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Toward Reproducibility in Preclinical Alzheimer's Research: The Case for Standardizing $A\beta_{1-42}$-Induced Rodent Models

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INTRODUCTION & AIM

Animal-induced models are essential for bridging the translational gap between transgenic models and clinical trials. Although several models are standard, experimental designs differ, and protocols are not standardized.
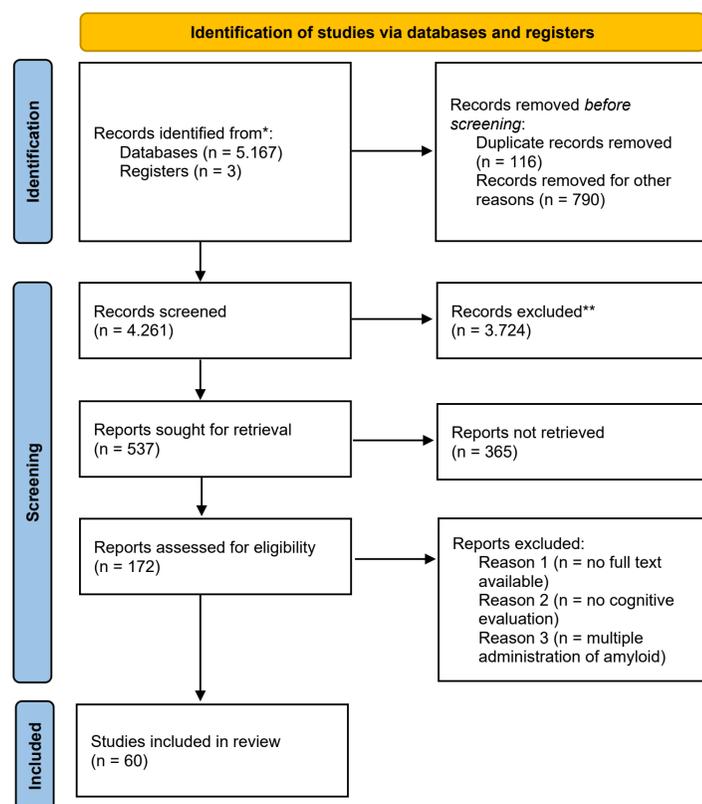
METHOD

A PRISMA-guided search was done in PubMed, Embase, and Cochrane, and 60 studies with Aβ1-42 injected into rats.

Primary outcomes were
- rat strain
- sex
- injection site
- Injected dose

Secondary outcomes followed the **time** between induction and **cognitive** testing.

Data was analyzed using JASP statistics program and applying descriptive statistics, t-tests, chi-square, and correlations.

Identification of studies via databases and registers

Identification

Records identified from*:
Databases (n = 5.167)
Registers (n = 3)

Records removed *before screening*:
Duplicate records removed (n = 116)
Records removed for other reasons (n = 790)

Screening

Records screened (n = 4.261)

Records excluded** (n = 3.724)

Reports sought for retrieval (n = 537)

Reports not retrieved (n = 365)

Reports assessed for eligibility (n = 172)

Reports excluded:
Reason 1 (n = no full text available)
Reason 2 (n = no cognitive evaluation)
Reason 3 (n = multiple administration of amyloid)

Included

Studies included in review (n = 60)

RESULTS & DISCUSSION: Primary Outcomes

Bilateral injections showed up in 65% of the studies, most often in Wistar rats (64%), and hit either the intracerebroventricular (i.c.v., 48.7%) or intrahippocampal (i.h.c., 51.3%) regions.
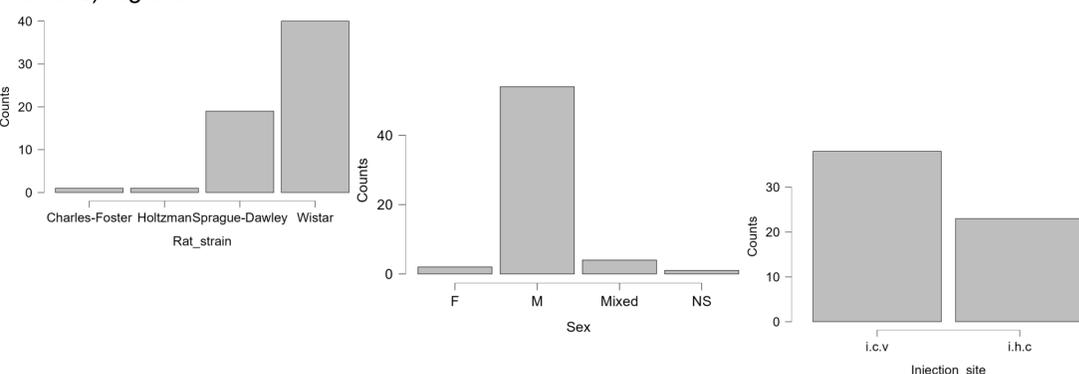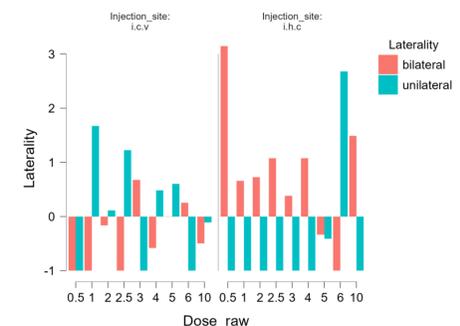

RESULTS & DISCUSSION: Secondary Outcomes

Most unilateral models—85.7%—used i.c.v. injections. On average, researchers injected 3.8 ± 2.1 µl in bilateral setups and 4.9 ± 2.6 µl in unilateral ones.

Frequencies for injection location

injectare uni/bi	injection location	Frequency	Percent
bilateral	i.c.v	19	48.7
	i.h.c	20	51.3
unilateral	i.c.v	18	85.7
	i.h.c	3	14.3

They ran cognitive testing about 18.4 ± 10.6 days after bilateral and 20.7 ± 12.9 days after unilateral injections.
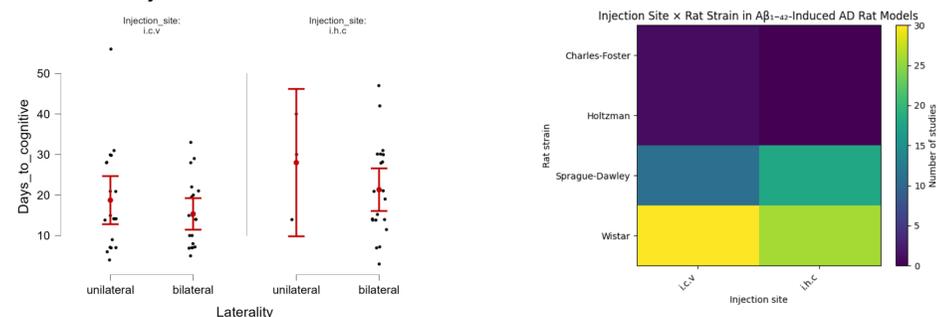
Statistically, those differences were not significant (p > 0.05).

CONCLUSION

This analysis highlights the substantial methodological heterogeneity underlying $A\beta_1–A\beta_{1-42}$-induced rat models of Alzheimer's disease.

Despite partial convergence in injected volumes and timing of behavioural assessments, critical experimental parameters—including rat strain, injection site, laterality, and dose reporting—remain highly variable across studies.

Importantly, no statistically significant differences were observed in injected dose or timing of cognitive testing between unilateral and bilateral approaches, underscoring that current practices are driven more by convention than by standardised evidence.

These findings emphasise the need for consensus-based reference parameters regarding injection site, dose metrics, and assessment timelines to improve reproducibility, comparability, and translational relevance of preclinical Alzheimer's research.

FUTURE WORK / REFERENCES

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