Sensory Measures as Biomarkers for Alzheimer's Disease Pathology

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BACKGROUND

Sensory changes, including in vision, smell, and hearing have previously been reported in patients with Alzheimer's disease and mild cognitive impairment (MCI) [1-3]. This study is designed to evaluate the independent and combinatorial ability of sensory measures from multiple sensory domains (vision, smell, hearing) to predict the presence of AD pathophysiology on neuroimaging measures (amyloid and tau deposition, neurodegeneration, altered brain connectivity), as well as clinical diagnosis and two-year progression. The study will include 150 individuals, including 40 cognitively normal older adults with minimal risk (CN), 70 cognitively normal at-risk due to subjective cognitive decline (SCD), *APOE* ε4 positive genotype, or amyloid positivity, and 40 MCI. Measures of visual function, olfaction, and auditory function will be collected along with amyloid and tau PET, as well as structural and functional MRI. A two-year follow-up visit with cognition, clinical, and sensory measures, as well as MRI will also be collected.

PRELIMINARY ANALYSIS METHODS

- Participants from the Indiana Memory and Aging Study, who are seen through the clinical core of the Indiana Alzheimer Disease Center, underwent sensory testing, amyloid and tau PET imaging, and structural and functional MRI.
- Visual studies included multiple tests, such as frequency doubling technology (FDT), which assesses visual contrast sensitivity.
- Olfactory identification was assessed using the University of Pennsylvania Smell Identification Test (UPSIT).
- Amyloid was measured using PET scans with either [^{18}F]florbetapir or [^{18}F]florbetaben. Scans were collected and processed using standard techniques and converted to centiloids [4].
- Tau deposition was evaluated using [^{18}F]flortaucipir PET scans. Scans were collected and processed using standard techniques.
- Voxel-wise analyses to assess the association of visual contrast sensitivity measures (Figure 1), as well as olfactory identification on the UPSIT (Figure 2), with amyloid and tau deposition on PET. Figure 1 is presented at voxel-wise p<0.05 (FWE), while Figure 2 is presented at voxel-wise p<0.001 (uncorrected).
- Combinatorial analyses were performed using a linear regression model using contrast sensitivity and olfactory identification together or independently to predict entorhinal cortex (EC) thickness.

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PRELIMINARY RESULTS

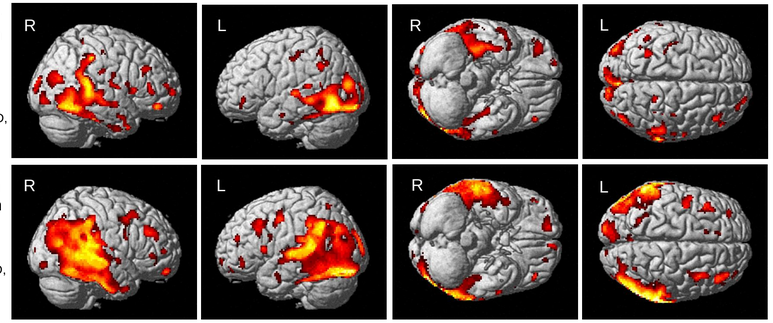
Figure 1. Visual Contrast Sensitivity Measures are Associated with Amyloid and Tau Deposition

A) Exam Duration vs. Amyloid

(n=74; 31 CN, 20 SCD, 16 MCI, 7 AD)

B) Mean Deviation vs. Tau

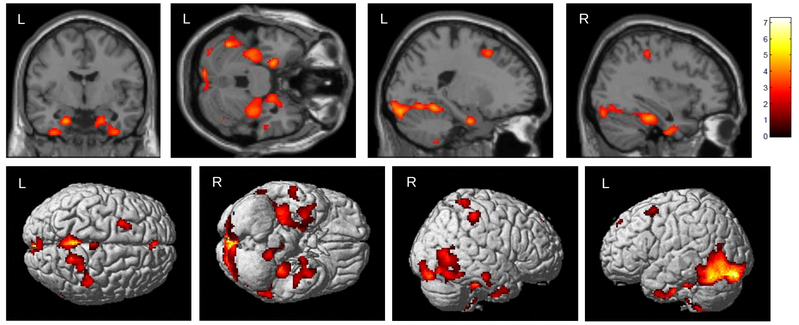
(n=46; 23 CN, 12 SCD, 9 MCI, 2 AD)



Visual contrast sensitivity (CS) was associated with widespread amyloid and tau deposition in AD-like patterns

Covaried for age and sex

Figure 2. Olfactory Identification is Associated with Tau Deposition



Olfactory identification was associated with tau deposition in primarily the medial and lateral temporal lobes. No association with amyloid was observed.

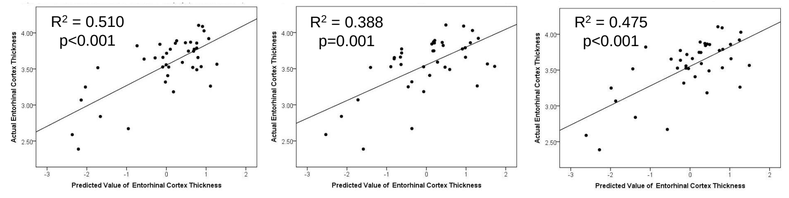
n=26 (14 CN, 7 SCD, 5 MCI)
Covaried for age and sex

Figure 3. Combining Olfactory and Visual Measures Better Predicts Medial Temporal (MTL) Atrophy

A) Residuals of Combined Prediction

B) Residuals of Visual Prediction

C) Residuals of Olfactory Prediction



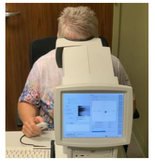
Combined olfactory and visual measures better predicts MTL atrophy than either measure alone.

n=40 (21 CN, 12 SCD, 6 MCI)
Covaried for age and sex

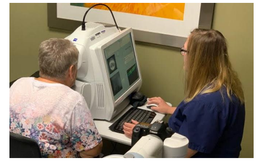
CURRENT STUDIES

Vision

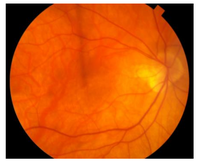
Frequency Doubling Technology (FDT)



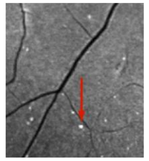
Optical Coherence Tomography (OCT)



Fundus Photography

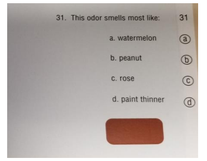


Neurovision Fluorescent Scan



Olfaction

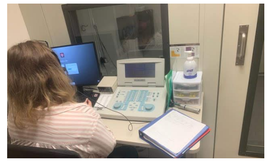
UPSIT



OLFACT Battery – smell identification, detection, and episodic recall

Hearing

Pure Tone Audiometry (PTA) and CUNY Sentences



Sentence in Noise (QuickSIN)

Auditory Letter-Number Sequencing

Test	Item	Response
1.	L-2	2-L
2.	R-4-D	4-D-R
3.	V-1-J-5	1-5-J-V

CONCLUSIONS

Visual and olfactory function are associated with biomarkers of AD pathophysiology such as amyloid and tau. Our current studies will expand on our preliminary findings to provide evidence as to whether sensory measures are useful non-invasive, easy to administer, and inexpensive screening tests for AD.

ACKNOWLEDGEMENTS

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