600. Real time cortical excitability in children with DRE and ESES and its correlation with treatment response: A TMS based study

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INTRODUCTION

- Enhanced cortical excitability is considered as the pathophysiologic substrate of epilepsies
- The above assumption may not be universally true citing the highly heterogenous nature and varying severity of epilepsy .
- Very few studies have assessed the motor cortex excitability in drug refractory epilepsy and epileptic encephalopathies such as electrical status epilepticus in sleep (ESES) in children
- The literature is variable and conflicting.
- Real time cortical excitability has also been proposed as a biomarker that correlates with treatment response . The same needs exploration in multiple settings across epilepsy severity grades

OBJECTIVES

• To compare the cortical excitability of children with focal drug refractory epilepsy(DRE) and Electrical status epilepticus in sleep(ESES) with typically developing children(TDC) using single pulse transcranial magnetic stimulation(TMS) parameters

•To study the correlation between treatment response and cortical excitability in DRE and ESES.

MATERIALS AND METHODS

• Children (5-14 years) diagnosed with DRE and ESES were enrolled. Standard definition for DRE was used for enrollment. ESES was defined as unexplained neurocognitive regression alongwith sleep potentiated discharges in EEG with spike-wave-index (SWI) > 50%

• TMS parameters: resting motor threshold (RMT) over dorsolateral premotor frontal cortex of dominant hemisphere, and short interval cortical inhibition (SICI) were measured at baseline and 8-12 weeks of therapy.

• Children with DRE received either antiseizure medications (ASM) alone or targeted low frequency (0.5 Hz) high intensity (110% of RMT) repetitive TMS (rTMS)(1200 pulses) for 10 days with figure of 8 coil alongcwith ASMs.

• ESES children uniformly received pulse i.v.methylprednisolone x 5 days followed by 6 weeks (2mg/kg) + 6 weeks tapering prednisolone

•For outcome assessment

- DRE were categorized as good responders(> 80% seizure reduction); partial responders (50-80% seizure reduction) and poor responders (< 50% seizure reduction).

RESULTS

• Forty-nine children with DRE, 20 with ESES and 20 age-matched TDC were enrolled at separate time-points.

• Baseline mean RMT in ESES 86.3 ±6.96; DRE 68.1 ±3.87; and TDC 58.0 ±4.71 were statistical different (p< 0.001).

•Similarly, SICI in ESES 39.20 ± 4.36; DRE 37.2 ± 2.82; TDC 55.45 ±4.78 was statistically different (p < 0.001)

•A high RMT and a low SICI suggest reduced excitability

•Among DRE, percentage seizure reduction at 8-10 weeks correlated with mean reduction in RMT (r = 0.74, p< 0.0001).

•Median RMT in good responders (n =16)(60.0; 58.0, 60.0) nearly reached TDC level.

•In ESES, RMT and SICI improved statistically and reached TDC levels in responders.

•Change in RMT and SICI in ESES correlated with change in SWI (r = 0.74 & -0.70 respectively, p < 0.007).

Figure 1: Comparison of cortical excitability (RMT & SICI) between children with ESES, DRE & TDC

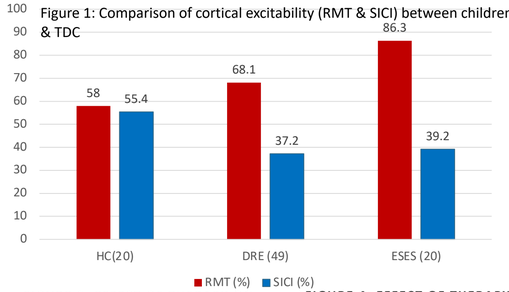


Figure 2: Post therapy reduction in RMT in ESES and DRE

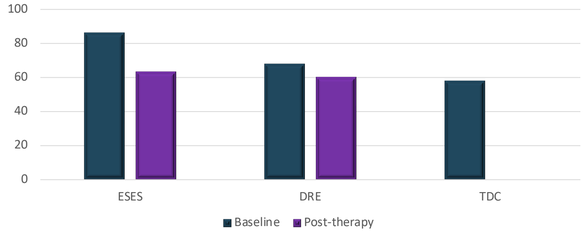


FIGURE 3: EFFECT OF THERAPY ON RMT IN CHILDREN WITH DRUG REFRACTORY EPILEPSY

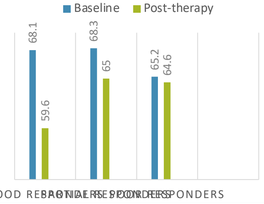


FIGURE 4: EFFECT OF THERAPY ON SICI IN CHILDREN WITH DRUG REFRACTORY EPILEPSY

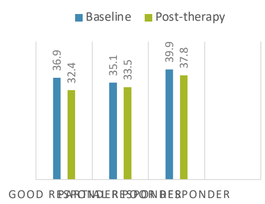


FIGURE 5: EFFECT OF THERAPY ON RMT IN CHILDREN IN ESES

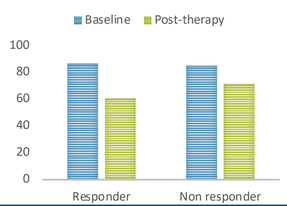
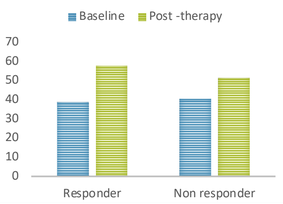


FIGURE 6: EFFECT OF THERAPY ON SICI IN CHILDREN WITH ESES



CONCLUSION

- Motor cortex is inhibited in Drug refractory epilepsy and Electrical status epilepticus in sleep syndrome compared to typically developing children
- Inhibition is graded and is maximal in ESES
- Motor cortex inhibition improves and reaches TDC levels with effective therapy both in DRE and ESES
- Among DRE, percentage seizure reduction at 8-10 weeks correlated with mean reduction in RMT
- In ESES, RMT and SICI correlated with change in SWI post therapy
- Cortical excitability may act as a biomarker of treatment efficacy in DRE and epileptic encephalopathies

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