

# Effects of levetiracetam in patients with generalized epilepsy on Transcranial Magnetic Stimulation

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## Purpose

- Cortical hyperexcitability is a key feature of epilepsy, and Transcranial Magnetic Stimulation (TMS), combined with electromyography (EMG), is a non-invasive method to study cortical excitability
- Different anti-epileptic drugs (AEDs) affect TMS measures of cortical excitability in healthy volunteers
- We evaluated the effects of levetiracetam on motor cortical excitability in patients with generalized epilepsy, to validate TMS as a valuable translational biomarker for early phase drug development of new AEDs

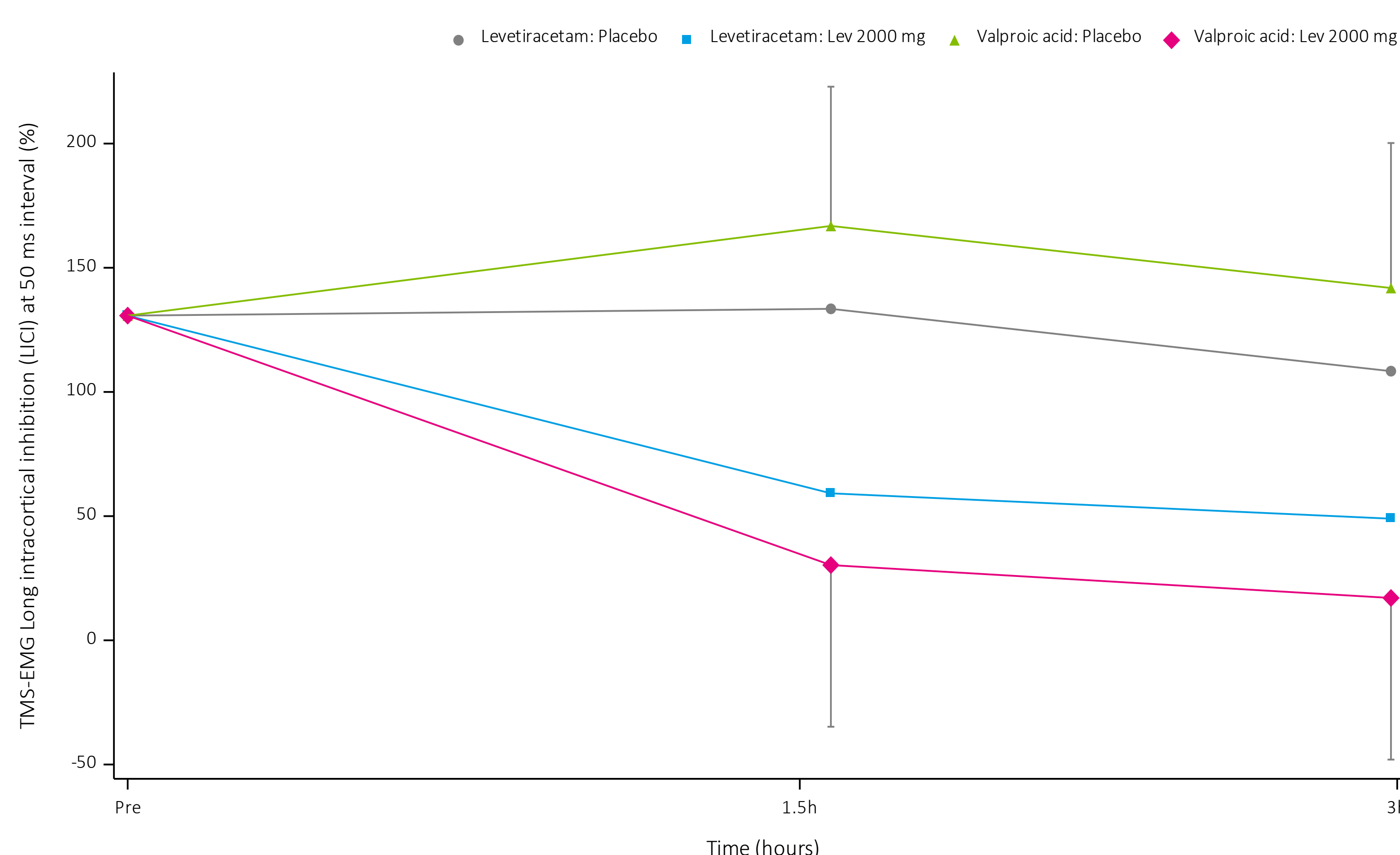


Fig. 2 Estimated means LICI<sub>50</sub> (%)

Placebo: patients on levetiracetam ● and valproic acid ▲

Levetiracetam 2000mg: patients on levetiracetam ■ and valproic acid ◆

## Results

- Levetiracetam significantly reduced single pulse MEP amplitude and paired pulse long intracortical inhibition at interstimulus interval (ISI) 50 msec (LICI<sub>50</sub>) in the combined group, with a greater effect in levetiracetam-naïve patients
- LICI<sub>100</sub> was only reduced in patients on levetiracetam monotherapy
- Resting motor threshold, short intracortical inhibition at ISI 2 msec (SICI<sub>2</sub>) and LICI<sub>300</sub> were not affected

## Conclusions

- Levetiracetam reduced cortical excitability in patients with generalized epilepsy, with a greater effect size in levetiracetam-naïve patients
- This is in line with findings in healthy volunteers, confirming the value of TMS-EMG as a translational biomarker for AED effects in generalized epilepsy patients

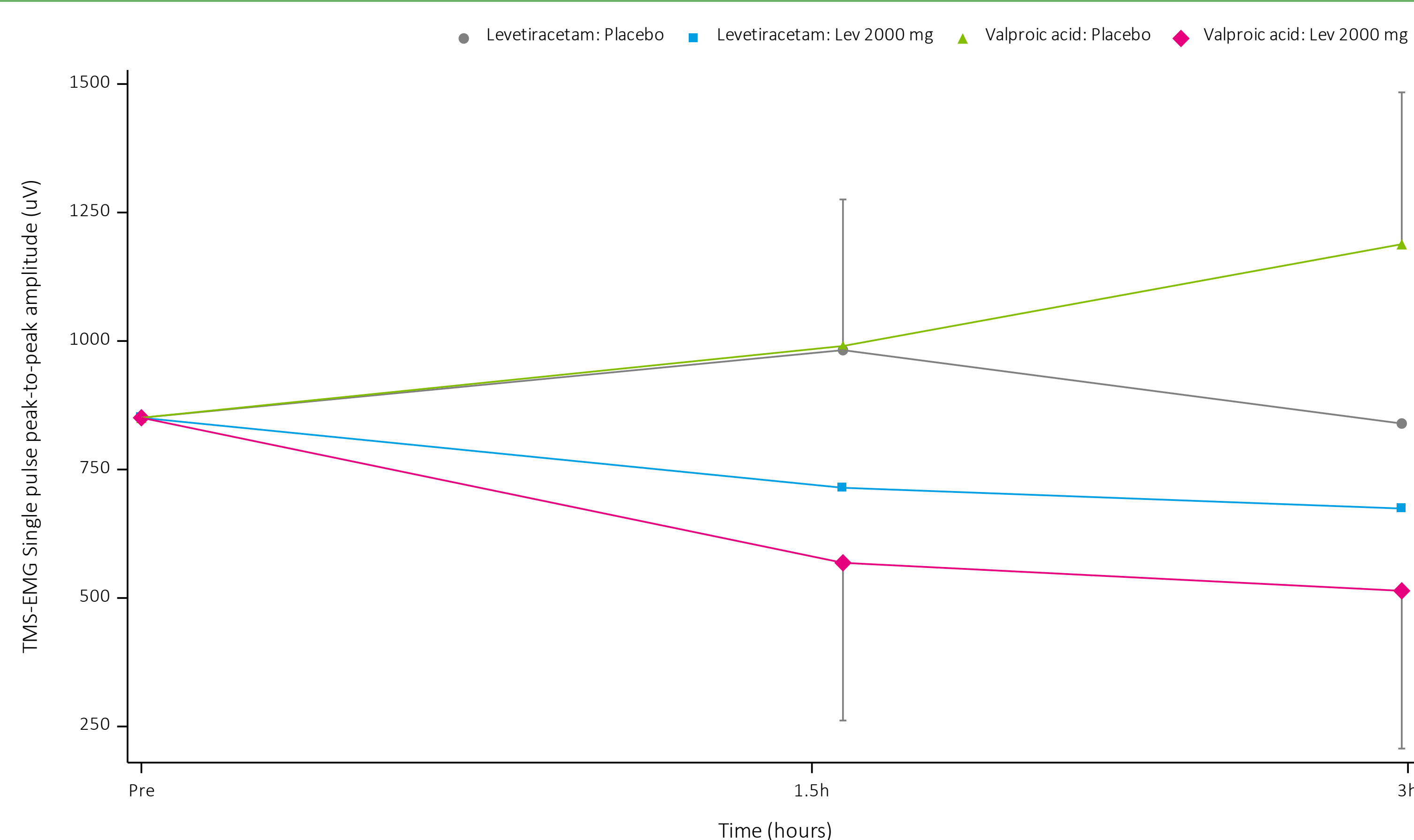


Fig. 1 Estimated means MEP amplitude (µV)

Placebo: patients on levetiracetam ● and valproic acid ▲

Levetiracetam 2000mg: patients on levetiracetam ■ and valproic acid ◆

## Methods

- Randomized, double-blind, placebo-controlled, two-way cross-over study
- Patients with generalized epilepsy on monotherapy: levetiracetam max. 2dd500mg, valproic acid max. 1000mg/day (levetiracetam-naïve)
- Single dose of levetiracetam 2000mg or placebo after refraining from morning AED dose
- Single- and paired-pulse TMS-EMG, measured pre-dose and 1.5 hours and 3 hours post-dose
- A mixed effects model analysis of variance with baseline as covariate was used

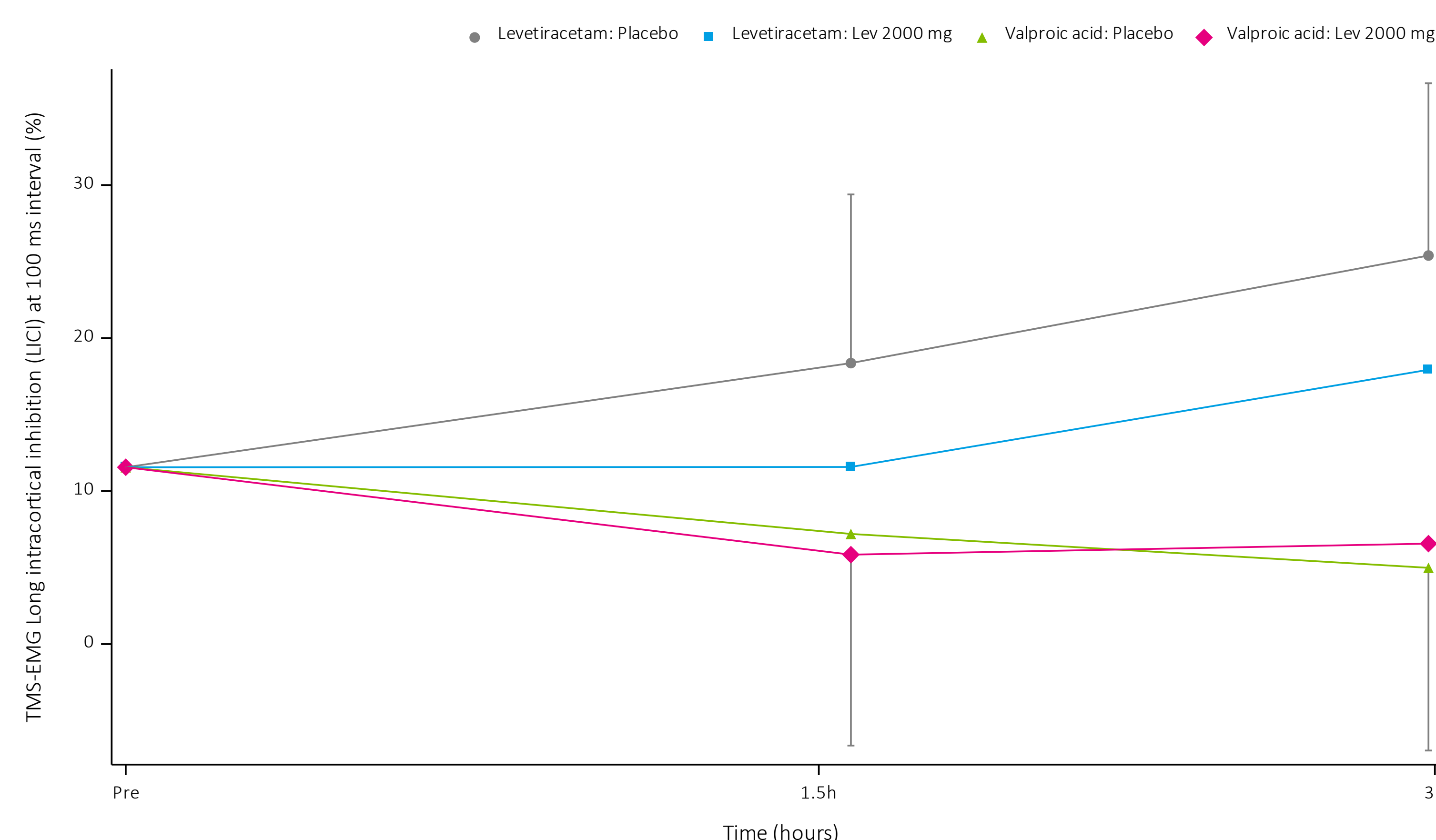


Fig. 3 Estimated means LICI<sub>100</sub> (%)

Placebo: patients on levetiracetam ● and valproic acid ▲

Levetiracetam 2000mg: patients on levetiracetam ■ and valproic acid ◆