Organization and Functional Roles of the Central Complex in the Insect Brain

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Annu. Rev. Entomol. 2014. 59:165–84

First published online as a Review in Advance on October 18, 2013

The *Annual Review of Entomology* is online at ento.annualreviews.org

This article's doi: 10.1146/annurev-ento-011613-162031

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Keywords

central body, protocerebral bridge, spatial orientation, polarization vision, spatial memory, place learning, motor control

Abstract

The central complex is a group of modular neuropils across the midline of the insect brain. Hallmarks of its anatomical organization are discrete layers, an organization into arrays of 16 slices along the right-left axis, and precise interhemispheric connections via chiasmata. The central complex is connected most prominently with the adjacent lateral complex and the superior protocerebrum. Its developmental appearance corresponds with the appearance of compound eyes and walking legs. Distinct dopaminergic neurons control various forms of arousal. Electrophysiological studies provide evidence for roles in polarized light vision, sky compass orientation, and integration of spatial information for locomotor control. Behavioral studies on mutant and transgenic flies indicate roles in spatial representation of visual cues, spatial visual memory, directional control of walking and flight, and place learning. The data suggest that spatial azimuthal directions (i.e., where) are represented in the slices, and cue information (i.e., what) are represented in different layers of the central complex.

INTRODUCTION

Central complex: group of midline-spanning neuropils in the insect brain, consisting of PB, CBU/FB, CBL/EB, and noduli

Upper division of the central body (CBU): in locusts, the larger superior/posterior part of the central body

Fan-shaped body (FB): in flies, the larger superior/posterior part of the central body

Lower division of the central body (CBL): in locusts, the smaller inferior/anterior part of the central body

Ellipsoid body (EB): in flies, the smaller inferior/anterior part of the central body

Noduli: bilateral pair of small globular neuropils of the central complex

PB: protocerebral bridge

The insect brain is composed of a number of modular neuropils that, in the central brain, are embedded in a matrix of coarse neuropil. These modular neuropils include the first stages of visual processing—the lamina, medulla, and lobula complex of the optic lobe—the antennal lobe; the primary olfactory brain area; and, in the central brain, the mushroom bodies and the central complex. The paired mushroom bodies receive massive input from the antennal lobes and play a key role in olfactory learning and memory (10, 11, 29). In contrast, the central complex is a group of unpaired midline-spanning neuropils with highly indirect sensory input, especially, but not exclusively, from the visual system (34, 38). Although the mushroom bodies have been studied intensely for many decades, the central complex has received increasing attention only in recent years following reports suggesting a key role of this brain area in locomotor control (97, 109), spatial orientation (39, 82, 97, 114), visual memory (66, 82, 83), and various forms of arousal (57, 64). Therefore, except for a few comparative studies, knowledge about the anatomical organization and functional roles of the central complex is based largely on studies of a few model species, including the discoid cockroach (*Blaberus discoidalis*), the desert locust (*Schistocerca gregaria*), the field cricket (*Gryllus campestris*), the monarch butterfly (*Danaus plexippus*), and the fruit fly (*Drosophila melanogaster*). Accumulating data from these and other species are largely converging on a common role of the central complex in space representation and spatial aspects of motor control. To stimulate further research on this brain area, we review comparative data on the anatomical organization and developmental and evolutionary origin of the insect central complex and focus on current evidence for and hypotheses on the physiological roles of the central complex in the insect brain. The nomenclature for brain areas used throughout this review was introduced by Ito et al. (52).

NEUROARCHITECTURE OF THE CENTRAL COMPLEX

Subunits and Internal Organization

The term central complex denotes a group of closely interconnected neuropils spanning the brain midline in all hexapod species. It consists of the protocerebral bridge (PB) in the posterior dorsal brain and, more anterior-ventrally, the central body, which is subdivided into an upper division (CBU, or fan-shaped body, FB) and a lower division (CBL, or ellipsoid body, EB) (**Figure 1**). In pterygote insects, two globular neuropils, the noduli, are ventrally attached to the central body. A PB and central body are also present in certain crustaceans (e.g., Malacostraca, Remipedia) and are strikingly similar in neuroarchitecture to their insect counterparts, but whether midbrain-spanning neuropils in other arthropods (Myriapoda, Chelicerata), termed central body or arcuate body, are phylogenetically related to the insect central complex is still under debate (38, 68, 108).

The PB is an elongated handlebar-shaped neuropil with ends bent posterior-ventrally. It spans between the calyces of the mushroom bodies and is slightly detached posteriorly from the protocerebral neuropil. From right to left, the PB is subdivided into 16 slices, 8 in each hemisphere, which are also called columns or segments. The two hemispheres of the bridge may appear to be continuous across the brain midline (desert locust, honey bee) or may be connected by a more or less prominent commissure (monarch butterfly) (23) (**Figure 2**).

The central body lies more anteriorly, immediately frontally (in certain species dorsally) from the medial antennal lobe tracts connecting the antennal lobes and calyces of the mushroom bodies. In all species, a large CBU/FB covers a smaller kidney-shaped, hemispheroidally or toroidally shaped CBL/EB (**Figure 1**). Depending on the taxon, the CBU may cover the CBL dorsally (as in the desert locust and honey bee) or posterior-ventrally (as in the monarch butterfly

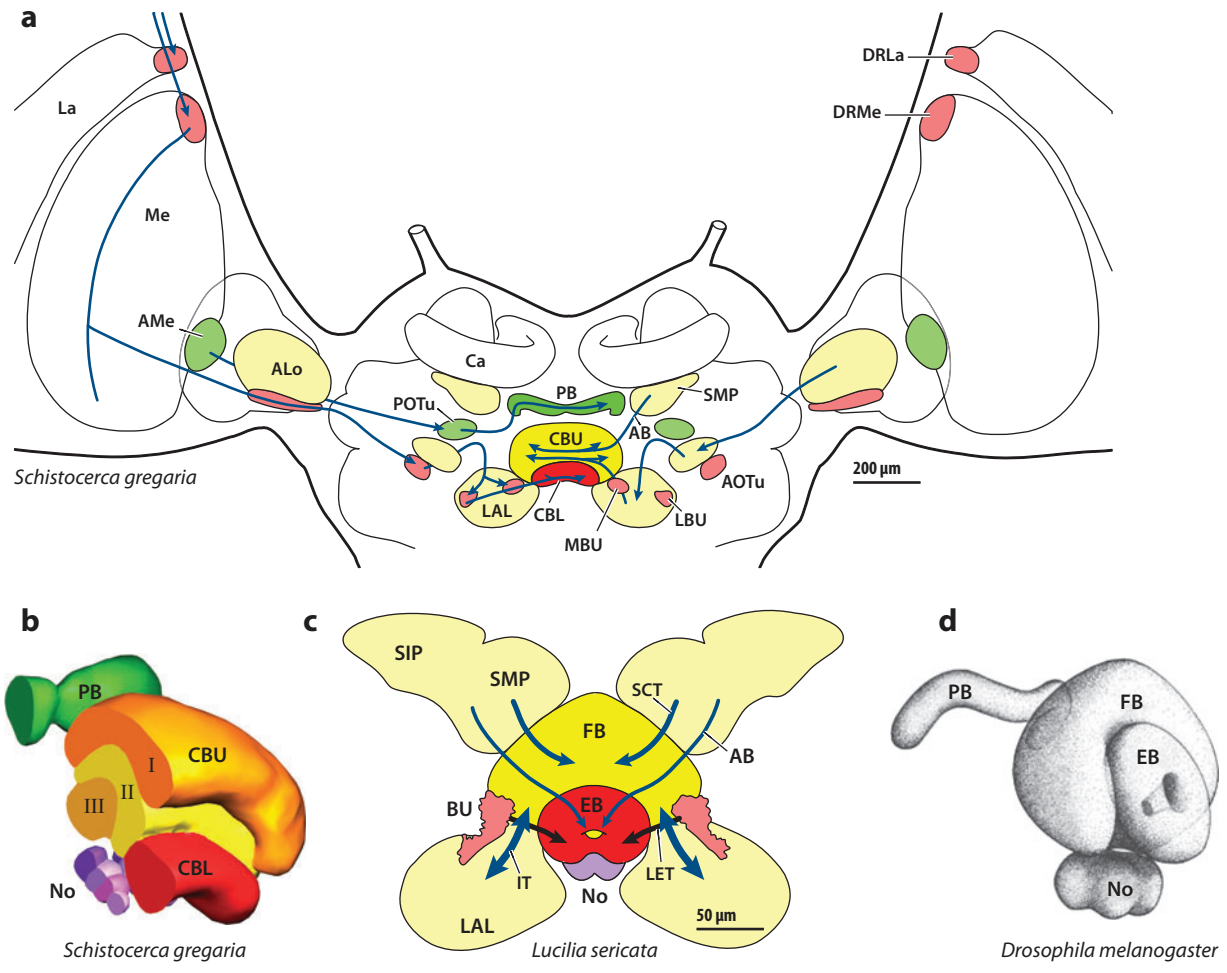

Figure 1

Subunits and connections of the insect central complex. (*a*) A frontal diagram of the brain of the desert locust, *Schistocerca gregaria*, illustrating fiber connections of the central complex. The anterior polarization pathway (*red*) connects the dorsal rim area of the lamina and medulla (DRLa, DRMe) via the ventral layer of the anterior lobe of the lobula (ALo), the lower unit of the anterior optic tubercle (AOTu), and the medial (MBU) and lateral (LBU) bulb to the lower division of the central body (CBL). A parallel pathway (*yellow*) originating in the ALo connects via the upper unit of the AOTu and lateral accessory lobe (LAL) to the upper division of the central body (CBU). The superior medial protocerebrum is connected to the CBU via the anterior bundles (AB). Finally, projections from the accessory medulla (AMe) extend to the posterior optic tubercle (POTu) and likely target tangential neurons entering the protocerebral bridge (PB; *green*). (*b*) Oblique three-dimensional view of the locust central complex. A sagittal cut reveals the positions of the PB, the three layers of the CBU (I, II, III), the CBL, and the four subunits of the noduli (No). (*c*) Fiber connections of the central body of the blow fly *Lucilia sericata*. The bulbs (BU) are connected through the lateral ellipsoid tracts (LET) to the ellipsoid body (EB). The isthmus tracts (IT) provide connections between the LALs and the fan-shaped body (FB). The superior intermediate protocerebrum (SIP) and superior medial protocerebrum (SMP) are connected to the FB via the AB and the superior central-body tract (SCT). (*d*) Oblique lateral view illustrating the subunits of the central complex of the fruit fly, *Drosophila melanogaster*; modified with permission from Reference 17.

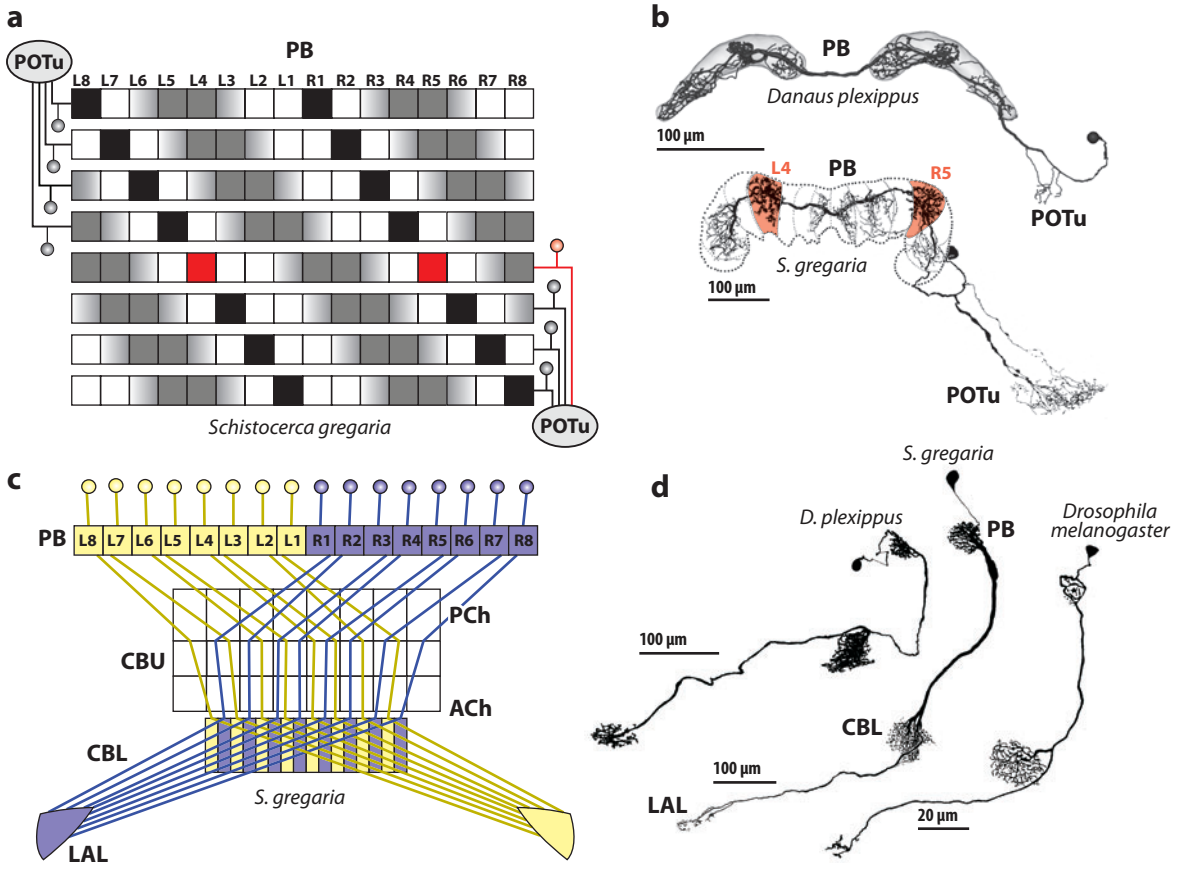

Figure 2

Tangential and columnar neurons of the central complex. (*a*) Schematic diagram of arborization patterns of TB1 tangential neurons of the protocerebral bridge (PB) of the desert locust, *Schistocerca gregaria*. Each line represents one TB1 neuron. Each neuron has ramifications in the posterior optic tubercle (POTu) and, in each hemisphere of the PB, invades one slice with varicose ramifications (*black/red*), and several slices with smooth ramifications (*gray*) in a pattern illustrated in the figure. Neurons marked in red indicate the locust TB1 neuron in panel *b*. (*b*) Single TB1 neurons from the monarch butterfly, *Danaus plexippus* (*top*), and *S. gregaria* (*bottom*; slices with varicose ramifications marked in red). (*c*) Wiring scheme of 16 CL1 columnar neurons in the central complex of *S. gregaria*. Neurons provide precise right-left connections between the PB, lower division of the central body (CBL), and their axonal terminals in a small subfield of the lateral accessory lobe (LAL). (*d*) Single CL1 neurons from *D. plexippus* (*left*), *S. gregaria* (*middle*), and the fruit fly, *Drosophila melanogaster* (*right*). Abbreviations: CBU, upper division of the central body; ACh, anterior chiasma of the central complex; PCh, posterior chiasma of the central complex. Panel *a* modified with permission from Reference 25, panel *b* from References 23 and 25, panel *c* from Reference 26, and panel *d* from References 17, 23, and 76.

and tobacco hornworm). Both subdivisions are internally organized into horizontal layers and 16 or, more often, 8 vertical slices, 4 in each hemisphere. Neurons connect the PB and central body via four bilateral pairs of fiber bundles termed w-, x-, y-, and z-bundles (123) that give rise to a highly regular scheme of interhemispheric fiber crossings in the posterior chiasma (between the PB and central body) and anterior chiasma (between the CB and lateral complex) (**Figure 2**). In pterygote species, a pair of globular neuropils, the noduli, is posterior-ventrally attached to the central body (**Figure 1*b–d***). The noduli consist of stacked subunits (four in *S. gregaria*, *D. melanogaster*, and *D. plexippus*), but they do not show a columnar organization. Fiber connections

between the central body/PB and noduli again show interhemispheric crossings via the posterior chiasma of projections. In the desert locust there is evidence for a topographical relationship between noduli subunits and central-body layers (26): Each nodulus consists of a lower unit that is exclusively connected to the CBL and an upper unit with three layers that are largely topographically connected to the three major layers of the CBU.

Connections with Other Brain Areas

The central complex is connected to many areas in the surrounding protocerebrum, but except for a few direct connections with the optic lobe documented for crickets and locusts (46, 47) and two pairs of SIFamide-immunoreactive descending neurons (32), it is connected only indirectly to sensory brain areas and the ventral nerve cord. Reports of direct innervation of the PB by ocellar interneurons in *Schistocerca gregaria* (12), *Periplaneta americana* (59), and *Acheta domesticus* (59) have not been confirmed by others (74). Tracing studies, single cell dye injections, and data from immunolabelling studies across several species showed that connections with other brain areas occur via three major pathways: (*a*) the isthmus tracts, (*b*) the anterior bundles, and (*c*) fiber bundles entering/leaving the lateral tips of the PB (**Figure 1*a*,*c***). In addition, more diffuse connections with other brain areas via the ventral face of the PB and the dorsal and posterior face of the CBU are made by small numbers of neurons with individual fiber trajectories. Connections with the mushroom bodies that frame the central complex on both sides are conspicuously absent, except for a single reported neuron in monarch butterflies (23).

The isthmus tracts encompass several fiber bundles passing through the isthmus, a small neuropil connection between the ventrolateral edges of the central body and the lateral complex (lateral accessory lobe and bulb). In flies they include the lateral ellipsoid tract and the FB isthmus tract (17, 105) (**Figure 1*c***). The majority of input and output projections of the central complex occurs via these pathways. The connections are topographic: The lateral and medial bulbs (previously termed lateral triangles, median olives), condensations of microglomerular synaptic complexes, are connected to the CBL, whereas subfields of the lateral accessory lobes communicate largely with the CBU (**Figure 1*a*,*c***). In the honey bee, desert locust, and monarch butterfly, parallel visual pathways from the anterior optic tubercles contact central-complex neurons in the lateral complex (23, 41, 75, 88, 89). The polarization-sensitive dorsal rim areas of the compound eyes of those insects provide specific indirect visual input via the anterior optic tract, lower unit of the anterior optic tubercle, and bulb to the CBL (**Figure 1*a***). A parallel visual pathway originating in the medulla and lobula connects to neurons of the CBU via the lateral accessory lobe. Synaptic contacts in the lateral and medial bulbs of the desert locust occur via unique microglomerular synaptic complexes with multiple active zones, presumably for strong and precisely timed synaptic transmission (113). The lateral accessory lobes are further connected to posterior brain areas; they are also invaded by intersegmental ascending and descending neurons (36, 53, 84), which provide a link to motor control centers in the ventral nerve cord.

The anterior bundles (17, 123), also termed oblique ellipsoid tracts (105), and the superior central-body tracts (superior protocerebrum-superior arch commissure; 91) connect the superior and inferior protocerebrum to the CBU. The fiber tracts project obliquely from the superior protocerebrum toward the anterior face of the central body from where neurons invade particular layers of the CBU (**Figure 1*a*,*c***).

Fascicles connecting the PB and posterior lateral protocerebrum have been documented in desert locusts and monarch butterflies (25, 28). A distinct neuropil in the posterior brain, called the posterior optic tubercle, is connected to the PB via a distinct fiber bundle (**Figure 1*a*** and **Figure 2*a*,*b***). In desert locusts, the posterior optic tubercle receives input via the posterior optic

Isthmus tracts: groups of fiber bundles connecting the lateral complex (LAL and bulb) with the central body

Lateral accessory lobe: major projection area of central-complex neurons

Bulb: condensation of microglomerular synaptic complexes lateral to the central body; in locusts the bulb is divided into two subregions, the medial bulb (previously median olive) and lateral bulb (previously lateral triangle)

tract from the accessory medulla in the optic lobe, the site of the circadian clock in the fruit fly and Madeira cockroach (9, 31, 43). In locusts and flies, additional fibers provide input from wide areas in the posterior protocerebrum (44, 58, 90). Although physiological studies provided evidence for antennal mechanosensory and chemosensory input (33, 98), as well as mechanosensory input from wings and other body parts [honey bee (33); desert locust (36)], specific sensory pathways to the central complex for these modalities have not yet been demonstrated in any insect.

Amacrine neurons: neurons lacking an axonal process (anaxonal)

Pontine neurons: neurons connecting arborization domains in two slices or in different layers of the same slice of the CBU

TB neurons: tangential neurons of the PB

TU neurons: tangential neurons of the CBU; in flies termed F neurons (fan-shaped neurons)

TL neurons: tangential neurons of the CBL; in flies termed R neurons (ring neurons)

TN neurons: tangential neurons of the noduli

Neuronal Cell Types

The central complex is innervated by a large variety of neuronal cell types. These may occur as single neurons with unique morphology or as small groups of isomorphic neurons. On the basis of principal differences in arborization patterns, four categories of neurons can be distinguished: tangential neurons, amacrine neurons, pontine neurons, and columnar neurons.

Tangential neurons have proximal ramifications outside the central complex and tangentially innervate the PB (TB neurons), particular layers in the upper (TU neurons) or lower division of the central body (TL neurons), or the noduli (TN neurons). Ramifications of TU and TL neurons usually extend through all slices of a particular central-body layer (17, 23, 28, 33, 76, 90, 91, 103, 105), but TB neurons may omit certain slices of the PB (**Figure 2*a***). With some exceptions, distinct brain areas are connected to the different central-complex subunits: (*a*) Tangential neurons of the CBL (termed TL or R neurons) have small dendritic tufts in the bulbs and form the postsynaptic elements of the bulbs' microglomeruli (113). Distinct subtypes of these neurons (TL1–3 in *S. gregaria*; R1–R4 in *D. melanogaster*) ramify in different layers/zones of the CBL/EB (17). (*b*) Tangentials of the CBU/FB have wide ramifications in the superior protocerebrum, large subfields of the LALs, and areas in the inferior lateral and ventromedial protcerebrum. (*c*) Tangentials of the PB, finally, ramify in the posterior optic tubercles or wider areas in the posterior brain (**Figure 2*b***). Ramifications outside the central complex are usually smooth but sometimes bear spines, suggesting dendritic input regions, and arborizations within the central complex are varicose or beaded, suggesting output areas. Notable exceptions are TB1 tangential neurons connecting the posterior optic tubercle and PB in desert locusts and monarch butterflies. These neurons have varicose ramifications in two slices of the bridge, which are eight slices apart and have smooth ramifications in about three different slices in each hemisphere. In *S. gregaria*, four subtypes of these neurons provide regular connections throughout all slices of the bridge (**Figure 2*a***). Similar neurons with slice-specific ramifications have also been found in *Apis mellifera* (33) and *D. melanogaster* (17, 128), but in those insects, the neurons lack projections outside the PB.

Anaxonal, amacrine neurons are rare and have been reported only from the CBU. A single neuron innervating several slices in the CBU has been identified in *S. gregaria* and amacrine neurons innervating lateral parts of the FB have been reported for *D. melanogaster* (16). Pontine neurons are intrinsic neurons of the central body. They occur only in the CBU and typically interconnect single heterolateral slices in a precise pattern. Their somata are in the pars intercerebralis. Proximal dendritic ramifications invading single or pairs of slices are connected by an axon to varicose ramifications in slices of the contralateral hemisphere that are exactly eight slices apart, giving rise to isomorphic sets of neurons. In *D. melanogaster*, *S. gregaria*, and *D. plexippus*, several subtypes were distinguished based on innervations of different layers of the CBU (17, 23, 26). In *D. melanogaster*, additional types of pontine neurons not reported in other taxa connect adjacent slices or different layers within the same slice (17, 90).

Columnar neurons have arborization domains in single or pairs of slices and interconnect slices of the PB and central body in a highly regular way. Their cell bodies are in the pars intercerebralis.

Columnar neurons have two or three distinct arborization domains. Neurons either link slices of the PB to other substructures or spare the PB and connect the CBU to the CBL (reported only in flies), noduli, lateral accessory lobe, or anterior lip. Ramifications of columnar neurons in the PB are usually spiny, suggesting that they are dendritic. A notable exception has been found in a single cell type with spiny ramifications in the CBL/EB and varicose terminals in the PB [fruit fly (17); desert locust (26); monarch butterfly (23)]. These neurons are believed to provide polarized-light visual input from the CBL to the PB in desert locusts and monarch butterflies (see below). Axonal projections of columnar neurons may extend to subfields of the lateral accessory lobe, to single layers of a nodulus, or to the anterior inferior protocerebrum. Therefore, in addition to communication between different subunits, columnar neurons can be regarded as the principal output elements of the central complex. Based on different innervation domains, some 50 different types have been estimated to be present in *S. gregaria* and about 37 in *D. melanogaster*. Most types occur as isomorphic sets of 16 neurons, one neuron per slice or multiples thereof, but certain types may be present only in particular slices. Neurites from columnar neurons give rise to the chiasmal fiber crossings between the PB and the central body or lateral accessory lobe. The scheme of right-left columnar connectivity differs among different types of neurons, but in many types, neurons innervating corresponding slices in the right and left hemispheres of the bridge (e.g., R1-L8, R2-L7) have closely adjacent (or identical) columnar domains in the central body, thereby reducing recognizable slice numbers from 16 in the PB to 8 in the central body.

DEVELOPMENT OF THE CENTRAL COMPLEX

The time of appearance of the central complex and its subunits during development varies considerably between different insect taxa (86). In hemimetabolous species (grasshoppers, crickets, cockroaches) the central complex develops during embryogenesis and is present in adult-like appearance in first instar larvae (86). In holometabolous species, the PB likewise is already present in larvae, but the central body may be completely absent in first instar larvae (*A. mellifera*, *D. melanogaster*), whereas in others (*Bombyx mori*, *Manduca sexta*, *Tenebrio molitor*) only the CBU is present. In the PB and CBU of larval *M. sexta* (13) and *T. molitor* (118, 119), neuroactive substances were detected immunocytochemically, indicating a larval function, whereas the development of the CBL is delayed until early pupal stages (40, 96). In *D. melanogaster*, the FB and PB can first be identified in the third instar larva, followed again by delayed appearance of the EB in the early pupae (127). Synaptic markers, however, are not expressed in the central body until the early pupal period (87), indicating that in *D. melanogaster* the central body is functionally an adult brain structure. Panov (86) concluded that the late development of the CBL coincides with the differentiation of compound eyes, and that the early presence of the CBU in beetles and moths but not in flies may be related to the presence of larval walking legs (106).

In *S. gregaria* and *D. melanogaster*, cell lineages giving rise to central-complex neurons have been analyzed (5, 6, 51, 87). In both species columnar and pontine neurons originate from four bilateral pairs of neuroblasts in the pars intercerebralis that produce large lineages of cells via unique intermediate neural progenitors. The outgrowing neurites from these cells form fascicles and give rise to the w-, x-, y-, and z-bundles in the posterior chiasma. Each lineage consists of two hemilineages, which finally result in the 16-fold columnar organization of the central complex. Additional neuroblasts in the pars intercerebralis, the inferior, the ventromedial, and the superior lateral cell body rind give rise to clusters of tangential neurons (51, 87, 129). Outgrowing neurites from tangential neurons cross the brain midline and interact with incoming fibers from the w-, x-, y-, and z-bundles. How topological organization within these bundles is maintained and changed

during fascicle switching to generate the columnar neuroarchitecture of the central complex is currently under investigation.

NEUROTRANSMITTERS AND NEUROPEPTIDES

Supplemental Material

Corresponding to the diversity in morphological cell types, a large number of neuroactive substances have been reported in central-complex neurons, usually by immunocytochemical or histochemical studies (**Supplemental Table 1**; follow the **Supplemental Material link** from the Annual Reviews home page at **http://www.annualreviews.org**). Glutamate and acetylcholine appear to be major transmitters in the central complex, but the identity of cholinergic and glutamatergic neurons has not been revealed in any species. Of particular functional significance may be the conserved distribution of γ-aminobutyric acid (GABA), dopamine, octopamine, and histamine across a variety of species (**Supplemental Table 1**). GABA appears to be the transmitter of many TL neurons and a few TU neurons in all species studied, including the polarization-sensitive TL neurons in desert locusts, field crickets, and monarch butterflies (e.g., 42, 45, 72, 102). Histamine and dopamine have been found in certain TU neurons with somata in the lateral pars intercerebralis (e.g., 79, 120), and octopamine has been found in unique midline neurons ascending from the subesophageal ganglion to the CBU and a pair of deutocerebral neurons invading the PB (7, 44) (**Supplemental Table 1**). The distribution of serotonin appears to be more variable and includes various types of columnar and tangential neurons (e.g., 35). Using GAL4 technology, Kasahi et al. mapped metabotropic receptors to several transmitters in the central complex of *D. melanogaster* and usually matched the distribution of their respective ligands (54).

In addition to classical transmitter substances, various neuropeptides have been detected immunocytochemically in the central complex (37, 78, 80, 81), but their distribution is often highly species specific (**Supplemental Table 1**). An exception is SIFamide, which in all insects studied is expressed in two pairs of descending neurons with cell bodies near the frontal brain midline and ramifications in certain or all subdivisions of the central complex (32, 56). Other neuropeptides may be present in columnar and/or tangential neurons (**Supplemental Table 1**). Double-label experiments demonstrated colocalization with acetylcholine (fruit fly: tachykinin, short neuropeptide F, myoinhibitory peptide), GABA (desert locust: allatostatin, tachykinin, RFamides), and serotonin (desert locust: allatostatin, allatotropin), suggesting a cotransmitter function (56, 81). The gaseous transmitter nitric oxide (NO) has been detected in diverse populations of columnar, pontine, and tangential neurons through citrulline immunostaining and NADPH-diaphorase histochemistry (63, 77, 104, 122).

In contrast to mapping studies, only few studies have addressed the functional role of neuroactive substances in the central complex. These include reports on the roles of distinct dopaminergic neurons in *D. melanogaster* in several forms of arousal (1, 57, 67, 115) and on the role of tachykinin and short neuropeptide F in modulation of locomotor behavior (55), as well as pharmacological studies on grasshoppers suggesting that acetylcholine, GABA, and NO interact in the central body to control sound production (61).

SENSORY SIGNAL PROCESSING

The central complex is a multisensory neuropil that processes a variety of visual, mechanosensory, and olfactory signals. In desert locusts, field crickets, and monarch butterflies, neurons within the central complex are sensitive to the plane of polarized light (24, 27, 28, 101, 116). During stimulation with a dorsally presented rotating polarizer, the activity of these neurons is modulated such that the electrical field vectors (*E*-vectors) eliciting an activity peak (Φ_{max}) and the *E*-vector

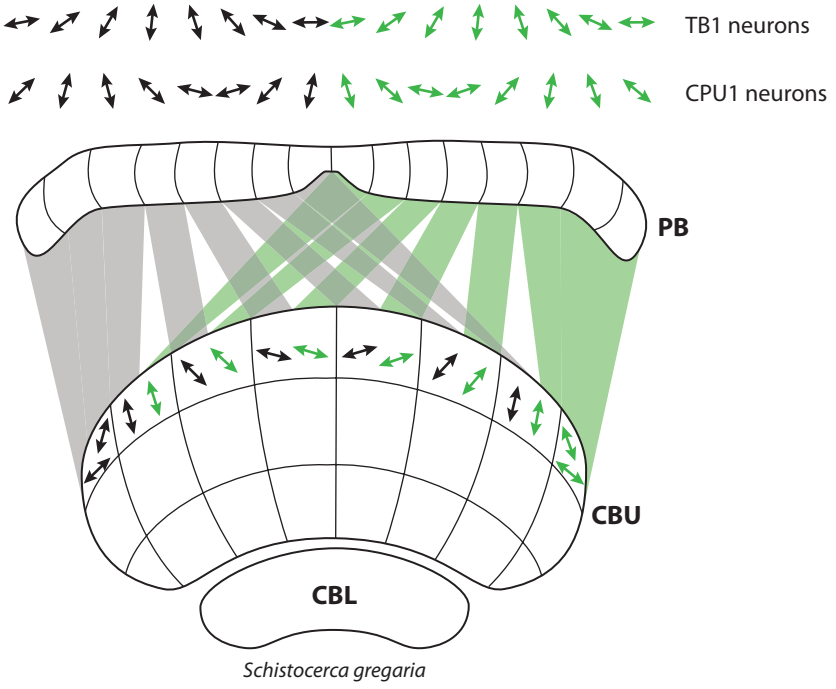

Figure 3

Topographic representation of zenithal electrical field vector (*E*-vector) preferences in the central complex of the desert locust, *Schistocerca gregaria*. In the protocerebral bridge (PB), *E*-vector tunings of TB1 tangential neurons and CPU1 columnar neurons cover a range of roughly 2 × 180°. Through right-left interactions in the upper division of the central body (CBU) the range of *E*-vector tunings is transformed by CPU1 columnar neurons to about 2 × 140°. Modified with permission from Reference 25. Abbreviation: CBL, lower division of the central body.

eliciting an activity trough (Φ_{min}) are separated by 90°. Most of these neurons display polarization opponency; i.e., they are excited at Φ_{max} and inhibited at Φ_{min}.

In desert locusts, the main input to this system is provided by the anterior polarization vision pathway, which connects the polarization-sensitive dorsal rim area of the compound eye via intercalated interneurons to the bulbs of the lateral complex, where contact to GABAergic TL neurons is established (41, 89, 113). Through the 16 slices of the PB, TB1, CPU1, CP1, and CP2 neurons constitute a polarotopic representation of preferred *E*-vector orientations (**Figure 3**). The columnar cell types occur as sets of 16 (or multiples thereof) individual neurons, each of which ramifies in a different PB slice. Preferred *E*-vector orientations of neurons in neighboring slices differ from 24° to 30°, so that the entire PB covers a range of 2 × 180° (25) (**Figure 3**). Each possible *E*-vector orientation will therefore lead to a maximum excitation of one PB slice in each brain hemisphere. The PB can be regarded as a neural substrate for instantaneous *E*-vector detection and might thus serve as an internal sky compass.

Because polarized light has a periodicity of 180°, i.e., *E*-vector orientations of 0° are identical to 180°, a polarotopic compass alone cannot unambiguously represent the entire azimuthal range of 360°. Additional information is needed to discern the solar and the antisolar hemispheres of the sky. Polarization-sensitive neurons in the central complex of monarch butterflies are also

responsive to the azimuth of an unpolarized light spot and could therefore resolve this ambiguity using spectral gradients of the blue sky (28).

rutabaga: gene coding for a calcium/calmodulin-sensitive adenylyl cyclase

foraging: gene coding for a cGMP-dependent protein kinase (PKG)

Although sky-compass cues are certainly not the only visual information processed by the central complex, other visual cues have so far received less attention. Phillips-Portillo (90) reported excitatory responses to dorsally presented unpolarized light stimuli in a variety of neurons of the EB, FB, and PB of the flesh fly *Neobellieria bullata*. Some of these neurons showed pronounced directionally sensitive responses to the translational movement of a bar. One type of ring neuron of the EB and one type of tangential neuron of the FB responded to air puffs delivered to the head in addition to visual stimuli.

Neurons of the central complex in honey bees responded to visual (lights on/off, moving gratings), mechanical (air puffs), and olfactory (geraniol) stimuli. Many of the neurons were sensitive to more than one modality (33, 73). Polarized light was not used as a stimulus in those studies.

Multisensory visual and mechanosensory responses of central-complex neurons have also been observed using intracellular recordings from the desert locust *Schistocerca gregaria* and extracellular multiunit recordings from the discoid cockroach *Blaberus discoidalis* (36, 98). TL3 neurons in *S. gregaria* respond to polarized dorsal light, to unpolarized dorsal and frontal light, and to an air flow directed at the head (36, 116). A variety of central-complex neurons in *S. gregaria* respond to looming stimuli. Some of these neurons are also sensitive to small moving objects and/or polarized light (99). In *B. discoidalis*, Ritzmann et al. investigated responses to the passive displacement of the antennae and also tested simple on/off light stimuli. Seventy-eight percent of all units responded to the visual stimulus. Of those, 58% also responded to displacement of the antennae (98).

Although single cell recordings in these different insect species provide yet another hint that the basic layout of the central complex is conserved, these results do not allow us to draw a coherent picture of the central complex in functional terms. This is owed to the different stimulus regimes used in different species. It is therefore desirable in future studies to broaden the range of stimuli in all species investigated for better interspecific functional comparability. Taken together these studies do, however, show that across different insect species a manifold of neuron types within the central complex integrate multisensory information.

VISUAL AND SPATIAL MEMORY

The role of the central complex in learning and memory has been studied predominantly in *D. melanogaster*, using mutants with structural defects in different compartments of the central body and enhancer trap lines, allowing researchers to manipulate distinct subsets of central-complex neuron populations. Several structural mutant strains are deficient in visual (66, 82, 83), olfactory (30), and gustatory (4) learning paradigms that involve a spatial component.

Operant conditioning paradigms using a flight simulator showed that the FB is involved in visual pattern memory (**Figure 4*c***). Neurons in a dorsal layer (F5 neurons) and a ventral layer (F1 neurons) of the FB are required to recognize the elevation and contour orientation of objects, respectively (**Figure 4*a*,*c***). For functional visual pattern memory, F5 neurons are required to have a functional NO system and both F1 and F5 neurons need to express the *rutabaga* gene (*rut*), which codes for a Ca^{2+}/calmodulin and G-protein-regulated adenylyl cyclase (48, 66). Experiments with a *rut* null mutant showed that *rut* expression is required not only in F1/F5 neurons, but also in R2/4m ring neurons of the EB for learning of contour orientation, elevation, and other visual features (85). Of similar importance is the expression of the *foraging* gene (*for*), which codes for a cGMP-dependent protein kinase (PKG). Expression of *for* in R2/4m neurons of the EB in for^s mutant fruit flies that normally have reduced PKG activity restores their ability to learn both

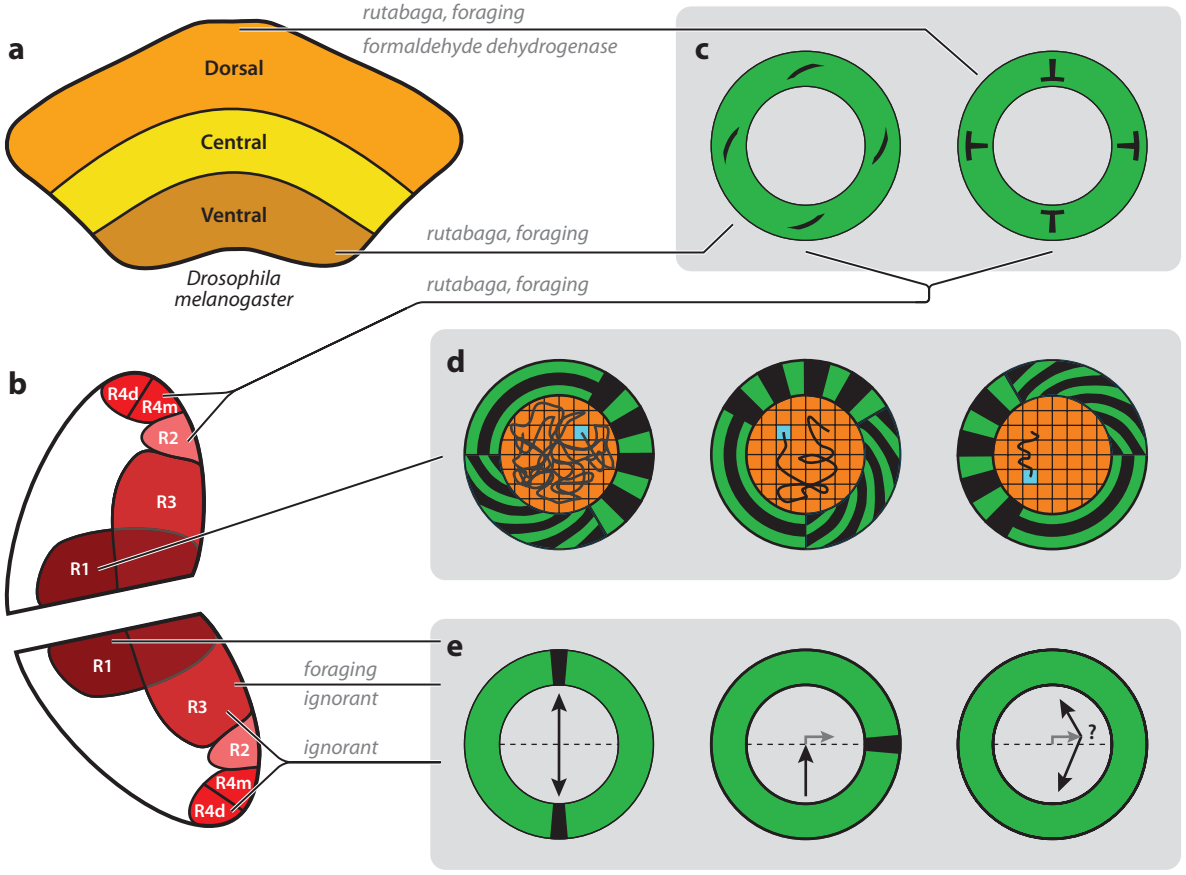

Figure 4

Layers and their functions in the *Drosophila melanogaster* central complex. (*a*) The fan-shaped body is subdivided into dorsal, central, and ventral layers. (*b*) Sagittal section through the ellipsoid body shows the spatial arrangement of the four ring neuron systems (R1–R4). (*c–e*) Schematics of visuospatial behavioral paradigms. (*c*) Arenas used to test visual memory for the parameters contour orientation (*left*) and elevation (*right*) in a closed-loop situation in tethered flying *D. melanogaster*. Neurons in a dorsal layer (F5) of the fan-shaped body are necessary to learn elevation; the parameter "contour orientation" requires neurons in a ventral layer (F1). R2/R4m neurons are required for both parameters. (*d*) *D. melanogaster* heat maze. With increasing numbers of trials (*left to right*) flies walking on a hot surface (*orange*) learn to find a cool tile (*turquoise*) using only visual cues provided by the surrounding LED arena. R1 neurons are critically important to solve this task. (*e*) Detour paradigm used to investigate spatial working memory. Flies walking back and forth between two stripes (*left*) are distracted by a third stripe appearing at a perpendicular direction when the original stripes disappear (*middle*). Upon disappearance of the distractor stripe, wild-type flies remember their original heading (*right*). R1, R3, and R3/4d neurons are required for this task. The arrows are labeled to indicate the genes required for proper function of the respective memory. Panel *a* based on data from Reference 128; panel *b* based on data from References 83, 95, and 128; panel *d* modified with permission after Reference 83; and panel *e* based on data from Reference 82.

elevation and contour orientation, whereas *for* expression in F1 or F5 neurons restores learning deficits selectively for either of the parameters (65, 117).

A different set of EB ring neurons (R1) are required for visual place learning (**Figure 4*b*,*d***). In an arena where fruit flies were challenged to find a cool tile on an otherwise hot floor, using the visual panorama as the sole orientation cue, individuals with silenced R1 neurons failed (83).

The EB is also required for spatial working memory, which can be tested by the fly's ability to remember the azimuth of a disappearing visual cue in the so-called detour paradigm (82) (**Figure 4*e***).

Silencing of R1 or R3 or R3/R4d neurons leads to a loss of spatial working memory in this paradigm (**Figure 4*b*,*e***). Rescue experiments showed that ribosomal S6 kinase (*ignorant*, $ign^{58/1}$) is critically important in R3 and/or R4d neurons for this type of memory. Expression of *for* is necessary only in R3 neurons upstream of *ignorant* (62).

***ignorant*:** gene coding for ribosomal S6 kinase II

Although most learning and memory studies on the central complex converge on visuospatial memory, there is controversial evidence for a role in consolidation of olfactory/gustatory memory. Silencing of NMDA receptor genes in R4m neurons of the EB disrupts consolidation of long-term memory in an olfactory associative conditioning paradigm (126). Krashes & Waddell (60), however, point out that the fly line used in that study (Feb170;uas-shi^{ts1}) is impaired in locomotion, failed an olfactory acuity test, and might therefore not be suited for an olfactory conditioning paradigm. Although the central complex seems to play an important role in a variety of different types of memory, the common denominator emerging from most of these studies is the representation of space.

ROLE IN MOTOR CONTROL

As suggested by its topological position in the middle of the brain, the central complex is not only a center of sensory integration but also a premotor center and serves important functions in motor control tasks, such as walking, flight, acoustic communication, and courtship. Whereas the neural firing patterns necessary for basic, straight walking are generated in central pattern generators of the thoracic ganglia, the central complex is important for the initiation and maintenance of walking activity, as well as the fine-tuning of motor patterns, e.g., unilateral alterations in stride length that lead to curve walking (reviewed in 106, 109).

In an early study by Huber (49), electrical stimulation within the central complex of crickets led to increased walking activity, whereas complete ablation decreased walking activity. Electrophysiological recordings in the discoid cockroach *Blaberus discoidalis* and the desert locust *Schistocerca gregaria* provided further evidence for the central complex's role in regulating locomotor activity. Bender et al. (3) showed that electrical activity of extracellularly recorded units in the central complex of *B. discoidalis* was correlated to and in some cases predictive of stepping frequency. In the same study the authors were able to manipulate walking speed by injecting current through the recording electrodes. Increased discharge of some central-complex neurons in desert locusts preceded wind-induced activity of flight muscles (36) and thus provided additional support for a role in motor control.

In accordance with these data, fruit flies with structural mutations of the central complex or genetically manipulated neuron populations of the central complex exhibit decreased levels of locomotor activity (92, 111), shorter activity duration (70), lower walking speed (92, 110), and a change in walking time intervals (55, 69). GAL4-targeted gene silencing and activation showed that specific tangential neurons of the central complex control activity levels and sleep-wake states, largely through dopamine signaling (1, 8, 57, 64, 67, 115). Both stress-induced arousal and ethanol-induced hyperactivity are mediated by dopamine receptors in ring neurons of the EB (57, 64). Dopaminergic neurons of the dorsal FB instead mediate wake-promoting effects (67, 115), whereas dopaminergic tangentials of the PB and central FB layer control the level of aggressiveness (1). Taken together these studies show that various forms of arousal and activity states are mediated by the central complex, largely involving dopamine signaling.

Beyond its global function of regulating arousal and locomotor activity levels, an increasing body of research reveals a role of the central complex in goal-directed locomotor behaviors. Large lesions of the *B. discoidalis* central complex resulted in abnormal turning behaviors; i.e., the animals

were unable to turn away from an obstacle or a mechanical stimulus to one antenna, or turned toward obstacles, or ran in circles (96). Extracellular recordings in tethered walking cockroaches showed that changes in firing activity of some central-complex neurons preceded changes in turning speed of a particular direction (14). *D. melanogaster* mutant flies with structural defects within the PB or the EB and FB were severely impaired in straight walking (109, 111) and showed deficits in visual flight control (50). The PB mutants *ocelliless* and *tay bridge* were impaired in a visual targeting paradigm in which the fruit flies had to surmount a gap. Although they executed the correct motor action to cross the gap, they did so into a seemingly random direction, indicating that they were not able to align their body at the proper angle with the sensory representation of the environment (114).

Although all the former publications address the role of the central complex in selecting or maintaining a direction in the horizontal plane, i.e., control of the yaw axis, there is also evidence for an involvement of the central complex in controlling the pitch axis. Focal electrolytic lesions in the cockroach brain revealed that damage within the CBL and the lateral accessory lobe led to abnormalities in block climbing or negotiation of shelf-like objects (18). In *D. melanogaster*, silencing of R1 or R3/R4d neurons of the EB led to abnormal behavior in a gravitaxis maze, in which flies walking toward a light source had to make a series of up/down decisions (2). Centrophobic behavior (i.e., the avoidance of the center zone in an arena) was enhanced following knockdown of *D. melanogaster* tachykinin in columar or tangential neurons of the FB (55).

Other behaviors in which the central complex is involved are courtship and acoustic communication. Silencing of neurons in the *D. melanogaster* FB or structural mutation within the central complex reduced courtship activity (93, 100). In the grasshopper *Omocestus viridulus*, two species of crickets (*Acheta domesticus*, *Gryllus campestris*), and the fruit fly *Drosophila melanogaster*, the central complex is involved in acoustic communication. This was first shown by Huber (49), who was able to elicit sound production by focal electric stimulation of the cricket central complex. The evoked songs were, however, atypical and never observed under natural circumstances. Similarly, structural central-complex mutants of *D. melanogaster* exhibit variable, unstable song patterns with unusual temporal properties (94). In the grasshopper *O. viridulus*, sound production can be elicited by injection of cholinergic agonists into the central body (20–22, 121). Muscarine-induced stridulation can be suppressed by injecting pharmacological agents that activate the NO/cGMP pathway (122). NO-induced inhibition of stridulation is mediated via GABAergic neurons and is believed to reside in the CBL (61).

Taken together, the central complex's motor function is the precise control of the temporal structure and amplitude of motor actions. This can be the mere control of the onset and offset of a behavior to sophisticated tasks such as the temporal control of single legs or wings for goal-directed locomotion.

COMPARISON TO VERTEBRATE BRAIN REGIONS

Two vertebrate motor control centers in the brain, the cerebellum (106, 112) and the basal ganglia (107), have been proposed to be analogous to or even share deep homology with the central complex. The central complex and cerebellum have similar roles in motor coordination, posture, and balance; both structures are characterized by highly regular, layered modular architectures that may underlie the neural basis of motor instruction wiring. Strausfeld & Hirth (107) have more recently suggested homology between the central complex and the vertebrate basal ganglia. The authors show that the development of the central complex and basal ganglia requires similar programs of gene expression and regulation, leading to commonalities

in modular neuroarchitectures. Both structures share a number of neurotransmitter systems, most prominently a rich supply of GABAergic and dopaminergic neurons, which might play similar roles in controlling motor behavior and activity levels. In contrast, there appears to be no equivalence in basal ganglia for the specific supply of the central complex with sky compass signals and its role in spatial orientation, which is rather served by the vertebrate hippocampal formation.

TOWARD A UNIFIED CONCEPT OF CENTRAL COMPLEX FUNCTION

Converging lines of research on the neuroarchitecture and fiber connections of the central complex, on sensory signal processing, and on the role of the central complex in motor control have considerably sharpened current understanding of the functional role of the central complex and suggest that this brain area serves a common basic function for a wide range of insect species. The processing of sky compass signals, documented for two orthopteroid species and the monarch butterfly, strongly points to a role of this brain area in spatial orientation. More specifically, the topographic representation of zenithal *E*-vector tunings in the slices of the PB in the desert locust suggests that azimuthal space is represented in the slices of the central complex, which would allow the animals to monitor and control heading directions relative to solar azimuth. This finding lends strong support to the hypothesis that the central complex is the site of an internal sun compass used in seasonal migrations and for homing (39, 71). An intriguing addition to this concept, based on data from *D. melanogaster*, is strong evidence for a role in place and landmark learning, pointing to particular systems of tangential neurons (fan-shaped neurons, ring neurons) of the central body as crucial elements (66, 83). Many tangential neurons may therefore represent particular landmark or object parameters that give rise to a memory trace when interacting with columnar elements at a particular slice/azimuth. Columnar neurons are the principal outputs of the central complex and, as an ensemble, apparently control the right-left balance of descending motor control pathways in flight and walking. It is conceivable that other aspects of spatial orientation, such as path integration, are likewise computed in the central-complex network, but experimental evidence is presently not at hand. Nevertheless, network models computing path integration that show striking resemblance to central-complex architectures have already been proposed (15, 19, 125). Beyond a role in goal-oriented behavior, general levels of arousal and motor activity, including aggressiveness and sleep-wake states, are regulated via the central complex, largely through parallel systems of dopaminergic neurons. Evidence is based so far on data from *D. melanogaster* but, given the similarity of dopaminergic innervation in fruit flies, honey bees, and desert locusts, is probably valid across species.

Little positive evidence across species exists for a role of the central complex in chemosensory processing, which is the domain of the antennal lobe/mushroom body axis. Accordingly, there is a dearth of evidence for direct interaction between the mushroom body and the central complex. Perhaps olfactory and visually dominated spatial and memory tasks are processed in fundamentally different ways, and signals from these two brain areas may interact only at the level of descending neurons exiting the brain.

SUMMARY POINTS

1. The central complex is an assembly of midline brain neuropils in insects characterized by topographic interhemispheric connections and layered organization.

2. The late appearance of the central complex in the development of holometabolous insects concurs with the development of compound eyes and the ability for legged locomotion.
3. The central complex is involved in visual signal processing, including sky polarization signals (desert locust, field cricket, monarch butterfly) and visual object parameters (fruit fly, desert locust), and receives mechanosensory input (desert locust, discoid cockroach, honey bee).
4. Noduli appear to be present only in pterygote insects, consistent with a possible role in flight control.
5. Dopaminergic neurons of the central complex in fruit flies control states of arousal including stress-induced arousal, wakefulness, ethanol-induced hyperactivity, and aggression.
6. Genetic lesions in fruit flies and electrolytic lesions and electrical stimulations in cockroaches provide strong evidence for a role in spatial control of flight and walking.
7. Experiments on transgenic and mutant fruit flies suggest a key role of the central complex in spatial visual memory and place learning.

DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

ACKNOWLEDGMENTS

The authors are grateful to the German Science Foundation (Deutsche Forschungsgemeinschaft) and the US Air Force Office of Scientific Research for financial support.

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115. Shows that dopaminergic neurons of the dorsal fan-shaped body of *Drosophila melanogaster* are involved in the regulation of sleep-wakefulness.

124. Demonstrates through meticulous fiber reconstructions the topographic interhemispheric fiber connections and the columnar organization of the central complex.

Annual Review of Entomology

Volume 59, 2014

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