Nerve cell function and synaptic mechanisms

Allan Fletcher

Abstract

Nerve cells (neurones) are 'excitable' cells that can transduce a variety of stimuli into electrical signals, continuously sending information about the external and internal environment (in the form of sequences of action potentials) to the central nervous system (CNS). Interneurones in the CNS integrate this information and send signals along output (efferent) neurones to various parts of the body for the appropriate actions to be taken in response to environmental changes. Networks of neurones have been arbitrarily classified into various nervous systems that gather and transmit sensory information and control skeletal muscle function and autonomic function, etc. The junctions between neurones (synapses) are either electrical or chemical. The former permit the direct transfer of electrical current between cells, whereas the latter utilize chemical signalling molecules (neurotransmitters) to transfer information between cells. Neurotransmitters are mainly amino acids, amines or peptides (although other molecules such as purines and nitric oxide are utilized by some cells), and can be excitatory or inhibitory. Individual neurones within the CNS may receive synaptic inputs from thousands of other neurones. Therefore, each neurone 'integrates' this vast complexity of inputs and responds accordingly (either by remaining silent or firing action potentials to other neurones). Adaptations in the function and structure of chemical synapses in particular (synaptic plasticity) are thought to underlie the mechanisms mediating cognitive functions (learning and memory).

Keywords Neurone; synapse; synaptic integration; synaptic plasticity

Royal College of Anaesthetists CPD Matrix: 1A01

Learning objectives

After reading this article, you should be able to:

- distinguish between the functions of an afferent neurone, efferent neurone and interneurone, and be able to draw and label a 'typical neurone'
- compare and contrast the origin, ionic basis and role of an end-plate potential, an excitatory post-synaptic potential and an inhibitory post-synaptic potential
- illustrate how the neurone fulfils its role of acting as an integrator of the many inputs it receives, and the role of the axon hillock in this process

Nerve cells (neurones), together with muscle cells, are 'excitable' in the sense that their plasma membranes can respond to external stimuli by generating changes in electrical potential difference across the membrane – this leads to the initiation of a self-propagating 'wave' of depolarization (the action potential; see pages 204–208 of this issue). This excitable property allows sensory (afferent) neurones to respond rapidly to changes in the internal or external environment, and to send information about these changes to the central nervous system (CNS). The human CNS contains at least 10^{11} neurones, whose functions are to integrate this vast quantity of sensory information and to issue commands via efferent neurones in order to react appropriately to environmental changes. Taking appropriate action also usually requires the recall of previous experience (i.e. CNS neurones have the ability to store information and modify behaviour accordingly – learning and memory). Junctions between neurones (and between neurones and target cells such as muscle tissue) are critically important for transferring information between cells – these junctions are termed 'synapses', and are usually chemical in nature (signalling molecules are released from one cell to initiate responses in the second cell). Changes in synaptic function are thought to underlie the cognitive functions of learning and memory. The basic nature of neuronal function and the ways in which information is passed between neurones (synaptic function) will be reviewed in this article.

Neuronal networks

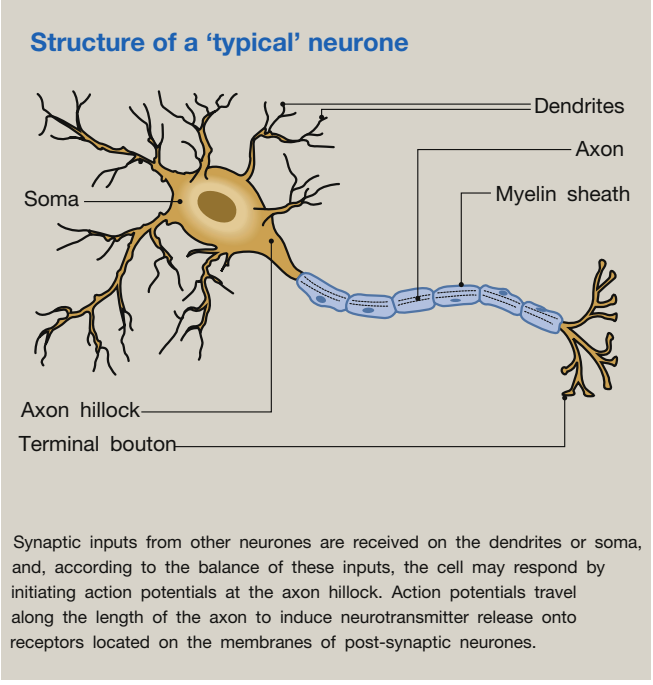
The billions of neurones within the human body are organized into complex neuronal networks that have been arbitrarily divided into different 'nervous systems' according to their main physiological roles. The broadest subdivision distinguishes the 'central nervous system' (brain and spinal cord) from the 'peripheral nervous system'. The terminology 'afferent' and 'efferent' refers, respectively, to neurones sending information into the CNS or transmitting commands out from the CNS. The peripheral nervous system comprises the autonomic nervous system (sympathetic and parasympathetic), the somatic nervous system (motor neurones controlling skeletal muscle) and systems of afferent neurones that transmit sensory information into the CNS. Functionally, the neurones constituting these nervous systems can be broadly classified as follows.

- Sensory (afferent) neurones that transduce sensory stimuli into electrical potential changes. The nature of the stimuli ranges from those of the five senses to internal stimuli such as changes in blood pressure (baroreceptors respond to changes in stretch of vascular walls) and interstitial fluid osmolarity (detected by osmoreceptors in the hypothalamus). Proprioceptors in skeletal muscle, tendons and skeletal joints continuously monitor muscle stretch and contraction and the orientation of joints.
- Interneurones in the CNS integrate information from afferent neurones, allowing information processing, storage and retrieval.
- Efferent neurones that transmit commands arising from the activity of interneurones, in order to execute appropriate reactions to external and internal stimuli.

Allan Fletcher *BSc is currently an e-tutor for the Department of Biomedical Sciences, University of Ulster, UK. Conflicts of interest: none.*

Neuronal morphology

As a reflection of the many different specialist functions of neurones throughout the body's nervous systems, the shape and size of these specialized cells varies enormously. However, most neurones have many common morphological features that we can consider in a 'typical' neurone, for example a spinal motor neurone (Figure 1). Neurones have a 'polar' structure such that one end of the cell is specialized to receive incoming information from other neurones, and the other end makes synaptic contacts in order to transmit information to other (post-synaptic) cells. The roughly spherical central part of a 'typical' neurone, which contains the cell nucleus, is the soma, and is about 20 μm in diameter. Dendrites are processes extending out from the soma that receive synaptic input from pre-synaptic neurones. According to the activity of these pre-synaptic neurones, an action potential (or a train of action potentials) may be triggered in a 'typical' neurone. These action potentials travel along the axon — a long process (emerging from the soma) that divides into terminal branches, each of which forms a synapse with a post-synaptic cell (another neurone or, in the case of a motor neurone, a skeletal muscle cell). The initial portion of the axon where it emerges from the soma is called the axon hillock — this is an important region of the plasma membrane because it is where the action potential is usually initiated, depending on the balance of the inputs of many pre-synaptic neurones (see below). The axons of most neurones are myelinated (i.e. they are wrapped in an insulating sheath, consisting mainly of myelin [a lipoprotein], which is formed by glial cells [Schwann cells or oligodendrocytes in the peripheral or central nervous systems, respectively]). The myelin sheath is discontinuous such that it is separated into segments, approximately 1 mm long, by nodes of Ranvier. Myelination allows action potentials to travel much more rapidly along the length of the axon by saltatory conduction (see pages 204–208 of this issue). The speed of action potential propagation is a crucial aspect of nervous system function — the basic survival of an organism depends on its ability to respond rapidly to environmental changes. This, in turn, is determined by the rates of information transfer between neurones. In general, the larger the diameter of an unmyelinated axon, the faster it can conduct action potentials. Myelination permits smaller-diameter axons to conduct action potentials more rapidly. Large-diameter myelinated axons in the human body can conduct action potentials at speeds of over 100 m/second, whereas small-diameter unmyelinated fibres (e.g. C fibres, which transmit some types of pain signals) may operate at conduction speeds of only 0.5–2 m/second.



Synaptic inputs from other neurones are received on the dendrites or soma, and, according to the balance of these inputs, the cell may respond by initiating action potentials at the axon hillock. Action potentials travel along the length of the axon to induce neurotransmitter release onto receptors located on the membranes of post-synaptic neurones.

Figure 1

The synapse

The connections, or junctions, between neurones are termed synapses. Although there are many neurones in the body, the true complexity of the body's central nervous system is reflected particularly in the astonishing total number of interconnections, or synapses, between neurones. The human brain comprises approximately 10^{11} neurones, each of which may receive thousands of synaptic contacts from other neurones, such that the cerebral cortex alone probably contains at least 10^{14} synapses. Modifications in synaptic function (so-called 'synaptic plasticity') are believed to underlie the brain's most complex and advanced functions (learning, memory and 'thinking'). Most synapses are 'chemical' in the sense that intercellular communication is achieved by the release of signalling molecules; however, the contact between some cells is sufficiently intimate to allow the formation of electrical synapses where the direct intercellular passage of ionic current occurs.

Electrical synapses

Electrical synapses are found in the CNS and occur at specialized intercellular contact regions called gap junctions where the membranes of the two cells involved are separated by only approximately 3 nm. Integral membrane proteins called connexins combine to form channels (connexons, each comprising six connexins) in each cell membrane. The connexons of the two cells are aligned to form gap junction channels that span the gap between the cells and allow the direct passage of ions from one cell to the other (Figure 2). The two cells are said to be electrically coupled — an action potential arriving from one cell acts extremely rapidly to induce a potential change (post-synaptic potential; PSP) in the second cell. The potential change caused by current flowing through an electrical synapse is small, so several synapses on the same cell must be active simultaneously in order to trigger an action potential (an example of synaptic integration). One of the main functions of electrical synapses is thought to be the synchronization of the activity of groups of neurones (or glial, cardiac muscle, epithelial or liver cells which can also form gap junctions).

Chemical synapses

At a chemical synapse the terminal of an axon branch is expanded into a terminal bouton where the chemical signalling molecules (neurotransmitter) are synthesized and packaged in spherical membrane vesicles awaiting release. Between the