhejiang University, Hangzhou, Zhejiang 310058, China; ^bDepartment of Molecular and Cell Biology, University of California, Berkeley, CA 94720-3200; and ^cCollege of Life Sciences, Sichuan University, Chengdu, Sichuan 610064, China

Edited* by David J. Anderson, California Institute of Technology, Pasadena, CA, and approved March 10, 2015 (received for review September 16, 2014)



Regulation of starvation-induced hyperactivity by insulin and glucagon signaling in adult *Drosophila*

Yue Yu^{1,2+}, Rui Huang^{1,2++}, Jie Ye^{1,2}, Vivian Zhang³, Chao Wu^{1,2}, Guo Cheng^{1,2}, Junling Jia^{1,2}, Liming Wang^{1,2*}

Starvation induces hyperactivity of adult flies





Food Cues Suppress Starvation-Induced Hyperactivity.

Neuronal AKHR is required for starvation-induced hyperactivity but not food consumption.



d





AKHR+ neurons are required for starvation-induced hyperactivity



silencing of AKHR+neurons

С





facilitating the activation of of AKHR+neurons





High-fat diet enhances starvation-induced hyperactivity via sensitizing hungersensing neurons in Drosophila

Yinjun Tian⁴, Xuan Dong⁴, Liming Wang⁴*

HFD promotes starvation-induced hyperactivity in adult Drosophila.



Rui Huang^{1,2†}*, Tingting Song^{2†}, Haifeng Su^{3†}, Zeliang Lai^{1,2}, Wusa Qin²,


AKHR protein levels were upregulated by HFD feeding.



	ns		
Gene	ND	HFD	
AKHR	30.924 (±5.02)	40.096 (±2.351)	
InR	2.329 (±0.363)	2.294 (±0.235)	





AKHR⁺neurons are more sensitive to AKH upon HFD feeding.

AKHR accumulation is induced by the suppression of <u>autophagy</u>

(lysosome-dependent protein degradation pathw HFD suppressed autophagy via activating AMPK-TOR signaling

How feeding exert effect on the AKHR+ neurons?





working model:





nature > communications biology > articles > article

Article Open Access Published: 07 June 2021

Metabolic control of daily locomotor activity mediated by tachykinin in Drosophila

Sang Hyuk Lee, Eunjoo Cho, Sung-Eun Yoon, Youngjoon Kim & Eun Young Kim 🗠

Communications Biology 4, Article number: 693 (2021) Cite this article

Journal's Impact IF 2021-2022

5.489



HSD extended morning activity but not evening activity.





ISD, high sucrose die 30% sucrose

High-temperature augmented this effect.

Extended M activity after the startle response was more prominent in the 16L:8D













DTk levels were increased in DTk neurons in flies fed a HSD.



Neuropeptide DTk and the DTk receptor TkR86C were required for M activity extension in HSD.



DTk neurons and DN1_Ps were anatomically and functionally connected.



Subsets of DN1_ps were TkR86C-positive and were required for M activity extension in HSD.

29°C, ZT2



TkR86C²⁰²⁰³⁶ > UAS-mCD8::GFP







d TkR86C²⁰²⁰³⁶ > UAS-mcd8::GFP R18H11-LexA > LexAop-CD2-RFP





temperature

RESEARCH ARTICLE Drosophila

Daniela Ostrowski^{¤a}, Autoosa Salari^{¤b}, Melissa Zars, Troy Zars*

Division of Biological Sciences, University of Missouri, Columbia, Missouri, United States of America

A biphasic locomotor response to acute unsignaled high temperature exposure in



Increase then depression of locomotor activity after high temperature experience.



Depressed locomotor activity is not due to fatigue and is a general phenomenon.



The role of octopamine / Tyramine and serotonin in changes of locomotor activity following high temperature exposure.

Journal of **Experimental Biology**

Andrea Soto-Padilla, Rick Ruijsink, Ody C. M. Sibon, Hedderik van Rijn, Jean-Christophe Billeter 🔤 💿

2021-2022

RESEARCH ARTICLE | 22 MAY 2018

Thermosensory perception regulates speed of movement in response to temperature changes in Drosophila

melanogaster **FREE**

Α

Drosophila melanogaster increases speed at increasing temperature following a model based on enzyme-catalyzed temperature performance.

Intact central thermal sensing is necessary for flies to increase speed according to temperature changes.

Gr28b(D) gene, encoding a peripheral thermosensor

Disease model

STRESS 2021, VOL. 24, NO. 1, 96–106 https://doi.org/10.1080/10253890.2020.1759547

ORIGINAL RESEARCH REPORT

Stress-mediated hyperactivity and anhedonia resistant to diazepam and fluoxetine in *drosophila*

Ana Belén Ramos-Hryb^{a,b}* (), Mauro Federico Ramirez^a, Cilene Lino-de-Oliveira^{b,c} and Mario Rafael Pagani^a

^aInstituto de Fisiología y Biofísica (IFIBIO) Bernardo Houssay, Grupo de Neurociencia de Sistemas, Universidad de Buenos Aires, CONICET, Buenos Aires, Argentina; ^bPostgraduation Program in Pharmacology, CCB, Federal University of Santa Catarina, Florianópolis, Brazil; ^cDepartment of Physiological Sciences, CCB, Federal University of Santa Catarina, Florianópolis, Brazil

Stress

The International Journal on the Biology of Stress

Check for updates

Journal's Impact IF 2021-2022 3.493 ~ 12.6%

provoke stress-induced phenotypes in Drosophila

short-term variable stress

SVS protocol induces hyperlocomotion and centrophilia in adult flies.

Metabolism influences locomotor behaviors:

temperature

disease model

short-term various stimuli, SVS

The Locomotion Transmitters

The locomotion neurotransmitters of Drosophila melanogaster 李小龙 2022-2-24

Neurotransmitter

• What is transmitter?

神经递质 (neurotransmitter) 是神经元之间或神经元与效应器细胞之间传递信 息的化学物质。

Neurotransmitter

Classification: 胆碱类、单胺类、氨基酸类和神经肽类等。

Development, growth, feeding, metabolism, reproduction, homeostasis, and longevity, as well as Function neuromodulation in learning and memory, olfaction and locomotor control.

The locomotion neurotransmitters of Drosophila melanogaster

The locomotion neurotransmitters of Drosophila melanogaster

How many neurotransmitters are there in Drosophila?

Table 1

Neuropeptides and peptide hormones identified in Drosophila melanogaster.

Neuropeptide name ^a	Acronym	
Adipokinetic hormone	АКН	
Aupokinetie normone	ANT	
Allatostatin A (AstA)	AstA-1	
	AstA-2	
	AstA-3	Drosulfakinins
	AstA-4	
Allatostatin B (AstB; MIP)	MIP-1	Dromussumpressin
	MIP-2	Dromyosuppressin
	MIP-3	Ecdysis-triggering hormon
	MIP-4	Eclosion hormone
	MIP-5	Hugin-pyrokinin
Allatostatin C (AstC)	AstC	
Bursicon (Burs α)	BURS	Ion transport peptide
Partner of bursicon (Burs β)	PBURS	
CAPA-PVK/PK	CAPA-PVK-1	Leucokinin
	CAPA-PVK-2	
	CAPA-PK	Neuropeptide F
	СРРВ	Neuropeptide F (short NPF
ССАР	CCAP	
CCHamide	CCH1	
	CCH2	
Corazonin	CRZ	NPLP1
Diuretic hormone 44	DH44	
Diuretic hormone 31	DH31	
dFMRFamides	dFMRFa-1	NPLP2
	dFMRFa-2	NPLP3
	dFMRFa-3	
	dFMRFa-4	NPLP4
	dFMRFa-5	Pigment-dispersing factor
	dFMRFa-6	Proctolin Prothoraciostropic hormon
	dFMRFa-7	Sex peptide ^e
	dFMRFa-8	SIFamide

dFMRFa-1 dFMRFa-2 dFMRFa-3 dFMRFa-4 dFMRFa-5 dFMRFa-6 dFMRFa-7 dFMRFa-8 DSK-0	Tachykinin-related	DTK-1 DTK-2 DTK-3 DTK-4 DTK-5 DTK-6
DSK-1 DSK-2		
DMS		
ETH-1 ETH-2 EH		
hug-PK hug-γ		
DrmITP DrmITPL1 DrmITPL2		
LK		
NPF		
sNPF-1 sNPF-1 ⁴⁻¹¹ sNPF-2 sNPF-2 ¹²⁻¹⁹ sNPF-3 sNPF-4		
MTYamide IPNamide APK VQQ		
NEF		
SHA VVIamide		
YSY PDF		
PTTH SP SIFa		

Dick R. Nassel, et al., 2010, Prog Neurobiol

Drosophila life cycle

> J Comp Neurol. 2012 Nov 1;520(16):3764-85. doi: 10.1002/cne.23152.

The role of octopamine and tyramine in Drosophila larval locomotion

Mareike Selcho¹, Dennis Pauls, Basil El Jundi, Reinhard F Stocker, Andreas S Thum

Affiliations + expand

PMID: 22627970 DOI: 10.1002/cne.23152

The role of octopamine and tyramine in Drosophila larval locomotion

Tyramine is a biosynthetic precursor of octopamine

Octopaminergic/tyraminergic neurons within the ventral nerve cord are necessary for larval locomotion

Tdc2-Gal4;tshGal80

> Proc Natl Acad Sci U S A. 2019 Feb 26;116(9):3805-3810. doi: 10.1073/pnas.1813554116. Epub 2019 Feb 11.

Tyramine action on motoneuron excitability and adaptable tyramine/octopamine ratios adjust *Drosophila* locomotion to nutritional state

Natalie Schützler ¹, Chantal Girwert ¹, Isabell Hügli ¹, Giriram Mohana ², Jean-Yves Roignant ², Stefanie Ryglewski ³, Carsten Duch ³

OA and TA Adjust Drosophila Larval Locomotion to Nutritional State

TDC2 Neurons Contact MNs in Central Ventral Nerve Cord Neuropils

Summary

• OA and TA are important for *Drosophila* Larval Locomotion

The locomotion neurotransmitters of adult Drosophila melanogaster

Dimorphism is regulated by dilp2 in Drosophila

Belgacem YH, et al., 2002, PNAS

Belgacem YH, et al., 2006, J Neurobiol

Octopamine mediates starvation-induced hyperactivity



Zhe Yang, et al., 2015, PNAS



AKH mediates starvation-induced hyperactivity

Gene name	Gene ID	Putative Ligand	Baseline locomotion (fed)	Locomotion upon starvation	Increase in locomotion (fed vs. starved)	Statistical significance (fed vs. starved)
Control			865.2(±33.9)	1391.9(±77.6)	60.8%(±9.0%)	***
Adipokinetic hormone receptor	CG11325	Adipokinetic hormone	773.9(±39.0)	897.9(±67.4)	16.0%(±8.7%)	NS
CCHamide-1 receptor	CC30106	CCHamide-1	940.9(±76.9)	1153.1(±73.4)	22.5%(±7.8%)	*
Neuropeptide F receptor	CG1147	Neuropeptide F	1003.0(±44.3)	1265.1(±72.6)	26.1%(±7.2%)	**
Leucine-rich repeat-containing G protein-coupled receptor 1	CG7665	Glycoprotein hormone alpha2/beta5	744.1(±38.9)	939.3(±63.4)	26.2%(±8.5%)	*
Diuretic hormone 44 receptor 1	CG8422	Diuretic hormone 44	719.1(±42.6)	910.2(±72.6)	26.6%(±10.1%)	*
Proctolin receptor	CG6986	Proctolin	734.2(±37.3)	940.3(±84.5)	28.1%(±11.5%)	*
Allatostatin C receptor 2	CG13702	Allatostatin C	766.1(±69.7)	1001.4(±54.9)	30.7%(±7.2%)	*
Cholecystokinin-like receptor at 17D1	CG42301		706.3(±39.7)	925.1(±75.9)	31.0%(±10.7%)	*
	CG10738	Eclosion hormone	686.3(±49.6)	927.6(±73.8)	35.2%(±10.7%)	**
Rickets	CG8930	Bursicon	806.1(±66.4)	1092.3(±68.5)	35.5%(±8.5%)	**
Leucokinin receptor	CG10626	Leucokinin	769.6(±43.1)	1049.9(±75.9)	36.4%(±9.9%)	**
Tachykinin-like receptor at 99D	CG7887	Tachykinin/Drotachykinin	783.3(±58.9)	1074.8(±96.5)	37.2%(±12.3%)	*
Pyrokinin 1 receptor	CG9918	CAPA-PVK/PK	614.8(±29.9)	843.8(±57.0)	37.2%(±9.3%)	***
SIFamide receptor	CG10823	SIFamide	516.3(±31.1)	718.0(±58.3)	39.1%(±11.3%)	**
Myosuppressin receptor 1	CG8985	Myosuppressin/ dromysosuppressin	758.7(±43.3)	1060.9(±62.4)	39.8%(±8.2%)	***
Allatostatin C receptor 1	CG7285	Allatostatin C	855.2(±30.2)	1204.4(±87.8)	40.8%(±10.3%)	***
Corazonin receptor	CG10698	Corazonin	803.3(±32.3)	1157.6(±77.1)	44.1%(±9.6%)	***
FMRFamide Receptor	CG2114	FMRFamide	735.8(±38.6)	1062.4(±81.1)	44.4%(±11.0%)	***
Pyrokinin 2 receptor 1	CG8784	Hugin	732.0(±41.6)	1091.2(±79.3)	49.1%(±10.8%)	***
Myosuppressin receptor 2	CG43745		794.1(±42.5)	1190.0(±71.2)	49.9%(±9.0%)	***
Allatostatin A receptor 1	CG2872	Allatostatin A	828.7(±46.9)	1252.9(±68.4)	51.2%(±8.3%)	***
Torso	CG1389	Prothoracicotropic hormone	723.8(±46.6)	1095.3(±58.1)	51.3%(±8.0%)	***
Allatostatin A receptor 2	CG10001	Allatostatin A	679.7(±44.1)	1039.6(±75.8)	52.9%(±11.1%)	***
Crustacean cardioactive peptide receptor	CG33344		884.3(±61.3)	1356.9(±77.9)	53.4%(±8.8%)	****
Capability receptor	CG14575	CAPA-PVK/PK	959.6(±49.1)	1482.5(±79.4)	54.5%(±8.3%)	***
Pyrokinin 2 receptor 2	CG8795	Hugin	648.1(±28.2)	1018.9(±60.4)	57.2%(±9.3%)	****
Ecdysis-triggering hormone receptor	CG5911	Ecdysis-triggering hormone	990.3(±55.4)	1566.4(±93.7)	58.2%(±9.5%)	***
Pigment-dispersing factor receptor	CG13758	Pigment-dispersing factor	678.3(±27.8)	1099.5(±80.5)	62.1%(±11.9%)	***
Diuretic hormone 31 Receptor	CG32843	Diuretic hormone 31	519.3(±50.3)	857.9(±93.6)	65.2%(±18.0%)	**
Tachykinin-like receptor at 86C	CG6515	Tachykinin/Drotachykinin	749.3(±43.7)	1279.2(±98.1)	70.7%(±13.1%)	***
Short neuropeptide F receptor	CG7395	Short neuropeptide F	820.0(±49.3)	1414.3(±95.7)	72.5%(±11.7%)	***



Yu Y, et al., 2016, Elife



Insulin signaling suppresses starvation-induced hyperactivity via AKHR+neurons



Yu Y, et al., 2016, Elife



Octopamine signaling mediates the effect of AKHR+ neurons on starvation-induced hyperactivity



Yu Y, et al., 2016, Elife



Summary

- OA and TA are important for *Drosophila* Larval Locomotion
- Octopamine signaling mediates the effect of AKHR+ neurons on starvation-induced hyperactivity

Activation of VNC Serotonergic Neurons Slows Walking Speed



Howard CE, et al., 2019, Curr Biol



VNC Serotonergic Neurons regulate Walking Speed



Howard CE, et al., 2019, Curr Biol



HSD extended morning activity but not evening activity



Lee SH, et al., 2019, Commun Biol



HSD extended much morning activity in 16L:8D condition



Lee SH, et al., 2019, Commun Biol



Neuropeptide tachykinin was required for M activity extension in flies on a HSD



elav >d2, w1118 or neuropeptide Ri



24



Lee SH, et al., 2019, Commun Biol



Summary

- OA and TA are important for *Drosophila* larval locomotion
- Octopamine signaling mediates the effect of AKHR+ neurons on starvation-induced hyperactivity for Drosophila adult locomotion
- VNC Serotonergic Neurons regulate Walking Speed

• Neuropeptide tachykinin was required for M activity extension in flies on a HSD

Thanks!