

Pain

Benefits and control

Although we would rather avoid experiencing pain, in most circumstances it is an extremely important sensation, signalling potential or actual tissue damage. It urges us to act to prevent or minimise that damage. In this article Shelley Davies outlines how nerves work and describes how pain activates the nervous system and tells the brain about injury to the body, a topic she is researching.

The nervous system coordinates and controls rapid activities of the body, especially those involving interactions with the outside world. Figure 1 shows the various parts of the nervous system and also how information flows around it.

NERVE CELLS

Information is rapidly transferred around the nervous system via nerve cells, or **neurones** (see

Figure 2), separated from each other by a microscopic gap — the **synaptic cleft**. A neurone has two major functions:

- When *stimulated* it generates a nerve impulse (see Box 1, page 16) along its axon.
- It transmits this signal from one neurone to another neurone across the synaptic cleft, or to effector cells (in muscles or glands) which show a *response*.

SHELLEY DAVIES

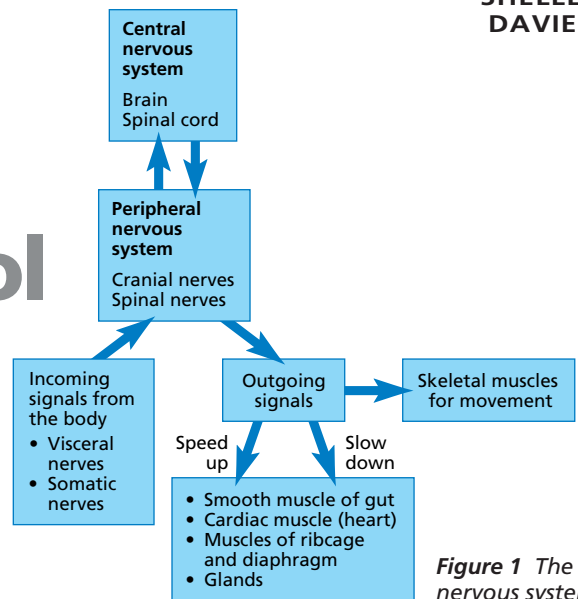


Figure 1 The nervous system.

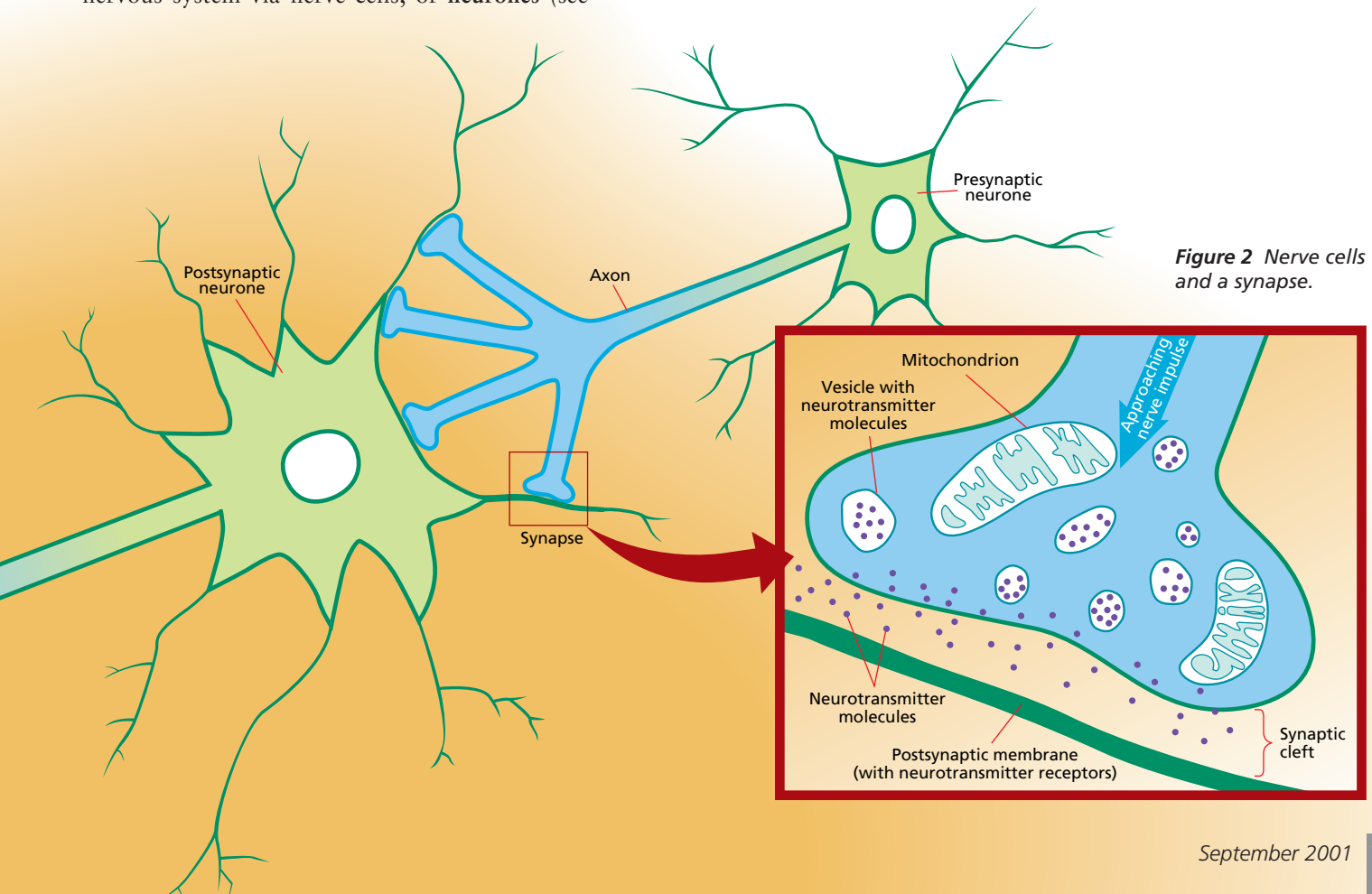


Figure 2 Nerve cells and a synapse.

BOX 1 NERVE IMPULSES

When a nerve cell is at rest there are greater numbers of positively-charged ions outside the axon membrane than inside (Figure 3). When the nerve is stimulated, channels made of protein open up and sodium and potassium ions move across the membrane. A local current flows. This prompts changes in the next section of membrane and so on, carrying the impulse along the cell (Figure 3). Normal distribution of ions is re-established promptly by pumping them back across the membrane.

Research on damaged nerves

When a nerve is damaged it becomes spontaneously active, without normal stimulation. This results in abnormal sensations of pain. I am carrying out research on the possible mechanisms of this **neuropathic** (nerve injury) pain. It can result from trauma, diseases such as diabetes, or late-stage cancer. The pain experience can range from mild to excruciating. Indeed, some patients are unable to work or walk or sleep; some can hardly wear clothes because contact with the skin feels like unbearable burning.

Unfortunately neuropathic pain cannot be relieved by standard painkillers like aspirin and paracetamol. Various ways of dealing with it are described in Table 3. Local anaesthetics relieve pain by preventing sodium ions moving through the membrane. This means that a nerve impulse cannot pass. Recently scientists have identified a number of different types of sodium ion channels. My research involves looking at how these different sodium channels change following nerve injury. I am trying to find out how they are involved in neuropathic pain. By identifying specific targets involved in neuropathic pain we can develop new drugs that promise great benefits for patients suffering from nerve injuries.

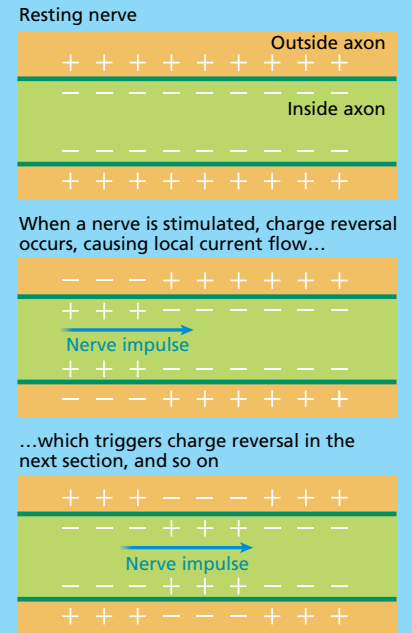


Figure 3 How nerve impulses work.

Table 1 Neurotransmitters

Neurotransmitter	Comments
Acetylcholine	Transmits signals to muscles. Nerve gases and some insecticides <i>prolong</i> its effect, leading to spasm. Some snake venoms <i>inhibit</i> its release, leading to paralysis
Noradrenaline	A feel-good neurotransmitter. Release is <i>enhanced</i> by amphetamines. Removal is <i>blocked</i> by some anti-depressant drugs and by cocaine
Dopamine	As for noradrenaline. Parkinson's disease is caused by dopamine deficiency in the brain
Serotonin	Plays a role in sleep, appetite, nausea, migraines and the regulation of mood. Activity is blocked by LSD. Re-uptake is blocked by drugs such as Prozac that alleviate anxiety and depression
Endorphins	Dull the senses, reducing pain. Their effects are mimicked by morphine, heroin and methadone

At a synapse, chemicals called **neurotransmitters** bridge the gap. They are synthesised in the nerve ending and stored in membrane-bound vesicles. When a nerve impulse arrives at the terminal it stimulates the release of neurotransmitter molecules into the cleft. The neurotransmitters diffuse across the synaptic cleft and bind briefly to receptor molecules on the surface of the next neurone. There are different types of receptor — some initiate a new nerve impulse, some inhibit this.

Once the neurotransmitter has done its job it must be removed. It is either quickly pumped back into the presynaptic nerve terminals, or destroyed by enzymes near the receptors, or diffuses into the surrounding area and is destroyed.

Neurotransmission involves many stages and chemicals, so it is perhaps no surprise that drugs can modify the process. Some, such as hallucinogens, cause adverse effects. Many neurological and psychiatric diseases involve problems of neurotransmission, which can sometimes be corrected by the

use of drugs, such as antipsychotics. Table 1 lists some neurotransmitters, together with the way in which various substances affect them.

PAIN

Pain is nature's way of telling the brain about injury to the body. So, how do painful stimuli such as toothache activate the nervous system?

There are specialised receptors in the skin and internal organs that are sensitive to painful stimuli. These receptors are called **nociceptors**. Nociception is the response of the nervous system to painful stimulation. There are four basic types of nociceptors (Table 2). The two most commonly involved in pain production are the chemical and mechanical nociceptors.

Some nociceptors, clustered in sensitive areas, respond very quickly to intense stimulation. They have an insulating fatty myelin sheath, wrapped around the axon. At intervals there are gaps in the

Table 2 Types of nociceptor

Nociceptor	Function
Thermonociceptor	Responds to temperatures greater than 45°C or less than 18°C
Chemonociceptor	Stimulated by increased levels of chemicals naturally present in the body, such as lactic acid, potassium, peptides and histamine, and of foreign irritants such as insect venom
Mechanonociceptor	Requires mechanical stimulation, especially by sharp objects and physical distortion of tissues
Polymodal nociceptor	Responds to many types of unpleasant stimuli

Table 3 Pain relief

Method	Mechanism
Operations to relieve pain	A neurosurgeon may cut a nerve close to the spinal cord or cut bundles of nerves in the spinal cord to interrupt nerve pathways. After such operations patients are more likely to injure the affected area because they no longer have the protective reflexes of pain, pressure or temperature
Local anaesthetics	Block nerve impulses by decreasing the permeability of nerve membranes to sodium ions. They prevent both generation and conduction of a nerve impulse
Transcutaneous electric nerve stimulation (TENS)	Mild electric currents are applied to selected areas of the skin by two electrodes. The small electrical impulses seem to interfere with pain sensations. The current can be adjusted so that the sensation is pleasant and relieves pain. Pain relief lasts beyond the time that the current is applied
Acupuncture	Special needles are inserted into the body at certain points at specific angles and depths. Particular groups of acupuncture points are believed to control specific areas of pain sensation
Hypnosis	No one knows how hypnosis works to control pain. During hypnosis a person is very receptive to suggestions made by the hypnotist. To relieve pain, the hypnotist may suggest that pain will be gone when a person 'wakes up'

The tiny change in charge distribution as ions move can be measured and is called an **action potential**.

sheath, called nodes of Ranvier. The impulse jumps from node to node, moving at high speeds of about 20 m/s. In nociceptors without myelin sheaths conduction is slower — about 2 m/s. These fibres are responsible for the longer-lasting but duller pain which follows an initial sharp pain.

Discovery of nociceptors has led to an understanding of how pain arises. Studying nociceptors

altered by injury may result in improved methods of pain relief. Box 1 describes research into how pain may be relieved. ■

Shelley Davies studied biomedical science at Wolverhampton University. She is now doing research in neuroscience for her PhD at the University of Sheffield.

● A tremendous website for learning about the nervous system is: <http://faculty.washington.edu/chudler/neurok.html>