Supplementary Methods

Methods

Participants

Community-dwelling individuals in the state of Massachusetts responded to advertisements placed in the local media and at health fairs and underwent telephone screening; the screen failure rate for in-person visits was approximately 18%. Participants diagnosed as CN elderly met the following criteria: at the initial visit, participants were ages 65-90 (inclusive), in general good health without any unstable medical conditions, did not have an active psychiatric disorder, and had a study partner who could serve as a collateral source of information about the participant's cognition and daily functioning. Participants were included if they had completed olfaction testing and either magnetic resonance imaging (MRI) or PiB PET imaging. The initial sample included 287 participants; this was reduced to 215 (2 missing olfaction testing, 32 with active cold at time of olfaction testing, and 38 missing both MR and PiB data). The resulting group was compared to a further reduced group (n=136) that did not have any nasal pathology on the screening questionnaire (see appended questionnaire) in domains felt to be pertinent to performance on the UPSIT (no nasal congestion, difficulty breathing through one nostril, history of broken nose, nasal surgery, or radiation/chemotherapy). There were no significant differences between these groups in terms of demographic and dependent variables used in the primary analyses (p>0.05 for all variables). Therefore, all subsequent analyses were conducted on the larger sample.

Clinical assessments

Participants completed an extensive set of neuropsychological tests used to derive cognitive

domain factors of executive function, episodic memory, and processing speed, as previously described. In the current study, we only used the memory factor score. Tests that comprised that score included the cued recall names and cued recall occupations scores from the Face-Name Associative Memory Exam^{1, 2}, the delayed recall score from the Six-Trial Selective Reminding Test³, and List 2 free recall from the Memory Capacity Test.⁴

Structural MRI acquisition and processing

Bilateral hippocampal volume was adjusted for intracranial volume (ICV) by performing a linear regression with hippocampal volume and ICV as the dependent and independent variables respectively; residuals from this model were added to mean hippocampal volume, yielding an adjusted hippocampal volume value representative of typical values in order to facilitate interpretation.

References

- 1. Rentz DM, Amariglio RE, Becker JA, et al. Face-name associative memory performance is related to amyloid burden in normal elderly. Neuropsychologia 2011;49:2776-2783.
- 2. Amariglio RE, Frishe K, Olson LE, et al. Validation of the Face Name Associative Memory Exam in cognitively normal older individuals. J Clin Exp Neuropsychol 2012;34:580-587.
- 3. Masur DM, Fuld PA, Blau AD, Crystal H, Aronson MK. Predicting development of dementia in the elderly with the Selective Reminding Test. J Clin Exp Neuropsychol 1990;12:529-538.

4. Rentz DM, Locascio JJ, Becker JA, et al. Cognition, reserve, and amyloid deposition in normal aging. Ann Neurol 2010;67:353-364.