Facial pain increases nausea and headache during motion sickness in migraine sufferers

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Summary
The aim of this study was to determine whether trigeminal nerve discharge associated with painful stimulation of the temple would intensify symptoms of motion sickness in migraine sufferers. If so, this would support the notion that symptoms such as nausea and headache interact with each other during attacks of migraine. Symptoms of motion sickness were rated at 2 min intervals during 15 min of optokinetic stimulation in 27 migraine sufferers and 23 age- and sex-matched controls. To document changes in frontotemporal blood flow, pulse amplitude was monitored with photoelectric pulse transducers. To induce facial pain, ice was applied to the temple for 30 s, three times at 4 min intervals during optokinetic stimulation. On another occasion, pain was induced during optokinetic stimulation by immersing the non-dominant hand in 2°C ice water for 30 s, three times at 4 min intervals. On a third occasion, measures were obtained during optokinetic stimulation alone. Migraine sufferers rated themselves as being generally more susceptible to motion sickness than controls. In addition, symptoms of motion sickness provoked by optokinetic stimulation were greater in migraine sufferers than in controls. Painful stimulation of the temple intensified nausea and headache during optokinetic stimulation, whereas painful stimulation of the hand did not. Since nausea also intensifies facial pain during motion sickness, nausea and headache may reinforce each other in a vicious circle. In the absence of painful stimulation, increases in pulse amplitude during optokinetic stimulation were greater in migraine sufferers than controls, possibly because the discomfort associated with motion sickness triggered extracranial vasodilatation in migraine sufferers as part of a fight-or-flight (defense) response. Extracranial vasodilatation did not differ between migraine sufferers and controls when ice was applied to the temple or hand during optokinetic stimulation, implying that the additional discomfort associated with painful stimulation of the head and hand evoked a defense response in controls. These findings suggest that a mechanism which boosts extracranial neurovascular reflexes to stress and which heightens symptoms of motion sickness, increases susceptibility to migraine.

Keywords: migraine; motion sickness; nausea; headache; extracranial vasodilatation

Abbreviations: DNIC = diffuse noxious inhibitory controls; SE = standard error


Introduction
Migraine sufferers are particularly susceptible to motion sickness (Barabas et al., 1983; Kayan and Hood, 1984; Golding 1998). Since vestibular disturbances are frequently associated with migraine (Kuritzky et al., 1981a; Olsson, 1991), it has been assumed that episodic ischaemia of the labyrinth during attacks of migraine damages the vestibular apparatus and increases susceptibility to motion sickness (Kuritzky et al., 1981b). However, this may not be the only link between motion sickness and migraine. We recently reported that an optokinetic effect (the illusion of movement induced by watching vertical stripes move past) provoked nausea more readily in migraine sufferers than controls (Drummond, 2002); in addition, headache and light-induced pain persisted longer after optokinetic stimulation in migraine sufferers than controls. Since this form of stimulation does not involve the vestibular apparatus, nausea and headache could not have been due to vestibulocochlear dysfunction. The similarity of symptoms during motion sickness and migraine suggests that the same mechanism contributes to
both conditions. For example, brainstem nuclei that are active during attacks of migraine (Weiller et al., 1995) might mediate nausea and headache during optokinetic stimulation (Drummond, 2002).

Alloodynia to thermal and tactile stimulation spreads from the region of headache to involve the limbs during attacks of migraine (Burstein et al., 2000). To determine whether motion sickness also influences the perception of pain, mechanical hyperalgesia was assessed in the forehead and fingertips before and after optokinetic stimulation (Drummond, 2002). Hyperalgesia increased in the forehead of the most nauseated subjects, and hyperalgesia increased in the fingertips of migraine sufferers but not controls. These findings, together with the persistence of headache and light-induced pain after optokinetic stimulation, suggest that normal inhibitory modulation of pain is disrupted in migraine sufferers during motion sickness.

Loss of normal inhibitory pain modulation may cause headache and symptoms such as photophobia to escalate in a vicious circle during attacks of migraine. In support of this hypothesis, experimentally-induced facial pain was found to increase the intensity of photophobia in migraine sufferers (Drummond and Woodhouse, 1993; Drummond, 1997). Conversely, the intensity of experimentally-induced facial pain increased after exposure to bright light (Drummond, 1997; Kowacs et al., 2001). A persistent deficit in normal inhibitory modulation of trigeminal nerve activity could account for mild photophobia in migraine sufferers during the headache-free interval (Drummond, 1986; Main et al., 1997; Vanagaite et al., 1997) and for neurophysiological signs of trigeminal sensitization (Sandrini et al., 2002).

Patients often report that nausea and headache build up together during attacks of migraine and subside after a bout of vomiting. To investigate the association between these symptoms in the present study, migraine sufferers were subjected to facial pain during optokinetic stimulation. As noted above, normal pain modulation may fail during motion sickness and migraine; in addition, migraine sufferers are particularly susceptible to motion sickness. Therefore, we hypothesized that facial pain would intensify symptoms such as nausea, dizziness and headache in migraine sufferers during optokinetic stimulation.

Trigeminal nerve discharge associated with cranial pain provokes parasympathetic vasodilator reflexes (Lambert et al., 1984; Drummond, 1992; Izumi, 1999) and perivascular neurogenic inflammation (Moskowitz, 1984; Williamson and Hargreaves, 2001). More generally, facial pain induces bilateral extracranial vasodilatation (Drummond, 1997), presumably mediated by active sympathetic vasodilatation or release of sympathetic vasoconstrictor tone as part of a fight-or-flight (defense) response coordinated in the periaqueductal gray (Bandler and Shipley, 1994). Since blood flow through dilated pain-sensitized cranial arteries is a source of pain in at least some attacks of migraine (Graham and Wolff, 1938; Drummond and Lance, 1983; Iversen et al., 1990), headache and dilatation of cranial arteries could build up in a positive loop. The scalp vessels of migraine sufferers dilate readily to painful stimulation of the face (Drummond, 1997) and the hand (Drummond and Granston, 2003). Therefore, we hypothesized that pain-induced extracranial vasodilatation would be greater in migraine sufferers than controls during optokinetic stimulation. We also explored the association between headache and changes in extracranial vasodilatation to determine whether vasodilatation mediated increases in headache.

Methods

Subjects

Participants were recruited by advertisements in local and state newspapers, from the local Migraine Support Group, and the university population. The migraine sample consisted of 22 females and five males (mean age ± SD = 40.7 ± 11.2 years; range = 20–59 years) who met International Headache Society criteria for migraine. Three patients whose attacks were sometimes preceded by a visual aura were included in the present series because, in other respects, their attacks were similar to those of the remainder of migraine without aura patients. Participants did not take prophylactic medication for migraine and had no other major medical conditions. Headache frequency averaged two per month. Five subjects took sumatriptan and three took ergotamine to relieve attacks, whereas the remainder took analgesic, anti-inflammatory, anti-emetic or caffeine-based remedies. The control group consisted of 17 females and six males (mean age = 39.7 ± 11.8 years; range = 18–62 years) who reported less than 12 headaches per year that did not meet diagnostic criteria for migraine. Analgesics, when used, relieved the headache within 20 min. Twenty-three migraine sufferers reported a family history of migraine, whereas only five control subjects had a similar family history. None of the control subjects (including those with a family history of migraine) had experienced an attack of migraine. Each participant provided informed consent for the procedures, which were approved by the Murdoch University Human Research Ethics Committee.

Experiments were carried out when subjects were free from headache for at least 4 days. Participants abstained from medication and alcohol for at least 24 h, and from food, drink and cigarettes for at least 2 h before testing. Females were tested between menstrual periods. All but four migraine sufferers and one control subject attended three sessions separated by at least 3 weeks. Two migraine sufferers began prophylactic medication after participating in one session and were not tested further, and the other two withdrew from the experiment after the first session because of prolonged headache and nausea. A control subject withdrew because of time constraints.

Subjects answered the question: "Do you regard yourself as susceptible to motion sickness?" as 'not at all' (scored as 0), 'slightly' (1), 'moderately' (2) or 'very much as' (3). They also rated how often in the past 10 years they had felt nauseated (never, rarely, sometimes, frequently or always; scored from 0–4) when travelling in cars, buses, trains, aircraft, small boats and ships, when playing on swings, roundabouts and funfair rides [these items were taken from Golding’s Motion Sickness Susceptibility Questionnaire (Golding, 1998)], when watching widescreen movies and other movement simulators (e.g. arcade games), and when reading in the car. A mean score for those items that had been experienced at least once in the past 10 years was calculated.
Procedures

The procedures were carried out in a laboratory maintained at 22 ± 1.5°C. To monitor changes in extracranial vasodilatation, photoelectric pulse transducers (photoplethysmographs, Grass Instrument Company, Quincy, IL, USA.) were attached with double-sided adhesive washers to the frontotemporal region ~4.5 cm rostral and 8.5 cm medial to the ears in the vicinity of anterior branches of the superficial temporal artery. A black elastic headband was stretched slightly and placed over the transducers to screen out changes in background illumination that would otherwise have interfered with the signal. The pulsatile component of the photoplethysmograph signal reflects changes in the calibre of cutaneous arterioles and thus mirrors changes in cutaneous blood flow (Hertzman et al., 1946; Drummond and Lance, 1981; Kamal et al., 1989). Pulses recorded from the left and right temples were sampled at 100 Hz by an MP100 Biopac Systems analogue/digital data acquisition system and displayed on a computer monitor with AcqKnowledge software (Biopac Systems, Goleta, California, USA). Beat-by-beat changes in pulse amplitude were later calculated off-line using AcqKnowledge software.

Optokinetic stimulation

To provoke symptoms of motion sickness, the subject sat on a stationary chair with his or her head and shoulders inside an illuminated drum 50 cm in diameter, 70 cm in height, and painted internally with 24 pairs of vertical black and white stripes each 3.3 cm wide (Hu et al., 1997). The drum revolved 10 × per minute for 15 min or until the subject was about to vomit. To enhance the illusion of movement created by the moving stripes, the subject was asked to focus on a distant point rather than to watch the stripes moving past. Every 2 min, the subject rated headache, nausea and dizziness on scales ranging between 0 (not at all) to 10 (extreme). In two of the sessions, optokinetic stimulation was combined with painful stimulation of the temple or hand. The session order varied randomly across subjects.

Painful stimulation of the temple

Four minutes after the start of optokinetic stimulation, the subject applied an ice block with a surface area of 12.25 cm² to the temple near the point of emergence of the superficial temporal artery in front of the ear for 30 s. The subject held onto the ice block with a short stick that was embedded in the ice. The ice was applied to the usual side of headache in migraine sufferers and to right (nine subjects) or left side (14 subjects) in controls. Shortly after the ice was removed, subjects rated headache, dizziness, nausea, and the intensity of pain during the application of the ice. In particular, subjects were asked to distinguish between the pain induced locally by the ice and headache elsewhere. The ice was applied twice more at 4 min intervals during optokinetic stimulation.

Painful stimulation of the hand

Two minutes after the optokinetic drum started revolving, the subject immersed the fingers and palm of their non-dominant hand (in all but two cases this was the left hand) to the level of the thumb in 32°C water for 2 min to establish a thermal baseline. Next, subjects moved their palm and splayed fingers around in 2°C ice water for 30 s. Shortly after placing their hand back in the warm water, subjects rated headache, dizziness, nausea, and the intensity of pain during immersion of their hand in the ice water. This cycle was repeated twice more at 4 min intervals.

Data reduction and statistical analysis

Preliminary analyses indicated that nausea and dizziness were minimal before optokinetic stimulation; however, some migraine sufferers reported mild headache. Nausea and dizziness ratings, averaged across the period of optokinetic stimulation, were investigated in 2 × 3 [Group (migraine, control) × Task (optokinetic stimulation alone, optokinetic stimulation with ice on the temple, optokinetic stimulation with the hand in ice water)] analyses of variance with planned contrasts between optokinetic stimulation alone and optokinetic stimulation with head or hand pain. Analysis of headache ratings contained an additional factor of Period (before versus during optokinetic stimulation). Pain ratings, averaged across the three trials, were investigated in a 2 × 2 [Group (migraine, control) × Task (head pain, hand pain)] analysis of variance.

Pulse amplitude was measured in 30 s blocks before, during and after each painful stimulus, and for equivalent periods during optokinetic stimulation alone. Since photoelectric pulse transducers do not measure vessel calibre or flow in absolute terms, changes in pulse amplitude were expressed as the percent change from the level recorded for 30 s before optokinetic stimulation. Vascular responses, averaged across the three trials, were investigated separately for each of the three tasks. Mean changes in pulse amplitude during optokinetic stimulation alone were compared between migraine sufferers and controls with Student’s t-test. Vascular responses during the other two procedures were investigated in 2 × 2 × 3 [Group (migraine, control) × Side (ipsilateral to painful stimulation, contralateral to painful stimulation) × Block (before, during, and after painful stimulation)] analyses of variance. Planned contrasts were made between the level before painful stimulation and levels during and after painful stimulation. Responses are reported as the mean ± standard error (SE) and P < 0.05 was considered to be statistically significant.

Results

Ratings of motion sickness

Ratings to the question: "Do you regard yourself as susceptible to motion sickness?" averaged 1.65 ± 0.22 in migraine sufferers (corresponding to slightly to moderately susceptible) and 0.70 ± 0.17 in controls (i.e. not at all to slightly susceptible) [t(48) = 3.30, P < 0.01]. More specifically, mean nausea ratings to various forms of motion sickness induction were greater in migraine sufferers than controls [1.18 ± 0.90 (rarely to sometimes nauseated) versus 0.56 ± 0.15 (never to rarely nauseated)], t(48) = 2.68, P < 0.01).

Twenty-eight percent of migraine sufferers withdrew from optokinetic stimulation when it was combined with painful stimulation of the temple compared with only 4% of controls (P < 0.05, Table 1). The withdrawal rate did not differ between migraine sufferers and controls during the other two sessions.

The pain induced by immersing the hand in ice water was greater than the pain evoked by applying ice to the temple [F(1,43) = 19.4, P < 0.001] (Fig. 1). Pain ratings were greater in migraine sufferers than controls during both of these
procedures \[F(1,43) = 10.5, P < 0.01\], but were unrelated to differences between groups in susceptibility to motion sickness as judged by ratings of nausea during various forms of motion sickness induction [covariation between pain and nausea ratings, \(F(1,42) = 1.86\), not significant].

As shown in Fig. 2, optokinetic stimulation provoked greater nausea \([F(1,43) = 12.9, P < 0.001]\) and dizziness \([F(1,43) = 9.2, P < 0.01]\) in migraine sufferers than controls. To determine whether these symptoms were associated with the migraine predisposition or with a general susceptibility to motion sickness, the analyses were run again with the mean nausea rating to various forms of motion sickness induction included as a covariate. The association between the migraine predisposition and nausea during optokinetic stimulation \([F(1,42) = 6.8, P < 0.05]\) was independent of the association between the index of susceptibility to motion sickness and nausea during optokinetic stimulation \([F(1,43) = 21.5, P < 0.001]\). Similarly, dizziness during optokinetic stimulation was associated both with the migraine predisposition \([F(1,42) = 4.8, P < 0.05]\) and with susceptibility to motion sickness \([F(1,42) = 16.3, P < 0.001]\). Application of ice to the temple intensiﬁed nausea during optokinetic stimulation \([F(1,43) = 4.1, P < 0.05]\), whereas immersing the hand in ice water did not. Neither applying ice to the temple nor immersing the hand in ice water inﬂuenced ratings of dizziness.

Headache ratings were greater in migraine sufferers than controls both before and during optokinetic stimulation [main effect for Group, \(F(1,43) = 19.7, P < 0.001\] (Fig. 3). This effect was associated both with the migraine predisposition \([F(1,42) = 13.0, P < 0.001]\) and with susceptibility to motion sickness \([F(1,42) = 7.0, P < 0.05]\). Headache increased in migraine sufferers during optokinetic stimulation, but was minimal in controls [Group \(\times\) Period interaction, \(F(1,43) = 16.4, P < 0.001\]. Headache generally developed at the usual site of migraine, or across the forehead and behind the eyes. Applying ice to the temple during optokinetic stimulation increased headache in migraine sufferers [Group \(\times\) Task interaction, \(F(1,43) = 4.2, P < 0.05\]. Immersing the hand in ice water also increased headache ratings slightly, but ratings were not signiﬁcantly greater than during optokinetic stimulation alone.

**Extracranial vascular reactivity**

In the absence of painful stimulation, pulse amplitude increased in the frontotemporal region during optokinetic stimulation—more so in migraine sufferers than controls [mean increase 32 \(\pm\) 5% versus 10 \(\pm\) 2%, \(t(45) = 4.03, P < 0.001\]. However, painful stimulation of the temple and hand modiﬁed this response (Figs 4 and 5). In particular, vascular responses did not differ signiﬁcantly between migraine sufferers and controls, when ice was applied to the temple, due to an increase in pulse amplitude in controls (Fig. 4). During hand immersion, pulse amplitude decreased bilaterally in migraine sufferers, but remained stable in controls [Group \(\times\) Block (before versus during hand immersion) interaction, \(F(1,43) = 4.5, P < 0.05\] (Fig. 5). After the hand was removed from the ice water, pulse amplitude increased in the ipsilateral frontotemporal region both in migraine sufferers and controls [main effect for Side, \(F(1,43) = 16.9, P < 0.001\]; Block (before versus after immersion) \(\times\) Side interaction, \(F(1,43) = 9.5, P < 0.01\]; increase on the ipsilateral side from before to after immersion, \(t(44) = 3.27, P < 0.01\]. Including the mean nausea rating to various forms of motion sickness induction as a covariate did not alter the outcome of these analyses, suggesting that differences in vascular reactivity between migraine sufferers and controls were unrelated to differences in susceptibility to motion sickness.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Migraine</th>
<th>Controls</th>
<th>(\chi^2)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optokinetic stimulation without pain</td>
<td>4/25 (16%)</td>
<td>1/22 (5%)</td>
<td>1.61</td>
<td>0.20</td>
</tr>
<tr>
<td>Optokinetic stimulation with temple pain</td>
<td>7/25 (28%)</td>
<td>1/23 (4%)</td>
<td>4.82</td>
<td>0.03</td>
</tr>
<tr>
<td>Optokinetic stimulation with hand pain</td>
<td>4/23 (17%)</td>
<td>2/22 (9%)</td>
<td>0.67</td>
<td>0.41</td>
</tr>
</tbody>
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Fig. 1 Mean pain ratings (+SE) in migraine sufferers (ﬁlled bars) and controls (open bars) during application of ice to the temple and immersion of the hand in ice water. Ratings were greater during immersion of the hand than during application of ice to the temple, and were greater in migraine sufferers than controls during both procedures (*\(P < 0.05\)).
Within the migraine group, extracranial vasodilatation was unrelated to headache intensity during optokinetic stimulation alone \( r(23) = 0.07 \), not significant \] or when optokinetic stimulation was combined with painful stimulation of the head \[ \text{ipsilateral to pain, } r(23) = 0.23, \text{ not significant}; \text{contralateral to pain, } r(23) = -0.39, \text{ not significant} \] or hand \[ \text{ipsilateral to pain, } r(21) = -0.23, \text{ not significant}; \text{contralateral to pain, } r(21) = -0.27, \text{ not significant} \].
Discussion

Symptoms of motion sickness

Interaction between sensory stimuli and the sensitized trigeminal system of migraine sufferers may account for certain symptoms associated with migraine (Drummond, 1997). In the present study, the aim was to determine whether trigeminal nerve discharge provoked by painful stimulation of the temple would intensify symptoms common to motion sickness and migraine. If so, this would support the notion that symptoms such as nausea and headache escalate in a vicious circle.

We found that nausea induced by optokinetic stimulation increased during painful stimulation of the temple. It seems unlikely that this reflected an overall increase in discomfort or a general reaction to pain, because nausea did not increase during painful stimulation of the hand. Furthermore, neither cranial pain nor hand pain influenced ratings of dizziness, indicating that the association was specific to nausea and headache. Pathways between the trigeminal nucleus caudalis and neurons in the medullary nuclei of the solitary tract (Goadsby and Hoskin, 1997; Ruggiero et al., 2000) may allow direct communication between centres that process head pain and those that respond to emetic stimuli. Thus, one explanation for the present finding is that trigeminal nerve discharge, induced by painful stimulation of the temple, converged upon solitary tract neurons to intensify nausea. If this explanation is correct, similar convergence of gastrointestinal and cranial nociceptive sensations might intensify nausea during attacks of migraine. Conversely, decreases in headache after the administration of anti-migraine drugs (e.g. triptans) may secondarily decrease nausea. Although nausea increased to the same extent in migraine sufferers and controls during painful stimulation of the temple, in absolute terms nausea was greater in migraine sufferers than controls during this and other procedures. Since a greater proportion of migraine sufferers than controls withdrew from optokinetic stimulation when it was combined with painful stimulation of the temple, ratings of nausea may have been limited by a ceiling effect in some migraine sufferers.

Immersion of the hand in ice water was employed to investigate non-specific effects of painful stimulation on symptoms of motion sickness. Painful stimulation of the arm inhibits the second component of the blink reflex (Ellrich and Treede, 1998), which is mediated in part by trigeminal nociceptive afferents. Presumably this involves ‘diffuse noxious inhibitory controls’ (DNIC) that originate in the subnucleus reticularis dorsalis of the caudal medulla and modify activity in wide dynamic range neurons in the dorsal horn and its trigeminal extension (Villanueva et al., 1995). Gastrointestinal discomfort exerts an inhibitory effect on the withdrawal reflex elicited by painful stimulation of the sural nerve (Bouhassira et al., 1994), indicating that visceral sensations can trigger DNIC. Thus, it might be expected that the intense pain provoked by painful stimulation of the hand would inhibit minor symptoms of motion sickness such as mild headache and nausea. Surprisingly, however, symptoms persisted after immersing the hand in ice water. Mechanical hyperalgesia increases in the fingertips of migraine sufferers after optokinetic stimulation, and scalp tenderness increases in the most nauseated subjects (Drummond, 2002). Thus, it would be interesting to determine whether activation of
certain brainstem nuclei during motion sickness (and, by implication, migraine) disrupts pain inhibitory mechanisms such as DNIC.

Ratings of nausea, dizziness, headache and ice-induced pain were consistently higher in migraine sufferers than controls throughout the experimental procedures, independent of differences in self-reported susceptibility to motion sickness. Our data do not allow us to determine whether heightened ratings of discomfort were due to a reporting bias or point to real differences in sensation between migraine sufferers and controls. However, since migraine is associated with objective signs of trigeminal sensitization (Kaube et al., 2002; Sandrini et al., 2002), vestibular disturbances (Kuritzky et al., 1981a), and a low threshold for vomiting (Cerbo et al., 1997; Jan et al., 1997), it seems plausible that heightened ratings of discomfort reflect the sensory experience of migraine sufferers. Heightened discomfort to noxious stimuli would be consistent with a deficit in normal inhibitory pain modulation that persists between attacks of migraine.

Although symptoms of motion sickness were greater in migraine sufferers than controls, the rate of withdrawal from optokinetic stimulation was similar in both groups except when combined with painful stimulation of the temple. Discomfort provoked by standard noxious stimulation often begins sooner in migraine sufferers than controls (Marlowe 1992; Nicolodi et al., 1994; Hassinger et al., 1999). Nevertheless, tolerance of discomfort does not generally differ between migraine sufferers and controls, despite higher ratings of discomfort in migraine sufferers (Drummond, 1987, 1997; Bishop et al., 2001). Perhaps migraine sufferers learn to tolerate heightened levels of discomfort during repeated episodes of migraine.

**Extracranial vascular reactivity**

In the absence of painful stimulation, extracranial vasodilation was greater in migraine sufferers than controls during optokinetic stimulation. Vessel calibre and blood flow were not measured in absolute terms in the present study; thus, it is possible that differences in vascular activity at baseline contributed to the enhanced response in migraine sufferers. Since facial pallor is usually associated with motion sickness, it may seem surprising that scalp vessels dilated during optokinetic stimulation. However, similar findings have been reported previously (Kolev et al., 1997); presumably, flow through dermal arterioles bypassed the vascular network responsible for skin colour during optokinetic stimulation. A similar response might account for facial pallor associated with distended scalp arteries during attacks of migraine.

The mechanism of the vasodilator response to optokinetic stimulation is uncertain, but could involve active sympathetic vasodilatation provoked by the discomfort associated with motion sickness (Money et al., 1996). Short periods of stressful stimulation induce extracranial vasodilatation in migraine sufferers (Wolff, 1953; Drummond, 1982, 1985; Arena et al., 1985; Rojahn and Gerhards, 1986; Kroner-Herwig et al., 1993), particularly in a subgroup of patients with painful, distended scalp vessels during attacks of
migraine (Drummond, 1984). Conversely, scalp vessels appear to constrict more tightly in migraine sufferers than controls during extended periods of stress (Haynes et al., 1990; Passchier et al., 1993). Drummond (1982) reported that dilatation of the superficial temporal artery was greater in migraine sufferers than controls during stressful mental arithmetic, but not during other laboratory tasks (isometric exercise, rebreathing carbon dioxide, immersing the foot in ice water, heating the trunk or head-up or head-back tilt). Thus, differences between migraine sufferers and controls may depend more on central processing of stressful stimuli than on differences in intrinsic vascular hyper-reactivity.

We previously found that painful stimulation of the face (Drummond, 1997) and hand (Drummond and Granston, 2003) provoked greater extracranial vasodilatation in migraine sufferers than controls. In the present study, however, responses did not differ between groups when pain was provoked during optokinetic stimulation. The present findings suggest that the discomfort induced by optokinetic stimulation facilitated extracranial vasodilatation to pain in controls. The extracranial vasodilator response to pain may form part of a general defense response to noxious or threatening stimulation (Bandler and Shipley, 1994). Applying ice to the temple for 30 s did not induce vasoconstriction in the terminal distribution of the superficial temporal artery, probably because sympathetic vasoconstrictor tone is weak in this part of the face (Blair et al., 1961; Fox et al., 1962).

Immersion of one hand in ice water provokes ipsilateral extracranial vasodilatation (Drummond and Granston, 2003). This response also developed during optokinetic stimulation in the present study, but an additional weak bilateral vasoconstrictor response opposed vasodilatation in migraine sufferers when the hand was immersed in ice water. Further study is required to identify the stimulus characteristics that induce extracranial vasoconstriction as opposed to vasodilatation. In general, however, it seems reasonable to conclude that the extracranial vasculature of at least a subgroup of migraine sufferers is more reactive than that of controls, both in terms of vasoconstriction and vasodilatation. Since there is no evidence that the vessels themselves are hyper-reactive (Skarby et al., 1982; Edvinsson et al., 1983), exaggerated psychological reactions or excitable neurovascular circuits may be responsible for this reactivity.

Although headache and extracranial vasodilatation were greater in migraine sufferers than controls during optokinetic stimulation, there seemed to be no direct association between headache intensity and vascular changes within the migraine group. Furthermore, headache intensified when ice was applied to the temple whereas scalp pulsations remained unchanged. The transient headache that develops during motion sickness is usually described as a dull ache across the forehead, in the temples or behind the eyes (Drummond, 2002). In contrast to motion sickness, intense or prolonged trigeminal nerve discharge during attacks of migraine may provoke perivascular neurogenic inflammation and sensitize cranial vessels to pain (Moskowitz, 1984; Williamson and Hargreaves, 2001). Once the vessels become inflamed, vasodilatation in response to stress or pain might exacerbate headache, leading to further vasodilatation and pain.

**Conclusions**

The present findings suggest that migraine sufferers experience pain more intensely and develop symptoms of motion sickness more readily than controls, and provide additional evidence that stress-linked extracranial neurovascular responses are greater in migraine sufferers than controls. Thus, a mechanism that heightens nausea and other symptoms of motion sickness, and that boosts extracranial neurovascular responses to stress, may increase susceptibility to migraine. The findings also show that facial pain increases the intensity of nausea and exacerbates headache during motion sickness. Since nausea appears to intensify facial pain during motion sickness (Drummond, 2002), nausea and headache could reinforce each other in a vicious circle.

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**References**


