Abnormal motor cortex plasticity in juvenile myoclonic epilepsy

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| Background

Abnormal cortical plasticity has been hypothesized to play a crucial role in the pathogenesis of juvenile myoclonic epilepsy (JME). To study the motor cortical plasticity we used paired associative stimulation (PAS). When a repetitive electrical stimulus to the median nerve is paired with a transcranial magnetic stimulus (TMS) pulse over the controlateral motor cortex with an interstimulus interval (ISI) of 21.5–25 ms, a long term potentiation (LTP)-like synaptic plasticity is induced in the corticospinal system. Aim of this study was to investigate the motor cortex LTP-like synaptic plasticity by means of PAS in patients with JME.

| Methods

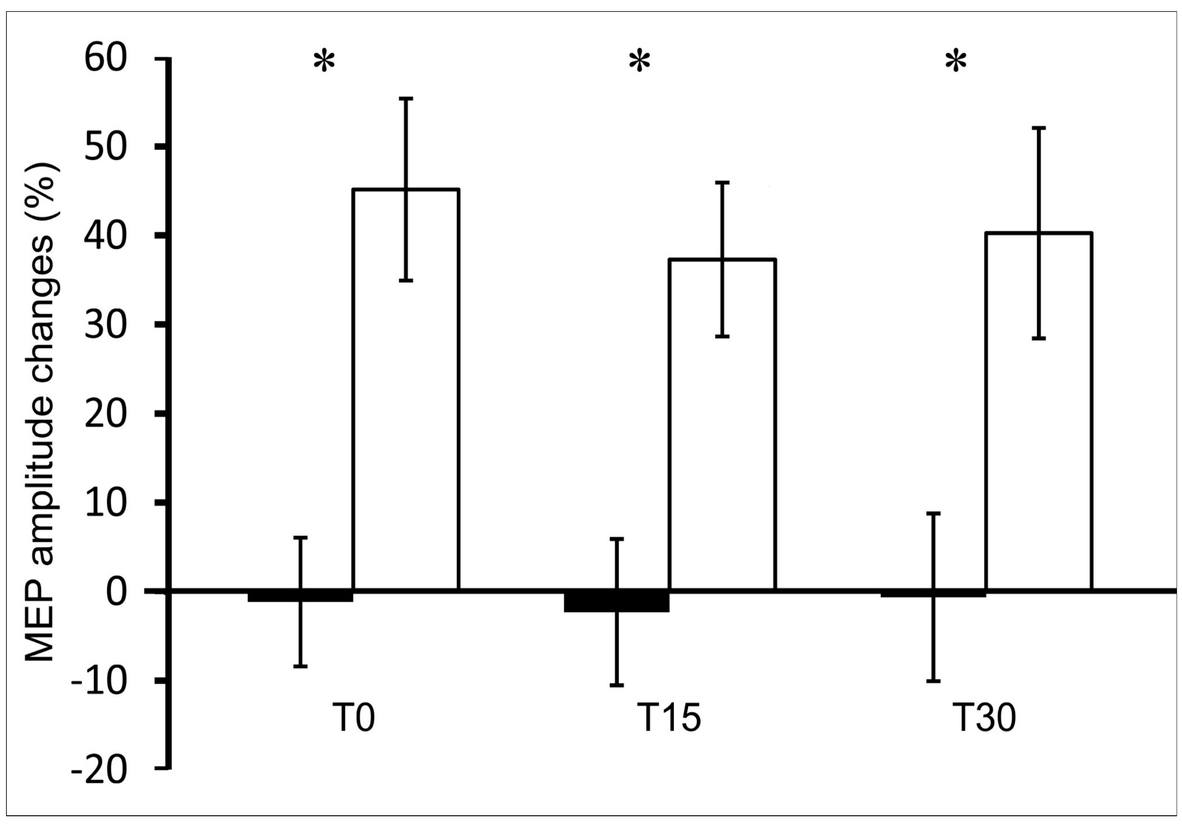
Twelve adult patients with JME were compared with 13 healthy subjects (HS) of similar age and sex. PAS consisted of 180 electrical stimuli of the right median nerve paired with a single TMS over the hotspot of right abductor pollicis brevis (APB) at an ISI of 25 ms (PAS25). We measured motor evoked potentials (MEPs) before and after each intervention for up to 30 min (T0, T15, T30). Data entered repetitive measure ANOVAs for statistical analysis. A p value <0.05 was significant. All data are given as mean ± standard error of the mean (SEM).

	HS	JME	Differences
	13	12	n.s.
Age	27.9 ± 1.5	32.8 ± 3.1	n.s.
Sex (female)	10	10	n.s.
RMT (%)	40.2 ± 1	44.7 ± 2.5	n.s.
PsT (mA)	2.2 ± 0.2	2.6 ± 0.2	n.s.
SI1mV (%)	51.8 ± 2.5	55.3 ± 3.2	n.s.
Baseline MEP (mV)	0.94 ± 0.07	1.08 ± 0.08	n.s.

HS: healthy subjects; JME: juvenile myoclonic epilepsy patients; MEP: motor evoked potential; psT: peripheral sensory threshold; RMT: resting motor threshold; SI1mV: intensity required to elicit a 1mV MEP; n.s.: non-significant.

| Results

In HS the PAS25 protocol was followed by a significant increase of the MEP amplitude (p < 0.001). On the contrary, in patients with JME, the MEP amplitude did not change.



Grand average of normalized MEPs at T0, T15 and T30 to baseline in patients (black) and controls (white). Asterisks indicate a significant difference (p < 0.05).

MAIN FEATURES OF PATIENTS				
Patient	Age	Sex	Treatment (mg/die)	Photosensitivity
1	26	F	400 LTG	Yes
2	48	F	1300 VPA + 1000 LEV	Yes
3	22	F	100 LTG	Yes
4	49	F	800 VPA	No
5	45	F	800 VPA	No
6	25	M	900 VPA	No
7	42	F	1000 VPA + 100 PB	Yes
8	24	F	400 LTG	Yes
9	28	M	300 VPA	Yes
10	26	F	1000 LEV	Yes
11	38	F	115 PB	Yes
12	21	F	800 VPA	No

LEV: levetiracetam; LTG: lamotrigine; PB: phenobarbital; VPA: valproic acid.

| Conclusion

We suggest three possible mechanisms involved in the disruption of the motor cortical plasticity in patients with JME:

•during epileptogenesis, a pathological form of plasticity may occur, leading into an unbalance between excitatory and inhibitory neural circuits in specific networks (i.e. motor cortex). Abnormal cortical plasticity may be the neurophysiological background for the development of myoclonus;

•seizures themselves may lead to structural and functional alterations of neuronal circuits accompanied by declining cognitive and behavioural functions. These manifestations might include an impairment of cortical plasticity;

•the antiepileptic treatment itself may induce long lasting changes in cortical plasticity.

REFERENCE:

Strigaro G, Falletta L, Cerino A, Pizzamiglio C, Tondo G, Varrasi C, Cantello R. Abnormal motor cortex plasticity in juvenile myoclonic epilepsy. *Seizure*. 2015;30:101-5.