

**EXPLORING THE EFFECT OF AGING AND  
NEURODEGENERATION ON DECISION-  
MAKING AND THE UNDERLYING  
MECHANISMS USING RODENT-IOWA  
GAMBLING TASK**

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**Exploring the Effect of Aging and Neurodegeneration on  
Decision-Making and the Underlying Mechanisms using Rodent-  
Iowa Gambling Task**

by

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A thesis submitted in fulfilment of the requirements

for the degree of

**DOCTOR OF PHILOSOPHY**

to the



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April 2026

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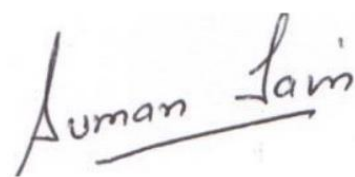
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Aging, Neurodegeneration, Alzheimer’s disease, Rodent Iowa Gambling Task, Decision-making, Hippocampus-amygdala circuitry, Working memory, Spatial memory, Cognitive impairment, Rodent models

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## **Abstract**

Decision-making is a fundamental cognitive process that depends on attention, motivation, memory, reward evaluation, and adaptive learning. These functions are highly vulnerable to the effects of aging and neurodegeneration. Alzheimer's disease (AD), in particular, is characterized by progressive impairment of hippocampal and amygdalar circuits that are central to memory and value-based choice. The present study investigated how aging, AD, and disruption of the basolateral amygdala (BLA) independently and interactively influence decision making and memory in a rodent model.

Using the rodent Iowa Gambling Task (r-IGT) alongside complementary behavioural assays, this thesis assessed decision-making, spatial memory and recognition memory across ten experimental groups, including young and aged healthy controls, AD sham surgery groups, AD-induced groups, BLA lesion groups, and combined AD+BLA lesion groups. Neurochemical correlates were examined through ELISA-based assays of dopamine and serotonin, while histological and immunohistochemical analyses were used to quantify neuronal degeneration and serotonergic expression within the hippocampus and BLA.

Results demonstrated that aging alone produced modest deficits in feedback-based learning and spatial memory. AD exacerbated these impairments, with aged AD rats showing pronounced deficits in long-term advantageous choice and recognition memory. BLA lesions further disrupted adaptive decision making, impairing the ability to link affective outcomes with context. Notably, the AD+BLA lesion group exhibited the most severe impairments across all tasks, highlighting the critical interaction between hippocampal and amygdalar systems in guiding flexible, adaptive behaviour. Neurochemical analyses revealed significant reductions in dopamine and serotonin levels in AD and BLA groups, with the lowest levels observed in the AD+BLA group, suggesting a molecular basis for the observed cognitive impairments.

Overall, these findings provide novel insight into how aging, AD, and amygdalar dysfunction converge to disrupt decision-making and memory processes. By highlighting the hippocampus–amygdala interaction as a central mechanism of vulnerability, this work advances our understanding of the circuit-level and neurochemical underpinnings of cognitive decline. These results have translational implications for identifying biomarkers and therapeutic targets to preserve decision-making capacity and cognitive autonomy in aging populations and individuals at risk of Alzheimer’s disease.

## Abstract in Hindi (सारांश)

निर्णय लेना एक बुनियादी संज्ञानात्मक प्रक्रिया है जो ध्यान, प्रेरणा, स्मृति, पुरस्कार मूल्यांकन और अनुकूली सीखने पर निर्भर करती है। ये कार्य उम्र बढ़ने और न्यूरोडीजेनरेशन (तंत्रिका-क्षरण) के प्रभावों के प्रति अत्यधिक संवेदनशील होते हैं। विशेष रूप से, अल्जाइमर रोग (AD) की विशेषता हिप्पोकैम्पल और एमिग्डालर सर्किट का बढ़ता हुआ क्षरण है, जो स्मृति और मूल्य-आधारित चुनाव के लिए केंद्रीय होते हैं। वर्तमान अध्ययन ने इस बात की जांच की कि उम्र बढ़ना, AD, और बेसोलेटरल एमिग्डाला (BLA) का व्यवधान, एक कृतक मॉडल में निर्णय लेने और स्मृति को स्वतंत्र रूप से और परस्पर रूप से कैसे प्रभावित करते हैं।

कृतक आयोवा गैबलिंग टास्क (r-IGT) का उपयोग करते हुए, साथ ही पूरक व्यवहारिक परीक्षणों के माध्यम से, इस शोध-पत्र ने दस प्रायोगिक समूहों में निर्णय लेने, स्थानिक स्मृति और पहचान स्मृति का मूल्यांकन किया; इन समूहों में युवा और वृद्ध स्वस्थ नियंत्रण समूह, AD शम सर्जरी समूह, AD-प्रेरित समूह, BLA घाव समूह, और संयुक्त AD+BLA घाव समूह शामिल थे। डोपामाइन और सेरोटोनिन के ELISA-आधारित परीक्षणों के माध्यम से न्यूरोकेमिकल सहसंबंधों की जांच की गई, जबकि हिप्पोकैम्पस और BLA के भीतर तंत्रिका-क्षरण और सेरोटोनर्जिक अभिव्यक्ति की मात्रा निर्धारित करने के लिए हिस्टोलॉजिकल और इम्यूनोहिस्टोकेमिकल विश्लेषणों का उपयोग किया गया।

परिणामों ने प्रदर्शित किया कि अकेले उम्र बढ़ने से प्रतिक्रिया-आधारित सीखने और स्थानिक स्मृति में मामूली कमी आई। AD ने इन कमियों को और बढ़ा दिया, जिसमें वृद्ध AD चूहों ने दीर्घकालिक लाभकारी चुनाव और पहचान स्मृति में स्पष्ट कमियां दिखाईं। BLA घावों ने अनुकूली निर्णय लेने की प्रक्रिया को और बाधित किया, जिससे भावनात्मक परिणामों को संदर्भ से जोड़ने की क्षमता क्षीण हो गई। विशेष रूप से, AD+BLA घाव समूह ने सभी कार्यों में सबसे गंभीर कमियां प्रदर्शित कीं, जो लचीले और अनुकूली व्यवहार को निर्देशित करने में हिप्पोकैम्पल और एमिग्डालर प्रणालियों के बीच महत्वपूर्ण परस्पर क्रिया

को उजागर करता है। न्यूरोकेमिकल विश्लेषणों ने AD और BLA समूहों में डोपामाइन और सेरोटोनिन के स्तरों में महत्वपूर्ण कमी का खुलासा किया, जिसमें AD+BLA समूह में सबसे कम स्तर देखे गए; यह प्रेक्षित संज्ञानात्मक कमियों के लिए एक आणविक आधार का सुझाव देता है।

कुल मिलाकर, ये निष्कर्ष इस बात की नई अंतर्दृष्टि प्रदान करते हैं कि कैसे उम्र बढ़ना, AD, और एमिग्डालर शिथिलता मिलकर निर्णय लेने और स्मृति प्रक्रियाओं को बाधित करते हैं। हिप्पोकैम्पस-एमिग्डाला परस्पर क्रिया को संवेदनशीलता के एक केंद्रीय तंत्र के रूप में उजागर करके, यह कार्य संज्ञानात्मक गिरावट के सर्किट-स्तरीय और न्यूरोकेमिकल आधारों के बारे में हमारी समझ को आगे बढ़ाता है। इन परिणामों के अनुवादकीय निहितार्थ हैं, जो वृद्ध आबादी और अल्जाइमर रोग के जोखिम वाले व्यक्तियों में निर्णय लेने की क्षमता और संज्ञानात्मक स्वायत्तता को बनाए रखने के लिए बायोमार्कर और चिकित्सीय लक्ष्यों की पहचान करने में सहायक हो सकते हैं।

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## List of Abbreviations

AD – Alzheimer’s Disease

BLA – Basolateral Amygdala

r-IGT – Rodent Iowa Gambling Task

OFT – Open Field Test

OLT – Object Location Test

NORT – Novel Object Recognition Test

STZ – Streptozotocin

ICV – Intracerebroventricular

ELISA – Enzyme-Linked Immunosorbent Assay

DA – Dopamine

5-HT – 5-Hydroxytryptamine (Serotonin)

PBS – Phosphate Buffered Saline

PBST – PBS + Tween-20

BSA – Bovine Serum Albumin

DAPI – 4',6-diamidino-2-phenylindole (nuclear stain)

ROI – Region of Interest

TIFF – Tagged Image File Format

PFA – Paraformaldehyde

ANOVA – Analysis of Variance

SEM – Standard Error of the Mean

IAEC – Institutional Animal Ethics Committee

CPCSEA – Committee for the Purpose of Control and Supervision of Experiments on Animals

H&E – Hematoxylin and Eosin