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POSTER PRESENTATION

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Multimodal assessment of locus coeruleus integrity is associated with late-life memory performance

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Abstract

Background: Abnormally phosphorylated tau, an indicator of Alzheimer's disease, accumulates in the first decades of life in the locus coeruleus, the brain's main norepinephrine supply. Recent advances in brainstem magnetic resonance imaging (MRI) suggest an association between in-vivo locus coeruleus integrity and Alzheimer's-related neuropathology. However, while MR sequences have demonstrated their sensitivity for the locus coeruleus, a complete understanding of the underlying contrast mechanisms is still lacking.

Method: To investigate whether common locus coeruleus imaging approaches measure the same construct, younger and older participants of the Berlin Aging Study-II (n ~ 320) underwent 3T-MRI. The imaging protocol included three scans sensitive for the locus coeruleus—a Fast-Spin-Echo [FSE] sequence focused on the brainstem, and a Magnetization-Transfer sequence, acquired once with a dedicated magnetic saturation pulse [MT] and once without, resulting in a proton-density like image [noMT]. Participants moreover completed a comprehensive cognitive battery, including tests of fluid intelligence, episodic and working memory, to assess whether different imaging protocols relate to similar aspects of late-life cognition.

Locus coeruleus MR-intensity ratios, a non-invasive proxy for neuronal density, were semi-automatically extracted from FSE, MT, and noMT scans in standard space. We integrated locus coeruleus ratios across imaging modalities to derive a latent, multimodal factor expressing locus coeruleus integrity. Similarly, we used a previously established cognitive factor structure to integrate performance across multiple cognitive tasks to retrieve latent measures of fluid intelligence, episodic and working memory.

Result: Locus coeruleus-related hyperintensities were reliably detected across imaging modalities (see Figure 1). Crucially, locus coeruleus ratios derived from different imaging modalities were strongly interrelated in younger and older adults (see Figure 2), indicating a common construct. However, age-group differences in locus coeruleus ratios were modality-specific, warranting caution in cross-study comparisons. Merging neural and cognitive models, we found that higher locus coeruleus ratios were related to better episodic memory performance in later life. This association was observed for multimodal locus coeruleus integrity and was replicated for each imaging modality (see Figure 3).

Conclusion: Our findings support the utility of brainstem MRI as proxy for locus coeruleus integrity and highlight a role of the noradrenergic system in late-life memory decline.

Fig. 1: Locus coeruleus-related hyperintensities are detected across imaging modalities and are reliably captured by a locus coeruleus mask (red)

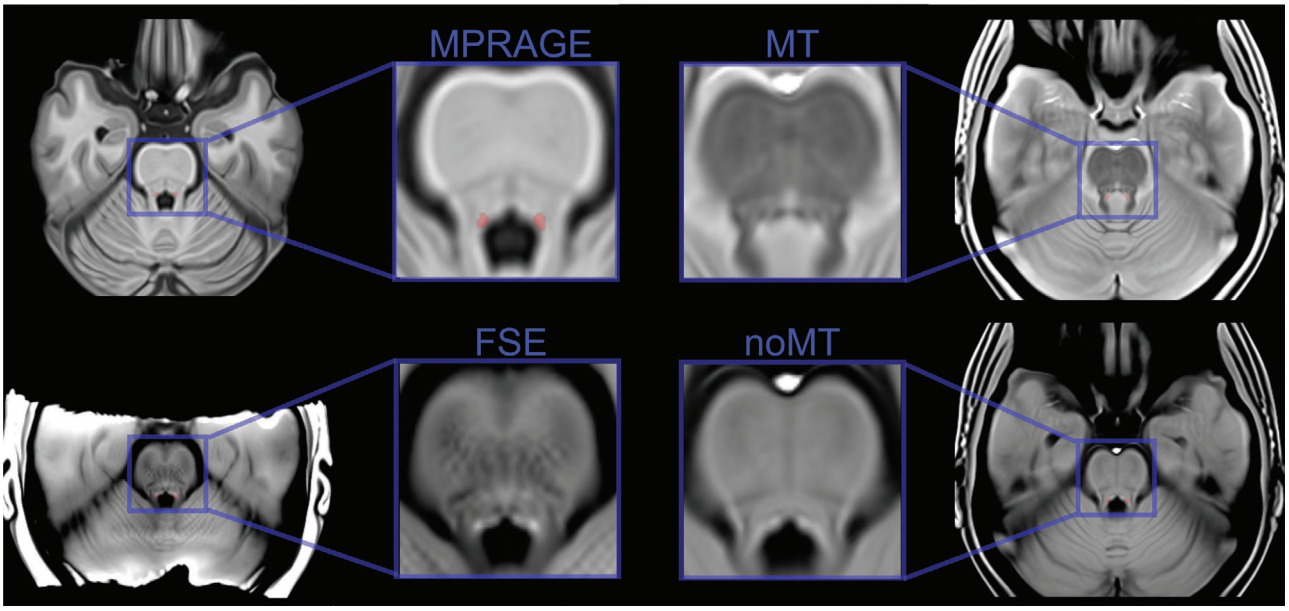

FIGURE 1

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Fig. 2: Locus coeruleus intensity ratios are interrelated across MRI modalities
In older adults, intensity ratios based on Fast Spin Echo (FSE) and Magnetization-Transfer sequences with (MT) and without preparation pulse (noMT) are correlated

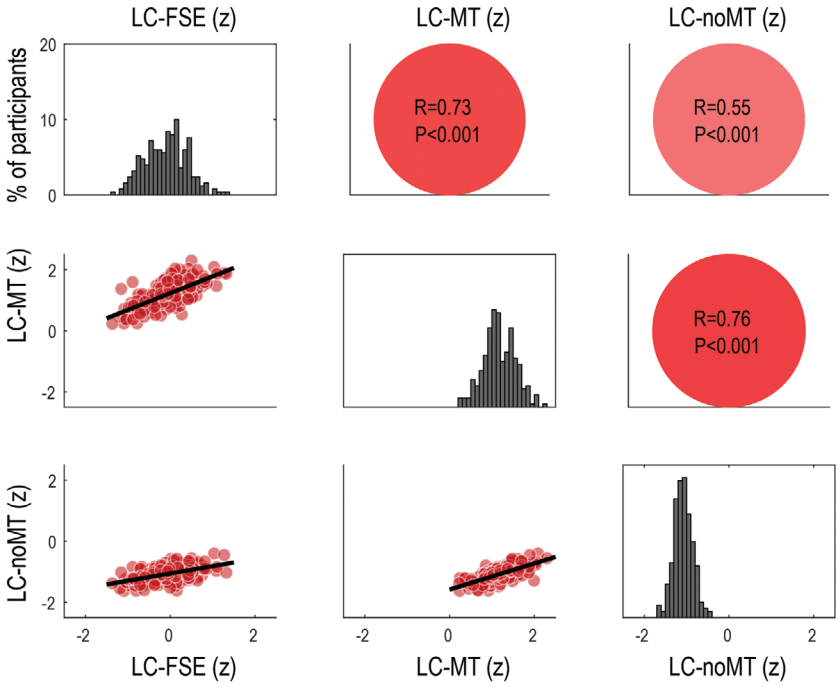

FIGURE 2

Fig. 3: Multimodal and modality-specific locus coeruleus integrity is associated with late-life episodic memory performance

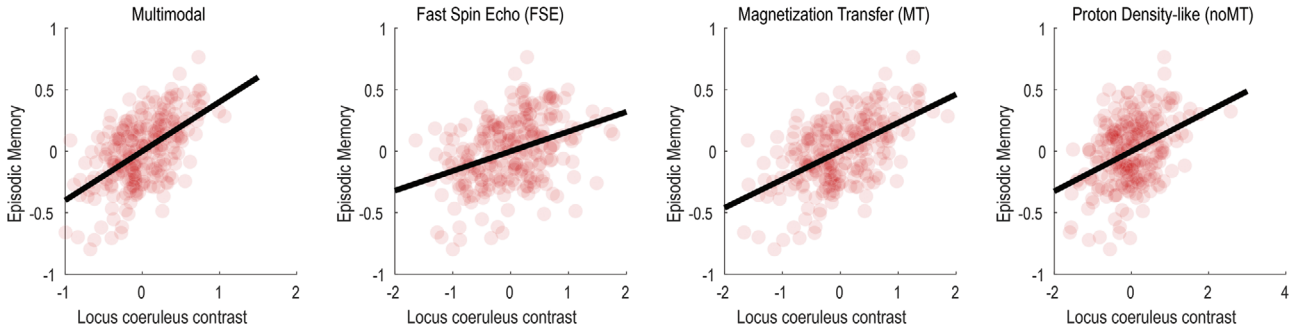

FIGURE 3