

The Need for Funding and Services in the Treatment of Migraine and Comorbidities

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Migraine is a widespread health issue affecting as many as 4.9 million Australians (Deloitte Access Economics, 2018). It is more common in people of working age (Blumenfeld et al., 2010) and twice as prevalent among women (Woldeamanuel & Cowan, 2017). There are two major types of migraine according to the Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition (ICHD-3; 2018). The first is migraine without aura, which is diagnosed after five long-lasting headaches accompanied by nausea/vomiting and/or photophobia and phonophobia, with at least two of the following: the headache is unilaterally-located, associated with pulsating, causes moderate-to-severe pain and is aggravated by physical activity (IHS ICHD-3, 2018). The second type includes aura (IHS ICHD-3, 2018). Aura describes a range of disorienting experiences of neurological origin, including colour flashes, tingling and light-headedness (Goadsby, 2004). For diagnosis of migraine with aura, criteria stipulate two or more attacks involving visual, sensory, speech/language, motor, brainstem and/or retinal aura symptoms and at least three of the following: aura spreading progressively over five minutes, two or more concurrent aura symptoms, long-lasting aura symptoms, one or more unilateral aura symptoms, one or more positive aura symptoms (e.g. tingling) and subsequent or simultaneous headache (IHS ICHD-3, 2018). There are also variations in aura profile and migraine chronicity, with chronic migraine (CM) consisting of headaches occurring on 15 or more days per month for over three months, while episodic migraine (EM) occurs on less than 15 (Lipton & Silberstein, 2015). Although EM is more common (Deloitte Access Economics, 2018), CM creates more personal and societal problems due to extended disability periods (Lipton & Silberstein, 2015). Indeed, approximately 30% of migraineurs have Major Depressive Disorder (MDD) and some form of anxiety disorder

(Breslau, Davis, & Andreski, 1991), which puts strain on familial relationships (Buse et al., 2016) and increases community burden (Friedman, Zhong, Gelaye, Williams, & Peterlin, 2017). Despite these effects, the aetiology of migraine and its comorbidities are still not understood (Levy, 2012). Migraine is underdiagnosed and inadequately treated (Miller & Matharu, 2014), and management methods have some way to go before migraine burden is sufficiently reduced. This document will explore the bio-psycho-social implications of migraine to show why it should receive more funding from the Victorian Government Royal Commission into Mental Health. Evidence will be presented for the need to improve pharmacological treatment options and prescription pharmaceuticals. The need for research into anti-inflammatory drugs and the necessity of pensions for improving availability of psychological treatments is also addressed.

Effects of Migraine

More studies are needed to uncover the neurobiological causes of migraine (Levy, 2012). Some research suggests ion channel dysfunction in neurons leads to neuronal hyper-excitability, thereby lowering the threshold at which nociceptive messages are propagated (Vincent & Hadjikhani, 2008). If excessive nociceptive signals are sent through the trigeminal nerve in the brainstem, they could spread to adjacent nuclei (e.g. the rostral ventromedial medulla, locus coeruleus and parts of the tegmentum) and then proliferate throughout the brain (Dahlem, 2013). Resultant hyper-excitability in the hypothalamus may explain why migraineurs often exhibit depression and anxiety, since hypothalamic pathways play a role in mood regulation and stress (Plotsky, Owens, & Nemeroff, 1998). Additionally, these brainstem triggers have been associated with widespread electrical waves that spread across the cortex in a phenomenon called cortical spreading depression (Vincent & Hadjikhani, 2008). Besides the possibility that

spreading depression causes the varied sensations of aura (Lauritzen, 1994), it is also thought to trigger the release of neuromodulators that cause inflammation in the meninges (Levy, 2012).

Besides the aforementioned neurobiological links between migraine and affective comorbidities, the psychological effects of pain itself are also significant (Deloitte Access Economics, 2018). Pain plays a major role in promoting reduced participation in social and occupational activities and can lead to financial difficulties and strained familial relationships (Buse et al., 2016). Migraine is associated with higher rates of divorce/separation and can have adverse psychological implications for children (Buse et al., 2016). A review of over 156 million hospitalisations found that migraineurs below 50 were more than two times as likely to engage in suicidal behaviours (Friedman et al., 2017). The greater societal costs of migraine cannot be overstated, either. In 2018, migraine cost the Australian health system over \$14.2 billion and was responsible for at least \$16.3 billion in lost productivity (Deloitte Access Economics, 2018). More funding is needed for research into the aetiology of migraine and associated comorbidities to minimise suffering and its extensive follow-on effects.

Management & Treatment

Migraine treatment aims to reduce pain and headache frequency, restore daily functioning and address comorbidities (Lipton & Silberstein, 2015). Although several approaches exist, few have been studied sufficiently (Sun-Edelstein & Rapaport, 2016) and many patients show wide-ranging treatment unresponsiveness (Lipton & Silberstein, 2015).

Multiple pharmacological treatments are used for preventing EM, including blood pressure medications and anticonvulsants (Lipton & Silberstein, 2015). Unfortunately, patients with CM have fewer options (Lipton & Silberstein, 2015). The only treatment available for CM prophylaxis is OnabotulinumtoxinA (Botox) injection (Sun-Edelstein & Rapoport, 2016), and

while Botox has been approved in Australia by the Therapeutic Goods Administration (Therapeutic Goods Administration, 2011), availability is limited (Miller & Matharu, 2014). Botox is thought to inhibit nociception by blocking substance P and other chemical mediators in sensory terminals (Ashkenazi & Blumenfeld, 2013). It achieved significant reduction of headache frequency and increased quality of life in a double-blind placebo-controlled trial with 705 participants (Diener, Dodick, & Aurora, 2010).

For acute migraine treatment, patients unresponsive to over-the-counter painkillers are commonly prescribed a class of pharmaceuticals called triptans, which are selective serotonin agonists thought to reduce pain by constricting cranial vasculature and decreasing inflammation (Benemei et al., 2017). Triptans were shown to have a significant effect on reducing pain, nausea, photophobia and phonophobia in a randomised placebo-controlled trial with 469 participants (Goldstein et al., 2012).

These treatments also benefit the families of migraineurs and the community by reducing interpersonal and occupational avoidance and improving daily functioning (Buse et al., 2016). Unfortunately, the efficacy of many treatments may be diminished by comorbid mental illness and patients with MDD and anxiety are often less satisfied with pharmaceuticals (Lantéri-Minet, Radat, Chautard, & Lucas, 2005). More funding is needed to expand on research and improve methods for treating CM and drug-resistant patients.

Long-term Actions & Recommendations

Emerging drugs that reduce inflammation by targeting the calcitonin gene-related peptide (CGRP) pathway may help individuals suffering from both EM and CM treat acute attacks and prevent migraine onset (Edvinsson, 2017). A randomised double-blind controlled trial with 656 participants found antagonism of the CGRP receptor significantly reduced migraine frequency

(Tepper et al., 2017). It is suggested that further investments be made into research on novel therapies, which could shorten disability periods and reduce strain on family members and communities. Allocation of resources to better inform practitioners of treatment options is also suggested, since Australian physicians may be undereducated in this area (Stark, Valenti, & Miller, 2007).

It is also recommended that disability pensions be adjusted to improve the availability of psychological treatment and that targeted advertisement be implemented to ensure migraineurs are adequately informed about available options. There are three main psychological approaches for migraine prevention and associated mental health issues: cognitive behavioural therapy (CBT), relaxation training (RT), which constitutes activities like meditation and yoga, and biofeedback (BF; Sullivan, Cousins, & Ridsdale, 2016). BF gives patients real-time physiological information, allowing them to make minor bodily adjustments to deaccelerate internal feedback mechanisms that trigger migraines (Stubberud, Varkey, McCrory, Pedersen, & Linde, 2016). A review of 24 studies examining psychological migraine interventions revealed participant improvement rates of 20-67% and reduced depression among 60%, but found no difference in effectiveness between approaches (Sullivan et al., 2016). A randomised controlled trial found the greatest reduction in migraine frequency occurred when all three approaches were combined in conjunction with prophylactic drugs (Holroyd et al., 2010). Nevertheless, there appears to be a lack of knowledge about these options among migraineurs (Lipton & Silberstein, 2015)

There is a paucity of research into migraine management at the community level. Some evidence shows chronic pain support groups can help improve functional ability, educate sufferers and address mental illness (Subramaniam, Stewart, & Smith, 1999), but further research

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is needed (Friedman et al., 2017). Since migraine remains underdiagnosed and inadequately treated (Miller & Matharu, 2014) and surveys reveal a communal lack of sympathy for migraineurs (Deloitte Access Economics, 2018), education in the community and among specialists about the impacts of migraine is of great importance.

Migraines and affective comorbidities cause substantial personal and societal burden. Chronic pain and related neurological factors result in diminished life satisfaction, disrupted relationships, reduced participation in social and occupational settings, higher rates of suicide and psychological inflictions upon others. It is recommended that the Victorian Government seriously consider allocating additional funding for the development, promotion and delivery of existing treatment options. To implement long-term solutions, it is recommended that funding be provided for additional research into new anti-inflammatory pharmaceuticals and to make psychological treatments more available.

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