Beta-frequency electrophysiological bursts: BOLD correlates and relationships with psychotic illness

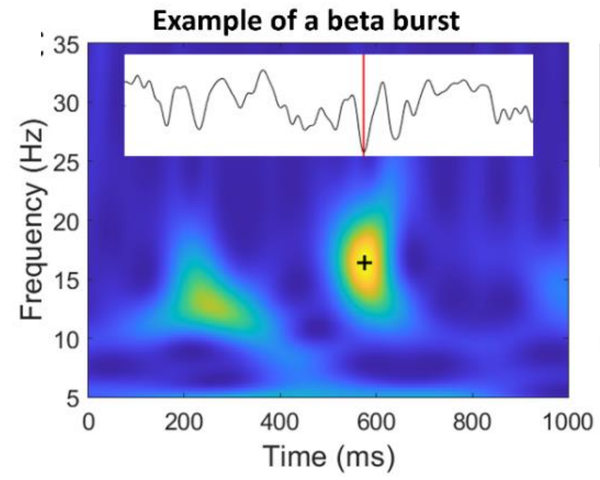
Paul M. Briley[1,2], Elizabeth B. Liddle[1], Molly Simmonite[1], Marije Jansen[1], Thomas P White[1], Vijender Balain[1,3], Lena Palaniyappan[1,4-6], Richard Bowtell[7], Karen J. Mullinger[7,8] & Peter F. Liddle[1]
Email: paul.briley@nottingham.ac.uk

BACKGROUND

- Electrophysiological activity in the beta (13-30 Hz) frequency band is abnormal in psychosis
- In particular, the usual increase in beta-frequency power following a motor response (post-movement beta rebound, "PMBR") is reduced in psychosis
- This reduction in PMBR is correlated with both symptom severity and functional impairment
- Recent evidence indicates that beta oscillations occur as transient bursts (Jones, 2016, PMID: 27400290)
- We used this discovery to identify the BOLD correlates of beta bursts using simultaneous fMRI/EEG
- Spitzer and Haegens (2017, PMID: 28785729) recently proposed that beta bursts are content-specific and support the transition between latent and active neural assemblies encoding that content
- We compared beta-burst rates, as well as the magnitude and extent of BOLD activation associated with beta bursts, between patients with schizophrenia, patients with bipolar disorder, and healthy controls

METHODS

- Data from 78 participants were included in this study: 32 patients with schizophrenia or schizoaffective disorder, 16 patients with bipolar disorder, and 30 healthy control participants
- Participants completed an N-back working memory task at three levels of difficulty: 0-back, 1-back, and 2-back, interspersed with short rest periods
- 31-electrode EEG data were recorded simultaneous with 3T BOLD fMRI
- EEG recordings underwent pre-processing including per-participant artefact correction, then data from all participants were submitted to a group independent component analysis (ICA) to identify a representative source of beta-frequency electrophysiological activity
- This source was used in individual participant datasets to extract time courses of brain activity
- Time-frequency spectrograms were used to identify beta-frequency peaks in these time courses – the timings of beta-frequency peaks were used as event markers in the fMRI analyses
- fMRI design matrices included 0-back, 1-back and 2-back sub-blocks modelled as rectangles convolved with the SPM canonical haemodynamic response function, as well as motor responses and beta-bursts modelled as impulses convolved with the same function

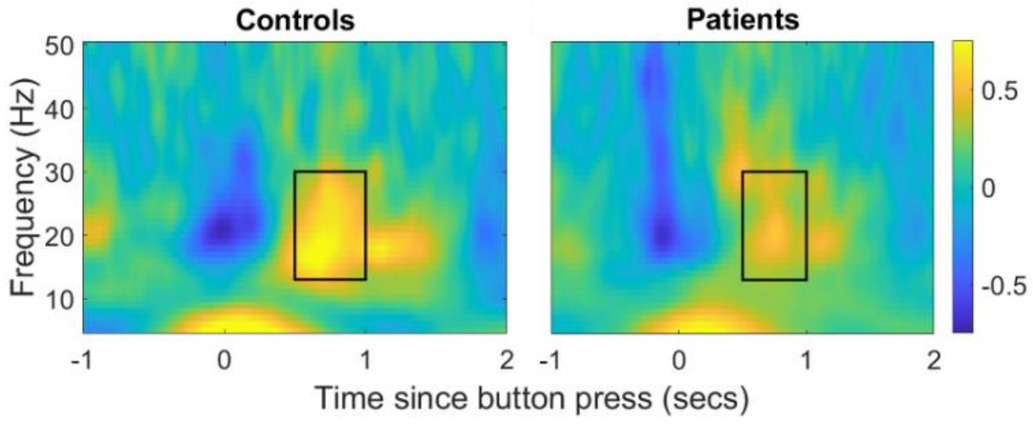


Schematic of N-back task: 0-back: z… y… y… k… n… k… **x**
(targets in each condition are shown in red) 1-back: z… y… **y**… k… n… k… x
2-back: z… y… y… k… n… **k**… x

Above: Schematic of the N-back task

Left: Example of a suprathreshold beta burst identified in a time-frequency spectrogram (marked with a plus sign), with inset showing the corresponding neural activity time course measured with EEG

Below: Time-frequency spectrograms averaged across responses, showing the reduced rebound of beta power following a motor response in patients than controls (black rectangle: post-movement beta rebound, "PMBR", window)

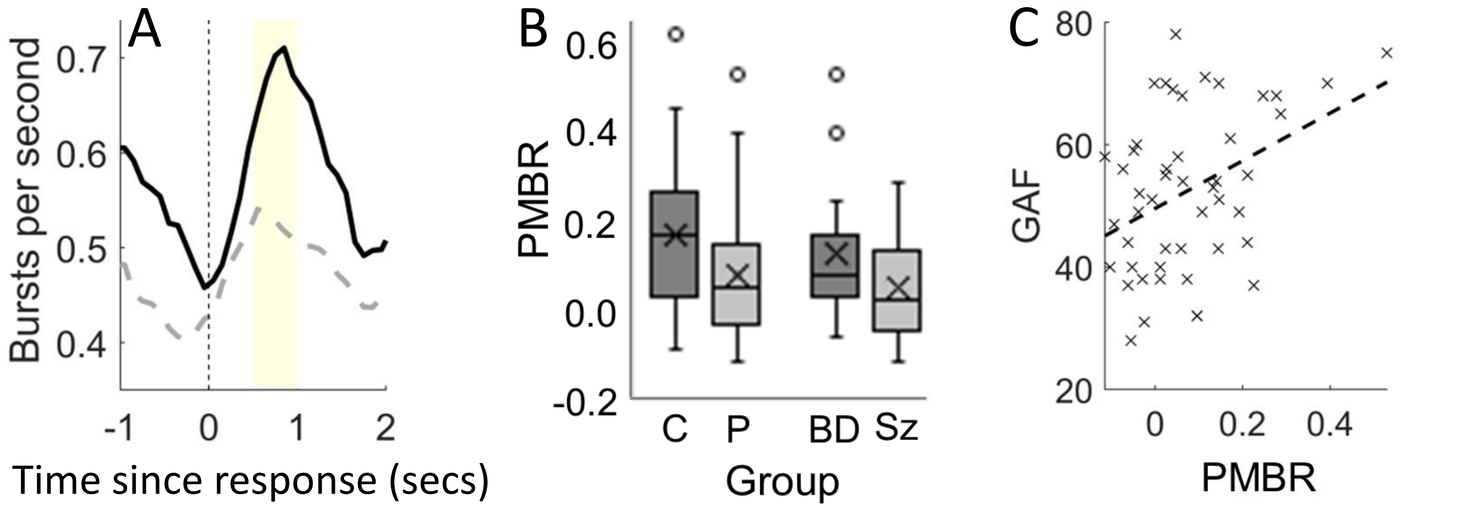


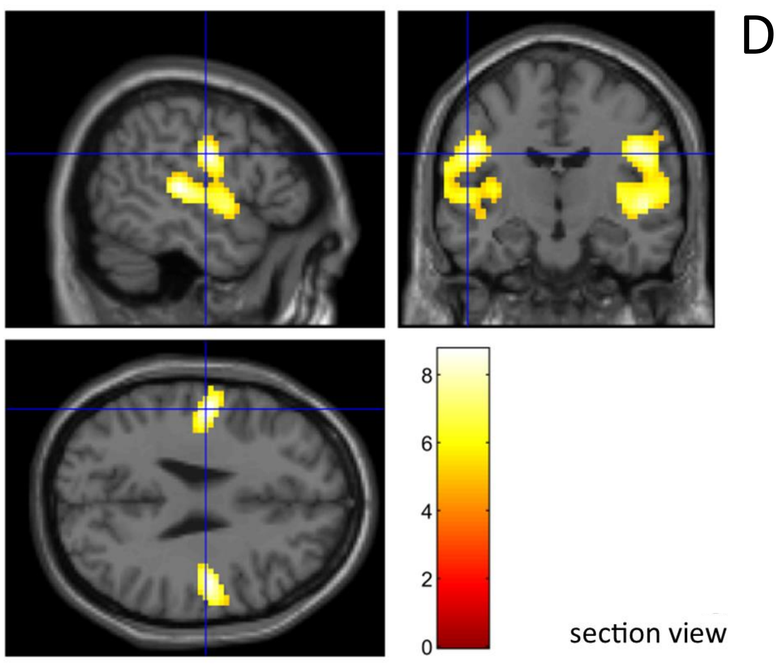
RESULTS

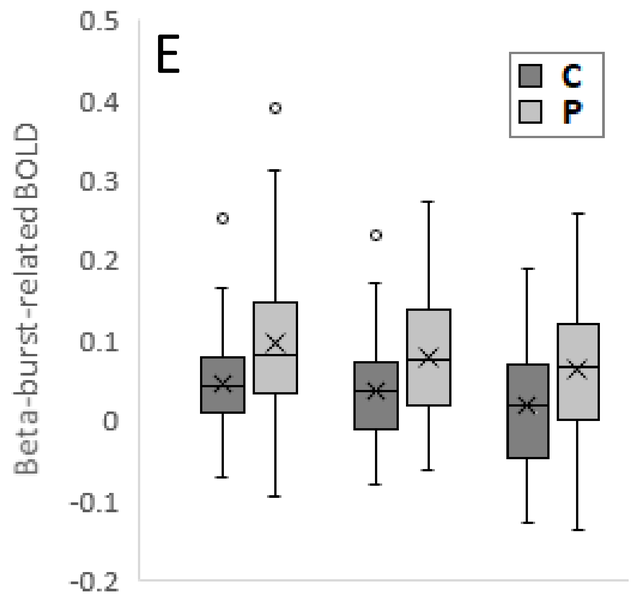
A: Beta burst rate relative to the timing of motor responses, calculated in sliding time windows. PMBR peaked in the window 0.5-1 second post response (yellow shaded area). Solid black line = controls, dashed grey line = patients

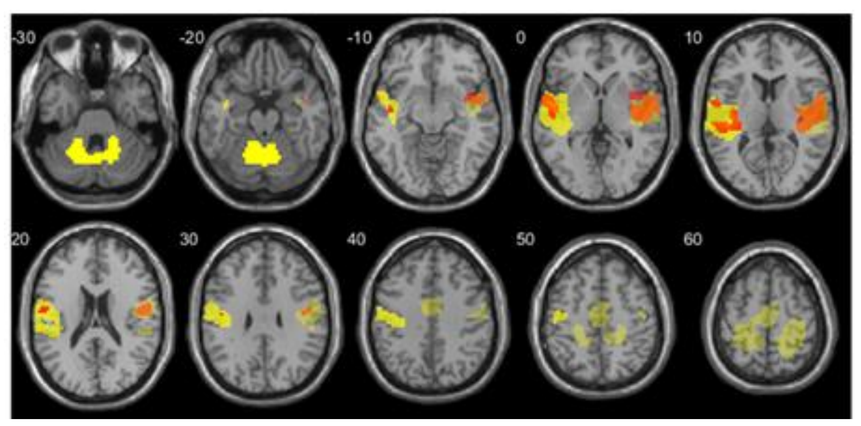
B: PMBR was significantly smaller in patients (P) than controls (C). PMBR did not differ significantly between patients with bipolar disorder (BD) or schizophrenia (Sz)

C: In patients, PMBR was significantly correlated with Global Assessment of Functioning score (GAF). In addition, smaller PMBR was significantly associated with poorer performance on a digit symbol substitution test, and with greater persistence of symptoms of disorganisation (not shown)









D: Areas of increased BOLD activation positively associated with beta bursts. The largest cluster of activation associated with beta bursts in each hemisphere, termed the sensorimotor-verbal (SM-verbal) cluster, included the Rolandic operculum as well as superior temporal gyrus and Heschl's gyrus. These areas are involved in the motor execution of speech and the processing of speech sounds and language, including covert speech

As the N-back task involves remembering the names of previously-seen letters, this is consistent with Spitzer and Haegens' (2017) theory that beta bursts serve to reactivate latent content-specific representations (in this case, the phonological representations of speech and motor representations of required responses)

E: In all clusters of activation, patients ("P") showed greater BOLD activation positively-associated with beta bursts than controls ("C"). Sensorimotor-verbal clusters (SM-verbal); sensorimotor-manual clusters (SM-manual – this included superior pre/post-central gyrus, in the vicinity of the hand area of the motor/somatosensory homunculus) and left cerebellum (Ce). In the above, SM-verbal and SM-manual are collapsed across hemispheres

F: Whole brain analyses revealed more extensive clusters of activation in patients (yellow) than controls (red). Contrasting patients and controls showed two clusters of increased activation in patients – a medial cluster that included regions of the salience network, and a cluster in left sensorimotor cortex

CONCLUSIONS

The BOLD correlates of beta bursts included task-relevant areas involved in the motor and sensory representations of speech sounds and associated responses, consistent with Spitzer & Haegens' theory that beta bursts serve to reactivate content-specific representations held latently in working memory

Despite reduced PMBR measured with EEG, and consistent relationships between reduced PMBR and poorer functioning and increased disorganization, BOLD responses to beta bursts were larger and more extensive in patients. This is consistent with an inefficiency hypothesis of brain activation in psychosis, and suggests that the latent content-specific representations re-activated by beta bursts are less precisely or reliably specified in psychosis, potentially leading to the working memory impairments and loosening of associations characteristic of disorganization

[1]Institute of Mental Health, University of Nottingham; [2]Nottinghamshire Healthcare NHS Foundation Trust; [3]Burnaby Centre for Mental Health & Addiction, Canada; [4]Department of Psychiatry, University of Western Ontario, Canada; [5]Robarts Research Institute, University of Western Ontario, Canada; [6]Lawson Health Research Institute, Canada; [7]Sir Peter Mansfield Imaging Centre, University of Nottingham; [8]School of Psychology, University of Birmingham

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