

Pain sensitivities predict prophylactic treatment outcomes of flunarizine in chronic migraine patients: A prospective study

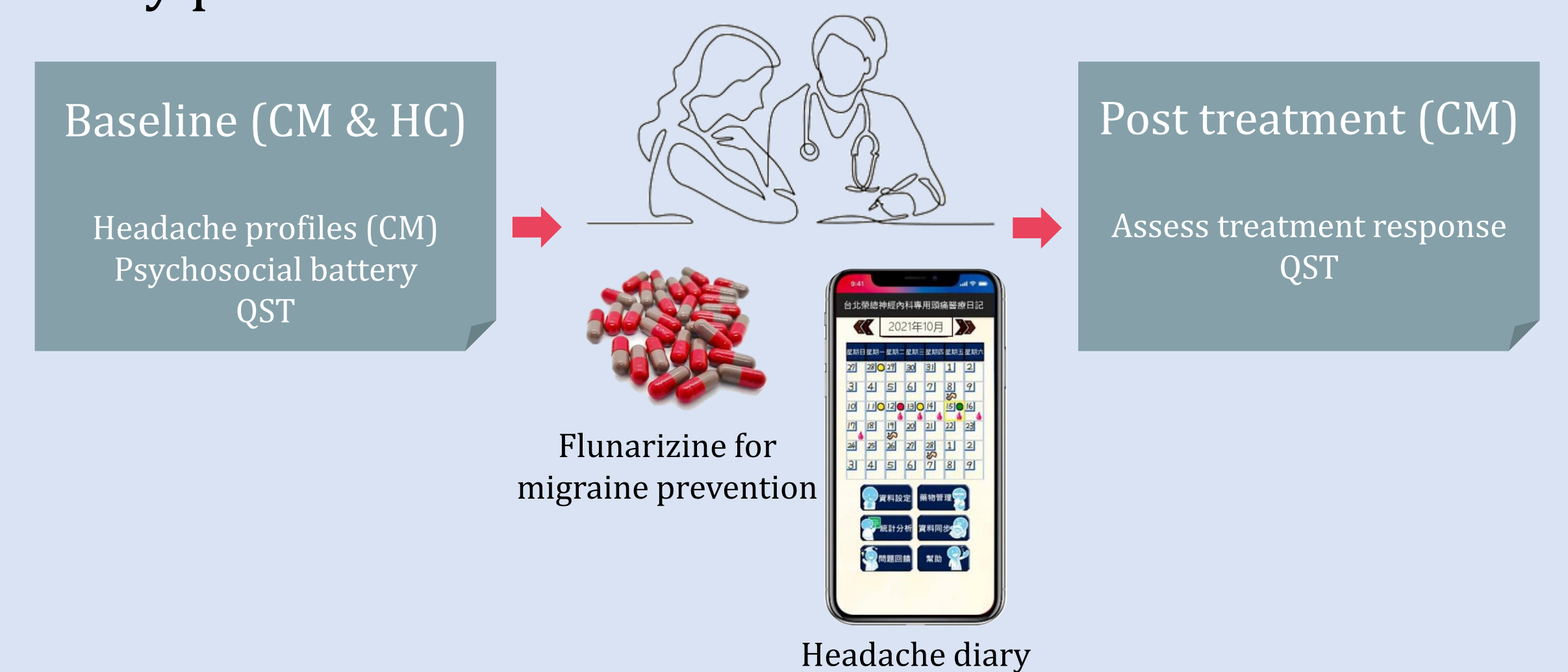
Li-Ling Hope Pan, Yen-Feng Wang, Yu-Hsiang Ling, Kuan-Lin Lai, Shih-Pin Chen, Wei-Ta Chen, Rolf-Detlef Treede, Shuu-Jiun Wang

Brain Research Center & School of Medicine,
National Yang Ming Chiao Tung University
Department of Neurology, Neurological Institute,
Taipei Veterans General Hospital
Mannheim Center for Translational Neurosciences, Medical Faculty
Mannheim, Heidelberg University, Germany

Aims

- To assess the differences in quantitative sensory testing (QST) between chronic migraine (CM) and healthy controls (HCs)
- To explore the association between pain sensitivities and outcomes in CM following preventive treatment

Methods



- Study procedures
- Independent t-tests or Mann-Whitney *U* tests: HC vs. CM or responders vs. non-responders
- One-way analysis of variance (ANOVA) tests with post-hoc least significant difference (LSD) test: comparison between HC, responders, and non-responders
- Chi-squared automatic interaction detection (CHAID) decision tree was applied with ≥ 10 cases/parent node & ≥ 2 cases/child node

Results

- Treatment naïve CM patients (by the International Classification of Headache Disorders, 3rd edition) and HC were recruited.
- Cold, heat, mechanical punctate, and pressure pain thresholds (CPT, HPT, MPT, PPT) over the dermatomes of first branch of trigeminal nerve (V1) and first thoracic nerve (T1) were measured by QST
- Instrument
 - CPTs & HPTs: Medoc TSA-II NeuroSensory Analyzer with a 30 mm x 30 mm Thermode (Medoc Ltd., Israel)
 - MPTs: standard rigid electronic von Frey filament (ITTC 2392, IITC Life Science Inc., USA)
 - PPTs: 1-cm² probe on a hand-held electronic algometer (Algometer Type II, SBMEDIC Electronics, Sweden)
- Prophylactics: flunarizine (5-10 mg per day)
- Abortive medication: sumatriptan or NSAID
- Treatment response: $\geq 50\%$ reduction in the number of monthly headache days (MHD) over the 12-week treatment period
- 84 CM and 50 age-and-sex-matched HCs were included. (Table 1)

Table 1. Demographic data and headache profiles of CM and HC

	CM	HC	<i>p</i>
N	84	50	-
Age (yrs.)	38.3 ± 11.5	37.4 ± 9.2	0.620
Sex (M/F)	6/78	8/42	0.105
BMI (kg/m ²)	23.1 ± 5.4	23.3 ± 3.6	0.506 [†]
MHD (days)	21.7 ± 6.0	NA	NA
Disease duration (yrs.)	18.9 ± 11.5	NA	NA
MIDAS	38.6 ± 46.5	NA	NA
MOH	19 (23%)	NA	NA
HADS-A	8.3 ± 3.9	3.9 ± 3.4	<0.001*
HADS-D	6.4 ± 3.4	2.7 ± 2.9	<0.001*
PSS	26.2 ± 8.1	21.2 ± 9.1	0.001*
Presence of migraine during QST	44 (52%)	NA	NA

**p* < 0.05; [†]calculated with the Mann-Whitney *U* test

CM: chronic migraine; HC: healthy control; BMI: body mass index; MHD: monthly headache days; MIDAS: Migraine Disability Assessment; MOH: medication overuse headache; HADS-A/D: Hospital Anxiety and Depression Scale-Anxiety/Depression Scale; PSS: Perceived Stress Scale; QST: quantitative sensory testing; NA: not applicable

- Demographics and headache profiles were comparable between the responders (*n* = 24) and non responders (*n* = 60).
- Significant differences in pain sensitivities were found between responders, non-responders, and HC. (Table 2)
- CM with higher (closer to normal) HPT or MPT over the supraorbital area were more likely to have a favorable outcome following preventive treatment with flunarizine.
- The cutoff values for treatment responders are HPT >44.9°C or MPT >158 g.

Table 2. QST results of the responders, non-responders, and HC

	R	nR	HC	ANOVA <i>p</i>	R vs. nR <i>p</i>	R vs. HC <i>p</i>	nR vs. HC <i>p</i>
V1 CPT (°C) [†]	18.8 ± 7.7	21.8 ± 7.5	15.2 ± 7.9	0.001*	0.239	0.079	<0.001*
HPT (°C)	42.7 ± 4.1	39.9 ± 3.5	43.8 ± 3.4	<0.001*	0.002*	0.208	<0.001*
MPT (g) [†]	123 ± 55	96 ± 34	110 ± 32	0.027*	0.023*	0.586	0.030*
PPT (kPa) [†]	182 ± 64	150 ± 59	173 ± 59	0.026*	0.026*	0.653	0.026*
T1 CPT (°C) [†]	17.7 ± 9.1	21.4 ± 7.7	13.4 ± 9.8	0.001*	0.243	0.052	<0.001*
HPT (°C) [†]	41.7 ± 3.6	40.0 ± 3.7	42.2 ± 3.8	0.010*	0.066	0.631	0.004*
MPT (g)	106 ± 58	88 ± 35	103 ± 42	0.108	-	-	-
PPT (kPa)	265 ± 68	228 ± 75	284 ± 97	0.002*	0.061	0.373	0.001*

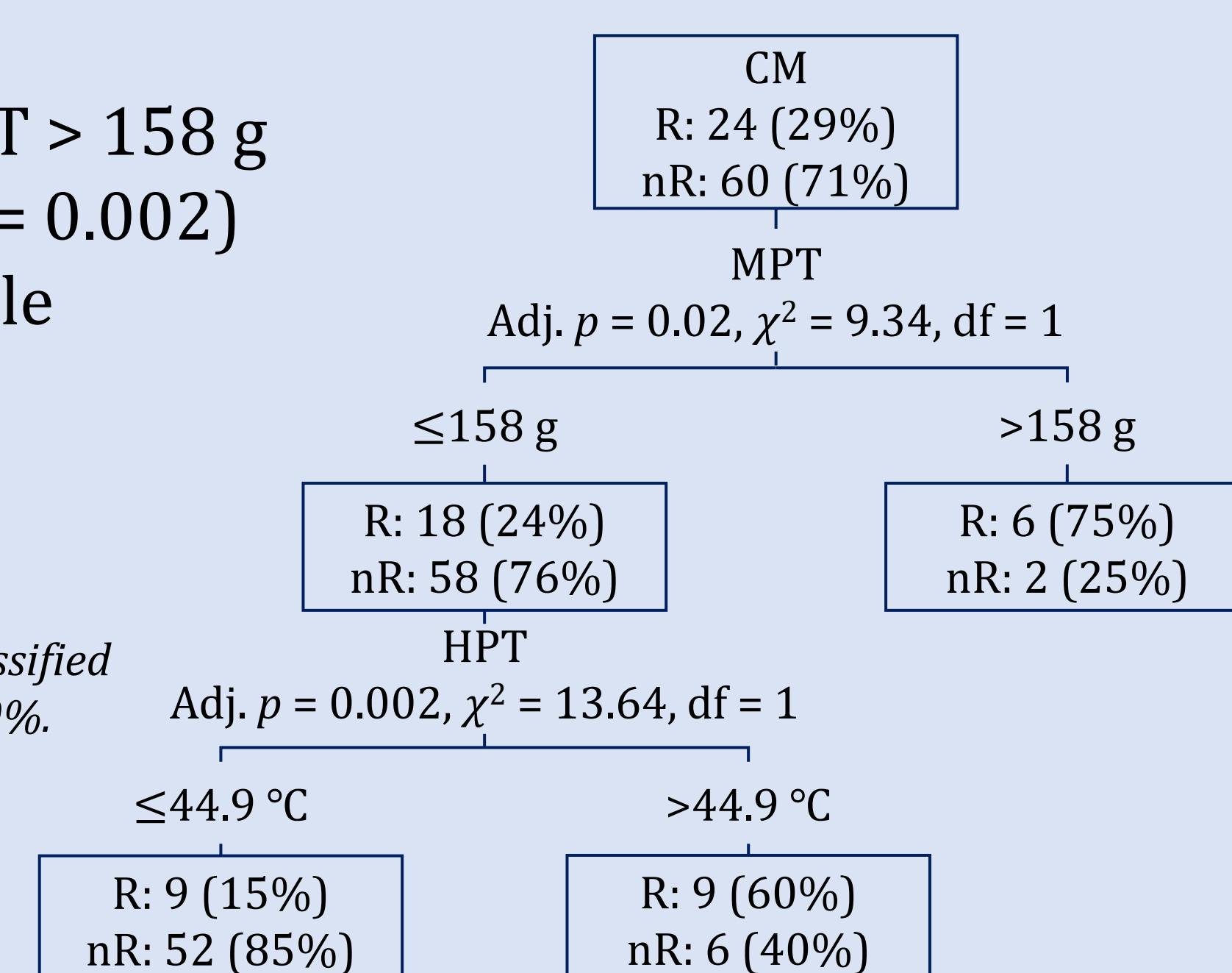
**p* < 0.05; [†] not normally distributed, calculated with log transformed data;

R: responders; nR: non-responders; HC: healthy control; V1: first branch of trigeminal nerve; T1: first thoracic nerve; CPT: cold pain threshold; HPT: heat pain threshold; MPT: mechanical punctate pain threshold; PPT: pressure pain threshold.

- Decision tree analysis: V1 MPT > 158 g (*p* = 0.02) or HPT > 44.9°C (*p* = 0.002) was associated with a favorable treatment outcome (Fig. 1)

Fig.1 The responders and non-responders were classified based on HPT and MPT with overall accuracy of 80%.

CM: chronic migraine; R: responders; nR: non-responders; V1: first branch of trigeminal nerve; MPT: mechanical punctate pain threshold; HPT: heat pain threshold.



Conclusion

SJW's Headache Study Group in Taiwan
王署君醫師榮陽頭痛研究團隊

