**To be emailed to** [**mri.admin@mrc-cbu.cam.ac.uk**](mailto:mri.admin@mrc-cbu.cam.ac.uk)**, and signed version given to:**

**Neuroimaging Facilities Manager, MRC CBSU, 15 Chaucer Road, Cambridge, CB2 7EF**

**SLOTS WILL NOT BE ALLOCATED UNTIL SIGNED DOCUMENTS ARE RECEIVED**

**Part A: Details**

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| **1.** | **Project and PI details:** |  |
| 1.1 | Name of Project: | The Role of DMN in Context Representation during Task Switches |
| 1.2 | Researchers involved: | Ashley Zhou, Daniel Mitchell, John Duncan |
| 1.3 | Primary contact address, telephone number and email: | [Ashley.zhou@mrc-cbu.cam.ac.uk](mailto:Ashley.zhou@mrc-cbu.cam.ac.uk)  +44 7311131662 |
| 1.4 | If any of the researchers involved are not CBSU staff, please give their visitor status: |  |
| 1.5 | List all researchers involved in running the scans: | Ashley Zhou, Daniel Mitchell |
| **2.** | **If an internal (CBSU) project:** |  |
| 2.1 | At what stage are previous projects led by the PI of this project (if none, write “N/A”)? | N/A |
| 2.2 | When was the project presented at a CBSU Research Group Meeting (if not, why not)? | 25/03/22 |
| 2.3 | When was the project presented at the Project presentation meeting (PPM) (if not, why not)? | 04/04/22 |
| 2.4 | If all or partially QQ-funded, give QQ code and % of funding to come from QQ (e.g. 100%) | SUAG/045 G101400 |
| 2.5 | If all or partially grant-funded via CBSU, give CBSU grant code and % of funding to come from grant (e.g. 100%) |  |
| 2.6 | If all or partially funded by external collaborators, give % of funding to come from external collaborators (and complete Section 3) |  |
| 2.7 | If with external collaborators, has a collaboration agreement been signed (if not, why not)? |  |
| **3.** | **If an external project:** |  |
| 3.1 | Who is the Sponsor of the study (all studies must have a sponsor, as defined by the NHS Research Governance Framework)? |  |
| 3.2 | Do you wish to run data analyses on CBSU computers (in which case, you will be invoiced a additional amount), or do you only want access to the raw (DICOM) data? |  |
| 3.3 | What is the MRC CBSU purchase order code for paying for scans? (usually generated by your finance dept) |  |
| 3.4 | If also partially funded by MRC CBSU, please give % of external funding and state where the remaining CBSU component is being paid from |  |
| **4.** | **Ethics/Insurance (both internal and external):** |  |
| 4.1 | Ethics approval received from:  (note: if NHS patients\* involved, must be NRES) | CPREC |
| 4.2 | What is the ethics reference number?  (have you emailed mri.admin your ethics application and approval?) | CPREC2010.16 |
| 4.3 | What is the insurance code for any non-MRC staff involved in scanning |  |
| 4.4 | If this is a clinical trial, give Authorisation Number (CTA) (and any ISRCTN or EudraCT number) |  |
| **5** | **Request Details:** |  |
| 5.1 | How many slots are you requesting? | 40 |
| 5.2 | How many volunteers are you testing? Please give justification for number (e.g., power). | 2 tailed t-test, = 0.05, Power(1-) = 0.8, *d* = 0.5, **N = 34** (calculated by G\*power). We are requesting a few more to allow for exclusions. |
| 5.3 | How many pilots (additional to above) do you want to run (>2 weeks beforehand)? If none then please justify… | 4 |
| 5.4 | Are the volunteers patients**\* or from a special population that inhibits the use of backups**? If so, please detail | No |
| 5.5 | What is the total time required in the scanner per slot? (in minutes) | 60-90 |
| 5.6 | What is the total EPI time per slot? | ~50 |
| 5.7 | Do you want the 20 32 64 channel headcoil? | 32 |
| 5.8 | Is this project standard or high priority?  If high please give your reasons | Standard priority |
| 5.9 | When will you be ready to start? | As soon as possible |
| 5.10 | Will you be able to take slots available from last minute cancellations by others? | Yes |
| 5.11 | By when do you want to finish the scanning? | As soon as possible |
| 5.12 | What dates are you unavailable (eg away)? | August 8-19th |
| 5.13 | Are consecutive slots a problem? | NO |
| 5.14 | Can you scan on Saturdays?  Can you scan in the evenings (5:30-8pm)? If not, why? | YES  YES |
| 5.15 | Any non-standard setup/equipment/procedures – e.g. EYE TRACKER (please detail)? | NO |
| 5.16 | Have you submitted a pre-registration report, eg on OSF website or to a journal? If not, why not? | Yes, submitted on OSF: osf.io/e3ntu |

**\***The term patient means 'stable' patients; that is, participants who have a neurological history, but who do not require ongoing medical attention and for whom MRI poses no significant risks over and above those that apply to a normal healthy participant.

**Part B: Procedures, protocols and predictions**

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| **Proposal background and basic procedure:**  **(If you have pre-registered this study, you can just provide a link, eg to OSF page)**  **Link to pre-registration: osf.io/e3ntu** |
| **Hypotheses and Predictions:**  **(If you have pre-registered this study, you can just provide a link, eg to OSF page)**  **Link to pre-registration:**  osf.io/e3ntu   |  | | --- | | **Scanning protocol (please list from** [**http://imaging.mrc-cbu.cam.ac.uk/imaging/ImagingSequences**](http://imaging.mrc-cbu.cam.ac.uk/imaging/ImagingSequences)**). Please detail any non-standard sequences (and ensure you have checked with Radiographers).**  **Also, if using a non-licensed sequence (see above weblink), then please explain why.**   * CBU default imaging sequence (T1 weighted structural, T2 weighted, standard EPI, fieldmap) |   **Suggestions from PPM (if applicable). Please list each question and your response.**   * Tamar asked for elaboration on the controls for the multivariate analysis. Both visual and motor systems will be able to decode contexts/switches, how will you be able to account for these 'low level' contributions? How do you know the MVPA is not just picking up 'leakage'   + A supplementary analysis will use a whole-brain voxel-wise searchlight to pick up on other areas showing classification of context and then we might get a hint at whether there is leakage and where it is coming from.   + Also, the key question is whether there is modulation of episodic/context representations by the task-switch condition. Although we hypothesise to see this in the DMN, it would still be of interest if episodic representations in more domain-specific regions (e.g. PPA for the scene stimuli) were modulated by task switches.   + Finally, we are also considering (see below) an alternative behavioural response to the context switches, which would avoid the motor confound. * Jasmin asked with regard to control conditions, how do we ensure between task switching activity is context processing and not task orientation. Switching between domains can also be detachment of focus, which is shown before for DMN. Is DMN activity task relevant? Is DMN activity really active between task switches?   + We agree that the DMN responses in Crittenden *et al*. (2015) and Smith *et al*. (2018) could reflect detachment of focus from the main task at between-domain task switches. (Although this is unlikely to be “mind-wandering” in a typical sense given the fast-paced design and the objective difficulty of the between-domain switches.) Our primary hypothesis is that between-domain switches are accompanied by a refocussing of attention on the broader episode/context, which will be tested by decoding of the background scene. To test the possibility that attention is also less focused on the foreground task, we would also decode aspects of the foreground stimuli (the side of the word/object, and the side of the frame).   + For the last question, DMN activity for task switches is greater than DMN activity for task repeats, but less than DMN activity for switches to/from rest. (See Smith et al., 2018 for details). * Alex Woolgar asked whether we wanted to account for multiple comparisons in our power analysis. And also why we chose the CBU standard EPI.   + Regarding power analysis, we had sought advice from Peter Watson, who advised that adjusting the power analysis for multiple comparisons was not recommended, and that we should instead power for the smallest interesting difference. (In our case this is the unknown effect size for the primary MVPA analysis, which we set to a medium standardised effect size; this gives a sample size substantially larger than the two studies whose univariate results we hope to replicate.).   + Regarding the choice of EPI sequence, we feel that our scientific questions would benefit from prioritizing sensitivity over temporal or spatial resolution, and so we see little reason to deviate from the recommended default sequence. This is also the sequence that was used in Crittenden *et al.* (2015). However we are open to changing this if a different sequence is now recommended, and we are particularly interested in the multi-echo option. We will discuss this with Marta and Ajay before starting to scan. * Matt Lambon Ralph asked about the definition of context. He sees the coloured frames as also a kind of context, and is concerned that switching hands is also another an extra task. On that note, he wonders if all these rules demand too much of people's memory. He also points out that DMN is very active when one does episodic memory tasks, and that might be a source of generating context. He cites a few of Gina Humphrey's work in DMN and episodic memory retrieval, and wants to discuss further offline.   + We have subsequently had extensive email exchanges with Matt and Gina. We agree that “context” can be tricky to define and that its episodic nature is interesting and important. Indeed the motivation for the experiment was to test whether large task switches cause attentional refocussing on the broad task episode (externally defined). The hypothesis doesn’t depend on the scenes being “contextual” in a strong sense, just that they form temporally stable episodes in contrast to the rapidly changing frame colours.   + Given the interesting questions around (episodic) memory encoding/retrieval, we have now added two modifications to the design. (1) Within each run, half of the scene images associated with each condition will be completely novel and the other half will be repeated (within the run). Decoding of novel vs repeated would give evidence of a memory representation, and we could then test whether neural sensitivity to this memory representation varies across conditions. (2) After the scan, we will add a surprise memory test in which we ask participants to report the run in which the repeated scene images were presented. (This could also be done for the novel images, if not too difficult.). This would be done separately per condition, so a difference would give evidence that condition affects encoding of the scene/episode. Both of these modifications should be completely orthogonal to the original design and hypotheses.   + Although the task has a substantial memory demand, the previous studies (Crittenden *et al*., 2015; Smith *et al*., 2018) show that participants could handle six focal tasks with high accuracy (>95% correct), and we have reduced this set to four focal tasks. We agree that the hand-switch task adds an extra demand. If people struggled to implement this episodic hand-switch it would actually give us an interesting measure of goal neglect, which should be orthogonal to performance on the focal tasks. However we agree that it may unnecessarily complicate the design and interpretation (e.g. introducing the motor confound mentioned in Tamar’s question). We had discussed various alternative designs, and the dilemma of having the context be too task relevant or irrelevant. We are now considering replacing the hand-switch rule with a simple speeded press of a third button whenever the scene/episode changes category. We will make a final decision after behaviourally piloting both alternatives prior to scanning. |

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**PART C: Checklist and Disclaimer**

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| 1. I confirm that the ethics and other appropriate regulatory approvals, insurance and funding detailed above are all valid, and evidence of this has been provided to the CBSU Neuroimaging Facilities Manager: including hard-copies of the ethics approval letter, the certificate of insurance and confirmation of funding (if not CBSU-managed). An electronic version of the full ethics application must be provided promptly if requested. | √ |
| 2. I confirm that all researchers involved in scanning are named on the ethics, have read and understood the ethics, and have appropriate CRB clearance and Occupational Health clearance (as part of their CBSU staff or visitor status). | √ |
| 3. I confirm that all researchers involved in scanning have the appropriate training and expertise, including attending the CBU MRI Safety Course and signing and returning the form at the end of the SOPs to say they have read the SOPs, and will abide by local rules and safety procedures detailed in those SOPs. | √ |
| 4. I confirm that personal information about participants will be protected and will not shared with people either directly or indirectly other than as expected from consent given by participants and by the ethics approval. Anonymised data will also be handled in line with consent obtained and ethics approval, and I am aware of the potential for identification from facial information in some MRI data, and potential health-sensitive nature of MRI data. | √ |
| 5. I acknowledge that ensuring the project is conducted in accordance with the regulatory approvals given is my responsibility. | √ |
| 6. I agree to inform the MRI facilities manager of any safety incident or event that occurs that would affect persons or use of the MRI facilities. | √ |
| 7. I agree to acknowledge the MRC CBSU in any publication arising from this research. | √ |
| 8. I understand that slots cancelled with less than 10 working days notice may incur charges (and therefore it is advised that you cost for potential cancellations within your budget) | √ |
| 9. **If an internal (CBSU-administered) project:**  I understand that all recorded data are MRC/UCAM property; any data leading to publication will be stored at the CBSU Repository and anonymised data may be shared with others, subject to the ethical approval. | √ |

By signing below, you warrant that all information contained in this application is correct and that you will inform mri.admin@mrc-cbu.cam.ac.uk of any changes which may affect any access granted. To the extent permitted by law, MRC disclaims any liability associated with the hosting and conduct of the study.

Signed by Principal Investigator (PI)



This study has been peer-reviewed, signed by

(For internal studies, signatory must be CBU PL/PLT confirming study was stated in QQR programme, or if not, signatory must be an independent CBU PL/PLT; for external studies, signatory is confirming some form of independent peer-review)

(If external) Signed by PI’s Head of Department (pp. Signature NOT acceptable)

Print name (PI): Print name (HoD):

Date: Date:

Checked and Signed by Neuroimaging Facilities Manager: Date: