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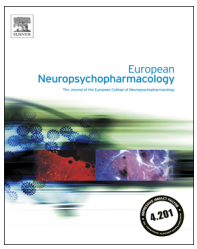

Topical ibuprofen inhibits blushing during embarrassment and facial flushing during aerobic exercise in people with a fear of blushing

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Abstract
The flush that develops during whole-body heat stress depends partly on prostaglandins production in the skin. Variations in the strength of this local mechanism may contribute to individual differences in susceptibility to blushing and associated anxiety. To investigate this in the present study, the anti-inflammatory agent ibuprofen (which blocks prostaglandins formation) was applied topically to a small area of the cheek in 16 participants with a fear of blushing and in another 14 without this fear. Changes in skin blood flow were monitored at the ibuprofen-treated site and at a mirror image control site while participants sang (to induce embarrassment and blushing) and during aerobic exercise (to induce flushing). The topical ibuprofen treatment inhibited increases in cheek blood flow in both groups during both of these tasks. However, increases in cheek blood flow were greater in participants with high than low fear of blushing immediately after exercise. These findings suggest that prostaglandins contribute to dilatation of facial blood vessels both during emotional arousal (embarrassment) and aerobic exercise. Furthermore, fear of blushing may be associated with mechanisms that delay the resumption of normal vascular tone after a period of vasodilatation. Whether topical ibuprofen gel is suitable for intermittent or long-term use as an aid for blushing control requires further investigation.

1. Introduction

Blushing refers to the transient facial redness that develops during emotions such as embarrassment, guilt or shame (Leary et al., 1992), whereas flushing refers to more-enduring facial redness triggered not only by strong emotions but also by vasodilators such as alcohol and by thermoregulatory adjustments to physical exercise and heat. Transient blushing involves an accumulation of red blood cells in the superficial venous plexus of the facial skin due to sympathetically-mediated dilatation of the arterial supply (Mellander et al., 1982; Drummond and Lance, 1987; Drummond, 1997, 2013). Similarly, the flush that develops during whole-body heating and exercise involves active

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sympathetic dilatation of cutaneous blood vessels (Drummond and Lance, 1987; Drummond and Finch, 1989; Charkoudian, 2010). These neurally-mediated increases in blood flow liberate substances such as nitric oxide from the vascular endothelium and prostaglandins from cutaneous cells which heighten and prolong the flush (Kellogg et al., 2003, 2008; McCord et al., 2006; Pyke and Tschakovsky, 2005).

During social encounters, people with social anxiety frequently experience autonomic and motor signs of anxiety, including blushing (Bögels et al., 2010). A subgroup of socially anxious people are particularly frightened of blushing (Voncken and Bögels, 2009; Pelissolo et al., 2012), primarily because they fear that others who notice the blush will regard them with derision or contempt. Surprisingly, during the majority of embarrassing laboratory tasks, the actual intensity of blushing is unrelated to perceived intensity or susceptibility to blushing (Drummond, 1997; Mulkens et al., 1997; Drummond and Su, 2012; but see Drummond, 2001) or to fear of blushing (Mulkens et al., 1999; Gerlach et al., 2001; Voncken and Bögels, 2009; but see Dijk et al., 2009). Nevertheless, blushing appears to build up over repeated episodes in people who report that they blush frequently (Drummond et al., 2003) or who are frightened of blushing (Drummond et al., 2007). The aetiology of this is unknown, but is consistent with a physiological predisposition that might delay recovery after a blush.

We recently reported that a local vascular mechanism may, in part, contribute to individual differences in susceptibility to blushing and associated anxiety. In particular, we found that a low dose of the vasodilator nicotinic acid (niacin) provoked greater increases in facial blood flow in people with high than low fear of negative evaluation (a cardinal feature of social anxiety), both when they sat quietly (Drummond and Lazaroo, 2012a) and during an embarrassing task (singing a children's song) (Drummond and Lazaroo, 2012b). Niacin dilates superficial blood vessels by releasing prostaglandin D_2 from epidermal Langerhans cells and prostaglandin E_2 from keratinocytes (Benyo et al., 2006; Hanson et al., 2010). Prostaglandins are potent vasodilators (Nagai, 2008; Shimura et al., 2010; Matsushima et al., 2011); thus, an exaggerated release or a heightened response to prostaglandins might amplify vasodilatation or delay resolution of blushing in people with social anxiety (Bouwer and Stein, 1998).

Non-steroidal anti-inflammatory drugs such as ibuprofen inhibit cyclooxygenase, an enzyme that mediates the production of prostaglandins (Ricciotti and FitzGerald, 2011). When applied topically to the skin in a gel, ibuprofen inhibits the inflammatory processes involving prostaglandins formation that contribute to musculoskeletal pain (Massey et al., 2010). Hence, to determine whether prostaglandins might contribute to blushing or exercise-induced flushing, ibuprofen gel was applied topically to a small area of the cheek in the present study. Changes in blood flow were measured at this site and at a comparable site in the contralateral cheek while participants sang (to induce embarrassment and blushing) and exercised (to evoke thermoregulatory flushing). It was hypothesised that ibuprofen would inhibit increases in cheek blood flow when participants exercised by blocking prostaglandins-mediated vasodilatation. As social anxiety is associated with a heightened response to prostaglandins (Drummond and Lazaroo, 2012a, 2012b), it was hypothesised that the inhibitory effect of ibuprofen would be greater in people with a fear of blushing than in people without this fear. We expected that participants who were frightened of blushing would report more embarrassment when they sang than participants without this fear, due to greater social anxiety in the high- than low-fear group (Voncken and Bögels, 2009; Dijk et al., 2009). Whether this heightened emotional arousal would augment blushing due to prostaglandins production was also explored.

2. Experimental procedures

2.1. Participants

Participants were selected from 286 undergraduate university students who rated their concerns about blushing on a screening questionnaire (Bögels and Reith, 1999; Heinrichs et al., 2006). The high fear group consisted of 12 women and four men aged between 17 and 37 years (mean $\pm$S.D., 22 $\pm$ 5 years) who scored between 29 and 55 out of a possible total of 60 on the screening questionnaire (i.e., between the 83rd and 100th percentile of the total group), and the low fear group consisted of six women and eight men aged between 18 and 53 years (27 $\pm$ 11 years) who scored between 0 and 9 on the screening questionnaire (i.e., between the 1st and 33rd percentile of the total group). None of the participants were pregnant, had asthma or other respiratory problems, liver or kidney disease, mental difficulties, took prescription medication for high blood pressure, regularly took ibuprofen or other analgesics, had a previous sensitivity to non-steroidal anti-inflammatory drugs or had inflamed facial skin. Participants each provided informed consent for the procedures, which were approved by Murdoch University Human Research Ethics Committee.

2.2. Measures and instruments

The screening questionnaire consisted of six items from the Blushing, Trembling and Sweating Questionnaire that measured the extent to which individuals were afraid of and hindered in their daily functioning by blushing (Bögels and Reith, 1999). Each item was rated on a 10 cm visual analogue scale, thus providing a total score between 0 and 60. To evaluate perceptions of blushing propensity and other broader aspects of social anxiety, participants filled out the Blushing Propensity Scale (Leary and Meadows, 1991) and the Fear of Negative Evaluation Scale (Watson and Friend, 1969). The Blushing Propensity Scale measures the degree to which people expect to blush in situations such as "talking to someone about a personal topic" and "when I've looked stupid or incompetent in front of others" (Leary and Meadows, 1991). Blushing propensity scores relate closely to measures of social anxiety (Leary et al., 1992; Edelmann and Skov, 1993). The Fear of Negative Evaluation Scale contains 30 items that assess apprehension and distress about being evaluated negatively by others, a fundamental component of social anxiety. The participants also completed the Social Interaction Anxiety and Social Phobia Scales which, respectively, assess anxiety associated with initiating and maintaining conversations and anticipatory and performance-related social anxiety (Mattick and Clarke, 1998). For each of these scales, the internal consistency and test-retest reliability over short intervals is high (Bögels and Reith, 1999; Leary and Meadows, 1991; Mattick and Clarke, 1998; Watson and Friend, 1969).

Changes in skin blood flow were detected with wide surface area laser Doppler flow probes (Moor Instruments, Axminster, UK) which were inserted into probe holders attached with double-sided adhesive washers to prepared sites in the cheeks. Signals were processed by a Moor Instruments MBF3D laser Doppler flowmeter and sampled at 200 Hz by a Biopac MP100 data acquisition system (Biopac Instruments, Goleta, California).