

# Prolonged migraine aura or TIA/stroke?

Ville Artto MD, PhD

Department of Neurology

Helsinki University Central Hospital



## Disclosures:

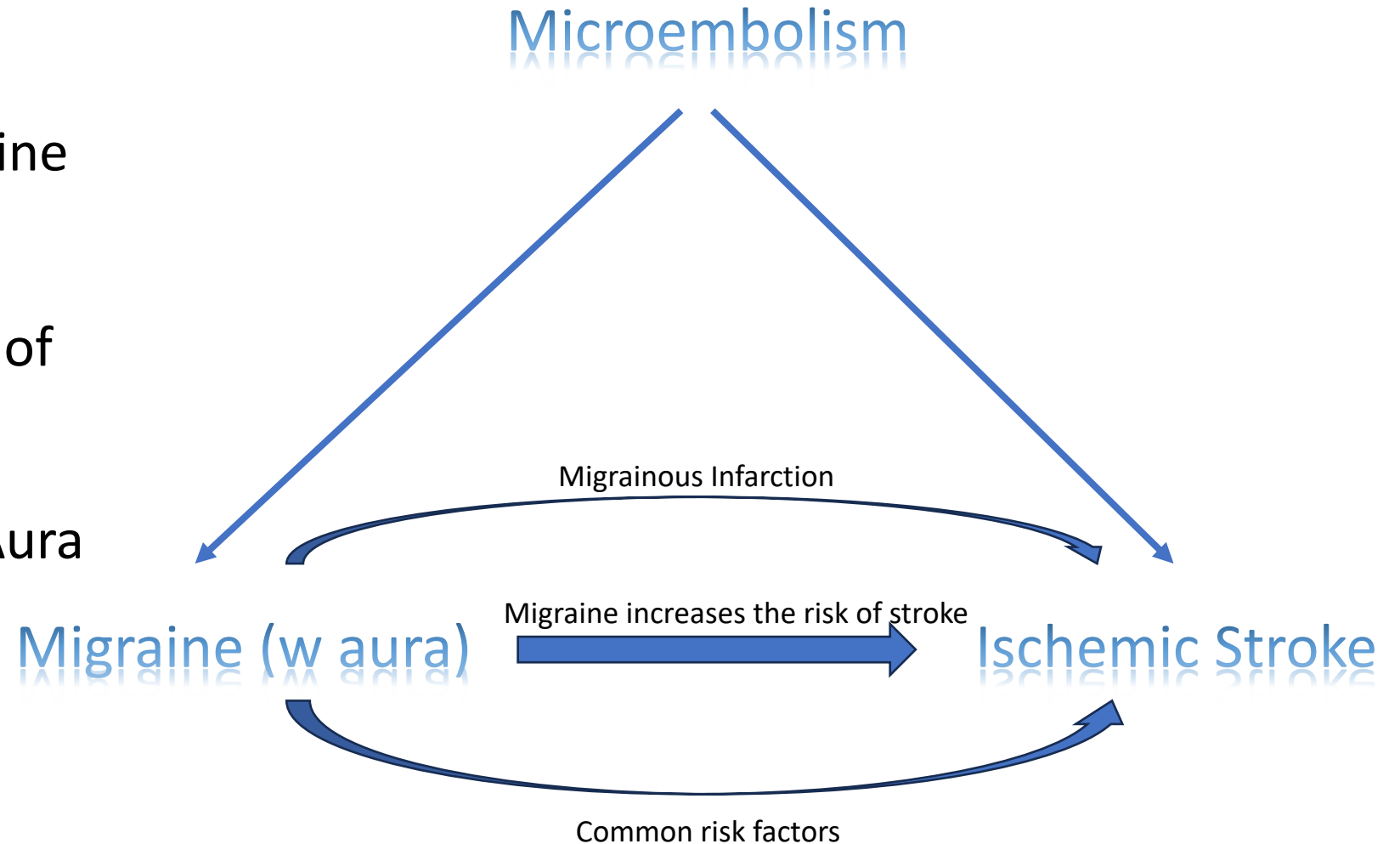
- Congress funding: Teva, Sanofi, Merck, Pfizer
- Speaker honoraria: Novartis, Teva, Lilly, Lundbeck, Pfizer, AbbVie
- Advisory board: Teva, Lilly, AbbVie, Lundbeck, Pfizer
- Other disclosures: HUCH/HUS, AAVA, ULP, Helsinki Sleep Clinic, Finnish Migraine Association

# Prolonged migraine aura or TIA/stroke?

- Comorbidity of migraine and stroke
- Possible mechanisms of the association
- Features suggesting Aura or TIA/stroke
- Imaging

# Prolonged migraine aura or TIA/stroke?

- Comorbidity of migraine and stroke
- Possible mechanisms of the association
- Features suggesting Aura or TIA/stroke
- Imaging

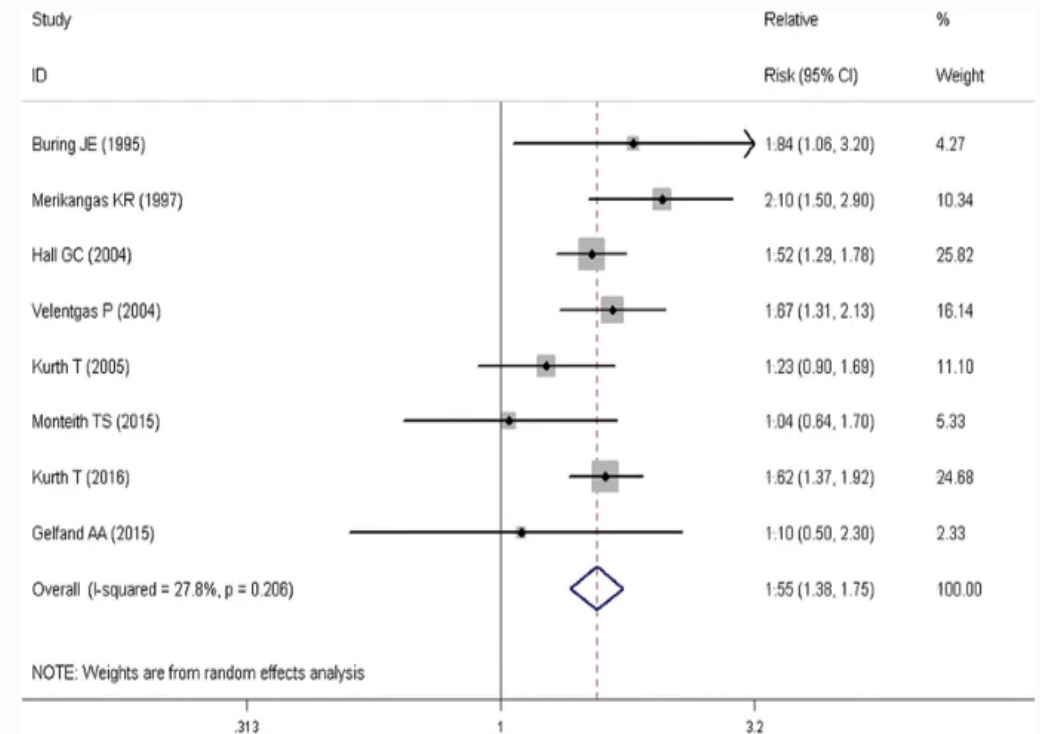


# Migraine and the risk of stroke

## Relative risk of Ischemic stroke

- for all migraineurs 1.64 (95% CI 1.22–2.20)
- for with aura 2.14 (95% CI 1.33–3.43)
- for without aura 1.02 (95% CI 0.68–1.51)

Fig. 2



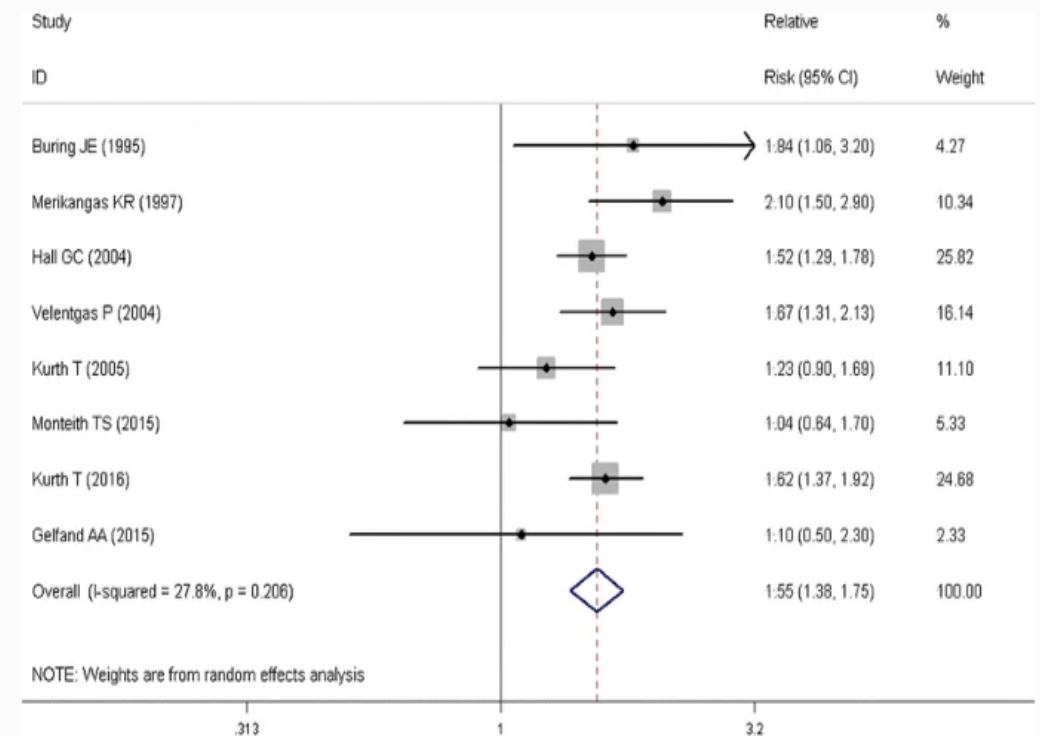
Association between migraine and the risk of total stroke

# Migraine and the risk of stroke

## Relative risk of ischemic stroke

- for all migraineurs 1.64 (95% CI 1.22–2.20)
- **for with aura 2.14 (95% CI 1.33–3.43)**
- for without aura 1.02 (95% CI 0.68–1.51)

Fig. 2



Association between migraine and the risk of total stroke

ARTICLE

Association between Migraine and Cryptogenic Ischemic Stroke in Young Adults

[View article page](#)

Nicolas Martinez-Majander, Ville Artto, Pauli Ylikotila, Bettina Sarnowski, Ulrike Waje-Andre ... [See all authors](#)

**TABLE 3. Odds Ratios and 95% Confidence Intervals from Conditional Logistic Regression on the Association between Migraine and Cryptogenic Ischemic Stroke**

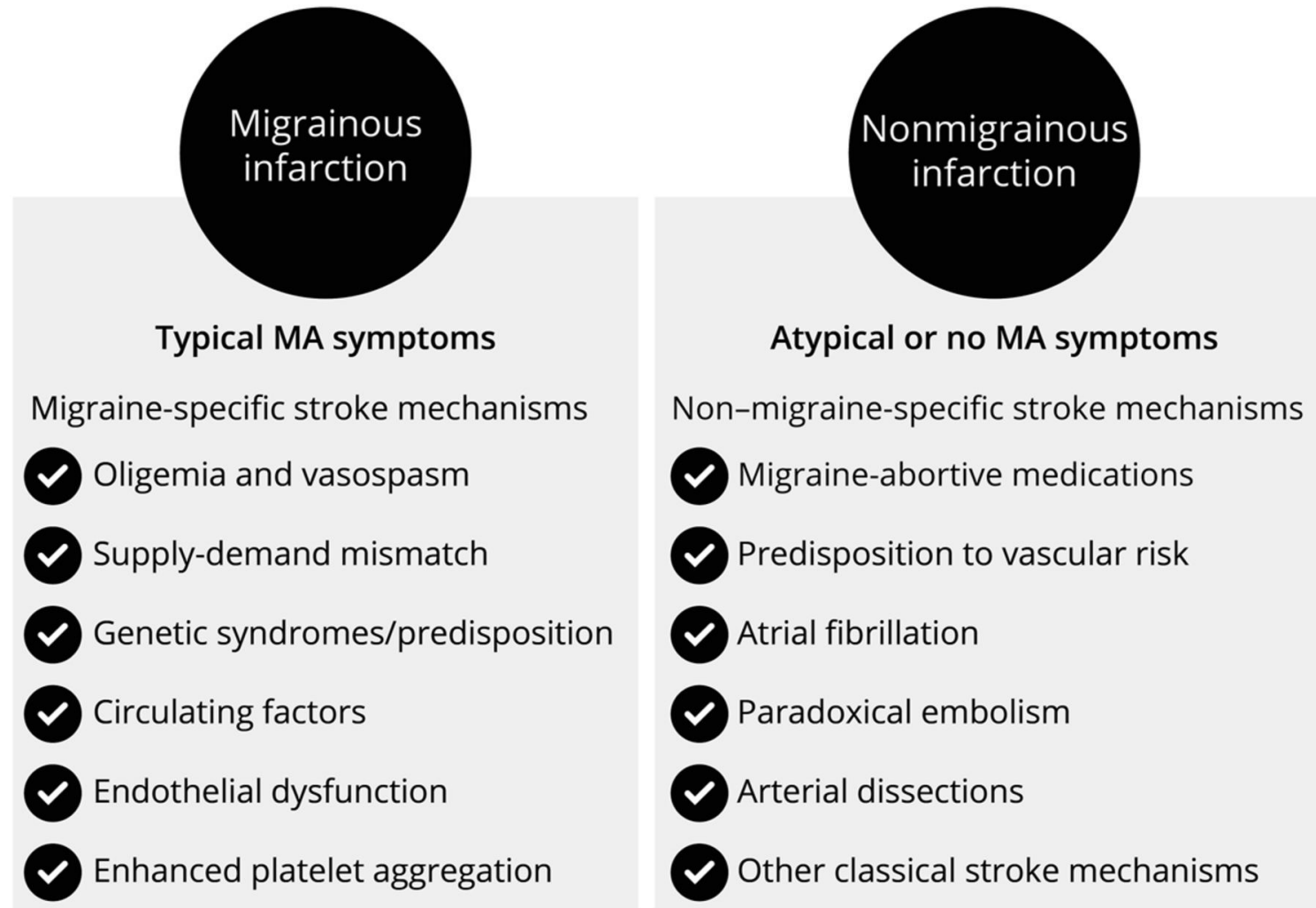
|                             | Model Adjusted for Age and Level of Education | Model Adjusted for Demographics and Vascular Risk Factors <sup>a</sup> |
|-----------------------------|---|--|
| <b>All</b>                  |   |  |
| Migraine status             |   |  |
| No migraine                 | Reference                                     | Reference  |
| Migraine with aura          | 3.40 (2.20–5.25)                              | 3.50 (2.19–5.61)   |
| Migraine without aura       | 0.66 (0.31–1.39)                              | 0.60 (0.27–1.31)   |
| Any migraine vs no migraine | 2.48 (1.68–3.65)                              | 2.48 (1.63–3.76)   |
| <b>Women</b>                |   |  |
| Migraine status             |   |  |
| No migraine                 | Reference                                     | Reference  |
| Migraine with aura          | 4.14 (2.22–7.73)                              | 4.32 (2.16–8.65)   |
| Migraine without aura       | 0.66 (0.31–1.39)                              | 0.63 (0.22–1.82)   |
| Any migraine vs no migraine | 3.04 (1.73–5.34)                              | 2.97 (1.61–5.47)   |
| <b>Men</b>                  |   |  |
| Migraine status             |   |  |
| No migraine                 | Reference                                     | Reference  |
| Migraine with aura          | 2.89 (1.54–5.41)                              | 3.61 (1.75–7.45)   |
| Migraine without aura       | 0.52 (0.16–5.41)                              | 0.56 (1.15–2.14)   |
| Any migraine vs no migraine | 2.04 (1.19–3.49)                              | 2.47 (1.32–4.61)   |

<sup>a</sup>Adjusted for age, level of education, hypertension, diabetes, current tobacco smoking, physical inactivity, heavy alcohol use, and waist-to-hip ratio. In women, models were further adjusted for oral estrogen use but not for diabetes due to its low frequency.

347 consecutive patients aged 18 to 49 years with a recent cryptogenic ischemic stroke (CIS) and 347 age- and sex-matched (5 years) stroke-free controls were enrolled

MA has a strong association with CIS in young patients, independent of vascular risk factors and presence of PFO

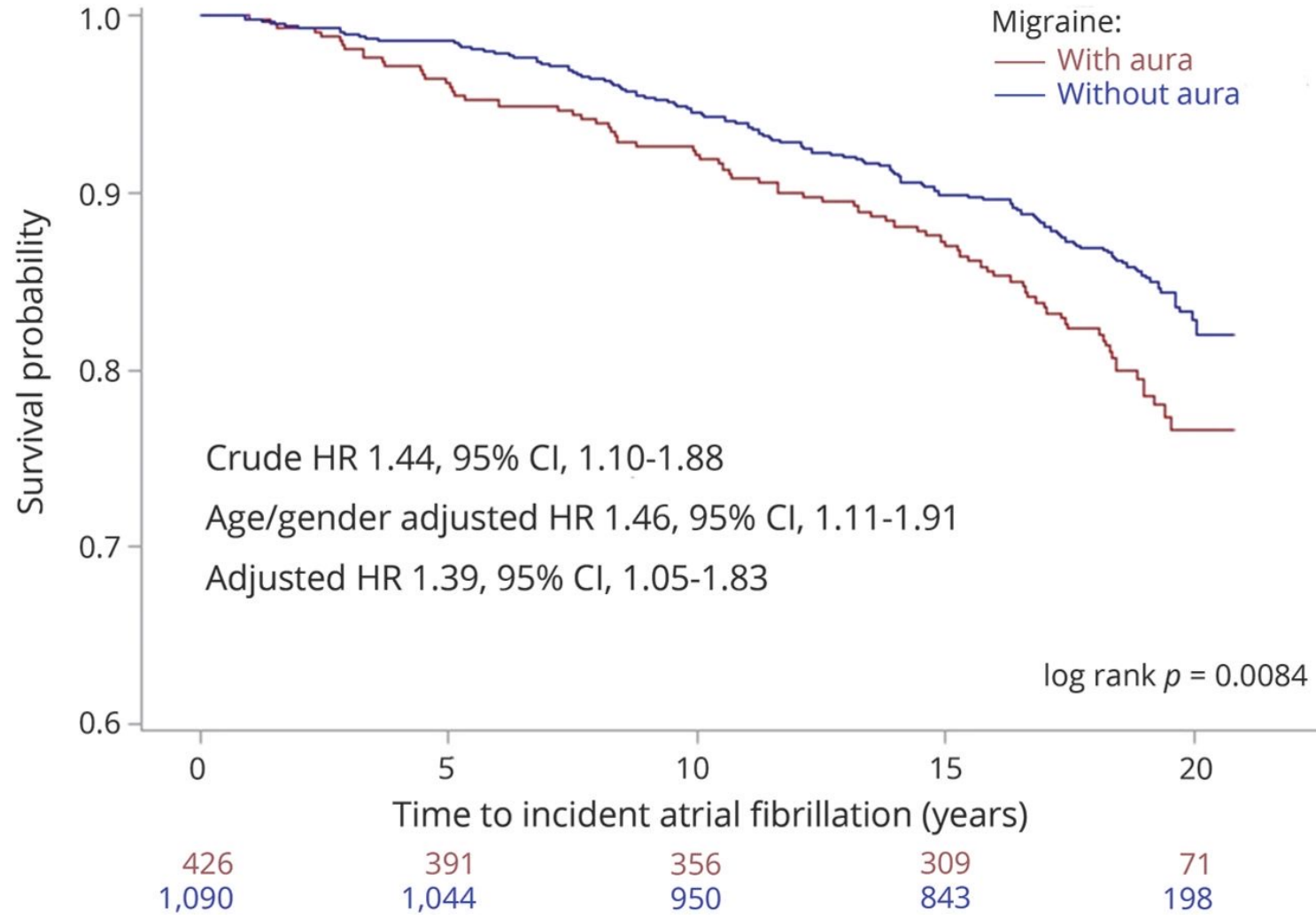
**Figure 2 Potential Mechanisms of Migrainous and Nonmigrainous Infarctions in Patients With Migraine**



Simona Sacco et al. *Neurology* 2023;100:716-726



**Kaplan-Meier curves depicting 20-year outcome of incident atrial fibrillation in participants with migraine with visual aura and those with migraine without aura**



Migraine with aura was associated with increased risk of incident AF

This may potentially lead to ischemic strokes

Souvik Sen et al. *Neurology* 2018;91:e2202-e2210




# Stroke mimics

- A stroke mimic is defined as a nonvascular disease that presents with stroke-like symptoms
- Stroke mimics include e.g. migraine, seizures metabolic disorder, infection, space-occupying lesion, syncope, and functional disorder
- Migraine with aura is the final diagnosis in more than 1% of patients evaluated in the emergency setting for the suspicion of acute ischemic stroke, and it is responsible for about 1.8% of thrombolytic treatments

## Review

### When migraine mimics stroke: A systematic review

Alberto Terrin<sup>1</sup>, Giulia Toldo<sup>1</sup>, Mario Ermani<sup>1</sup>, Federico Mainardi <sup>2</sup>, and Ferdinando Maggioni<sup>1</sup>

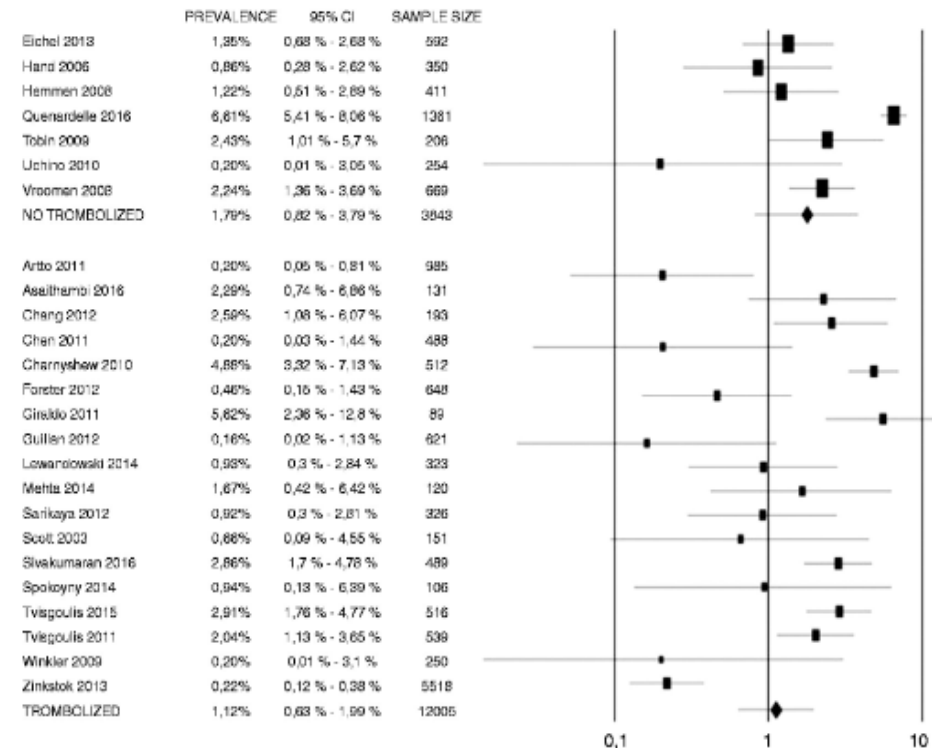


Figure 3. Absolute prevalence of migraine with aura (%) among patients evaluated in an emergency setting for a suspected acute ischemic stroke (first group) and among patients treated with rt-PA (second group).

## As a consequence

- If migraine patient is falsely diagnosed to suffer stroke – the patient is exposed to potentially hazardous treatments e.g. rTPA
- If stroke patient is falsely diagnosed to suffer migraine – the patient is left without stroke prevention and other stroke treatments

## Kallela Duodecim 2012;128(9):971-7 (Finnish) How do I distinguish migraine aura from TIA attack?

### Miten erotan migreeniauran TIA-kohtauksesta?



1959-2023

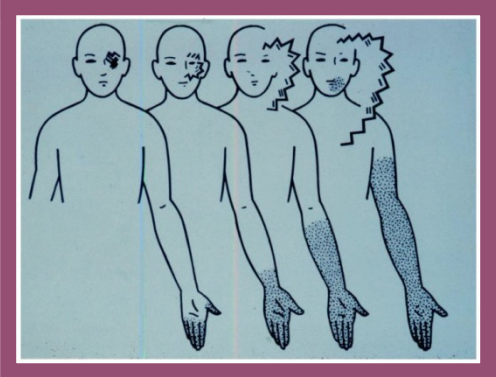
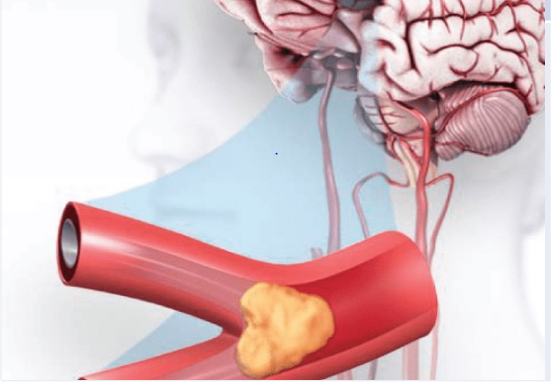
TAULUKKO 1. Migreeniauran ja TIA:n tyypilliset kliiniset piirteet.

| Migreeniaura   | TIA  | Kommentti   |
|--|--|---|
| Auratyypit yleisyysjärjestyksessä: visuaalinen, puhe, sensorinen (hyvin harvoin motorinen) | Motorinen, puheeseen liittyvä, sensorinen tai visuaalinen (vaihtelee iskemia-alueen paikan mukaan) | Motorinen oire (hemipareesi) liittyy harvinaiseen familiaaliseen hemiplegiseen migreeniin (FHM) Hemipareesi on TIA:n tyyppioire |
| Oireisto ilmaantuu ja väistyy asteittain   | Äkillinen alku ja nopea korjaantumisen   | Migreenioire vaikeutuu minuuttien ( $\geq 5$ min) aikana Aivoverenkierron häiriö saavuttaa huippunsa heti                       |
| Kohtaukset toistuvat vuosien aikana pitkälti samankaltaisina                               | Yksi tai useampi kohtaus päivien tai muutaman viikon sisällä                                       | Migreenitaipumus säilyy koko elämän TIA puolestaan enteilee pysyvää puutosoiretta (aivoinfarktia) lähipäivien aikana            |
| Oireet kestävät kymmeniä minutteja   | Oireet kestävät minutteja  | TIA on äkillisempi oire kuin migreeniaura   |
| Päänsärky seuraa neurologista oiretta (ja näin on tapahtunut usein aiemminkin)             | Päänsärkyä esiintyy harvoin, mutta se saattaa myös edeltää neurologista oiretta                    | Migreeniaura voi toisinaan esiintyä ilman päänsärkyä ("migreenin ekvivalentti")   |
| Kohtaukset alkavat alle 40 vuoden iässä (usein jo lapsena tai teini-iässä)                 | Kohtausten ilmaantuvuus lisääntyy iän myötä  | Potilas on nuori ja terve – epäile migreeniauraa<br>Potilas on vanha ja sairas – epäile TIA-kohtausta                           |
| Potilaalla ei useinkaan ole verenkiertosairautta tai sen riskitekijöitä                    | Potilaalla on useasti verenkiertosairaus tai sen riskitekijöitä                                    | Mitä suurempi ABCD <sup>2</sup> -pistemäärä, sitä suurempi aivoinfarktin riski  |
| Suvussa on migreenipotilaita (joilla on aurallinen tai hemipleginen migreeni)              | Suvussa esiintyy verenkiertosairauksia tai niiden riskitekijöitä, jopa nuorella iällä              | Sukanamneesi on tärkeä motorisen oireen selvittelystä (nimenomaan epäiltäessä familiaalista hemiplegistä migreeniä)             |

ABCD<sup>2</sup> (age, blood pressure, clinical duration, diabetes). A = ikä,  $\geq 60$  vuotta = 1 piste, B = verenpaine,  $\geq 140/90$  mmHg = 1 piste, C = oireisto, toispuolinen lihaskivertys = 2 pistettä, puhehäiriö ilman lihaskivertystä = 1 piste, D = oireen kesto, 10–59 minuuttia = 1 piste,  $\geq 60$  minuuttia = 2 pistettä, D = diabetes = 1 piste



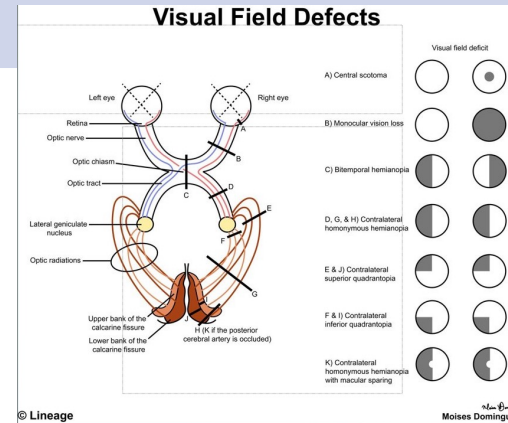
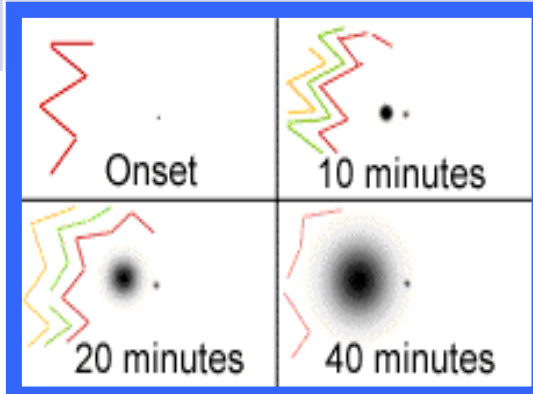
# Clinical features of migraine aura and TIA Kallela Duodecim 2012;128(9):971-7 (Finnish)


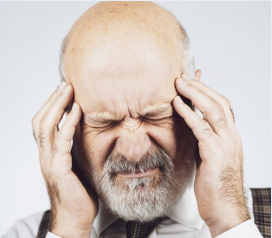
|                         | Aura  | TIA   | Comment  |
|-------------------------|---|---|--|
| Development of symptoms | Gradually (=march of symptoms)  | Sudden  | The aura symptoms worsen over minutes  |
| Prodromal symptoms?     | Prodrome symptoms (food cravings, mood changes, fatigue...)   | No prodrome symptoms  | Cerebrovascular disorder reaches its peak immediately  |
|                         |   |  |  |
| Symptoms                | <p>Aura symptoms in order of frequency:</p> <ol style="list-style-type: none"> <li>1. Visual (almost always)</li> <li>2. Aphasic</li> <li>3. Sensory</li> <li>(4. only rarely motor)</li> </ol> | Motor, aphasic, sensory or visual (varies by the location of the ischemic area)     | <p>Motor symptoms (hemiparesis) only associated with a rare hemiplegic migraine</p> <p>Hemiparesis is a typical symptom of TIA</p> |

# Clinical features of migraine aura and TIA

Kallela Duodecim 2012;128(9):971-7

|                               | Aura                            | TIA                                 | Comment   |
|-------------------------------|---------------------------------|-------------------------------------|---|
| Positive or negative symptoms | Zig zags<br>Flashes<br>Tingling | Loss of vision<br>Loss of sensation | Zigzag lines that are gradually floating across field of vision – Aura<br><br>Sudden amaurosis fugax or homonymous hemianopsia – TIA/Stroke |



|  | Aura  | TIA   | Comment   |
|--|---|---|---|
| <p>Duration</p>   | <p>The symptoms last for tens of minutes</p>  | <p>The symptoms last for minutes</p>                                    | <p>TIA is a more sudden attack than a migraine</p>                                  |
| <p>Headache</p>  | <p>Headache follows neurological symptoms</p> | <p>Headache is rare, but it may also precede a neurological symptom</p> | <p>Migraine aura can sometimes occur without a headache ("migraine equivalent")</p> |

# Clinical features of migraine aura and TIA


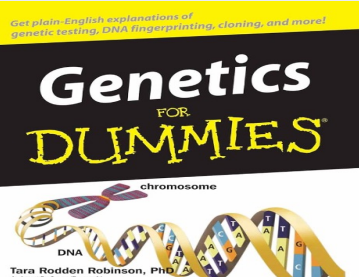
Kallela Duodecim 2012;128(9):971-7

|            | Aura   | TIA  | Comment   |
|------------|--|--|---|
| Recurrence | The attacks repeat themselves over the years in largely similar ways           | One or more attacks within a few days (or weeks) | Migraine tendency might remain throughout life<br><br>TIA might foreshadow a more permanent deficit (infarction) in the coming days |
| Age        | Attacks begin under the age of 40 (often already as a child or in adolescence) | The incidence of attacks increases with age      | The patient is young and healthy – suspect aura<br><br>The patient is old and sick – suspect a TIA                                  |





## Clinical features of migraine aura and TIA (continues...)

|  | Aura  | TIA   | Comment  |
|--|---|---|--|
| <p>Vascular risk factors</p>   | <p>The patient often does not have a vascular disease or its risk factors</p> | <p>The patient often has a vascular disease or its risk factors</p>  | <p>The larger the ABCD2 - score, the greater the risk of cerebral infarction</p>   |
| <p>Family history</p>  | <p>Migraine sufferers in the family</p>                                       | <p>Vascular diseases (or risk factors) in the family</p>  | <p>Family history is especially important when evaluating motor symptoms (e.g. when suspecting familial hemiplegic migraine)</p> |

# Explicit diagnostic criteria for transient ischemic attacks to differentiate it from migraine with aura

Elena R Lebedeva<sup>1,2</sup>, Natalia M Gurary<sup>3</sup>, Denis V Gilev<sup>4</sup>,  
Anne Francke Christensen<sup>5</sup> and Jes Olesen<sup>5</sup>

*Cephalalgia*

2018, Vol. 38(8) 1463–1470

© International Headache Society 2017

Reprints and permissions:

sagepub.co.uk/journalsPermissions.nav

DOI: 10.1177/0333102417736901

journals.sagepub.com/home/cep

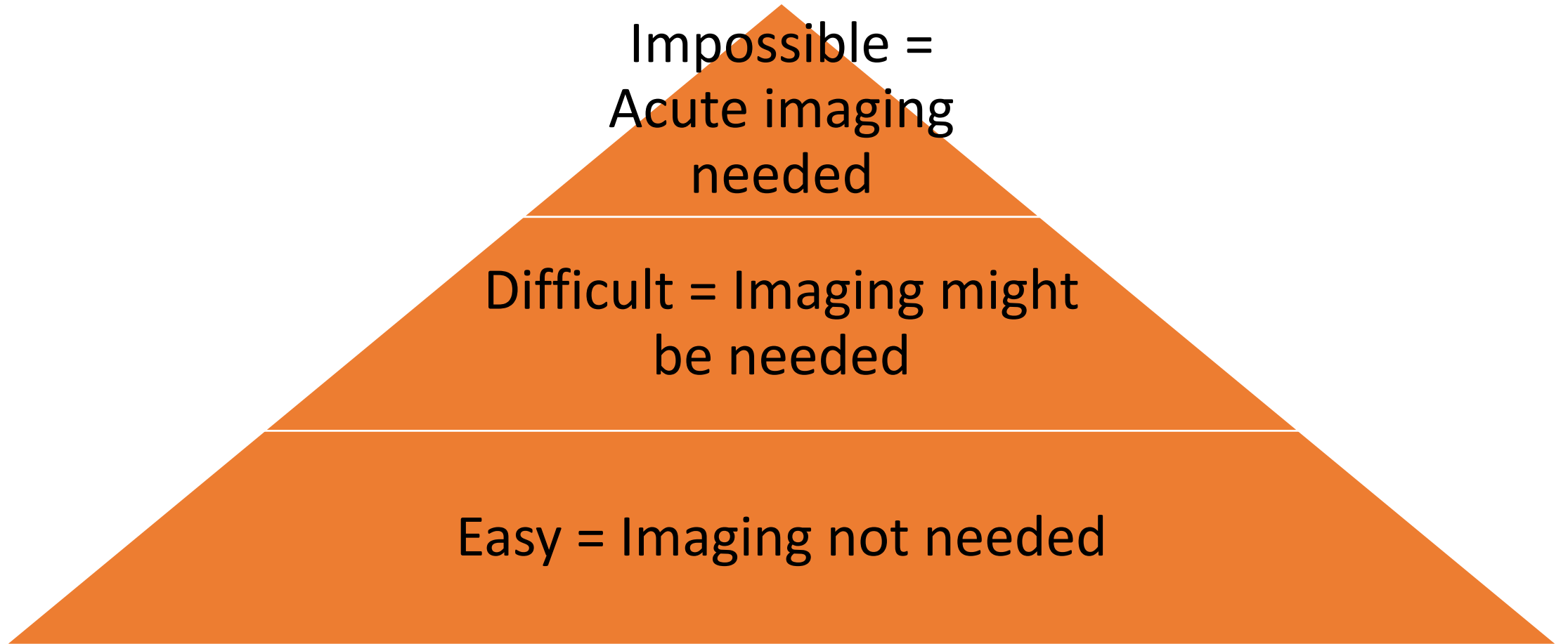


- A. Sudden onset of fully reversible neurological or retinal symptoms (typically hemiparesis, hemihypesthesia, aphasia, neglect, amaurosis fugax, hemianopsia or hemiataxia)
- B. Duration < 24 hours
- C. At least two of the following:
  1. At least one symptom is maximal in < 1 minute ( no gradual spread)
  2. Two or more symptoms occur simultaneously
  3. Symptoms in the form of deficits ( no irritative symptoms such as photopsias, pins and needles etc)
  4. No headache accompanies or follows the neurological symptoms within one hour
- D. None of the following isolated symptoms (can occur together with more typical symptoms): shaking spells, diplopia, dizziness, vertigo, syncope, decreased level of consciousness, confusion, hyperventilation associated paresthesias, unexplained falls, amnesia
- E. No evidence of acute infarction in the relevant area on neuroimaging

**Figure 1.** Proposed tissue based diagnostic criteria for transient ischemic attacks\*.

\*All letter headings must be fulfilled.

# Differential diagnosis between migraine aura and TIA



*Original Article*

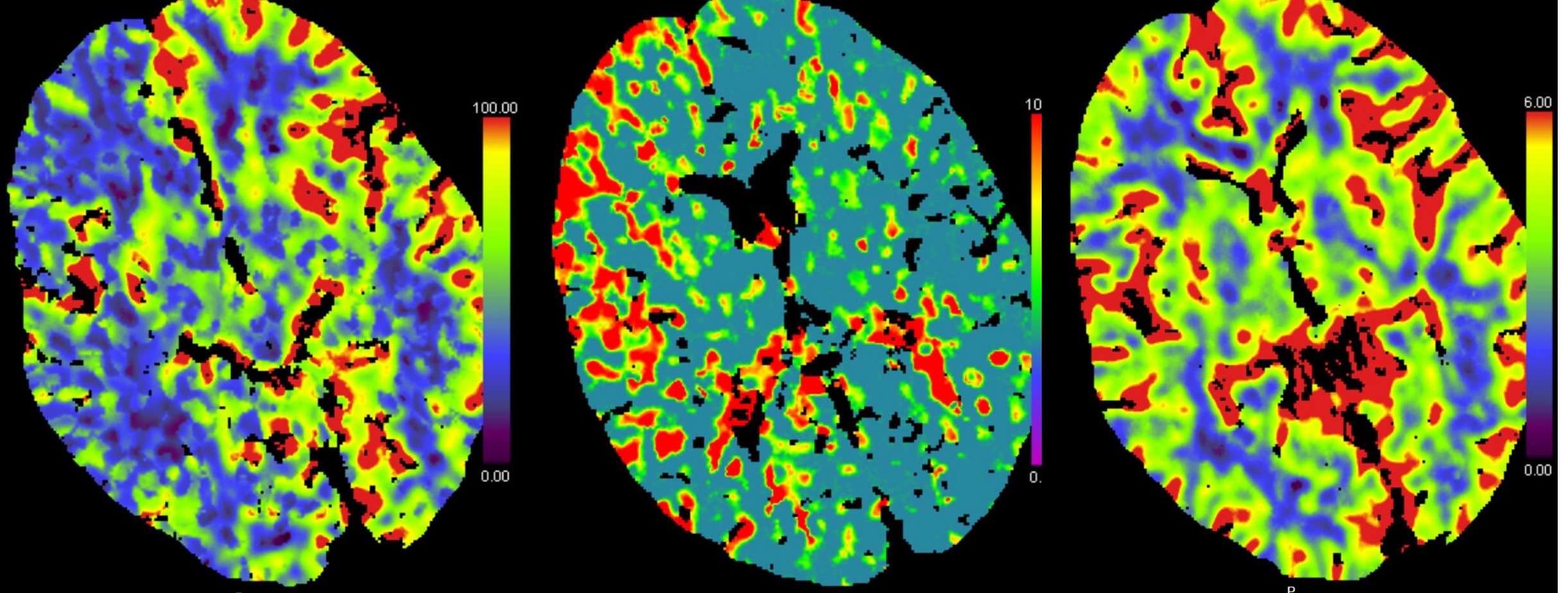
## **Perfusion patterns in migraine with aura**

Alex Förster<sup>1</sup>, Holger Wenz<sup>1</sup>, Hans U Kerl<sup>1</sup>, Marc A Brockmann<sup>1,2</sup>, and Christoph Groden<sup>1</sup>

- Migraine aura is usually associated with a perfusion deficit not limited to a specific vascular territory, and a moderate increase of time to peak (TTP)
- Hypoperfusion restricted to a single vascular territory with a marked increase of TTP and/or mean transit time (MTT) is atypical for migraine with aura and suggestive of acute ischemic stroke

# Case report of a young man

- No vascular risk factors
- Hemiplegic migraine from childhood
- Now the patient was brought to ER because sudden global aphasia and left side hemiparesis (aphasia was new symptom)
- Visual neglect
- NIHSS 12



CT-angiography was normal, however, CT-perfusion demonstrated hypoperfusion in the right ACA, MCA, and PCA territory, as well as in the left ACA territory (Cerebral Blood Flow and Mean Transit Time), but Cerebral Blood Volume was normal.

The depicted distribution of CT-perfusion deficit - not limited to a specific vascular territory - in the context of this patient case suggests aura.

## Conclusion

- Association between migraine and stroke is complex
- Migraine with aura increases the risk of ischemic stroke
- In most cases differentiation of the two is relatively easy
- Imaging might be considered in some cases (and of course always if stroke is suspected)

