Review

Classical and Non-Classical Neural Communications

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Abstract

This review was constructed to show how the connectome has evolved in motor command systems from simple command elements to complex systems of neurons utilizing parallel distributed processing and the possibility of quantum entanglement between groups of neurons. Scientific and medical interest in neural pathways and their connections have driven neuroscience and brain research for many decades so that specific systems and their feedback loops have been considered in detail. We review motor command systems in invertebrate and vertebrate nervous systems, using PubMed and more generalized searches. We contemplate the attractiveness of the command neuron concept and why it has been largely superseded by parallel distributed processing (PDP) in both vertebrate and invertebrate models. Action potentials, synaptic connectivity and communication within the nervous system are extremely important to understanding basic neurological and physiological functions. However, newer concepts suggest computation within nervous systems may resemble quantum phase computation and that computational action potentials are also quantal. We suggest that a

rational form of computation that can operate according to the physiological constraints of neurons and their connectivity is essential in further evaluating neuronal interactions. We also consider recent studies that indicate that quantum entanglement may occur in the human brain. Thus some brain functions may be non-classical, most likely the phenomena of consciousness and self-awareness. The significance of this review is that future studies on motor command should not just consider the connectome but should also consider computational systems within nervous systems and the likelihood of quantum entanglement between groups of neurons not currently indicated by the connectome.

Keywords

Neurons; brain; invertebrate; vertebrate; action potentials; interneurons; command neuron concept; central pattern generators; motor neurons; parallel distributed processing; neuronal redundancy; neural computation; connectome; non-classical connections; consciousness; magnetic resonance imaging; quantum entanglement

1. Introduction

Motor command elements exist in nervous systems with many examples in both vertebrates and invertebrates. The exact nature of those elements depends on the complexity of the nervous system in question. For example human nervous systems with 86 billion neurons [1] might be expected to be differently organized from those of invertebrates such as the pulmonate mollusk *Lymnaea stagnalis* (L.) with only about 25,000 neurons [2] or the lobster *Homarus gammarus* (L) with an estimated 100,000 neurons [3]. Motor output leading to locomotion and escape behavior of many sorts is a primary function of nervous systems and in vertebrates command systems of interneurons send signals via tracts of axons in the spinal cord to activate central pattern generators to instigate movements which may then be modulated by external events and appropriate feedback systems [4]. The three major components of motor commands are: excitation, inhibition and neuromodulation [5]. Because of the relative paucity of neurons in invertebrates, it was assumed that single command interneurons could initiate some specific behaviour patterns [6], but these were often described in tethered [7] or reduced preparations such as the crayfish abdomen [8-10]. However, Wine [11] demonstrated that the tail flip's escape circuitry, although exhibiting a high degree of autonomy, had several motor systems involved, with 90 pairs of efferents and 18 pairs of interneurons participating. This implies parallel distributed processing (see below) so that no individual neuron could act as a command neuron. However, some neurons had dual behavioral functions [12], by which time they were described as "*elements in a command group*", perhaps interacting with several central pattern generators (CPGs). The command neuron concept still has adherents or at least those who use the terminology [13-15]. However, in more complex animals, many now prefer to use terms such as command-like neurons, command systems of neurons or command areas in the nervous system [4]. However command neurons are now described in insects such as the fruit fly *Drosophila melanogaster*, where a single pair of interneurons command its feeding motor program [16] and a pair of commissural command neurons have been shown to induce wing grooming [17]. Furthermore, cells that may be command neurons control walking in

the cricket *Gryllus bimaculatus* were described in 1992 [18]. Two neurons transmitting sky compass command signals to the motor center in the brain of the desert locust *Schistocerca gregaria* and numerous other descending brain neurons have been described in this animal [19]. Arguments about motor command are still lively.

Modern neuroscience concepts strongly suggest that individual neurons have a computational function [20, 21] as well as their traditional functions of communication and modulation [22]. Furthermore, the brain may function as a quantum phase computer [23]. The first evidence for quantum entanglement in the human nervous system, possibly underlying consciousness, has recently been presented [24].

2. Methodology, Resources and Literature Searches

In preparing this article we reviewed literature acquired from the NIH National Library of Medicine – PubMed- and more generalized web searches as well as W Winlow's substantial publication archive collected over 56 years from 1967. Most of the work reviewed here was from laboratories using standard electrophysiological intracellular and extracellular recording techniques, but later work uses cell culture and molecular biological techniques. The work on conscious human beings was carried out using nuclear magnetic resonance (NMR) detection and magnetic resonance imaging (MRI).

3. The Attractiveness of the Command Neuron Concept

The command neuron concept was first introduced by Wiersma and Ikeda [6] to describe specific interneurons, which when directly stimulated, were capable of generating motor actions similar to elements of normal behavior in crayfish and related species. It was suggested by Wiersma and Ikeda [6] that single neurons could alter the beat of swimmerets in crayfish. Further reports of command neurons came from a variety of sources, mainly in arthropods and mollusks (e.g. [8-10, 25-31]) the Mauthner cells in fish and amphibians (e.g. [32]) and the squid giant fiber system [33]. Many workers adhered to this conclusion and examples of command neurons have been described or assumed in the following years (e.g. [15]). However, even in invertebrates, neural redundancy occurs, where multiple neural units can have similar or identical functions, leading to questioning the command fiber concept by Kupferman and Weiss [34]. They suggested that a command neuron must be both necessary and sufficient to induce the behavior ascribed to it. In addition, a command neuron has also been defined as an interneuron "*reproducibly releases motor action resembling a major piece of normal behaviour upon stimulation. Other than a neuron early in an afferent pathway or late in an efferent pathway*" [35]. Thus a command neuron should be both necessary and sufficient and be a true interneuron, but was the definition of an "interneuron" appropriate in all cases?

The earliest examples of presumed command neurons were described in the ladder-like nerve cords of arthropods where they were easiest to find. However, they only generated incomplete segments of full behavioral repertoires. More recently hermaphrodite specific command neurons (HSNs) have been described in *Caenorhabditis elegans* [36, 37], which has only 302 neurons, all specified. The HSNs are multifunctional, both serotonergic and neuropeptidergic, and are also involved in other behaviors such as high-speed locomotion [38]. Command-like neurons may also occur in mollusks, which do not have ladder-like nervous systems, but whose torted CNS may have been derived from archetypal bilaterally symmetrical proto-mollusks [39-43] perhaps with ladder-

like cords, as in the archaeogastropod *Haliotis* [39]. However, two extremes of neural development occur in this phylum when comparing gastropods and cephalopods (see also Figure 1). As mentioned above, there is a paucity of neurons in gastropods such as *Lymnaea* (25,000 neurons) and its relatives. In contrast, the nervous systems of cephalopods such as *Octopus vulgaris* and the squid, *Sepioteuthis lessoniana,* may contain 520 million neurons – (300 million of which are in the arms- Young 1963).

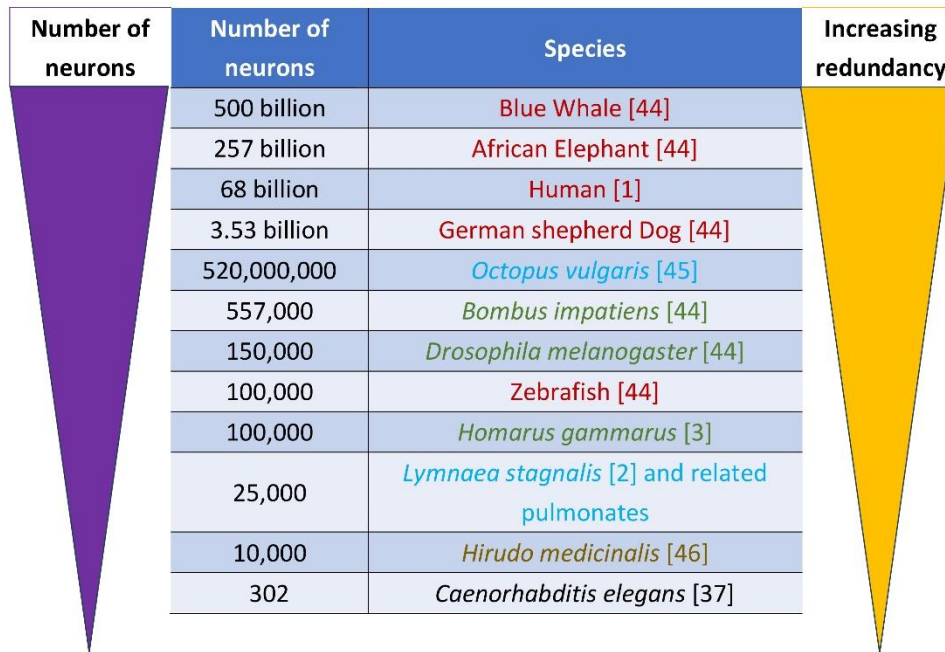| Number of neurons	Number of neurons	Species	Increasing redundancy
	500 billion	Blue Whale [44]	
	257 billion	African Elephant [44]	
	68 billion	Human [1]	
	3.53 billion	German shepherd Dog [44]	
	520,000,000	*Octopus vulgaris* [45]	
	557,000	*Bombus impatiens* [44]	
	150,000	*Drosophila melanogaster* [44]	
	100,000	Zebrafish [44]	
	100,000	*Homarus gammarus* [3]	
	25,000	*Lymnaea stagnalis* [2] and related pulmonates	
	10,000	*Hirudo medicinalis* [46]	
	302	*Caenorhabditis elegans* [37]	

Figure 1 A representation of the increasing complexity of nervous systems. As numbers of neurons increase there is a significant increase in their redundancy, reducing the requirement for individual command neurons and multiplying the number of feedback loops in the system. Colours represent animals in same phylum: Red for chordates (vertebrates); Green for arthropods; blue for molluscs; orange for the annelid *H. medicinalis* and black for the free-living nematode roundworm *C. elegans* [37, 44-46].

3.1 Gastropod Mollusks

Gastropod mollusks such as *Helix pomatia, Lymnaea stagnalis* and the related species *Helisoma trivolvis* and *Planorbis corneus* have been studied in detail because they possess neurons with giant cell bodies which are relatively easy to penetrate with glass microelectrodes. Recordings from these cells have shown their role in the control of behaviors such as feeding [47], locomotion [48, 49], respiration [50-52], defensive behaviors [53], etc. To take a specific example, in *Lymnaea stagnalis,* the giant multi-action neuron right pedal dorsal, RPeD1 [54] might be considered to be a command neuron [55, 56] as originally envisaged by Wiersma and Ikeda [6]. RPeD1 is a key component of the central respiratory generator of *Lymnaea*, which has been cultured in isolation ([57] and see Figure 2A) and which, in semi-intact preparations, can trigger the opening of the pneumostome in the absence of motor neuronal activity [55] as well as having direct synaptic connections to the motor neurons (Figure 2C). It thus acts as a motor neuron and an interneuron and participates in the

central pattern generator for aerial respiration. Thus RPeD1 fulfils the sufficiency criterion for being a command neuron, but is it also necessary to fulfil its behavioral role?
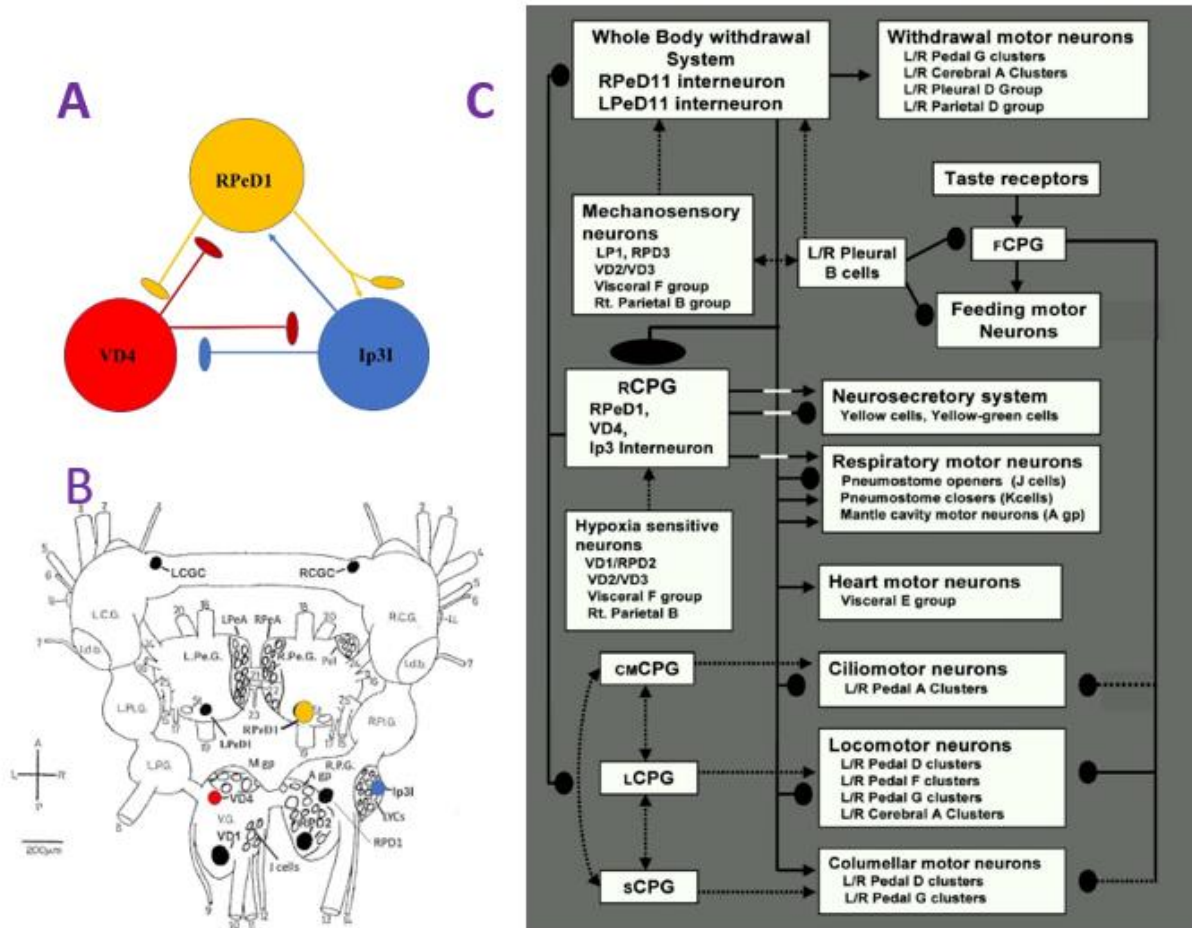

Figure 2 Connectivity in the brain of *Lymnaea stagnalis* (L.), an animal with only about 25,000 neurons in its nervous system, although its connectome is not yet completed. A) the neurons of the respiratory central pattern generator (RCPG), arrows indicate excitatory connections, while ovals indicate inhibitory connections: RPeD1- right pedal dorsal neuron 1; VD4 – visceral dorsal neuron 4; Ip3I – input 3 interneuron. B) A diagram of the brain, except for the buccal ganglia in which much of the feeding system is located. The RCPG neurons identified by colour as in A), showing its dispersed nature across three separate ganglia (modified from Winlow et al, 2018 [58]). C) A circuit diagram of the distributed, interacting systems within the brain of *Lymnaea*. Arrows again indicate excitatory synapses while ovals indicate inhibitory connections. Dotted lines indicate presumed connections. (From Winlow and Polese 2014 [43], with permission from Nova Science Publishers, Inc. and where further details can be found). FCPG, feeding CPG; CMCPG, ciliomotor CPG; LCPG, locomotor CPG; SCPG, shell movement CPG.

Experiments in Syed's laboratory in Calgary, using cell culture techniques designed to allow transplantation and functional integration of identified neurons into a host nervous system [59], have demonstrated that this is indeed the case. If the soma of RPeD1 was removed and its axons were allowed to degenerate, this significantly modified respiratory behavior. Complete ablation of

the RPeD1 cell body and all its branches by direct Pronase injection completely disrupted the respiratory rhythm [55], indicating that RPeD1 is necessary for normal respiratory behavior. Furthermore, following transplantation of a fresh RPeD1 into an animal whose original RPeD1 soma was excised and whose axons had completely degenerated, the transplanted cell reinnervated all its potential targets, allowing restoration of the respiratory rhythm [59, 60]. Thus both criteria for a command neuron can be fulfilled by a single neuron, but proving the necessity criterion is often difficult and time-consuming.

RPeD1 is not just an interneuron as it also has direct connections to motor neurons and participates in the respiratory central pattern generator, initiating its activity [56]. Indeed Davis [61] asked "Are command neurons also central pattern generators" in 1978 and RPeD1 certainly fulfils both roles. It is a constituent of the respiratory central pattern generator (RCPG) (Figure 2A), which is distributed across three ganglia within a multi-ganglionic neural network (Figure 2B, Figure 2C) [43, 62] and has been reconstructed *in vitro* [57]. The activity of the RCPG can be terminated by the action of the whole-body withdrawal neuron RPeD11 ([63] and see Figure 2C). However, it is currently unclear whether other neurons can contribute to whole animal withdrawal, which sits at the top of the behavioral hierarchy in *Lymnaea* [43, 62] and presumably in related species such as *Helisoma* and *Planorbis*.

3.2 Command Neurons in Simpler Nervous Systems

Classifying a multifunctional, multi-action neuron such as RPeD1 is difficult as it has several functions: it is an interneuron with a command element and also acts as a motor neuron. Perhaps this multifunctionality is forced upon it by the very paucity of neurons within the animal, thus driving the nervous system to develop a suitable behavioral repertoire using very few neurons. This suggests that command-like neurons most usually exist in simpler nervous systems and this view is supported by work on *C elegans* [36-38] and the medicinal leech, *Hirudo verbena,* whose CNS contains approximately 10,000 neurons [46], rather fewer than that of *Lymnaea*. *Hirudo* bilaterally paired neurons descend from the cephalic ganglion and their terminal arbors invade each of the 21 ipsilateral hemiganglia of the nerve cord. The neurons appear necessary and sufficient for intersegmental coordination during crawling [64] and, like RPeD1 in *Lymnaea*, they are multifunctional: they can command crawling or swimming movements. They are almost certainly command neurons, but detailed experiments such as those in Syed's' laboratory remain to be performed. Because of the greater neuronal redundancy in more complex nervous systems single command neurons are much less likely to exist than in simpler nervous systems, so we will now consider the situation in cephalopod mollusks, whose nervous systems are the most complex of all invertebrates [65].

3.3 Cephalopod Molluscs

Cephalopod mollusks include the decapodiform squids such as *Loligo spp* whose escape systems have been well documented [33, 66] and comprise first, second and third-order giant fibres. The two first-order neurons lie in the magnocellular lobe and integrate sensory inputs from the eyes sense organs on the tentacles, etc. These two cells have been assumed to be command interneurons [67]. They fuse in "the midline of the central paliovisceral lobe to form a chiasm where axoplasmic fusion occurs" [33, 68, 69] allowing synchronization of escape behavior on both sides of the body.

When activated they drive 2nd order giant neurons and in turn the third-order giant neurons, which are motor neurons innervating the circular muscles of the mantle [66, 70]. This system needs to be intact to facilitate fast jet propulsion swimming. Thus the first-order giant fibers have been described as command interneurons (e.g. [67]) but most of the support for this view comes from morphological and ultrastructural studies [33, 68, 71] and most electrophysiological studies have concentrated on the giant synapse between the 2nd and 3rd order neurons because of their accessibility and usefulness in understanding synaptic physiology [72]. However, even though the two first-order giant neurons can ensure bilateral, rhythmic contractions of the mantle they should not be considered command neurons because there are parallel motor axons that can generate the strong jet propulsion, associated with escape behavior, sometimes before the giant fiber system is utilized [73] and which presumably interact with them. Thus command-like multifunctional neurons may exist in smaller nervous systems but are much less likely to occur with increasing complexity, which leads to neuronal redundancy and multiple feedback mechanisms. These ideas indicate that there is much less linear neural processing in more advanced nervous systems, when compared with simpler systems with few neurons.

3.4 Command Systems of Neurons in the Vertebrates

Specific vertebrate behavior patterns are now known to be driven by command systems of neurons-see extensive review by Grillner and Manira [4]. For example the locomotor commands are generated by command centers in the mesencephalon and diencephalon, whose activities are modulated by the reticulospinal system, with simultaneous activation of respiration and cardiac output to match increased metabolic needs (see [4] for details). From here information is passed via multiple specialized command lines to specific spinal cord central pattern generators (CPGs) in practically all vertebrates (4). As sensory inputs modulate movements and gait changes the CPGs interact with one another as polymorphic neuronal ensembles as in parallel distributed processing (PDP – see below). However, one pair of vertebrate neurons have previously been classified as command neurons, the Mauthner cells of fish and amphibia [32, 74]: a pair of reticulospinal neurons involved in fish escape behaviors (the C-start) that are essential for survival by escaping predation. Further studies have shown that although the firing of Mauthner cells is correlated with escape behaviors, alternative parallel reticulospinal pathways [75] can initiate the behavior when the Mauthner cells are inactivated [76]. Thus, although important, Mauthner cells are part of a reticulospinal pathway and should not be thought of as command neurons. The Mauthner cells have become incorporated into escape behaviors in flying fish and anuran amphibians [75] and it is suspected that "*the most fundamental mechanisms for rapid motor control by the Mauthner system may extend even to mammals*" [77]. They are of phylogenetic importance [75] and it may well be that something similar happened with the giant fiber system of squids which later became incorporated into the current more complex escape system with many smaller parallel fibers. However, a recent paper by Hecker et al. 2020 [78], suggests that the M cell is essential for rapid escape behavior in zebrafish. However, following ablation of one Mauthner cell body in larval zebrafish this only becomes apparent after the giant axon has fully degenerated over many months. This directly affected survival in predator-prey assays, suggesting that if the Mauthner cells are not integrated into the escape system during development, fast escape becomes impossible, implying that "*even complex brains can trust vital functions to individual neurons*" [78]. Should the Mauthner

cells be considered command neurons, or do they normally work in parallel with other reticulospinal cells? In our view the latter supposition seems most likely, given that two separate command populations of glutamatergic neurons in the brainstem "*integrate environmental cues and hence generate flexible swimming movements to match the animal's behavioral needs*" [79] (Figure 1). In this figure animals were chosen to indicate that major differences have occurred both between and within Phyla during evolution, e.g., between the mollusks *L. Stagnalis* and *O. vulgaris*; between the arthropods *H. gammarus* and *B. impatiens*; between the Zebrafish and higher vertebrates. Animals such as the Zebrafish may represent an evolutionary situation where neural redundancy has not fully overtaken the need for individual command elements such as the Mauthner cells. The environment of each animal no doubt determines many of the specific connections in its nervous system, e.g., the zebrafish depends on the neural connections driving the C-start response for its survival.

4. Parallel Distributed Processing and Modulation of Motor Commands

Parallel distributed processing (PDP), sometimes known as connectionism, was first introduced in the 1980s by Hinton and Anderson [80] and summarised in two edited volumes by and Rumelhart and McClelland in 1986 [81]. In 1992, Kien, McCrohan and Winlow considered the basis of motor programme selection in both vertebrates and invertebrates [82]. They concluded that computation in nervous systems is usually by parallel distributed processing (PDP) rather than by command neurons, often described in reduced preparations, which were unable to behave with normal flexibility. Briefly, they suggested that:

- Small neural networks may be multifunctional when embedded in the CNS.
- In intact brains, behavioral flexibility is achieved by polymorphic neuronal ensembles of interacting networks to produce a wide range of outputs.
- Each behavior involves large numbers of neurons.
- Motor output is achieved by PDP not by single cells or nuclei, but from the complex, interacting networks in which these cells are embedded.

These concepts still appear to be relevant today. However, human findings suggest that PDP and much slower serial processing may both occur, particularly when individuals are required to perform two cognitive tasks simultaneously, due to a bottleneck at the decision stage when common circuitry is involved in both tasks [83]. A recent paper [84] suggests that sub-connections of the neocortex fluctuate and are rearranged in the first 200 ms following a visual stimulus in mice, but reach a stable format in 0.5 sec, suggesting sensory coding redundancy near the start of perception. This supports the concept of PDP. As does the Cognitive Evolution Theory (CET) proposed by Yurchenko [85] which considers consciousness to be "a discrete chain of momentary states" and that it has no special neural correlate in the brain but spreads over many brain regions. Given that the different visual stimuli arriving in the brain are divided into four very different components of color, motion, shape and depth [86], this seems an appropriate conclusion and supports the idea of PDP but does not explain consciousness and self-awareness in physiological terms. Interestingly, it has been suggested that people of high intelligence (based on IQ tests) have larger grey matter volumes in the parietal-frontal cortex than those of lesser intelligence. Such data should be treated with skepticism, but higher intelligence in healthy individuals is related to lower values of dendritic density and arborization. In addition, the brains of intelligent people show less neural activity during

testing than those of less intelligent people, perhaps using a distributed neural network of "*efficiently organized neurons and axons underlying the expression of human intelligence*" [87], supporting the PDP concept.

5. Beyond the Connectome

There is more to the physiology of nervous systems than just connectivity and endocrine and neuroendocrine adjustments must be combined with the system. For example, we now realize that action potentials have three functions within nervous systems: communication, modulation and computation [22] using phase ternary, rather than binary computation [20]. The whole point is that nervous systems are likely to be much more complex than circuit diagrams or hormonal and neurosecretory actions can predict, particularly as there is also evidence that brains may function as quantum phase computers [23], exhibiting quantum entanglement [24]. These important concepts will eventually affect our understanding of neuroethology and the organization of animal behavior. Quantum approaches may also start to crack the problem of consciousness, which is unexplained at physiological and connectivity levels. However, philosophers, psychologists and physicists have assumed the importance of quantal organization for some time [88]. Thus there is a basic divide between those neuroscientists "*who believe that the way to understanding the brain is through looking at the nerve cells*" (i.e., the connectome of various species) and those "*physicists who suggest that the laws of quantum mechanics may have an influence on the dynamics of consciousness and the mind*" [89]. However, in real neural networks individual neurons appear to act as computational elements and to participate in parallel processing using phase ternary computation [22, 23] and in the view of Winlow and Johnson 2023*, "the brain acts as a quantum phase computer and would be expected to generate multiple non-classical brain functions in terms of connectivity across a nervous system*" [90], presumably interacting with polymorphic parallel distributed neural networks to generate behavior. In analogy, the frequencies of action potentials computed in parallel may be equivalent to central pattern generation. The combination frequencies at any moment will compute as an action, as in the retina [21]. We do not presume that such interactions only occur in the brains of advanced vertebrates, but that they may also occur in cephalopod brains, whose decentralized, distributed nervous systems make them prime candidates for PDP [91]. Whether this would be the case in less complex nervous systems is unknown. However, a possibility to be considered in future studies may be found in *Lymnaea* and related gastropods, whose RCPG neurons are distributed over several ganglia (Figure 2).

We already know that quantum tunneling occurs through closed voltage-gated channels in biological membranes where small particles can cross energy barriers and may affect the resting membrane potential [92]. Thus some quantal effects are already known in nerve cells and at a psychological level quantal probability has been suggested to provide a framework for understanding reasoning and similarity [93]. Furthermore, Larson [94] suggests the primacy of quantum logic in the cognitive sciences underlying subconscious decision-making. However, until recently there was no neurophysiological evidence for these logical but unproven ideas on non-classical brain functions, although in a recent journal special issue on quantum information applied in neuroscience Georgiev [95, 96] suggested that quantum information theory should have significant utility in our understanding of neuroscience and particularly in the precise timing of action potentials [97].

6. Evidence for Non-Classical Human Brain Functions by Quantum Entanglement Between Systems

A non-classical framework for cognitive science was suggested by Horgan and Tienson [98] derived to some extent from the proposals by David Marr in 1982 [99]. However, Marr had provided a useful framework for theorizing about cognition, which had been based on classical artificial intelligence ideas of cognitive science, in terms of three levels of description: cognitive function, algorithm and physical implementation. In 1994 Horgan and Tienson generalized this into a non-classical framework involving cognitive state transitions, mathematical/functional design and physical implementation or realization. Unfortunately they argued against a computational framework for cognitive science while accepting that connectionist networks (PDP) networks were important, which seems contradictory, particularly now that we know that in real neural networks individual neurons act as computational elements [20, 22]. However, evidence favoring non-classical brain functions due to quantum entanglement has recently emerged from Trinity College, Dublin in the work of Kerskens and Perez [24], thus supporting our view that the brain uses quantum computation [23].

Quantum entanglement is a perplexing quality of quantal mechanics, suggesting that quanta once entangled can remain so over vast distances. However, entanglement cannot be directly observed and is difficult to detect experimentally, but Rappaport et al [100] indicated that it may be detected indirectly using entanglement witnesses (EW) and this was the approach taken by Kerskens and Perez [24]. They adopted an idea, based on experiments to prove the existence of quantum gravity, postulating experiments in which a known quantum system might interact with an unknown system. If those systems entangle, the unknown must also be a quantum system. They suggested that proton spins of bulk brain water could act as quantum systems. Using nuclear magnetic resonance (NMR) detection they demonstrated, in conscious human volunteers at rest that, in the absence of classical neural signals, what appeared to be heartbeat-evoked potentials were evoked in most parts of the brain using nuclear magnetic resonance (NMR) detection. The volunteers were conscious of these non-classical connections, none detectable with magnetic resonance imaging (MRI). These observations require detailed verification, but suggest that there may be quantum entanglement between systems, not previously observed directly or physiologically identified.

7. Conclusions

The organization of advanced nervous systems is highly complex and motor control resides in command systems of neurons, rather than individual command neurons which appear to occur in simpler nervous systems with restricted numbers of neurons. In these restricted nervous systems, the command elements are often multifunctional and perhaps evolved due to environmental pressures, so that their nervous systems reflect the animal's physiology, environment and behaviour.

More complex nervous systems have substantial neuronal redundancy and multiple feedback systems to multiple specialised command lines driving central pattern generators (CPGs). Computation of sensory inputs, leading eventually to motor outputs, is most likely by parallel distributed processing achieved from complex interacting networks in which the CPGs are also embedded. This may also be true in some "simpler" nervous systems. The key steps in our understanding of motor command systems are summarised in Table 1.

Table 1 Key concepts in understanding motor command systems.

Introduction of the command neuron concept	Wiersma and Ikeda, 1964 [6]
Development of the concept	e.g. Davis and Kennedy, 1972 [8-10]; Bowerman and Larimer, 1973 [28, 29]; Gillette, Kovac and Davis, 1978 [31]
Querying the concept	Kupferman and Weiss, 1978 [34]
Direct evidence for command neurons in "simpler" nervous systems	e.g. Syed et al, 1992 [59]; Lee and Syed 2004 [60]; Puhl, 2015 [64]; Brewer et al, 2019 [38]
Overlap of command neurons and command systems of neurons	Hecker et al, 2020 [78]
Command systems of neurons	e.g. Bouvier, 2015 [14]; Grillner and Manira, 2020 [4] – extensive review article
Concept of parallel distributed processing	Hinton and Anderson, 1981 [80]; Rumelhart and McLelland, 1986 [81]; Kien, McCrohan and Winlow, 1992 [82]; Yurchenko, 2022 [85]
Computational and quantal nature of action potentials	Winlow and Johnson, 2021 [22]; Johnson and Winlow, 2021 [23]
Quantum entanglement between systems of neurons	Kerskens and Perez, 2022 [24]

Although connectivity within nervous systems is vital, this may include more than just a specific connectome because even individual neurons are capable of computation and computational action potentials are considered quantal. Recently quantum entanglement between neural systems in alert humans has been postulated based on physiological evidence indicating non-classical connections between some systems.

Now, we are entering a new and exciting research phase on nervous function, particularly in nonclassical brain connections, as we further investigate the connectome which appears to be underlain by interacting neurons connected by parallel distributed processing.

Author Contributions

WW provided the conceptual framework for this review and wrote the first draft. There were then significant inputs from both ASJ and RF. ASJ helped in rewriting the manuscript.

Competing Interests

We have no conflicts of interest, financial or otherwise.

References

1. Humphries M. The spike. Princeton, NJ: Princeton University Press; 2021.
2. Fodor I, Hussein AAA, Benjamin PR, Koene JM, Pirger Z. The unlimited potential of the great pond snail, Lymnaea stagnalis. Elife. 2020; 9: e5962.
3. Fraser P. Scientists say lobsters feel no pain. Guardian; 2005. Available from: https://www.theguardian.com/world/2005/feb/08/research.highereducation.
4. Grillner S, Marina AEl. Current principles of motor control with special reference to vertebrate locomotion. Physiol Rev. 2020; 100: 270-320.
5. Johnson MD, Thompson CK, Tysseling VM, Powers RK, Heckman CJ. The potential for understanding the synaptic organization of human motor commands via the firing patterns of motoneurons. J Neurophysiol. 2017; 118: 520-531.
6. Wiersma CAG, Ikeda K. Interneurons commanding swimmeret movements in the crayfish *Procambarus clarkii* (Girard). Comp Biochem Physiol. 1964; 12: 509-525.
7. Larimer JL, Eggleston AC. Motor programs for abdominal positioning in crayfish. Z Vergl Physiol. 1971; 74: 388-402.
8. Davis WJ, Kennedy D. Command interneurons controlling swimmeret movements in the lobster: I) Types of effects on neurons. J Neurophysiol. 1972; 35: 1-12.
9. Davis WJ, Kennedy D. Command interneurons controlling swimmeret movements in the lobster: II Interaction of effects on neurons. J Neurophysiol. 1972; 35: 13-19.
10. Davis WJ, Kennedy D. Command interneurons controlling swimmeret movements in the lobster: III) Temporal relationships among bursts in different neurons. J Neurophysiol. 1972; 35: 20-29.
11. Wine JJ. The structural basis of an innate behavioural pattern. J Exp Biol. 1984; 112: 283-319.
12. Murchison D, Larimer JL. Dual motor output interneurons in the abdominal ganglia of the crayfish *Procambarus clarkii*: Synaptic activation of motor outputs in both swimmeret and abdominal positioning systems by single neurons. J Exp Biol. 1990; 150: 269-293.
13. Zelenin PV, Grilllner S, Orlovsky GN, Deliagina TG. Heterogeneity of the population of command neurons in the lamprey. J Neurosci. 2001; 27: 7793-7803.
14. Bouvier J, Caggiano V, Leiras R, Caldeira V, Bellardita C, Balueva K, et al. Descending command neurons in the brainstem that halt locomotion. Cell. 2015; 163: 1191-1203.
15. Hsu LJ, Bertho M, Kiehn O. Deconstructing modular organization and real-time dynamics of mammalian spina; locomotor networks. Nat Commun. 2023; 14: 873.
16. Flood TF, Iguchi S, Gorczyca M, White B, Ito K, Yoshihara M. A single pair of interneurons commands the drosophila feeding motor program. Nature. 2013; 499: 83-87.
17. Zhang N, Simpson JH. A pair of commissural command neurons induces drosophila wing grooming. IScience. 2022; 25: 103792.

18. Böhm H, Schildberger K. Brain neurones in the control of walking in the cricket *Gryllus bimaculatus.* J Exp Biol. 1992; 166: 113-130.

19. Staudacher EM, Cigan ML, Wenz F, Pollun A, Beck S, Beck M, et al. Organization of descending neurons in the brain of the desert locust. J Comp Neurol. 2023; 531: 1350-1380.

20. Johnson AS, Winlow W. Computing action potentials by phase interference in realistic neural networks. EC Neurol. 2017; 5: 123-134.

21. Johnson AS, Winlow W. Are neural transactions in the retina performed by phase ternary computation? Ann Behav Neurosci. 2019; 2: 223-236.

22. Winlow W, Johnson AS. Nerve impulses have three interdependent functions: Communication, modulation and computation. Bioelectricity. 2021; 3: 161-170.

23. Johnson AS, Winlow W. Does the brain function as a quantum phase computer using phase ternary computation? Front Physiol. 2021; 12: 572041.

24. Kerskens MK, Lopez DL. Experimental indications of non-classical brain functions. J Phys Commun. 2022; 6: 105001.

25. Wiersma CAG, Mill PJ. Descending units in the commissure of the crayfish central nervous system and their integration of visual, tactile and proprioceptive stimuli. J Comp Neurol. 1965; 125: 67-94.

26. Kennedy D, Evoy WH, Hanawalt JT. Release of coordinated behavior in crayfish by single central neurons. Science. 1966; 154: 917-919.

27. Winlow W, Laverack MS. The control of hindgut motility in the lobster, *Homarus gammarus* (L). 3. Structure of the sixth abdominal ganglion (6A.G) and associated ablation and microelectrode studies. Mar Behav Physiol. 1972; 1: 93-121.

28. Bowerman RF, Larimer JL. Command fibres in the circumoesophageal connectives of crayfish: I. tonic fibres. J Exp Biol. 1974; 60: 95-117.

29. Bowerman RF, Larimer JL. Command fibres in the circumoesophageal connectives of crayfish: II. Phasic fibres. J Exp Biol. 1974; 60: 119-134.

30. Burrows M. Co-ordinating interneurones of the locust which convey two patterns of motor commands: Their connexions with flight motoneurones. J Exp Biol. 1975; 63: 713-733.

31. Gillette R, Kovac MP, Davis WJ. Command neurons of Pleurobranchaea receive synaptic feedback from the motor network they excite. Science. 1978; 199: 798-801.

32. Rock MK, Hackett JT, Brown DL. Does the Mauthner cell conform to the criteria of the command neuron concept? Brain Res. 1981; 204: 21-27.

33. Young JZ. Fused neurons and synaptic contacts in the giant nerve fibres of cephalopods. Phil. Trans R Soc B. 1939; 229: 465-503.

34. Kupferman I, Weiss KR. The command neuron concept. Behav Brain Sci. 1978; 1: 3-10.

35. Bullock TH, Orkand R, Grinnell A. Introduction to nervous systems. San Francisco, USA: Freeman; 1977.

36. Badhwar R, Bagler G. Control of neuronal network in Caenorhabditis elegans. PLoS One. 2015; 10: e0139204.

37. Huang YC, Luo J, Huang W, Baker CM, Gomes MA, Byrne AB, et al. A single neuron in C. elegans orchestrates multiple motor outputs through parallel modes of transmission. bioRxiv. 2023; 2023-04. doi: 10.1101/2023.04.02.532814.

38. Brewer JC, Olson AC, Collins KM, Koelle MR. Serotonin and neuropeptides are both released by the HSN command neuron to initiate Caenorhabditis elegans egg laying. PLoS Genet. 2019; 15: e1007896.

39. Spengel JW. Die geruchsorgane und das nervensystem der mollusken: Ein beitrag zur erkenntnis der einheit des molluskentypus. Z Wiss Zool. 1881; 35: 333-383.

40. Barnes RD. Invertebrate zoology. Philadelphia, USA: WB Saunders; 1969.

41. Kandel ER. Behavioral biology of Aplysia. San Francisco, USA: WH Freeman and Co; 1979.

42. McCrohan CR, Winlow W. Interganglionic co-ordination and bilateral symmetry in the nervous systems of gastropod molluscs. In: Bilateral and Intersegmental Co-ordination. Cambridge: Cambridge University Press; 1985. Pp. 33-62.

43. Winlow W, Polese G. A neuroplastic network underlying behaviour and seasonal change in *Lymnaea stagnalis*: A neuroecological standpoint. In: Neuroecology and neuroethology in molluscs: The interface between behaviour and environment. New York: Nova Science Publishers, Inc.; 2014. Pp. 145-176.

44. Wikipedia Free Encyclopedia. List of animals by number of neurons. San Francisco: Wikimedia Foundation, Inc.; 2023.

45. Young JZ. The number and sizes of nerve cells in octopus. Proc Zool Soc Lond. 1963; 140: 229-254.

46. Puhl J. Are medicinal leeches still a useful model for studying neurophysiology? Physiol News. 2015; 99: 24-26.

47. Benjamin PR. Distributed network organization underlying feeding behavior in the mollusk Lymnaea. Neural Syst Circuits. 2012; 2: 4.

48. Winlow W, Haydon PG. Locomotion of *Lymnaea stagnalis*: A behavioural and neuronal analysis. Comp Biochem Physiol. 1986; 83A: 13-21.

49. McKenzie JD, Caunce M, Hetherington MS, Winlow W. Serotonergic innervation of the foot of the pond snail *Lymnaea stagnalis*. J Neurocytol. 1998; 27: 459-470.

50. Syed NI, Winlow W. Respiratory behavior in the pond snail Lymnaea stagnalis. I. Behavioral analysis and the identification of motor neurons. J Comp Physiol. 1991; 169: 541-555.

51. Syed NI, Winlow W. Respiratory behavior in the pond snail Lymnaea stagnalis. II. Neural elements of the central pattern generator (CPG). J Comp Physiol. 1991; 169: 557-568.

52. Bell HJ, Syed NI. Control of breathing in invertebrate model systems. Compr Physiol. 2012; 2: 1745-1765.

53. Carew TJ, Kandel ER. Inking in Aplysia californica. I. Neural circuit of an all-or-none behavioural response. J Neurophysiol. 1977; 40: 692-707.

54. Winlow W, Benjamin PR. Postsynaptic effects of a multi-action giant interneurone on identified snail neurones. Nature. 1977; 268: 263-265.

55. Haque Z, Lee TKM, Inoue T, Luk C, Hasan SU, Lukowiak K, et al. An identified central pattern-generating neuron coordinates sensory-motor components of respiratory behavior in *Lymnaea*. Eur J Neurosci. 2006; 23: 94-104.

56. Janes T, Syed NI. Evolutionary sophistication of aerial respiratory behaviour in the freshwater mollusc *Lymnaea stagnalis*. In: Neuroecology and Neuroethology of Molluscs. New York, NY: Nova Science Publisher, Inc.; 2014. pp. 175-213.

57. Syed NI, Bulloch A, Lukowiak K. In vitro reconstruction of the respiratory central pattern generator of the mollusk *Lymnaea.* Science. 1990; 250: 282-285.

58. Winlow W, Polese G, Moghadam HF, Ahmed IA, Di Cosmo A. Sense and Insensibility-Appraisal of the effects of clinical anesthetics on gastropod and cephalopod molluscs as a step to improved welfare in Cephalopods. Front Physiol. 2018; 9: 1147.

59. Syed NI, Ridgway RL, Lukowiak K, Bulloch AGM. Transplantation and functional integration of an identified neuron in Lymnaea stagnalis. Neuron. 1992; 8: 767-774.

60. Lee KM, Syed NI. Transplantation and restoration of functional synapses between an identified neuron and its targets in the intact brain of *Lymnaea stagnalis*. Synapse. 2004; 51: 186-193.

61. Davis WJ. On the trail of the command neuron. Behav Brain Sci. 1978; 1: 17-19.

62. Winlow W, Moroz LL, Syed NI. Mechanisms of behavioural selection in *Lymnaea stagnalis.* In: Neurobiology of motor programme selection: New approaches to mechanisms of behavioural choice. Oxford: Pergamon Press; 1992. pp. 52-87.

63. Inoue T, Takasaki M, Lukowiak K, Syed NI. Inhibition of the respiratory pattern-generating neurons by an identified whole-body withdrawal neuron of *Lymnaea stagnalis.* J Exp Biol. 1996; 199: 1887-1898.

64. Puhl J, Masino MA, Mesce KA. Necessary, sufficient and permissive: A single locomotor command neuron important for intersegmental coordination. J Neurosci. 2012; 32: 17646-17657.

65. Budelmann BU. The cephalopod nervous system: What evolution has made of the molluscan design. In: The nervous systems of invertebrates: An evolutionary and comparative approach. 1995; 72: 115-138.

66. Young JZ. The functioning of the giant nerve fibres of the squid. J Exp Biol. 1938; 15: 170-185.

67. Grant P, Zheng Y, Pant HC. Squid (Loligo pealei) giant fiber system: A model for studying neurodegeneration and dementia? Biol Bull. 2006; 210: 318-333.

68. Pozzo-Miller LD, Moreira JE, Llinas RR. The first order giant neurons of the giant fibre system of the squid: Electrophysiological and ultrastructural studies. J Neurocytol. 1998; 27: 419-429.

69. Martin R. The structural organization of the intracerebral giant fibre system of cephalopods. The chiasm of the first order giant axons. Z Zellforsch. 1969; 97: 50-68.

70. Wang ZY, Ragsdale CW. Cephalopod nervous system organization. In: Oxford Research Encyclopedia of Neuroscience. Oxford: Oxford University Press; 2019.

71. Gervasio A, Martin R, Miralto A. Fine structure of synaptic contacts in the first order giant fibre system of the squid. Z Zellforsch. 1971; 112: 85-96.

72. Llinas RR. The squid giant synapse: A model for chemical transmission. Oxford: Oxford University Press; 1999.

73. Otis TS, Gilly WF. Jet-propelled escape in the squid *Loligo opalescens*: Concerted control by giant and non-giant motor axon pathways. Proc Natl Acad Sci USA. 1990; 87: 2911-2915.

74. Nissanov J, Easton C, DiDomenico R. The motor output of the Mauthner cell, a reticulospinal command neuron. Brain Res. 1990; 517: 88-98.

75. Sillar KT. Mauthner cells. Curr Biol. 2009; 12: R353-R355.

76. Eaton C, Lavender WA, Wieland CM. Alternative neural pathways initiate fast-start responses following lesions of the Mauthner neuron in goldfish. J Comp Physiol. 1982; 145: 485-496.

77. Eaton C, Lee RKK, Foreman MB. The Mauthner cell and other identified neurons of the brainstem escape network in fish. Prog Neurobiol. 2002; 63: 467-485.

78. Hecker A, Schulze W, Oster J, Richter DO, Schuster S. Removing a single neuron in a vertebrate brain forever abolishes an essential behavior. PNAS. 2020; 177: 3254-3260.

79. Berg EM, Mrowka L, Bertuzzi M, Madrid D, Picton LD, Manira AEl. Brainstem circuits encoding start, speed and duration of swimming in adult zebrafish. Neuron. 2023; 111: 372-386.

80. Hinton GE, Anderson JA. Parallel modes of associative memory. Hillsdale, NJ: Erlbaum; 1981.

81. Rumelhart DE, McClelland JL. Parallel distributed processing, Volume 1: Foundations; Volume 2: Psychological and biological models. Cambridge: MIT Press; 1986.

82. Kien J, McCrohan CR, Winlow W. Epilogue: Deciding what to do next. In: Neurobiology of Motor Programme Selection. Oxford: Pergamon Press; 1992. pp. 283-285.

83. Sigman M, Dehaene S. Dynamics of the central bottleneck: Dual-task and task uncertainty. PLoS Biol. 2006; 4: e220.

84. Ebrahimi S, Lecoq J, Rumyantsev O, Tasci T, Zhang Y, Irimia C, et al. Emergent reliability in sensory cortical coding and inter-area communication. Nature. 2022; 605: 713-721.

85. Yurchenko SB. From the origins to the stream of consciousness and its neural correlates. Front Integr Neurosci. 2022; 16: 928978.

86. Hubel DH, Wiesel TN. Brain and visual perception. New York, USA: Oxford University Press Inc.; 2005.

87. Genç E, Fraenz C, Schlüter C, Friedrich P, Hossiep R, Voelkle MC, et al. Diffusion markers of dendritic density and arborization in gray matter predict differences in intelligence. Nat Commun. 2018; 9: 1905.

88. Atmanspacher H. Quantum approaches to consciousness. In: Stanford Encyclopedia of philosophy archive. Stanford, CA: Stanford Encyclopedia of Philosophy; 2020.

89. Tarlaci S. Why we need quantum physics for cognitive neuroscience. Neuroqauntology. 2010; 8: 66-76.

90. Winlow W, Johnson AS. Neuronal connectivity and non-classical brain functions. EC Neurol. 2023; 15: 45-47.

91. Mather JA, Dickel L. Cephalopod complex cognition. Curr Opin Behav Sci. 2017; 16: 131-137.

92. Qaswal AB. Quantum tunnelling of ions through closed voltage-gated channels of the biological membrane: A mathematical model and implications. Quantum Rep. 2019; 1: 219-225.

93. Trueblood JS, Pothos EM, Busemeyer JR. Quantum probability theory as a common framework for reasoning and similarity. Front Psychol. 2014; 5: 322.

94. Larson CS. Primacy of quantum logic in the natural world. J Nat Soc Philos. 2015; 11: 326-340.

95. Georgiev DD. Quantum information in neural systems. Symmetry. 2021; 13: 773.

96. Georgiev DD. Special issue on quantum information applied in neuroscience. Symmetry. 2022; 14: 1212.

97. Singh P, Sahoo P, Saxena K, Manna JS, Ray K, Ghosh S, et al. Cytoskeletal filaments deep inside a neuron are not silent: They regulate the precise timing of nerve spikes using a pair of vortices. Symmetry. 2021; 13: 821.

98. Horgan T, Tienson J. A nonclassical framework for cognitive science. Synthesise. 1994; 101: 305-345.

99. Marr D, Vision A. A computational investigation into the human representation and processing of visual information. San Francisco: Freeman and Company; 1982.

100. Rappoport TG, Ghivelder L, Fernandes JC, Guimarães RB, Continentino MA. Experimental observation of quantum entanglement in low-dimensional spin systems. Phys Rev B. 2007; 75: 054422.