楊鈞百 醫師

台中光田醫院神經醫學部部長

台中光田醫院醫學研究部主任

台灣頭痛學會理事長

中興大學合聘教授

長庚大學臨床醫學研究所博士

美國史丹佛大學睡眠中心研究

Recent Publications

1. Wang, H.F, Liu, W.C., Zailani H, Yang, C.C., Chen, T.B., Chang, C.M., Tsai, I.J., **Yang, C.P.***, Su, K.P.* A 12-week randomized double-blind clinical trial of eicosapentaenoic acid intervention in episodic migraine. Brain, behavior, and immunity. 2024 May:118:459-467. (*共同通訊IF= 15.1)

2. Hou, T.W., Yang, C.C., Lai, T.H., Wu, Y.H.*, **Yang, C.P.*** Light Therapy in Chronic Migraine. Current pain and headache reports. 2024 Jun 12. doi: 10.1007/s11916-024-01258-y. (IF= 3.2)

3. Yu Aoh, Hou, T.W., Yang, C.C., Chang, C.M., Tsai, I.J., Cheng, C.W.*, **Yang, C.P.*** Update on gepants for the treatment of chronic migraine. Journal of the Chinese Medical Association. 2024; 87:350-356. (IF= 3.396)

4. **Yang, C.P.**, Tseng, P.T., Yang, C.C., Tsai, I.J., Su, K.P.*. Delirium prevention with age consideration- Reply to "Comment on Yang et al., 2020: Melatonergic agents in the prevention of delirium: A network meta-analysis of randomized controlled trials". Sleep Med Rev. 2023 (70) 101803. (IF: 10.5)

5. Chen, T.B., Chang, C.M., Yang, C.C., Tsai, I.J., Wei, C.Y., Yang, H.W., **Yang, C.P.***. Neuroimmunological Effect of Vitamin D on Neuropsychiatric Long COVID Syndrome: A Review. Nutrients. 2023 Aug 30;15:3802. (IF: 5.9)

6. **Yang, C.P.**, Yang, C.C., Tsai, I.J., Lin, T.S., Chiou, Y.L., Wang, H.F., Chang, C.M., Yih, K.H.*. The immediate effects of lavender-based essential oil inhalation on subsequent polysomnography in people with poor sleep quality. J Chin Med Assoc. 2023; 86:665-671. (IF: 3.396)

7. Lin, T.H., Yang, C.C., Lee, S.Y., Chang, C.M., Tsai, I. J., Wei, C.Y., **Yang, C.P.*.** The effect of bright light therapy in migraine patients with sleep disturbance: A prospective, observational cohort study protocol. 2023 Jan 19:14:1041076. Frontiers in Aging Neuroscience eCollection 2023. (IF:5.702)

8. **Yang CP**, Chang CM, Yang CC, Pariante CM, Su KP: Long COVID and long chain fatty acids (LCFAs): Psychoneuroimmunity implication of omega-3 LCFAs in delayed consequences of COVID-19. Brain Behav Immun 2022, 103:19-27. (IF: 19.23)

9. Chung CH, Chung SD, Cheng YH, **Yang CP***, Chien CT*: Long-Lasting Exendin-4-Loaded PLGA Nanoparticles Ameliorate Cerebral Ischemia/Reperfusion Damage in Diabetic Rats. J Pers Med 2022, 12. (共同通訊IF: 4.95)

10. **Yang, C.P.**, Liang, C.S., Chang, C.M., Yang, C.C., Shih, P.H., Yau, Y.C., Tang, K.T., Wang, S.J., Comparison of New Pharmacologic Agents With Triptans for Treatment of Migraine: A Systematic Review and Meta-analysis. JAMA Netw Open 2021, 4(10), e2128544. (IF: 8.485)

11. **Yang, C.P.**, Zeng, B.Y., Chang, C.M., Shih, P.H., Yang, C.C., Tseng, P.T., Wang, S.J., Comparative Effectiveness and Tolerability of the Pharmacology of Monoclonal Antibodies Targeting the Calcitonin Gene-Related Peptide and Its Receptor for the Prevention of Chronic Migraine: a Network Meta-analysis of Randomized Controlled Trials. Neurotherapeutics 2021. (IF: 7.62)

12. Yau, Y.C., **Yang, C.P.**, Lin, C.P., Tsai, I.J., Chang, C.M., Yang, C.C., Shih, P.H., Liao, Y.Y., The Morphological and Dynamic Changes of Ultrasound in the Evaluation of Effects of Oral Steroids Treatment for Patients with Carpal Tunnel Syndrome. Diagnostics (Basel) 2021, 11(8). (IF: 3.706)

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20. Guo, C.H., Chen, W.L., Liao, C.H., Huang, K., Chen, P.Y., **Yang, C.P.**, Effects of Chinese Medicinal Formula BNG-1 on Phosphodiesterase 3B Expression, Hepatic Steatosis, and Insulin Resistance in High Fat Diet-induced NAFLD Mice. Int J Med Sci 2018, 15(11), 1194-1202. (IF:3.738)

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台南市安南區安和路一段 40 號 Tel 06-2810700 Fax 06-2810702
Email: huang@livingwater.com.tw

黃子洲 (Tzu-Chou Huang) M.D.

學歷	1986-1993 醫學士	中國醫藥大學	台中市
經歷	1993-1993 內科部住院醫師	林口長庚醫院	桃園縣
	1993-1997 神經科住院醫師、總醫師	成大醫院	台南市
	1997-1998 內科主治醫師	省立新營醫院	台南縣
	1998-2001 主任兼醫師	台南縣安定鄉衛生所	台南縣
	2001-2006 神經科主治醫師、生理檢查中心主任、神經科主任	台南新樓醫院	台南市
	2005-2006 護理學系兼任講師	長榮大學	台南縣
	2006- 主治醫師	台南活水神經內科診所	台南市
	2008- 神經科兼任主治醫師	成大醫院	台南市
	2009- 副院長	台南活水、安河神經內科診所	台南市
	2011-2014 秘書長	台灣頭痛學會	
	2014- 理事	台灣頭痛學會	
	2018 訪問學者	NVVD, Johns Hopkins Hospital	Baltimore
資格	神經科專科醫師 老年醫學會專科醫師 睡眠醫學會專科醫師 IHS Headache Master, 2013		神專醫字 407 號 台老醫專字 0191 號 台睡醫字第 68 號 #181
近期著作	Huang TC, Lai TH, Taiwan Headache Society TGSOTHS. Medical Treatment Guidelines for Preventive Treatment of Migraine. Acta Neurol Taiwan. 2017;26(1):33-53.		
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	黃子洲：持續姿勢-知覺性頭暈(PPPD)。台灣醫學 Formosan J Med 2023;27:323-9		
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Emerging Therapies in Vestibular Migraine:

Focus on CGRP Monoclonal Antibodies and Beyond

活水神經內科診所

黃子洲

1.1 無預兆偏頭痛 Migraine without aura

A. 至少有5次發作符合基準B-D

B. 頭痛發作持續4-73小時 (未經治療或治療無效)

C. 頭痛至少具下列四項特徵其中兩項：

U 1. 單側 **U**nilateral

P 2. 搏動性 **P**ulsating

M 3. 疼痛程度中或重度 **M**oderate to severe

A 4. 日常活動會使頭痛加劇或避免此類活動(如走路或爬樓梯) **A**ggravated by **A**ctivity

D. 當頭痛發作時至少有下列一項：

噁 1. 噁心及/或嘔吐

怕 2. 畏光及怕吵

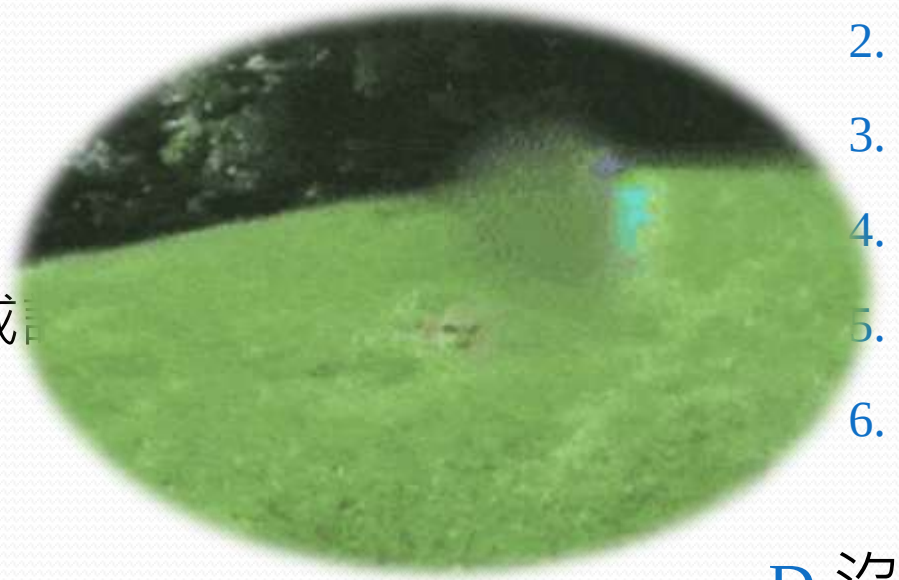
E. 沒有其他更合適的ICHD-3診斷

1.2 預兆偏頭痛 Migraine with aura

A.至少有兩次發作符合基準B及C

B.包括下列一或多項完全可逆的預兆症狀：

1. 視覺
2. 感覺
3. 說話及/或
4. 運動
5. 腦幹
6. 視網膜



C.至少具下列六項特徵其中三項：

1. 至少一種預兆症狀在 ≥ 5分鐘逐漸發展
2. 兩種或兩種以上的預兆症狀接續發生
3. 每一種個別的預兆症狀持續5-60分鐘
4. 至少有一種預兆症狀是單側的
5. 至少有一種預兆症狀是正向的
6. 預兆會同時伴隨頭痛或於預兆後60分鐘內頭痛

D.沒有其他更合適的ICHD-3診斷

偏頭痛六+一大特徵

1. 單側
2. 博動
3. 中重度
4. 日常生活影響

1. 噁心或嘔吐
2. 畏光及怕吵

1. **(視覺)預兆**

Vestibular migraine

TABLE II.
Outcome of Vestibular Meniere's Disease Group.

		Migraine
Continued vestibular Meniere's	21	17
Developed unilateral Meniere's	8	3
Became asymptomatic	7	1
Otosclerotic inner ear syndrome	1	0
Vascular compression syndrome	1	0
Total	38	21

81%

Laryngoscope. 1992;102:135-8.

Migraine and isolated recurrent vertigo of unknown cause

Hyung Lee*†, Sung Il Sohn*†, Doo Kyo Jung*†, Yong Won Cho*†, Jeong Geung Lim*†, Sang Doe Yi*† and Hyon Ah Yi*

*Department of Neurology, †Brain Research In

Chronic recurrent attacks of vertigo, not ass common reason for referral to our neurotolo some cases remain undiagnosed. We prospectively evaluated 72 consecutive patients who presented to the clinic with isolated recurrent vertigo of unknown cause. All patients underwent diagnostic evaluation to exclude identifiable causes of isolated recurrent vertigo. We compared the prevalence of migraine, according to the International Headache Society (IHS) criteria, in the isolated recurrent vertigo group, with a sex- and age-matched control group of orthopedic patients. The prevalence of migraine according to IHS criteria was higher in the isolated recurrent vertigo group (61.1%) than in the control group (10%; $p < 0.01$). Only 16.7% of patients had an abnormal vestibular function test. The most common abnormal finding was a unilateral vestibular weakness to caloric stimulation. Our results suggest that migraine should be considered in the differential diagnosis of isolated recurrent vertigo of unknown cause. [Neurol Res 2002; **24**: 663–665]

Keywords: Recurrent vertigo; migraine

72 isolated recurrent vertigo patients
61.1% fulfilled IHS migraine criteria

Neurol Res. 2002;24:663-5.

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T. Lempert

Journal of Vestibular Research 22 (2012) 167–172
DOI 10.3233/VES-2012-0453
IOS Press

Vestibular migraine: Diagnostic criteria

Consensus document of the Bárány Society and the International Headache Society

Thomas Lempert[a,*], Jes Olesen[b], Joseph Furman[c], John Waterston[d], Barry Seemungal[e], John Carey[f], Alexander Bisdorff[g], Maurizio Versino[h], Stefan Evers[i] and David Newman-Toker[j]

[a]*Department of Neurology, Schlosspark-Klinik, Berlin, Germany*
[b]*Danish Headache Center and Department of Neurology, University of Copenhagen, Copenhagen, Denmark*
[c]*Departments of Otolaryngology and Neurology, University of Pittsburgh, Pittsburgh, PA, USA*
[d]*Department of Neurology and Monash University Department of Medicine, Alfred Hospital, Melbourne, Australia*
[e]*Department of Clinical Neuroscience, Charing Cross Hospital, London, UK*
[f]*Department of Otolaryngology, Head and Neck Surgery, Johns Hopkins University School of Medicine, Baltimore, MD, USA*
[g]*Department of Neurology, Centre Hospitalier Emile Mayrisch, Esch-sur-Alzette, Luxembourg*
[h]*Department of Neurological Sciences University of Pavia, HSC and BCC National Neurological Institute IRCCS C. Mondino Foundation, Pavia, Lombardy, Italy*
[i]*Department of Neurology, University of Münster, Münster, Germany*
[j]*Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD, USA*

rology, Schlosspark-Klinik, Berlin, Germany. E-mail: Thomas. Lempert@schlosspark-klinik.de.

group to develop diagnostic criteria for vestibular migraine. The definition of vestibular migraine is part of

J. Olesen

J Vestib Res. 2012;22:167-172

Vestibular migraine

ICVD

A. At least 5 episodes with vestibular symptoms of moderate or severe intensity, lasting 5 min to 72 hours

B. Current or previous history of migraine with or without aura according to the International Classification of Headache Disorders (ICHD)

C. One or more migraine features with at least 50% of the vestibular episodes

- Headache with at least two of the following characteristics: one sided location, pulsating quality, moderate or severe pain intensity, aggravation by routine physical activity
- Photophobia and phonophobia
- Visual aura

D. Not better accounted for another vestibular or ICHD diagnosis

ICHD-3

A. At least five episodes fulfilling criteria C and D

B. A current or past history of 1.1 *Migraine without aura* or 1.2 *Migraine with aura*

C. Vestibular symptoms of moderate or severe intensity, lasting between 5 minutes and 72 hours

D. At least 50% of episodes are associated with at least one of the following three 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

A1.6.6 前庭偏頭痛

A. 至少有 5 次發作符合基準 C 及 D
B. 現在或過去有符合 1.1 *無預兆偏頭痛*或 1.2 *預兆偏頭痛*的病史
C. 前庭症狀嚴重程度中或重度，持續 5 分鐘到72 小時
D. 至少 50%的發作會合併以下 3 種偏頭痛特徵中至少 1 種：
   1. 頭痛，至少具下列 4 項特徵其中 2 項：
      a) 單側 Unilateral
      b) 搏動性 Pulsating
      c) 疼痛程度中或重度 Moderate to severe
      d) 日常活動會使頭痛加劇 Aggravated by daily activity
   2. 畏光及怕吵
   3. 視覺預兆
E. 沒有其他更合適的 ICHD-3 或其他前庭疾患的診斷

Vestibular migraine 的診斷

- The key points of diagnostic criteria for definite migrainous vertigo:
  - The diagnosis of migraine
  - Episodic vestibular symptoms
  - Temporal relationship between vestibular and migrainous symptoms
  - Exclusion of other causes

Probable vestibular migraine (ICVD)

A. At least 5 episodes with vestibular symptoms of moderate or severe intensity, lasting 5 min to 72 hours
B. Only one of the criteria B and C for vestibular migraine is fulfilled (migraine history or migraine features during the episode)
C. Not better accounted for another vestibular or ICHD diagnosis

J Vestib Res. 2012;22:167-172

極可能前庭偏頭痛 (ICVD)

A. 至少有五次前庭症狀的發作，嚴重程度為中度或重度，持續5分鐘到72小時

B. 只有符合前庭型偏頭痛的診斷準則B或C中的一項(偏頭痛病史或偏頭痛特徵)

C. 無法歸因於其他更好的前庭或ICHD的診斷

B. 現在或先前有符合國際頭痛分類(ICHD)偏頭痛(有預兆或無預兆)診斷的病史

C. 在至少50%的前庭症狀發作時同時有一項或多項偏頭痛特徵
- 頭痛，以下特徵至少符合兩種：單側，搏動性、疼痛程度為中或重度、日常活動會使頭痛加劇
- 怕光及怕吵
- 視覺預兆

J Vestib Res. 2012;22:167-172

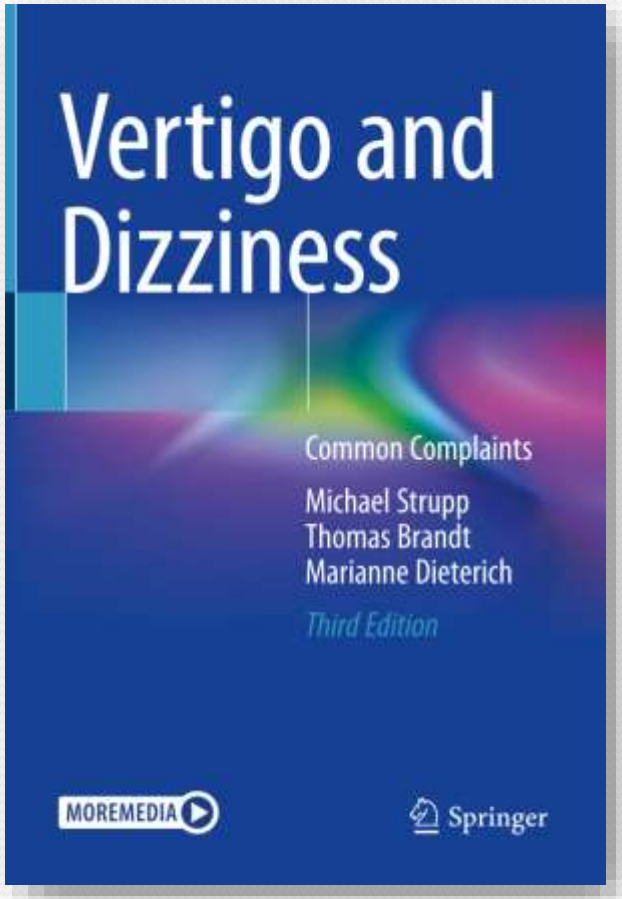
Prevalence

- Germany: 1%
- US: 2.7%

- Taiwan (Kinmen, middle-aged women): 5%

- Korea: 10% of migraineurs
- Taiwan (Tainan): 17.6% of migraineurs

Neurology 2006; 67: 1028–1033.
Otol Neurotol 2018; 39: 1037–1044.
Cephalalgia 2011; 31: 77–83.
Cephalalgia 2016; 36: 454–462.
XXVII Bárány Society Meeting, Uppsala 2012



Diagnosis	Frequency	
	n	%
1. Functional dizziness	6854	17.2
2. BPPV	5518	13.8
3. Central vestibular vertigo	5067	12.7
4. Vestibular migraine	5012	12.5
5. Menière's disease	4047	10.1
6. Unilateral vestibulopathy	3659	9.2
7. Bilateral vestibulopathy	2584	6.5
8. Vestibular paroxysmia	1234	3.1
9. Third mobile window syndrome	185	0.5
Unknown vertigo syndromes	1823	4.6
Other disorders	3926	9.8
	39,918	

Michael Strupp, Brandt T, Dieterich M, Strupp M. Vertigo and Dizziness: Common Complaints. London: Springer; 2023

Demographic Aspects

- Occurs at any age
  - 8-53 years (mid 30s-40s)
- Female preponderance
  - F/M: between 1.5 and 5 to 1
- Familial occurrence is not uncommon
- Migraine begins earlier in life than VM (6-15 years)
- Patients may develop vestibular symptoms after their headache attenuated during their lifetime.
- In women, vestibular symptoms can become more pronounced around the time of menopause.

Neurology 2006; 67: 1028
Cephalalgia. 2020;40:107-121
Braz J Otorhinolaryngol.2022;88(Suppl 3):S147-54.
J Laryngol Otol. 2001;115:782

Clinical presentations

Symptom duration

- About 30% of patients have symptoms lasting for **minutes**,
- 30% lasting for **hours**,
- 30% lasting for several **days** at a time, and
- about 10% report fluctuating daily symptoms

Symptom types

- **Spontaneous** vertigo,
- **Positional** vertigo,
- **Visually** induced vertigo,
- **Head motion**-induced **vertigo**, and
- **Head motion**-induced **dizziness** with **nausea**

Otological symptoms

- One-third may have otological symptoms, may not coincide with vestibular symptoms, always transient and mild

J Neurol.2016;263(Suppl 1):S82–S89
Curr Pain Headache Rep. 2024;28:613-620.

Pathophysiology

- Sensory Dysregulation and Central Mechanisms
- Brainstem and Neurotransmitter Pathways

Curr Pain Headache Rep . 2024;28:47-54.

Sensory Dysregulation and Central Mechanisms

- Cortical Spreading Depression (CSD)
- Sensory Hypersensitivity
- Visuo-Vestibular Dysfunction

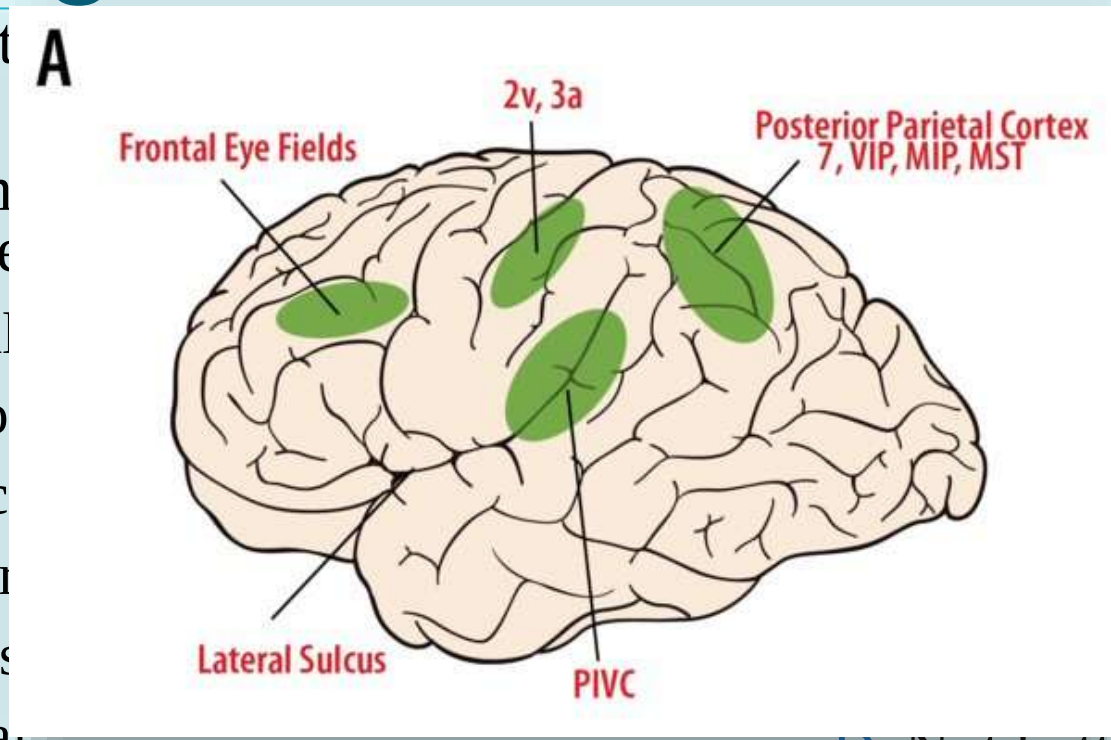
Curr Pain Headache Rep . 2024;28:47-54.

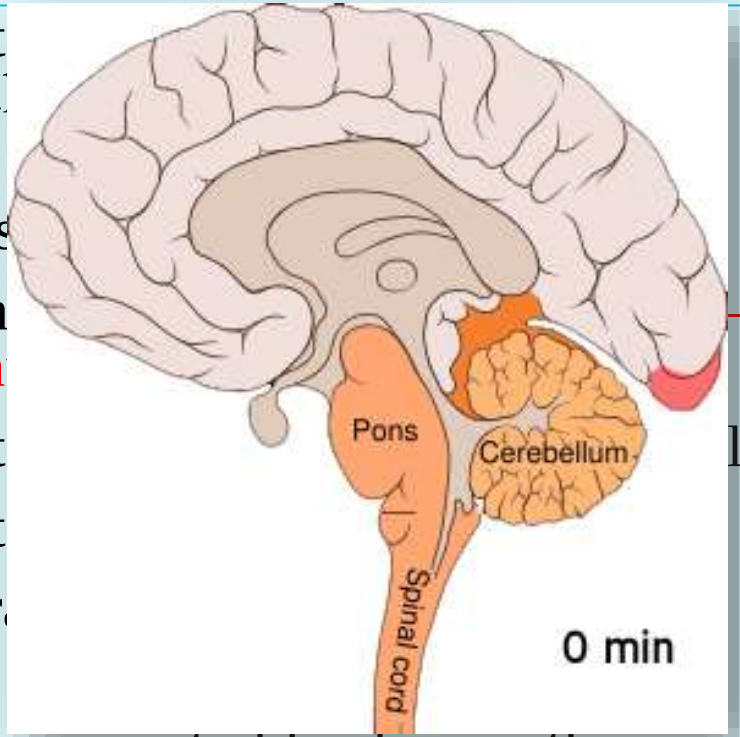
1.2 Migraine with aura

A. At least t
and C

B. One or m
reversible
1. visual
2. senso
3. speec
4. motor
5. brains
6. retina

C. At least three of the following six characteristics:





D. Not better accounted for by another ICHD-3 diagnosis.

Curr Pain Headache Rep . 2024;28:47-54.

Sensory Dysre… Mechanisms

- **Pathophysiology of migraine: a disorder of sensory processing.** *Goadsby PJ, Holland PR, Martins-Oliveira M, Hoffmann J, Schankin C, Akerman S.* Physiol Rev. 2017;553–622.
- **Central integration of canal and otolith signals is abnormal in vestibular migraine.** *King S, Wang J, Priesol AJ, Lewis RF.* Front Neurol. 2014;5:233.
- **Dynamic tilt thresholds are reduced in vestibular migraine.** *Lewis RF, Priesol AJ, Nicoucar K, Lim K, Merfeld DM*. J Vestib Res. 2011;21(6):323–30.
- **Abnormal motion perception in vestibular migraine.** *Lewis RF, Priesol AJ, Nicoucar K, Lim K, Merfeld DM.* Laryngoscope. 2011;121(5):1124–5.
- **Errors of upright perception in patients with vestibular migraine.** *Winnick A, Sadeghpour S, Otero-Millan J, Chang TP, Kheradmand A.* Front Neurol. 2018;9:892.
- **Abnormal visuo-vestibular interactions in vestibular migraine: a cross sectional study.** *Bednarczuk NF, Bonsu A, Ortega MC, Fluri AS, Chan J, Rust H, et al.* Brain. 2019;142(3):606–16.

CURRENT RE…

The brain… in migrai…

SK Aurora &…

Centre for Vision Res…

Acta Neurologica Belgica
https://doi.org/10.1007/s13760-021-01772-5

ORIGINAL ARTICLE

Check for updates

Clinical features of definite vestibular migraine through the lens

…ures are …taneous …) eluci- …ociated …hensive …specific …(26.5%) …the VM …stibular …erences …l group

…vide an insight … which have been … of central neuro… disturbance prec… increased neuron… genetic studies al… duced as a potent… (2). Mutant voltage-gated P/Q type calcium channel genes prob-…

had significant aura, severe disability, depression, tinnitus, sleep disorders, and widespread multimodal cutaneous allodynia. **Conclusions** VM and MwVS may be on the same spectrum of disorders. The VM group had significantly associated widespread multimodal cutaneous allodynia compared with the EM group, indicating that thalamic sensitization plays a key role in VM pathogenesis. Widespread allodynia may be a useful diagnostic aid for VM.

Keywords Allodynia · Cutaneous allodynia · Non-vestibular migraine · Thalamic sensitization

…occur with other primary headache disorders (7).

…47-54.

Brainstem and Ne ays

- Trigeminal-Vestibular Interac

Trigeminal Stimulation Elicits a Peripheral Vestibular Imbalance in Migraine Patients

Enrico Marano, MD; Vincenzo Marcelli, MD; Emanuela Di Stasio, MD; Salvatore Bonuso, MD; Giovanni Vacca, MD; Fiore Manganelli, MD, Elio Marciano, MD; Anna Perretti, MD

Objective.—The study explored the hypothesis that spontaneous nystagmus (Ny) in migraine patients can be triggered or modulated by painful trigeminal stimulation, providing evidence of a functional connection between vestibular and trigeminal systems.

Background.—Vertigo attacks are reported by subjects with migraine or a familiar history of migraine, also independently of headache episodes. Idiopathic vertigo is three times more frequent in migraine patients than in controls. Vestibular investigations in migraine patients have consistently demonstrated spontaneous Ny both of central and peripheral origin.

Design.—In the first phase of the study 10 outpatients experiencing migraine without aura (MO) and 10 healthy volunteers were submitted to the registration of spontaneous primary-position Ny in the dark by Ulmer's video-ocular-nystagmographic equipment. Two electrodes for electrical stimulation were applied on the supraorbital point of one side of the head and the intensity of stimulation corresponding to pain threshold was calculated. Spontaneous ocular movements were recorded for 5 minutes at baseline and after a sequence of five electric pulses (square waves of .5 Hz frequency and 50 μs duration, at pain threshold intensity). Nystagmographic responses were expressed as latency after stimulation, direction of the quick phase, and duration. The second phase of the study explored, with the same procedure, the effects on Ny of supraorbital versus median nerve stimulation in other 10 MO patients. Responses to stimulation were considered the appearance of *de novo* Ny after stimulation in subjects without baseline Ny, or the change of the frequency (at last a 50% variation) or of the direction of Ny after stimulation in subjects with baseline Ny. The latency and the duration of responses to stimulation were also calculated.

Results.—In the first series supraorbital painful electric stimulation was able to modify or to evoke Ny in 8 of 10 migraineurs and in none of 10 volunteers (Fisher's exact test, $P < .01$). Both the baseline and the induced Ny were second degree, stationary persistent, with a linear slow phase and were suppressed by visual fixation. In the second series, supraorbital nerve stimulation was able to induce or modify Ny in all of 10 patients but only in 1 patient Ny was induced by median nerve stimulation. Characters of Ny were the same as previously described. Statistical comparison of the responses at the two sites of stimulation was significant (Fisher's exact test, $P < .01$). In those 7 patients who presented *de novo* Ny after stimulation it was possible to calculate Ny latency and duration. The mean latency was 25 s (SD: 16, range: 14 to 60). The mean duration was 120 s (SD: 94, range: 20 to 290).

Conclusion.—The main result of our study is that in migraine patients painful trigeminal stimulation elicits *de novo*, or modifies pre-existing spontaneous Ny, generally increasing it. The finding was obtained after trigeminal stimulation, but not after median nerve stimulation. We suggest that painful trigeminal stimulation can induce an imbalance of the vestibular system in migraine patients and possibly explain their predisposition to vertigo. Our data require confirmation by other studies.

Key words: migraine, vertigo, trigeminus nerve

Headache 2005;45:325-331

Curr Pain Headache Rep . 2024;28:47-54.

Trigeminovascular-Vestibular Interactions

- A glutamatergic TNC-VN (trigeminal nucleus caudalis to vestibular nuclei) circuit involved in vestibular dysfunction has been identified in a rat model.
- Calcitonin gene-related peptide (CGRP)–expressing neurons in the VN receive glutamatergic projections from the TNC neurons, suggesting a therapeutic role for CGRP blockade.

Curr Pain Headache Rep . 2024;28:47-54.

Calcitonin gene-related peptide facilitates sensitization of the vestibular nucleus in a rat model of chronic migraine

Yun Zhang[1], Yixin Zhang[1*], Ke Tian[2], Yunfeng Wang[1], Xiaoping Fan[1], Qi Pan[1], Guangcheng Qin[3], Dunke Zhang[3], Lixue Chen[2] and Jiying Zhou[1]

Abstract

Background: Vestibular migraine has recently been recognized as a novel subtype of migraine. However, the mechanism that relate vestibular symptoms to migraine had not been well elucidated. Thus, the present study investigated vestibular dysfunction in a rat model of chronic migraine (CM), and to dissect potential mechanisms between migraine and vertigo.

Methods: Rats subjected to recurrent intermittent administration of nitroglycerin (NTG) were used as the CM model. Migraine- and vestibular-related behaviors were analyzed. Immunofluorescent analyses and quantitative real-

mRNA (LV-CGRP vs. LV-NC = 1.0 ± 0.1 vs. 2.1 ± 0.2) in the VN, further attenuating vestibular dysfunction after CM.

Conclusions: These data demonstrates the possibility of sensitization of vestibular nucleus neurons to impair vestibular function after CM, and anti-CGRP treatment to restore vestibular dysfunction in patients with CM.

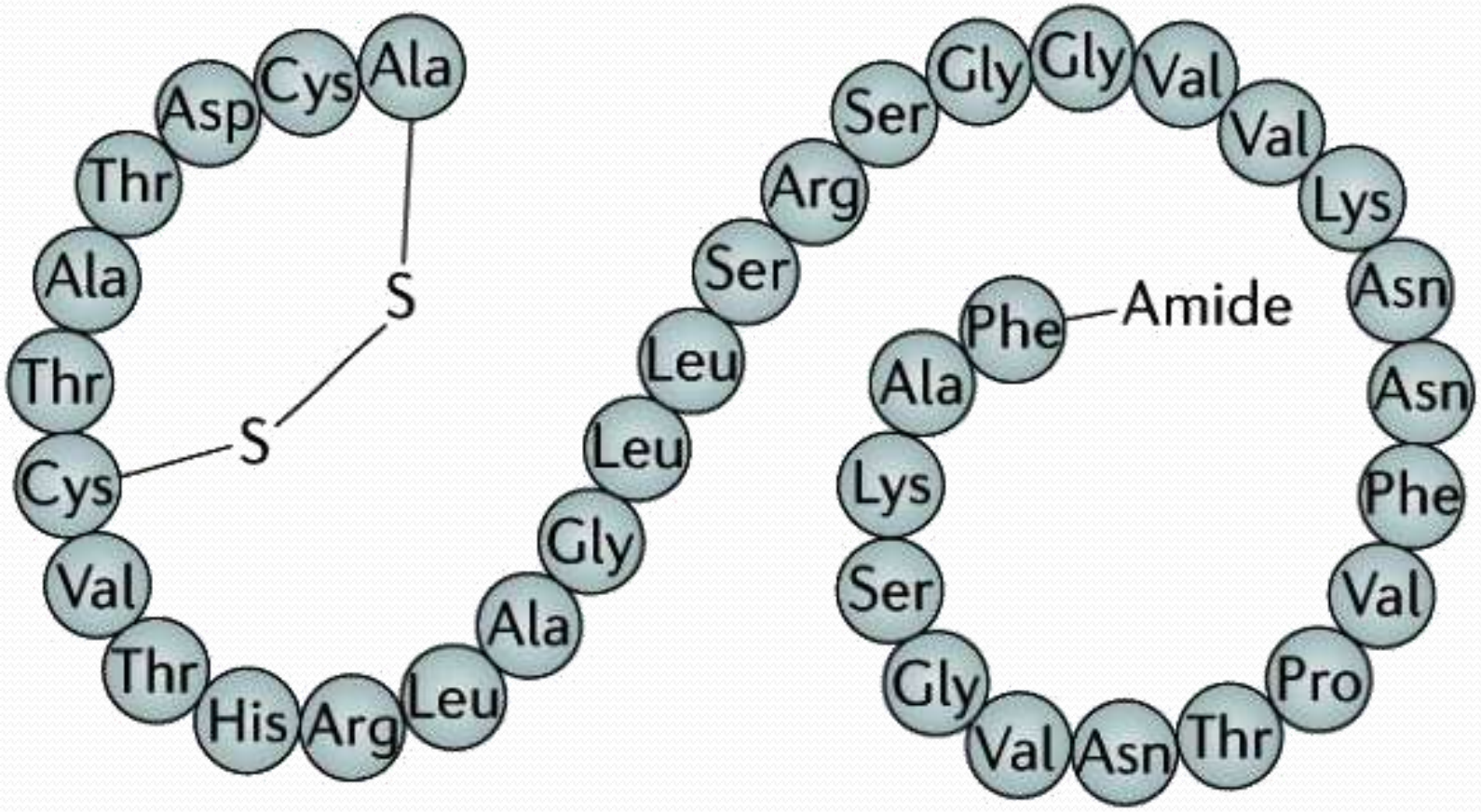
Keywords: CGRP, Vestibular migraine, Trigeminal nucleus caudalis, Vestibular nucleus, Central sensitization, Anti-CGRP treatment

Conclusions

In conclusion, we demonstrated the sensitization of vestibular nucleus neurons in a preclinical model of CM, and down-regulation of CGRP after CM could improve vestibular dysfunction, suppress neuronal activation, and reduce CGRP expression in the VN. Therefore, anti-CGRP might be a promising treatment strategy for ameliorating vestibular dysfunction in migraine patients with vestibular symptoms.

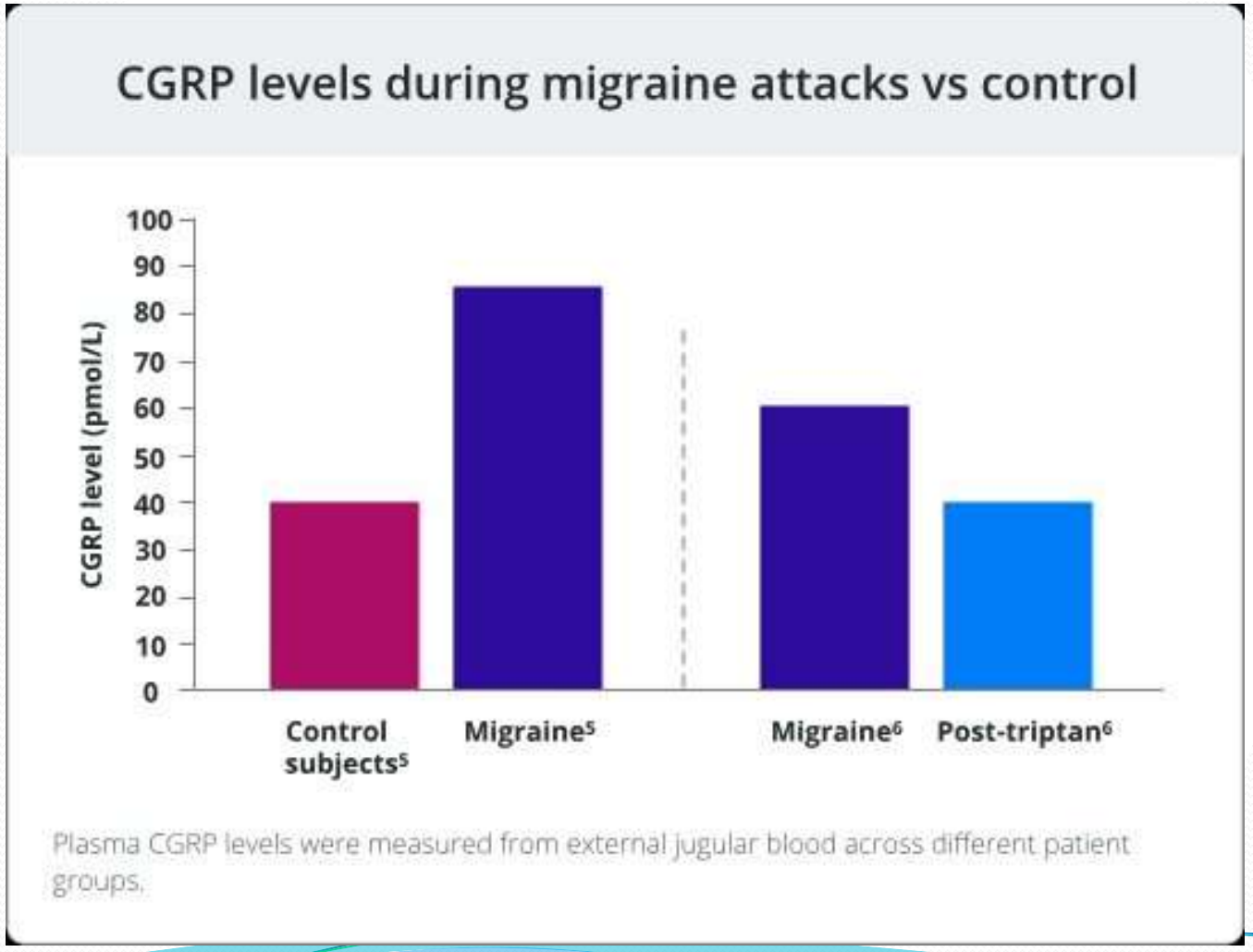
J Headache Pain. 2020;21:72.

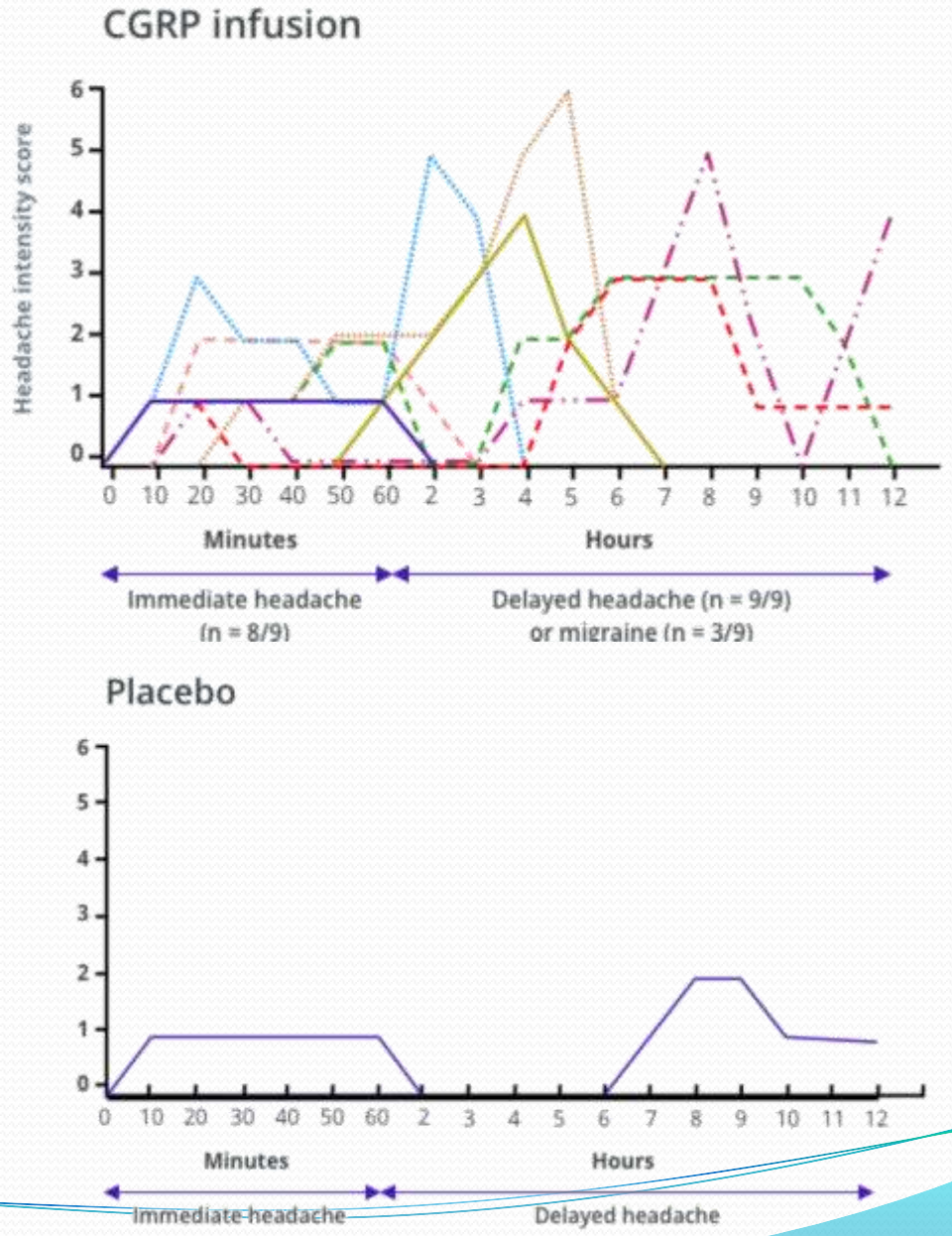
Calcitonin gene-related peptide (CGRP)
抑鈣素基因相關肽



Nat Rev Neurol . 2018;14:338-350.

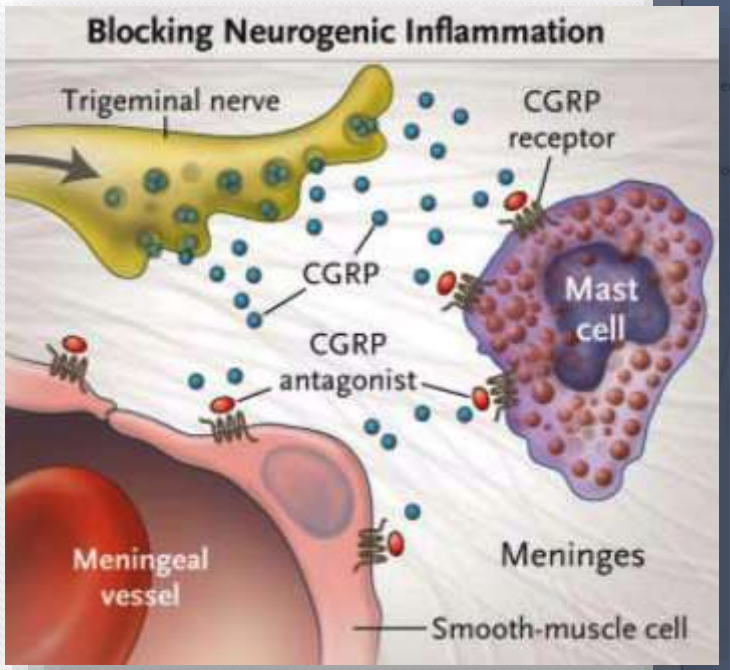
CGRP 是偏頭痛重要的mediator
而且是治療的target

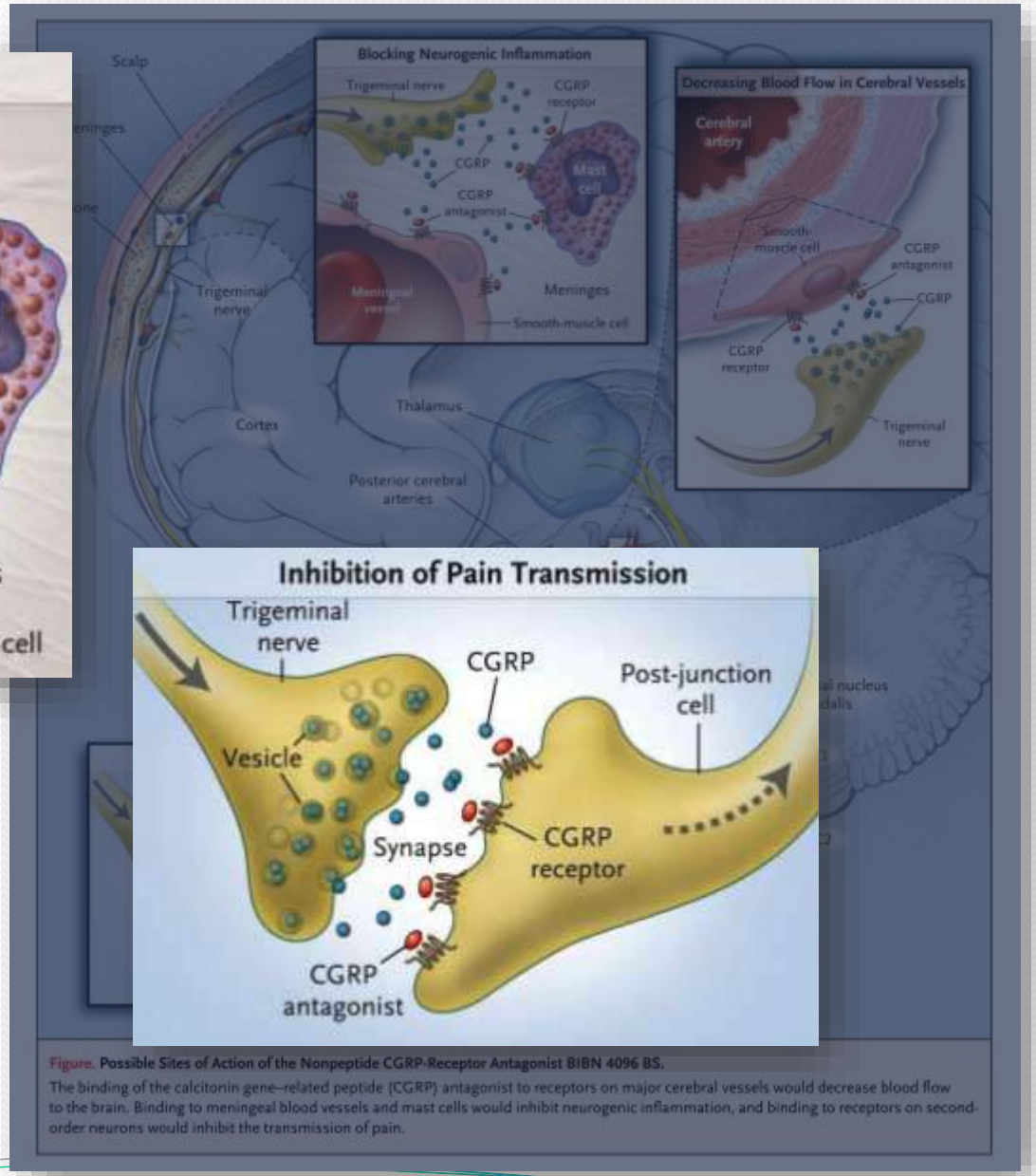


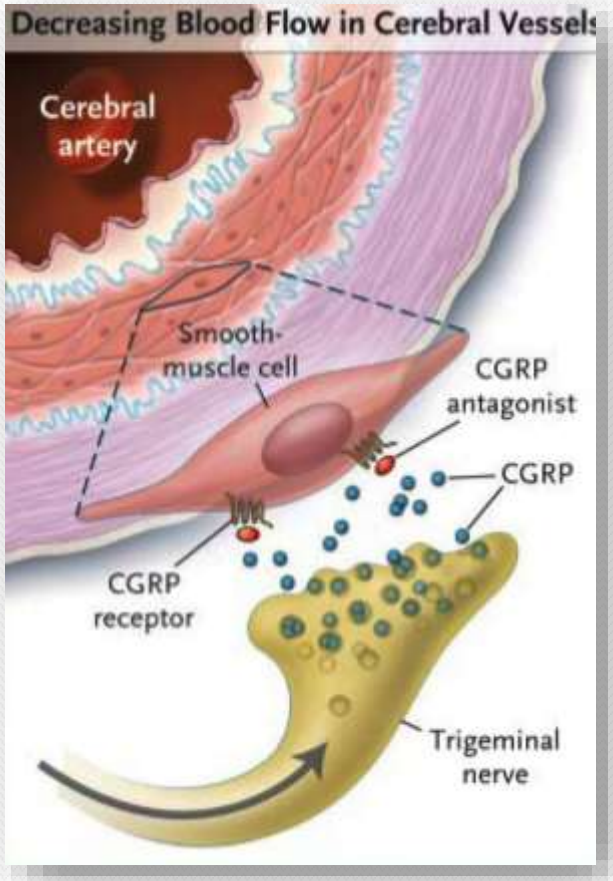


*CGRP levels in blood and saliva[4]
CGRP, calcitonin gene-related peptide; ODT, orally disintegrating tablet

1. Ho T, et al. Nat Rev Neurol. 2010;6:573-582; 2. Noseda R, Burstein R. Pain. 2013;154(Suppl 1):S44-53; 3. Schuster N, Rapoport A. Nat Rev Neurol. 2016;12:635-650; 4. Ashina M, et al. Pain. 2000;86:133-138.





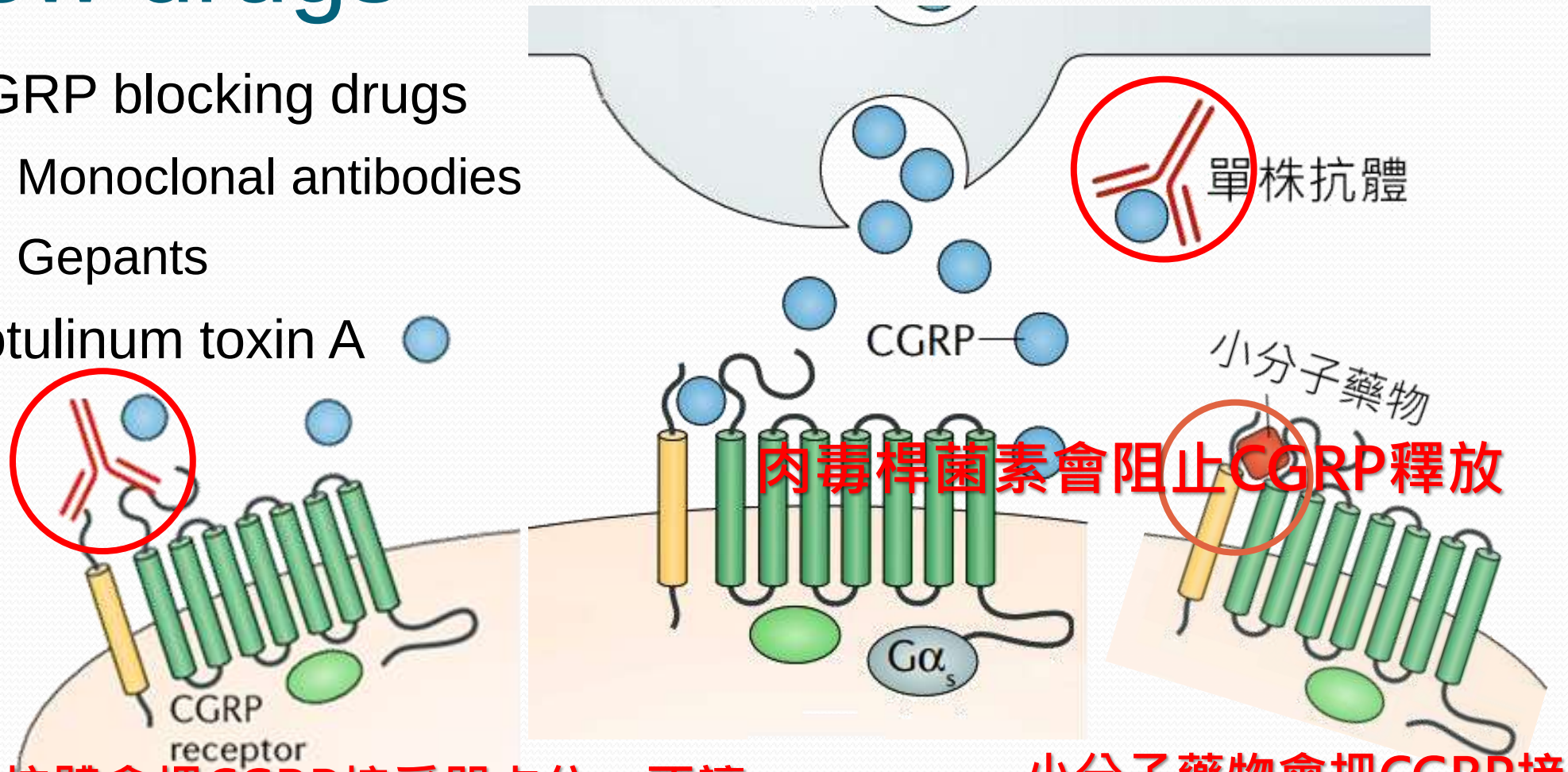


N Engl J Med . 2004;350:1073-5.

New drugs

- CGRP blocking drugs
  - Monoclonal antibodies
  - Gepants
- Botulinum toxin A

單株抗體會把CGRP抓住，不讓它作用



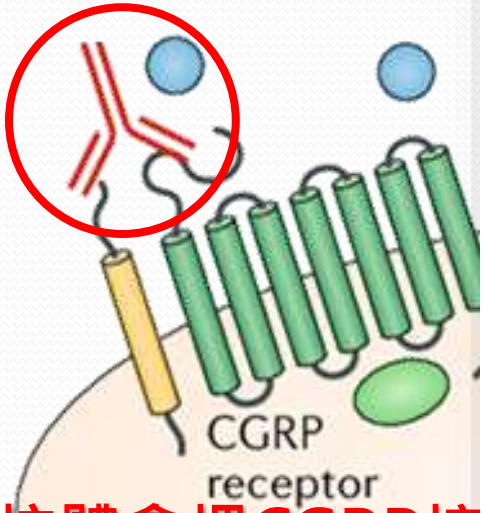
肉毒桿菌素會阻止CGRP釋放

單株抗體會把CGRP接受器卡住，不讓它作用

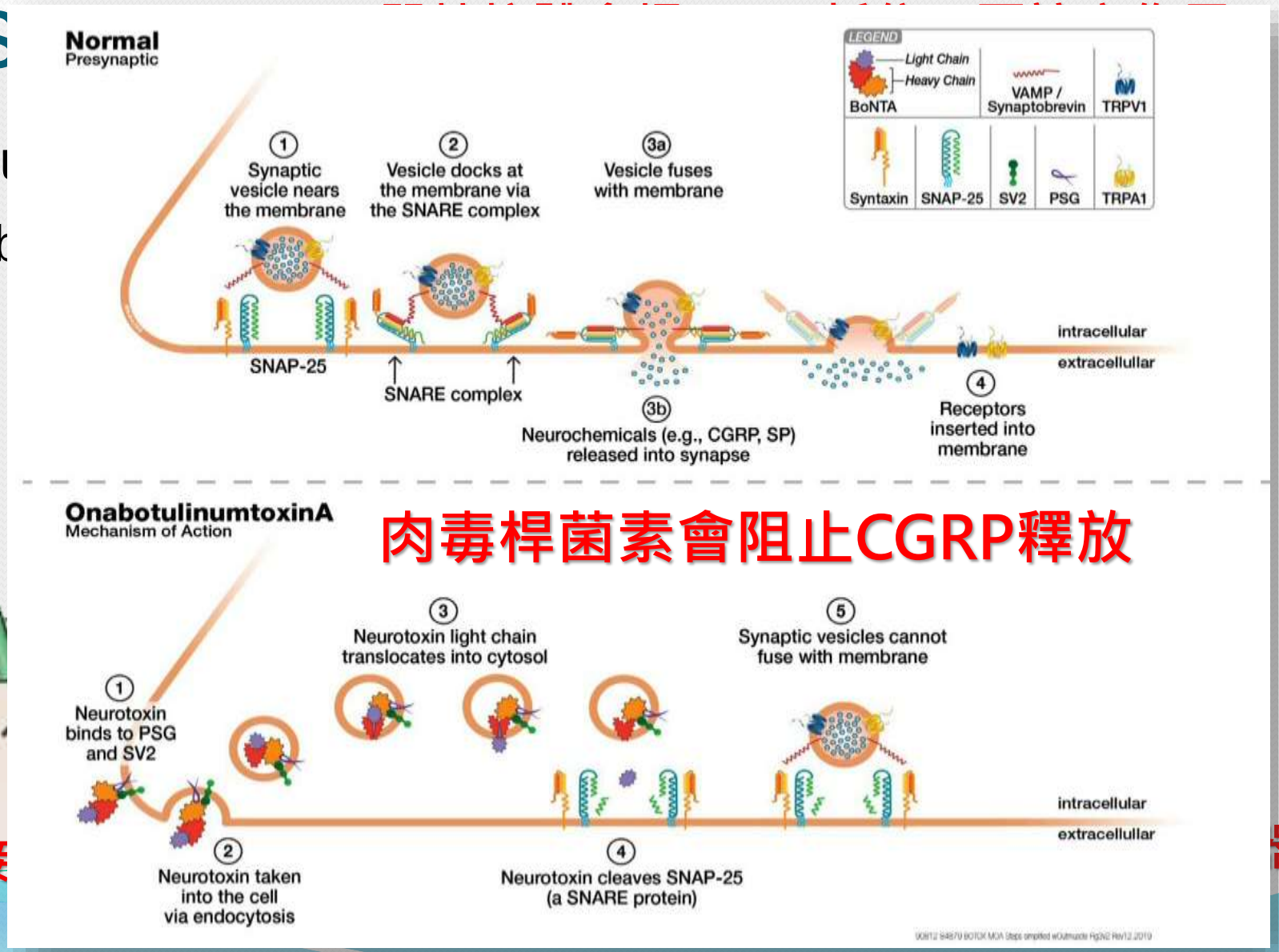
小分子藥物會把CGRP接受器卡住，讓真的CGRP無法作用

New drugs

- CGRP blocking dru
  - Monoclonal antib
  - Gepants
- Botulinum toxin A



單株抗體會把CGRP接 器卡住，
它作用



CGRP monoclonal antibodies

學名	商品名	中文名	途徑	使用頻次	用途	衛服部核准	健保給付
Erenumab	Aimovig	安莫疼	皮下注射	每月	預防治療	Yes → No	No
Fremanezumab	Ajovy	艾久維	皮下注射	每月或每季	預防治療	Yes	Yes
Galcanezumab	Emgality	恩疼停	皮下注射	負荷劑量後每月	預防治療	Yes	Yes
Eptinezumab	Vyepti		靜脈注射	每季	預防治療	No	No

Gepants

學名	商品名	中文名	途徑	用途	衛服部	健保給付
Rimegepant	Nurtec ODT	紐舒泰	口服	急性治療+預防治療	Yes+No	No
Atogepant	Aquipta	艾妥達	口服	預防治療	Yes	No
Ubrogepant	Ubrelvy		口服	急性治療	No	No
Zavegepant	Zavzpret		鼻噴	急性治療	No	No

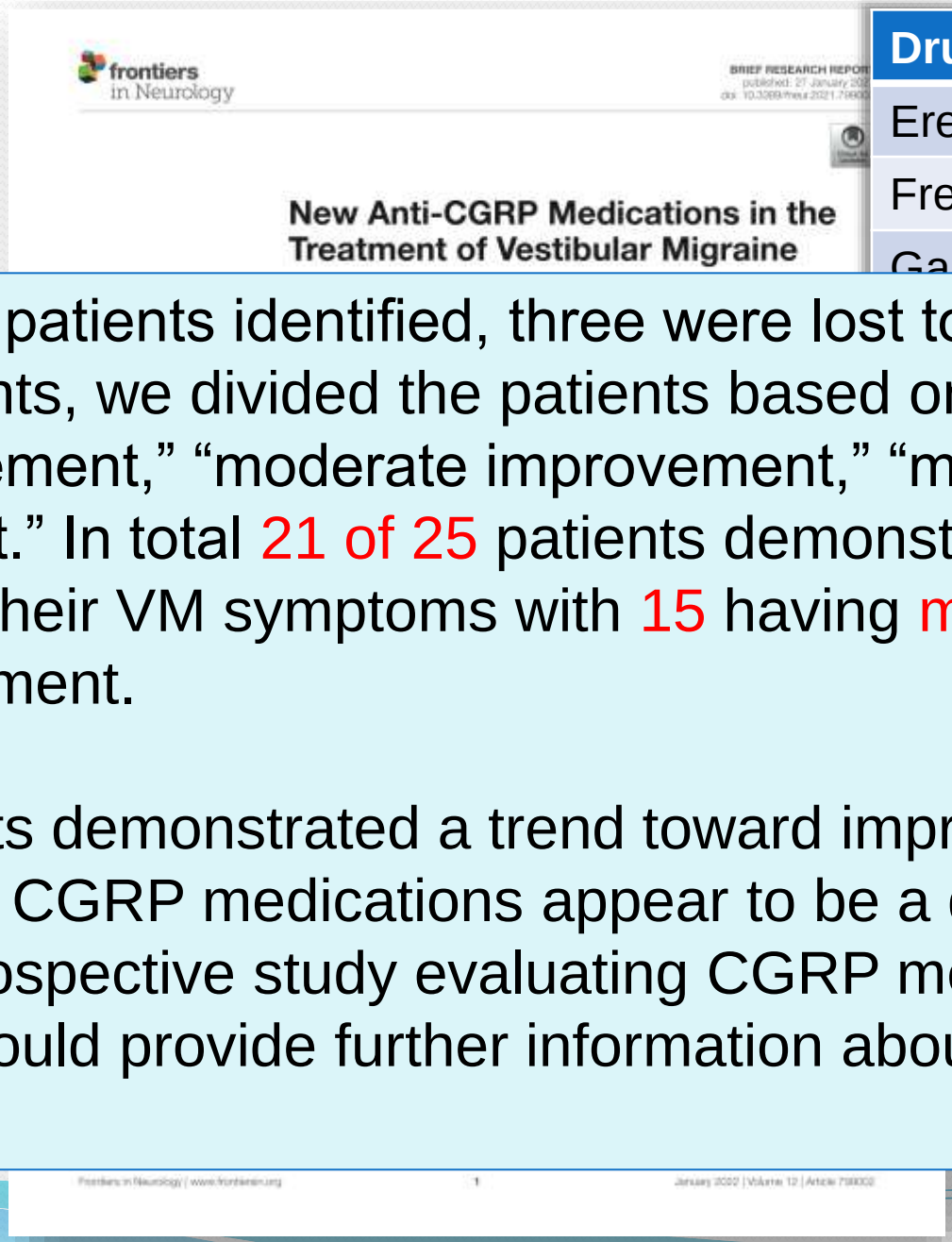
CGRP related drugs in Taiwan

- Anti-CGRP Monoclonal antibodies:
  - **Fremanezumab** (Ajovy)
  - **Galcanezumab** (Emgality)

- Small molecular CGRP antagonists (gepants):
  - **Rimegepant** (Nurtec): acute + preventive
  - **Atogepant** (Aquipta): preventive

CGRP單株抗體健保給付條件

1) 需經事前審查核准後使用。
2) 限神經內科或神經外科專科醫師診斷處方，並不得攜回注射。
3) 需符合慢性偏頭痛診斷：至少有3個月時間，每個月≧15天，每次持續4小時以上，且其中符合偏頭痛診斷的發作每個月≧8天。
4) 患者需經3種（含）以上偏頭痛預防用藥物（依據台灣頭痛學會發表之慢性偏頭痛預防性藥物治療準則之建議用藥，至少包括topiramate）治療無顯著療效，或無法忍受其副作用。
5) Galcanezumab第一次注射240mg (連續兩次皮下注射，每次120mg)做為負荷劑量(loading dose)，之後每月皮下注射120 mg的劑量；fremanezumab 為每月注射一次 225 mg，或每 3 個月注射一次 675 mg。
6) 首次申請給付3個月療程(galcanezumab共 4支；fremanezumab共3支)，3個月療程治療之後，評估每月頭痛天數，需比治療前降低50%以上，方可持續給付。
7) 接續得申請3個月療程，每月施打一次。療程完畢後半年內不得再次申請。
8) 若病況再度符合慢性偏頭痛診斷，得再次申請3個月療程時，需於病歷記錄治療後相關臨床資料，包括頭痛天數。
9) CGRP(calcitonin gene related peptide)單株抗體製劑僅能擇一使用且不得互換，並不得與 Botox 併用。



Drugs	Participants (n)
Erenumab	11
Fremanezumab	9
Galcanezumab	6

Results: Of the 28 patients identified, three were lost to follow up. For the remaining 25 patients, we divided the patients based on a scale of “significant improvement,” “moderate improvement,” “mild improvement,” or “no improvement.” In total 21 of 25 patients demonstrated some level of improvement in their VM symptoms with 15 having moderate to significant improvement.

Conclusion: Results demonstrated a trend toward improvement, suggesting that the CGRP medications appear to be a decent treatment option for VM. A prospective study evaluating CGRP medications in patients with VM would provide further information about this treatment option.

Front Neurol . 2022:12:799002.

Article

Monoclonal Antibodies Targeting CGRP: A Novel Treatment in Vestibular Migraine

Andrea Lovato [1,2,*], Caterina Disco [3], Andrea Frosolini [4], Daniele Monzani [5] and Francesco Perini [3]

1 Otorhinolaryngology Unit, Department of Surgical Specialties, Vicenza Civil Hospital, 36100 Vicen
2 Otorhinolaryngology Unit, Department of Surgical Specialties, San Gaetano Clinic, 36016 Thiene,
3 Neurology Unit, Department of Neuroscience, Vicenza Civil Hospital, 36100 Vicenza, Italy
4 Maxillofacial Surgery Unit, Department of Medical Biotechnologies, University of Siena, 53100 Siena, Italy
5 Otorhinolaryngology Unit, Department of Surgical Specialties, University of Verona, 37100 Verona, Italy

DHI 30.2 → 8.1
HDD 12.4→5.1

Conclusion:
VM patients using anti-CGRP mAbs experienced a reduction in the dizziness-derived handicap, as reported in the DHI questionnaire. Furthermore, these treatments were significantly associated with a normalization of vestibular instrumental analysis. These findings were not seen with conventional treatments. Treatment with anti-CGRP mAbs may be effective in VM patients who did not respond to conventional migraine treatments. These findings should be tested in large, randomized clinical trials.

Vestibular Migraine. *Medicina* **2023**, *59*, 1560. https://doi.org/10.3390/medicina59091560

Academic Editor: Vida Demarin

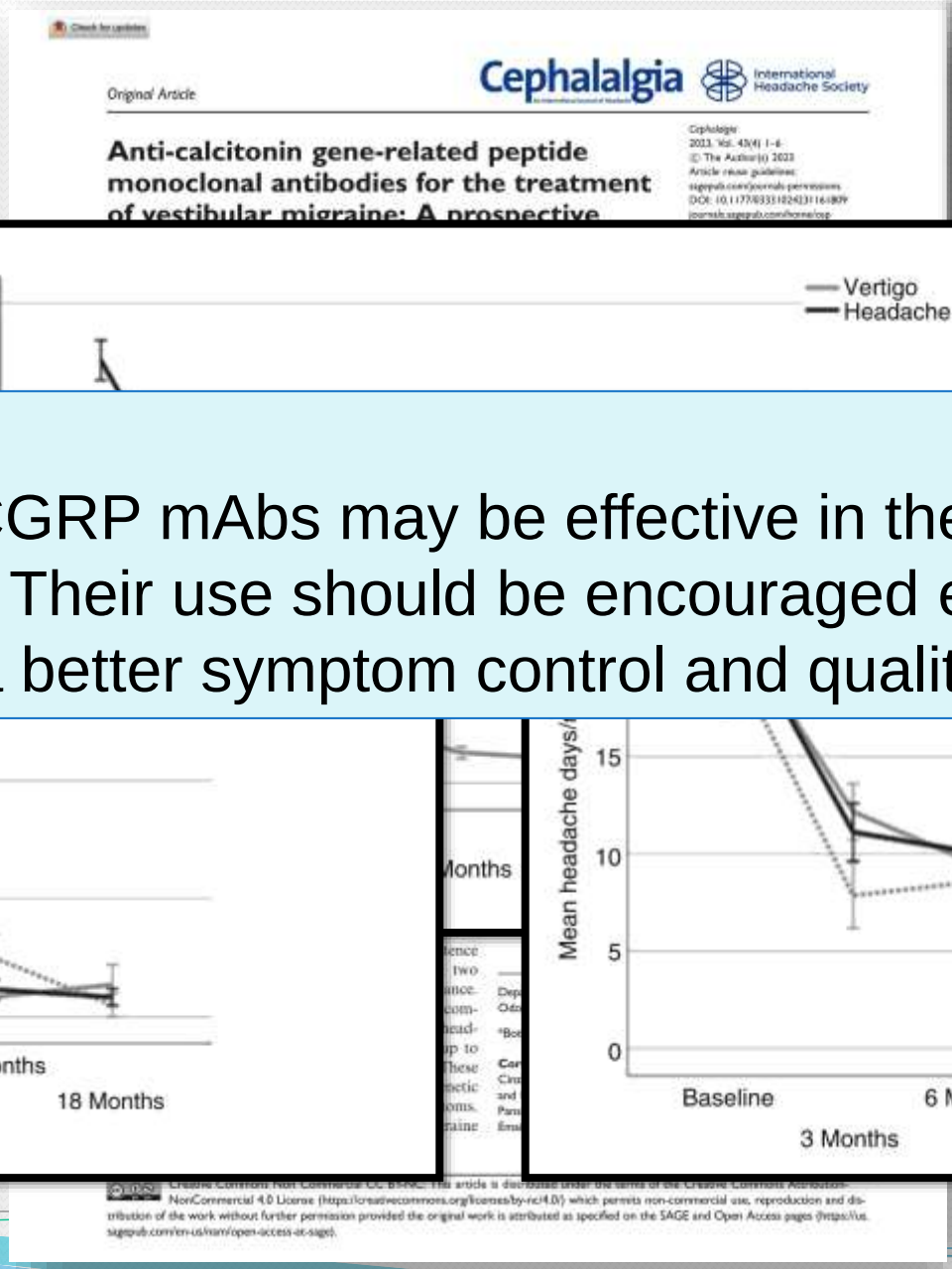
Received: 25 July 2023
Revised: 18 August 2023

instrumental analysis. These findings were not seen with conventional treatments. Treatment with anti-CGRP mAbs may be effective in VM patients who did not respond to conventional migraine treatments. These findings should be tested in large, randomized clinical trials.

Keywords: vestibular migraine; migraine; dizziness; monoclonal antibodies; nystagmus; vertigo

Medicina 2023, 59,1560.

Drugs	Participants (n)
Fremanezumab	25
Galcanezumab	18
Erenumab	7

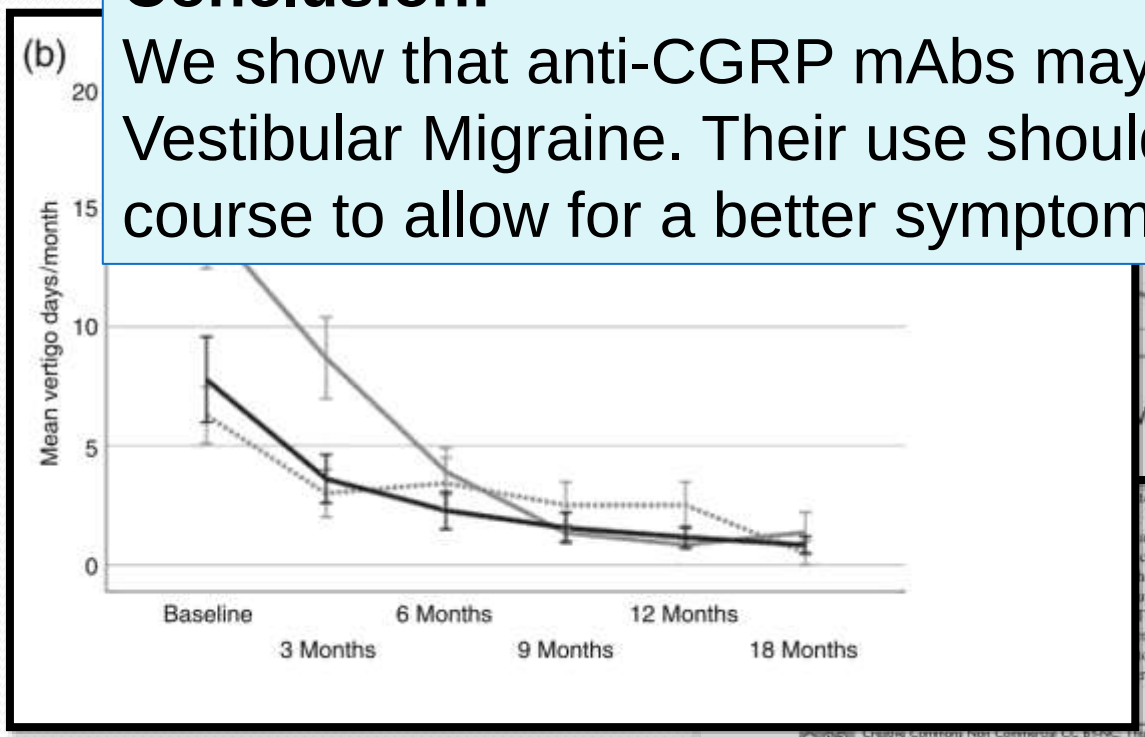

Cephalalgia

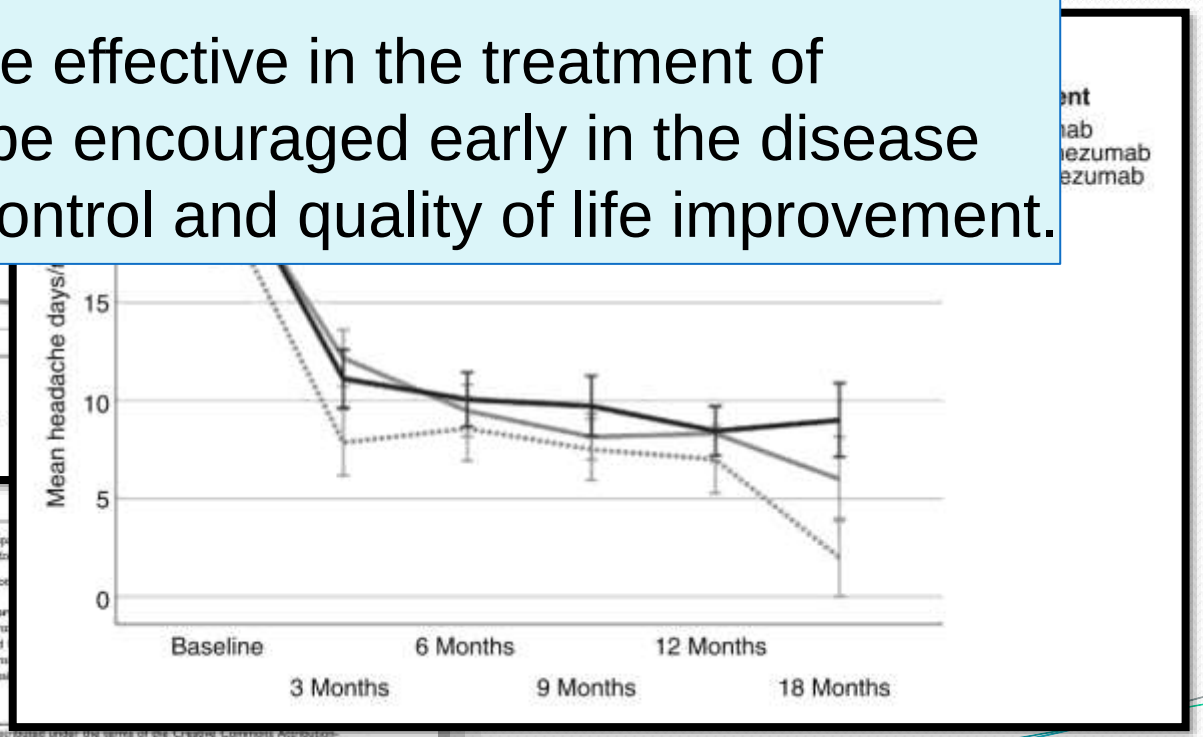
Original Article

Anti-calcitonin gene-related peptide monoclonal antibodies for the treatment of vestibular migraine: A prospective

Conclusion:

We show that anti-CGRP mAbs may be effective in the treatment of Vestibular Migraine. Their use should be encouraged early in the disease course to allow for a better symptom control and quality of life improvement.



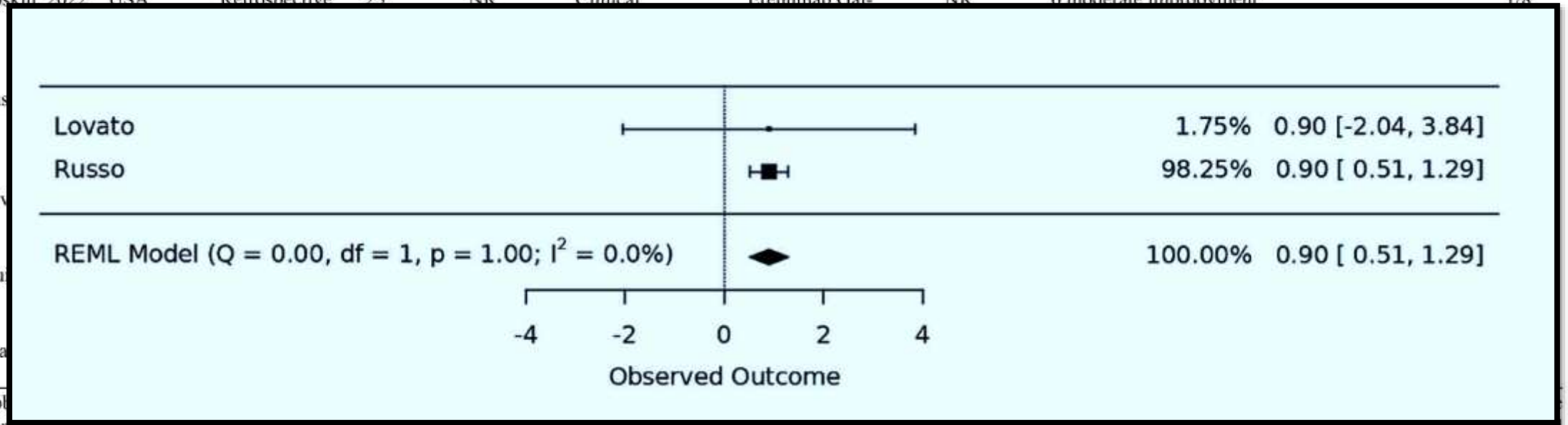


Cephalalgia.2023;43:3331024231161809.

Monoclonal Antibodies Targeting CGRP to Treat Vestibular Migraine: A

Table 2 Characteristics and main findings of included studies

1st Author, year	Country	Study Design	Sample	Diagnosis	Evaluation	Drugs (dose)	Study period	Enpoints	JBI's rating
Hoskin, 2022	USA	Retrospective	25	NR	Clinical	Erenumab Gal-	NR	6 moderate improovment	1/8



Abbreviations: ... Impact Test), MDD (Monthly Days with Dizziness), MDM (Monthly Days with Migraine), MIDAS (Migraine Disability Assessment), NR (Not Reported), PROMIS SF (Patient-Reported Outcomes Measurement Information System Short Form); PTA (Pure Tone Audiometry); RCT (Randomized Control Trial), VM-PATHI (Vestibular Migraine-Patient Assessment Tool and Handicap Inventory).

*the study is ongoing, protocol available at https://clinicaltrials.gov/study/NCT04417361#contacts-and-locations.

lish a more robust evidence base. Nonetheless, this treatment approach offers hope for the effective management of VM, potentially enhancing the well-being of affected individuals and reducing their associated disability.

RESEARCH SUBMISSION

A placebo controlled, randomized clinical trial of galcanezumab for vestibular migraine: The INVESTMENT study

Jeffrey D. Sharon MD[1] | Roseanne Krauter FNP[1] | Ricky Chae BA[1] | Adam Gardi BS[1] | Maxwell Hum BS[1] | Isabel Allen PhD[2] | Morris Levin MD[3]

[1]Department of Otolaryngology-Head and Neck Surgery, University of California, San Francisco, San Francisco, California, USA

[2]Department of Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, California, USA

[3]Department of Neurology, University of California, San Francisco, San Francisco, California, USA

Correspondence
Jeffrey D. Sharon, 6960 Norfolk Rd., Berkeley, CA 94075, USA.
Email: jeffrey.sharon@ucsf.edu

Funding information
Eli Lilly and Company

Abstract

Objective: To study if galcanezumab is effective for vestibular migraine (VM).

Background: There are currently no placebo-controlled trials showing that treatment is effective for VM. Therefore, we performed the first placebo controlled, randomized clinical trial of a calcitonin gene–related peptide–targeted monoclonal antibody for VM.

Methods: This was a single site, prospective, double-blind placebo controlled randomized clinical trial. Key inclusion criteria were as follows: participants aged 18–75 years with a diagnosis of VM or probable VM per Barany Society criteria. The primary outcome was change in VM-PATHI (Vestibular Migraine Patient Assessment Tool and Handicap Inventory) score, and secondary outcomes included change in DHI (Dizziness Handicap Inventory) score, and count of definite dizzy days (DDDs). Participants were randomized 1:1 to 3 months of treatment with galcanezumab or placebo via subcutaneous injection with a pre-filled syringe, 240 mg the first month, and 120 mg for the second and third months.

Results: Forty participants were randomized, and 38 participants were in the modified intent to treat analysis. VM-PATHI score was reduced 5.1 points (95% confidence interval [CI] −13.0 to 2.7) for placebo ($N=21$), and 14.8 points (95% CI −23.0 to −6.5) for galcanezumab ($N=17$), a difference of −9.6 (95% CI −20.7 to 1.5, $p=0.044$). DHI dropped 8.3 points in the placebo arm (95% CI −15.0 to 1.6), and 22.0 points in the galcanezumab arm (95% CI −31.9 to −12.1), a difference of −13.7 (95% CI −20.4 to −8.5, $p=0.018$). The count of DDDs per month dropped from 18 days (standard deviation [SD] 7.6) in the baseline month to 12.5 days (SD 11.2) in month 4 for those in the placebo arm, and from 17.9 days (SD 7.9) in the baseline month to 6.6 days (SD 7.3) in month 4 for those in the galcanezumab arm, a difference of −5.7 days (95% CI −10.7 to −0.7, $p=0.026$). No serious adverse events were observed.

Conclusions: In this pilot study, galcanezumab was effective in treating VM.

Plain Language Summary

Vestibular migraine is a common cause of dizziness. In this study, we investigated whether treatment with a drug called galcanezumab worked better than placebo for

Headache. 2024;64:1264–1272.

TABLE 1 Baseline demographics for the INVESTMENT trial.

	Placebo	Galcanezumab	Total
N	22	18	40
Diagnosis (%VM)	19 (86%)	16 (89%)	35 (88%)
Sex (% female)	16 (73%)	14 (78%)	30 (75%)
Age	47.3 (SD 14.5)	55.0 (SD 11.0)	50.8 (SD 13.5)
Race (% White)	16 (73%)	14 (78%)	30 (75%)
Race (% Asian)	2 (9%)	1 (6%)	8%
Race (% Black)	0 (0%)	1 (6%)	3%
Race (% other)	4 (18%)	2 (11%)	15%
History migraine (%)	90%	94%	93%
Family history migraine (%)	59%	61%	60%
Count of triggers	8.9 (SD 7.6)	9.4 (SD 7.8)	9.1 (SD 3.0)
Count of associated symptoms	4.6 (SD 1.3)	4.2 (SD 1.7)	4.4 (SD 1.5)
Count of migraine prophylactic medications	16	17	33
SV2 VM-PATHI score	45.7 (SD 9.9)	47.3 (SD 12.0)	46.4 (SD 10.8)
SV2 DHI score	56.7 (SD 19.1)	61.4 (SD 14.9)	58.8 (SD 17.3)
DDD baseline	18 (SD 7.6)	17.9 (SD 7.9)	18.0 (SD 7.7)

Note: *p*-value uses chi-squared test for categorical variables, *t*-test for numeric variables.

Abbreviations: DDD, definitive dizzy day; DHI, Dizziness Handicap Inventory; INVESTMENT, Investigating Vestibular Migraine Emgality Treatment; SD, standard deviation; SV2, study visit 2; VM, vestibular migraine; VM-PATHI, Vestibular Migraine Patient Assessment Tool and Handicap Inventory.

TABLE 2 Summary of outcomes for the INVESTMENT trial.

	Placebo	Galcanezumab	Difference	*p*-value	Effect size
N (mITT)	21	17			
Change in VM-PATHI score	−5.1 (SD 17.3)	−14.8 (SD 16.1)	−9.6 (95% CI −20.7 to −1.5)	0.044*	0.56
Change in DHI	−8.3 (SD 15.0)	−22.0 (SD 19.3)	−13.7 (95% CI −20.4 to −8.5)	0.017	0.98
Change in DDD Count	−5.6 (SD 7.9)	−11.3 (SD 7.2)	−5.7 (95% CI −10.7 to −0.7)	0.026	1.02
Effectiveness	1.1 (SD 1.2)	2.1 (SD 1.1)	1.1 (95% CI 0.3 to 1.8)	0.0067	0.89
GAD-7	−2.0 (SD 0.86)	−3.9 (SD 4.2)	−1.9 (95% CI −4.6 to 0.7)	0.152	
PHQ-9	−3.0 (SD 4.4)	−4.9 (SD 5.4)	−1.9 (95% CI −5.2 to 1.3)	0.232	
PROMIS SF Global Health v1.2- Physical Subscale	1.9 (SD 6.4)	5.3 (SD 7.0)	3.4 (95% CI −1.0 to 7.8)	0.129	
PROMIS SF Global Health v1.2- Mental Subscale	3.2 (SD 8.3)	4.8 (SD 5.3)	1.6 (95% CI −3.1 to 6.3)	0.494	
HIT-6	−1.8 (SD 4.4)	−3.5 (SD 3.3)	−2.9 (95% CI −7.2 to 1.4)	0.184	

Note: Shown is the difference between questionnaire scores for SV2 and SV4. For change in DDD count, it is the difference between the baseline month, and the fourth (final) treatment month.

Abbreviations: CI, confidence interval; DDD, definitive dizzy day; DHI, Dizziness Handicap Inventory; GAD-7, Generalized Anxiety Disorder-7; INVESTMENT, Investigating Vestibular Migraine Emgality Treatment; mITT, modified intent to treat; PHQ-9, Patient Health Questionnaire-9; PROMIS SF, Patient Recorded Outcome Measurement Information System Short Form; SD, standard deviation; SV, study visit; VM-PATHI, Vestibular Migraine Patient Assessment Tool and Handicap Inventory.

*One tailed *t*-test, if not stated than two-tailed *t*-test was used. Effectiveness is using a Likert scale for a single question given at SV4, "How effective was the medication you received in the trial?" Effect size measured with Cohen's *d*, provided only if $p < 0.05$.

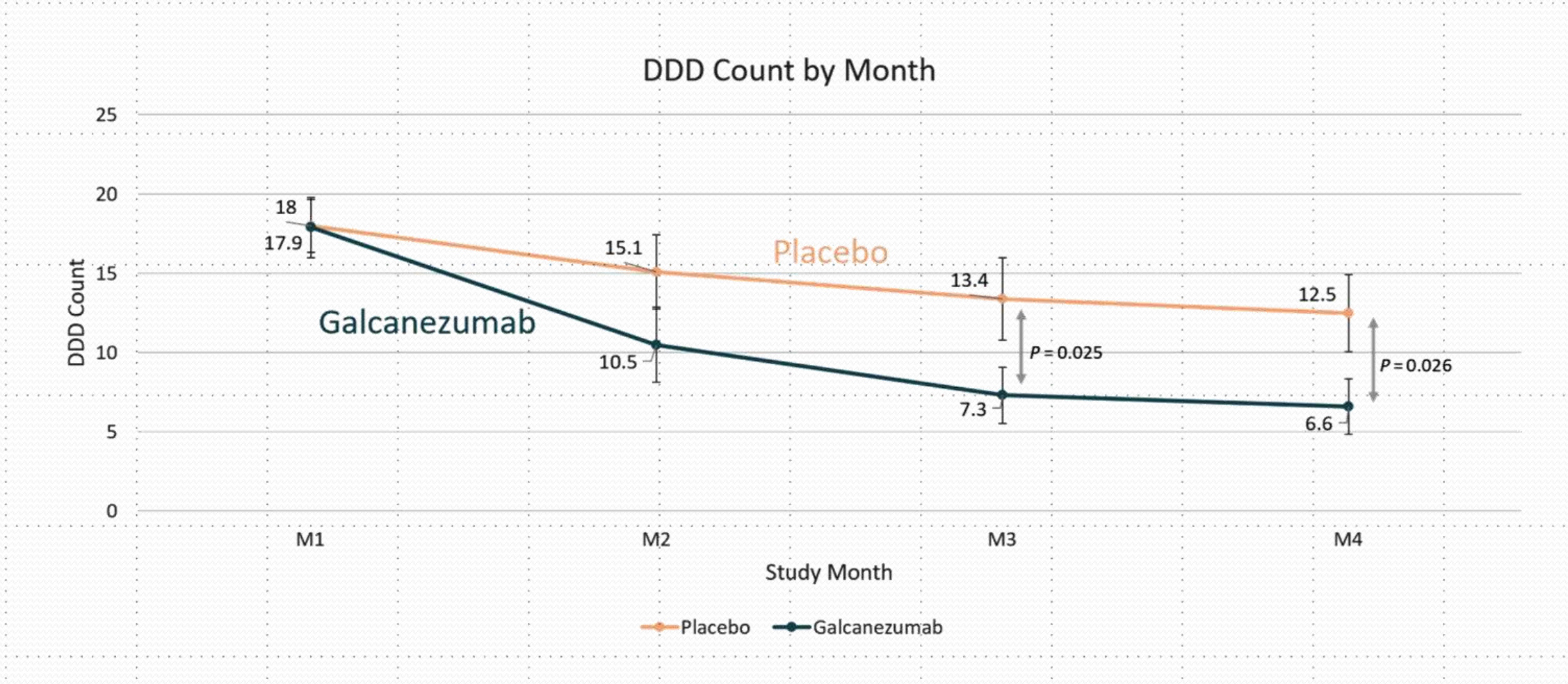


FIGURE 2 Count of definitive dizzy days (DDDs) by month, comparing placebo and galcanezumab arms ($N = 38$). Error bars show the standard error. [Color figure can be viewed at wileyonlinelibrary.com]

A preliminary trial of botulinum toxin type A in patients with

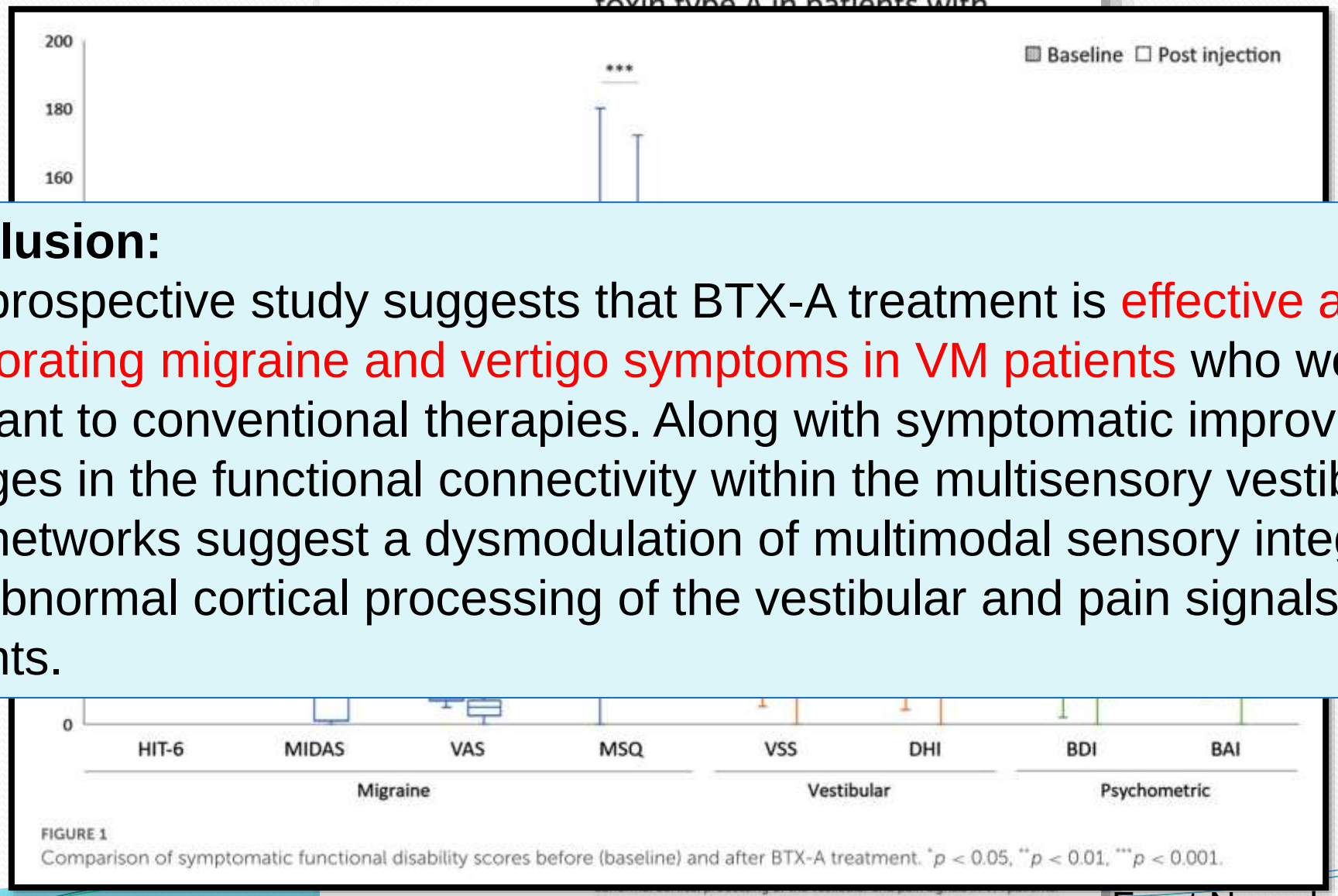


FIGURE 1
Comparison of symptomatic functional disability scores before (baseline) and after BTX-A treatment. $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$.

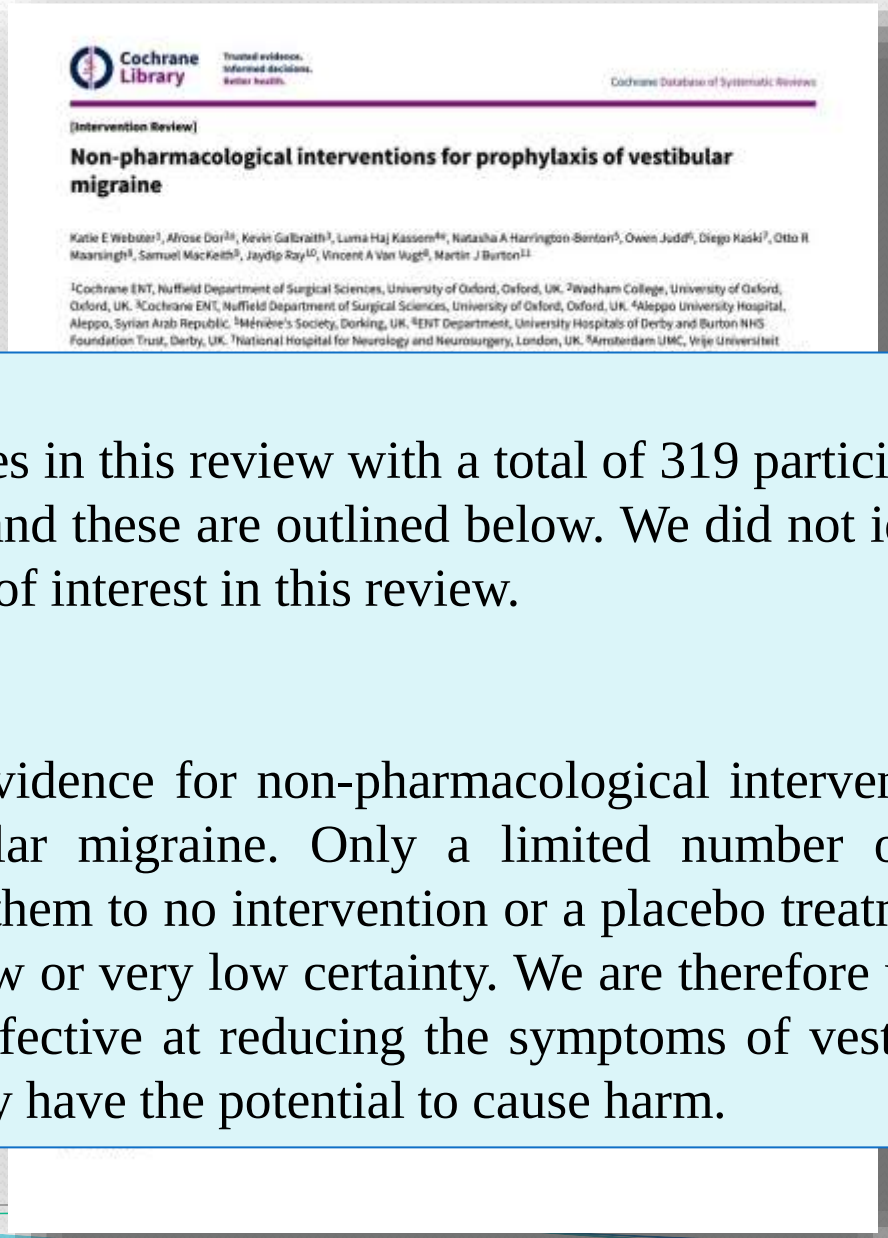
Conclusion:

This prospective study suggests that BTX-A treatment is effective at ameliorating migraine and vertigo symptoms in VM patients who were resistant to conventional therapies. Along with symptomatic improvements, changes in the functional connectivity within the multisensory vestibular and pain networks suggest a dysmodulation of multimodal sensory integration and abnormal cortical processing of the vestibular and pain signals in VM patients.

Front Neurol . 2022:13:955158.

Management for VM

- Explanation (education)
- Non-pharmacological treatment
- Acute treatment
- Preventive treatment



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[Intervention Review]

Non-pharmacological interventions for prophylaxis of vestibular migraine

Katie E Webster[1], Afrose Dor[2a], Kevin Galbraith[3], Luma Haj Kassem[4a], Natasha A Harrington-Benton[5], Owen Judd[6], Diego Kaski[7], Otto R Maarsingh[8], Samuel MacKeith[9], Jaydip Ray[10], Vincent A Van Vugt[8], Martin J Burton[11]

[1]Cochrane ENT, Nuffield Department of Surgical Sciences, University of Oxford, Oxford, UK. [2]Wadham College, University of Oxford, Oxford, UK. [3]Cochrane ENT, Nuffield Department of Surgical Sciences, University of Oxford, Oxford, UK. [4]Aleppo University Hospital, Aleppo, Syrian Arab Republic. [5]Ménière's Society, Dorking, UK. [6]ENT Department, University Hospitals of Derby and Burton NHS Foundation Trust, Derby, UK. [7]National Hospital for Neurology and Neurosurgery, London, UK. [8]Amsterdam UMC, Vrije Universiteit

Main results

We included three studies in this review with a total of 319 participants. Each study addressed a different comparison and these are outlined below. We did not identify any evidence for the remaining comparisons of interest in this review.

Authors' conclusions

There is a paucity of evidence for non-pharmacological interventions that may be used for prophylaxis of vestibular migraine. Only a limited number of interventions have been assessed by comparing them to no intervention or a placebo treatment, and the evidence from these studies is all of low or very low certainty. We are therefore unsure whether any of these interventions may be effective at reducing the symptoms of vestibular migraine and we are also unsure whether they have the potential to cause harm.

Cochrane Database Syst Rev . 2023;4:CD015321.

Non-pharmacological treatment

- Triggers avoidance
- Lifestyle modification*
- Dietary adjustments**
- Vestibular physical therapy
- Daily activities like dancing***

To improve perceptual functions related to motion tolerance and spatial orientation

Curr Pain Headache Rep. 2024;28:613-620.
*Otol Neurotol. 2021;42:e1537–43.
*Ann Otol Rhinol Laryngol. 2024;133:111-114.
**Otol Neurotol.2002;23:364-371.
***Cereb Cortex. 2015;25(2):554–62.

External trigeminal … vestibular migraine … nt for acute

Shin C. Beh*

Department of Neurology, UT Southwestern

ARTICLE INFO

Keywords:
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Vestibular migraine
Vertigo
External trigeminal nerve stimulation
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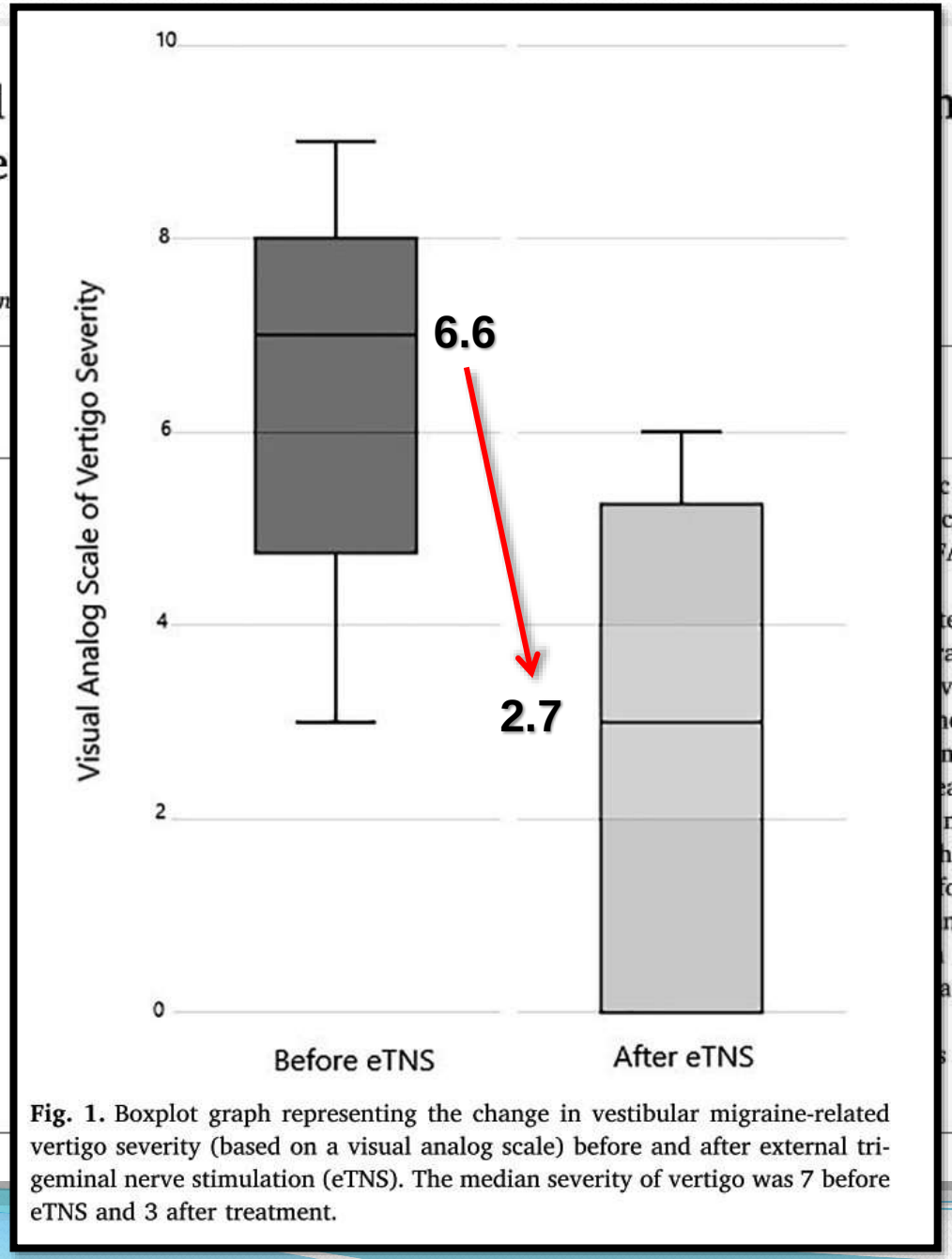


Fig. 1. Boxplot graph representing the change in vestibular migraine-related vertigo severity (based on a visual analog scale) before and after external trigeminal nerve stimulation (eTNS). The median severity of vertigo was 7 before eTNS and 3 after treatment.

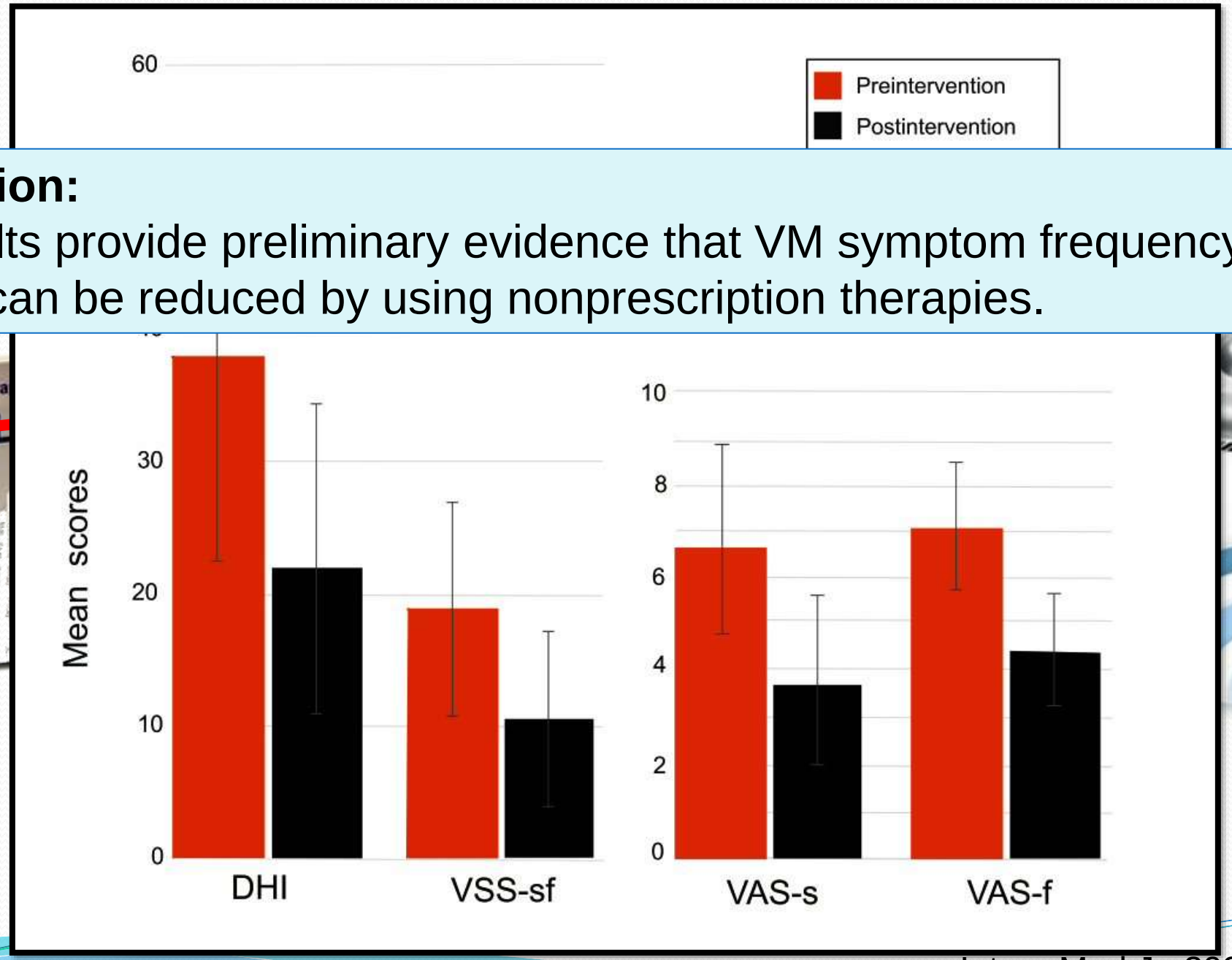
… cause of vertigo among adults. However, … cute VM attacks. This study describes how …ALY Technology, Seraing, Belgium) device …

…e VM attacks (seen between May 2018 and …aded the severity of their vertigo/headache …vertigo/headache, and 10 representing the …eir vertigo/headache using the same VAS …med before and after treatment.
…an vertigo severity was 6.6 (± 2.1; median … mean improvement in vertigo was 61.3% …headache. Mean headache severity was 4.8 …ollowing treatment; mean improvement in …mination was normal during VM attacks in … resolved after eTNS. Other improvements …acial pain. No intolerable side effects were …

… a novel, non-invasive, safe and effective …

J Neurol Sci . 2020:408:116550.

Conclusion:
The results provide preliminary evidence that VM symptom frequency and severity can be reduced by using nonprescription therapies.



Intern Med J . 2024;54:916-924.

Main results

We included two RCTs with a total of 133 participants, both of which compared the use of triptans to placebo for an acute attack of vestibular migraine. One study was a parallel-group RCT (of 114 participants, 75% female). This compared the use of 10 mg rizatriptan to placebo. The second study was a smaller, cross-over RCT (of 19 participants, 70% female). This compared the use of 2.5 mg zolmitriptan to placebo.

Triptans may result in little or no difference in the proportion of people whose vertigo improves at up to two hours after taking the medication. However, the evidence was very uncertain (risk ratio 0.84, 95% confidence interval 0.66 to 1.07; 2 studies; based on 262 attacks of vestibular migraine treated in 124 participants; very low-certainty evidence). We did not identify any evidence on the change in vertigo using a continuous scale. Only one of the studies assessed serious adverse events. No events were noted in either group, but as the sample size was small we cannot be sure if there are risks associated with taking triptans for this condition (0/75 receiving triptans, 0/39 receiving placebo; 1 study; 114 participants; very low-certainty evidence).

Authors' conclusions

The evidence for interventions used to treat acute attacks of vestibular migraine is very sparse. We identified only two studies, both of which assessed the use of triptans. We rated all the evidence as very low-certainty, meaning that we have little confidence in the effect estimates and cannot be sure if triptans have any effect on the symptoms of vestibular migraine. Although we identified sparse information on potential harms of treatment in this review, the use of triptans for other conditions (such as headache migraine) is known to be associated with some adverse effects.

We did not identify any placebo-controlled randomised trials for other interventions that may be used for this condition. Further research is needed to identify whether any interventions help to improve the symptoms of vestibular migraine attacks and to determine if there are side effects associated with their use.

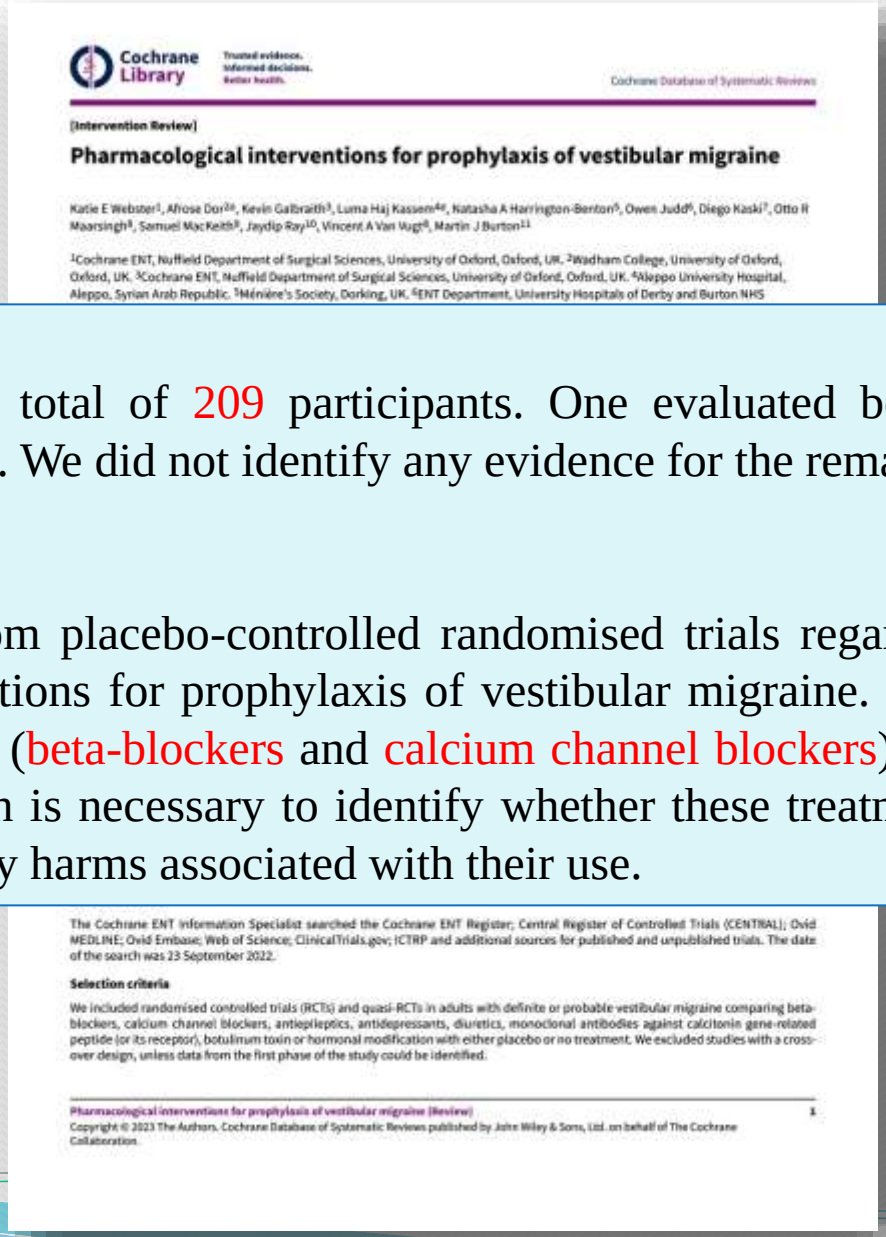
Cochrane Database Syst Rev. 2023;4:CD015322.

Acute treatment

- *Neuhauser H, Radtke A, von Brevern M, Lempert T* **Zolmitriptan for treatment of migrainous vertigo: a pilot randomized placebo-controlled trial.** *Neurology (2003) 60:882–883*
- *Furman JM, Marcus DA, Balaban CD* **Rizatriptan reduces vestibular-induced motion sickness in migraineurs.** *J Headache Pain (2011) 12:81–88*

- Symptomatic treatment for acute episodes is similar to treatment for acute vertigo with peripheral vestibular cause.* (benzodiazepines, antiemetics, antihistamines)

*Lancet Neurol 2013; 12: 706–15



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[Intervention Review]

Pharmacological interventions for prophylaxis of vestibular migraine

Katie E Webster[1], Afrose Dor[2,a], Kevin Galbraith[3], Luma Haj Kassem[4,a], Natasha A Harrington-Benton[5], Owen Judd[6], Diego Kaski[7], Otto R Maarsingh[8], Samuel MacKeith[9], Jaydip Ray[10], Vincent A Van Vugt[8], Martin J Burton[11]

[1]Cochrane ENT, Nuffield Department of Surgical Sciences, University of Oxford, Oxford, UK. [2]Wadham College, University of Oxford, Oxford, UK. [3]Cochrane ENT, Nuffield Department of Surgical Sciences, University of Oxford, Oxford, UK. [4]Aleppo University Hospital, Aleppo, Syrian Arab Republic. [5]Ménière's Society, Dorking, UK. [6]ENT Department, University Hospitals of Derby and Burton NHS

Main results

We included three studies with a total of 209 participants. One evaluated beta-blockers and the other two evaluated calcium channel blockers. We did not identify any evidence for the remaining interventions of interest.

Authors' conclusions

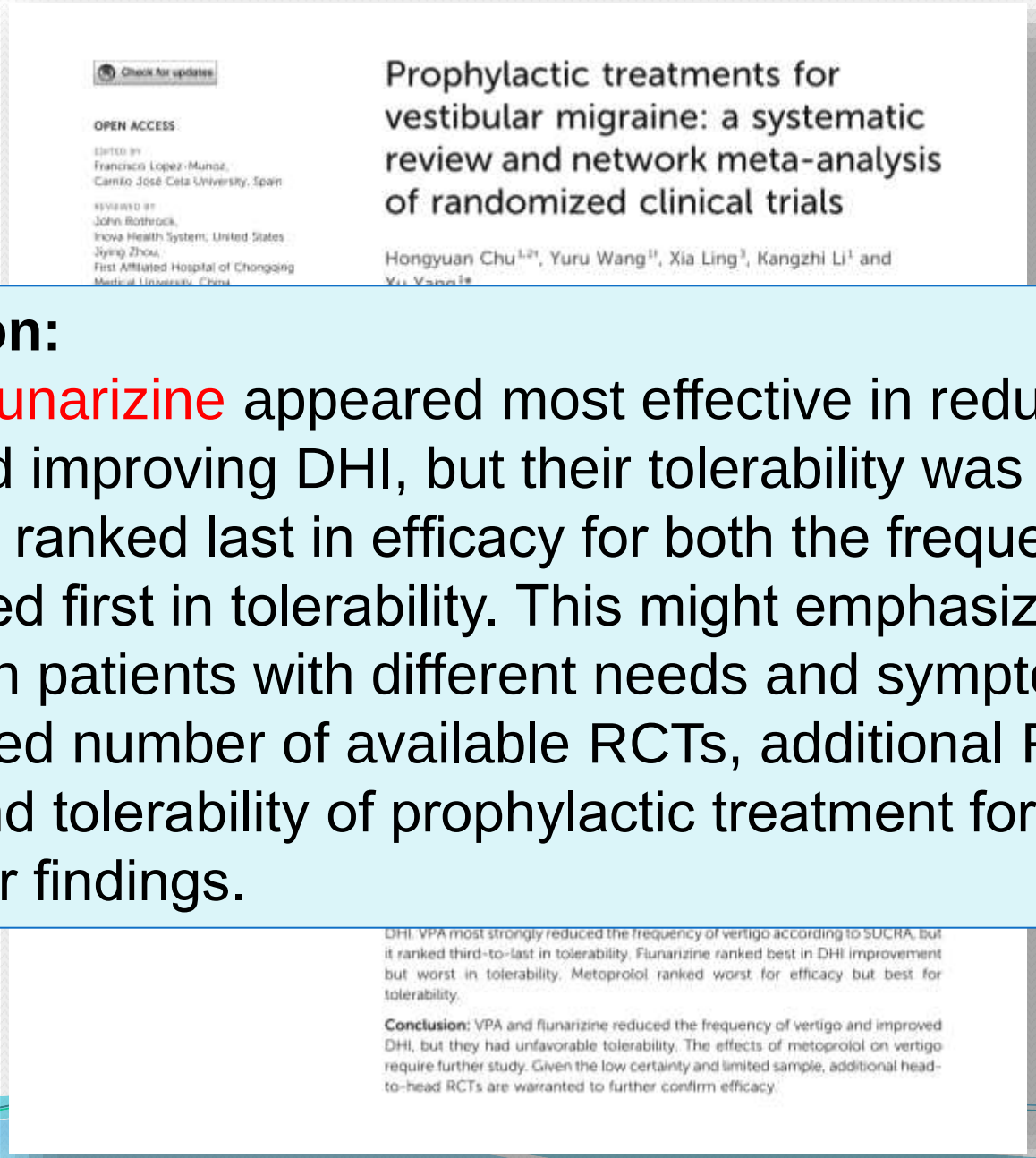
There is very limited evidence from placebo-controlled randomised trials regarding the efficacy and potential harms of pharmacological interventions for prophylaxis of vestibular migraine. We only identified evidence for two of our interventions of interest (beta-blockers and calcium channel blockers) and all evidence was of low or very low certainty. Further research is necessary to identify whether these treatments are effective at improving symptoms and whether there are any harms associated with their use.

The Cochrane ENT Information Specialist searched the Cochrane ENT Register; Central Register of Controlled Trials (CENTRAL); Ovid MEDLINE; Ovid Embase; Web of Science; ClinicalTrials.gov; ICTRP and additional sources for published and unpublished trials. The date of the search was 23 September 2022.

Selection criteria

We included randomised controlled trials (RCTs) and quasi-RCTs in adults with definite or probable vestibular migraine comparing beta-blockers, calcium channel blockers, antiepileptics, antidepressants, diuretics, monoclonal antibodies against calcitonin gene-related peptide (or its receptor), botulinum toxin or hormonal modification with either placebo or no treatment. We excluded studies with a cross-over design, unless data from the first phase of the study could be identified.

Cochrane Database Syst Rev.2023(4):CD015187



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Francisco Lopez-Munoz,
Camilo José Cela University, Spain

REVIEWED BY
John Rothrock,
Inova Health System, United States
Jiying Zhou,
First Affiliated Hospital of Chongqing
Medical University, China

Prophylactic treatments for vestibular migraine: a systematic review and network meta-analysis of randomized clinical trials

Hongyuan Chu[1,2†], Yuru Wang[1†], Xia Ling[3], Kangzhi Li[1] and
Xu Yang[1*]

DHI. VPA most strongly reduced the frequency of vertigo according to SUCRA, but it ranked third-to-last in tolerability. Flunarizine ranked best in DHI improvement but worst in tolerability. Metoprolol ranked worst for efficacy but best for tolerability.

Conclusion: VPA and flunarizine reduced the frequency of vertigo and improved DHI, but they had unfavorable tolerability. The effects of metoprolol on vertigo require further study. Given the low certainty and limited sample, additional head-to-head RCTs are warranted to further confirm efficacy.

Conclusion:

VPA and flunarizine appeared most effective in reducing the frequency of vertigo and improving DHI, but their tolerability was unfavorable. Conversely, metoprolol ranked last in efficacy for both the frequency of vertigo and DHI, but it ranked first in tolerability. This might emphasize the need for precision medicine in patients with different needs and symptoms. However, because of the limited number of available RCTs, additional RCTs comparing the efficacy and tolerability of prophylactic treatment for VM are warranted to confirm our findings.

Front. Pharmacol. 2023,14:1332973.

CNS Drugs (2023) 37:837–847
https://doi.org/10.1007/s40263-023-01037-0

ORIGINAL RESEARCH ARTICLE

Network Meta-analysis of Different Treatments for Vestibular Migraine

Jiann-Jy Chen[1,2] · Bing-Syuan Zeng[3,4] · Kuan-Pin Su[5,6,7] · Yi-Cheng Wu[8] · Yu-Kang Tu[9,10] · Brendon Stubbs[11,12,13] · Tien-Yu Chen[14,15] · Bing-Yan Zeng[16] · Yen-Wen Chen[2] · Chih-Wei Hsu[17] · Ping-Tao Tseng[2,4,18,19]

Accepted: 24 August 2023 / Published online: 7 September 2023

Abstract

Introduction Although one of the major presentations of vestibular migraine is dizziness with/without unsteady gait, it is still classified as one of the migraine categories. However, in contrast to ordinary migraine, vestibular migraine patients have distinct characteristics, and the detailed treatment strategy for vestibular migraine is different and more challenging than ordinary migraine treatment. Currently, there is no conclusive evidence regarding its management, including vestibular migraine prophylaxis.

included. We determined that only valproic acid (standardized mean difference [SMD] −1.01, 95% confidence interval [CI] −2.69, −0.54), propranolol (SMD −1.36, 95% CI −2.55, −0.17), and venlafaxine (SMD −1.25, 95% CI −2.32, −0.18) were significantly associated with better improvement in vestibular migraine frequency than the placebo/control groups. Furthermore, among all the investigated pharmacologic/non-pharmacologic treatments, valproic acid yielded the greatest decrease in vestibular migraine frequency among all the interventions. In addition, most pharmacologic/non-pharmacologic treatments were associated with similar acceptability (i.e. dropout rate) as those of the placebo/control groups.

Conclusions The current study provides evidence that only valproic acid, propranolol, and venlafaxine might be associated with beneficial efficacy in vestibular migraine treatment.

Trial registration CRD42023388343.

Conclusion:
The current study provides evidence that only valproic acid, propranolol, and venlafaxine might be associated with beneficial efficacy in vestibular migraine treatment.

1 Introduction

Despite the symptomatology of dizziness during a migraine attack, vestibular migraine is considered a distinct subtype of migraine [1–3]. Vestibular symptoms can occur in the absence of headache or migraine episodes in patients with vestibular migraine. Unlike ordinary migraine, vestibular migraine has distinct characteristics [4]. Specifically, patients with vestibular migraine had a significantly higher balance

Jiann-Jy Chen and Bing-Syuan Zeng contributed equally to this work as first authors.

Chih-Wei Hsu and Ping-Tao Tseng contributed equally to this work as corresponding authors.

Extended author information available on the last page of the article

CNS Drugs.2023,37:837–847

Communication

Vestibular Migraine Therapy: Update and Recent Literature Review

Laura Zanandrea [1,2,*], Bruno Colombo [1] and Massimo Filippi [1,2]

[1] Neurology Unit, IRCCS San Raffaele Scientific Institute, 20132 Milan, Italy; colombo.bruno@hsr.it (B.C.); filippi.massimo@hsr.it (M.F.)
[2] Faculty of Medicine, Vita-Salute San Raffaele University, 20132 Milan, Italy
* Correspondence: zanandrea.laura@hsr.it

Conclusions

Despite the new evidence available, the overall evidence base for the treatment of VM remains sparse. The efficacy of flunarizine and botulinum toxin A as preventive medications in VM patients has recently been investigated, with encouraging results. Also, medications targeting the CGRP pathway have recently shown clinical benefits in VM patients. In the field of non-pharmacological interventions, resistance exercise has recently been described as effective for reducing vestibular symptoms. However, because of several limitations of the studies, the evidence remains of low quality. Therefore, this paper highlights the need for further studies in order to identify effective treatments for VM patients.

Keywords: vestibular migraine; vertigo; treatment; prophylaxis

Audiol. Res. 2023,13, 724–729.

Preventive treatment for VM

- Beta-blockers (propranolol)
- Calcium channel blockers (flunarizine)
- Valproic acid
- Venlafaxine
- Botulinum toxin A
- CGRP blockers

https://doi.org/10.1093/brain/awac264 BRAIN 2022: 145; 3741–3754 | 3741

BRAIN
REVIEW ARTICLE

Vestibular migraine treatment: a comprehensive practical review

Duncan Smyth,[1] Zelie Britton,[1] Louisa Murdin,[2,3] Qadeer Arshad[4] and Diego Kaski[1]

Vestibular migraine is an underdiagnosed but increasingly recognized neurological condition that causes episodic vertigo associated with other features of migraine. It is now thought to be the most common cause of spontaneous (non-positional) episodic vertigo, affecting up to 1% of the population. A meta-analysis of preventative treatments for vestibular migraine was published in 2021, but the authors were unable to establish a preferred treatment strategy due to low quality of evidence and heterogeneity of study design and outcome reporting. Therefore, there remains a clinical need for pragmatic management guidelines specific to vestibular migraine using the available evidence. Here, we provide a practical review utilizing a systematic qualitative assessment of the evidence for abortive and preventative interventions in adults. The overall evidence base for vestibular migraine treatment is of low quality. Nevertheless, we provide practical treatment recommendations based on the available evidence and our experience to help guide clinicians treating patients with vestibular migraine. We also discuss how future clinical trials could be designed to improve the quality of evidence in this condition.

1 Department of Neuro-Otology, National Hospital for Neurology and Neurosurgery, London, UK
2 Department of Ear, Nose and Throat, Guy's and St Thomas' NHS Foundation Trust, London, UK
3 Ear Institute, Faculty of Brain Sciences, University College London, London, UK
4 Department of Neuroscience, Psychology and Behaviour, University of Leicester, Leicester, UK

Correspondence to: Dr Diego Kaski
Department of Neuro-Otology
National Hospital for Neurology and Neurosurgery
Queen Square, London WC1N 3BG, UK
E-mail: d.kaski@ucl.ac.uk

Keywords: vestibular migraine; treatment; prophylaxis; outcomes; clinical trials

Treatment options for management of vestibular migraine based on efficacy and side-effect profile data

- **All patients**
- **Abortive treatment**—use less than 10 days per month
- **Preventative treatment**—
  1. best efficacy evidence and lower rates of serious unwanted effects
  2. evidence of efficacy but risk of more serious unwanted effects
  3. limited efficacy evidence in VM—could be considered if failure of multiple other options
  4. currently undergoing evaluation
- **Vestibular rehabilitation**

BRAIN 2022: 145; 3741–3754

All patients

- Lifestyle advice—discuss sleep, exercise, stress, avoidance of fasting, potential dietary triggers, alcohol, caffeine

BRAIN 2022: 145; 3741–3754

Abortive treatment

—use less than 10 days per month

- Simple analgesics/NSAIDs/triptans for headache
- Vestibular sedatives (cyclizine, prochlorperazine, cinnarizine) for vertigo
- Consider prochlorperazine, cyclizine, cinnarizine, or domperidone for nausea

Preventative treatment 1

—best efficacy evidence and lower rates of serious unwanted effects

- **Tricyclics** (amitriptyline, nortriptyline)—consider if comorbid pain or insomnia.

  Start 10 mg at night and titrate up in 10 mg increments every 1–2 weeks. Usual dose range 10–150 mg at night. Lower doses are often effective for VM symptoms; higher doses (≥75 mg) may benefit patients with anxiety/depression, although in our experience patients with VM rarely tolerate this much.

- **Propranolol**—generally well-tolerated in studies. Avoid in asthma, bradycardia, hypotension, and use with caution in type 1 diabetes mellitus.

  Start at 20 mg twice daily and titrate up every 1–2 weeks by 20–40 mg twice daily. Usual dose range 20–80 mg twice daily.

- **Flunarizine**—consider if comorbid insomnia. Many patients report side effects (e.g. somnolence, weight gain) but rates of discontinuation are low. Need long-term monitoring to check for parkinsonism, so use with caution in elderly.

  Start at 10 mg at night (no need for dose titration) in younger patients, or 5 mg at night in older patients (>65 years).

BRAIN 2022: 145; 3741–3754

Preventative treatment 2

—evidence of efficacy but risk of more serious unwanted effects

- **Topiramate**—consider in obese patients. Avoid in underweight patients, women of childbearing potential (unless on reliable contraception) and those with uncontrolled low mood (risk of depressive symptoms/suicidality).

  Start at 25 mg at night and slowly titrate up by 25 mg every 2 weeks as effective/tolerated. Often poorly tolerated at higher doses. Usual dose range 25–100 mg twice daily.

- **Sodium valproate**—avoid in obese patients. Contraindicated in women of childbearing potential.

  Start at 200 mg twice daily and titrate up by 200–400 mg every 1–2 weeks. Usual dose range 200–1000 mg twice daily.

- **Venlafaxine**—consider if comorbid low mood. Note: can raise blood pressure and risk of withdrawal syndrome—essential to counsel patients to avoid sudden cessation.

  Start at 37.5 mg daily and titrate up by 37.5–75 mg every 2–4 weeks. Usual dose range 37.5–225 mg daily.

Preventative treatment 3

—limited efficacy evidence in VM—could be considered if failure of multiple other options

- **Lamotrigine**—generally well tolerated. Very slow titration needed due to risk of rash/Stevens–Johnson syndrome. Note interaction with sodium valproate.

  Start at 12.5 mg daily (in patients not on sodium valproate). See British National Formulary (https://bnf.nice.org.uk/drug/lamotrigine. html) for titration instructions. Usual dose range 50–100 mg twice daily.

- **Candesartan**—safe and well-tolerated. Consider if comorbid hypertension, although caution needed with respect to renal artery stenosis. No studies in VM.

  Start at 2 mg daily and titrate up by 2–4 mg every 4 weeks. Usual dose range 2–16 mg daily.

- **Nutraceuticals (riboflavin/coenzyme Q10/magnesium)**—safe and well-tolerated. May be used separately or in combination. Useful in patients desiring ‘natural’ treatment. No studies in VM. (1 study 2024)

  Dose riboflavin 400 mg daily, coenzyme-Q10 150 mg daily, magnesium 400–600 mg daily (no need for dose titration).

- **Botulinum toxin A**—likely to be more effective for headache than vestibular symptoms. Could be considered as a last resort in very refractory patients if available, if they have prominent headache and if other treatments have failed.

BRAIN 2022: 145; 3741–3754

Preventative treatments currently undergoing evaluation

- Calcitonin gene-related peptide (CGRP) inhibitors

  (some evidence already, 2024)

- Acupuncture

BRAIN 2022: 145; 3741–3754

Vestibular rehabilitation

- Consider in patients refractory or intolerant of pharmacological treatment and in patients desiring a non-pharmacological approach.
- Particularly useful if attacks are very frequent, concurrent persistent postural-perceptual dizziness (PPPD) or disabling avoidance behaviours.
- Availability and expertise may be limited in some centres so consider referring to tertiary centre.

BRAIN 2022: 145; 3741–3754


Thank you.