Motor-related transient bursts in schizophrenia

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Overview

- The acute symptoms of schizophrenia include hallucinations and delusions which can be well-controlled by medication in most cases. In the established phase, persisting core symptoms and disabilities, including poor cognitive, social and occupational function, are more prominent than delusions and hallucinations
- We have previously shown that the extent of suppression of a well-established cortical response, the post-movement beta rebound (PMBR), is significantly correlated with the severity of persisting symptoms and deficits [1]
- Recent work [2] suggests that trial-averaged beta responses are actually comprised of transient 'bursts' on a trial-by-trial basis, offering additional information on beta-related signalling
- The current study [3] sought to investigate possible changes in beta oscillatory behaviour in early-phase and established phases of schizophrenia during a visuo-motor task

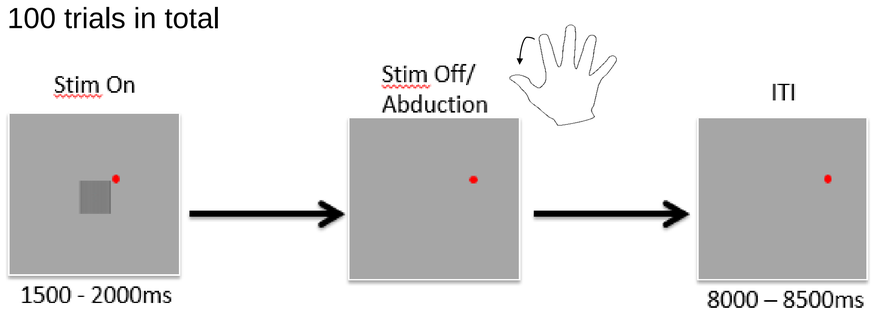
Methods

SPRING study background

- Large multi-site study looking at changes in recent-onset and established schizophrenia
- Measures include ^{13}C MRS at 3T and 7T, PET, MEG, structural MRI, cognitive and clinical scores
- MEG tasks: Visuomotor task,10 minutes eyes open resting state, Sternberg

Visuo-motor task

- Single right index finger abduction when visual grating disappears, subject looks at red dot throughout, 100 trials in total



Participants (Nottingham and Cardiff):

- 29 early-phase patients (<5 years diagnosis, <3 months medication treatment; mean age 24(std dev 5.6), 6F)
- 35 established patients (>10 years diagnosis; mean age 40 (std dev 7.2), 9F)
- 42 healthy controls (10 matched with each patient group; mean age 32 (std dev 9.9), 12F)

Acquisition:

- 275 channel CTF Omega MEG system, 3rd order gradiometers, sample rate 1200 Hz, continuous head localisation, recorded upright

Analysis:

- Fieldtrip [4] LCMV beamformer data covariance derived for -1.5-8 s around grating offset across 5 mm MNI warped volumetric grid for 13-30 Hz frequency using singleshell forward model
- Source power estimates obtained for movement-related beta decrease (MRBD; 0.2-1.2 s) and PMBR (2-3 s) compared with baseline (7-8 s), giving peak co-ordinates of percentage change from baseline
- Time-frequency using multitaper in the frequency domain and virtual electrode data computed from peak locations
- Virtual electrode data filtered 1-48 Hz and Hidden Markov Model (HMM) applied, based on 3 hidden states, to find high amplitude transient beta events. The state output most correlated with beta envelope was selected as chosen 'burst state'

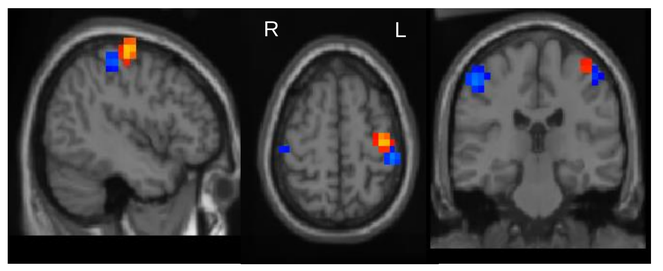
Conclusions

- Established patient group shows a significantly suppressed PMBR compared to the matched healthy controls. PMBR likely reflects long-range connectivity and inhibition.
- Degree of PMBR suppression correlates with clinical disorganization score in established cases, supporting a link between impaired long-range connectivity and persisting disability
- Results support our previous work in established patients [1], and extend this to show abnormal patterns of transient burst characteristics, indicating greater abnormality in established than recent-onset cases
- Analysis of different illness phases extends understanding of likely role of processes of PMBR impairment in pathophysiology of schizophrenia

REFERENCES [1] Robson et al. (2017) Abnormal visuomotor processing in schizophrenia. NeuroImage: Clinical. 12, pp.869-78 **[2]** Shin et al. (2017) The rate of transient beta frequency events predicts behaviour across tasks and species. eLife 6:e29086 **[3]** Gascoyne et al. (2021) Motor-related oscillatory activity in schizophrenia according to phase of illness and clinical symptom severity. NeuroImage: Clinical. 29: 102524 **[4]** Oostenveld et al. (2011) FieldTrip: Open Source Software for Advanced Analysis of MEG, EEG, and Invasive Electrophysiological Data. Computational Intelligence and Neuroscience, Volume 2011, Article ID 156869

Results

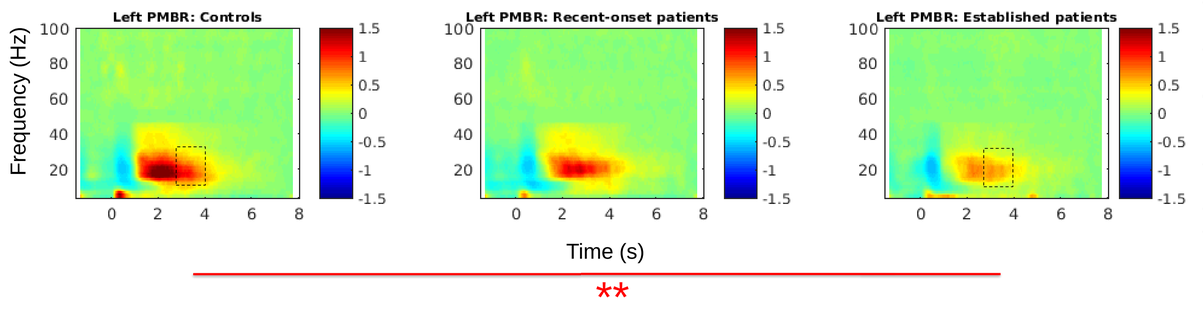
1 Peak locations of MRBD (blue) and PMBR (yellow / red) for all subjects



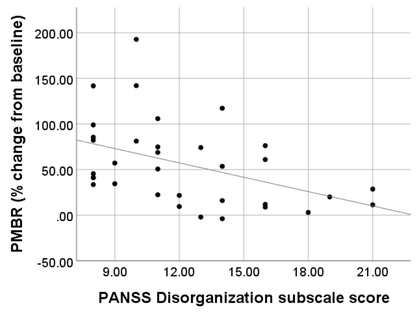
Peak LCMV beamformer activation for MRBD (blue) and PMBR (yellow/red) compared to baseline. MRBD is bilateral, and PMBR occurs in contralateral sensorimotor region

Activations are shown in radiological view (right on left, left on right)

2 Time-frequency representations for each group at PMBR peak location

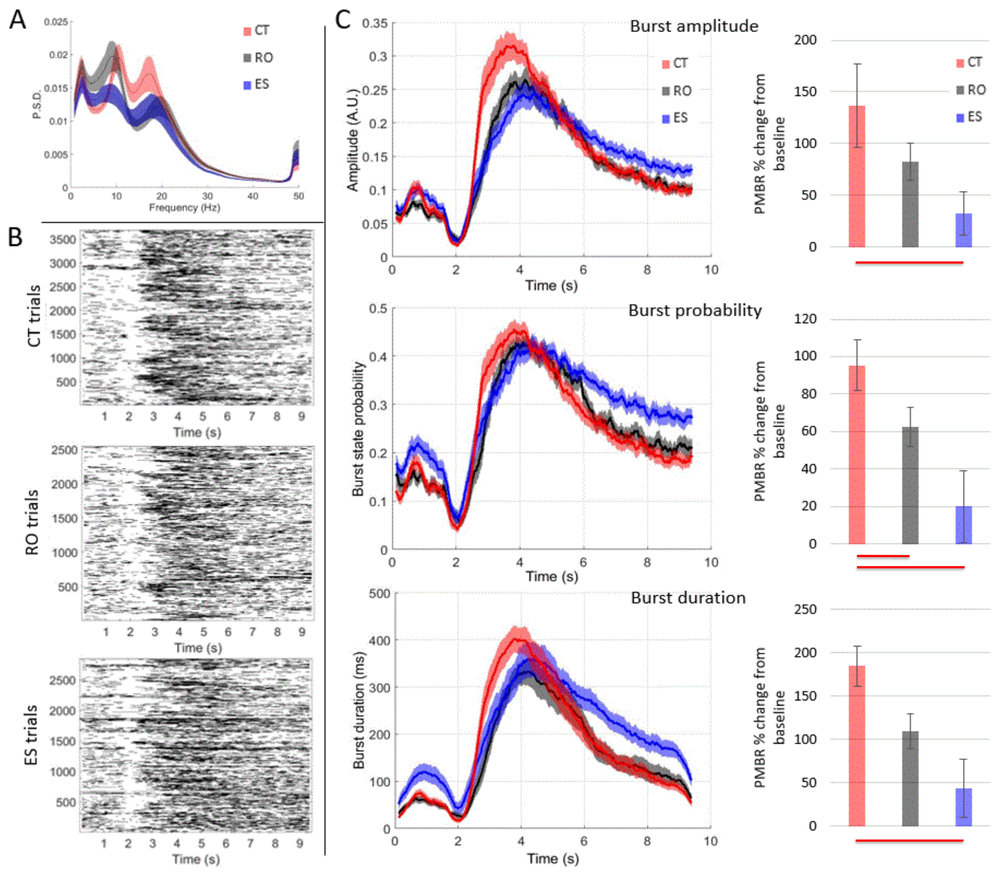


Post-movement beta rebound is significantly reduced in established patients compared to matched controls (t = -4.4(54), p < 0.00)



Extent of PMBR reduction in established patients correlates significantly with PANSS disorganization subscale score
(r(28) = -.42, p = .02)

3 Transient burst events over time at peak PMBR location using HMM



(A) Spectral analysis, (B) Binarised burst raster over trial duration, (C) Time courses of 3 different burst characteristics (amplitude, probability, duration), and change from baseline to PMBR window (bar chart). Burst amplitude, probability and duration increase during PMBR window relative to baseline in all groups. Significant reduction in burst amplitude, duration and probability of bursts for established patients vs controls. Further, we see significant reduction in burst probability for recent-onset patients vs controls, showing patient group differentiation.