



Cutaneous Allodynia – A Predictor of Migraine Chronification: Results of the American Migraine Prevalence and Prevention Study



Sait Ashina, MD¹, Dawn C. Buse, PhD^{1,3}, Marcelo E. Bigal, MD, PhD^{1,4}, Daniel Serrano, MS⁵, Michael Reed⁵, PhD, Richard B. Lipton, MD^{1,2,3}
Departments of ¹Neurology, ²Epidemiology and Population Health, ³Montefiore Headache Center, Albert Einstein College of Medicine, Bronx, NY;
⁴Merck Research Laboratories, Global Center for Scientific Affairs, Neuroscience, Whitehouse Station, NJ; ⁵Vedanta Research, Chapel Hill, NC

BACKGROUND

- Cutaneous allodynia (CA) is a marker of increased excitability of central nociceptive neurons, (i.e. central sensitization)¹.
- CA is more prevalent in chronic migraine (CM) than episodic migraine (EM)².
- Each year, approximately 2.5% of EM sufferers can develop CM, i.e. migraine chronification
- We hypothesize that CA may predict the new onset of CM among EM sufferers.

OBJECTIVE

- To explore the relationship between CA and new onset CM in individuals with EM.

METHODS

- Data were collected from the American Migraine Prevalence and Prevention Study (AMPP), a longitudinal, prospective, population-based, mailed questionnaire study. Respondents were identified in 2004 by screening 120,000 US households to identify 24,000 individuals with severe headache who have been followed in 2005, 2006 and 2007.
- The AMPP survey included demographic data and headache symptomology which allowed for the computation of headache type according to ICHD-2 criteria among other data
- Respondents who met ICHD-2 criteria for migraine and provided the necessary data were included in analyses. They were categorized into the following groups:
 - CM (ICHD-2 diagnosis of migraine with ≥ 15 headache days/month)
 - EM (ICHD-2 diagnosis of migraine with 0-14 headache days/month)

METHODS

- Migraine chronification was defined as development of new-onset CM in persons with EM.
- The 12-item Allodynia Symptom Checklist (ASC)³ was used to assess the frequency of CA symptoms during headache. Each of 12 items was scored on a 3-point scale with response options: never/rarely (0), less than 50% of the time (1) and 50% of the time or more(2).
- Total ASC score of ≥ 3 indicated presence of CA. The ASC also identified 3 non-mutually exclusive subtypes of CA: thermal, mechanical static and mechanical dynamic. Scores of ≥ 2 indicated presence of an allodynia subtype.
- Total allodynia and subtypes were also used as continuous variables in analyses.
- Logistic regression was used to model the odds of new-onset of CM in 2006 and 2007.
- Odds ratios (ORs) were adjusted for depression (PHQ-9), anxiety (self-report), body mass index, headache-related disability (assessed by MIDAS), household income, sex and age.

RESULTS

- The sample included persons with EM in 2005 (n=6657) or 2006 (n=7042) who provided data in the subsequent year.
- In total 304 subjects developed CM: 160 in 2006 and 144 in 2007.
- Subjects with CA were significantly more likely to progress from EM to CM, even after adjusting for demographic factors, headache-related disability, depression and anxiety. Odds ratios are presented in Tables 1 and 2.

RESULTS

TABLE 1. CUTANEOUS ALLODYNIA (DICHOTOMIZED VARIABLE) AS A RISK FACTOR FOR NEW ONSET CM

Type of allodynia (ASC cut score)	OR	95 % CI	P value
Total allodynia (score ≥ 3)	1.74	(1.32 - 2.28)	< 0.001
Thermal allodynia (score ≥ 2)	1.25	(0.98 - 1.61)	0.076
Mechanical dynamic allodynia (score ≥ 2)	1.49	(1.15 - 1.94)	0.003
Mechanical static allodynia (score ≥ 2)	1.75	(1.36 - 2.26)	< 0.001

TABLE 2. CUTANEOUS ALLODYNIA (CONTINUOUS VARIABLE) AS A RISK FACTOR FOR NEW ONSET CM

Type of allodynia (ASC score range)	OR	95 % CI	P value
Total allodynia (range: 0-24)	1.05	(1.03 - 1.08)	< 0.001
Thermal allodynia (range: 0-10)	1.09	(1.03 - 1.14)	0.0016
Mechanical dynamic allodynia (range: 0-4)	1.14	(1.05 - 1.23)	0.001
Mechanical static allodynia (range: 0-10)	1.11	(1.06 - 1.16)	< 0.001

CONCLUSIONS

- In persons with EM, CA is associated with the new-onset of CM after adjusting for demographic variables, headache features, and comorbid conditions.
- Central sensitization may be a marker for brain events which predispose to headache chronification.

REFERENCES

1. Burstein R, Yarnitsky D, Goor-Aryeh I, et al. An association between migraine and cutaneous allodynia. Ann Neurol 2000; 47(5):614-24.
2. Bigal ME, Ashina S, Burstein R, et al. Prevalence and characteristics of allodynia in headache sufferers: a population study. Neurology 2008; 70(17):1525-33.
3. Lipton RB, Bigal ME, Ashina S, et al. Cutaneous allodynia in the migraine population. Ann Neurol 2008; 63(2):148-59.