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Neurons with names: Descending control and sensorimotor processing in insect motor control

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Abstract

Technical and methodological advances in recent years have brought new ways to tackle major classical questions in insect motor control. Particularly, significant advancements were achieved in comprehending brain descending control by characterizing descending neurons, their targets in the ventral nerve cord (VNC), and how local networks there integrate sensory information. While physiological experiments in larger insects brought us a better understanding of how sensory modalities are processed locally in the VNC, the development and improvement of genetic tools, principally in *Drosophila*, opened the door to individually characterize actors at these three levels of information flow in behavioral control. This brief review brings together the names and roles of some of those actors, by highlighting the most significant findings from our perspective.

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Keywords

Neural circuits, Sensorimotor processing, Distributed processing, Descending control, Locomotion.

Introduction

For more than 100 years, insects have been study objects in scientists' strive to understand the generation of motor behaviors in animals (reviews in Refs. [1,2]). Insects have been ideal for this, because they exhibit a broad repertoire of motor behaviors from stereotypic behaviors like grooming, locomotion, and postural control to complex behavioral sequences, such as courtship, foraging, or nest-building (e.g. Ref. [3]). Still, we are far from understanding how insects select, generate, adapt, and modify the output of their nervous systems when executing motor behaviors to achieve such task-specificity. However, considerable progress has recently been made in elucidating how descending control by the brain of an insect acts, how this control affects downstream networks in the ventral nerve cord (VNC), and how these downstream networks in the VNC operate. This progress has been possible because of the implementation of neurogenetic tools in combination with electrophysiology and the use of semi-intact preparations. This review highlights the most significant findings in this area of research in recent years from our perspective. Due to space restrictions, we cannot refer to all literature available, but we will give reference to appropriate review articles for further reading. The interested reader is invited to consult additional recent broader reviews on the topic, for example, Refs. [2,4–6].

Identification of neurons in the insect CNS which can initiate and control motor actions: what does their location tell us about motor control in insects?

Initiation, maintenance, and task-specific modification of most motor behaviors is controlled by higher order centers in the insect brain. In recent years, research in the field of motor control has focused on the role of descending control in the generation of behaviors in general, as well as adaptivity in particular.

In this context, descending neurons (DNs) from the brain to the VNC are prime targets for addressing this question. DNs have shown a striking degree of conservation in number and organization, with few exceptions in the number or organization (i.e., clusters) of neurons across insects [7–11]. The role of DNs is best studied in *Drosophila*, owing to its ever-growing genetic toolbox and rich behavioral repertoire. The ability to target narrow/sparse sets of neurons, combined with advances in computation and electronics, prompted a new generation of detailed anatomical studies and high-throughput behavioral screening. With these new tools, the role of hundreds of DNs could be almost individually assessed [••8,12]. These studies have led to the morphological assessment of 190 bilateral pairs of DNs (from ∼1100 DNs) that could not be classified based on their soma location (distributed over six clusters,

[7]), but rather their VNC target area, from which three major pathways could be identified: (1) posterior slope of the brain to dorsal VNC neuropils, (2) Gnathal Ganglia (GNG) to leg neuromeres, and (3) distributed regions in the brain to the tectulum (Figure 1a). These pathways are not mutually exclusive: DNs located in one of the three brain areas can project to neurons in any VNC target area.

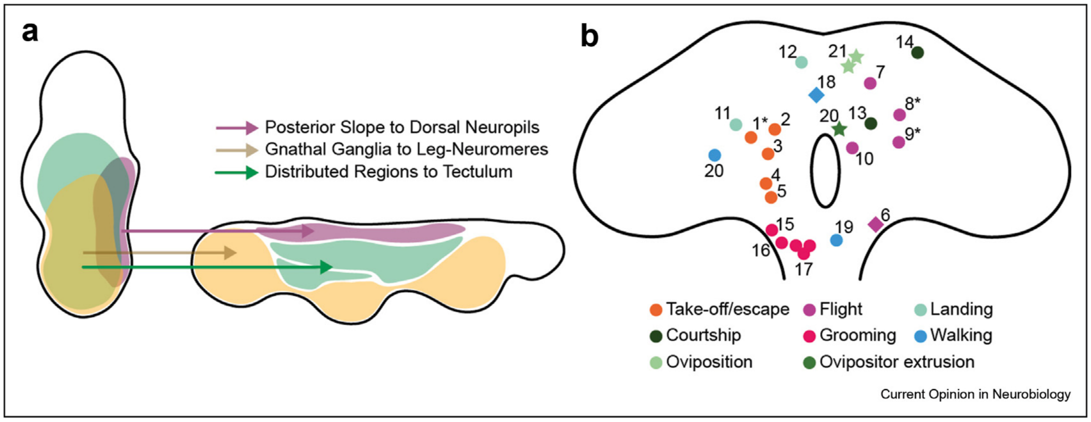
To date, 22 DN types in *Drosophila* have been characterized as command-like neurons (Figure 1b). The giant fibers (GF), whose inputs and outputs have been described in *Drosophila* and also several other insect species, are among the best-studied DNs (reviewed in Ref. [13]). In perched flies, GFs are necessary and sufficient for visually evoked short-duration take-off escapes upon approaching looming stimuli, whereas long-duration escapes rely on a parallel pathway [14]. Four DN groups on the posterior surface of the brain that receive inputs from looming-sensitive neurons have been implicated to contribute to take-off escapes [15]. Of these, DNp02, DNp04, and DNp11 receive direct inputs from looming-sensitive visual projection neurons LC4, just like the GF. The activation of DNp04 and DNp11 elicited only long-duration take-off escapes, and the activation of DNp02 or DNp11 produces take-offs with a bias direction. Final take-off direction, however, seems to be controlled in a population-coding fashion [15].

There are several DNs that contribute to maintenance/regulation of flight. A total of 15 bilateral DNs in the GNG, DNg02, regulate wingbeat amplitude via a population code, determining steering and thrust [16], while ipsilateral activation and contralateral inhibition of a pair of anterior DNs, called AX, correlates with rapid turning during flight [17]. The last identified group of DNs related to flight are DNOVS1, DNOVS2 (both homologous to DNs in blowflies), and DNHS1. Together, they integrate the output of nine large-field visual interneurons and encode self-motion around the three distinct body axes [18].

As described above, approaching looming stimuli promotes take-off behavior in perched flies. In flying flies, however, the same looming stimuli elicit a landing response. The initiation of this behavior involves two bilateral pairs of DNs with somas on the posterior surface, as well as putative inputs from visual projection neurons near GF inputs, DNp07, and DNp10 [19]. Both DNs promote landing upon experimental activation during flight, that is, a state-dependent response to looming stimuli. Their spike rate encodes for leg extension amplitude.

Descending command-like neurons have also been studied in the context of two non-locomotor behaviors, that is, grooming and courtship. Grooming is a sequence of cleaning movements, in which early occurring motor

Figure 1



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Schematics depicting the levels of control of motor behavior in insects. (**a**) Illustration of the three major descending sensory–motor pathways. Adapted from Namiki et al., 2018. Sagittal depiction of the *Drosophila* brain and ventral nerve cord. Each color represents the areas of DN types in the brain and the areas of their projections in the VNC· (**b**) Schematics of the soma location of individually characterized DN types in *Drosophila*. Somas were anatomically placed in a *Drosophila* brain illustration according to original publications and/or data in [••8]. Color code is used to group DN according to the behavior modulated by them. All DN types depicted are bilateral but have been drawn unilaterally for clarity (references are given in the main text). Circles symbolize individual DNs, while diamonds symbolize populations. Stars symbolize female-specific DNs **(1)** giant fiber. **(2)** DNp02. **(3)** DNp04. **(4)** DNp06. It was identified, but it was not characterized in depth in the original publication; therefore, it is included here but excluded from the main text [15]. **(5)** DNp11. **(6)** DNg02. **(7)** AX. **(8)** DNOVS1. **(9)** DNOVS2. **(10)** DNHS1. **(11)** DNp07. **(12)** DNp10. **(13)** pIP10. **(14)** aSP22. **(15)** DNg11. **(16)** DNg12. **(17)** aDN1, aDN2, and aDN3, somas of these three types are not easily distinguishable. aDN3 was identified, and a putative role was given, but it was not characterized in depth in the original publication [21]. **(18)** MDN. **(19)** Pair1. **(20)** DNp09. **(20)** DNp13. **(21)** oviDNa and oviDNb. * means homologs or putative homologs identified in other insects.

program elements, for example, cleaning of the eyes, suppress those that happen later, for example, cleaning of posterior body parts (for more information on the organization of behavioral sequences, see contribution by J.H. Simpson, this issue). Thus, cleaning probabilities of body regions change over time due to changes in the dirtiness of the body parts of higher hierarchy that, in turn, release hierarchical inhibition over the following body part to be clean [20]. Dusted flies start by cleaning their eyes and then focus on the antennae, orderly progressing later on along the posterior body parts. Each routine of body part cleaning comprises cyclic transitions between sweeps of the targeted region and rubbing of the legs against each other. Interestingly, some DNs are related to a specific subroutine, while others can mediate several sequential movements [21,22]. The activation of bilateral DNg12 located in the GNG induces front leg rubbing alternating with head sweeps on the ventral side, whereas the activation of bilateral DNg11 in the same region exclusively causes front leg rubbing. A third group of antennal DNs, aDN1 to 3, located in the posteroventral subesophageal zone evokes head sweeps targeting the antenna. Remarkably, generating an artificial conflicting descending drive by co-activating DNg11 and aDN1 caused alternation between behavioral modules, demonstrating that VNC neurons resolve the conflicting command in an orderly fashion [22]. Interestingly, courtship DNs, which control either individual elements of the behavior, or their sequencing were described. In particular, two pairs of DNs were identified, plP10, whose somas are located in the medial posterior brain [23], and aSP22, whose somas are located in the dorsal brain [••24] (see next section for more details).

DNs can also be sex-dimorphic and command sex-specific behaviors. So far, two groups of DNs have been identified exclusively in females and have been related to female-specific behaviors. Oviposition descending neurons (oviDNs) were found to be necessary and sufficient for egg laying, promoting the full sequence of events upon activation, which include abdomen bending, ovipositor extrusion, and egg deposition [25] (for more information on the organization of behavioral sequences, see contribution by J.H. Simpson, this issue). Interestingly, another DN pair, DNp13, has been linked to ovipositor extrusion, but in the context of mating acceptance or rejection, they respond to male courtship song via pC2l auditory neurons [26,27].

Although the activation of many DNs promotes locomotion in behavioral screening [12], only a few DNs have been characterized in independent studies. A group of two bilateral DNs with somas in the medial posterior protocerebrum were identified as command-like neurons for backward walking [28] (see below). Called *moonwalker descending neurons* (MDNs), these neurons activate a second group of bilateral DNs in the medial subesophageal zone, called Pair1, which remain active during backward walking and suppress forward walking [29]. Another pair of bilateral DNs, DNp09, has been implicated in controlling changes in walking direction. Unilateral activation of DNp09 [30] induces forward walking with an ipsilateral turning component [••31]. DNp09 receives inputs from courtship-promoting neurons and visual projection neurons, and participates in visually guided pursuit as seen during courtship.

One important conclusion from this summary is that descending command-like neurons can be well classified according to their output regions [8]. The DNs presented here (Figure 1a) possess somas located in different regions of the brain, for example, MDN and Pair1 (see Ref. [29], for anatomical details). Interestingly, DNs implicated in the same or related motor patterns tend to partially project to the same regions not only in the VNC but also in the brain, as exemplified by grooming-related DNg11 and DNg12 or take-off-related DNp02, DNp04, DNp06, and DNp11 (see Ref. [••8] for details).

Another striking finding is the numerous types of information coding used to command and control motor behaviors through DNs. DNs can act in concert, simultaneously, or sequentially to organize different aspects of the behavior. In other cases, their actions appear to be coded for by population activity. DNs can suppress or promote behaviors or act together. How these different influences cooperate in a behaving animal, and how information from several DNs is decoded in VNC local circuits remains largely unknown. Technical progress has been achieved recently on this regard: DN population activity patterns can now be recorded simultaneously in tethered behaving flies [•32], but it will be equally important to identify specific downstream partners in the VNC.

Information processing in the ventral nerve cord

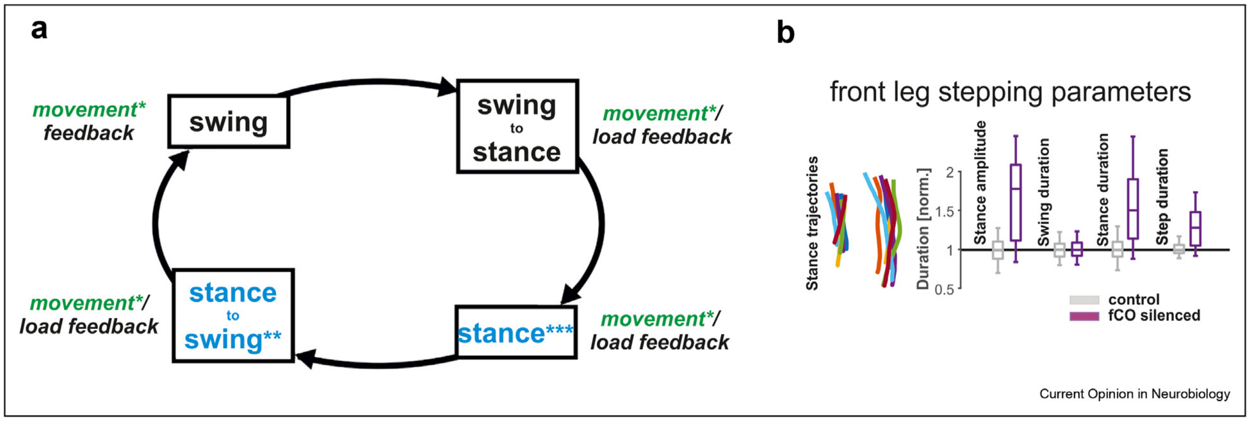
VNC component neurons for the generation of motor behavior

As outlined above, ample information has been collected on the identity of individual neurons in an insect brain serving initiation, maintenance, and control of motor behaviors. Who are those neurons connecting to in the VNC and what behaviors do they control? By activating identified descending pathways, it is possible to study the organization and function of downstream neural circuits in the VNC. Again, this proved especially profitable in the fruit fly, where the mentioned technical advantages allow manipulation of individual neurons in the downstream neural circuits [33,34] to study their role in VNC circuitry and operation. The conceptual progress has been best characterized for two motor behaviors of the fruit fly, courtship, and walking.

Courtship behavior of a male fruit fly consists of a sequence of behavioral elements: orientation, tapping, singing, licking, abdomen bending, and copulation [35] generated in sequence. The courtship song important for mating success and species recognition is composed of two components, an initial sine song during which one wing is vibrating with a frequency of 140–170Hz and the pulse song component, which almost always follows the sine song [36–38]. The pulse song consists of 2–50 pulses, each being composed of 1–3 cycles per pulse (CPP) of wing movement with a frequency of 150–300Hz and an interpulse interval (IPI) of approx.35 ms. As already mentioned, DNs identified for courtship appear to cooperate using two different mechanisms in descending control: while the elements of courtship are initiated sequentially along an increasing activation of aSP22 [24], individual elements of courtship are controlled by additional individual descending pathways, for example, courtship song by pIP10 [23]. The activation of the descending interneuron aSP22 was found to control the whole behavioral sequence in fruit fly courtship, while plP10 was found to activate three local neurons, the dPR1 in the prothoracic neuromere, and the vPR6 and vMS11 in the mesothoracic neuromere, all of which contribute only to individual aspects of pulse song generation [23]. While the activation of vMS11 appears to control wing extension and CPP, the activation of dPR1 and vPR6 lead to modification in IPI. This gives rise to the conclusion that these three local neurons are component neurons in central premotor circuits, reminiscent of central pattern generators (CPG) controlling features of pulse song in courtship, that is, CPP and IPI. Notably, the authors found sexual dimorphisms for each of these neurons, potentially indicative of the reason why only males sing [23].

The other motor behavior we would like to discuss here is walking: in insects, as across the animal kingdom, it is well established that the motor output for leg stepping results from the interaction of activity of central neural circuits, CPGs, able to generate rhythmic and alternating activity in the antagonistic motoneuron pools that supply muscles of each leg segments with proprioceptive feedback about movements and load/force generated. This interaction allows ongoing motoneuron activity and transitions in motoneuron activity to become a functional and coordinated motor output for leg stepping (for review, see Refs. [4,39,40]). There are four phases of leg stepping, which all depend on this interaction (Figure 2a): *leg swing* is primarily under the control of movement feedback, but *swing-to-stance*, *leg stance*, and *stance-to-swing transitions* are under the control of movement and load feedback. Component neurons have been identified that serve the generation of motor activity for leg stepping (e.g., Refs. [41–43]), but the detailed topology of the underlying premotor networks for insect walking is still unknown. Also, and importantly, until recently, it has been unclear how the VNC circuits in charge are accessed by DNs to initiate leg stepping, and how these neurons impinge on local neurons generating the motor output for leg stepping and the associated inter-joint coordination needed.

Figure 2



(a) Summary scheme depicting proprioceptive feedback signals and their contribution to generating leg stepping in insects. Movement and load feedback from leg proprioceptors influence the generation of all four phases of leg stepping (schematic summary based on [39]). (*) Movement signals from a single leg proprioceptor contribute to the generation and timing of all four phases, that is, stance, stance-to-swing transition, swing, and swing-to-stance transition of leg stepping [67]; (**) Local interneuron LUL130 was shown to serve the stance-to-swing transition in backward stepping [••44]; (***) Local interneuron LBL40 was shown to serve generation of stance in backward stepping [••44]. (**b**) Influence of optogenetic silencing of two subpopulations of movement-sensitive sensory neurons in a single leg proprioceptor, the femoral chordotonal organ (fCO). Left: comparison of individual average stance trajectories under control condition and when optogenetically jointly silencing “club” and “hook” fCO sensory neurons [61] in legs of a walking fruit fly, shown for the front leg (redrawn from [•67]; each color represents data from one out of seven flies). Right: modification of leg stepping parameters due to jointly silencing of these two subpopulations in front leg stepping (stance amplitude, swing duration, stance duration, and step duration) normalized to mean values in control condition; grey–box plots of average values for the control condition; purple–box plots of average values for the optogenetically induced silenced condition (see [•67] for further information).

A paradigm was needed, which allowed to induce walking experimentally by controlling descending commands. Although fruit flies have a general behavioral tendency to walk forward, this condition was found by the optogenetic activation of previously mentioned MDN [28] inducing backward walking [••44]. More than two dozen neurons in the VNC, regularly coming with segmental repetitions in the three neuromeres, were identified, which receive synaptic drive from the MDNs. This finding gives an idea about the connectivity of DNs that serve command-like functions in the VNC. Subsequent functional testing of each of these neurons by means of optogenetic silencing identified two local neuron types in the metathoracic neuromere which were most effective at suppressing MDN-induced backward walking, that is, neurons MF01 (LBL40) and MF09 (LUL130; [••44]). These two neurons underlie the generation of leg motor output for one particular phase in the step cycle: LBL40 was found to be instrumental for generating leg stance, while LUL130 was found to be similarly crucial for the transition from stance to swing of the hind leg (Figure 2a). Interestingly, it appears both neurons receive simultaneous excitatory synaptic drive from MDN. This supports the conclusion that their phase-specific action needs to be controlled at the level of the VNC networks by means of local interaction within the operating circuits.

Sensorimotor processing in the ventral nerve cord

There has been significant progress in determining the topology and operation of neuronal circuits in the insect VNC serving sensorimotor processing. Task-specific operation of these circuits plays an important role for generating a functional motor output with the processing of movement and force/load feedback playing a pivotal role [39,45]. Feedback signals on individual sensory modalities, for example, movements, as provided by the femoral chordotonal organ (fCO [46]; review in Ref. [47]), are processed in distributed premotor networks with parallel antagonistic pathways (e.g. Refs. [47–49]; reviews in Refs. [50,51]), a principle of processing first shown for pressure signals in the leech [52,53]. We are now beginning to understand how multimodal proprioceptive signals, for example, those arising from movement sensors and force/load sensors, like campaniform sensilla (CS), are processed in the insect leg muscle control system [54]. Recent studies have shown that multimodal sensory modalities are co-processed in one common, but distributed premotor network [55,56]. Sensory feedback from both modalities influences each other by presynaptic afferent inhibition of the associated sensory neurons, and it is processed downstream by the same intercalated network of premotor interneurons, which are in part laterally connected with each other. All component neurons contributing to the network process both movement and load/force feedback signals. This form of processing underlies the reduction of feedback gain for movement signals by strengthening opposing pathways relative to supporting pathways in this distributed network [••57].

What is the topological organization of such distributed sensorimotor circuits in the insect VNC? The methodological toolbox for the fruit fly was recently upgraded significantly and offers new approaches: (i) lineage mapping based on molecular similarities has resulted in individual lines of fruit flies, which specifically label single classes of neurons in the VNC [58], (ii) the trans-tango technique makes it possible to identify postsynaptic partners of individual neurons in the VNC of the fruit fly [59], and (iii) the VNC connectome will allow us to identify the connectivity between VNC neurons [•60].

The strength of the combined use of such approaches together with already existing ones can be exemplified by recent results elucidating neuronal pathways that underlie the processing of proprioceptive signals from the legs by participating neurons in the fruit fly VNC. Again, we focus on a proprioceptor in the insect leg, the fCO, which signals position, movement, and vibration of the tibia to the VNC [61]. By combining mechanical stimulation of the tibia and anatomical classification of neurogenetically different driver lines with *in vivo* calcium imaging three different classes of sensory neurons were identified that selectively report directional and bidirectional movement, position, and vibration of the tibia. Follow-up work has looked at their connectivity to VNC neurons [62,•63]. These results show that there are individual as well as jointly used processing pathways for these three movement parameters [62]. Divergence in neural processing may result in one class of sensory neurons, for example, those reporting tibia position, to connect to up to seven identifiable classes of VNC neurons (Figure 2b; [•63]). While we are still not at the point of understanding the functional architecture for processing of proprioceptive signals, it should now be possible to unravel the role that individual neurons play in sensorimotor networks of the insect VNC.

Mechanisms contributing to the generation of leg stepping

In both legged vertebrates and invertebrates, it is clear that sensory feedback plays an important role in generating the functional motor output for leg stepping [39,40,64,65]. All four phases of a leg step (leg stance, the stance-to-swing transition, leg swing, and the swing-to-stance transition) appear to be influenced by sensory feedback signals about movement, force/load, and ground contact (Figure 2a). Experiments on reduced and semi-intact preparations and subsequent modeling studies have provided evidence that signals about tibial position and movement reported by the fCO contribute to the motor activity that underlies stance as well as the swing-to-stance and stance-to-swing transitions (summaries in Refs. [39,65,66]). Yet, the test of these conclusions *in vivo* was missing. This has been addressed, as the specific contribution of fCO sensory feedback to the generation of leg stepping kinematics *in vivo* has now been shown by transiently silencing exclusively the fCOs in each leg of a walking fruit fly [•67]. This approach is reminiscent of the removal of muscle spindle afferent feedback in mammalian walking (see Ref. [68]), however, with the advantage of focusing on one sense organ only. Selective or joint silencing of the three subpopulations of sensory neurons in the fCO described above [61] resulted in marked alterations of leg stepping kinematics in the case of “club” and “hook” neurons, that is, those reporting movement of the tibia by affecting both swing-to-stance and stance-to-swing transition. These findings close the analytical loop and substantiate earlier conclusions on the role of movement feedback in generating the motor output for leg stepping from restrained preparations (for review see Ref. [39]).

What is next? In light of the reported advances, some issues appear particularly prevalent for guiding future research, for example, do properties and actions of descending control specifically relate to the motor behaviors controlled for, or, how do descending control and local processing of sensory information cooperate mechanistically in the VNC, given the fact that sensorimotor processing in the VNC markedly relies on distributed processing, just to name two of these.

Authors’ contributions

Ansgar Büschges: conceptualization, preparing figures, writing – original draft, writing – review & editing. **E. Axel Gorostiza**: conceptualization, preparing figures, writing – original draft, writing – review & editing

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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