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Autonomic features in cluster headache. Exploratory factor analysis

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Abstract The objective is to identify the pathogenesis of each autonomic manifestation in cluster headache (CH). Through a deductive statistics method (factor analysis) we analysed the type of autonomic symptoms reported by 157 CH patients. Three principal components were identified in the analysis: parasympathetic activation (lacrimation, conjunctival injection and rhinorrhoea), sympathetic defect (miosis and ptosis) and parasympathetic mediated effect (nasal congestion, eyelid oedema and forehead sweating). This work suggests that there are three different mechanisms underlying autonomic manifestations in CH.

Key words Cluster headache • Autonomic symptoms • Factor analysis

Introduction

Autonomic disturbances in cluster headache (CH) are thought to result from parasympathetic stimulation [1] and from ocular sympathetic deficit [2] with expression of a Horner-like syndrome. Forehead sweating is though to be a consequence of a postganglionic lesion in sympathetic sudomotor fibres [3], with adaptive supersensitivity of the forehead sweat glands [4]. Facial flushing could result from a unilateral increase in extracranial blood flow, demonstrated during cluster attacks [5, 6] as a consequence of trigeminal nociceptive activation [6, 7].

Principal component analysis is a data reduction method that explores correlations among the variables of a problem, producing a set of independent factors that resume the relation within the original variables – the principal components. We applied this deductive statistical method to the autonomic manifestations of a series of CH patients, trying to elucidate the relationships between these symptoms.

Methods

The Cluster Headache Outpatient database of Santa Maria's Hospital in Lisbon was used to select ICHD-II [8] CH patients. All patients included in this database was observed by neurologists with experience in headache. Clinical data were analysed, including age at first consultation, gender, duration of illness, follow-up time, pattern (episodic/chronic), presence of autonomic symptoms and number and type of autonomic symptoms (mio-

sis, ptosis, lacrimation, nasal congestion, rhinorrhoea, eyelid oedema, conjunctival injection and forehead sweating).

Statistical analysis was performed with the SPSS for Windows Software v 11.5, using descriptive statistics and exploratory factor analysis (method: principal component analysis; rotation method: varimax with Kaiser normalisation). Kaiser-Meyer-Olkin (KMO) and Bartlett's test of sphericity were used as measures of sampling adequacy. Factor and global model reliability was analysed through Cronbach's alpha. The significance level (α) considered was 0.05.

Results

The series consisted of 157 CH patients, 125 (79.6%) males and 32 (20.3%) females with an average age of 40.5 years, standard deviation (sd) of 12.4 years. Mean follow-up time is 2.8 years (sd 1.0) and mean disease duration 15.3 years (sd 9.2).

One hundred and thirty-one patients (83.4%) were classified as definite CH, 119 (75.8%) episodic and 12 (7.6%) chronic. Twenty-six (16.6%) were probable CH. One hundred and forty-eight patients (94.3%) experienced at least one of the usual autonomic symptoms, but 9 (5.7%) did not; of these only 4 fulfilled the ICDH-II criteria for definite CH because of restlessness.

The mean number of autonomic symptoms reported was 3.1 (sd 1.5, median 3), ranging from 0 to 7. The most frequent autonomic symptom reported was lacrimation (126 patients), then conjunctival injection (101), ptosis (100), rhinorrhoea (60), nasal congestion (52), eyelid oedema (26), miosis (16) and forehead sweating (2) (Table 1).

Factor analysis identified three factors explaining 52.5% of the autonomic symptom variability. KMO was 0.57 and Bartlett's test of sphericity was significant (Chi-Square 81.64, $p<0.0001$). Cronbach's alpha of the global model was 0.50 (Table 2).

Table 1 Frequency and factor analysis of autonomic symptoms in CH

	Frequency (%)	Factors		
		1 PS activation	2 S defect	3 PS mediated effect
Lacrimation	126 (80.3)	0.758		
Conjunctival injection	101 (64.3)	0.691		
Rhinorrhoea	60 (38.2)	0.604		
Miosis	16 (10.2)		0.806	
Ptosis	100 (63.3)		0.636	
Nasal congestion	52 (33.1)	0.368		0.674
Eyelid oedema	26 (16.6)			-0.531
Sweating	2 (1.3)		0.485	0.521

Values represented are absolute values on the rotated component matrix. Absolute values were suppressed if inferior to 0.35
PS, parasympathetic; *S*, sympathetic

Table 2 Factors, variance and reliability

	Variance explained, %	Cronbach's alpha
Parasympathetic activation (Factor 1)	20.7	0.53
Lacrimation		
Conjunctival injection		
Rhinorrhoea		
Ocular sympathetic defect (Factor 2)	17.0	0.40
Miosis		
Ptosis		
Parasympathetic mediated effect (Factor 3)	14.8	0.08
Nasal congestion		
Eyelid oedema		
Sweating		
Global model	52.5	0.50

The first factor included lacrimation, conjunctival injection and rhinorrhoea, therefore being identified as parasympathetic activation, and explained 20.7% of the variance; the second (responsible for 17% of variance) included miosis and ptosis and was identified as sympathetic defect. The third (14.8% of variance) included nasal congestion, eyelid oedema and forehead sweating and was denominated parasympathetic/trigeminal mediated effect. Nasal congestion can also be partially attributed to parasympathetic activation and forehead sweating to ocular sympathetic defect.

Discussion

The series of patients reported is similar to larger published series of CH patients in both the demographic features and the reported autonomic symptoms [9, 10]. The relatively low occurrence of symptoms like miosis, eyelid oedema and forehead sweating might be due to underreporting, because they may be subtle or subclinical, in contrast to the other more evident signs like lacrimation or rhinorrhoea. The total absence of autonomic symptoms in our series was 5.7%, which is in conformity to other series, which range from 2.8% [9] to 6.9% [10].

The use of principal component analysis in this study demonstrated that autonomic symptoms do not occur randomly during CH attacks, but tend to cluster according to the functional architecture of the cranial autonomic system. The analysis identified three main factors, which can be attributed to specific anatomic and functional modules:

1. Parasympathetic activation. Both the secretory and vasomotor parasympathetic innervation originate in the salivatory nuclei of the brainstem [2], but preganglionic secretory fibres travel through the greater superficial petrosal nerve and vasomotor fibres through the facial and glossopharyngeal nerves [2]. They synapse at the sphenopalatine ganglion and postganglionic fibres are then distributed to the lacrimal glands and nasal mucosal (causing lacrimation, rhinorrhoea and nasal congestion) and to various structures in the eye (explaining conjunctival injection).
2. Sympathetic defect. Oculomotor, vasomotor and sudomotor neurons from the cervical sympathetic pathway descend trough the medulla and spinal cord and leave the spinal cord in slightly different levels [2]. The preganglionic sympathetic fibres synapse in the superior cervical ganglion maintaining somatotopic organisation, in which fibres from the rostral end of the ganglion project into the internal carotid nerve plexus and innervate the eyes (explaining ptosis and miosis) and forehead (explaining forehead sweating) [2].
3. Parasympathetic/trigeminal mediated effect. Nasal congestion and eyelid oedema can be mediated by vasodilatation, with or without plasma extravasation. There is evidence that the increased cranial blood flow and vessel permeability verified in CH are mediated by acetylcholine and VIP released from parasympathetic efferents [7] in response to trigeminal-autonomic reflex, through a somato-autonomic response to pain. Forehead sweating might result from a postganglionic lesion in sympathetic sudomotor fibres [3], with parasympathetic cross-innervation of the sweat glands of the forehead [4].

The global model obtained has a good consistency but only explains 50.5% of the total variance; Cronbach's alpha reveals reasonable reliability.

Although the results obtained are appealing, for they are in accordance with the structural organisation of the cranial autonomic system and suggest the complementary involvement of several autonomic pathways, there are limitations to their interpretation. Firstly, the study is based in patient reports and not in clinical observations corroborated by functional autonomic testing. It is possible that symptoms reported are biased towards those that are more obvious or troublesome to the patients. Secondly, the role of the trigeminal activation was not considered in this analysis except for its interpretation, although it undoubtedly plays a pivotal role in the pathophysiology of CH.

Systematic studies performed during cluster attacks are necessary to corroborate these results, to understand the role of the Vth nerve in the model and the reciprocal interaction between the subsystems involved.

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