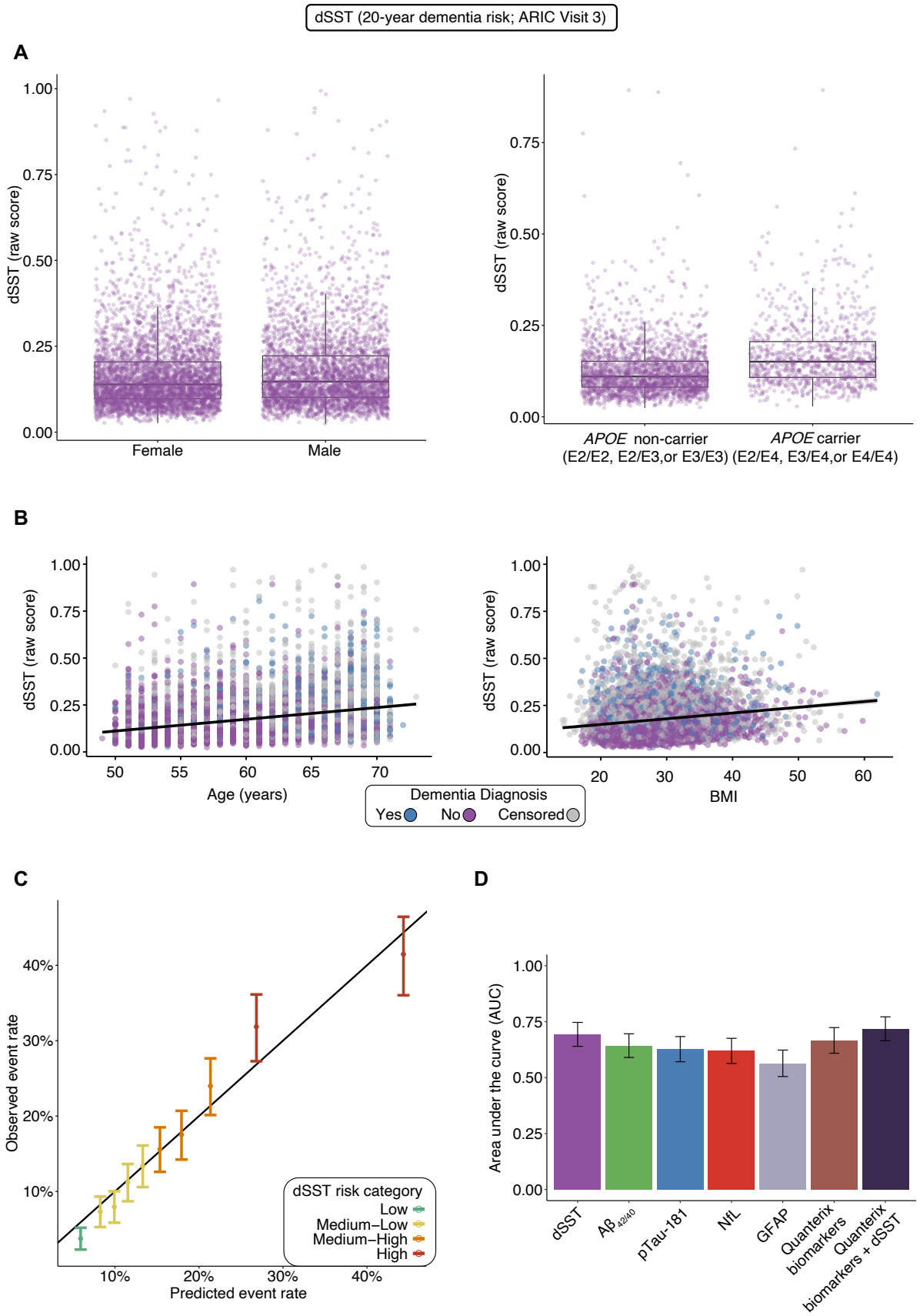
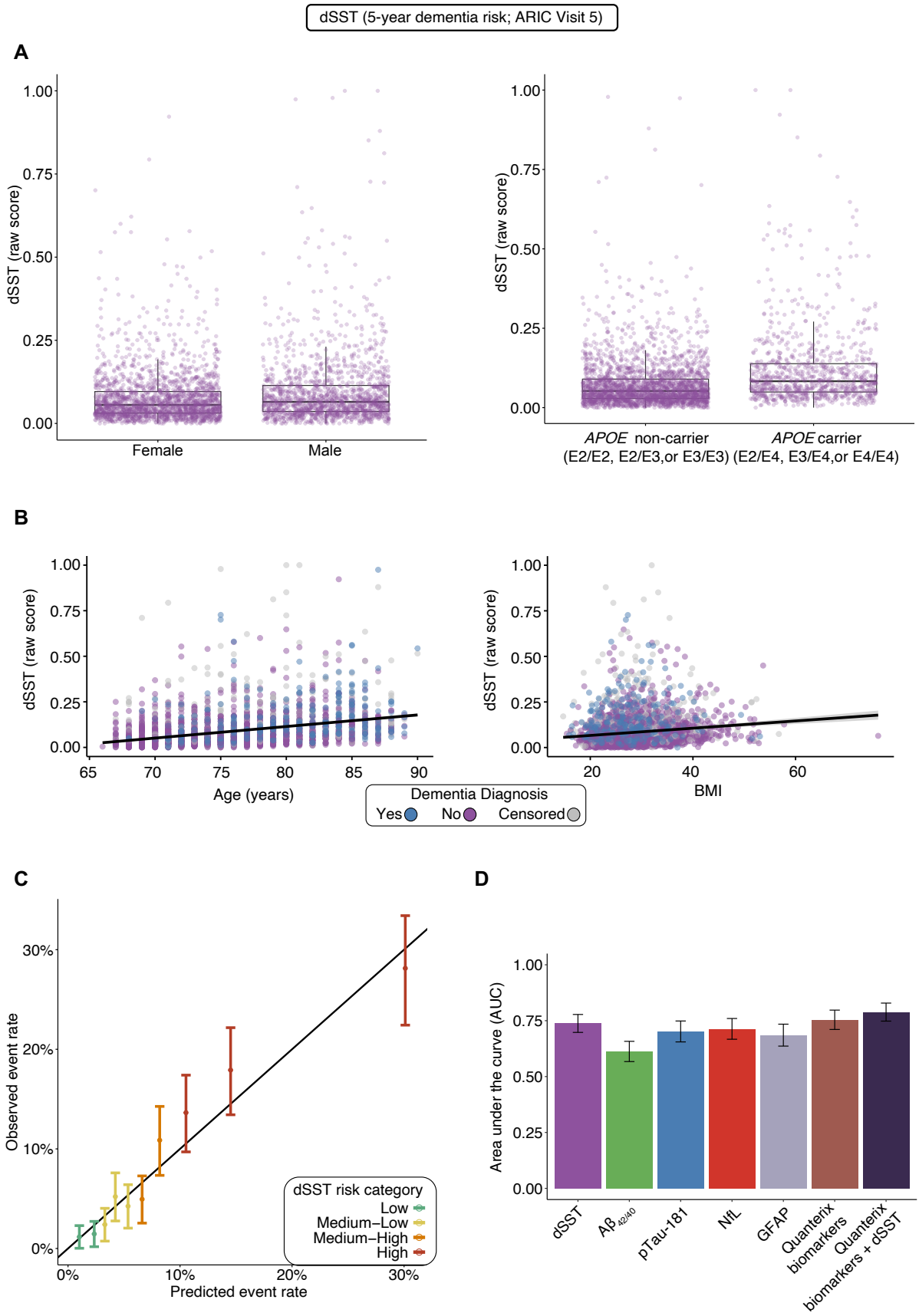
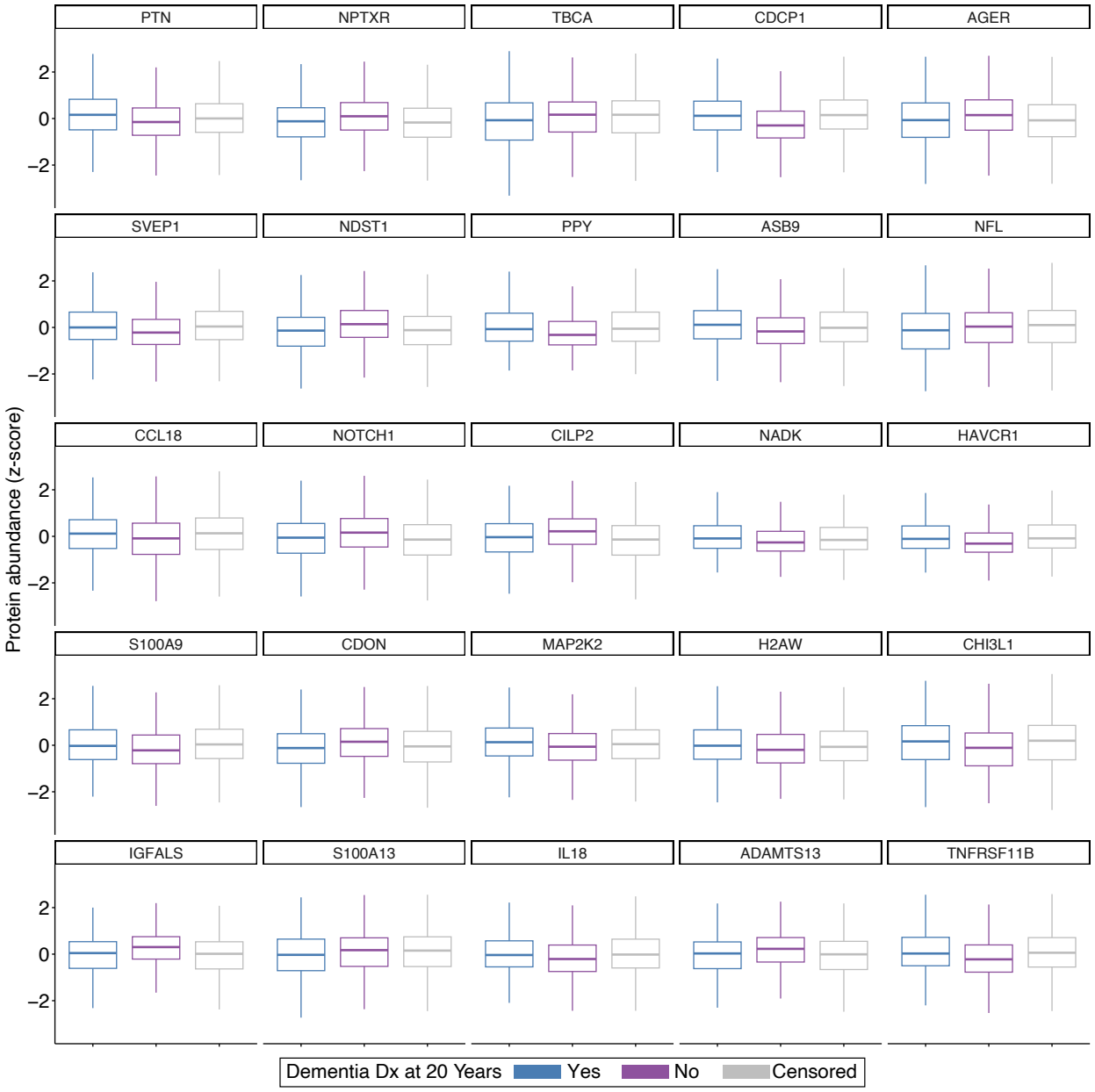


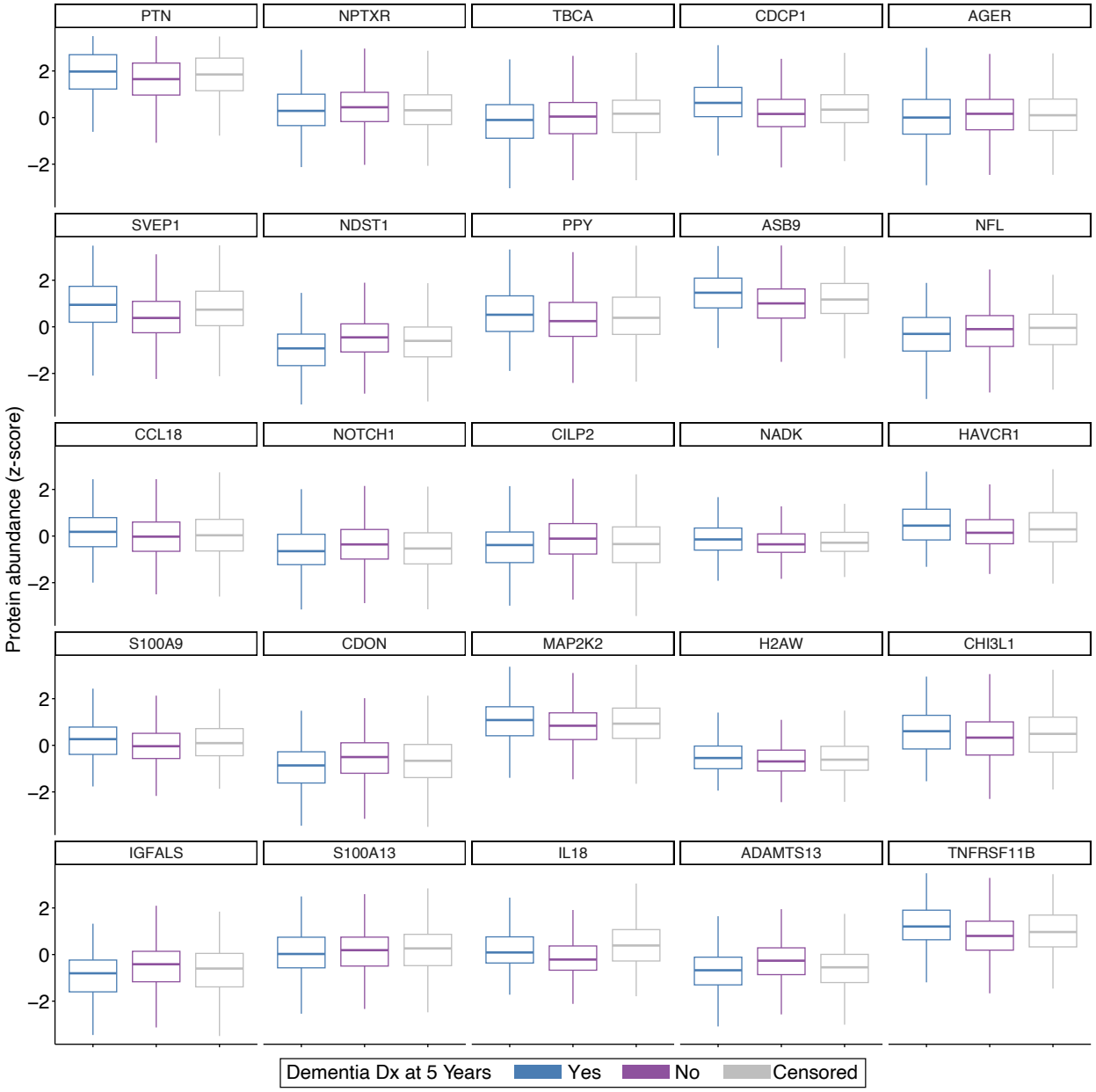
sFigure 1. The Dementia SomaSignal Test (dSST)'s relationship with physiological variables, its calibration according to deciles, and its performance in relation to ADRD plasma biomarkers using data from the Atherosclerosis Risk in Communities (ARIC) study participants at Visit 3. A Boxplots show the distribution of dSST scores according to sex and *APOE* genotype in the training dataset. B Scatterplots and lines of best fit show the distributions of dSST scores across baseline age and body mass index (BMI) in the training dataset. C Calibration plot shows the observed and predicted event rates according to the 20-year dSST deciles in the training dataset. The black line corresponds to diagonal y = x demonstrating perfect calibration. Predicted event rates were calculated as the mean dSST score for each decile. D Bar chart shows the area under the curve (AUC) of dSST scores and ADRD biomarker levels ($A\beta_{42/40}$, GFAP, NfL, pTau-181) in discriminating 20-year dementia risk. Results derived from Cox proportional hazard regression models. Key: Aβ, amyloid beta; ARIC, the Atherosclerosis Risk in Communities study; APOE, apolipoprotein-E; BMI, body mass index; dSST, Dementia SomaSignal Test; GFAP, glial fibrillary acidic protein; NfL, neurofilament light; pTau, phosphorylated tau.



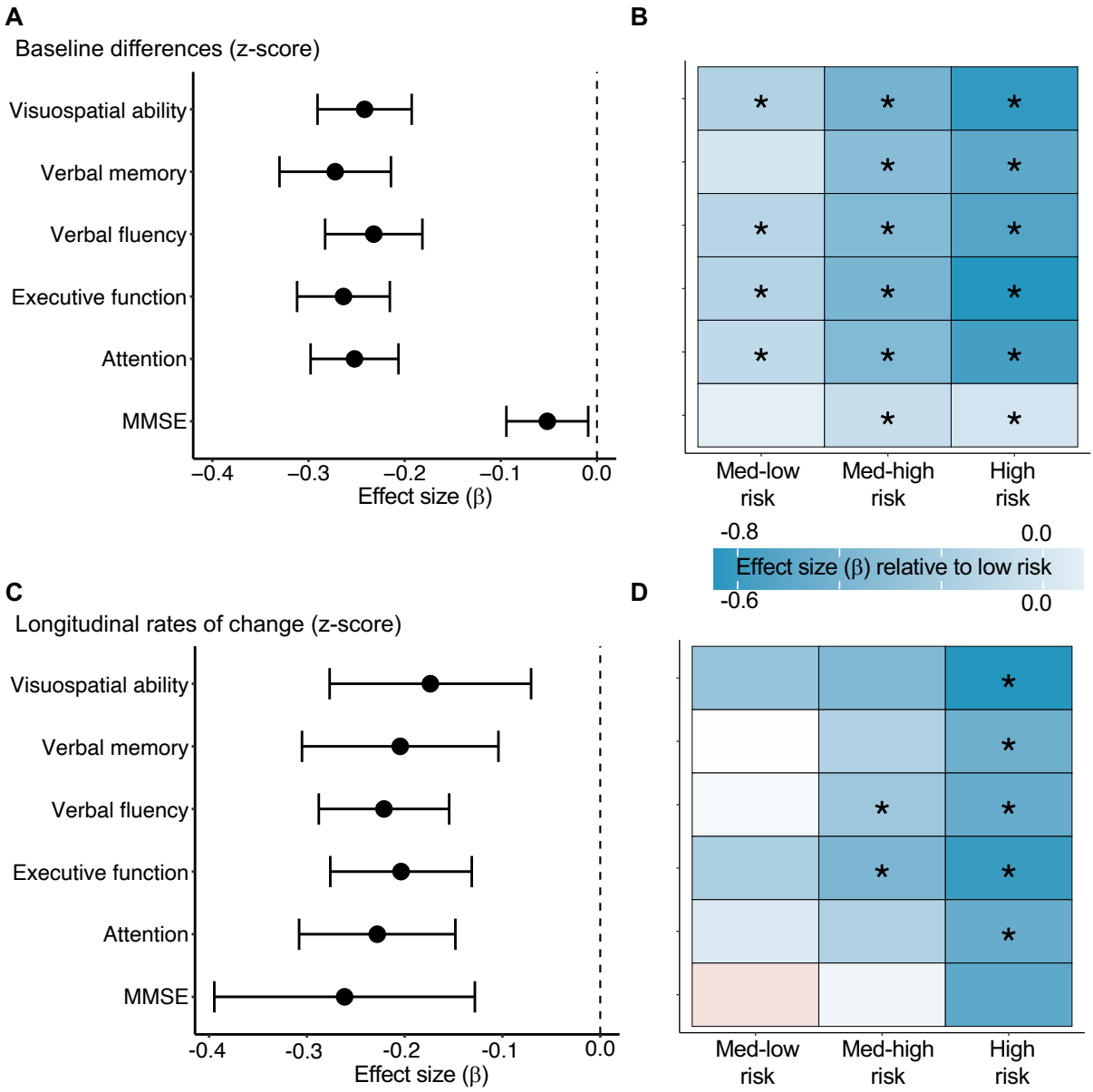
sFigure 2. The Dementia SomaSignal Test (dSST)'s relationship with physiological variables, its calibration according to deciles, and its performance in relation to ADRD plasma biomarkers using data from the Atherosclerosis Risk in Communities (ARIC) study participants at Visit 5. A Boxplots show the distribution of dSST scores according to sex and *APOE* genotype in the training dataset. B Scatterplots and lines of best fit show the distributions of dSST scores across baseline age and body mass index (BMI) in the training dataset. Predicted event rates were calculated as the mean dSST score for each decile. C Calibration plot shows the observed and predicted event rates according to the 5-year dSST deciles in the training dataset. The black line corresponds to diagonal y = x demonstrating perfect calibration. Predicted event rates were calculated as the mean dSST score for each decile. D Bar chart shows the area under the curve (AUC) of dSST scores and ADRD biomarker levels ($A\beta_{42/40}$, GFAP, NfL, pTau-181) in discriminating 5-year dementia risk. Results derived from Cox proportional hazard regression models. Key: Aβ, amyloid beta; ARIC, the Atherosclerosis Risk in Communities study; APOE, apolipoprotein-E; BMI, body mass index; dSST, Dementia SomaSignal Test; GFAP, glial fibrillary acidic protein; NfL, neurofilament light; pTau, phosphorylated tau.



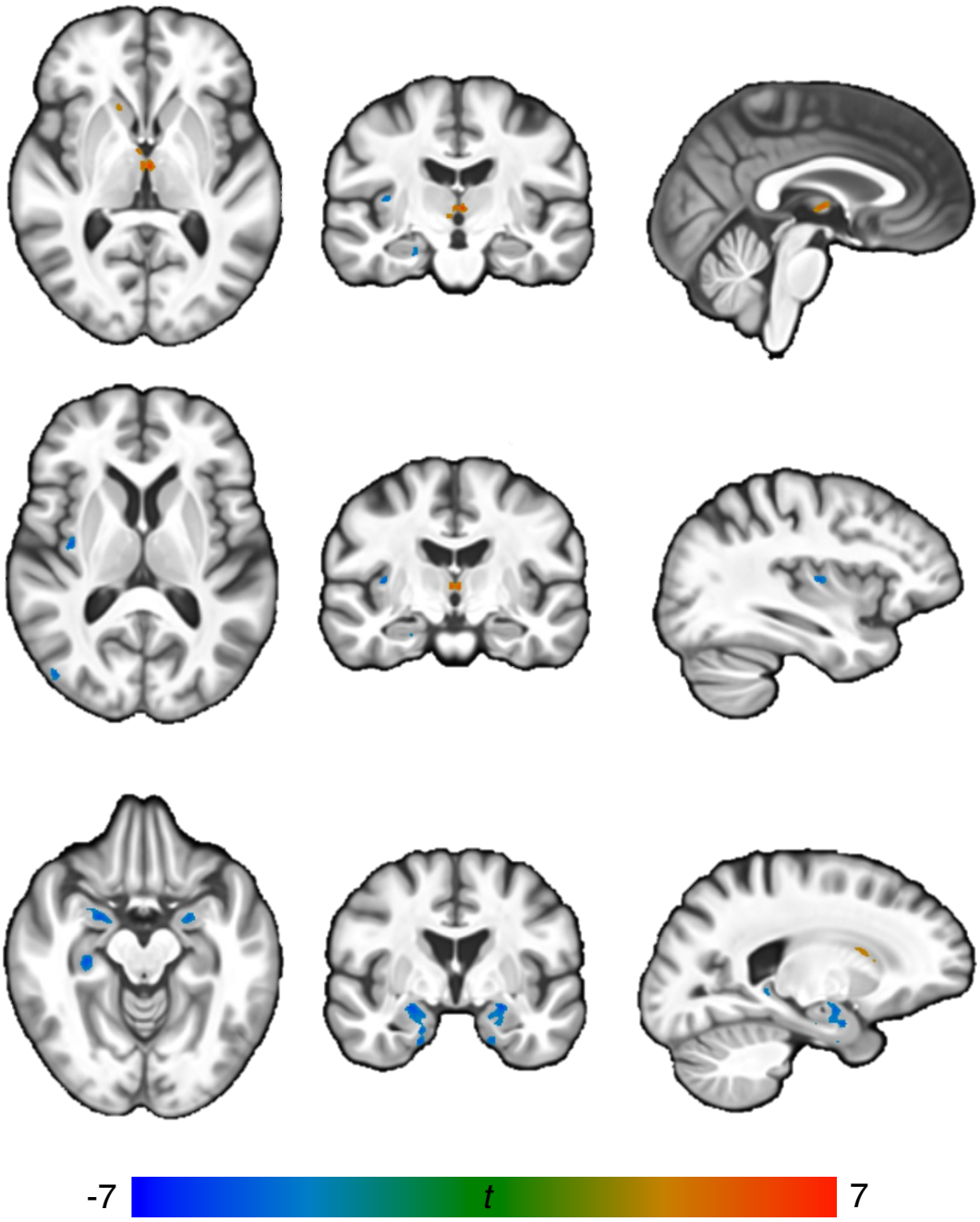
sFigure 3. Boxplots display levels of individual proteins (at ARIC Visit 3) used in dSST calculations.



sFigure 4. Boxplots display levels of individual proteins (at ARIC Visit 5) used in dSST calculations.



sFigure 5. The Dementia SomaSignal Test (dSST) relates to differences in baseline and longitudinal cognitive performance in the Baltimore Longitudinal Study of Aging (BLSA). **A** Forest plot and **B** heatmap show the associations of dSST scores and its risk categories (relative to the low-risk category) with cross-sectional differences in standardized performance across five cognitive domains and the MMSE. **C** Forest plot and **D** heatmap show the associations of dSST scores and its risk categories (relative to the low-risk category) with longitudinal differences in standardized performance across five cognitive domains and the MMSE. Differences in baseline and annual rates of change in standardized cognitive domain scores associated with dSST scores and its risk categories were derived from linear mixed-effects regression models. Key: MMSE, Mini-Mental State Exam.



sFigure 6. The Dementia SomaSignal Test (dSST) relates to differences longitudinal brain atrophy in the Baltimore Longitudinal Study of Aging (BLSA). Axial, coronal, and sagittal images show the associations of dSST scores with voxel-wise longitudinal differences in gray matter volumes. A threshold of 50 voxels with an uncorrected $p<0.001$ was used to define significant clusters. Differences in annual rates of change in voxels associated with dSST scores were derived from linear mixed-effects regression models.