Trigeminal Neuralgia, Migraine and Sympathetic Hyperactivity in a Patient with Parry-Romberg Syndrome

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Abstract

We investigated trigeminal and cervical sympathetic function in a woman with right-sided trigeminal neuralgia, migraine, and atrophy of subcutaneous tissues in the supraorbital region of the right-forehead (Parry-Romberg syndrome). We found loss of sensitivity to innocuous sensations (light touch, warmth, and cold), associated with heightened sensitivity to noxious pressure and heat in the atrophic region in the forehead and, to a lesser extent, in the cheek. Above the sensory detection threshold, light touch and cold evoked abnormal pain sensations that spread from the site of stimulation on the affected side. In addition, weak electrical stimulation of the supraorbital nerve evoked pain and blink reflexes more readily on the affected than unaffected side. The onset of body heating provoked substantial release of sympathetic vasoconstrictor tone on the affected side of the forehead. Similarly, prolonged body heating augmented sweating on the affected side of the forehead, consistent with heightened sympathetic sudomotor activity. These findings support the hypothesis that aberrant trigeminal and cervical sympathetic discharge, possibly resulting from an inflammatory process that attacks cranial blood vessels and nerves, is associated with the atrophic process in Parry-Romberg syndrome.

Key words: Parry-Romberg syndrome; migraine; trigeminal neuralgia; sympathetic nervous system; hyperalgesia; blink reflex

Introduction

Parry-Romberg syndrome is a rare disorder of unknown etiology that involves slowly progressive but self-limited wasting of subcutaneous tissues on one side of the face (1), usually in the distribution of a branch of the trigeminal nerve. In an internet survey of 205 people on the mailing list of the "Romberg's Connection" site, 52% reported suffering from migraine and 46% from facial pain, almost always affecting the same side as the atrophy (2). Headaches and facial pain have also featured in case reports (1,3-7), sometimes in association with an intracranial aneurysm (8,9) or radiological signs of ipsilateral brain pathology (10-12).

We had the opportunity to examine trigeminal and cervical sympathetic nerve function in a woman with right-sided Parry-Romberg syndrome, migraine and trigeminal neuralgia. We wished to determine whether signs of trigeminal or cervical sympathetic hyperactivity were associated with the facial hemiatrophy, because aberrant cranial nerve function has been implicated in the pathophysiology of Parry-Romberg syndrome (1,11,12).

Case Report

A 32 year old woman with a long history of right hemifacial pain had developed atrophy and hyperpigmentation in the right supraorbital region in childhood, which was diagnosed as Parry-Romberg syndrome. When she was 15 years old, scalp tissue was moved forward over the atrophic region. Migraine without aura started about ten months after the cosmetic surgery. Initially the headaches recurred every few months but the frequency increased progressively. When seen in June, 2005, the headaches lasted around three days with only a few days or a week of freedom before the next attack. The patient reported that the headaches were strictly right-sided, and began as an ache in the cheek, temple and supraorbital notch. The

ache then gradually intensified into a stabbing sensation, and eventually radiated to the right occipital region, down the right arm and into the fifth finger. The headaches were associated with photophobia, phonophobia, nausea and vomiting. She reported that the right nostril became stuffy and the right eyelid felt heavy and drooped slightly during the attacks. Alcohol triggered the headache within about 30 minutes. Other triggers included fatigue, stress, perfumes, repetitive stimulation of the forehead, cold wind on the right side of her face, and light touch particularly on the right cheek. The migrainous attacks did not respond to ergotamine or triptan medications.

The patient also described a continuous jabbing neuralgic pain and tingling sensation in the right cheek and angle of the jaw, which was aggravated by cold wind and light touch on the right side of her face (e.g., shower water), particularly near the hairline and cheek. She reported that these light sensations produced a persistent ache that could linger for ten minutes or more, and that could intensify into a migraine headache. The neuralgic pain responded weakly to gabapentin and carbamazepine, but these drugs were discontinued because of severe side effects. Approximately 12 months before attending the laboratory botulinum toxin was injected bilaterally above the ears, but the neuralgic pain remained unchanged.

MRI scans in 2001 and 2003 identified several isolated foci in the subcortical and periventricular white matter of the right frontal lobe, suggestive of deep white matter ischaemic change. No abnormality was seen in Meckel’s caves or along the course of the trigeminal nerves.

Sensory tests

Tactile sensitivity was investigated on each side of the face with graded nylon filaments (Senselab von Frey Aesthesiometer, Somedic Sales AB, Hörby, Sweden). The touch threshold was two steps greater on the right side of the forehead than the

left (filament 5 versus filament 3), and one step greater on the right cheek and chin than the left (filament 4 versus filament 3). At the touch threshold on the right forehead, an electric shock sensation spread into her cheek, the angle of the jaw and right occipital region. Similarly, a tingling sensation at the touch threshold on the right cheek spread to the right occipital region.

The pressure-pain threshold was investigated on each side of her face with a spring-loaded algometer (13). The pressure-pain threshold was roughly symmetrical except across the forehead, where pain developed at less than 250 gm on the right but around 1,000 gm on the left.

To investigate sensitivity to cold, the circular end of a cylindrical metal bar (10 cm long, 1.3 cm wide, 2^{o}C) was applied for a few seconds to the forehead, cheek and chin while the patient rated coldness between 0 (not cold at all) and 10 (extremely cold). The cold sensation was rated as 3-4 on the right side of the forehead and 7-9 elsewhere in the face. In addition, a burning sensation developed when the bar was applied to the right forehead and cheek.

Warmth and heat pain thresholds were investigated on each side of her face with a servo-controlled radiant heat lamp that increased skin temperature at 0.5^{o}C/second. She was unable to detect warmth on the right side of the forehead but as the heat intensified a stinging sensation developed around 42^{o}C. In contrast, warmth was detected on the left side of the forehead at 39^{o}C and pain at 45^{o}C. Warmth and heat pain thresholds were 4-5^{o}C greater on the right cheek than the left, but were symmetrical in the chin.

Blink reflexes

Standard plate electrodes were attached bilaterally with the cathode over the supraorbital notch and the anode 2-3 cm away in the forehead. Current intensity was

increased in 0.1 to 0.3 mA steps to establish the sensation, pain and blink reflex thresholds (monopolar square wave pulses, 0.3 milliseconds duration, interstimulus interval greater than 15 seconds). The stimulation procedure was repeated with concentric electrodes consisting of a central wire cathode and annular anode attached to the supraorbital region of the forehead, to selectively stimulate trigeminal nociceptive afferents (14). Blink reflexes were recorded bilaterally from miniature surface electrodes attached below the lower eyelids over the obicularis oculi muscles and 2-3 cm laterally.

As shown in Figure 1, a smaller intensity of electrical current on the right side of the forehead than the left was required to induce the threshold of sensation (a rating of 1), the pain threshold (a rating of 2) and the R2 component of the blink reflex, both for stimuli delivered from normal plate electrodes and from concentric electrodes. The R1 component of the blink reflex began at around 1 mA for stimuli delivered from normal plate electrodes, both on the affected and unaffected sides.

Autonomic tests

To investigate thermoregulatory facial sweating and flushing, the patient was covered in blankets and heated with warm air from a fan heater for 30 minutes. As shown in Figure 2, increases in amplitude of the pulse waveform (which reflects cutaneous blood flow) initially were greater on the right side of the forehead than the left, but ultimately responses were symmetrical. Vascular responses were symmetrical in the cheeks. Electrodermal activity (which reflects sweating) was greater on the right side of the forehead than the left during the final ten minutes of heating (Figure 2), and beads of sweat were more noticeable on the right than the left side of the forehead after 30 minutes of heating.

Pupil diameter was measured from photographic negatives on black-and-white infrared film. The right pupil was marginally greater than the left in darkness (6.5 mm versus 6.0 mm) but the pupils were symmetrical in dim and bright light and constricted normally. In addition, eyelid separation was symmetrical.

Discussion

The prevalence of migraine and facial pain appears to be far greater in Parry-Romberg syndrome than in the general population (2). Moreover, as trigeminal neuralgia is uncommon (15), its association with Parry-Romberg syndrome is unlikely to be due to chance. Although injury to trigeminal afferents during cosmetic surgery cannot be discounted in the present case, it seems unlikely that surgery in the ophthalmic division of the trigeminal nerve would produce neuralgia in the maxillary division. Taken together, these observations suggest a causal link between Parry-Romberg syndrome, migraine and neuralgic pain. It is interesting to note that hemifacial atrophy preceded the onset of migraine headaches by several years.

Loss of sensitivity to innocuous sensations (light touch, warmth, and cold) was accompanied by heightened sensitivity to noxious pressure and heat in the atrophic region of the forehead and, to a lesser extent, in the cheek. Indeed, innocuous stimuli such as light touch and cold induced abnormal pain sensations that spread from the site of stimulation. Furthermore, weak electrical stimulation of the supraorbital nerve evoked pain and blink reflexes more readily on the affected than unaffected side. Abnormal excitability and sustained afterdischarge of trigeminal nociceptive afferents is characteristic of trigeminal neuralgia. This may arise as a result of electrical or chemical cross-talk between Aβ touch afferents and nociceptive neurons in the trigeminal ganglion or trigeminal root due to demyelination or axonal injury (15).

Abnormal trigeminal excitability might also increase susceptibility to migraine headaches through a process of central sensitization (16).

Although sympathetic involvement in Parry-Romberg syndrome has been suspected for some time (1,11,12), formal investigation of this aspect of the syndrome is limited. In the present case, sympathetic activity appeared to be greater on the affected than unaffected side of the forehead both before and during body heating. In particular, the rapid increase in pulse amplitude on the affected side of the forehead implies that the initial period of body heating evoked substantial release of sympathetic vasoconstrictor tone. Similarly, prolonged body heating augmented sweating on the affected side of the forehead, consistent with heightened sympathetic sudomotor discharge. Sympathetic activity was symmetrical in regions other than the affected side of the forehead, suggesting an association between sympathetic hyperactivity and subcutaneous atrophy.

Chronic sympathetic hyperactivity, possibly triggered by an inflammatory process that attacks cranial blood vessels and nerves (11,17), has been put forward as a mediator of tissue destruction in Parry-Romberg syndrome (1,12). According to this hypothesis, cross-excitation of sensory neurons in trigeminal nerve branches that distribute sympathetic fibres to the skin results in a trophic disturbance in tissues supplied by these fibres (1). Several investigators have also proposed that cranial vasculitis in Parry-Romberg syndrome is responsible for trigeminal neuralgia and radiological signs of brain pathology (6,10,11). In support of this possibility, Pensler et al. (17) identified lymphocyte infiltration in neurovascular bundles and abnormalities of the vascular endothelium and basement membrane in clinically-evolving skin lesions. Although an inflammatory process might account for facial

atrophy and central and peripheral nervous system manifestations (10), the primary trigger of Parry-Romberg syndrome remains obscure.

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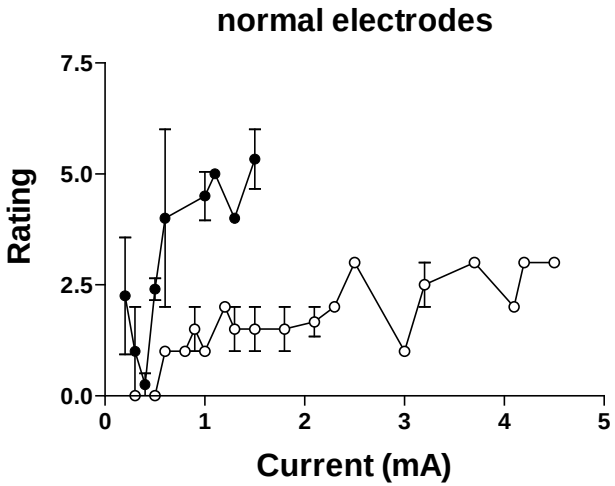
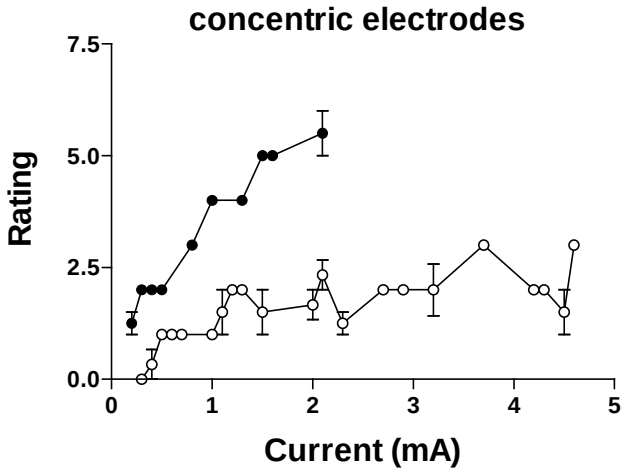
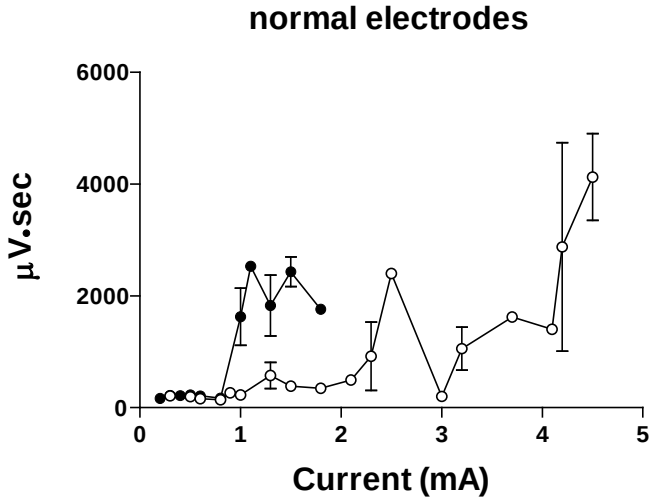
Figure legends

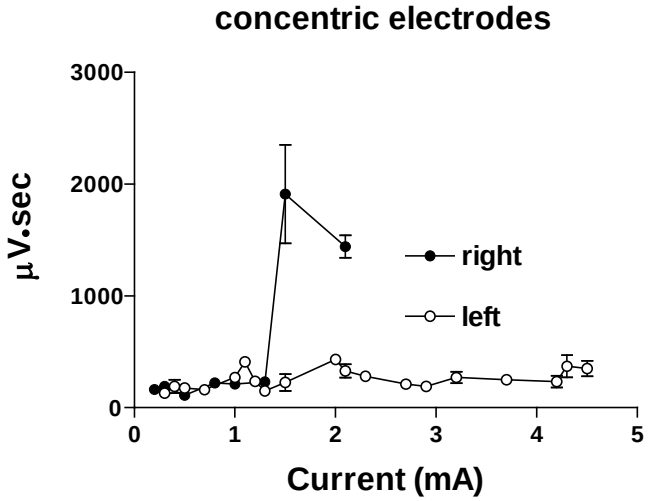
Figure 1. Pain ratings (+ S.E.M.) and blink reflexes (area under the rectified curve of the R2 component measured between 27 and 87 milliseconds after stimulus onset) to electrical stimuli delivered supraorbitally from normal plate electrodes and from concentric electrodes. A rating of 0 indicates that no sensation was detected, 1 corresponds to a painless sensation, and a rating between 2 and 10 indicates pain ranging between very mild (2) and extreme (10).

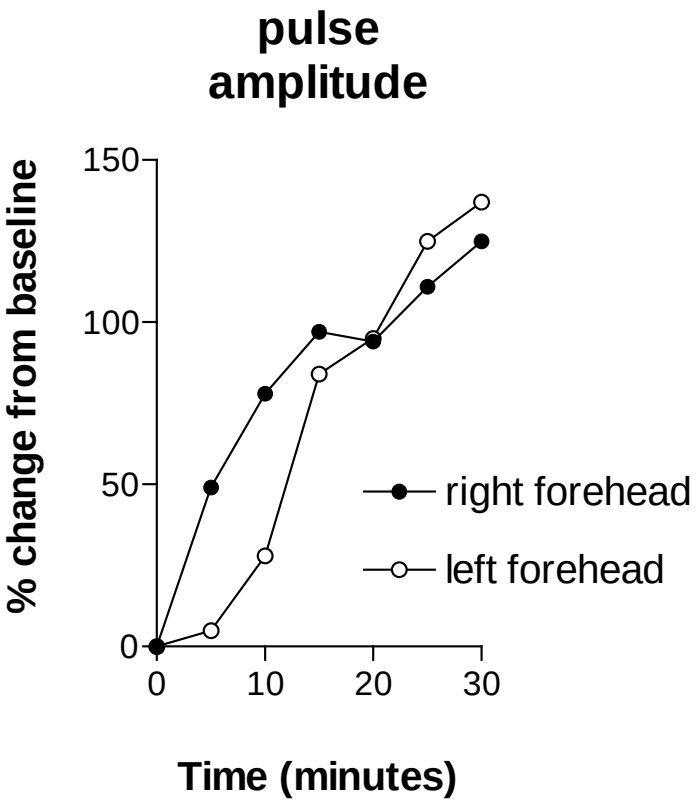
Figure 2. Increases in supraorbital pulse amplitude (expressed in relation to levels before heating) and electrodermal activity during 30 minutes of body heating.

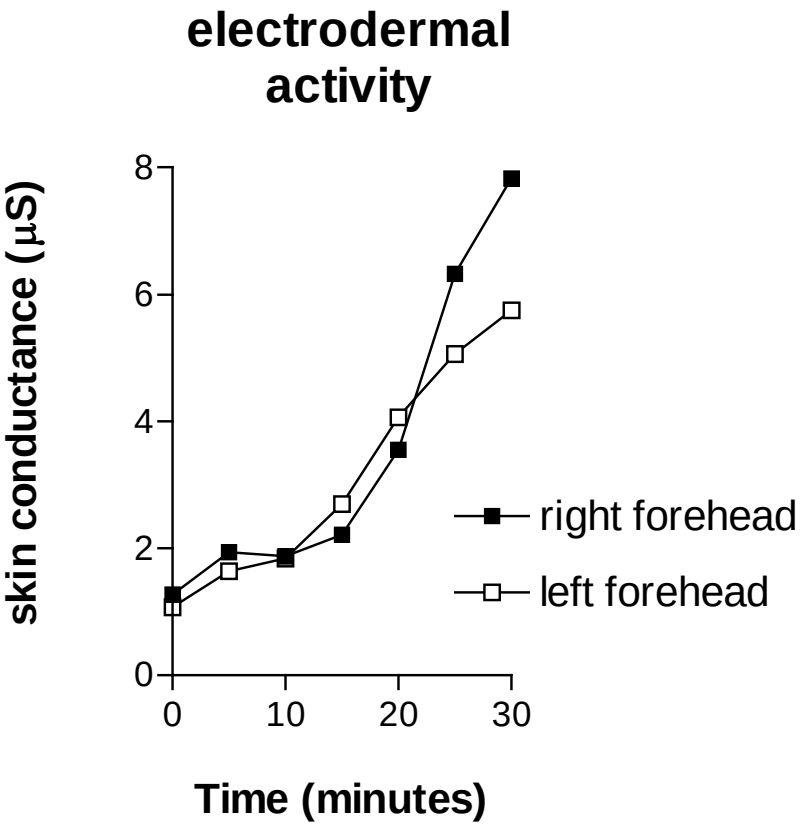

normal electrodes
Rating
7.5
5.0
2.5
0.0
0
1
2
3
4
5
Current (mA)


concentric electrodes
Rating
7.5
5.0
2.5
0.0
0
1
2
3
4
5
Current (mA)


normal electrodes
µV•sec
6000
4000
2000
0
0
1
2
3
4
5
Current (mA)


concentric electrodes
µV•sec
3000
2000
1000
0
0
1
2
3
4
5
Current (mA)
right
left


pulse amplitude
% change from baseline
150
100
50
0
0
10
20
30
right forehead
left forehead
Time (minutes)


electrodermal activity
skin conductance (μS)
8
6
4
2
0
0
10
20
30
right forehead
left forehead
Time (minutes)