Multifunctional Neuron CC6 in Aplysia Exerts Actions Opposite to Those of Multifunctional Neuron CC5

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Xin, Yuanpei, Klaudiusz R. Weiss, and Irving Kupfermann. Multifunctional neuron CC6 in Aplysia exerts actions opposite to those of multifunctional neuron CC5. J. Neurophysiol. 83: 2473–2481, 2000. The controls of somatic and autonomic functions often appear to be organized into antagonistic systems. This issue was explored in the bilaterally paired C cluster neuron, CC6, which was found to have properties that suggested that it might function antagonistically to the previously identified multiaction neuron, CC5. Similar to CC5, CC6 is an interganglionic neuron that sends its sole axon to the ipsilateral and contralateral pedal and pleural ganglia. Synaptic inputs to CC6 were opposite to those of CC5. For example, CC6 receives inhibitory inputs from mechanical touch to the lips and tentacles and is excited by firing of C-PR, a neuron involved in the control of a head extension response. Also during rhythmic buccal mass movements CC6 receives synaptic inputs that are out of phase with those received by CC5. CC6 is inhibited during a fictive locomotor program, whereas CC5 is excited, but unlike CC5, the inputs to CC6 are not rhythmic. CC6 has extensive mono- and polysynaptic outputs to many identified and unidentified neurons located in various central ganglia. Firing of CC6 evoked ipsilateral contraction of the transverse muscles of the neck, whereas CC5 contracts longitudinal neck muscles. CC6 monosynaptically inhibits the pedal artery shortener neuron, whereas CC5 monosynaptically excites the pedal artery shortener neuron. Specific motor neurons in the pedal ganglion receive synaptic inputs of opposite sign from CC5 and CC6. Although the inputs and most of the effects of CC6 were opposite to those of CC5, both cells were found to produce polysynaptic excitation of the abdominal ganglion neuron RBhe, a cell whose activity excites the heart. CC5 and CC6 appear to be multifunctional neurons that form an antagonist pair.

INTRODUCTION

Research in a number of invertebrate species as well as in some vertebrates has shown that behavior and the activity of pattern-generating circuits can be initiated or modulated by the firing of single or relatively few higher order interneurons (Arshavsky et al. 1988, 1989; Bartos and Nusbaum 1997; Delaney and Gelperin 1990; Didomenico et al. 1988; Frost and Katz 1996; Kupfermann and Weiss 1978; Rosen et al. 1991; Wiersma and Ikeda 1964). Some of these higher order neurons exert relatively large effects and have been called various names, including command neurons (Kupfermann and Weiss 1978; Wiersma and Ikeda 1964), commandlike neurons (Deodhar et al. 1994), or influential neurons (Arshavsky et al. 1988). In Aplysia a commandlike neuron (CC5) has been recently described, which is of special interest because it is active in many different behaviors (Xin et al. 1996a,b). All of the diverse behaviors in which CC5 participates involve neck shortening, and CC5 evokes both somatic and visceral concomitants of this response. The precise functional contribution of CC5, however, is different for the various behaviors in which it participates. Because the nervous system may be organized into groups of neurons that exert opposite actions (Marder and Calabrese 1996; Schneirla 1959; Sharp et al. 1996), we have attempted to find other neurons with complex outputs similar to that of CC5, but serving opposite functions. In this paper we describe one such bilaterally paired neuron, which we term CC6.

METHODS

Animals

Experiments were performed on 200- to 300-g wild-type Aplysia californica (Marinus, Long Beach, CA). A total of ~200 animals were used. The Us for most experiments were 3–5 and are indicated in the figure legends. The animals were maintained at 14–16°C in holding tanks containing aerated, filtered artificial seawater (ASW; Instant Ocean, Aquarium Systems; composition in mM: 543 Cl, 467 Na, 9.9 Ca, and 54 Mg) and held for 3–6 days before being used for experiments.

Preparations

Before dissection, animals were injected with isotonic magnesium chloride at 25% of their body weight. Three types of preparations were utilized: 1) isolated head ganglia, 2) semi-intact preparations, and 3) reduced preparations. The isolated head preparation consisted of all of the structures in the head and included the cerebral, buccal, and pedal-pleural ganglia. The ganglia were pinned to a silicone elastomer (Sylgard) floor of a recording chamber containing instant ocean ASW. The cerebral and pedal-pleural ganglia were pinned dorsal side up.

The semi-intact preparations consisted of head ganglia and portions of the head including the mouth, lips, anterior tentacles, and cephalic artery that supplies the head region. The preparations were set in a clear Lucite recording chamber consisting of two compartments containing ASW. The head ganglia were pinned in one compartment in the same orientation described above for the isolated ganglia preparation. The mouth, lips, anterior tentacles, and the cephalic artery were set in the second compartment. The second compartment was deeper than the first chamber, so that the tissue could be completely immersed in the ASW. The partition between the two compartments contained fine grooves that allowed the peripheral nerves to pass through. The grooves were filled with petroleum jelly (Vaseline) to maintain a watertight seal between two compartments. The cephalic artery was cannulated, and fresh ASW was pumped into the vascular...
system at a rate of ~0.5 ml/min to perfuse the tissue and to simulate the hydrokeleton of the animal. A suction tube for the outflow was set in the compartment to control the fluid level. The preparation could be presented with mechanical or chemical stimuli. Mechanical stimuli were provided by the tip of a heat-sealed glass Pasteur pipette. Combined chemo-mechano stimulii consisted of pieces of moistened dried seaweed (Laver, Vega Trading, New York, NY), which were applied to the lips or tentacles with a blunt forceps. A pure chemical stimulus consisted of a seaweed extract solution that was applied by a 1-ml syringe and slowly injected into the ASW 1 cm near one side of the lip and tentacle region (Susswein et al. 1978).

Reduced preparations included the head ganglia and neck muscles with attached pedal nerves that connect the muscles to the pedal ganglion.

Electrophysiology

All in vitro experiments were carried out at room temperature (19–21°C). For the intracellular recording and stimulation, neurons were impaled with double-barreled microelectrodes that were made of thin-walled glass (World Precision Instruments) filled with 2 M potassium acetate. The electrodes were flow beveled so that their impedances ranged from 10 to 15 MΩ. To identify neurons and examine their morphology, the potassium acetate in one barrel was replaced by a solution of 3% 5(6)-carboxyfluorescein dye (Kodak) in 0.1 M potassium citrate, titrated to pH 8.0 with KOH (Rao et al. 1986). These electrodes were beveled so that the impedance of the electrodes containing the dye was 15–20 MΩ and the impedance of the potassium acetate electrode was 10–15 MΩ. To test for monosynapticity of connections between cells, the threshold for action potential generation was raised by bathing the ganglia in a high divalent cation solution (3 times Ca2+, 30 mM, and 3 times Mg2+, 450 mM; or 2 times Mg2+, 300 mM, and 5 times Ca2+, 50 mM).

For extracellular recording or stimulation of various nerves, the cut ends of nerves were drawn into small-diameter polyethylene suction electrodes. Nerve recordings were made with AC amplifiers (A-M Systems), and electrical stimulation of the nerves was provided by a Grass 88 stimulator. An isotonic transducer (Harvard Bioscience) was used to record muscle movement (Xin et al. 1996a).

Morphology

Because many identified cells have distinctive morphologies, to aid the identification of cells, neurons were routinely filled with 3% 5(6)-carboxyfluorescein dye. Successful intracellular labeling was achieved by iontophoretic injection of the dye for 15–30 min, followed by a 48-h incubation at 4°C to allow the dye to fully fill the processes. To reduce active transport of the dye from the cells during incubation, the bathing ASW solution included 10 mM probenecid (Sigma) final concentration (Rosen et al. 1991; Steinberg et al. 1987). The living ganglia were cleared in 50% glycerol in ASW, and the fluorescence was visualized with a Nikon fluorescence microscope, and the labeled cell body with its processes was photographed, or drawn with the aid of a camera lucida.

RESULTS

Morphology

CC6 is located bilaterally on the dorsal surface of cerebral ganglion, within a distinct cluster of neurons that comprise the cerebral C cluster (Jahan-Parwar and Fredman 1976). CC6 was generally found anterior and lateral to the previously described neuron, CC5 (Xin et al. 1996a,b). The size of its cell body is ~80–100 μm. CC6 sends some processes into the region deep to the somata in the C cluster. Its main axon enters the ipsilateral pedal ganglion via the cerebral-pedal connective, and then continues to the contralateral pedal ganglion via the pedal-artery commissure. It sends out small processes in both pedal ganglia, and the processes extend to both pleural ganglia (Fig. 1). No axons of CC6 were observed to enter any peripheral nerves. Dye backfills (data not shown), indicate that in addition to CC6, there is another cell in the cerebral C cluster that sends its axon to the ipsilateral cerebral-pedal connective. This other cell is located anterior-medial to CC6, and its cell body is much smaller than that of CC6. Firing of this cell could evoke rhythmic activity in pedal nerves (data not shown), suggesting that it may be one of the previously described locomotor commandlike neurons (Fredman and Jahan-Parwar 1983). CC6 was usually identified on the basis of the characteristic inhibition it produces in the pedal artery shortener neuron (PAS, see CC6 inhibits the pedal artery shortener neuron).

Inputs to CC6

CC6 receives inputs from different sources. Application of seaweed to the anterior tentacle or lip evoked inhibition in CC6 (Fig. 2A). The preparations used in these studies did not typically exhibit feeding responses, and seaweed stimuli may have elicited defensive withdrawal responses rather than appetitive

FIG. 1. Morphology CC6 based on a composite of 30 cells labeled by means of intracellular dye injection. The diagram shows a dorsal view of the cerebral, pedal, and pleural ganglia. CC6 has processes that ramify mainly in the region of the C cluster. Its single axon projects to the ipsilateral pedal ganglion via the ipsilateral cerebral-pedal connective (C-PC). The axon, after reaching the ipsilateral pedal ganglion, continues to the contralateral pedal-pleural ganglia via the pedal-artery commissure (P-P comm.) and the short pedal-pleural commissures. ATn, anterior tentacular nerve; C-BC, cerebral buccal commissure; C-PC, cerebral-pedal commissure; C-PIC, cerebral-pleural commissure; LLABn, lower labial nerve; P, pedal nerve; Pl-ABC, pleural-abdominal commissure; P-P comm., pedal-artery commissure; ULABn, upper labial nerve.
feeding responses. We found that pure mechanical stimulation of the lip or tentacles, provided by a polished glass pipette, also evoked inhibition in CC6, and the response was indistinguishable from that evoked by seaweed. Previously we reported that tactile stimuli applied to the tentacles of the animal evoked excitatory responses in CC5 (Xin et al. 1996b).

In preparations consisting of the head ganglia and buccal mass, mechanical stimuli applied to the buccal mass produced several cycles of buccal mass forward and backward movements, and during the movements, CC6 received cyclic inhibitory inputs that were in phase with each backward movement of the buccal mass (Fig. 2B). The phase of this input is opposite to that previously reported for CC5 (Xin et al. 1996b).

We next examined the connections between CC6 and C-PR, a neuron involved in the head lifting component of appetitive feeding responses (Nagahama et al. 1993; Teyke et al. 1990). Firing of C-PR produced excitation of CC6 (Fig. 3A). In preparations in which intracellular records were obtained simultaneously from CC5 and CC6, firing of C-PR resulted in excitation of CC6 and inhibition of CC5 (Fig. 3B).

To determine whether CC6 receives synaptic input in phase with a locomotor program, we electrically stimulated a P9 nerve (Jahan-Parwar and Fredman 1998). Simultaneous extracellular recordings from the P9 and P10 nerves were obtained to monitor fictive locomotor activity. It was found that stimulation of P9 evoked a long-duration hyperpolarization in CC6 (Fig. 4A) and inhibited firing of the cell. The hyperpolarization persisted during the time that a fictive (presumably escape) motor program was present, as indicated by bursts of firing of units in the P9 and P10 nerves (Fig. 4B). Previously, we showed that during a fictive locomotor program CC5 received excitatory input (Xin et al. 1996b), but unlike the tonic hyperpolarization seen in CC6, the excitation was phasic. Direct firing of CC6 during an evoked locomotor program could excite activity of one or more units in P9 and P10 and could temporarily suppress rhythmic output recorded from the nerves (Fig. 5). Although the activity evoked in the nerves appeared to be tonic, we cannot rule out the possibility that rhythmic activity of small units might be obscured by the larger tonic units. Rhythmic activity of the large unit returned when the

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**FIG. 2.** Inputs to CC6. A: touching the lip (horizontal lines) with a piece of moist seaweed produces a short-duration inhibition of CC6 (n = 5). Touching with the tip of a glass pipette produced similar inhibition (data not shown). B: in a preparation in which the buccal mass and buccal ganglion was included, CC6 was inhibited during what appeared to be retraction movements of the buccal mass (indicated by double lines). Bouts of buccal mass movements were evoked by brief mechanical stimulation of the buccal musculature (n = 5).

**FIG. 3.** Effect of firing of C-PR on CC6. A: firing of C-PR by means of a depolarizing pulse, produced a slow excitatory input to CC6 (n = 5). B: in preparations in which both CC6 and CC5 were recorded and slightly hyperpolarized, firing of C-PR excited CC6 and produced signs of inhibition in CC5 (n = 3).

**FIG. 4.** Synaptic inputs to CC6 shown in relation to the presence of fictive locomotor programs. Fictive locomotor programs were evoked by a brief train of electrical stimulation applied to the P9 nerve (horizontal line). To reduce stimulus artifacts extracellular recording from the P9 and P10 nerves contralateral to the stimulated side were obtained. These recordings revealed that the stimulation evoked a regular rhythmic output of the pedal ganglia. CC6 was inhibited at the onset of the stimulation of the P9 nerve, and it largely remained inhibited during the period that the rhythmic program was active (n = 4). B: termination of rhythmic activity, typically was associated with a return of spontaneous nonrhythmic firing of CC6.
depolarizing current injected into CC6 was terminated and CC6 no longer fired (Fig. 5).

**Effect of CC6 on neck muscles**

To explore the effect of CC6 on neck muscles, extracellular records were obtained from pedal nerves (P3, P4, P5) that innervate the neck (Bablanian et al. 1987; Jahan-Parwar and Fredman 1978). Firing of CC6 strongly excited unit activity in neck nerves as well as other pedal nerves including P7, P9, and P10 (Fig. 6, A–C). We therefore examined the effect of firing of CC6 on neck muscles. By adjusting the plane of movement of the movement transducer, we could distinguish transverse from longitudinal contractions. We observed that firing of CC6 produced distinct transverse contractions of neck muscles (Fig. 7). Such transverse contractions should result in extension of the neck, and indeed CC6 firing evoked a distinct lengthening of the neck that was of sufficient magnitude that it could be observed visually without a microscope. This effect of CC6 contrasts with that of CC5, whose firing results in neck shortening (Xin et al. 1996b).

Intracellular recordings from unidentified pedal neurons that send axons into pedal nerves revealed that many of them were either excited (Fig. 8), or inhibited (Fig. 9) when CC6 was fired. Typically the excitation or inhibition of these presumptive pedal motor neurons was not associated with synaptic potentials that were one-for-one with the CC6 spikes, suggesting that the effects were polysynaptic. In some instances, however, discrete excitatory postsynaptic potentials (EPSPs)
that were time-locked to CC6 were obtained from the presumptive pedal motor neurons (Fig. 8B). In three experiments in which both CC5 and CC6 were recorded simultaneously, we found presumptive pedal motor neurons that received a synaptic input of one sign (either excitatory or inhibitory) when CC5 was fired but received input of the opposite sign (either inhibitory or excitatory) when CC6 was fired (Fig. 10, A and B). In experiments in which CC5 and CC6 were recorded simultaneously, it was observed that firing of CC5 or CC6 could evoke a weak slow membrane potential shift in the cell that was not fired, but mutual effects were not always observed (e.g., Fig. 10B), and we have not specifically investigated the sources of possible interaction between the cells.

**CC6 inhibits the pedal artery shortener neuron**

We previously reported (Xin et al. 1996a) that neuron CC5 controls the pedal artery shortener neuron (PAS), which contracts the pedal artery (Skelton and Koester 1992) during various behaviors that involve shortening of the neck. Because our data indicated that CC6 extends or lengthens the neck muscle, we hypothesized that CC6 would be involved in lengthening of the pedal artery and might therefore inhibit the pedal artery shortener neuron (PAS). Initially we obtained extracellular recordings from the pedal artery nerve (PAn) to monitor the activity of PAS, which is the only cell to send a large-diameter axon into the nerve (Skelton and Koester 1992). In these experiments we recorded simultaneously from CC5 and CC6. Firing of CC6 inhibited the firing of the PAS unit recorded in the ipsilateral pedal artery nerve. Confirming pre-
vious results, firing of CC5 was found to excite the P_{AS} unit recorded in the ipsilateral pedal artery nerve (Fig. 10, A and B).

Simultaneous recordings from the left and right pedal artery nerves and a single CC6 cell showed that, in addition to strongly inhibiting the ipsilateral P_{AS} unit in the nerve, CC6 had a weak inhibitory action on the contralateral unit (Fig. 11). Conversely, simultaneous recordings from a CC5 cell on the opposite side of the CC6 cell showed that CC5 had no effect or a very weak excitatory effect on the contralateral P_{AS} unit, but strongly excited the ipsilateral unit.

We next directly examined the synaptic connectivity of CC6 to P_{AS} by recording directly from the P_{AS} neuron cell body. Firing of CC6 produced strong inhibition in the P_{AS} neuron (Fig. 12A), and at a fast sweep speed, small inhibitory postsynaptic potentials (IPSPs) one-for-one with CC6 spikes could be observed (Fig. 12B). The IPSPs persisted in a high divalent cation solution (Fig. 12C), suggesting that they are monosynaptic.

**Effects of CC6 on neurons in the abdominal ganglion**

CC5 and a number of cells located near CC5 and CC6 in the C cluster have been found to produce varied effects on neurons in the abdominal ganglion (unpublished observations). For example, it was previously reported that firing of CC5 evokes polysynaptic excitation of RB_{he}, a neuron whose activity excites the heart (Mayeri et al. 1974) and is involved in a general arousal response of the animal (Koch et al. 1984). Whereas CC5 and CC6 typically have opposite actions, CC6 had the same action as CC5 on RB_{he}, that is, it excited the cell (Fig. 13A). The excitation of RB_{he} appeared to be polysynaptic, as would be expected because CC6 does not send an axon to the abdominal ganglion. Additional polysynaptic effects of CC6 on abdominal ganglion neurons included excitation of left upper quadrant (LUQ) cells (Fig. 13B), neurons involved in kidney function (Koester and Alevizos 1989), and excitation of...
L9 (Fig. 13C), a motor neuron that contracts the gill (Kupfermann and Kandel 1969).

Effects of CC6 on neurons in the cerebral ganglion

Firing of CC6 evoked polysynaptic input to a number of neurons whose cell bodies are located in the cerebral ganglion. Firing of CC6 evoked fast, polysynaptic potentials in the metacerebral cell (MCC; Fig. 14, A and B), a serotonergic neuron that modulates feeding behavior (Rosen et al. 1989). The occurrence of the individual synaptic potentials outlasted the firing of CC6, and they were not one-for-one with the CC6 spikes. Although the evoked synaptic potentials appeared to be depolarizing, they were not associated with an increase of the rate of firing of the MCC (Fig. 14A), but rather with a small but distinct decrease (note the increased interspike interval of the MCC immediately following the firing of CC6). It is possible that the evoked synaptic potential represents an example of the conjoint EPSP-IPSP previously described to occur in the MCC (Weiss and Kupfermann 1976), but when the MCC was prevented from spiking by means of a low level of hyperpolarizing current, the synaptic potentials did not exhibit any obvious multiple components.

Because the connections of CC6 suggested that it may be involved in head extension, we determined whether it might inhibit cerebral buccal interneuron 1 (CBI-1), which appears to be involved in buccal mass withdrawal, and presumably head withdrawal (Rosen et al. 1991). CBI-1 was identified by the presence of the characteristic bilateral axons that it sends into the cerebral-buccal connectives, as established by dye fills. We found that firing of CC6 strongly inhibited CBI-1 (Fig. 15). Similarly, Bn cells, which have been shown to be involved in head withdrawal (Teyke et al. 1989), were strongly inhibited by CC6 (Fig. 16). As was the case for CBI-1, the inhibition of spiking in Bn cells was associated with a smooth hyperpolarization (Fig. 16A) or with no clear membrane potential shift.

FIG. 15. Firing of CC6 inhibited cerebral to buccal neuron 1 (CBI 1). Extracellular recordings of P9 and PAn exhibited the characteristic responses to firing of CC6 (n = 3).

FIG. 14. CC6 evoked polysynaptic inputs to the metacerebral cell (MCC). A: when the MCC was depolarized so that it continuously fired at a low rate, firing of CC6 evoked fast depolarizing inputs in the MCC, but the MCC firing rate decreased. B: when the MCC was hyperpolarized so that it did not fire, firing of CC6 continued to produce a burst of fast depolarizing potentials. The fast potentials outlasted the firing of CC6 and were not one for one with CC6 spikes (n = 4).

FIG. 16. Firing of CC6 inhibited the spiking of Bn cells, neurons that are involved in head withdrawal. CC6 was identified by its position and its characteristic effect on PAn (A) or the P10 nerve (B). Inhibition of a Bn cell spiking could be associated with either a smooth hyperpolarization (A), or with no obvious shifts of membrane potential (B; n = 4).
(Fig. 16B). We have not attempted to determine whether this inhibition might be monosynaptic.

DISCUSSION

It has been suggested that somatic (Schneirla 1959) as well as autonomic (Patton 1989) responses are often controlled by antagonistic functional mechanisms. The present results suggest that the multifunctional neurons CC5 and CC6 comprise a functional antagonist pair that contributes importantly to the control of opposing movements. Previously, it was shown that CC5 is active in a variety of behaviors, all of which involve shortening of the neck. The current data support the hypothesis that CC6 is a counterpart of CC5, but is involved in lengthening of the neck. In some sense the two cells operate like a half-center pair. The notion of half-centers (Marder and Calabrese 1996; Sharp et al. 1996), however, has been traditionally applied to sets of mutually inhibitory neurons that can form an oscillatory circuit. Our data do not indicate that CC5 and CC6 are integral parts of an oscillatory pattern-generating circuit. Furthermore, head shortening and lengthening often occur as independent components of behaviors, such as feeding and defensive withdrawal, and presumably in these behaviors the activity of the two cells will not be directly linked.

Three lines of evidence support the idea that CC6 produces, actions that are antagonistic to those of CC5. First, the two cells have opposite synaptic inputs (either direct or polysynaptically) from common sources. For example, the higher order neuron C-PR excites CC6 but inhibits CC5. Furthermore, the two cells receive opposite sensory inputs following tactile stimulation of the head. The observed inhibition in CC6 following tactile stimuli to the head is consistent with a role of CC6 in responses that involve lengthening of the neck muscles, because such tactile stimuli typically produce head withdrawal and bilateral shortening of the neck (Teyke et al. 1989). A second line of evidence indicating an antagonist relationship between CC5 and CC6 comes from examination of their monosynaptic and polysynaptic effects on various follower neurons. A prominent feature of CC5 is that it produces strong monosynaptic excitation of the pedal artery shortener neuron, P_{AS} (Skelton and Koester 1992). In contrast, CC6 inhibits the P_{AS} and similar to CC5 the synaptic effect appears to be monosynaptic. Many other cerebral and pedal neurons receive polysynaptic input of opposite sign from the two neurons. The final evidence of antagonist actions of CC5 and CC6 is that firing of the individual cells indirectly evokes strong muscle contractions that produce opposing directions of movement of the neck.

Interestingly, although in most cases the responses and outputs of CC6 are diametrically opposite to those of CC5, this is not always the case. For example, during a locomotor program elicited by a presumably noxious stimulus, CC5 fires rhythmically (Xin et al. 1996b), whereas CC6 is completely inhibited rather than firing rhythmically in antiphase to CC5. These observations, however, do not preclude the possibility that the cells may exhibit antiphasic burst activity during locomotion that is not elicited by a strong noxious stimulus. It is also noteworthy that the two cells do not appear to provide strong mutual inhibition of one another, which is often, but not always (Lu et al. 1999), a feature of theoretical and actual neural systems that mediate opposing or conflicting actions (Blitz and Nusbaum 1997; Brooks 1986; Dickinson 1995; Edwards 1991; Jing and Gillette 1995; Krasne and Lee 1988; Kristan and Shaw 1997; Maes 1990; Redgrave et al. 1999; Svoboda and Fetcho 1996).

A second type of nonopposite behavior of CC6 and CC5 is seen in their effects on the heart exciter neuron Rbhe, which is located in the abdominal ganglion. CC6 as well as CC5 produces polysynaptic excitatory input to Rbhe (Fig. 16A). Similar to CC5, CC6 does not send an axon to the abdominal ganglion, so that its effect on Rbhe presumably involves intermediary interneurons located in head ganglia. The example of similarity of action of CC6 and CC5 may reflect the operation of a common “arousal-like” function, in which various motor activities, even opposing actions, nevertheless engage certain common functions, particularly “autonomic” responses that aid in the execution of motor output.

In addition to effects on Rbhe CC6 also has actions on other abdominal ganglion neurons. Similar to CC5, CC6 appears to be involved in the control of both somatic as well as visceral muscles, and thus is involved in generating a highly complex behavioral response rather than a simple component of a response.

Studies of CC5 have shown that it is involved in a large number of ostensibly different behaviors (Xin et al. 1996a,b) and that its specific functional role in each of the responses is different. In some behaviors CC5 appears to be necessary and sufficient for a component (arterial shortening) of a complex withdrawal response, and thus functions as a command neuron for that component. We have now provided evidence that CC6 may similarly play multiple roles in different behaviors, but based on its parallel, albeit opposite effects to those of CC5, it seems likely that it is a member of a growing class of multifunctional neurons that exert widespread actions. Definitive elucidation of the behavioral role of CC6 will require lesion and recording experiments in intact animals. These experiments are currently unfeasible but may become possible with future technical advances.

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