INVESTIGATING THE CONTRIBUTIONS OF NARROWBAND GAMMA AND BROADBAND GAMMA TO POSITIVE AND NEGATIVE BOLD RESPONSES

METHODS & PLANNED ANALYSIS

I. PARTICIPANTS

12 healthy participants with no history of psychiatric and/or neurological disorders; with normal or corrected-to-normal vision will be recruited through the Research Participation Scheme. Written, informed consent will be obtained from all participants; the study is approved by the Research Ethics Board of University of Birmingham.

II. STIMULI

Stimuli will be generated by running Psychotoolbox (www.psychtoolbox.org) on Windows computer. Images will be projected onto mirror at a distance of 60 cm from the participants. First visual stimulus (a) is a 100% contrast black and white checkerboard (16Hz), half circle with the diameter of 6 degree. Second visual stimulus (b) is a 100% contrast black and white grating with 3 cpd and 6 Hz drift frequency. Lastly, an auditory stimulus (c) will be delivered via in-ear ear phones with 1kHz beeps at 6Hz with 0,1,2 deviants (+/- 50Hz tones) per trial.

III. EXPERIMENTAL DESIGN

MEG: 3 different sensory tasks: (a) checkerboard, (b) grating, (c) auditory target detection task will be assessed by the participants. Two runs of each visual stimuli (a) or (b) with two conditions (right or left visual field stimulation) will be acquired and lasting 16 minutes. (a) and (b) will consist repeated 6 seconds ‘on’ and 6 seconds ‘off’ periods across 40 trials per run with pseudorandomised right or left stimuli presentation. The stimulus will be presented after randomly ordered green or red coloured fixation dot in the middle of the screen (averaging 3 seconds). The participants will have to response via button pressing to green coloured fixation dot to ensure the active cooperation and maintenance of attention. The one auditory run (c) will last 8 minutes with 40 trials. The participants will listen to beeps and decide the heard beeps is played on higher or lower tone, then indicate the

heard differences via button pressing. Minimised head and eye movements will be asked from participants.

fMRI: The participants will have to take part in the same 3 sensory tasks (a, b, c) as for the MEG session. Differences will be presented in the length of the stimulus and the number of trials. Each visual stimulus (a) or (b) will be in the same order and consist two runs across 20 trials per run with repeated 6 seconds 'on' and 15 seconds 'off' periods, therefore each run will last 7 minutes. The participants will assess the same (c) auditory run for 7 minutes with 20 trials.

IV. SIGNAL ACQUISTION

MEG: The data will be acquired continuously with whole-head 306 channel Neuromag TRIUX MEG system (204 planar gradiometers and 102 magnetometers) at sampling rate of 1000Hz. Head localisation coils will be attached to the participant at the nasion and preauricular points as fiducial markers. The data acquisition will start and end with head localisation in the MEG helmet to track the location and movements of the head. To achieve coregistration between the anatomy of participants' brain and MEG sensor geometry, digitised head shape (relative to the head coils location) will be generated with 3D digitiser (Polhemus, USA). Digitised head surface and the head surface from the anatomical MR images will be coregistered.

EYE TRACKER: Eye movements will be recorded during the MEG signal acquisition by EyeLink 1000 (SR Research Ltd., Osgoode, ON, Canada) at the rate of 1000Hz.

The total duration of the data acquisition will be approximately 40 minutes with additional 5 minutes initial set up and 15 minutes coil registration, head-shape and eye tracker calibration.

fMRI: fMRI data will be obtained a 3T Siemen's Prisma MR scanner at Centre Human Brain Health (CHBH). Echo-planar imaging (EPI) data will be acquired from 56 slices by multiband 6 sequence (2.4mm isotropic voxel size, TR=1000ms, TE=38ms, flip angle=55°) with a full head coverage. Additional high resolution T1-weighted anatomical images will be acquired using 1 mm isotropic Magnetization Prepared Rapid Gradient Echo (MPRAGE, TR=2000ms, TE=2ms, TI = 880ms, flip

angle=8°, FOV 256x256) sequence. To reduce the possible fatigue side effect, individual runs will be separated by 1-minute intervals.

The total duration of the data acquisition will be approximately 35 minutes and an additional 15 mins initial set up.

V. DATA ANALYSIS

MEG: Recorded MEG data will be visually inspected for possible interferences (e.g. due to SQUID resets or excessive muscle activity) with FieldTrip (FieldTrip toolbox, www.fieldtriptoolbox.org). We will apply the Noise-pool PCA algorithm which was published by Kupers et al. (Kupers et al., 2018). The algorithm is based on identifying 100 MEG sensors that is not containing stimulus-locked responses and estimating noise components. The algorithm will be trained on the data from checkerboard task to identify sensors with the lowest stimulus-locked signal-to-noise ratio; these channels will be collected as the 'noise-pool'. Same noise-pool with included sensors of auditory region will be applied on the auditory data. MEG recordings of each conditions of each stimulus will be divided into 6 – 6 non-overlapping 1-s epochs as 'data-blocks'. 6 blocks of the 'active' periods (0 to 6-, relative to trigger marker at stimulus onset) and 6 blocks of the 'control' periods (-6 to 0s).

All data-blocks will be filtered to remove signals that will not be used to estimate broadband components.

Principal component analysis will be applied on the filtered noise-pool; principal components will be computed separately for each 1-s epochs (active or control data-blocks) to identify the noise components. The identified noise components will be projected out from all sensors. Then, the denoised data will be bandpass filtered (1-150Hz) and decomposed to four frequency bands of interests (alpha, beta, NBG, BBG). The projected and filtered data will be analysed by using a scalar Linearly Constrained Minimum Variance (LCMV) beamformer to localise contralateral visual cortex response region and provide further noise rejection. We will extract time-courses of active and

control periods of the MEG data (in four frequency bands of interest) to compare the source reconstructed data to the corresponding haemodynamic response.

fMRI: Imaging data will be processed and analysed using FSL v6.0 (FMRIB's Software Library, www.fsl.fmrib.ox.ac.uk/fsl). First steps will include brain extraction using BET and motion correction with MCFLIRT**.** Cardiorespiratory data will be simultaneously recorded using the scanner physiological monitoring. Statistical analysis will be conducted using general linear models. For the first-level analysis, images will be spatially smoothed with Gaussian kernel of FWHM 5mm. Highpass temporal filtering (Gaussian weighted least-squares straight line fitting with sigma = 30s) will be applied. Followed by FILM (FMRIBs Improved Linear Model) time-series statistical analysis with local autocorrelation correction. The EPI data will be linearly registered (with FLIRT) to high resolution anatomical T1-weighted images of each participants (7 DOF). The high-resolution anatomical images will be linearly registered (12 DOF) to standard MNI 152 space. To create regressors of interest, model will include active and control periods for each stimulus with positive and negative contrasts; cardiorespiratory data will be added as nuisance regressors. Each event will be convolved with double-gamma haemodynamic response. The two runs of visual data will be combined with fixed-effects at second-level, then will be modelled with mixed effect (FLAME – Stage 1 only) and outlier deweighting at third-level. Results will be thresholded on the whole-brain level using Gaussian random field theory, with cluster-thresholded $z > 2.3$ and corrected $p < 0.05$.

MEG - fMRI COMPARISONS: The extracted time-courses of active and control periods from the MEG data will be compared to created pseudo t-statistical maps of the imaging data to investigate whether the observed gamma event-related-synchronisation (ERS) and alpha/beta event-related-desynchronisation (ERD) to the visual stimulus are reflected in the haemodynamic response as PBR and NBR.

VI. EXPECTED RESULTS

We aim to identify activated and deactivated regions in the visual cortex. We expect to find (in the imaging data) activation in the contralateral hemisphere (right) to the (left) visual field stimulation, while deactivated regions are expected to be in the ipsilateral hemisphere (left). We expect the opposite activation (left) and deactivation (right) pattern to the opposite visual field stimulation (right). We expect the source reconstructed time-courses (from the MEG data) of the activate and control periods will show associations with obtained positive (PBR) and negative (NBR) haemodynamic responses in the visual cortex. Ipsilateral visual cortex deactivation to stimulus is believed to contribute to NBR and represented in decreased alpha and beta activity in the MEG signal. In contrast, the contralateral visual cortex activation (to the stimulus) are assumed to be associated with PBR and expressed in increased gamma oscillation. We expect to observe strong evoked stimulus-locked activations in the auditory cortex (of both hemisphere) to auditory stimulus and deactivations in the nearby regions.

VII. IMPLICATIONS

The study aims to help understanding the contributions of difference frequency bands (mainly gamma band) to the haemodynamic response. Measuring NBR is an excellent opportunity to establish a functional map of the deactivated neuronal system and provide information about the inhibitory feature. Our study will try to establish a clearer characterisation of gamma band respects to NBG and BBG. The denoising algorithm is an excellent alternative to increase the signal-to-noise ratio of non-invasive imaging techniques and to obtain more accurate recording of the neural activity.

REFERENCE

Kupers, E. R., Wang, H. X., Amano, K., Kay, K. N., Heeger, D. J., & Winawer, J. (2018). A non-invasive, quantitative study of broadband spectral responses in human visual cortex. *PloS one*, *13*(3).