Trimodal EEG-fMRI-PET Imaging for Depression Research: Preliminary Findings of Simultaneous Acquisition with [18F]SynVesT-1

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Introduction

- Major depressive disorder (MDD) is a common & disabling psychiatric disorder with a high burden of disease[1]
- Despite its prevalence & impact, neurobiological correlates are incompletely understood (likely due to symptom heterogeneity).
- Alterations in synaptic density may contribute to both mood symptoms & cognitive impairment in MDD.[2,3]
- The tracer **[^{18}F]SynVesT-1** enables *in vivo* quantification of synaptic density in the brain using positron emission tomography (PET) imaging.[4]
- Combining electroencephalography (EEG), functional magnetic resonance imaging (fMRI) with PET, i.e., **simultaneous trimodal imaging (EEG+fMRI+PET)**, might provide a more comprehensive characterization of MDD by integrating neural dynamics, brain activation patterns, and synaptic density under identical experimental conditions.

Aims

- Evaluate the feasibility of a simultaneous trimodal EEG-fMRI-PET imaging protocol using the synaptic density tracer [^{18}F]SynVesT-1.
- Establish analytic pipelines for acquisition & integration of molecular, functional & electrophysiological measures relevant to MDD during attentional and working memory processes.

Methods

Participants: 9 individuals with MDD & 6 controls.
Procedure: Simultaneous EEG-fMRI-PET ([^{18}F]SynVesT-1) acquisition with 3T scanner (Siemens Biograph mMR PET-MR) & 32-channel Ag/AgCl EEG cap (Brain Products). Tasks will assess resting activity, attention (**Fig. 1**) & working memory (**Fig. 2**).

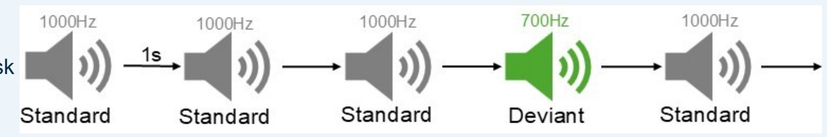


Fig.1. Auditory Oddball Task

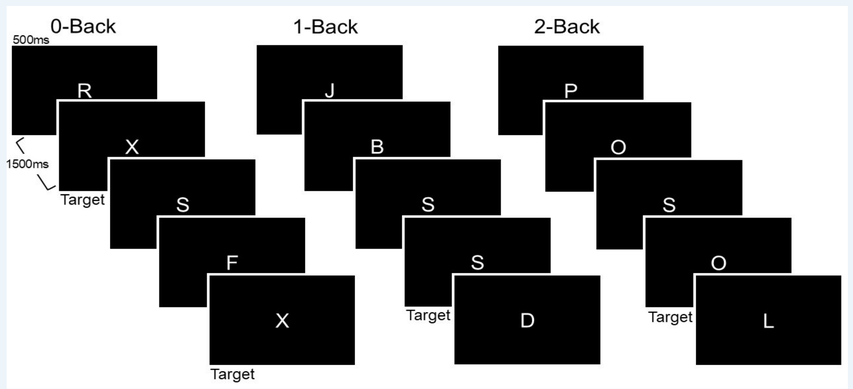


Fig.2. Working Memory N-Back Task

Results

EEG data were processed using BrainVision Analyzer, including magnetic resonance **gradient artifact** correction, **cardioballistic** artifact removal & **filtering** (**Fig. 3**).

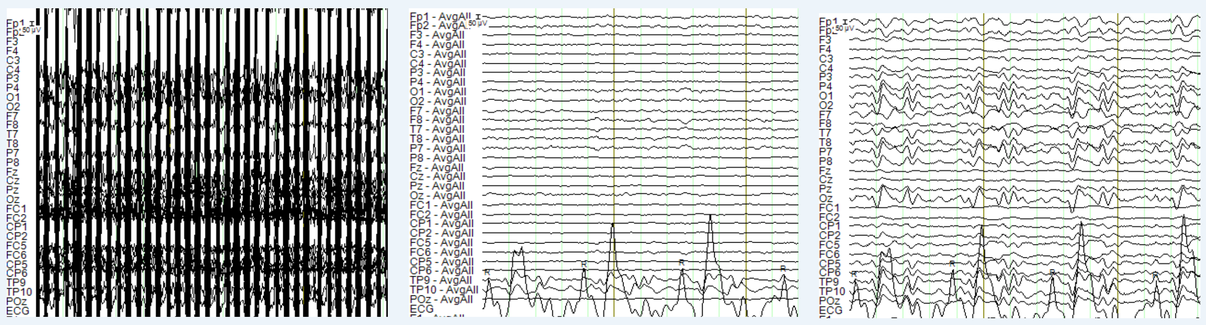


Fig. 3 A. Sample 64-channel EEG data acquired during simultaneous fMRI (EEG+fMRI) collected at Brain Imaging Center (BIC) as part of a past study (2018-2024). **B.** Post clean-up of scanner artifacts. **C.** Post clean-up of EKG artifact & further scrubbing (final dataset).

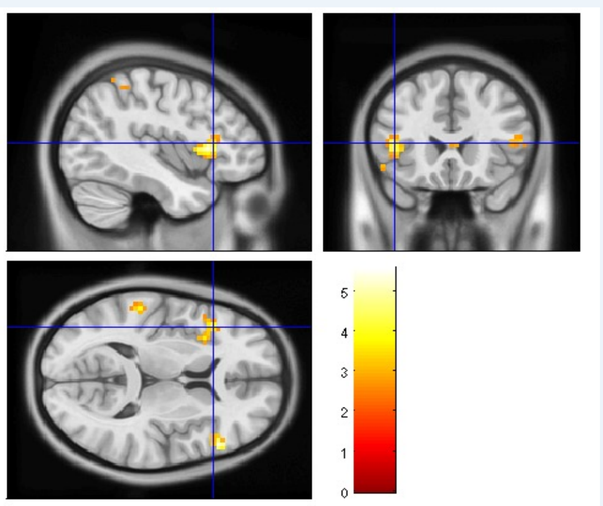


Fig. 7. Auditory oddball fMRI results (Deviant > Standard)

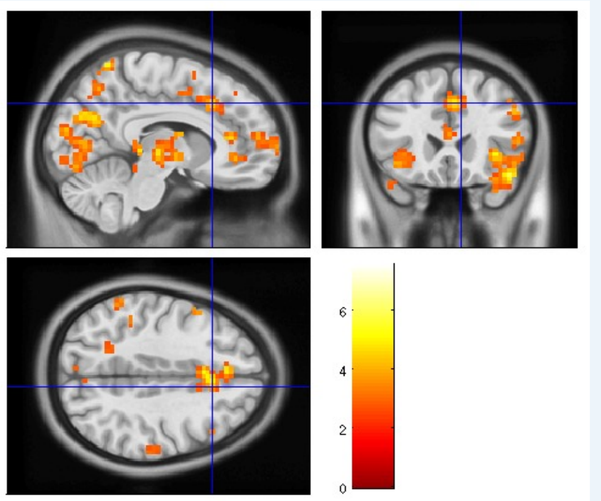


Fig. 8. N-back fMRI results (2-back > 0-back)

EEG: Successful artifact removal pipeline implementation demonstrates recovery of meaningful neural signals during MRI acquisition during the auditory oddball analyses (**Fig. 5**) and during the N-Back analyses (**Fig. 6**)

fMRI: Data were preprocessed & analyzed using standard task-based activation pipelines. Auditory oddball analyses revealed activation within **lateral temporal regions** during target detection (**Fig. 7**); N-back analyses demonstrated increasing **prefrontal cortex activation** with greater working memory load (**Fig. 8**). These were consistent with expected task-related responses.

PET: Data analyzed using the simplified reference tissue model with basis functions (*centrum semiovale* as reference region). Parametric maps of non-displaceable binding potential (BP_{ND}) were generated & values extracted using FreeSurfer-defined cortical/subcortical regions of interest. Regional BP_{ND} estimates showed expected spatial distributions (**Fig. 9**) & moderate correspondence with previous work.

Ongoing analyses:

- EEG modulation of fMRI responses & incorporation of regional [^{18}F]SynVesT-1 measures as regressors of interest, & advanced multimodal integration analyses (e.g., conjunction & multimodal fusion).
- Integration of cognitive, behavioral & clinical measures to inform biomarker discovery.
- Continued development of imaging and data-management pipelines through the Cardio-Neuro-Mind Data Platform.

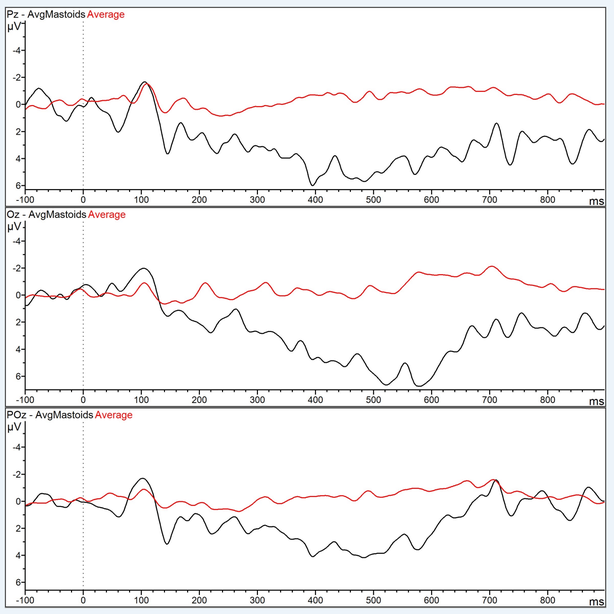


Fig. 5. Auditory oddball EEG (deviant [black]; standard [red])

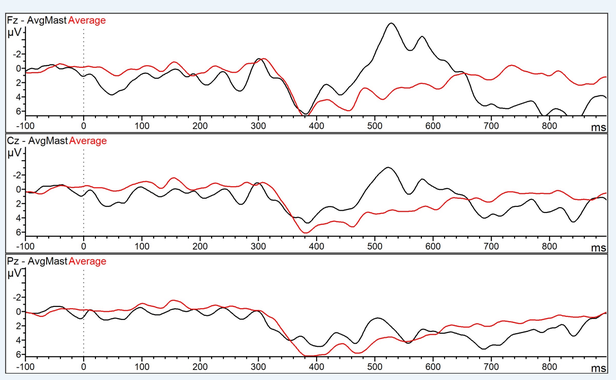


Fig. 6. N-back EEG (target [black]; standard [red])

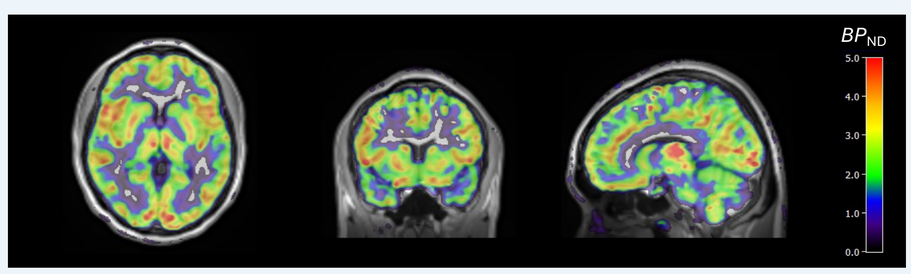


Fig. 9. BP_{ND} parametric images resampled in standard space (MNI152NLin2009c) and overlaid on MR image

Conclusion

- Preliminary test data support the feasibility of the proposed trimodal imaging acquisition, processing, and analysis pipelines, as expected electrophysiological, functional, and molecular signals were successfully identified across modalities, supporting progression to full participant recruitment.
- By integrating complementary temporal, spatial & molecular brain measures, this might facilitate multimodal biomarker discovery & support future precision psychiatry applications in MDD.

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References: **1.** Ferrari AJ, et al. Burden of Depressive Disorders by Country, Sex, Age, and Year: Findings from the Global Burden of Disease Study 2010. PLOS Med 2013;10:e1001547. **2.** Han K-M, et al. A study combining whole-exome sequencing and structural neuroimaging analysis for major depressive disorder. J Affect Disord 2020;262:31–9. https://doi.org/10.1016/j.jad.2019.10.039. **3.** Lyoo IK, et al. Altered prefrontal glutamate-glutamine-gamma-aminobutyric acid levels and relation to low cognitive performance and depressive symptoms in type 1 diabetes mellitus. Arch Gen Psychiatry 2009;66:878–87. https://doi.org/10.1001/archgenpsychiatry.2009.86. **4.** Naganawa M, et al. First-in-Human Evaluation of 18F-SynVesT-1, a Radioligand for PET Imaging of Synaptic Vesicle Glycoprotein 2A. J Nucl Med 2021;62:561–7. https://doi.org/10.2967/jnumed.120.249144.