Normalized Amygdala fMRI Response during Emotional Processing as Marker of Recurrence Severity of MDD in the UK Biobank

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INTRODUCTION

- Studies have consistently shown increased amygdala activity measured in BOLD response in Major Depressive Disorder (MDD) during emotional tasks involving facial stimuli, namely the Hariri task[1].
- Such increase was not found by Tamm et al.[2] in the UK Biobank (UKBB), one of the largest population studies to date, collecting the median BOLD response of faces-shapes contrast masked to the amygdala (see Figure 1).
- Tamm's analysis[2] assessed associations with concurrent depressive symptoms, focusing on state rather than trait factors of depression.
- Normative Modeling is an emerging new tool to combat heterogeneity in neuroimaging (see Figure 2).

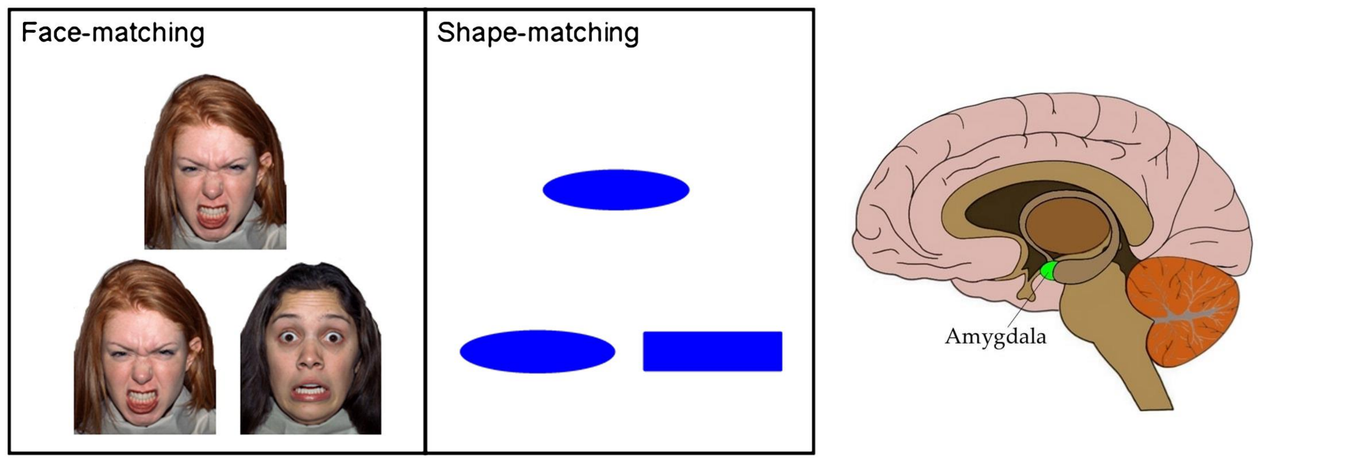

Figure 1 – The left shows examples of the Hariri task, consisting of alternating Face-matching and Shape-matching blocks. The median BOLD response is taken from the contrast between these two and masked to the amygdala (shown on the right).

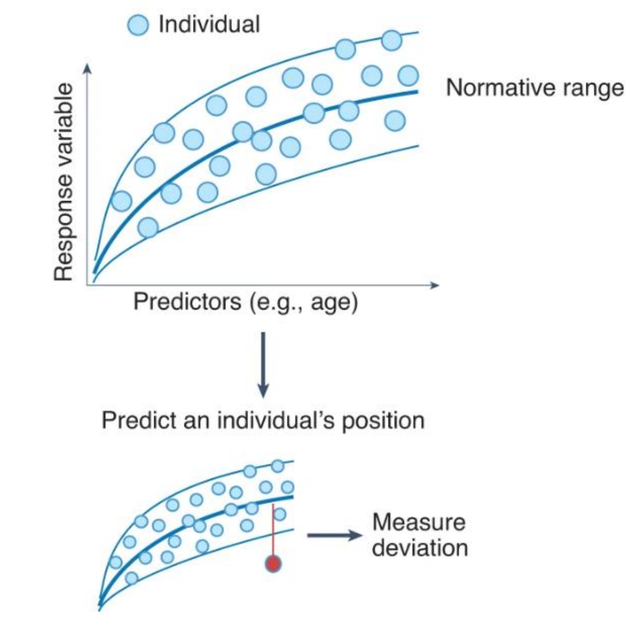

Figure 2 –Normative Modeling for individual prediction.

AIM OF STUDY

- Analyse and distinguish **state** from **trait** associations of MDD in a multilevel analysis of the BOLD response in the Amygdala measured during the Hariri task, to find out whether the BOLD-contrast signal associates with longterm recurrence-severity of MDD or current onset.
- Regress out associated covariates (age and sex) and determine whether the BOLD response in this experiment is a potential biomarker for MDD.

METHODS

- Using **Normative Modeling**, we calculate deviation scores of depressed individuals relative to healthy controls, and regress out unwanted effects induced from age and sex. For determining the normative range, a sample of 6442 healthy individuals is used (separated from testing) to fit a Bayesian Linear Regression model.
- Using questionnaire data, we determine patient history of depressive episodes, categorized by single episode, moderate recurrence (2-5 episodes) and severe recurrence (5+ episodes). To determine remission/ occurence of an episode on day of scanning, the Recent Depressive Symptoms (RDS) is used by summing up the score of four questions closely related to the PHQ-9.

RESULTS

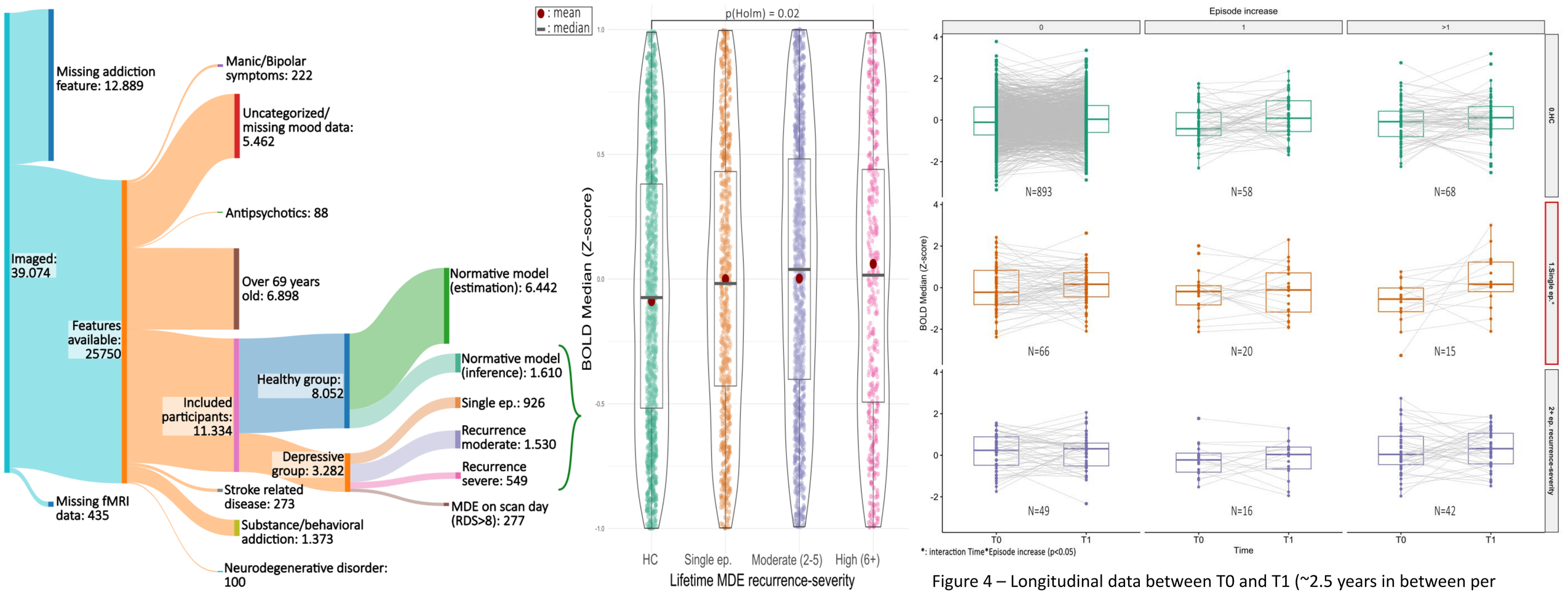

Figure 3 – Inclusion from UKBB, with median BOLD response of healthy, single episode, moderate- and severe recurrent MDD (in remission; RDS<9) participants from left to right respectively. Fisher's test is reported above, with a bar representing the pairwise significance post-hoc test between healthy controls and severe recurrent MDD.

Figure 4 – Longitudinal data between T0 and T1 (~2.5 years in between per participant), divided into recurrence-severity at T0 (rows) and relative increase of episodes at T1 (columns).

DISCUSSION AND CONCLUSION

- Normative Modeling **increased predictive power** of the amygdala BOLD feature as marker for MDD recurrence, without inherently 'training' for it.
- Population studies introduce more heterogeneity both in labels and neurological data; Normative Modeling is a step to overcome this.
- **No effect was found in symptom-severity**, in line with Tamm et al.[2]
- A significant increase in the BOLD signal was found within **severe recurrence** of MDD (5+ episodes), as well as in longitudinal analysis in the **advancement of single episode to further recurrence** of MDD episodes.

A significant effect in the recurrence-severity stages was found ($p=0.02$, $\eta^2=0.002$), with post-hoc analysis indicating a significant differencte between healthy controls and **severe recurrence** (Holm-adjusted $p=0.02$) (Fig. 3). A significant interaction time * episode increase ($p=0.02$, $\eta^2=0.03$) within the **single episode** group was found, highlighted in red (Fig. 4).

References: [1] Li X, Wang J. DOI: 10.1007/s11682-020-00299-2
[2] Tamm, Sandra, et al. DOI: 10.1176/appi.ajp.21050466