Apathy as a Loss of Prior Precision in the Bayesian Brain

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Abstract

Apathy is defined as a reduction in goal-directed behaviour. It is pervasive in dementia and is associated with poor prognosis. Treatments remain elusive. We propose and test a new model of apathy based on Bayesian brain principles. We propose that apathy arises from a reduction in precision of beliefs regarding action outcomes. Here, we test a potential mechanism for prior precision, in the GABAergic gain of superficial pyramidal neurons in the prefrontal cortex.

Fifty healthy adults (aged 50-85) undertook a goal-directed task during magnetoencephalography (MEG, Hezemans et al, 2020). Apathy was assessed using the Apathy-Motivation Index (AMI). Generative modelling was implemented to assess the involvement of three nodes in the prefrontal (PFC), premotor (PMC) and primary motor cortex (M1). See preregistration: https://tinyurl.com/wbt6rpx9.

There was strong evidence confirming the negative correlation between prior precision and apathy (B=12.2, p<0.01). There was very strong evidence that lower prior precision was associated with reduced gain on the superficial pyramidal neurons in the PFC and PMC, but not M1.

These results support the proposed mechanism of apathy, in terms of cognitive process (prior precision) and neural underpinning (frontal cortical gain). This opens novel avenues for the treatment of apathy.

Keywords: Apathy; Bayesian; MEG; Generative models

Introduction

Apathy is defined as a reduction in goal-directed behavior (Robert et al., 2018). It is prevalent in many neurological and psychiatric conditions. In dementia, it predicts caregiver burden (Basu & Mukhopadhyay, 2022), functional decline (Lansdall et al., 2019), and mortality (Murley et al., 2021). There are no approved treatments (Azhar et al., 2022). An improved understanding of the neural mechanisms underpinning apathy is crucial in identifying new therapeutic targets.

In this study, we propose and test a new model of apathy based on the reduction of prior precision in the context of a “Bayesian brain” (Yon & Frith, 2021). Under this model, action is motivated by a perceived discrepancy between prior expectations and sensory observations of reality. Apathy may therefore result from a loss of precision in these prior expectations meaning there is rarely a sufficient discrepancy between expected and observed outcomes to motivate action.

In this study we use psychophysics network modelling to explore the link between apathy and prior precision as well as addressing how prior precision may be represented across the prefrontal-motor decision-making hierarchy.

Methods

Participants. Fifty participants aged 50-85 were recruited from the Cognition & Brain Sciences Healthy Volunteer Panel. Participants had no neurological disease and no history of major psychiatric disorders or seizures. Five participants were removed prior to analysis due to data quality.

Experimental Measures. Participants completed the Apathy Motivation Index (AMI; Ang et al., 2017) and Cambridge Questionnaire for Apathy & Impulsivity (CamQUAIT; Lansdall et al., 2024).
Participants also completed the ‘Goal Priors Assay’ task in MEG. In this task, participants are asked to land a virtual ball on target by pressing on a force pad. On a pseudo-random subset of trials, the ball disappears, and participants estimate the landing position (see FIG 1). Each participant completed 4 blocks (120 trials total, including 40 catch trials).

Analysis. Our primary analyses use Bayesian statistics, interpreted in line with established conventions (Kass & Raftery, 1995).
Prior precision was calculated as the regression slope of estimation error on performance error for each participant (Hezemans et al., 2020).

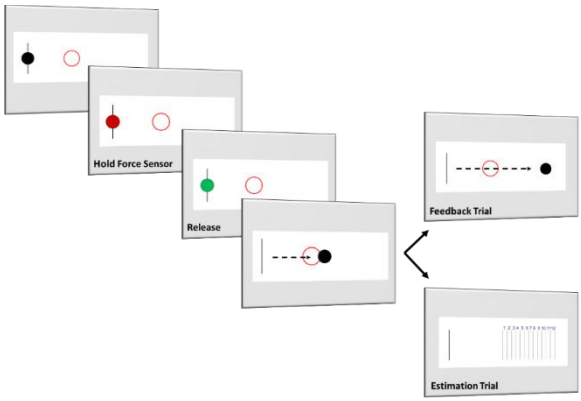

Figure 1: pipeline of the 'Goal Prior Assay' task originated by Hezemans et al (2020)

Generative modelling of MEG data was conducted using dynamic causal modelling of local-field potentials. Nodes were selected as the nearest local peak in activity to preregistered coordinates: right inferior frontal gyrus (pars orbitalis) [56; 26; -12], left premotor cortex [-14; 16; 58], and left motor cortex [-37; -25; 64].

Results

There was strong evidence for a correlation between prior precision and total score on the AMI (r=0.42, B=12.1, p<0.01) as well as moderate evidence for a correlation between prior precision and the motivation subscale of the CamQUAIT (r=0.37, B=4.34, p=0.02; see FIG 2).

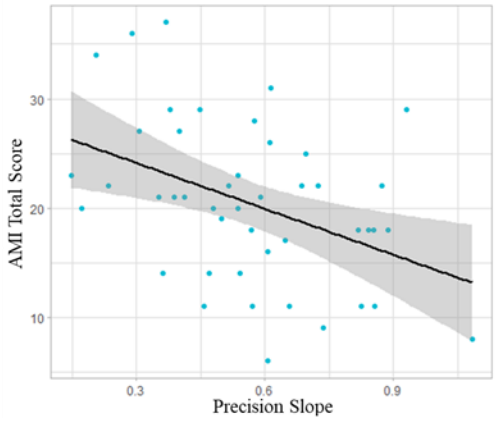

Figure 2: Correlation between AMI total score and prior precision.

Generative modelling of MEG data showed strong evidence that lower levels of prior precision were associated with higher GABA time constants and self-inhibition on superficial pyramidal neurons, particularly in the prefrontal cortex (see FIG 3).

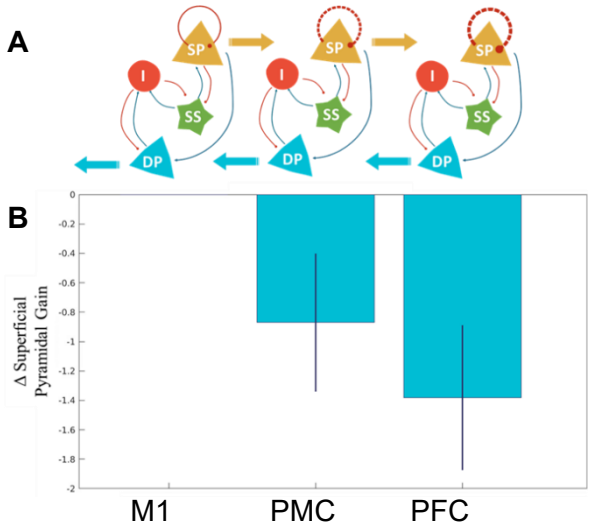

Figure 3: (A) The microcircuit used at each node with the superficial pyramidal gain marked as a dashed red circle. (B) Regions where the superficial pyramidal self-inhibitory connection was modulated by prior precision with a posterior probability >0.99

Discussion

We found strong evidence for an association between prior precision and apathy, in healthy controls. We examined the potential neural correlates for prior precision using generative modelling, confirming the association between prior precision and the gain of the superficial pyramidal neurons, particularly in the prefrontal cortex.

This opens new avenues for interventions in the treatment of apathy. Future studies could generalise these findings to new groups, other tasks that quantify goal priors, and with imaging modalities that are more sensitive to deep brain structures.

Acknowledgements

This study was funded by the Medical Research Council (MC_UU_00030/14; MR/T033371/1), the

NIHR Cambridge Biomedical Research Centre (NIHR 203312); and the Wellcome (220258). The views expressed are those of the authors and not necessarily those of the NIHR or the Department of Health and Social Care.

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