Improvements of Mice Models to Best Represent Alzheimer's Disease

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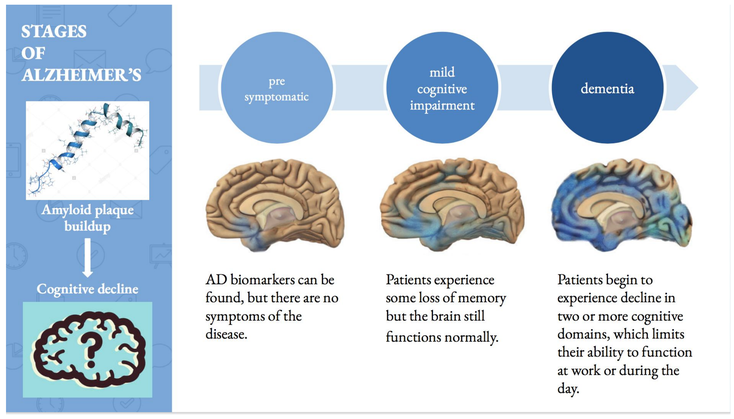
INTRODUCTION

- Current mice models for modeling Alzheimer's disease in humans have several **flaws in their representation of human symptoms** (APP 1).
- Despite some success of Alzheimer's treatments in mice, there has been **no successful translation** to human patients.
- A possible cause of this problem is a lack of research focusing on **finding the specific flaws** of Alzheimer's disease mouse models and how they can accurately model the disease in humans.



RESEARCH METHODOLOGIES

Inquiry approaches:

- Action research: focused on studying a system and attempting to correct the flaws within that system
- Needs assessment research: allowed for a process to determine the needs of an accurate Alzheimer's disease model and make decisions on how to improve the standing models

Data collection tools:

- Database: provided an organized system to collect and review data on the success or failures or different types of current mouse models (Google Spreadsheets)
- Measurements: quantitative data
- Observations: qualitative data

Data analysis techniques:

- Summaries: used to describe data and facts without outside opinions or interpretations

DATA AND FINDINGS

Mice Model	Mutation	Neuronal Loss	Plaques	Tangles	Gliosis	Synaptic Loss	Changes in LTP/LTD	Cognitive Impairment
TauΔK280 ("Proaggregation mutant")	MAPT K280del	Absent	Absent	Present	Unknown	Present	Present	Present
ARTE10	APP KM670/671NL (Swedish), PSEN1 M146V	Absent	Present	Absent	Present	Present	Unknown	Present
TASTPM (TAS10 x TPM)	APP KM670/671NL (Swedish), PSEN1 M146V	Absent	Present	Absent	Present	Unknown	Unknown	Present
TAS10 (thy1-APPswe)	APP KM670/671NL (Swedish)	Absent	Present	Absent	Present	Present	Absent	Present
APP NL-F Knock-in	APP KM670/671NL (Swedish), APP I716F (Iberian)	Absent	Present	Absent	Present	Present	Unknown	Present
APP NL-G-F Knock-in	APP KM670/671NL (Swedish), APP I716F (Iberian)	Absent	Present	Absent	Present	Present	Unknown	Present
APP(V717I)	APP V717I (London)	Absent	Present	Absent	Present	Unknown	Absent	Absent
PDAPP(line109)	APP V717F (Indiana)	Absent	Present		Present	Present	Present	Present
Tg2576	APP KM670/671NL (Swedish)	Absent	Present	Absent	Present	Unknown	Present	Present
rTgTauEC	MAPT P301L	Present	Absent	Present	Present	Present	Present	Present
TauRDΔK280 ("Proaggregation mutant")	MAPT K280del	Present	Absent	Present	Present	Present	Present	Present
APP E693Δ-Tg (Osaka)	APP E693del (Osaka)	Present	Absent	Absent	Present	Present	Present	Present
hTau.P301S	MAPT P301S	Present	Absent	Present	Present	Unknown	Unknown	Present
Tau P301L	MAPT P301L	Unknown	Absent	Present	Present	Unknown	Present	Present
JNPL3(P301L)	MAPT P301L	Present	Absent	Present	Present	Unknown	Unknown	Unknown
Tau P301S (Line PS19)	MAPT P301S	Present	Absent	Present	Present	Present	Present	Present
rTg9191	APP KM670/671NL (Swedish), APP V717I (London)	Present	Present	Absent	Present	Unknown	Unknown	Absent
PS/APP	APP KM670/671NL (Swedish), PSEN1 M146L (A>C)	Present	Present	Absent	Present	Unknown	Unknown	Present
APP23	APP KM670/671NL (Swedish)	Present	Present	Absent	Present	Absent	Absent	Present
TgCRND8	APP KM670/671NL (Swedish), APP V717F (Indiana)	Present	Present	Absent	Present	Present	Present	Present
APPPS1	APP KM670/671NL (Swedish), PSEN1 L166P	Present	Present	Absent	Present	Present	Present	Present
APP(V717I) x PS1(A246E)	APP V717I (London), PSEN1 A246E	Unknown	Present	Absent	Present	Unknown	Present	Present
5xFAD	APP KM670/671NL (Swedish)	Present	Present	Absent	Present	Present	Present	Present
APP(Swedish) (R1.40)	APP KM670/671NL (Swedish)	Unknown	Present	Absent	Present	Present	Unknown	Unknown
APPswe/PSEN1dE9	APP KM670/671NL (Swedish), PSEN1: deltaE9	Present	Present	Absent	Present	Present	Present	Present
J20 (PDGF-APPSw,Ind)	APP KM670/671NL (Swedish), APP V717F (Indiana)	Present	Present	Absent	Present	Present	Present	Present

Figure 1: This table displays the commonly used mouse models for Alzheimer's Disease and whether the certain symptoms were absent (pink highlight), present, or unknown. When the symptoms are found to be absent, the model has successfully treated an area of the disease.

DISCUSSION AND ANALYSIS

- Despite evidence of success in mice models (Figure 1), there is **currently no cure for Alzheimer's disease**, as no treatment found to be successful in mice has worked in humans.
- Certain mice models have shown absence of symptoms of the disease when treated with specific drugs.
- When **symptoms are found to be absent in mice**, they might not have cured the disease but rather **eliminated one factor**.
- However, no success has been found in humans when using the same drugs because **no drugs have passed stage 3** of the clinical trial process.
- Since success has been found in mice but not humans, the **mouse model does not accurately display the disease as it is found in humans**.

CONCLUSIONS AND IMPLICATIONS

- Biomarkers and cognitive developments in the brain are difficult to model in mice, as **numerical change can be observed but mental progression can not**.
- It is **challenging to track regression and progression of Alzheimer's disease** because the cognitive abilities of mice can not be measured to the same extent as humans
- Further research needs to be conducted to **focus on targeting a specific area or symptom** of the disease

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