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SCIENCE DIRECT
Developmental Biology 288 (2005) 126 – 138
DEVELOPMENTAL BIOLOGY
www.elsevier.com/locate/ydbio

Are dendrites in *Drosophila* homologous to vertebrate dendrites?

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Received for publication 4 July 2005, revised 1 September 2005, accepted 9 September 2005
Available online 11 October 2005

Abstract

Dendrites represent arborising neurites in both vertebrates and invertebrates. However, in vertebrates, dendrites develop on neuronal cell bodies, whereas in higher invertebrates, they arise from very different neuronal structures, the primary neurites, which also form the axons. Is this anatomical difference paralleled by principal developmental and/or physiological differences? We address this question by focussing on one cellular model, motorneurons of *Drosophila* and characterise the compartmentalisation of these cells. We find that motorneuronal dendrites of *Drosophila* share with typical vertebrate dendrites that they lack presynaptic but harbour postsynaptic proteins, display calcium elevation upon excitation, have distinct cytoskeletal features, develop later than axons and are preceded by restricted localisation of Par6-complex proteins. Furthermore, we demonstrate in situ and culture that *Drosophila* dendrites can be shifted from the primary neurite to their soma, i.e. into vertebrate-like positions. Integrating these different lines of argumentation, we propose that dendrites in vertebrates and higher invertebrates have a common origin, and differences in dendrite location can be explained through translocation of neuronal cell bodies introduced during the evolutionary process by which arthropods and vertebrates diverged from a common urbilaterian ancestor. Implications of these findings for studies of dendrite development, neuronal polarity, transport and evolution are discussed.

Keywords: Dendrite; Compartmentalisation; Mosaic analysis; Cytoskeleton; Transmitter receptors; *Drosophila*

Introduction

Neurons in vertebrates and arthropods are functionally similar (Laurent, 1999) and are believed to have common evolutionary roots (Ghysen, 2003; Nübler-Jung and Arendt, 1994). However, nerve cords of vertebrates and arthropods are very differently organised (Fig. 1; Bullock and Horridge, 1965; Ramón y Cajal, 1909, 1911). Neuronal cell bodies in the vertebrate nerve cord lie in the synaptic core area (grey matter). They are heteromultipolar (Bullock and Horridge, 1965), i.e. two functionally and structurally distinct types of neurites (postsynaptic dendrites and presynaptic axons) emanate directly from their cell bodies. Ascending and descending axons connecting brain and spinal cord are myelinated and placed in the outer non-synaptic layer of the spinal cord (white matter). In contrast, in the arthropod nerve cord, ascending and descending axons are placed in the synaptic core area (neuropile), whereas the outer non-synaptic layer (cortex) harbours the neuronal cell bodies. These cell bodies are unipolar in their majority, each displaying usually only one primary neurite which projects into the synaptic core area (neuropile) and branches thereafter into neurites of mostly poorly defined synaptic nature.

Given these organisational differences, we have to ask to which degree unipolar and heteromultipolar neurons are structurally comparable and develop on common principles. Here, we approach this question by focussing on one cellular model, motorneurons in the *Drosophila* nerve cord, and characterise the compartmentalisation of these cells. Various features have been described for these motorneurons: they send usually one primary neurite into the neuropile from where they

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doi:10.1016/j.ydbio.2005.09.026

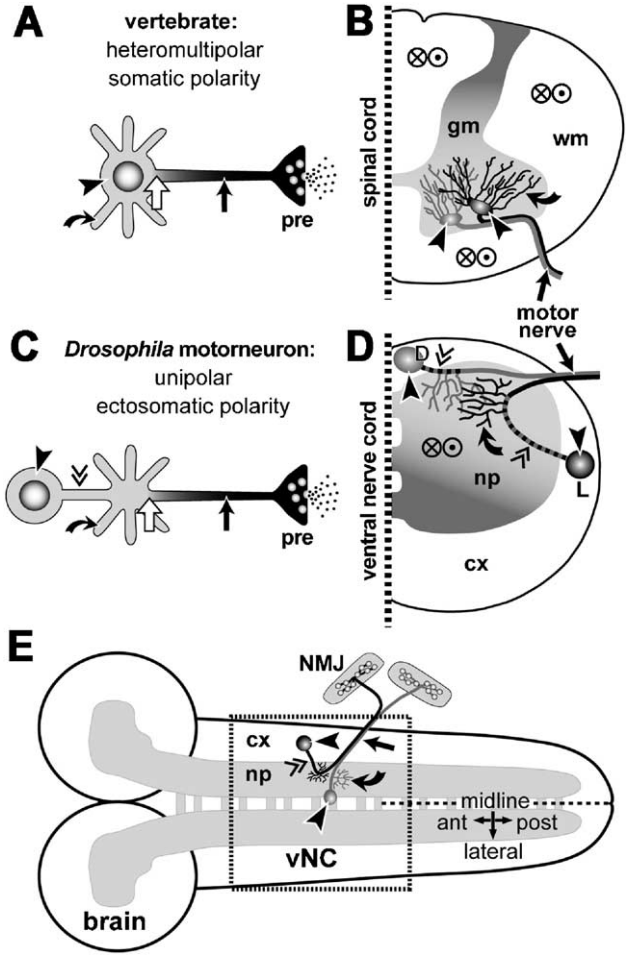

Fig. 1. Comparing motorneurons in vertebrate spinal cord and *Drosophila* ventral nerve cord. Symbols are used consistently throughout the figure. (A) A typical vertebrate neuron is heteromultipolar: postsynaptic dendrites (curved arrow) and presynaptic axon (black arrow) both emanate from the soma (arrowheads). The centre of functional polarity (axon hillock; white arrow) lies at the cell body, referred to as somatic polarity. (B) Saggital section (one body half; dashed line is midline) through the vertebrate spinal cord; somata of vertebrate neurons lie in the synaptic core area (grey matter; gm; here: two motorneurons in the ventral horn) amongst dendritic and axonal projections, whereas the outer layer (white matter; wm) harbours ascending and descending axons (circles with × or dot, respectively); the sensory input area (darker shaded) lies in the dorsal horn. (C) A typical *Drosophila* motorneuron is unipolar: only one primary neurite emanates from its cell body (double chevron) terminating in a presynaptic ending (pre) and budding off dendrites on its way through the neuropile. In analogy to motorneurons of larger insects (Burrows, 1996) and based on our results, the centre of functional polarity (spike initiation zone; white arrow) is expected to lie at the dendrite base away from the cell body (ectosomatic polarity). (D) In contrast to vertebrates, ascending and descending axons lie in the synaptic core area (neuropile, np), whereas neural somata lie in the outer layer (cortex, cx); regardless of their soma position (here: D = dorsal, L = lateral) dendrites of motorneurons are placed in the dorsal region of the neuropile, whereas the sensory input region lies ventral (Landgraf et al., 2003b). (E) Scheme of a *Drosophila* CNS in horizontal view showing the same two motorneurons as in panel B (dashed line, midline; ant, anterior; post, posterior; NMJ, neuromuscular junctions on two muscles); dashed box illustrates sector of most images shown in Figs. 2–5 and 8) and Supplementary Fig. 1.

enter the dorsal motor nerves (Fig. 1D). All motorneurons form side branches in the dorsal neuropile (Landgraf et al., 2003b). These side branches are commonly referred to as dendrites. They display tree-like shapes which could be classified as partial spherical radiation type when using nomenclature for vertebrate dendrites (Fiala and Harris, 1999; Figs. 1, 2). They are arranged into somatotopic maps which are roughly comparable to motor columns in the ventral horn of the vertebrate spinal cord (Landgraf et al., 2003a; Tsuchida et al., 1994). Thus, dendrites of *Drosophila* motorneurons and of vertebrates show similarities at the gross morphological level. But are they similar also at the molecular and developmental level? Although extensive work has been carried out on dendrites in a number of arthropods (Laurent, 1999), the available data about their molecular properties are not sufficient to address this question satisfactorily (see discussion for details). Even if they shared a wider range of molecular properties, would dendrites in both systems have to be considered analogous or homologous given their strikingly different position (on cell bodies vs. primary neurites)? These questions are of interest in the light of ongoing discussions about the evolution of vertebrates and arthropods (Ghysen, 2003; Nübler-Jung and Arendt, 1994), and they are pivotal in the context of ongoing work on dendrite formation with respect to translatability of insights from invertebrate to vertebrate models (Jan and Jan, 2003; Kim and Chiba, 2004).

Here, we show that dendrites of vertebrates and of *Drosophila* motorneurons share essential properties and are likely to share the same developmental roots. We propose that dendrites of arthropods and vertebrates are homologous and suggest modes in which they may have evolved from a common urbilaterian ancestor.

Materials and methods

Fly stocks

The following fly strains were used for this project: *OK6-Gal4* (courtesy of B. McCabe; Aberle et al., 2002; Landgraf et al., 2003a), *eve-Gal4* (*RRK* and *RN2* alleles; courtesy of J. Janes; Fujioka et al., 1999; Landgraf et al., 2003b; Löhr et al., 2002), *MzVUM-Gal4* (Landgraf et al., 2003b), *scabrous-Gal4* (Budnik et al., 1996), *elav-Gal4* (Bloomington stock centre; Luo et al., 1994), *UAS-Synaptotagmin-hemagglutinin* (*UAS-syt-HA*; courtesy of I. Robinson; Löhr et al., 2002; Robinson et al., 2002), *UAS-tau-myc* (courtesy of S. Thor; Thor et al., 1999), *UAS-GFP-α-tub84B* (courtesy of C. Boekel; Grieder et al., 2000), *UAS-GFP-Shot-L(A)* (courtesy of P. Kolodziej; Lee and Kolodziej, 2002), *UAS-nod-lacZ* (courtesy of S. Sweeney; Clark et al., 1997), *UAS-actin-GFP* (*UAS-Act5C.T:GFP*$^{127.37.2}$ and *UAS-Act5C.T:GFP*$^{127.18.4}$; Bloomington Stock Centre; Kelso et al., 2002), *UAS-mCD8-GFP* (courtesy of L. Luo; Lee and Luo, 1999), *UAS-cdc42*^{V12} (courtesy of E. Martin-Blanco; Luo et al., 1994), *UAS-Cameleon2.1* (Diegelmann et al., 2002), *UAS-homer-myc* (courtesy of U. Thomas; Diagana et al., 2002), *Df(3)Synapsin*^{97} (courtesy of E. Buchner; Godenschwege et al., 2004; Löhr et al., 2002).

Immunohistochemistry

Antibodies used in these studies are directed against Synapsin (mouse, 1:10; Klagges et al., 1996), CD8 (rat, 1:10, Caltag Laboratories), Fasciclin2 (Developmental Studies Hybridoma Bank; mouse, 1:10; VanVactor et al., 1993), haemagglutinin (HA; rat, 1:100; Boehringer-Mannheim), Lgl and Par-6 (both courtesy of J. Knoblich; rabbit, 1:100 and 1:1000, respectively; Betschinger et al., 2003; Petronczki and Knoblich, 2001), aPKC (courtesy of A. Wodarz; rabbit, 1:1000; Sigma), Bazooka (rabbit; 1:1000), GFP (Molecular Probes; rabbit, 1:200), Myc (mouse, 1:20; Calbiochem), Tubulin (mouse, 1:1000; Sigma), and β-Galactosidase (Cappel; rabbit, 1:2000), Horseradish