

Characterizing auditory dysfunction in mild cognitive impairment: rationale and design of an ongoing clinical phenotyping study - The SAPHIR Study

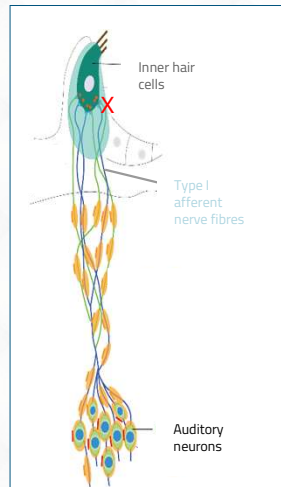
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Background:

Hearing loss is increasingly recognized as a major potentially modifiable risk factor for dementia.¹ Beyond age-related threshold elevation, altered auditory processing, particularly impaired speech intelligibility in noisy environments, has been linked to increased cognitive load and early cognitive decline.² Cochlear synaptopathy, defined by the degeneration of synapses between inner hair cells and auditory nerve fibers, has been proposed as a peripheral mechanism underlying degraded auditory signal transmission despite preserved pure-tone audiometry.^{3,4} However, comprehensive auditory phenotyping across the cognitive continuum remains limited. Improved characterization of auditory dysfunction may therefore provide critical insights into the auditory-cognitive interface in individuals at risk for Alzheimer's disease.

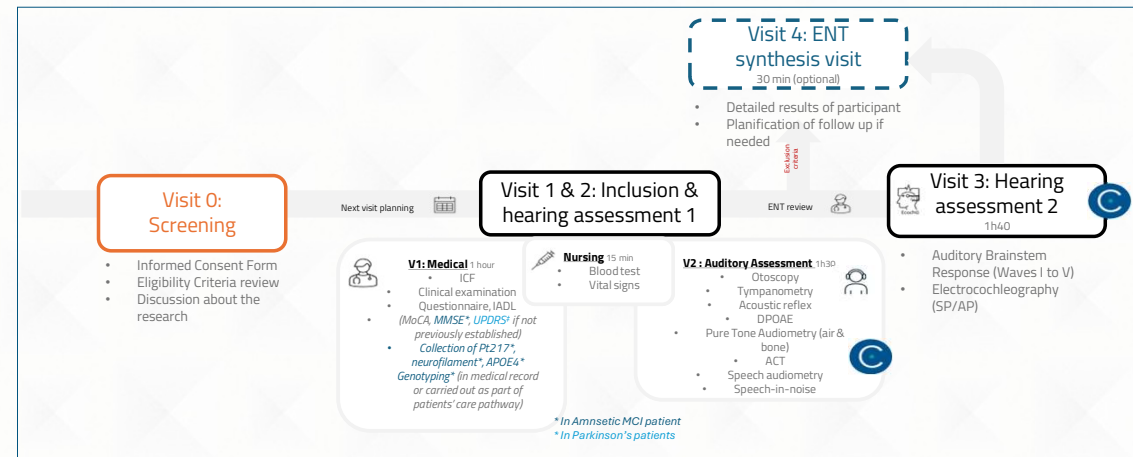
Methods:

SAPHIR (NCT07083089) is an ongoing, multicenter clinical phenotyping study designed to characterize auditory function in cognitively unimpaired individuals and participants with amnesic mild cognitive impairment (MCI), defined by predominant episodic memory. At inclusion, participants undergo standardized neuropsychological assessment, detailed medical and hearing history, quality-of-life questionnaires, plasma tau217 analysis. Plasma biomarkers are collected for a high-sensitivity multiplex analysis. Auditory evaluations include speech perception in quiet and in noise, and electrophysiological recordings (auditory brainstem responses and electrocochleography) targeting auditory nerve function and markers consistent with cochlear synaptopathy. Interim feasibility assessments monitor recruitment and tolerability.



Results:

As of July 5th 2026, recruitment is ongoing across 6 clinical centers, with a seventh center planned. 31 participants with amnesic MCI and 89 controls have been enrolled, towards a target of 103 participants per group. Interim analysis is due mid-July 2026. Early discontinuations after the inclusion visit were primarily due to audiological exclusion criteria identified at baseline, including conductive hearing loss (26%), abnormal otoscopy (31%) or tympanometry (28%), asymmetric hearing loss (10%), single-sided deafness (3%).



Conclusion:

Our ongoing study implements a standardized and comprehensive framework for auditory phenotyping in cognitively unimpaired individuals and those with amnesic MCI, addressing a critical gap in the clinical characterization of auditory dysfunction along the AD continuum. SAPHIR aims to elucidate potential associations between early auditory abnormalities and blood-based biomarkers of early-AD, thereby informing future preventive and interventional strategies.

Keywords: cochlear synaptopathy; hearing impairments; Mild Cognitive Impairment; Alzheimer's disease; neurodegenerative disease

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