

MVPA-based fMRI Neurofeedback For Modulating Auditory Verbal Imagery: A Pilot Study In Healthy Volunteers

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Introduction

Auditory verbal hallucinations (AVH) are a critical feature in schizophrenia, affecting 70-80% of patients, and are associated with distress and functional disability (Toh, Moseley and Fernyhough, 2022). Furthermore in 30% of patients, AVH do not respond to anti-psychotic drugs (Dyck *et al.*, 2016), highlighting the need for novel interventions.

Real-time fMRI neurofeedback (rt-fMRI-NFB) has recently emerged as a promising technique that enables voluntary control over neuronal activity and can be used to modify behaviour and reduce symptom severity in psychiatric disorders (Pindi *et al.*, 2022).

In addition, recent advances in machine learning now allow the use of multivoxel pattern analysis (MVPA) to discriminate between brain states with high sensitivity, enabling neurofeedback based on participants' proximity to targeted neural patterns rather than just activity in specific regions or networks. MVPA-based neurofeedback has been successfully applied in healthy samples to train shifts toward or away from defined brain states (Finelli *et al.*, 2026).

Moreover, previous studies have provided preliminary evidence of the use of rt-fMRI-NFB in patients with refractory AVH (Dyck *et al.*, 2016; Orlov *et al.*, 2018; Morfini *et al.*, 2024). However, no previous study has used MVPA-based rt-fMRI-NFB to modulate brain states thought to underpin AVH. In this proof-of-concept study we tested the feasibility of MVPA-based rt-fMRI NFB to train healthy participants to modulate Auditory Verbal Imagery (AVI)-related brain activity, used as a proxy for AVH brain states.

Methods

Twenty healthy participants completed four visits, including two training sessions followed by two rt-fMRI-NFB sessions. During training, participants learned two cognitive strategies to modulate brain states: Subvocalization (SVA) and Meditation (MED). During each rt-fMRI-NFB session (completed in two consecutive days), participants performed both strategies in a counterbalanced order, attempting to volitionally shift their brain activity away from the AVI-state. During each rt-fMRI-NFB session, participants received real-time feedback derived from a support vector machine (SVM) classifier trained to discriminate AVI from non-AVI brain states. Feedback scores reflected the current brain state's distance from the classifier hyperplane.

Learning was assessed by comparing rt-fMRI-NFB scores between early (runs 1–2) and late runs (runs 5–6), reflecting changes in distance from the classifier hyperplane across runs. To evaluate neural modulation, representational similarity analysis (RSA) was used to quantify neural distances between AVI and strategy-specific brain activation patterns, comparing early and late runs. RSA was performed within predefined ROIs associated with each strategy (SVA: inferior frontal gyrus (IFG), superior temporal gyrus (STG), and supplementary motor area (SMA); MED: insula (Ins), middle frontal cortex (MFC), anterior cingulate cortex (ACC), and middle frontal gyrus (MFG)).

Results

rt-fMRI-NFB scores showed no significant change between early and late runs (runs 1–2 vs runs 5–6) for the SVA strategy ($t(19) = -0.26$, $p = 0.79$), while the MED strategy showed higher, but not significant, feedback scores in late compared to early runs ($t(19) = 1.91$, $p = 0.07$).

RSA revealed changes in neural dissimilarity between AVI and strategy-related brain states across training. For the SVA strategy, significant increases in dissimilarity were observed in all ROIs (STG ($t(19) = 2.99$, $p = 0.007$, $d = 0.86$), IFG ($t(19) = 3.03$, $p = 0.006$, $d = 0.76$), and SMA ($t(19) = 2.17$, $p = 0.04$, $d = 0.58$)) indicating greater separation from AVI-related patterns from early to late runs. In contrast, MED-related regions showed no significant changes in dissimilarity across training (MFG ($t(19) = -0.59$, $p = 0.55$, $d = -0.14$), ACC ($t(19) = 0.48$, $p = 0.63$, $d = 0.12$), Ins ($t(19) = -0.32$, $p = 0.75$, $d = -0.08$), and FMC ($t(19) = -0.69$, $p = 0.49$, $d = -0.14$)).

Conclusions

Our findings provide initial support for the use of MVPA-based rt-fMRI-NFB to target AVI-related brain states in healthy participants. While no significant changes in hyperplane distance were observed for the SVA strategy and only a trend towards increased distance was found for MED, RSA revealed increased neural dissimilarity between AVI and SVA-related activation patterns across several ROIs. In contrast, no changes in neural dissimilarity were observed for MED. Together, these findings suggest that SVA and MED may engage distinct neural processes and highlight that different analytical approaches may capture different aspects of neural state modulation.

Although both hyperplane distance and RSA quantify relationships between brain states, they reflect fundamentally different properties of neural representations (Kriegeskorte, 2008). While hyperplane distance measures movement along a classifier-defined dimension, RSA preserves information about the multidimensional representational space (Popal, Wang and Olson, 2019). Furthermore, the SVM classifier was trained at the between-subject level, relying on spatial correspondence of activation patterns across individuals, while RSA assessed within-subject changes in representational structure.

Overall, this proof-of-concept study demonstrates the successful implementation of an MVPA-based rt-fMRI neurofeedback paradigm targeting AVI-related brain states. These insights will inform the design of a forthcoming multi-centre clinical trial in patients with schizophrenia and treatment-resistant AVH, guiding protocol optimisation and supporting the potential use of different cognitive strategies to modulate AVH-related networks.

References

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