Artificial intelligence in migraine management

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AJO-DK-NP-00084

Disclosures

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Speaker at Teva

Artificial Intelligence (AI): what are we talking about?

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Xu Y., Zhou Y., Sekula P., Ding L. Machine learning in construction: From shallow to deep learning. Dev. Built Environ. 2021;6:100045. doi: 10.1016/j.dibe.2021.100045.

Artificial Intelligence (AI): what are we talking about?

Artificial intelligence
A machine that mimics natural intelligence.

Machine learning (ML): a subset of AI that aims to identify patterns from pre-existing data to teach a machine how to perform a specific task

Non-machine learning AI: a machine that mimics natural intelligence but operates on a specific set of rules (e.g. chess softwares)

Predictive AI: uses ML algorithms to undestand patterns and predict outcomes

Generative AI: uses ML to create original content or data (text, images, sound, video)

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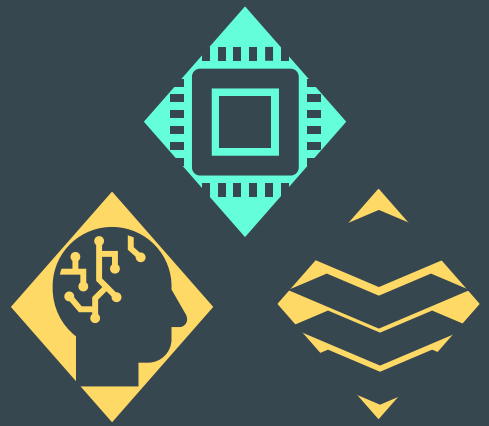
Artificial Intelligence (AI): what are we talking about?



Shallow learining

Supervised learining: learns a pattern from labeled data and uses it to predict the outcome of new data. Used mostly for data classification

Unsupervised learning: finds pattern from unlabeled data. Used for data reduction and clustering problems

Reinforcement learning: based on the Markov decision process. It does not need labeled data. The «teacher» provides feedback (*reward*), which the agent tries to maximize

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Artificial Intelligence (AI): what are we talking about?

Deep learning

Utilizes multiple layers of neural networks. Data follow a chain of transformation from input to output that allows more in-depth analyses (e.g. in image analyses, one layer analyses colour, another shapes, another elements that are relevant to human perception, etc.). Deep learning includes a wide number of possible architectures (Convolutional Networks, Transformers, Recurrent Neural Networks, Restricted Boltzmann Machines, Deep Belief Networks)

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Artificial Intelligence (AI): why migraine?

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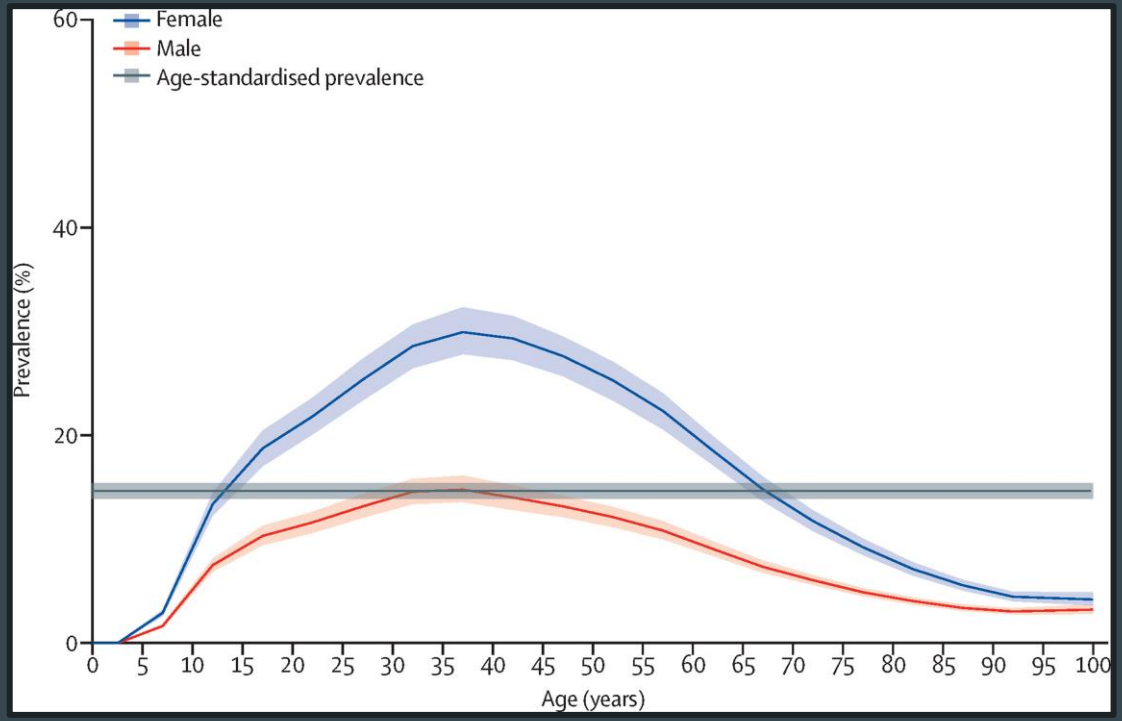
Artificial Intelligence (AI): why migraine?

High prevalence
Migraine is one of the most prevalent neurologic diseases worldwide

Burden of disease
Migraine is in the top 20 causes of disability worldwide, and it affects mostly the working population

High rate of misdiagnosis
Migraine is in the top 20 causes of disability worldwide, and it affects mostly the working population



Ashina M, Katsarava Z, Do TP, Buse DC, Pozo-Rosich P, Özge A, Krymchantowski AV, Lebedeva ER, Ravishankar K, Yu S, Sacco S, Ashina S, Younis S, Steiner TJ, Lipton RB. Migraine: epidemiology and systems of care. Lancet. 2021 Apr 17;397(10283):1485-1495. doi: 10.1016/S0140-6736(20)32160-7. Epub 2021 Mar 25. PMID: 33773613.

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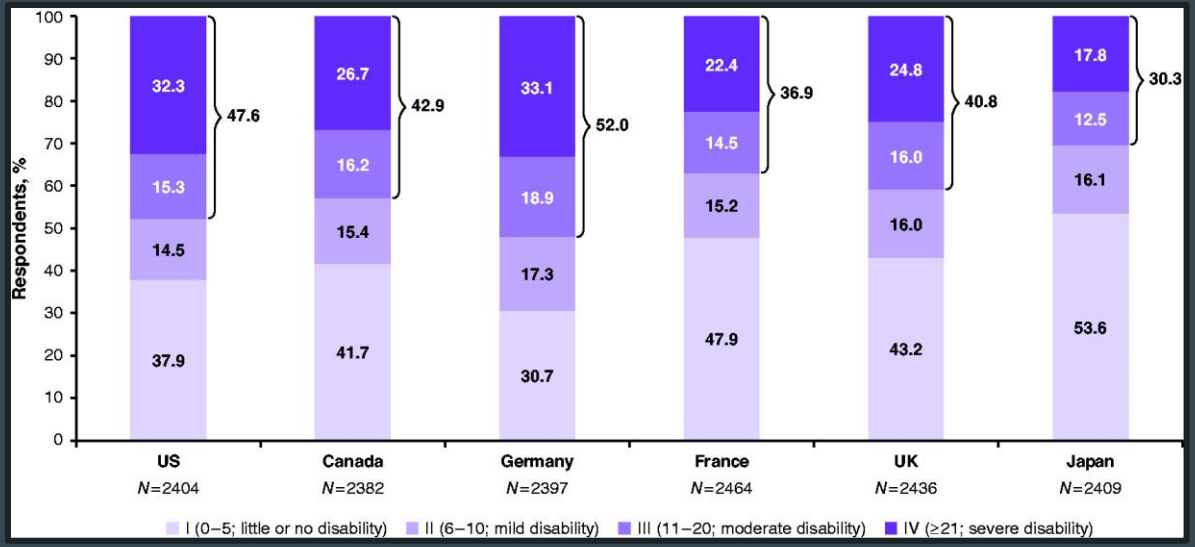

Adams AM, Buse DC, Leroux E, Lanteri-Minet M, Sakai F, Matharu MS, Katsarava Z, Reed ML, Fanning K, Sommer K, Lipton RB. Chronic Migraine Epidemiology and Outcomes - International (CaMEO-I) Study: Methods and multi-country baseline findings for diagnosis rates and care. Cephalalgia. 2023 Jun;43(6):3331024231180611. doi: 10.1177/03331024231180611. PMID: 37314231.

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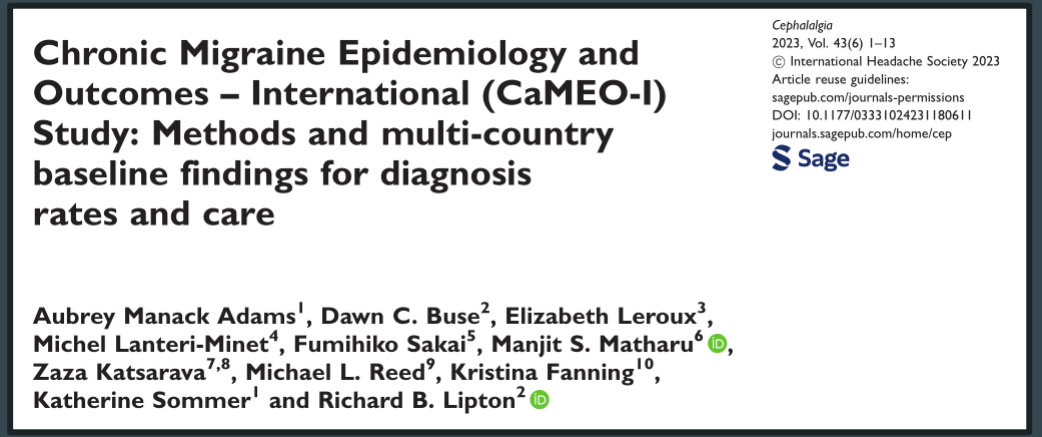

Chronic Migraine Epidemiology and Outcomes – International (CaMEO-I) Study: Methods and multi-country baseline findings for diagnosis rates and care

Cephalalgia
2023, Vol. 43(6) 1–13

DOI: 10.1177/03331024231180611
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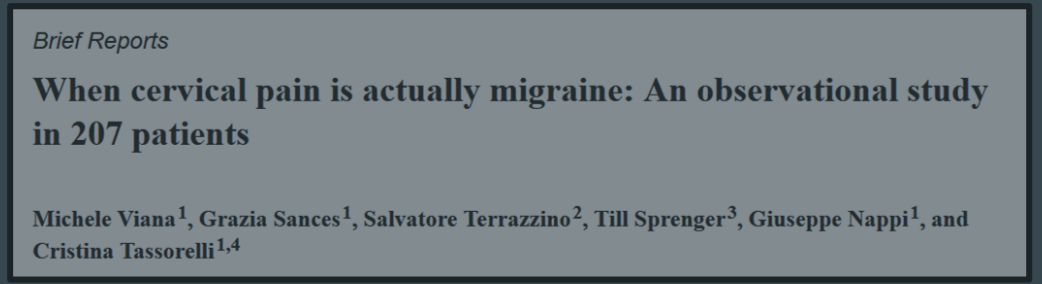
Aubrey Manack Adams[1], Dawn C. Buse[2], Elizabeth Leroux[3], Michel Lanteri-Minet[4], Fumihiko Sakai[5], Manjit S. Matharu[6], Zaza Katsarava[7,8], Michael L. Reed[9], Kristina Fanning[10], Katherine Sommer[1] and Richard B. Lipton[2]



Brief Reports

When cervical pain is actually migraine: An observational study in 207 patients

Michele Viana[1], Grazia Sances[1], Salvatore Terrazzino[2], Till Sprenger[3], Giuseppe Nappi[1], and Cristina Tassorelli[1,4]

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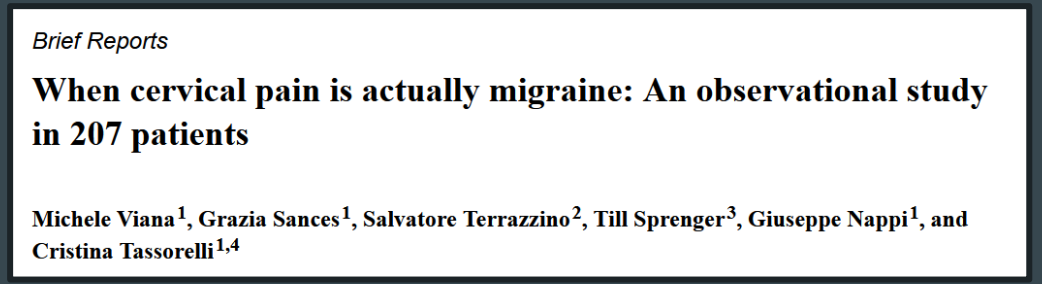

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Artificial Intelligence (AI): what role?

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Diagnosis and patient profiling

Automatic migraine classification using artificial neural networks

Paola A Sanchez-Sanchez [1,a], José Rafael García-González [1], Juan Manuel Rúa Ascar [1]

▸ Author information ▸ Article notes ▸ Copyright and License information

PMCID: PMC8564744 PMID: 34745568

- Data obtained from 400 retrospective medical records
- Data are used as inputs to five different classification models, including a multilayer perceptron-type artificial neural network (MLP), a logistic regression model, an SVM model, a nearest neighbor model and and an optimized classification and regression tree (CART)
- 97% diagnostic accuracy with 23 variables, 98% with 18 variables

	Description	Name		Description	Name
1	Patient's age	Age	13	Lack of speech coordination	Dysphasia
2	duration of last episode in days	Duration	14	Disarticulated sounds and words	Dysarthria
3	Frequency of episodes per month	Frequency	15	Dizziness	Vertigo
4	Unilateral or bilateral pain location	Location	16	Ringing in the ears	Tinnitus
5	Throbbing or constant pain	Character	17	Hearing loss	Hypoacusis
6	Pain intensity, i.e., mild, medium, or severe	Intensity	18	Double vision	Diplopia
7	Nauseous feeling	Nausea	19	Simultaneous frontal eye field and nasal field defect and in both eyes	Visual defect
8	Vomiting	Vomit	20	Lack of muscle control	Ataxia
9	Noise sensitivity	Phonophobia	21	Jeopardized conscience	Conscience
10	Light sensitivity	Photophobia	22	Simultaneous bilateral paresthesia	Paresthesia
11	Reversible visual symptoms	Visual	23	Family background	Family
12	Reversible sensory symptoms	Sensory	24	Diagnosis of migraine type	Type

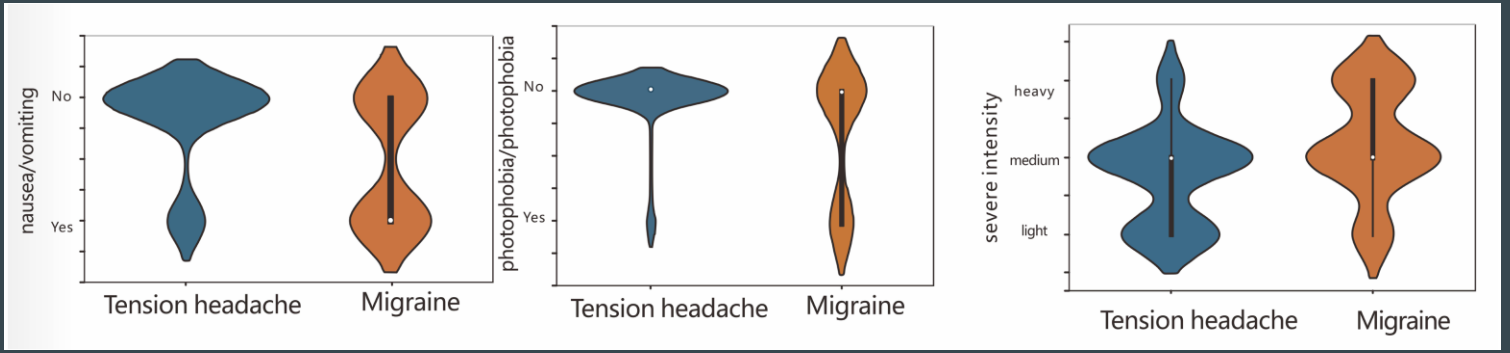
Sanchez-Sanchez PA, García-González JR, Rúa Ascar JM. Automatic migraine classification using artificial neural networks. F1000Res. 2020 Jun 16;9:618. doi: 10.12688/f1000research.23181.2. PMID: 34745568; PMCID: PMC8564744.

A decision support system for primary headache developed through machine learning

Fangfang Liu, Guanshui Bao, Mengxia Yan and Guiming Lin

Shanghai Jiao Tong University, School of Medicine, Shanghai Ninth People's Hospital, Shanghai, Huangpuqu, China

- Differential diagnosis between migraine and tension-type headache (TTH)
- Decision tree, random forest, logistic regression, gradient boosting algorithm and support vector machine (SVM) were used to create a model based on data from 173 patients
- The model reached an accuracy of 0.84
- The absence of nausea/vomiting and photophobia/phonophobia were the most important discriminating factors among the others (gender, pain quality and severity, change after activities, course), with an accuracy of 0.74



Liu F, Bao G, Yan M, Lin G. A decision support system for primary headache developed through machine learning. PeerJ. 2022 Jan 11;10:e12743. doi: 10.7717/peerj.12743. PMID: 35047235; PMCID: PMC8759354.

Original Article

Developing an artificial intelligence-based headache diagnostic model and its utility for non-specialists' diagnostic accuracy

Masahito Katsuki [1], Tomokazu Shimazu [2], Shoji Kikui [3], Daisuke Danno [3], Junichi Miyahara [3], Ryusaku Takeshima [4], Eriko Takeshima [5], Yuki Shimazu [6], Takahiro Nakashima [7], Mitsuhiro Matsuo [8], and Takao Takeshima [3]

- AI model (shallow learning) trained with medical records by 4000 patients (2800 training, 1200 testing)
- 5 non-headache specialists were asked to select the correct headache diagnosis of 50 patients basing on questionnaire sheets
- Diagnostic accuracy improved from 46% to 83.20% with AI assistance

Questions
01. Age
02. Sex
03. Height
04. Weight
05. Headache onset age
06. Headache frequency
07. Headache duration
08. Site of headache
09. Headache characteristics
10. Headache severity
11. Presence of aggravation or improvement by exercise
12. Concomitant symptoms
13. Presence of aura
14. Times when headaches are most likely to occur
15. Inducement of headache
16. Use of acute medication
17. Does anybody in your family have a headache?

Katsuki M, Shimazu T, Kikui S, Danno D, Miyahara J, Takeshima R, Takeshima E, Shimazu Y, Nakashima T, Matsuo M, Takeshima T. Developing an artificial intelligence-based headache diagnostic model and its utility for non-specialists' diagnostic accuracy. Cephalalgia. 2023

Application Value of a Machine Learning Model in Predicting Mild Depression Associated with Migraine without Aura

Sheng-wei Cui[1], Pei Pei[1,*], Wen-ming Yang[1,2,3,*]

Migraine with aura associates with a higher artificial intelligence: ECG atrial fibrillation prediction model output compared to migraine without aura in both women and men

Chia-Chun Chiang MD[1] | Nikita Chhabra DO[2] | Chieh-Ju Chao MD[3] | Han Wang MD, MPH[4] | Nan Zhang MS[5] | Elisabeth Lim MPH[5] | Abraham Baez-Suarez PhD, MS[3] | Zachi I. Attia PhD[3] | Todd J. Schwedt MD[2] | David W. Dodick MD[2] | Fred M. Cutrer MD[1] | Paul A. Friedman MD[3] | Peter A. Noseworthy MD[3]

- Depression is frequently comorbid to migraine and might compromise response to treatment; mild depression may undergo unnoticed
- AI model (shallow learning) trained with medical records by 178 MWoA patients (140 training, 38 testing)
- Depression diagnosis was assessed according to DSM-V criteria and HAMD scale; mild depression was defined by the presence of typical symptoms for ≥2 weeks with a mild intensity (HAMD score ≤7)
- AI can effectively predict the risk of mild depression basing on headache characteristics

Cui SW, Pei P, Yang WM. Application Value of a Machine Learning Model in Predicting Mild Depression Associated with Migraine without Aura. Br J Hosp Med (Lond). 2024 Sep 30;85(9):1-12. doi: 10.12968/hmed.2024.0208. Epub 2024 Sep 19. PMID: 39347670.

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- MwA patients are more at risk for AF and stroke; however, standard ECG have a low diagnostic accuracy and prolonged cardiac monitoring is not routinely feasible in MwA patients
- ECGs with normal sinus rhythm from 40.002 migraine patients were examined with an AI-ECG algorithm that calculates the probability of paroxysmal or impending AF
- Comparisons between MwA and MwoA were conducted, adjusting for sex, age and other vascular comorbidities
- Patients with MwA have a significantly higher AF prediction model output (+0.7%), especially ≤55 years

Chiang CC, Chhabra N, Chao CJ, Wang H, Zhang N, Lim E, Baez-Suarez A, Attia ZI, Schwedt TJ, Dodick DW, Cutrer FM, Friedman PA, Noseworthy PA. Migraine with aura associates with a higher artificial intelligence: ECG atrial fibrillation prediction model output compared to migraine without aura in both women and men. Headache. 2022 Sep;62(8):939-951. doi: 10.1111/head.14339. Epub 2022 Jun 8. PMID: 35676887.

Artificial Intelligence (AI): what role?

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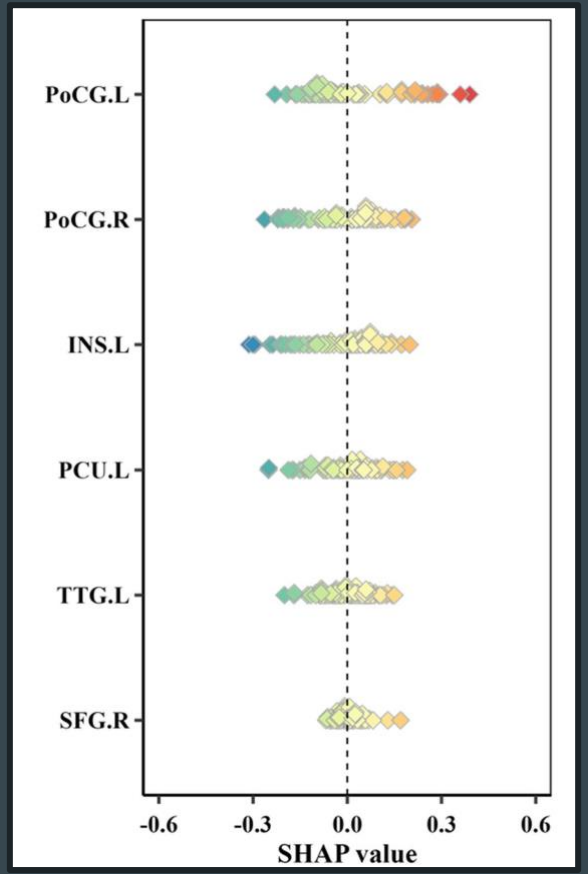
Treatment selection

RESEARCH Open Access

Exploring potential neuroimaging biomarkers for the response to non-steroidal anti-inflammatory drugs in episodic migraine

Heng-Le Wei[1,2†], Yu-Sheng Yu[2†], Meng-Yao Wang[2], Gang-Ping Zhou[2], Junrong Li[4*], Hong Zhang[2*] and Zhengyang Zhou[1,3*]

- NSAIDS are considered first-line medications for migraine attacks. However, there are no biomarkers that can accurately predict response to treatment.
- 59 NSAIDS responders and 59 non-responders underwent fMRI to train an AI-model basing on six variables: PerAF of left insula and left transverse temporal gyrus; and GMV of right superior frontal gyrus, left postcentral gyrus, right postcentral gyrus, and left precuneus
- AI model can predict response to NSAIDS in migraine with a sensitivity of 0.976



Wei HL, Yu YS, Wang MY, Zhou GP, Li J, Zhang H, Zhou Z. Exploring potential neuroimaging biomarkers for the response to non-steroidal anti-inflammatory drugs in episodic migraine. J Headache Pain. 2024 Jun 21;25(1):104. doi: 10.1186/s10194-024-01812-4. PMID: 38902598; PMCID: PMC11191194.

Article

Searching for the Predictors of Response to BoNT-A in Migraine Using Machine Learning Approaches

Daniele Martinelli [1,*], Maria Magdalena Pocora [1,2], Roberto De Icco [1,2], Marta Allena [1], Gloria Vaghi [1,2], Grazia Sances [1], Gloria Castellazzi [1] and Cristina Tassorelli [1,2]

- BoNT-A and anti-CGRP revolutionized the landscape of migraine prophylactic treatment; however, it is difficult to predict the response to treatment in single patients; therapy selection still heavily relies on clinician's expertise, evaluation of co-morbidieties and controindications
- An increasing number of studies is addressing the issue by developing AI algorithms to effectively predict response to treatment

Machine-learning-based approach for predicting response to anti-calcitonin gene-related peptide (CGRP) receptor or ligand antibody treatment in patients with migraine: A multicenter Spanish study

Alicia Gonzalez-Martinez[1] | Josué Pagán[2] | Ancor Sanz-García[3] | David García-Azorín[4] | Jaime Samuel Rodríguez-Vico[5] | Alex Jaimes[5] | Andrea Gómez García[5] | Javier Díaz de Terán[6] | Nuria González-García[7] | Sonia Quintas[1] | Rocío Belascoaín[1] | Javier Casas Limón[8] | Germán Latorre[9] | Carlos Calle de Miguel[9] | Álvaro Sierra[4] | Ángel Luis Guerrero-Peral[4] | Cristina Trevino-Peinado[10] | Ana Beatriz Gago-Veiga[1]

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- 212 patients treated with BoNT-A
- Random forest, SVM, ANFIS, MLP and fuzzy clustering ML was applied to a dataset that included migraine characteristics, MIDAS, MMD, acute medication intake, HIT-6 and ASC-12
- Endpoints: **MMD reduction**, acute medication intake reduction, MIDAS reduction
- The algorithm could predict response to BoNT-A with an accuracy of 0.85
- The most relevant discriminating factors were: migraine age onset, MIDAS, HADS-A score, use of opioids as acute medication

Martinelli D, Pocora MM, De Icco R, Allena M, Vaghi G, Sances G, Castellazzi G, Tassorelli C. Searching for the Predictors of Response to BoNT-A in Migraine Using Machine Learning Approaches. Toxins (Basel). 2023 May 29;15(6):364. doi: 10.3390/toxins15060364. PMID: 37368665; PMCID: PMC10303214.

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- 712 patients treated with anti-CGRP mAbs
- Variables assessed: headache days/month, migraine days/month and HIT-6
- The algorithm calculates the probability of response to anti-CGRP mABs at 6, 9 and 12 months basing on headache days before treatment and after 3 months and the HIT-6 score after 3 months, with an area under the
- receiver-operating curve score range of 0.87–0.98

Gonzalez-Martinez A, Pagán J, Sanz-García A, García-Azorín D, Rodríguez-Vico JS, Jaimes A, García AG, de Terán JD, González-García N, Quintas S, Belascoaín R, Casas Limón J, Latorre G, Calle de Miguel C, Sierra Á, Guerrero-Peral ÁL, Trevino-Peinado C, Gago-Veiga AB. Machine-learning-based approach for predicting response to anti-calcitonin gene-related peptide (CGRP) receptor or ligand antibody treatment in patients with migraine: A multicenter Spanish study. Eur J Neurol. 2022 Oct;29(10):3102-3111. doi: 10.1111/ene.15458. Epub 2022 Jul 12. PMID: 35726393.

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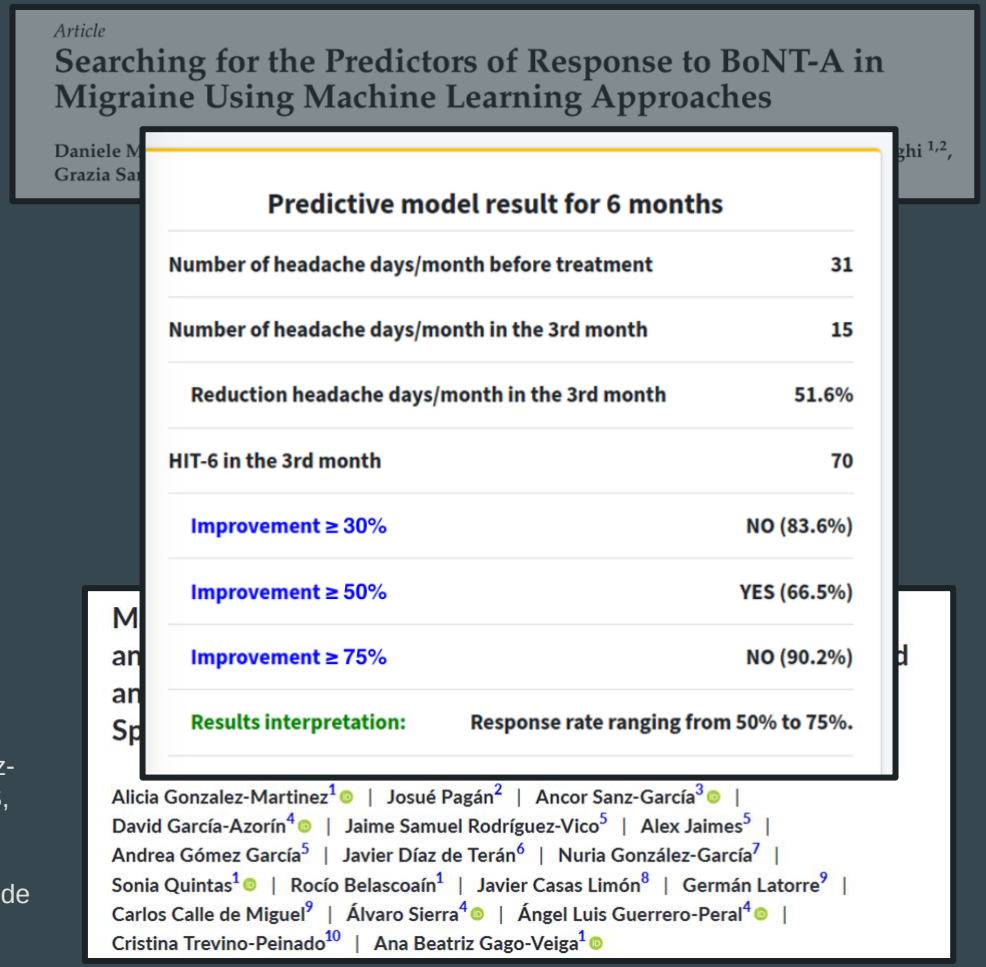

Article

Searching for the Predictors of Response to BoNT-A in Migraine Using Machine Learning Approaches

Daniele M… Grazia Sa… …ghi [1,2],

Predictive model result for 6 months

Number of headache days/month before treatment	31
Number of headache days/month in the 3rd month	15
Reduction headache days/month in the 3rd month	51.6%
HIT-6 in the 3rd month	70
Improvement ≥ 30%	NO (83.6%)
Improvement ≥ 50%	YES (66.5%)
Improvement ≥ 75%	NO (90.2%)
Results interpretation:	Response rate ranging from 50% to 75%.

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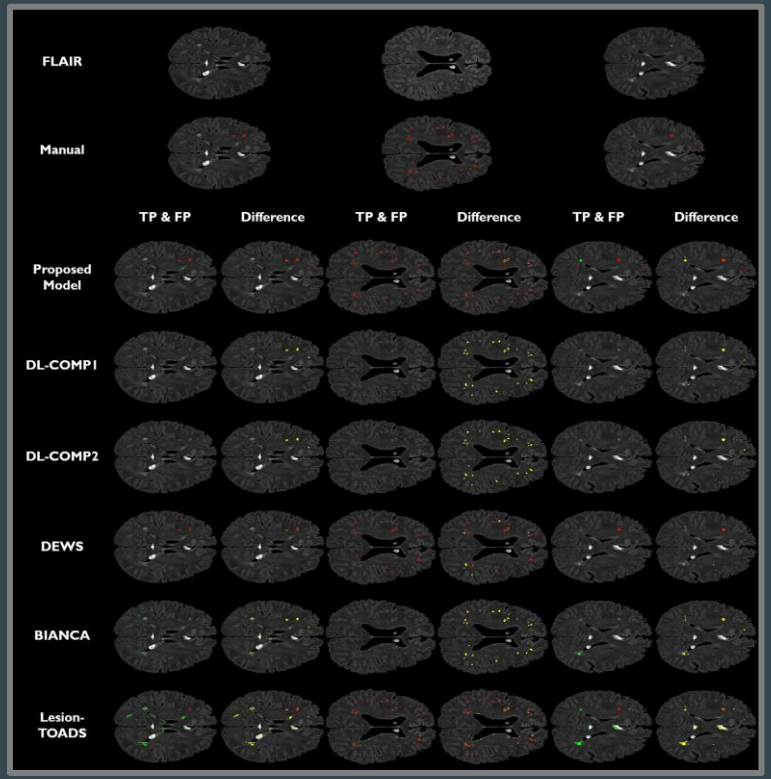
Neuroimaging analysis

Two-step deep neural network for segmentation of deep white matter hyperintensities in migraineurs

Jisu Hong[a,b], Bo-yong Park[a,b], Mi Ji Lee[c], Chin-Sang Chung[c], Jihoon Cha[d], Hyunjin Park[b,e,*]

- WMHs are common in migraineurs; periventricular WMHs are associated with a decline in cognitive function and cerebral blood flow, and deep WMHs are of hypoxic/ischemic origin.
- A deep neural network algorithm was used to quantify deep WMH, developing an automatic model that reached a true positive rate of 0.88 and a false discovery rate of 0.13, thus performing better than other existing models



Hong J, Park BY, Lee MJ, Chung CS, Cha J, Park H. Two-step deep neural network for segmentation of deep white matter hyperintensities in migraineurs. Comput Methods Programs Biomed. 2020 Jan;183:105065. doi: 10.1016/j.cmpb.2019.105065. Epub 2019 Sep 5. PMID: 31522090.

Artificial Intelligence (AI): what role?

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Attack prediction

Investigating the effects of weather on headache occurrence using a smartphone application and artificial intelligence: A retrospective observational cross-sectional study

Masahito Katsuki MD[1] | Muneto Tatsumoto MD, PhD[2] | Kazuhito Kimoto MD[3] | Takashige Iiyama BS[4] | Masato Tajima BS[4] | Tsuyoshi Munakata[4] | Taihei Miyamoto BS[4] | Tomokazu Shimazu MD, PhD[5]

- Weather conditions (barometric pressure, temperature, humidity, rainfall, seasons, time zone) can trigger migraine attacks
- Data from 4375 migraineurs were analyzed with DL-based models to assess the impact of weather conditions on migraine
- low barometric pressure, barometric pressure changes, higher humidity, and rainfall were significantly temporally related to migraine attacks

Original Article

Forecasting migraine with machine learning based on mobile phone diary and wearable data

Anker Stubberud [1,2], Sigrid Hegna Ingvaldsen[1,3], Eiliv Brenner[4], Ingunn Winnberg[4], Alexander Olsen[2,3,5], Gøril Bruvik Gravdahl [1,2,4], Manjit Singh Matharu [1,2,6], Parashkev Nachev[6], and Erling Tronvik[1,2,4]

Katsuki M, Tatsumoto M, Kimoto K, Iiyama T, Tajima M, Munakata T, Miyamoto T, Shimazu T. Investigating the effects of weather on headache occurrence using a smartphone application and artificial intelligence: A retrospective observational cross-sectional study. Headache. 2023 May;63(5):585-600. doi: 10.1111/head.14482. Epub 2023 Feb 28. PMID: 36853848.

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- Timely assumption of acute medication is crucial in the management of migraine attacks. Moreover, the unpredictability of attacks causes anxiety and is linked to a worse QoL
- 18 migraineurs completed a headache diary (388 total entries) and underwent optional self-administered app-based biofeedback sessions, which measured HR, peripheral skin temperature and muscle tension
- ML was used to construct a predictive model (4:1 training-test ratio) which could correctly predict an acute attack with an AUC of 0.62

Stubberud A, Ingvaldsen SH, Brenner E, Winnberg I, Olsen A, Gravdahl GB, Matharu MS, Nachev P, Tronvik E. Forecasting migraine with machine learning based on mobile phone diary and wearable data. Cephalalgia. 2023 May;43(5):3331024231169244. doi: 10.1177/03331024231169244. PMID: 37096352.

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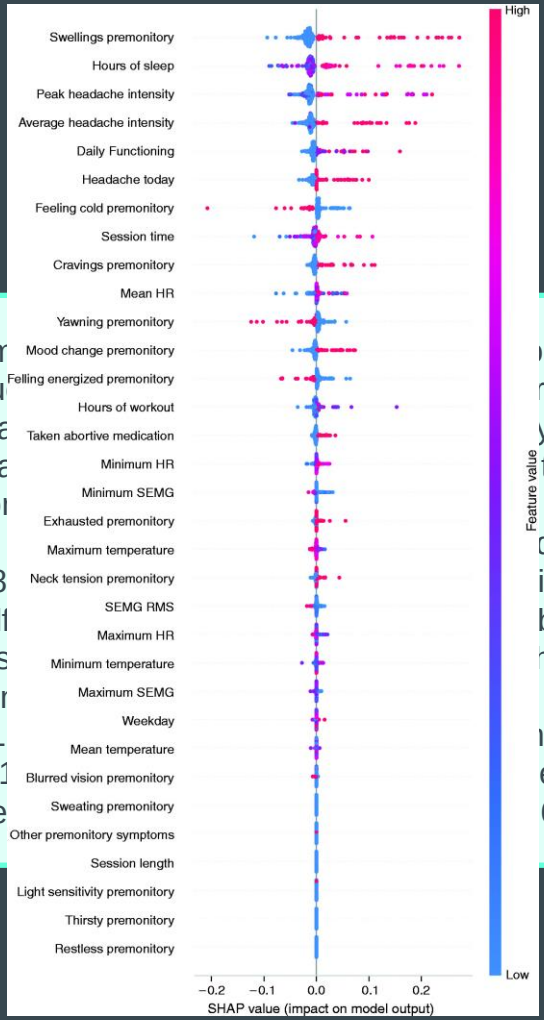
- 18 … (38… self… ses… ski…
- ML… (4:1… pre…

…on is …raine …y of …to a …diary …ional …back …neral …odel …ectly …62



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Artificial Intelligence (AI): future perspectives

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Homogeneity of approaches

Larger study samples

More powerful deep learning techniques

Programs to implement AI in routine practice

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Thank you for your attention!

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