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Ipsilateral cortical motor desynchronisation is reduced in Benign Epilepsy with Centro-Temporal Spikes

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HIGHLIGHTS

- On a MEG motor task in children with Benign Epilepsy with Centro-Temporal Spikes (BECTS) we found reduced ipsilateral cortical desynchronisation.
- This reduced ipsilateral cortical desynchronisation was linked to poorer motor skills and more recent seizures.
- Our findings suggest disrupted inter-hemispheric interactions during motor control in BECTS.

ABSTRACT

Objective: Magnetoencephalography (MEG) and a simple motor paradigm were used to study induced sensorimotor responses and their relationship to motor skills in children diagnosed with Benign Epilepsy with Centro-Temporal Spikes (BECTS).
Methods: Twenty-one children with BECTS and 15 age-matched controls completed a finger abduction task in MEG; movement-related oscillatory responses were derived and contrasted between groups. A subset of children also completed psycho-behavioural assessments. Regression analyses explored the relationship of MEG responses to manual dexterity performance, and dependence upon clinical characteristics.
Results: In children with BECTS, manual dexterity was below the population mean ($p = .002$) and three showed severe impairment. Our main significant finding was of reduced ipsilateral movement related beta desynchrony (MRBDi) in BECTS relative to the control group ($p = .03$) and predicted by epileptic seizure recency ($p = .02$), but not age, medication status, or duration of epilepsy. Laterality scores across the entire cohort indicated that less lateralised MRBD predicted better manual dexterity ($p = .04$).
Conclusions: Altered movement-related oscillatory responses in ipsilateral motor cortex were associated with motor skill deficits in children with BECTS. These changes were more marked in those with more recent seizures.
Significance: These findings may reflect differences in inter-hemispheric interactions during motor control in BECTS.

1. Introduction

Benign Epilepsy with Centro-Temporal Spikes (BECTS) is a common childhood epilepsy syndrome characterised by focal facial and

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laryngeal sensorimotor seizures, with age of seizure onset between 3–14 years (peak at 8–9 yr) (Panayiotopoulos et al., 2008). The EEG shows characteristic high amplitude centro-temporal interictal spikes (Pataraia et al., 2008), and clinical MR brain imaging is normal to visual inspection. An expanding literature suggests disordered neurodevelopment with varying presentations of language and motor deficits, ranging from what is considered benign, with few clinical or social implications (Camfield and Camfield, 2014), to more severe deficits particularly in language and attention (Kavros et al., 2008; Monjauze et al., 2011; Verrotti et al., 2011; Smith et al., 2012) and motor domains (Scabar et al., 2006; Ayaz et al., 2013). The causes of BECTS remain unknown, it has been considered part of a genetic and syndromic spectrum extending to Landau–Kleffner Syndrome and Epilepsy with Continuous Spike and Wave during Slow Wave Sleep (CSWS), with complex heritability (Rudolf et al., 2009; Lemke et al., 2013).

Neurophysiological studies in BECTS have mostly focused on the spontaneously occurring centro-temporal EEG/MEG spike; its frequency, morphology and dipole localization (Wolff et al., 2005; Pataraia et al., 2008; Perkins et al., 2008). Whilst there appears to be a correlation between incidence of sleep centro-temporal spikes and impaired reading ability (Overvliet et al., 2010; Ebus et al., 2011), the spike frequency on routine EEG, location or morphology do not appear to correlate well with psycho-behavioural measures (Northcott et al., 2005; Riva et al., 2007). Given the hyperexcitable sensorimotor cortex in BECTS (Manganotti et al., 1998; Manganotti and Zanette, 2000), it would be reasonable to hypothesise a localised deficit in inhibitory control, associated with motor deficits. We therefore chose to study neurophysiological induced responses in this area; namely, task-dependent modulations of localised resting beta band oscillations (15–30 Hz), comprising frequency-specific power decreases on movement initiation (movement-related beta desynchronisation; MRBD) and a post-movement beta rebound (PMBR) upon movement cessation (Neuper and Pfurtscheller, 2001; Pfurtscheller et al., 2005; Jurkiewicz et al., 2006; Gaetz et al., 2010). An earlier study investigated these responses in adults with juvenile myoclonic epilepsy, a syndrome in which focal motor seizures also feature, and found a reduction in MRBD relative to non-epileptic controls (Hamandi et al., 2011).

These beta-band responses are likely modulated by GABA activity, with agonism of GABA-A receptors via administration of benzodiazepines (Hall et al., 2011), and increased endogenous GABA levels via blockage of GABA re-uptake (Muthukumaraswamy et al., 2013), both leading to enhanced MRBD. Increased endogenous GABA also reduces PMBR, whereas the movement-related gamma synchronisation (MRGS) that occurs in contralateral primary motor cortex, maximal just after movement electromyographic onset (Crone et al., 1998; Muthukumaraswamy, 2010; Wilson et al., 2010) is unaffected by GABAergic modulation (Hall et al., 2011; Muthukumaraswamy et al., 2013).

Investigation of motor responses in three separate age groups (young children, adolescents and adults) has shown an increase in MRBD and PMBR with age (Gaetz et al., 2010), perhaps reflecting reduced GABAergic motor inhibition in young children, facilitating neural plasticity. The same study found contralateral emphasis of MRBD for adults and adolescents, but not for young children, who demonstrated no significant differences in MRBD between hemispheres contralateral and ipsilateral to the movement (Gaetz et al., 2010). The significance of this altered laterality is as yet unknown, but may reflect increased lateralisation of function as the motor system develops.

Given that BECTS is closely related to childhood development in its age of onset and remission, and with the defining feature of sensorimotor seizures and co-occurrence of psycho-behavioural difficulties, we used MEG and a simple motor paradigm to study induced sensorimotor responses and their relationship to diagnosis and psychological measures. We hypothesised that induced sensorimotor responses in BECTS would differ from controls and that the parameters that differed would correlate with psycho-behavioural deficits.

2. Methods

2.1. Participants

Twenty-one right-handed children (11 males) aged 8 y1 m–14 y11 m (M = 10 y8 m, SD = 1 y9 m) with a diagnosis of BECTS were recruited from paediatric neurology clinics in South Wales. Supplementary material S1 details patients' clinical characteristics. Fifteen typically-developing right-handed children (5 males) aged 8 y5 m–15 y0 m (M = 11 y1 m, SD = 2 y2 m) were recruited as controls (the 'TD' group) via electronic and physical notice boards at Cardiff University and the University of South Wales, and email advertisements sent to Cardiff University staff. The children did not significantly differ in age between groups ($F(1,32) = 0.17$, $p > .6$), between genders ($F(1,32) = .01$, $p > .9$), or as an interaction of group and gender ($F(1,32) = 1.93$, $p > .17$). Parents/guardians of all participants gave written informed consent and children gave written assent to participate in the study. The study was approved by NHS ethics review, and the Cardiff and Vale research and development, committees.

The diagnosis of BECTS was based upon clinical history and EEG features of lateralised focal motor seizures initially affecting orofacial regions and prominent interictal EEG spikes over centro-temporal regions, along with normal neurological examination. All diagnoses were reviewed by a paediatric neurologist (FG, JtWN). There was no history of neurological or psychiatric diagnoses in the TD group and they were screened via parental questionnaires prior to participation to ensure no history of atypical development in domains of movement, language or numeracy.

2.2. MEG recording

MEG recordings were made using a whole-head CTF-Omega 275-channel radial gradiometer system sampled at 1200 Hz (0–300 Hz bandpass). An additional 29 reference channels were recorded for noise cancellation purposes and the primary sensors were analysed as synthetic third-order gradiometers (Vrba and Robinson, 2001). Three channels were turned off due to excessive sensor noise. Participants were fitted with three electromagnetic head coils (nasion and pre-auriculars), which were localised relative to the MEG system immediately before and after the recording session. Simultaneous EMG recordings were made from participants' first dorsal interosseus (FDI) and digitised with the MEG data. Participants' index fingers were lightly taped to a small piece of plastic attached to an optical displacement system. This device gave a one-dimensional measure of displacement (in the direction of FDI abduction) that was continuously sampled together with the MEG data (see (Muthukumaraswamy et al., 2013) for details).

2.3. MRI acquisition

3D fast spoiled gradient-recalled (FSPGR) scans (inversion time = 450 ms; flip angle = 20; TR/TE = 7.9/3.0 ms) were used for MEG co-registration and acquired on a 3-T General Electric HDx scanner with an eight channel receive-only head RF coil (Medical Devices). For the majority of participants, 1 mm isotropic voxel resolution and field of view and matrix size of 256 × 256 × 192 were used, however, field of view and voxel resolution were reduced in order to shorten acquisition times for two participants who had