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Neck pain and dizziness, and their relation to migraine

The 5th Nordic Migraine Symposium

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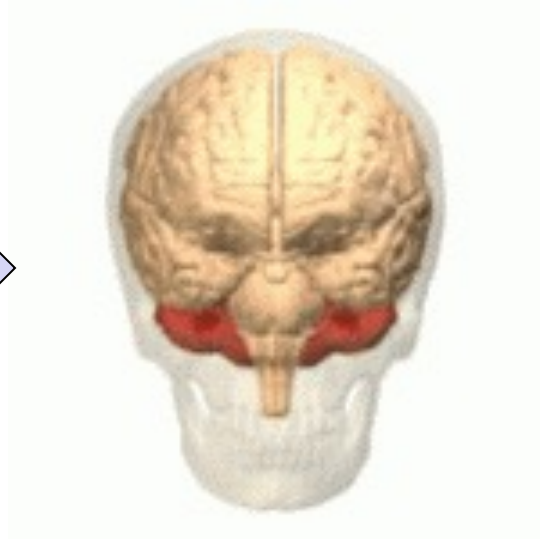
Disclosures

- Sait Ashina is a consultant for Abbvie/Allergan, Eli Lilly, Linpharma, Lundbeck, Satsuma, Teva, Theranica, Percept, Pfizer, Impel NeuroPharma

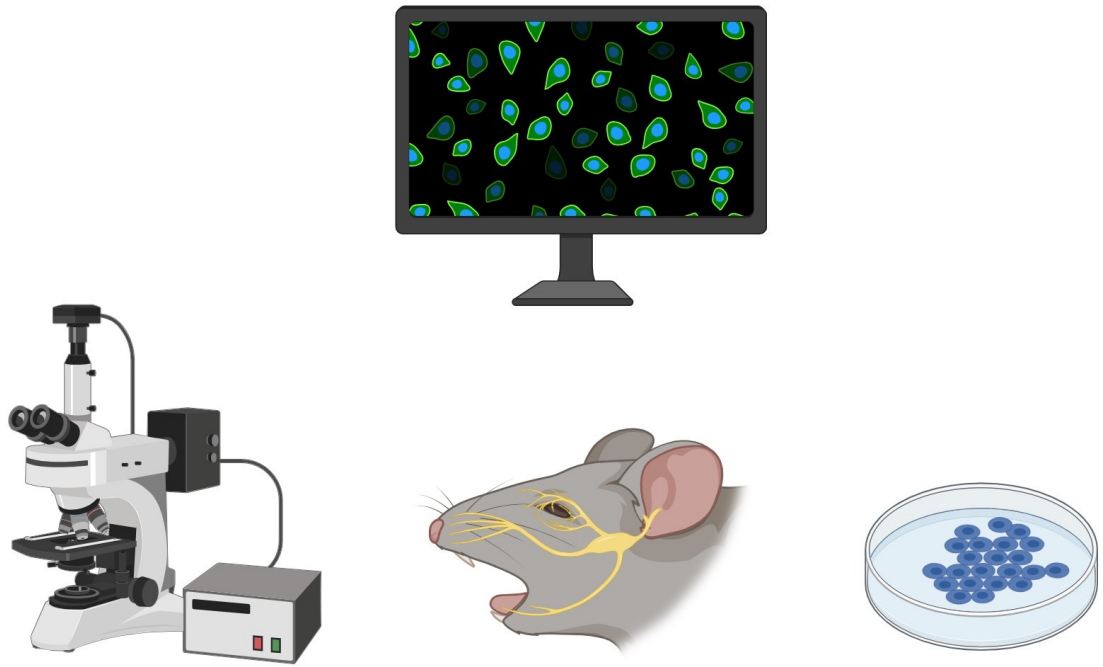
Background

Vestibular migraine



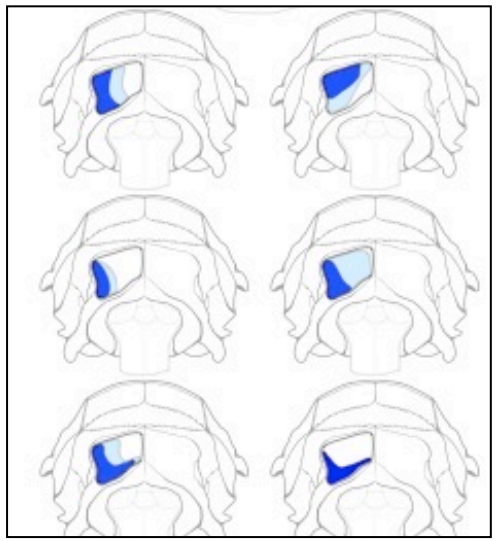
- Occipital headache
- Neck pain
- Neck muscle tenderness
- Dizziness

Preclinical studies

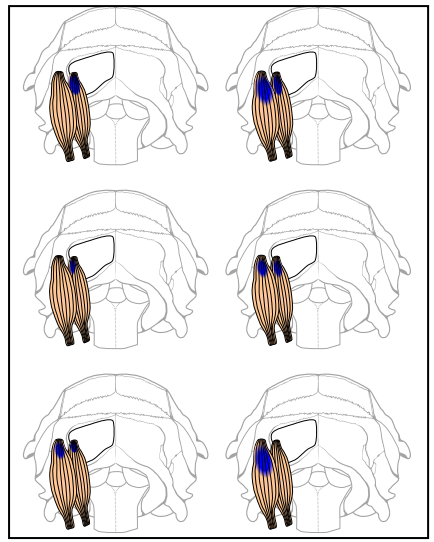


Receptive fields of cervicovascular neurons in C2-DRG

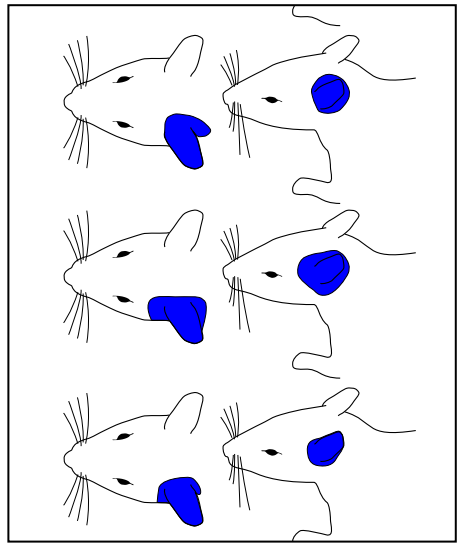
Occipital dura overlaying the cerebellum



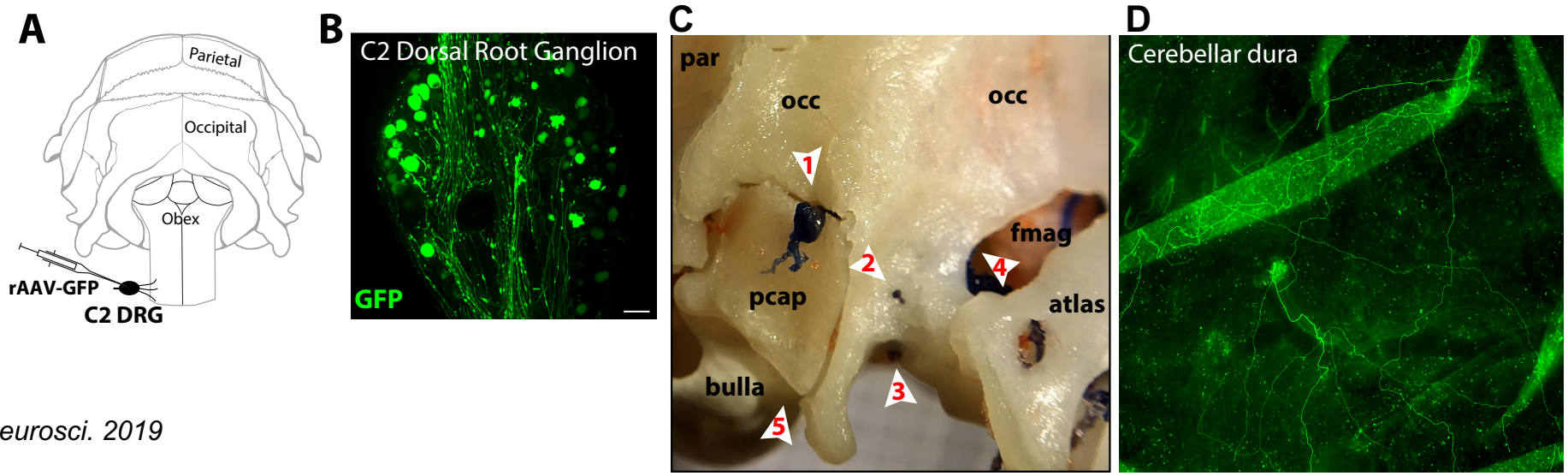
Tendons of occipital neck muscles



Occipital cutaneous areas



C2-DRG axons enter the calvaria and innervate the occipital dura

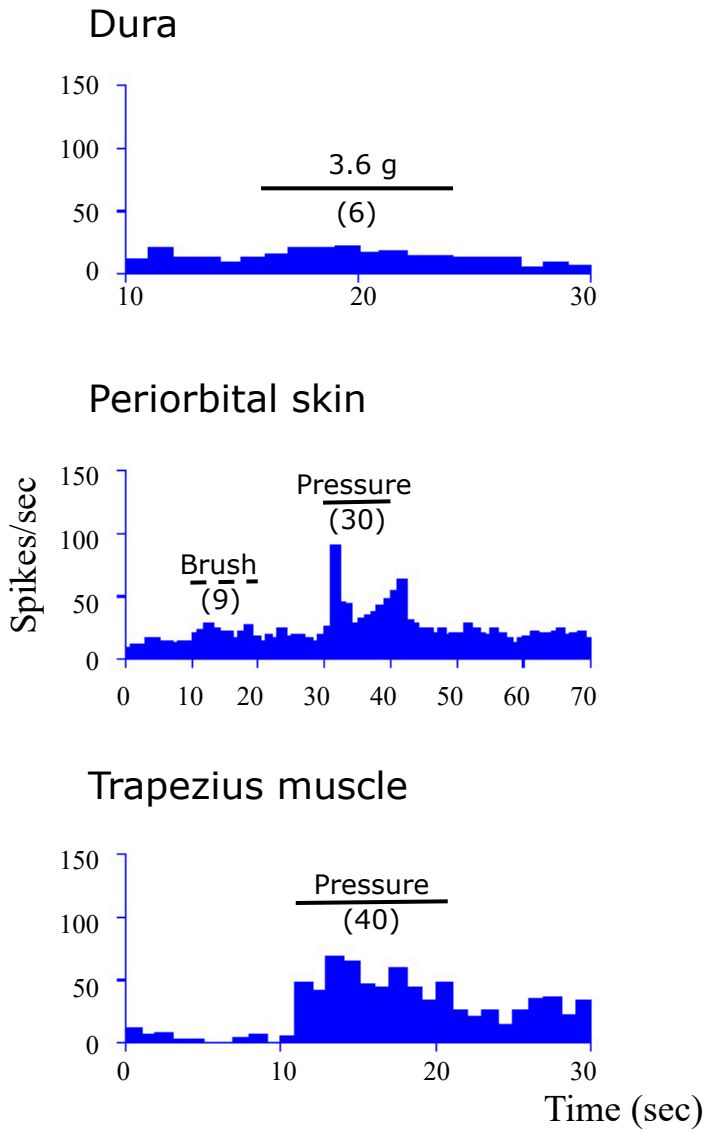


Noseda R et al. J Neurosci. 2019

Central sensitization (Skin, muscles, dura)

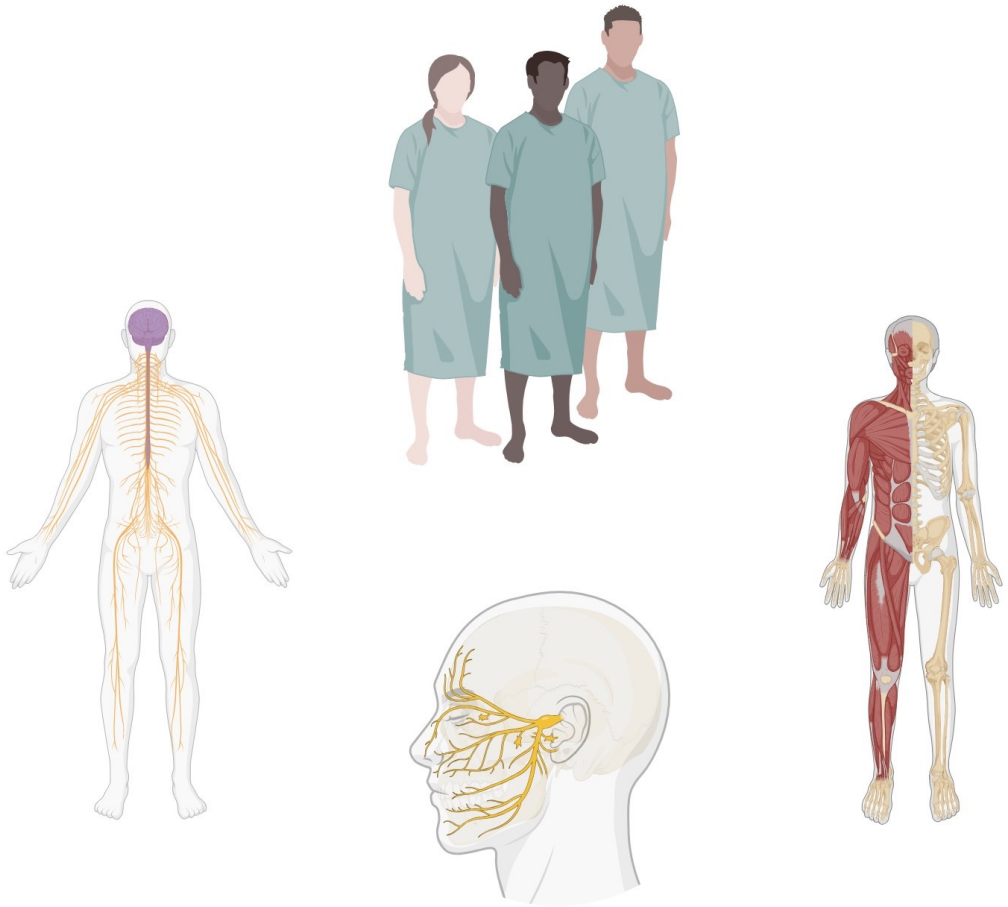
Before sensitization

After sensitization

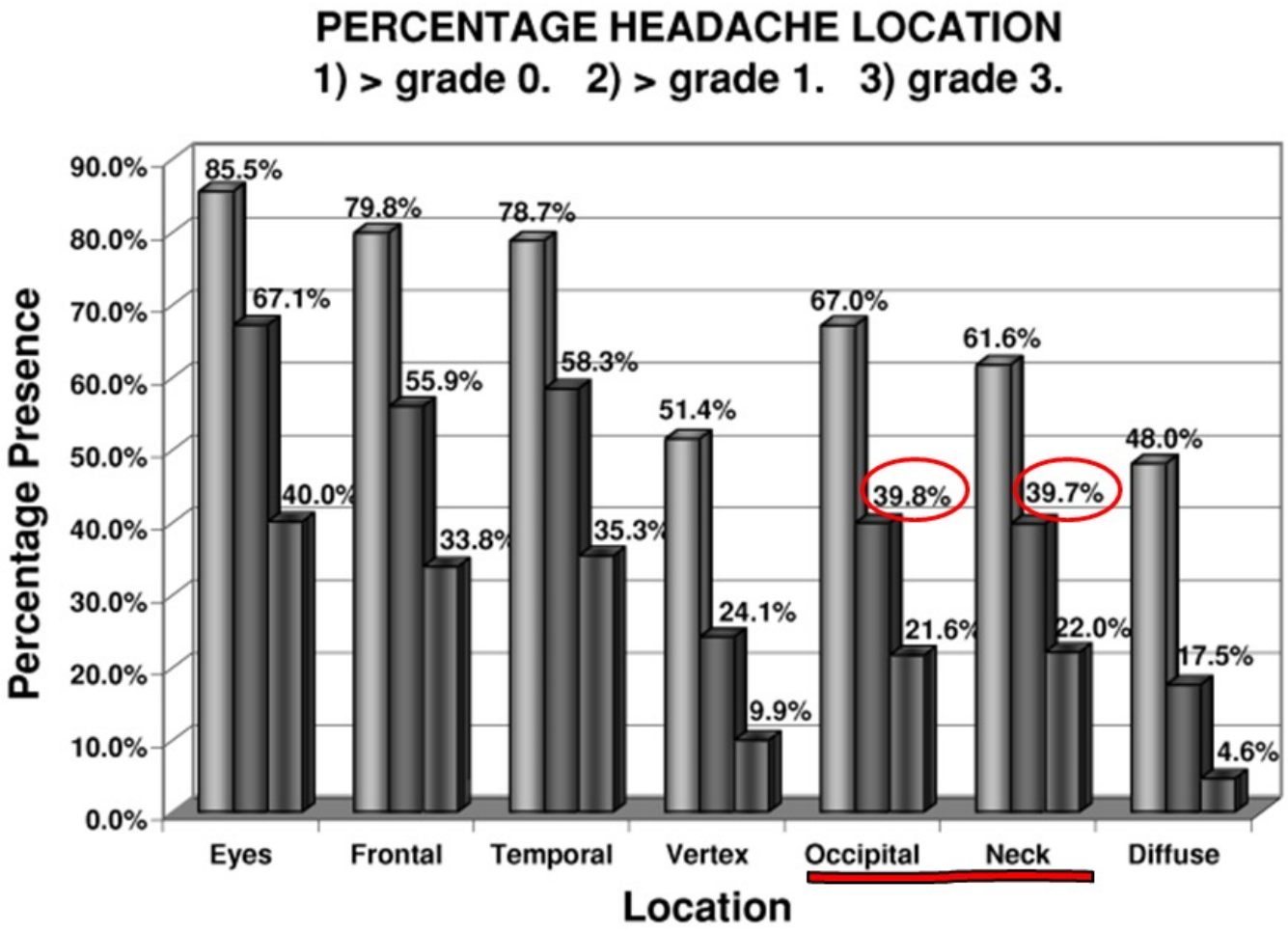


Noseda R et al. J Neurosci. 2019

Human studies



Migraine Pain Location:
A Tertiary Care Study of 1283 Migraineurs

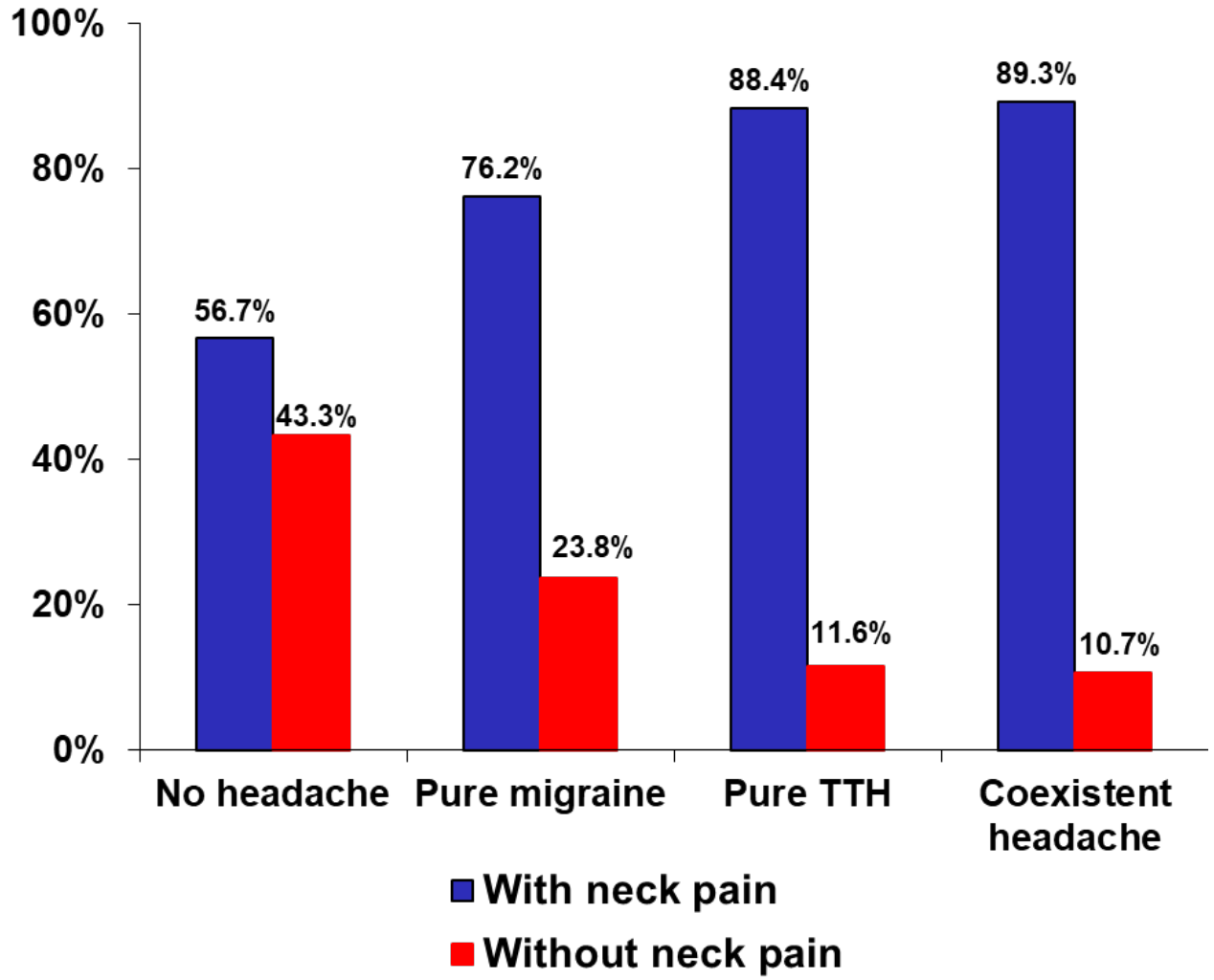


- ~40% of patients reported frequent location of pain in the occipital and neck regions greater than 1/3 of the time
- Occipital headache during migraine was often triggered by neck pain

Percentage headache location in migraine: (1) any occurrence, (2) greater than 1/3 time, (3) greater than 2/3 of time

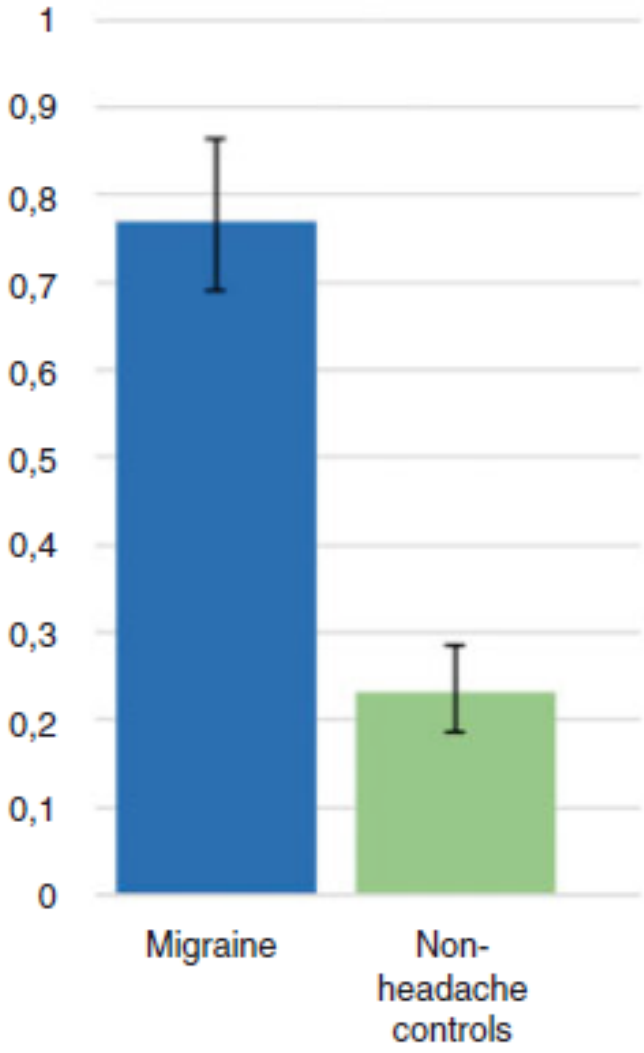
Kelman, Headache 2005

1-year prevalence of self-reported neck pain (n = 797)



Ashina S, Cephalalgia 2015

Mean Relative Frequency of Associated Neck Pain in Patients with Migraine vs. Non-Headache Controls

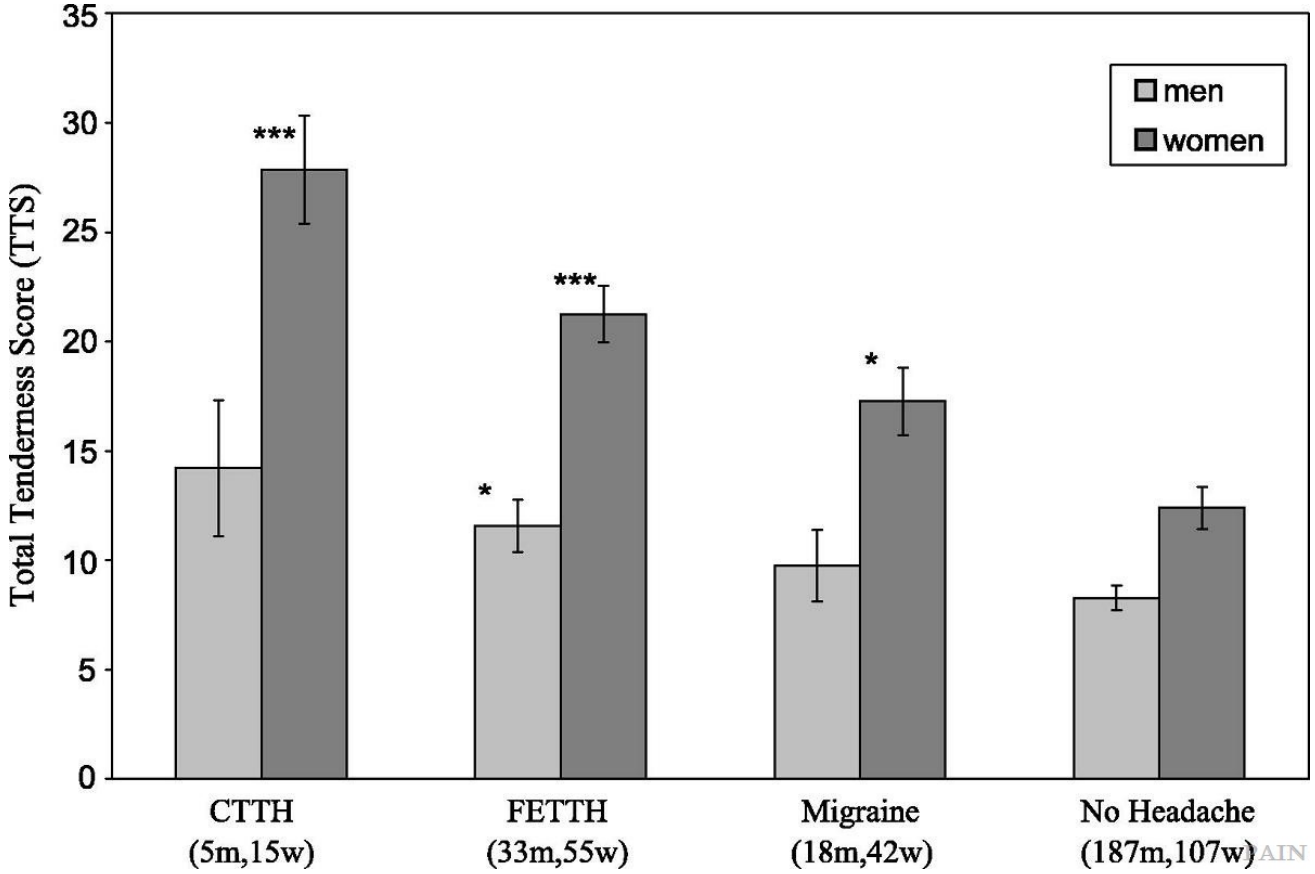


The meta-analysis for clinic-based studies: the pooled relative frequency of neck pain

- 77.0% (95% CI: 69.0–86.4) in the migraine group
- 23.2% (95% CI:18.6–28.5) in the non-headache control group

Al-Khazali HM et al. Cephalalgia. 2022

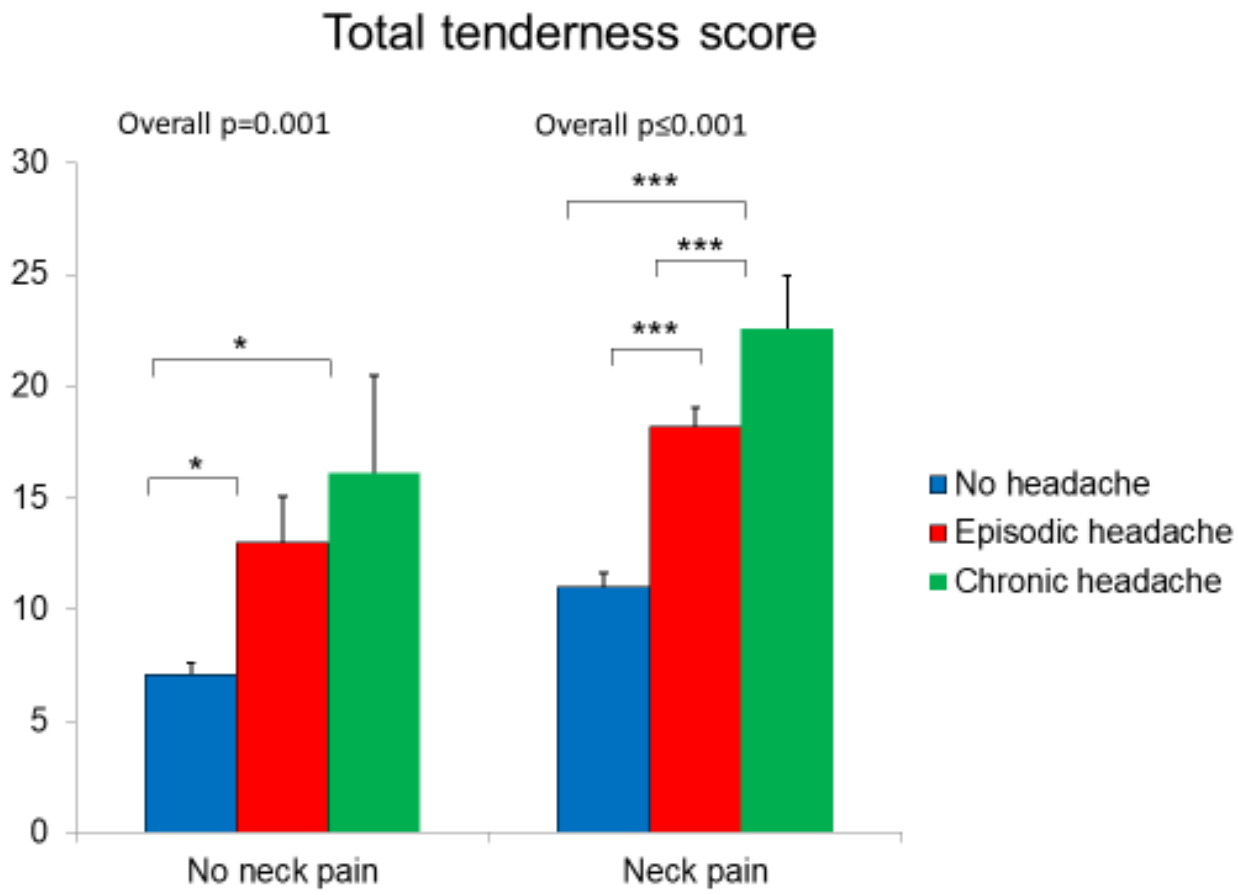
Pericranial tenderness according to different headache disorders



Mean TTS ± SEM. Multiple regression analysis (controlled for age difference): men: $F = 3.17$, $p = 0.025$; women: $F = 17.6$, $p < 0.001$. Pairwise comparison: (∗∗∗) Significant difference from subjects with no headache at the 0.01 level. (∗) Significant difference from subjects with no headache at the 0.05 level.

Buchgreitz, Pain 2006

Headache coexistent with neck pain



Ashina S et al., Scand J Pain 2022

Muscle tenderness and primary headache

- Muscle tenderness occurring before the onset of migraine attacks (or associated with TTH) is considered primary, possibly originating from activation of pericranial nociceptors

- Muscle tenderness that develops after the onset of headache is considered secondary, potentially resulting from pain referral by sensitized trigeminovascular neurons

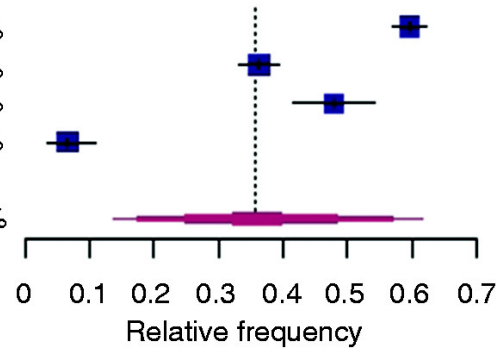
Burstein R et al. Curr Opin Neurol 2017

Relative frequency of dizziness in migraine

“Dizziness” in patients with migraine: 35.7%

Reference	Total relative frequency		95% CI	Weight
Bisdorff, 2010	1271	0.596	[0.569; 0.623]	25.2%
Kelman, 2006	1009	0.363	[0.333; 0.393]	25.2%
HSU, 2011	238	0.479	[0.416; 0.543]	24.9%
Carvalho, 2018	180	0.067	[0.034; 0.108]	24.8%
Random effects model 2698		0.357	[0.137; 0.615]	100.0%

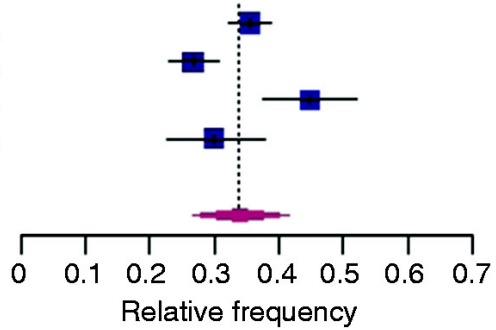
Heterogeneity: I^2 = 99% [99%; 99%], τ^2 = 0.0700, χ^2_3 = 300.90 (p < 0.01)



“Vertigo” in patients with migraine: 33.9%

Reference	Total relative frequency		95% CI	Weight
Akdal, 2015	871	0.355	[0.323; 0.387]	27.7%
Lampl, 2019	487	0.267	[0.229; 0.307]	26.7%
Carvalho, 2018	180	0.447	[0.375; 0.520]	23.3%
Menon, 2013	144	0.300	[0.228; 0.378]	22.2%
Random effects model 1682		0.339	[0.267; 0.415]	100.0%

Heterogeneity: I^2 = 87% [68%; 94%], τ^2 = 0.0055, χ^2_3 = 22.43 (p < 0.01)



Iljazi et al. Cephalalgia. 2020

Premonitory symptoms in migraine

An electronic diary study

Table 1 *Nonheadache features in the intention to treat population at baseline and during the study*

Nonheadache feature	Sessions where each nonheadache feature was reported, %		
	Premonitory (n = 803)	Headache (n = 559)	Postdrome (n = 425)
Tired/weary	72.5	84.3	88.2
Dizziness	22.9	31.1	
Lots of energy/hyperactivity	5.2	2.7	
Yawning	27.8	25.4	13.9
Pale face			21.4
Stiff neck	49.7	62.8	41.9
Light sensitive			36.0
Noise sensitive	38.4	*	31.8
Blurred vision	28.0	34.7	17.4
Sensitive skin	5.7	9.3	5.2

Giffin et al., Neurology, 2003

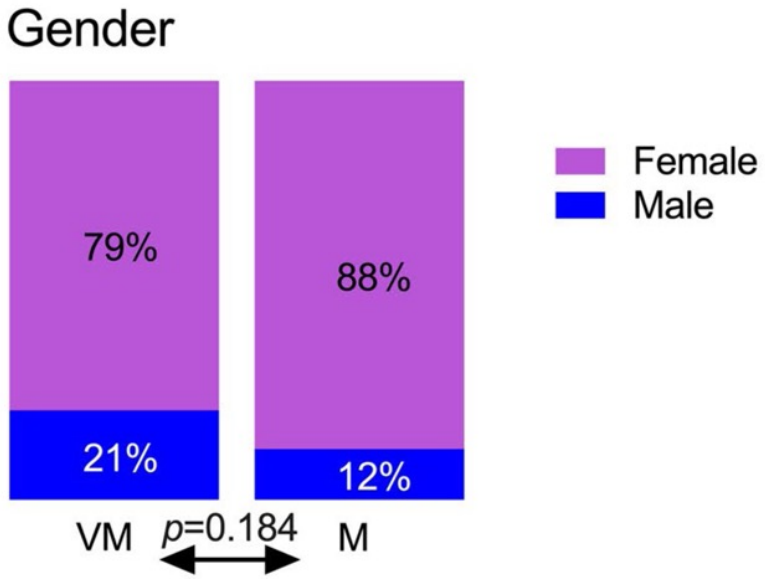
Vestibular migraine:
ICHD appendix diagnostic criteria

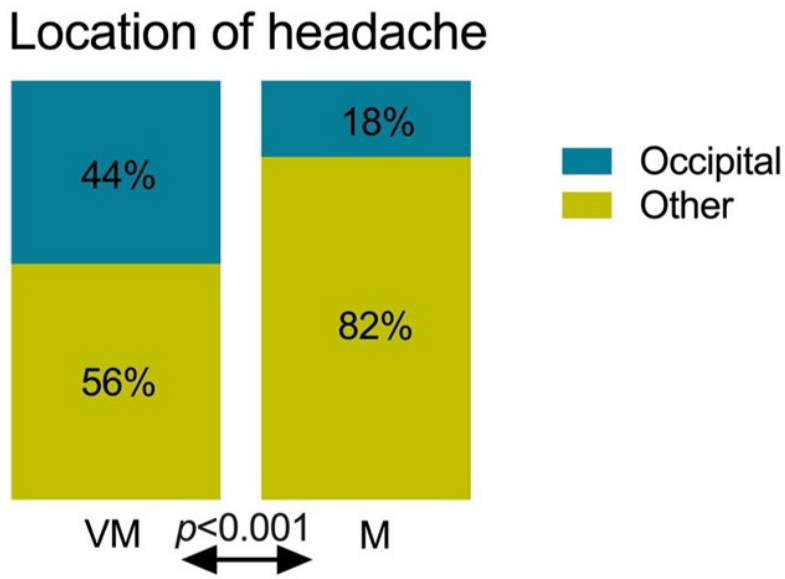
A. At least 5 episodes fulfilling criteria C and D
B. A current or past history of *Migraine without aura* or *Migraine with aura*
C. Vestibular symptoms[a] of moderate or severe intensity, lasting between 5 min and 72 hrs.
D. At least half of episodes are associated with at least 1 of the following 3 migrainous features:
    1. headache with at least two of the following four characteristics:
        a) unilateral location
        b) pulsating quality
        c) moderate or severe intensity
        d) aggravation by routine physical activity
    2. photophobia and phonophobia
    3. visual aura
E. Not better accounted for by another ICHD-3 diagnosis or by another vestibular disorder.

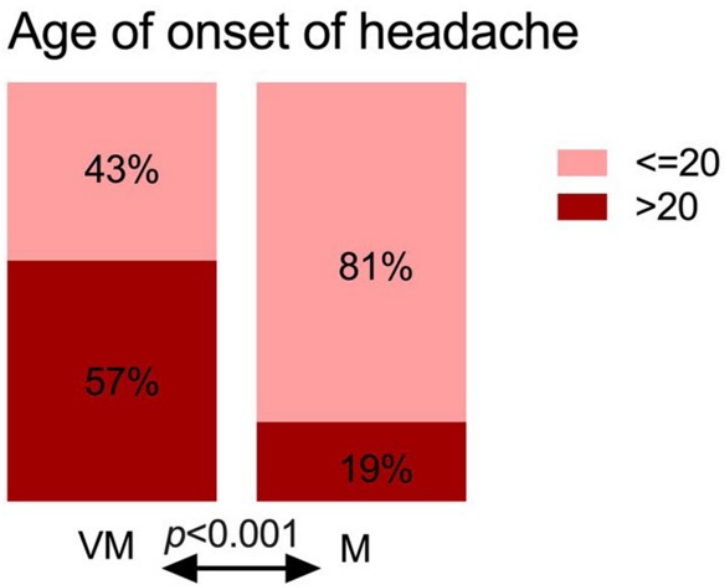
[a]defined by the Bárány Society's Classification of Vestibular Symptoms

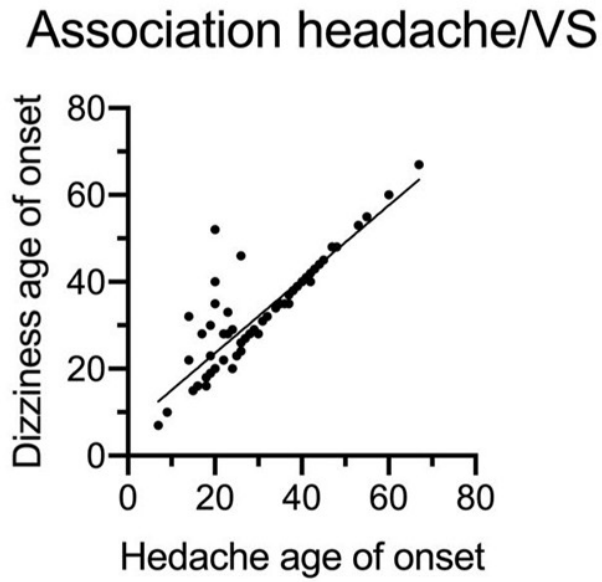
ICHD-3

Vestibular migraine (n=103) vs. migraine w/o vestibular symptoms (n=66)



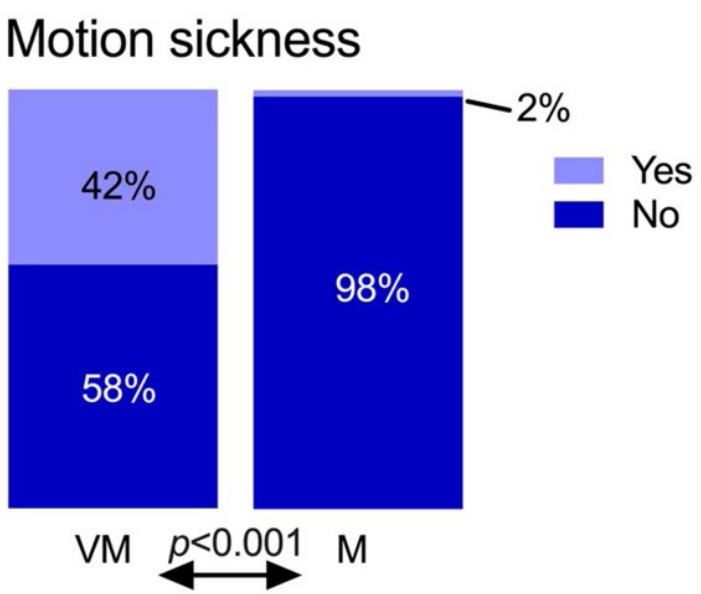


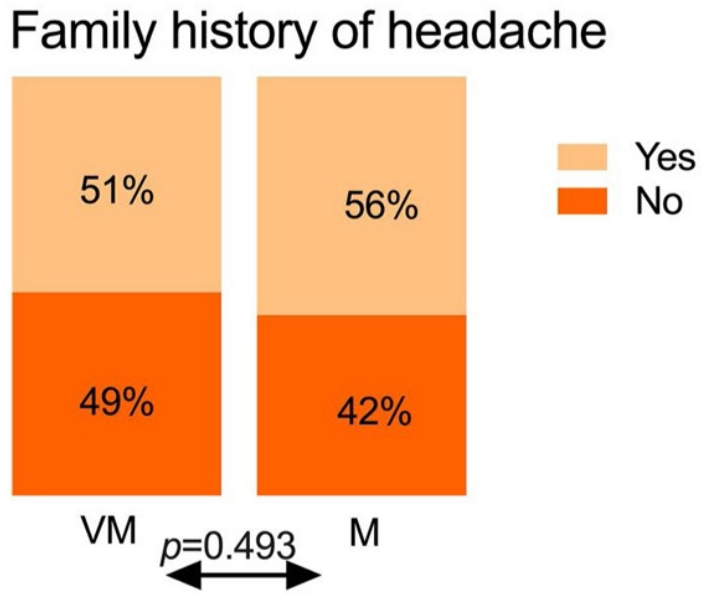


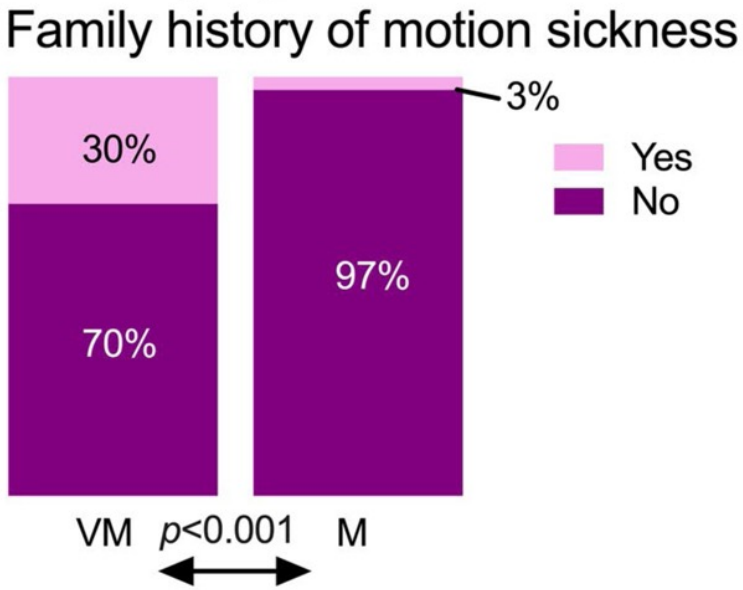


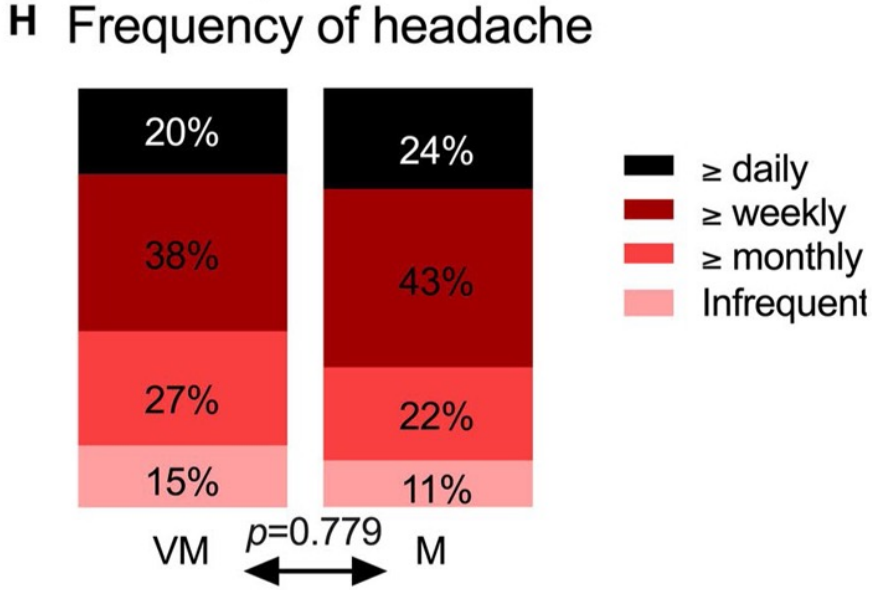
Wattiez et al. Headache. 2020

Vestibular migraine (n=103) vs. migraine w/o vestibular symptoms (n=66)



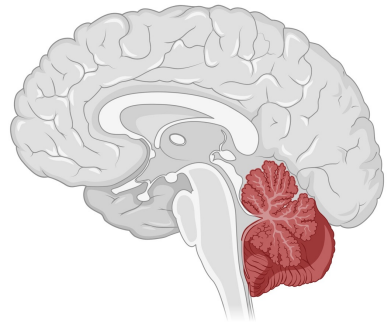






Wattiez et al. Headache. 2020

Cerebellum and nociception

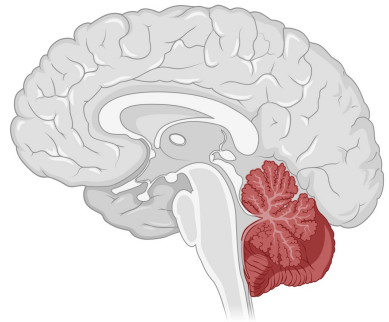


- Multisensory processing
- Associated with pain-related cognitive, autonomic, and somatovisceral regions in the human brain
- Specific reciprocal connections to trigeminal pain pathways
- Cerebellar activity during acute and chronic pain conditions, and in association with the emotional, cognitive, and motor responses to pain

Based on these brain dynamics, migraine varied symptomatology and emerging subclinical evidence: the role of the cerebellum has become highly relevant in the last two decades

Noseda R et al. J Neurosci. 2019

Migraine and cerebellar dysfunction



- Familiar hemiplegic migraine: ataxia
- Vestibular migraine: vertigo, dizziness
- Migraine with/without aura:
  - Ictal and interictal balance abnormalities
  - Abnormal nystagmus and decrease in saccadic eye-movement accuracy
  - Interictal lack of fine coordination
  - Pre and ictal dizziness, vertigo, reduced coordination

Vincent M, Hadjikhani N. Headache. 2007

Summary

- Neck pain is highly prevalent in patients with migraine
- Occipital headaches can be a prominent feature in migraine
- 1/3 of all migraines begin with tenderness of neck/shoulder muscles that gradually develop into a low-grade occipital headache
- Migraine is often preceded or accompanied by dizziness, vertigo, decreased motor coordination, instability, insecure walking, clumsiness, and reduced coordination
- Cerebellum may play a modulatory role in migraine, but role of cerebellum in migraine requires further exploration

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Additional slides

Vestibular symptoms

1. Spontaneous vertigo:
   - internal vertigo (a false sensation of self-motion)
   - external vertigo (a false sensation that the visual surround is spinning or flowing)

2. Positional vertigo, occurring after a change of head position
   - visually-induced vertigo, triggered by a complex or large moving visual stimulus
   - head motion-induced vertigo, occurring during head motion

3. Head motion-induced dizziness with nausea (dizziness is characterized by a sensation of disturbed spatial orientation; other forms of dizziness are currently not included in the classification of vestibular migraine)

ICHD-3

Vestibular symptoms

1. Duration of episodes
   - 30% of patients have episodes lasting minutes
   - 30% have attacks for hours
   - 30% have attacks over several days
   - 10% have attacks lasting seconds only, which tend to occur repeatedly during head motion, visual stimulation or after changes of head position. In these patients, episode duration is defined as the total period during which short attacks recur.
   - For some patients it can take 4 weeks to recover fully from an episode
   - Core episode rarely exceeds 72 hrs.
2. One symptom is sufficient during a single episode
3. Different symptoms may occur during different episodes
4. Associated symptoms may occur before, during or after the vestibular symptoms
5. Other symptoms: Transient auditory symptoms, nausea, vomiting, prostration and susceptibility to motion sickness

ICHD-3

Vestibular migraine (VM):
differential diagnosis

- Vestibular migraine is a clinical diagnosis, with currently no pathognomonic clinical sign or laboratory test that can verify its diagnosis

- History/physical examinations do not suggest another vestibular disorder, or such a disorder has been considered but ruled out by appropriate investigations or such a disorder is present as a comorbid condition, but episodes can be clearly differentiated

- Vestibular laboratory abnormalities are quite variable, which may reflect inconsistent findings regarding the existence of a peripheral vestibular component. Nevertheless, vestibular testing is still helpful to rule out other disorders considered in the differential diagnosis

- Migraine attacks may be induced by vestibular stimulation → differential diagnosis should include other vestibular disorders complicated by superimposed migraine attacks

ICHD-3

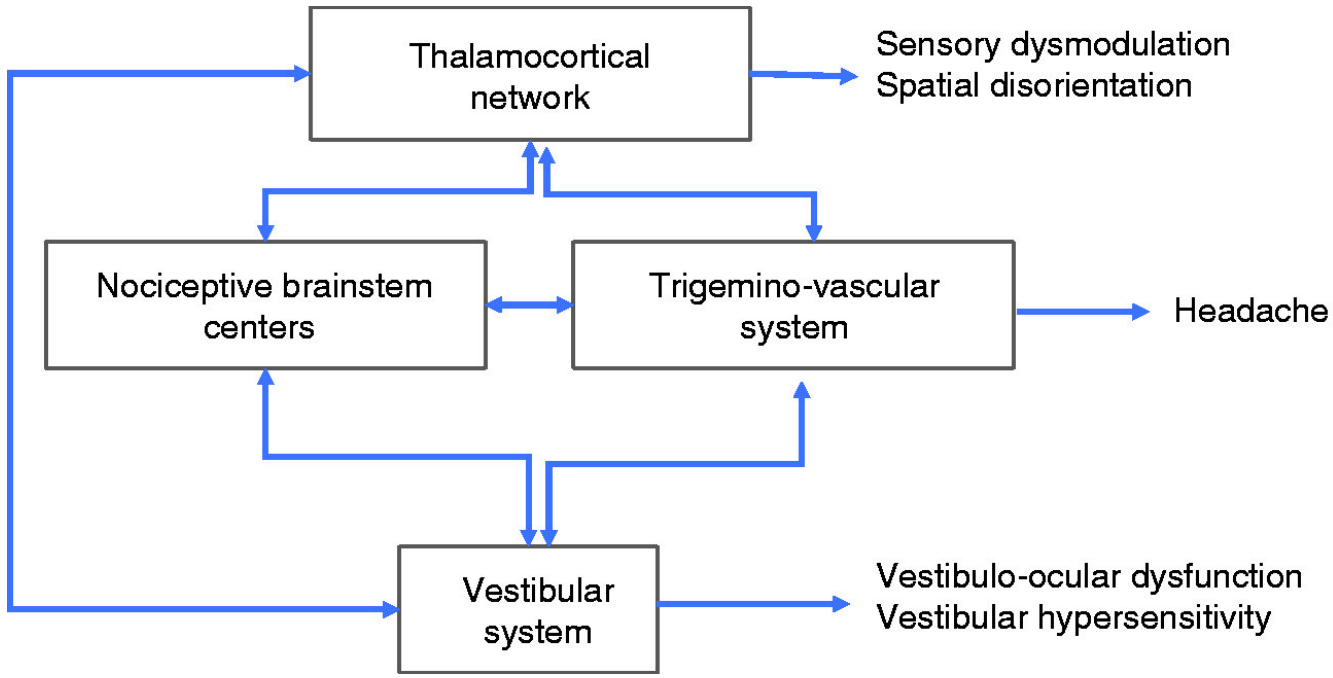
Vestibular migraine (VM)

- One-year prevalence in general population: 1-2.7%
- Relative frequency in specialized dizziness and headache clinics: 4–10%
- Female to male ratio: 1.5–5 to 1
- Age of onset for VM symptoms: 8-50 years old or even older (median ages being the mid-30s to 40s)
- Migraine headache tends to present first, and patients may be headache-free for years before the onset of vestibular symptoms

Huang et al. Cephalalgia 2020

Pathogenesis of vestibular migraine: possible mechanisms

- Abnormal sensory modulation or integration within the thalamo-cortical network could result in dizziness and spatial disorientation
- Hyperactivity within the trigeminovascular system (TVS) and nociceptive brainstem centers could result in headache
- Altered activity in the vestibular system could lead to transient vestibulo-ocular dysfunction or vestibular hypersensitivity associated with migraine features



Huang et al. Cephalalgia 2020