What happens in the brain during a migraine? And what medications can be used to treat it?

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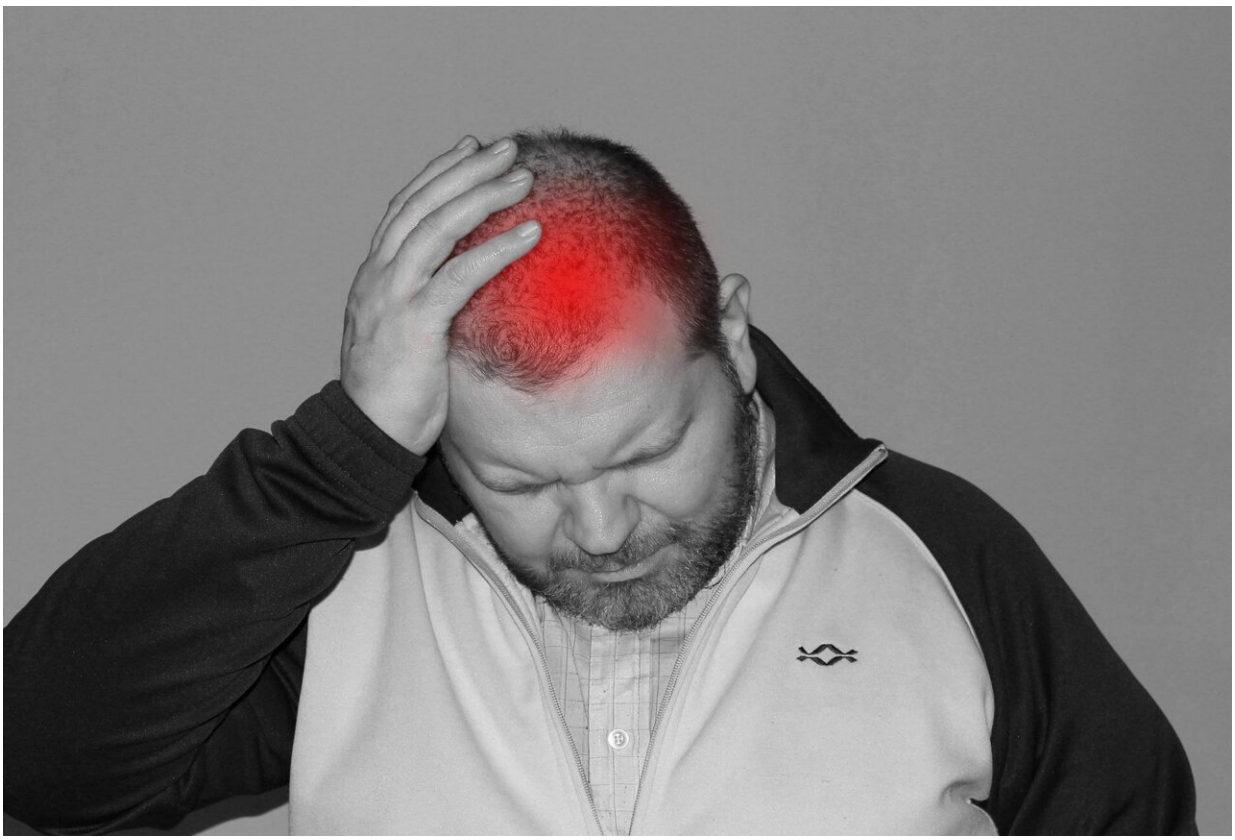

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Migraine is many things, but one thing it's not is "just a headache."

"Migraine" comes from the Greek word "hemicrania," referring to the common experience of migraine being predominantly one-sided.

Some people experience an "aura" preceding the headache phase—usually a visual or sensory experience that evolves over five to 60 minutes. Auras can also involve other domains such as language, smell and limb function.

Migraine is a disease with a huge personal and societal impact. Most people cannot function at their usual level during a migraine, and anticipation of the next attack can affect productivity, relationships and a person's mental health.

What's happening in my brain?

The biological basis of migraine is complex, and varies according to the phase of the migraine. Put simply:

The earliest phase is called the prodrome. This is associated with activation of a part of the brain called the hypothalamus which is thought to contribute to many symptoms such as nausea, changes in appetite and blurred vision.

Next is the aura phase, when a wave of neurochemical changes occurs across the surface of the brain (the cortex) at a rate of 3–4 millimeters per minute. This explains how usually a person's aura progresses over time. People often experience sensory disturbances such as flashes of light or tingling in their face or hands.

In the headache phase, the trigeminal nerve system is activated. This gives sensation to one side of the face, head and upper neck, leading to the release of proteins such as CGRP (calcitonin gene-related peptide). This causes inflammation and dilation of blood vessels, which is the

basis for the severe throbbing pain associated with the headache.

Finally, the postdromal phase occurs after the headache resolves and commonly involves changes in mood and energy.

What can you do about the acute attack?

A useful way to conceive of migraine treatment is to compare putting out campfires with bushfires. Medications are much more successful when applied at the earliest opportunity (the campfire). When the attack is fully evolved (into a bushfire), medications have a much more modest effect.

Aspirin

For people with mild migraine, non-specific anti-inflammatory medications such as high-dose aspirin, or standard dose non-steroidal medications (NSAIDS) can be very helpful. Their effectiveness is often enhanced with the use of an anti-nausea medication.

Triptans

For moderate to severe attacks, the mainstay of treatment is a class of medications called "triptans." These act by reducing blood vessel dilation and reducing the release of inflammatory chemicals.

Triptans vary by their route of administration (tablets, wafers, injections, nasal sprays) and by their time to onset and duration of action.

The choice of a triptan depends on many factors including whether nausea and vomiting is prominent (consider a dissolving wafer or an injection) or patient tolerability (consider choosing one with a slower

onset and offset of action).

As triptans constrict blood vessels, they should be used with caution (or not used) in patients with known heart disease or previous stroke.

Gepants

Some medications that block or modulate the release of CGRP, which are used for migraine prevention (which we'll discuss in more detail below), also have evidence of benefit in treating the acute attack. This class of medication is known as the "gepants."

Gepants come in the form of injectable proteins (monoclonal antibodies, used for migraine prevention) or as oral medication (for example, rimegepant) for the acute attack when a person has not responded adequately to previous trials of several triptans or is intolerant of them.

They do not cause blood vessel constriction and can be used in patients with heart disease or a previous stroke.

Ditans

Another class of medication, the "ditans" (for example, lasmiditan) has been approved overseas for the acute treatment of migraine. Ditans work through changing a form of serotonin receptor involved in the brain chemical changes associated with the acute attack.

However, neither the gepants nor the ditans are available through the Pharmaceutical Benefits Scheme (PBS) for the acute attack, so users must pay out-of-pocket, at a cost of approximately A$300 for eight wafers.

What about preventing migraines?

The first step is to see if lifestyle changes can reduce migraine frequency. This can include improving sleep habits, routine meal schedules, regular exercise, limiting caffeine intake and avoiding triggers such as stress or alcohol.

Despite these efforts, many people continue to have frequent migraines that can't be managed by acute therapies alone. The choice of when to start preventive treatment varies for each person and how inclined they are to taking regular medication. Those who suffer disabling symptoms or experience more than a few migraines a month benefit the most from starting preventives.

Almost all migraine preventives have existing roles in treating other medical conditions, and the physician would commonly recommend drugs that can also help manage any pre-existing conditions. First-line preventives include:

- tablets that lower blood pressure (candesartan, metoprolol, propranolol),
- antidepressants (amitriptyline, venlafaxine)
- anticonvulsants (sodium valproate, topiramate).

Some people have none of these other conditions and can safely start medications for migraine prophylaxis alone.

For all migraine preventives, a key principle is starting at a low dose and increasing gradually. This approach makes them more tolerable and it's often several weeks or months until an effective dose (usually 2- to 3-times the starting dose) is reached.

It is rare for noticeable benefits to be seen immediately, but with time

these drugs typically reduce migraine frequency by 50% or more.

'Nothing works for me!'

In people who didn't see any effect of (or couldn't tolerate) first-line preventives, new medications have been available on the PBS since 2020. These medications block the action of CGRP.

The most common PBS-listed anti-CGRP medications are injectable proteins called monoclonal antibodies (for example, galcanezumab and fremanezumab), and are self-administered by monthly injections.

These drugs have quickly become a game-changer for those with intractable migraines. The convenience of these injectables contrasts with botulinum toxin injections (also effective and PBS-listed for chronic migraine) which must be administered by a trained specialist.

Up to half of adolescents and one-third of young adults are needle-phobic. If this includes you, tablet-form CGRP antagonists for migraine prevention are hopefully not far away.

Data over the past five years suggest anti-CGRP medications are safe, effective and at least as well tolerated as traditional preventives.

Nonetheless, these are used only after a number of cheaper and more readily available first-line treatments (all which have decades of safety data) have failed, and this is also a criterion for their use under the PBS.

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