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Investigating structural brain change with heart failure using voxel-based morphometry

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Introduction

- While heart failure clearly shows clinical symptoms, such as fatigue, nausea and dizziness, the consequences to brain structure are not well understood.
- Few studies show regional gray matter (GM) decrease related to heart failure [1,2,3].
- Recent work showed both hippocampal GM loss [4] and blood flow abnormality [5] suggesting a link between brain damage and decreased blood flow due to a decreased heart pumping efficiency.
- We studied the potential correlation between gray matter density (GMD) and heart failure markers using voxel-based morphometry (VBM).

Methods

- All 50 heart failure patients (12 female, mean age=53.9y, std=5.4y) received a coronary stent during a percutaneous coronary intervention.
- Markers for heart failure: Ejection fraction (EF, mean=56.4%, std=11.8%) and N-terminal pro-hormone of brain natriuretic peptide (NT-proBNP, mean=220.6pg/mL, std=306.0pg/mL).
- Structural T1-weighted MP-RAGE brain images were acquired on a 3T Verio scanner (Siemens, Erlangen) with a 32-channel head coil using 176 sagittal slices, a field of view of 240×256mm^2, and a nominal resolution of 1×1×1mm^3.
- Imaging parameters according to the ADNI protocol: TR=2300ms, TE=3ms, TI=900ms.
- VBM was performed using gray matter density (GMD) images computed with the Computational Anatomy Toolbox (CAT) in combination with SPM12 and Matlab8.6.
- Statistical analysis was performed with a voxel threshold of $p<0.005$ using the general linear model to test for potential correlations between GMD and both markers of heart failure (EF, NT-proBNP) including age and total intracranial volumes as covariates.
- To correct for multiple comparisons, significant clusters were obtained using a family-wise error corrected cluster threshold of $p<0.05$ ($k>1000$ voxels).

Figures

1

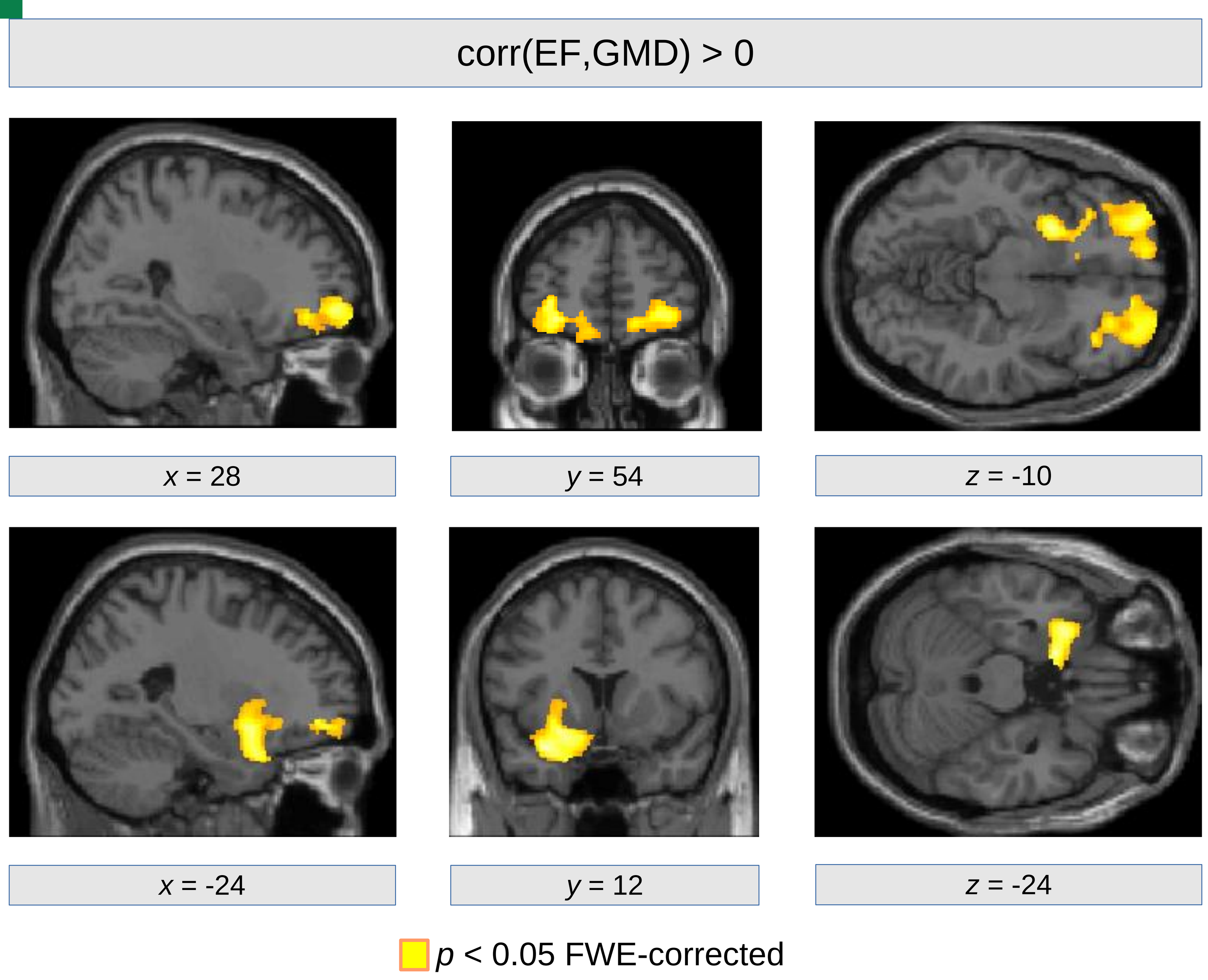

Figure 1. Orthogonal brain sections showing a significant positive correlation between ejection fraction (EF) and gray matter density (GMD) in a group of 50 heart failure patients. A decreased EF was related to a diminished GMD in orbitofrontal brain regions and left ventral striatum. Clusters are shown with family-wise error corrected $p<0.05$.

2

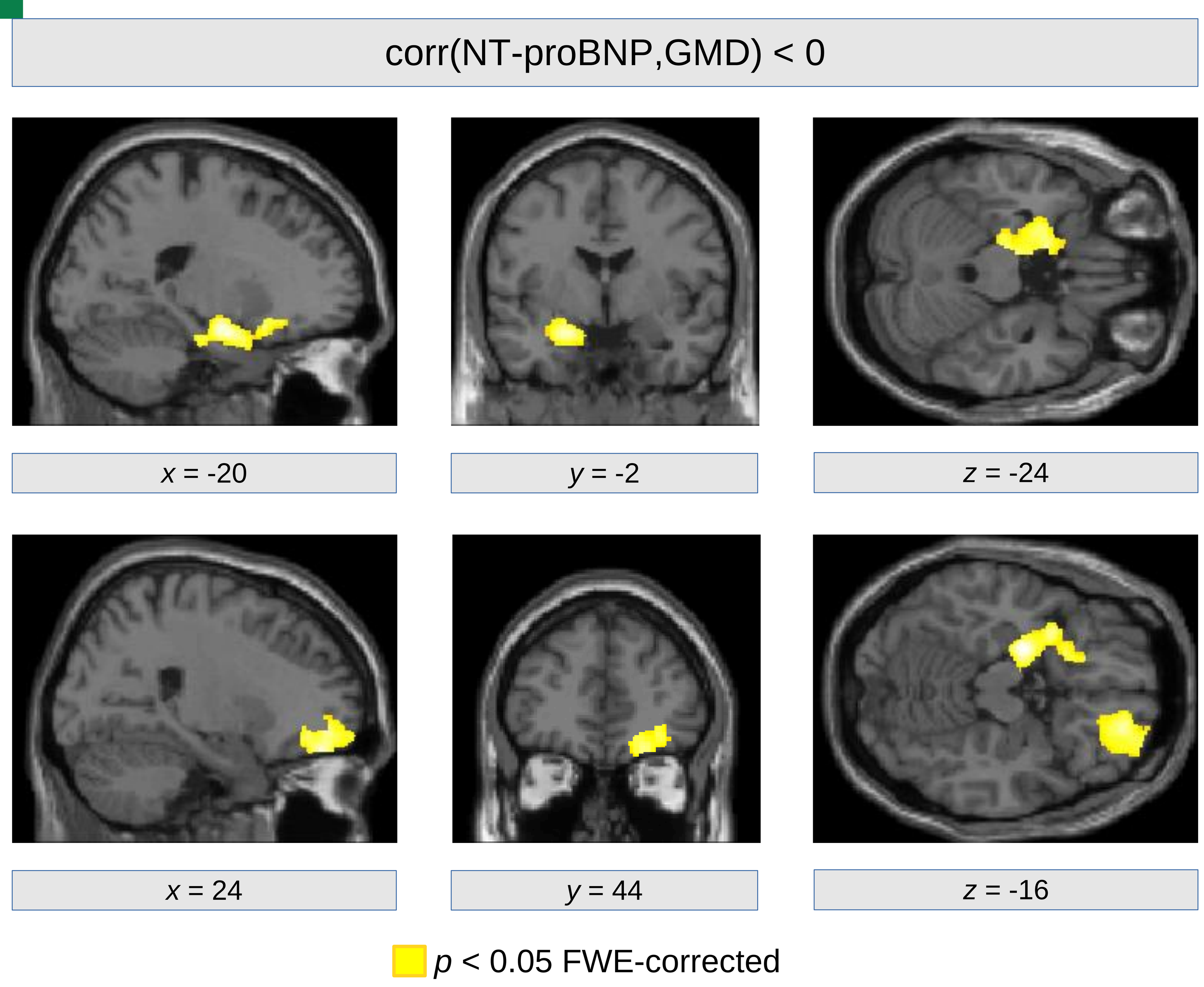

Figure 2. Significant negative correlation between N-terminal prohormone of brain natriuretic peptide (NT-proBNP) and gray matter density (GMD) in a sample of 50 heart failure patients. Increased NT-proBNP concentrations were associated with decreased GMD values in the right orbitofrontal cortex and the left hippocampus. Results are adjusted for multiple comparisons using family-wise error correction ($p<0.05$).

Results and Discussion

- We obtained significant correlations between brain structure and markers of heart failure including EF and NT-proBNP.
- A diminished GMD was found with decreased EF and increased NT-proBNP in orbitofrontal regions, which is in line with previous work showing a reduced cortical thickness in heart failure patients in these cortical regions [6].
- The orbitofrontal cortex plays a substantial role in blood pressure regulation [7] which might link reduced EF, potentially diminished blood flow, and structural brain change.
- We also found increased NT-proBNP with a diminished GMD in the hippocampus in our patient cohort.
- Structural abnormalities in the hippocampus were previously shown in rats with heart failure using VBM and probabilistic maps of the Wistar rat brain [4].
- In line with these observations, histological analysis revealed a decreased neurogenesis together with an increased number of astrocytes in the ventral hippocampus of rats suffering from heart failure compared with sham rats [4].
- Thus, the relationship between NT-proBNP concentrations and GMD might reflect brain injury due to changes in hippocampal blood flow in heart failure [5] .

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