Glutamate Receptor Ionotropic AMPA 3 (GRIA3) gene polymorphism influences cortical response to somatosensory stimulation in medication-overuse headache patients

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BACKGROUND

- Glutamate-mediated pathways seem to play a relevant role in the generation of somatosensory evoked potentials (SSEPs) in supragranular parietal layers (Salt et al., 1995), but also in induction and maintenance of central sensitization (Latremoliere and Woolf, 2009), a mechanism that may be responsible for medication overuse headache (MOH).
- MOH is a secondary form of chronic (>15 days/month) headache usually developed by migraine patients after prolonged (>3 months) symptomatic medication overuse.
- Here, we tested whether Glutamate Receptor Ionotropic AMPA 3 (GRIA3) rs3761555 polymorphisms may influence SSEPs sensitization and habituation in patients with MOH.

DESIGN & METHODS

- We recorded median nerve SSEPs (two blocks of 100 sweeps) in 60 MOH patients. We measured N20-P25 1st block amplitude, as a marker of sensitization, and amplitude changes between two sequential blocks, as a marker of habituation.
- According to their genotype, patients were divided in three groups: "T/T" (N=27), "T/C" (N=26) and "C/C" (N=7).

RESULTS

- Patients carrying T/T polymorphism had larger-amplitude block 1 SSEP than those carrying C/C (z=2.604; p=0.028), with T/C falling in between.
- No between groups differences were observed regarding the degree of delayed habituation.
- In T/T carriers, the habituation slope correlated positively with the duration of the overuse headache; this was not so for T/C and C/C carriers.

DISCUSSION

- In patients with MOH, GRIA3 rs3761555 polymorphisms influence somatosensory sensitization and habituation processes.
- These data suggest a key role of the glutamatergic system in the process of headache chronification.

Results: Clinical characteristics

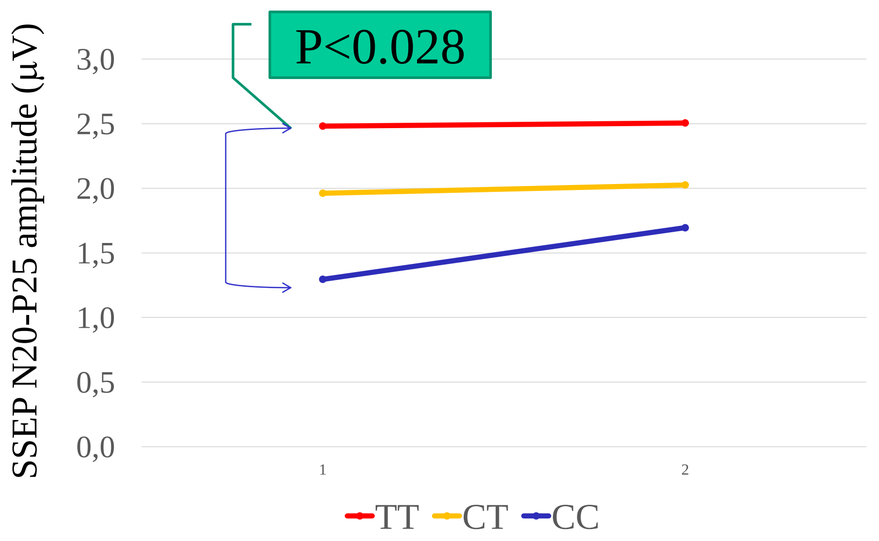
Demographic and clinical data	Whole sample (n=60)	Genotype		
		TT (n = 27)	CT (n = 26)	CC (n = 7)
Age (years)	42.52±12.8	42.37±12.02	41.46±14.09	47±11.37
Headache days/month	25.13±5.62	24.52±6.09	25.23±5.55	27.14±3.93
Years of headache	26.33±13.2	24.52±12.59	27.23±15.21	30±5.45
Months of chronicity	48.58±75.01	31.7±40.74	51.12±88.11	104.29±104.19
Months of drug overuse	39.84±64.28	22.69±17.11	39.81±72.18	103.71±104.77
Monthly drug number	41.44±36.38	39.93±30.83	38.56±41.78	57.57±36.64

Results: Basic SSEP parameters

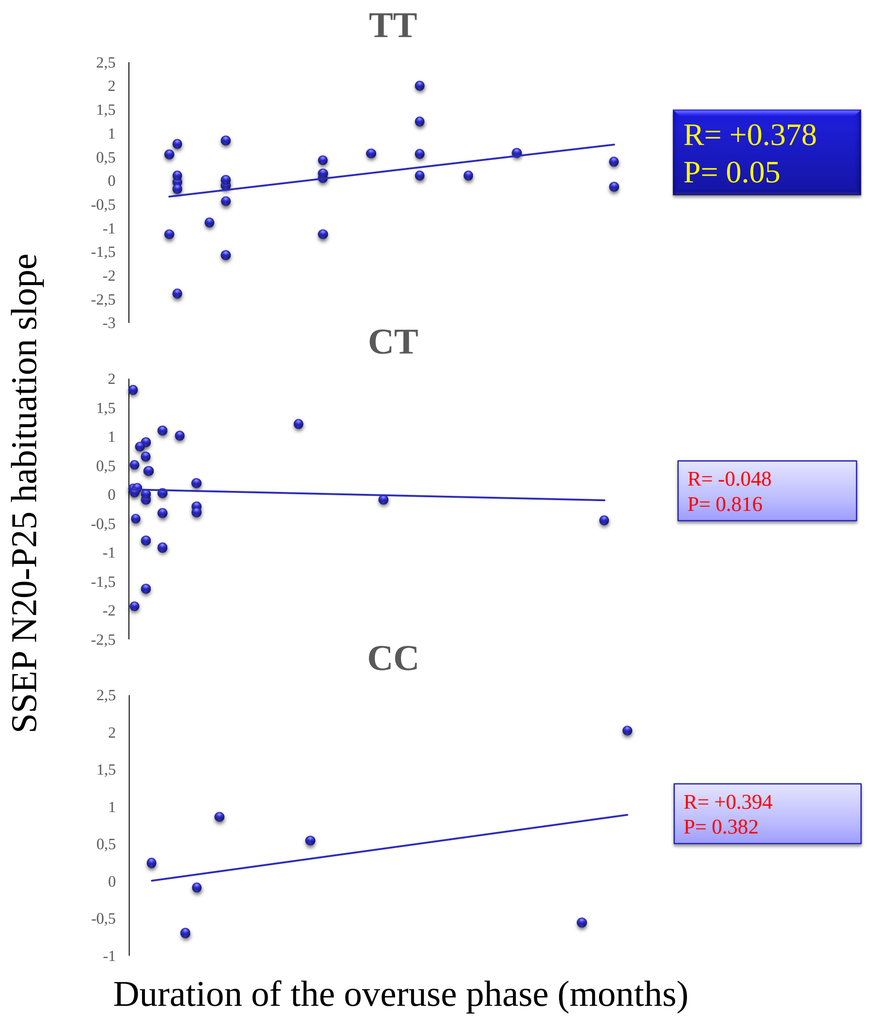
SSEP parameter	Genotype		
	TT (n = 27)	CT (n = 26)	CC (n = 7)
N9 (ms)	2.23 ± 1.26	2.21 ± 1.11	1.31 ± 0.99
N13 (ms)	1.35 ± 0.69	1.44 ± 0.92	1.14 ± 0.45
N20-P25 (μV)	1.97 ± 1.37	1.53 ± 0.77	1.28 ± 0.51
P25-N33 (μV)	1.28 ± 0.98	1.1 ± 0.64	1.35 ± 1.36
N20-P25 1st block (μV)	2.48 ± 1.35	1.96 ± 0.95	1.3 ± 0.43 (*)
N20-P25 2nd block (μV)	2.51 ± 1.32	2.03 ± 1.05	1.7 ± 0.91
N20-P25 slope2	0.02 ± 0.89	0.06 ± 0.84	0.33 ± 0.93

In the comparison of the three genotypes, the grand average of all the neurophysiological data did not emerge in terms of latencies and amplitudes (for each measure F(2, 60), p>0.05).

Results: Sensitization



Results: Correlations



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