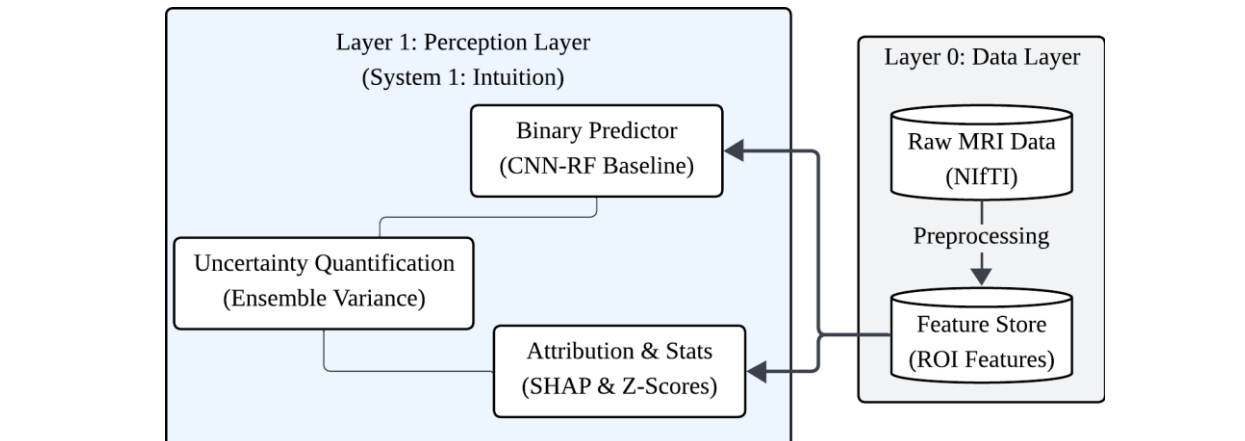
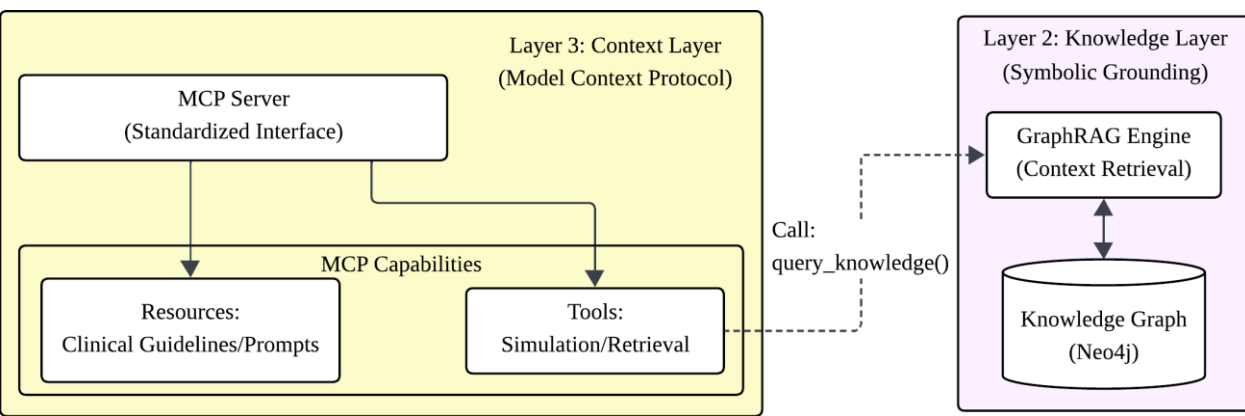
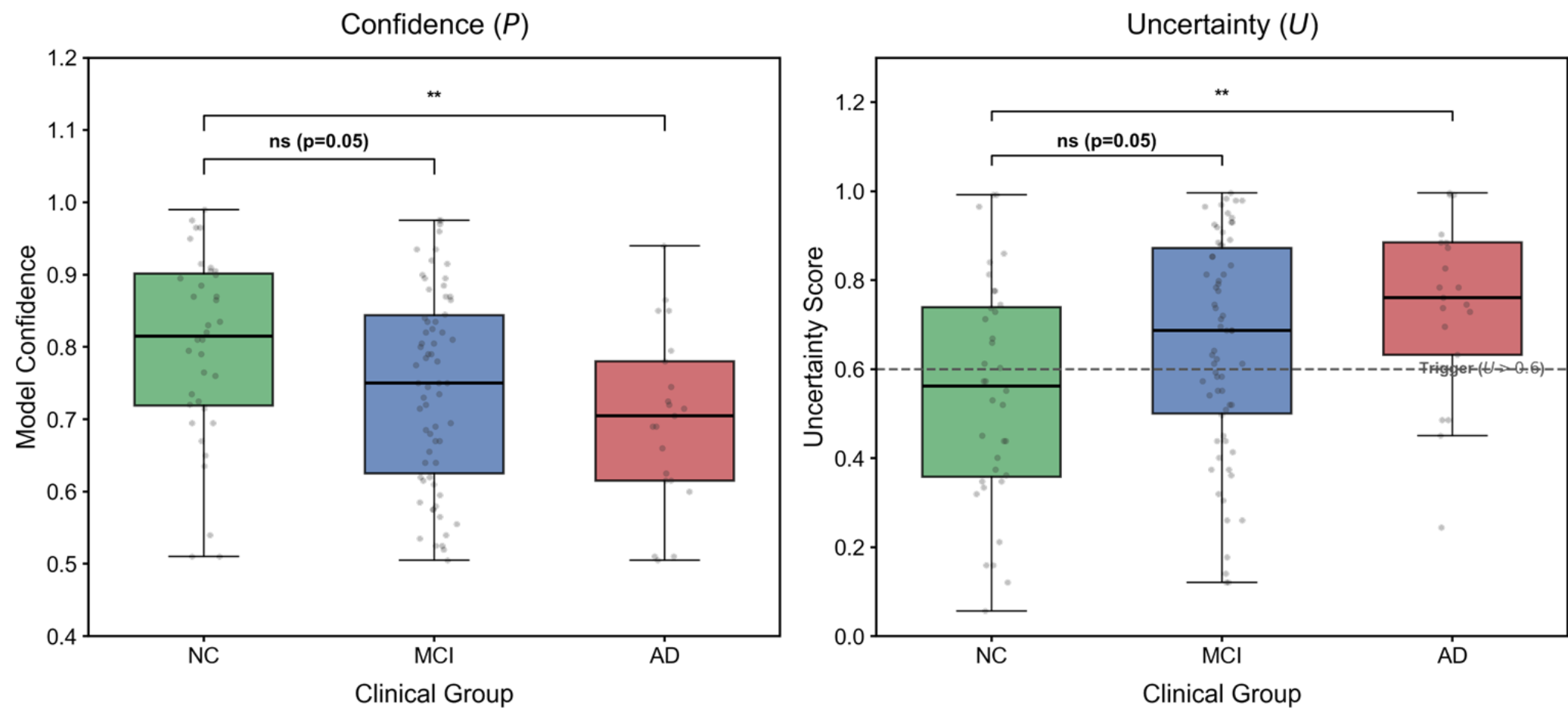
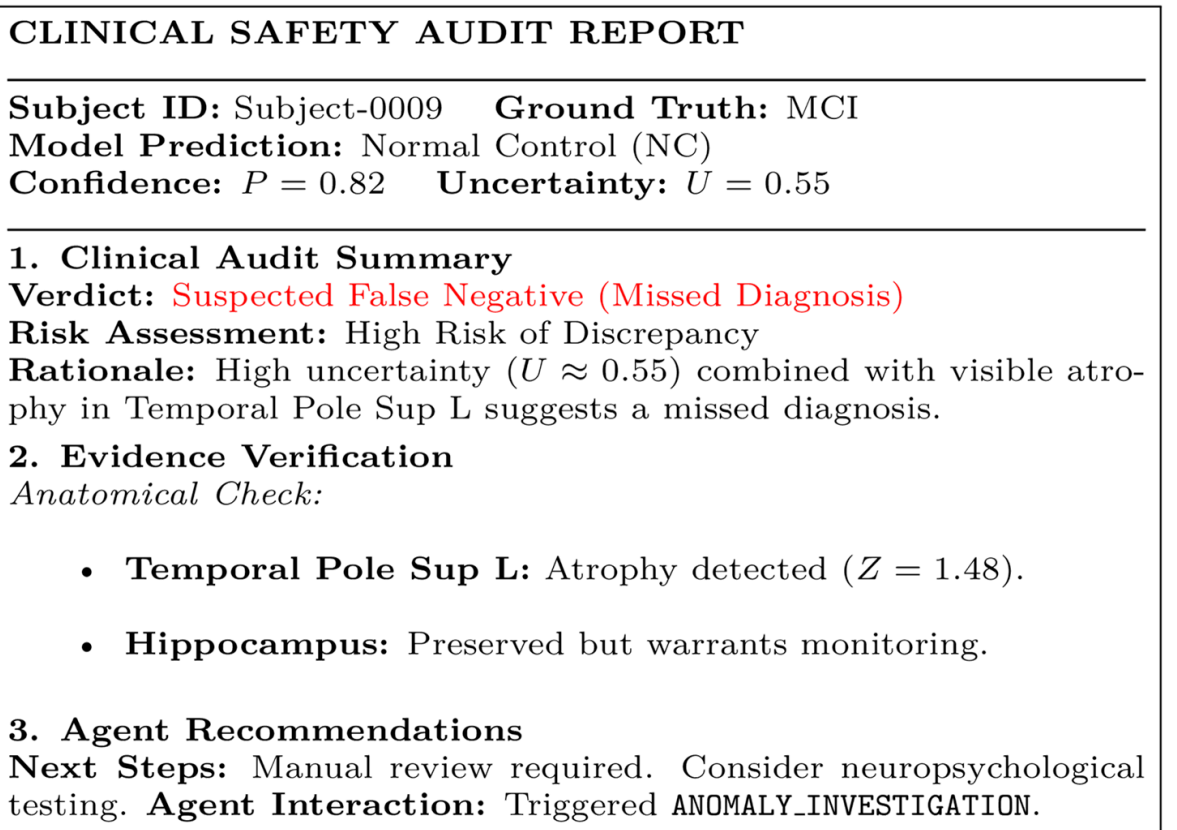


# A Neuro-symbolic Agentic Framework for Enhancing Diagnostic Safety in Alzheimer’s Disease

P2-07

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A decoupled Neuro-symbolic Agentic framework provides an automated clinical safety net, identifying 89.4% of ambiguous MCI cases by auditing neural predictions against anatomical logic.

| INTRODUCTION                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | METHODS                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | RESULTS                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | CONCLUSIONS                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
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| <p><b>Background:</b> Deep learning models excel in sMRI analysis for Alzheimer's disease (AD) but operate as opaque "black boxes".</p> <p><b>The Problem:</b> Classifiers suffer from overconfidence on ambiguous Mild Cognitive Impairment (MCI) cases, causing silent clinical failures. Passive XAI cannot actively intercept errors.</p> <p><b>Objective:</b> We propose a Neuro-symbolic Agentic Framework that decouples statistical perception from symbolic reasoning to act as an active safety net.</p> | <div><p><b>Context Layer (MCP):</b> Standardizes interface interactions via Model Context Protocol to translate agent reasoning into deterministic tool calls.</p><p><b>Knowledge Layer:</b> Hosts an anatomical knowledge graph via Neo4j for GraphRAG context retrieval.</p><div><p><b>Reasoning Layer:</b> Dual-LLM agents replicate clinical consultation:</p><p><i>Orchestrator (Phi-4-mini):</i> Triggers simulation if Uncertainty &gt; 0.6.</p><p><i>Safety Auditor (Llama-3.1-Aloe-8B):</i> Audits predictions against Z-scores.</p></div></div> | <p><b>Baseline Performance:</b> Achieved <b>80.70% binary accuracy</b> and <b>88.89% specificity</b> on clear NC/AD cases (N=57).</p> <p><b>MCI Safety Interception:</b> Successfully flagged and routed <b>89.39% (59/66)</b> of unseen, ambiguous MCI cases for intensive agentic auditing.</p> <p><b>Workstation Latency:</b> Average execution time of <b>33.62 seconds per subject</b> (17.0 reasoning steps) on a local NVIDIA RTX 5090 Laptop GPU.</p> <div><p>Confidence (P) and Uncertainty (U) box plots for NC, MCI, and AD groups. Significance levels: ns (p=0.05), ** (p&lt;0.01).</p></div> | <p><b>Preventing False Positives (Subject-0116):</b> Classifier predicted AD with high confidence (C = 0.82). The Safety Auditor detected preserved anatomical volumes (<math> Z  &lt; 2.5</math>), triggered a discrepancy alert, and blocked the error.</p> <p><b>Catching Missed Diagnoses (Subject-0009):</b> Classifier misclassified an MCI patient as Normal Control. Elevated uncertainty (<math>U = 0.55</math>) triggered a safety audit, capturing subtle temporal atrophy (<math>Z = 1.48</math>).</p> <div><p><b>CLINICAL SAFETY AUDIT REPORT</b></p><p>Subject ID: Subject-0009    Ground Truth: MCI<br/>Model Prediction: Normal Control (NC)<br/>Confidence: <math>P = 0.82</math>    Uncertainty: <math>U = 0.55</math></p><p><b>1. Clinical Audit Summary</b><br/>Verdict: <b>Suspected False Negative (Missed Diagnosis)</b><br/>Risk Assessment: High Risk of Discrepancy<br/>Rationale: High uncertainty (<math>U \approx 0.55</math>) combined with visible atrophy in Temporal Pole Sup L suggests a missed diagnosis.</p><p><b>2. Evidence Verification</b><br/>Anatomical Check:</p><ul style="list-style-type: none"><li><b>Temporal Pole Sup L:</b> Atrophy detected (<math>Z = 1.48</math>).</li><li><b>Hippocampus:</b> Preserved but warrants monitoring.</li></ul><p><b>3. Agent Recommendations</b><br/>Next Steps: Manual review required. Consider neuropsychological testing. <b>Agent Interaction:</b> Triggered ANOMALY_INVESTIGATION.</p></div> |
| METHODS                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | ACKNOWLEDGEMENT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | CONTACT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| <p><b>Clinical Dataset (N = 123):</b> Real-world sMRI neuroimaging cohort:</p> <p><i>Normal Control (NC; N = 36):</i> Cognitively unimpaired subjects.</p> <p><i>Alzheimer's Disease (AD; N = 21):</i> Diagnosed probable AD patients.</p> <p><i>Mild Cognitive Impairment (MCI; N = 66):</i> Unseen intermediate cohort.</p> <p><b>Perception Layer:</b> A hybrid CNN-RF pipeline trained on NC vs. AD baseline to build clear decision boundaries, outputting uncertainty (U) and confidence (C).</p>            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | <p>This research was supported by grants from the National Science and Technology Council (NSTC 114-2410-H-006-122-MY3, NSTC 114-2224-E-006-005-, and NSTC 114-2314-B-567-001-). This research was also supported by the Higher Education Sprout Project from the Ministry of Education (MOE) at National Cheng Kung University (NCKU).</p>                                                                                                                                                                                                                                                                                                                                                    | <p>Petersen, R. C. (2004). J Intern Med, 256(3), 183–194.</p> <p>Lundberg, S. M., et al. (2017). NeurIPS, 30.</p> <p>Anthropic. (2024). Model Context Protocol Documentation.</p> <p>Qamar, S., et al. (2023). Sci Rep, 13(1), 17818.</p> <p>Lakshminarayanan, B., et al. (2017). NeurIPS, 30.</p> <p>Edge, D., et al. (2024). arXiv:2404.16130.</p> <p>Microsoft Research. (2025). arXiv:2503.01743.</p> <p>Garcia-Gasulla, D., et al. (2025). arXiv:2505.04388.</p> <p>Dickerson, B. C., et al. (2009). Cereb Cortex, 19(3), 497–510.</p> <p>Avants, B. B., et al. (2011). NeuroImage, 54(3), 2033–2044.</p> <p>Kohavi, R. (1995). IJCAI, 2, 1137–1143.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
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