

Individual Differences in Cognitive Aging Rodent Datasets (ID-CARD): A collaborative platform for behavioral analysis across the lifespan

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ABSTRACT

Understanding cognitive aging requires approaches that capture individual variability while enabling integration across studies. In rodent models, behavioral data are central to this effort, yet cross-laboratory differences in experimental design limit comparability and constrain secondary analysis. To address this gap, we developed the Individual Differences in Cognitive Aging Rodent Datasets (ID-CARD), a first-of-its-kind collaborative repository aggregating trial-level Morris water maze data from multiple laboratories. ID-CARD is designed to support large-scale, integrative analyses and to facilitate secondary use of existing behavioral data in alignment with emerging data-sharing and transparency initiatives. Rather than imposing retrospective harmonization of experimental protocols, we implemented a normalization and modeling framework that enables comparison of learning trajectories while preserving meaningful variation across studies. Behavioral data from > 5000 rats spanning common strains, both sexes, and multiple ages were normalized in training and performance domains and fit with a logarithmic function to derive an error accumulation rate coefficient (EARC) as a measure of spatial learning. Age was strongly associated with increased EARC, indicating attenuated learning, even after adjusting for non-spatial cue performance. Analyses of goodness of fit revealed systematic structure in learning dynamics, where age was associated with reduced learning-curve conformity after accounting for overall performance. Inter-individual variability in spatial learning also increased with age, with strain-specific interactions. These findings demonstrate that integrated analysis of heterogeneous behavioral datasets can yield robust, individual-level insights into cognitive aging. ID-CARD provides a scalable resource and analytic framework to advance discovery in behavioral neuroscience by enabling reuse, integration, and comparative analysis of existing data.

1. Introduction

Advancing our understanding of brain and cognitive aging is a

central challenge for both basic and clinical neuroscience, with profound implications for public health as the global population continues to age. Age is the strongest risk factor for Alzheimer's disease (AD) and

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related dementias (Evans et al., 1989; Hebert et al., 1995; Kukull et al., 2002), and is also associated with modest, gradual declines in episodic memory across adulthood, even among otherwise healthy individuals (Salthouse, 2019). Human studies have identified key trajectories of age-related cognitive change and have highlighted factors associated with resilience that can delay or mitigate decline (Harrison et al., 2012; Rogalski et al., 2013; Stern et al., 2023). However, the inherent complexity of human populations, shaped by diverse genetic, environmental, and lifestyle influences, limits the ability to establish causal mechanisms. Preclinical models, particularly rodent models, therefore, provide a critical bridge by enabling controlled experimental manipulation and mechanistic investigation of hippocampus-dependent memory processes that are highly relevant to human aging and AD (Burke and Barnes, 2025, 2006; Foster, 2012; Gallagher and Rapp, 1997; McQuail et al., 2015; Morrison and Baxter, 2012).

In animal models, cognition is necessarily inferred from behavior, which provides the primary empirical link between internal neural processes and observable learning and memory performance (Krakauer et al., 2017). Central to the study of cognitive aging, therefore, is the availability of behavioral data that can be interpreted at the level of individual animals. Individual differences in learning and memory performance provide the basis for distinguishing vulnerability from resilience to age-related decline. The Morris water maze (MWM) has become one of the most widely used paradigms for assessing hippocampus-dependent spatial learning and memory, with extensive validation and methodological refinement spanning decades of research (D'Hooze and De Deyn, 2001; Morris, 1984; Vorhees and Williams, 2006). Across independent laboratories, diverse training procedures, multiple strains, and both sexes, age-associated decrements in MWM performance have been consistently observed in cross-sectional cohorts (Bizon et al., 2009; Faghihi et al., 2026; Gage et al., 1984; Gallagher et al., 1993; Guidi et al., 2014; McQuail and Nicolle, 2015; Rapp et al., 1987; Zempare et al., 2026).

Across studies, behavioral characterizations have been coupled with rich biological, physiological, and imaging datasets, including large-scale gene expression (Blalock et al., 2003; Haberman et al., 2011), ensemble electrophysiological recordings (Barnes et al., 1997; Wilson et al., 2005), and resting-state functional MRI (Ash et al., 2016). Increasingly, such datasets are being made publicly available for secondary analyses by researchers in behavioral neuroscience and cognitive aging. However, despite the availability of these biological resources, a major barrier to integrative and comparative research remains the absence of a shared behavioral framework that would enable meaningful cross-study analyses at the level of individual subjects.

With support from the National Institute on Aging (R24 AG061421), as well as the McKnight Brain Research Foundation, the Alzheimer's Association, AARP, and the Alzheimer's Drug Discovery Foundation, the Collaboratory on Research Definitions for Reserve and Resilience in Cognitive Aging and Dementia (R&R Collaboratory) convened to establish a framework for advancing research on cognitive reserve and brain resilience through shared definitions, measurement strategies, and collaborative infrastructure. As part of this initiative, a working group of behavioral neuroscientists studying cognitive aging in rodents committed to sharing raw MWM datasets, developing analytic approaches to improve comparability of behavioral outcomes across laboratories, and making these datasets publicly accessible for secondary analysis. This effort resulted in the creation of the Individual Differences in Cognitive Aging Rodent Datasets (ID-CARD) repository, a resource that emphasizes individual-level behavioral trajectories rather than only group-level effects. By aggregating detailed behavioral data across laboratories, ID-CARD enables systematic investigation at the population level of factors that confer vulnerability to age-related memory decline or support preservation of function.

The present work addresses the challenge of cross-laboratory behavioral heterogeneity by focusing on analytic strategies that support comparability without requiring retroactive harmonization of

experimental protocols. Rather than enforcing uniformity, this approach preserves variation across strains, sexes, and training procedures while enabling learning to be characterized in a common quantitative framework. More broadly, the primary contribution of this work is to demonstrate that large-scale aggregation and analysis of behavioral data in animal models is both feasible and informative. By enabling pooled, individual-level analyses across studies, this framework makes it possible to leverage existing data to address questions that are inaccessible within single experiments. By emphasizing learning trajectories rather than single endpoints, individual-level parameters can be extracted that capture distinct aspects of performance, including rate of spatial learning and the structure of learning dynamics. In this context, the analyses presented here serve as a proof-of-principle for discovery-oriented investigation using integrated behavioral datasets and provide a foundation for future integration with biological data as these resources continue to expand.

2. Materials and methods

2.1. Behavioral datasets

Participating research groups contributed a variety of both published and unpublished behavioral datasets from rats and mice, including wild-type strains and transgenic lines, all based on adaptations of the Morris water maze (Figure 1A). In these datasets, animals were trained to locate a fixed hidden platform location over repeated training trials. Individual laboratories varied in their specific protocols: some implemented massed training within a single day, whereas others distributed training across multiple days; some included interpolated probe trials, whereas others used a single final probe trial; and cued trials were incorporated either before or after hidden-platform training. Despite these procedural differences, the core task remained a spatial learning paradigm.

All datasets included acquisition, cue (visible-platform), and probe trial records, together with trial-level behavioral measures including proximity-based metrics (search error and cumulative proximity), path length, latency, and swim speed. Subject metadata included species, strain, biological sex, and age in months. Information regarding visual, motor, or health-related exclusion criteria and age-specific protocol adaptations was not systematically reported to or harmonized within ID-CARD; the availability of such ancillary information therefore varies across datasets. Users requiring additional information for individual datasets may need to consult the originating investigators. All contributed datasets were curated and standardized before being uploaded to GitHub and the R&R Collaboratory website (<https://reserveandresilience.com/animal-cohorts/>), ensuring consistent organization and reproducible analyses (Figure 1B).

2.2. Dataset access

Raw and processed datasets are available through the R&R Collaboratory website and associated repositories (i.e., GitHub). Trial structure and variable definitions are described in README files accompanying each dataset.

For high-level access to the data, we developed a custom graphical user interface (GUI) in Python (PySide6/Qt) to explore and analyze water maze datasets from multiple laboratories (Figure 1C). The GUI loads preprocessed data tables generated by a separate pipeline that standardizes variable names (metadata and trial-level measures) across datasets and combines them into a single analysis frame.

The main window consists of three components: (1) a filter panel, (2) a summary area, and (3) a data table. The filter panel provides collapsible sections for rat metadata (e.g., age, sex, strain, genotype), protocol metadata (e.g., PI, housing, pool diameter, water maze dates, lights on/off), and trial metadata (trial type: spatial/probe/visible; trial number ranges; latency/distance/speed measures). Filters are applied using range fields and multi-select checkboxes; only rows satisfying all

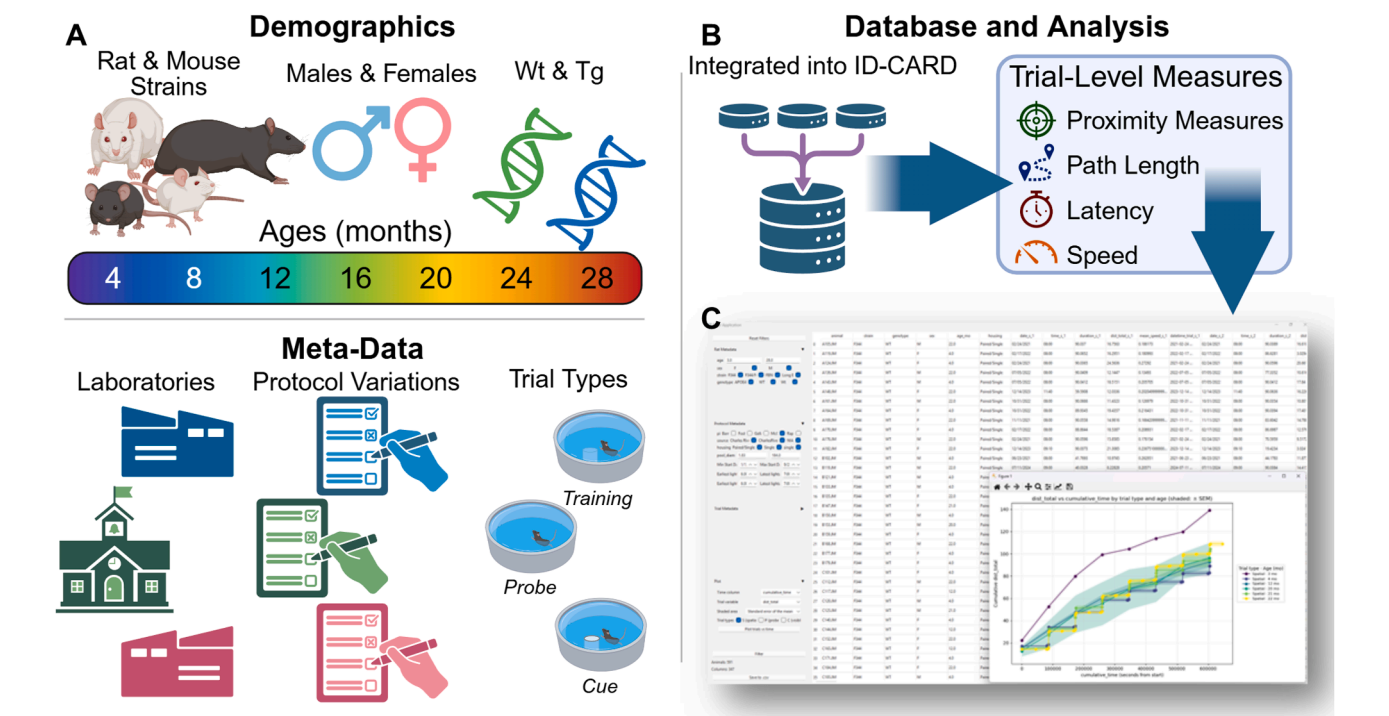


Fig. 1. Structure of contributing datasets and analytical framework in ID-CARD. A. Heterogeneous behavioral datasets integrated across studies. Subjects include rats and mice spanning multiple strains and genotypes (Wt: wild-type; Tg: transgenic), both sexes, and a broad age range. Data were collected across multiple laboratories using distinct experimental protocols. Trial types include training, probe, and cue trials. B. Integrated trial-level behavioral data and associated subject metadata are combined into a unified dataset, from which measures including proximity-based metrics (e.g., search error), path length, latency, and speed are derived. C. Screenshot of the ID-CARD graphical user interface (GUI) for data exploration and analysis. Users can filter data by species, sex, age, laboratory, protocol, and trial type, and visualize trial-level outcomes. Example plot shows accumulating search error as a function of age. The interface also provides access to underlying trial-level data tables for further analysis. Figure created with BioRender.com.

active criteria are retained. The current number of animals (rows) and variables (columns) remaining after filtering is displayed, and the filtered dataset is rendered in a table view. A reset function returns all filter widgets and the displayed data to their default, unfiltered state, and the resulting table can be exported as a CSV file.

An additional “Plot” section allows simple visualization of behavioral performance over training. For each selected dataset view, the GUI reshapes wide trial-level cumulative distance variables into long format, groups animals by age, and computes trial-wise means and variability (standard error, standard deviation, or 95% confidence intervals). It then plots cumulative distance across successive training trials with shaded error bands for each age group and overlays probe-trial performance as individual scatter points. This enables rapid comparison of acquisition and probe performance across ages and experimental conditions within a unified interface. Subsets of data may also be selected within the GUI and saved to CSV files for independent analysis.

2.3. Behavioral data normalization and curve fitting

The current analyses were conducted on a subset of the ID-CARD database selected according to predefined inclusion criteria. Eligible datasets were required to contain trial-level hidden-platform (acquisition) training data from wild-type rats (Table 1). All included datasets also contained visible-platform (cue) and probe trials, together with trial-level proximity measures, path length, latency, and swim speed. Acquisition trials served as the common behavioral framework for standardized normalization and curve fitting across laboratories, whereas cue-trial data were retained for secondary analyses. Restriction to wild-type rats was motivated by the substantially larger sample size, broader age coverage, and more even representation across strains and laboratories relative to mouse and transgenic datasets, which remain integral components of the repository and are intended to support future species-specific and comparative analyses. Probe trials were excluded because their implementation varied substantially across laboratories, including differences in the number, timing (interpolated versus terminal), and duration of probe trials. This heterogeneity precluded

Table 1
Characteristics of datasets included in the present analyses.

Strain	Laboratory	Hidden-Platform Training	Total N (M/F)	Mean Age (months)	Age Range (months)
F344	Barnes	4 trials/day × 5 days (20 trials)	281 (281/0)	16.2	6–25
F344	Foster	18 trials in 1 day (18 trials)	445 (445/0)	13.7	5–24
F344	McQuail	2–3 trials/day × 8 days (24 trials)	375 (191/184)	16.4	4–26
FBN	Nicolle	2–3 trials/day × 8 days (24 trials)	284 (284/0)	18.1	6–28
Long-Evans	Gallagher	2–3 trials/day × 8 days (24 trials)	3775 (3680/95)	20.1	6–24
Long-Evans	Rapp	2–3 trials/day × 8 days (24 trials)	118 (118/0)	18.5	6–24
Total			5278 (4999/279)	18.9	4–28

Only datasets meeting the inclusion criteria for these analyses are shown. Analyses were restricted to wild-type rats with complete hidden-platform acquisition data. Mouse and transgenic datasets contained within the ID-CARD repository were not included. Values in parentheses indicate male/female sample sizes.

consistent normalization of probe performance for quantitative comparison across studies. In contrast, acquisition trials were available across all contributing datasets and followed a sufficiently comparable structure to permit standardized normalization and curve fitting. Individual subjects were excluded if acquisition training data were incomplete (i.e., one or more training trials were missing), preventing reliable estimation of learning trajectories. This analytical strategy prioritizes cross-laboratory comparability while acknowledging that acquisition performance reflects a combination of spatial and non-spatial processes. Probe trials provide a more selective measure of spatial search strategy and memory precision and remain an important focus for future analyses as additional harmonized datasets become available.

Because ID-CARD is a retrospective aggregation of independently generated datasets, information regarding animal health, physical condition, and exclusion criteria reflected the documentation practices of the contributing laboratories rather than a prospectively standardized protocol. Each laboratory contributed complete water maze datasets for animals that underwent behavioral testing, but health- and procedure-related records outside the water maze protocol were not uniformly harmonized across laboratories and therefore were not incorporated into the present analyses. Consequently, no additional health- or motor-based exclusion criteria beyond complete acquisition training data were imposed.

Training trial data from multiple research groups were normalized in two dimensions, training and performance, to enable quantitative comparison of learning rates across laboratories using different protocols. To accommodate differences in the number of training trials, normalized training was calculated as $(n - 1) / (\max n - 1)$, where n is the trial number. This transformation produced values ranging from 0 (first trial, no prior training) to 1 (final trial, fully trained).

All datasets included trial-level measures of path length (or distance traveled), latency to reach the escape platform, swimming velocity, and proximity-based search error. For the present analyses, performance was operationalized using the proximity-based search-error measure originally described by Gallagher et al. (1993). For each subject and trial, this measure was normalized to the mean value of the corresponding laboratory study population. This normalization provided a common reference point across studies, minimizing between-laboratory offsets while preserving biologically meaningful differences among individuals and across age groups.

The cumulative normalized proximity data were then fit with a logarithmic function:

$$Y = \text{EARC} \cdot \ln(X + 1) + b$$

where X represents normalized training and Y represents cumulative normalized proximity (Supplementary Fig. S1). The error accumulation rate coefficient (EARC) quantified the rate at which cumulative proximity scaled with training and served as the primary measure of rate of spatial learning during acquisition. Here, “error” refers to deviation from the goal location as indexed by proximity-based measures, rather than a specific implementation of search error. A logarithmic function was selected because it captures the characteristic decelerating improvement observed during acquisition, with rapid early gains followed by asymptotic change, and provided a stable fit across heterogeneous datasets with differing numbers of training trials. Higher cumulative proximity values, and correspondingly higher EARC values, reflect slower and less effective spatial learning performance. This formulation is consistent with error-driven learning models in which behavior is updated based on prediction error (Rescorla and Wagner, 1972; Sutton and Barto, 2018). The intercept parameter b (“initial offset”) was retained in the fitting procedure but regarded as a nuisance variable, as it largely reflected scaling artifacts of normalization rather than true differences in initial performance.

Goodness of fit (R^2) was calculated for each individual curve to assess conformity to the fitted learning function. Parametric characterization

of learning trajectories is widely used in studies of skill acquisition, where performance is described using canonical nonlinear functions and evaluated based on their fit to individual learning data (Heathcote et al., 2000; Newell and Rosenbloom, 1980). Because R^2 values are bounded between 0 and 1 and typically non-normally distributed, they were Fisher Z-transformed ($Z = 0.5 \cdot \ln[(1 + \sqrt{R^2}) / (1 - \sqrt{R^2})]$) prior to statistical comparison across groups.

2.4. Statistical analysis

Data organization and preprocessing were performed in Microsoft Excel, with additional data transformation using Power Query. Curve fitting was conducted in GraphPad Prism (version 10). Processed data were then exported for statistical analysis in JASP (version 0.95.4), an open-source statistical platform. Analyses were performed on learning parameters derived at the individual subject level, with one observation per animal. Descriptive statistics and graphical methods, including histograms and Q–Q plots, were used to assess the distributions of learning parameters. Because of the large sample size and the bounded nature of derived measures, formal tests of normality were not used as a criterion for model selection. Instead, assumptions underlying linear models were evaluated using residual diagnostics, including residuals-versus-fitted plots and Q–Q plots of standardized residuals. Figures were generated in JASP and finalized for presentation using Microsoft PowerPoint.

The primary analysis examined the relationship between age (in months) and rate of spatial learning, quantified by EARC, using linear regression. Age was treated as a continuous predictor to preserve information across the full age range. Biological sex and strain were included as covariates to account for baseline differences in performance across groups. Strain was coded as Fischer 344 (F344; reference), Fischer 344 × Brown Norway F1 (FBN), and Long–Evans (LE). Laboratory was not included as an explicit factor because it was confounded with strain and training protocol; inter-laboratory differences were addressed through normalization procedures applied during data preprocessing.

To account for potential contributions of non-spatial performance, latency during cued (visible-platform) trials was summarized for each subject as the median cue latency. Because cue trials varied in duration across laboratories, values were z-transformed within laboratory to place performance on a common scale. This measure was included as a covariate in the EARC regression model to assess whether age-related effects persisted after accounting for variation in non-spatial performance.

Goodness of fit (GOF), quantified as the Fisher Z-transformed R^2 , was initially examined using linear regression models that included age, sex, and strain as predictors, paralleling the primary analysis of rate of spatial learning. Because GOF reflects conformity to a smooth learning function rather than behavioral reliability per se, it was treated as a secondary descriptive measure. To assess whether age-related differences in learning-curve conformity were present beyond overall rate of spatial learning, GOF was subsequently analyzed in models that included EARC as a covariate, allowing age-related effects on learning-curve conformity to be evaluated after accounting for differences in overall performance.

Inter-individual variability (IIV) in rate of spatial learning was quantified as the absolute residuals from the EARC model including age, sex, strain, and their interaction. This measure captures the magnitude of deviation from expected rate of spatial learning and reflects variability in performance, which has been characterized as a sensitive marker of cognitive aging and neural integrity (Hultsch et al., 2002; MacDonald et al., 2006). IIV was analyzed using the same predictors to assess whether variability changed with age and differed across groups.

Where appropriate, correlation analyses were conducted using both Pearson and Spearman methods to confirm robustness of effects. These statistics are reported in figures for descriptive purposes and were not used for primary inference, which was based on regression models. Statistical significance was evaluated at an alpha level of 0.05. Given the

large sample size, effect sizes and confidence intervals were emphasized alongside p-values.

3. Results

3.1. Age-related changes in rate of spatial learning

Learning-curve fits were successfully obtained for all subjects ($N = 5278$), yielding an error-accumulation rate coefficient (EARC) and goodness of fit estimate (GOF) for each rat. The distribution of EARC values was right-skewed, with a mean of 1.264 and a standard deviation of 0.606 (minimum = 0.056, maximum = 4.044; [Figure 2A](#)). Age (in months) was positively associated with EARC ([Figure 2B](#)). Correlation analyses confirmed a robust monotonic relationship between age and EARC (Pearson $r = 0.443$, $p < 0.001$; Spearman $\rho = 0.455$, $p < 0.001$). This relationship was further evaluated using linear regression with EARC as the dependent variable and age, sex, and strain as predictors. The full model was significant ($F(4, 5273) = 335.102$, $p < 0.001$) and explained approximately 20.2% of the variance in rate of spatial learning ($R^2 = 0.202$). Age was a strong positive predictor of EARC (unstandardized $B = 0.036$ per month, $SE = 9.959E-4$, $t = 36.445$, $p < 0.001$), indicating that older rats accumulated error more rapidly during training. Sex was not a significant predictor of rate of spatial learning ($B = 0.015$, $t = 0.429$, $p = 0.668$; [Figure 2C](#)). Strain was associated with significant differences in EARC after accounting for age and sex, with both FBN ($B = -0.141$, $SE = 0.037$, $t = -3.861$, $p < 0.001$) and LE ($B = -0.122$, $SE = 0.020$, $t = -6.219$, $p < 0.001$) exhibiting lower EARC than F344 rats (reference strain; [Figure 2D](#)), indicating slower learning (higher error accumulation) in F344 relative to the other strains.

To evaluate whether the association between age and EARC differed across independent laboratory implementations, an additional analysis was performed using only F344 rats, the only strain represented across three laboratories. Laboratory was included as a factor together with an age $\times$ laboratory interaction term. Although the interaction significantly improved model fit ($\Delta R^2 = 0.016$, $F(2, 1094) = 12.43$, $p < 0.001$), the estimated age slope remained positive in all three laboratories ([Supplementary Fig. S2](#); [Supplementary Table S1](#)).

To account for potential contributions of non-spatial performance, median cue-trial latency (z-transformed within laboratory) was included as a covariate. The model including cue performance remained significant ($R^2 = 0.277$), and age continued to be a strong positive predictor of EARC ($B = 0.033$, $SE = 9.588E-4$, $t = 34.765$, $p < 0.001$). Cue latency was also positively associated with EARC in this model ($B = 0.171$, $SE = 0.007$, $t = 23.162$, $p < 0.001$), indicating that slower performance during cued trials was associated with greater error accumulation (data not shown). When an age $\times$ cue interaction was included, the overall model fit improved modestly ($R^2 = 0.286$), and age remained a strong predictor ($B = 0.035$, $SE = 9.665E-4$, $t = 35.875$, $p < 0.001$). The interaction term was significant ($B = 0.009$, $SE = 0.001$, $t = 8.250$, $p < 0.001$), whereas the main effect of cue latency was not ($B = -0.009$, $SE = 0.023$, $t = -0.398$, $p = 0.691$), indicating that the association between poorer cue performance and higher EARC increased with age (data not shown). Notably, the inclusion of cue performance did not attenuate the primary effect of age on EARC.

3.2. Rate of spatial learning, goodness of fit, and age-related learning dynamics

Because GOF reflects the degree to which individual learning

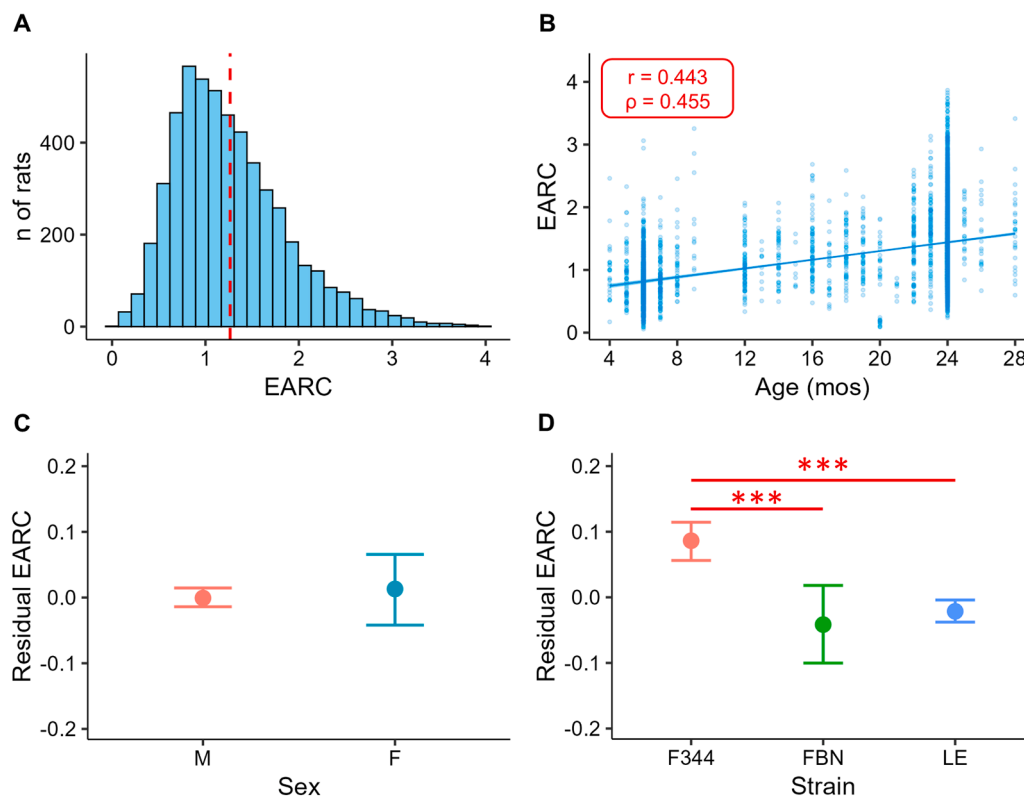


Fig. 2. Distribution of error accumulation rate coefficient and its relationship with age and demographic factors. **A.** Distribution of the error accumulation rate coefficient (EARC) across all subjects. Histogram illustrates the distribution of rate of spatial learning, with vertical line indicating the sample mean. **B.** Relationship between EARC and age (months). Each point represents an individual subject. The solid line indicates the fitted linear regression, with shaded area representing the standard error (SE). Correlation coefficients are shown for both Pearson (r) and Spearman (ρ) analyses. **C.** Residual EARC by sex after accounting for age and strain. Points represent group means of residual EARC values and error bars indicate 95% CIs. **D.** Residual EARC by strain after accounting for age and sex. Points represent group means of residual EARC values and error bars indicate 95% CIs. *** $p < 0.001$ for indicated comparisons.

trajectories conform to a smooth logarithmic function, we next examined how GOF was structured by rate of spatial learning and whether age-related effects on learning dynamics could be distinguished from differences in overall performance. EARC and GOF were strongly and positively associated (Pearson $r = 0.527$, $p < 0.001$; Spearman $\rho = 0.514$, $p < 0.001$; Figure 3A), indicating that rats that accumulated error more rapidly exhibited more stereotyped learning trajectories that closely followed the fitted model.

Inspection of scatterplots revealed an asymmetric, wedge-shaped relationship between EARC and GOF. Rats with greater EARC showed uniformly high GOF, whereas rats with low EARC exhibited substantially greater variability in GOF. This pattern indicates that poor learners tended to exhibit constrained, highly predictable behavior, while better learners showed greater flexibility and variability in learning trajectories that deviated from a smooth monotonic function. Thus, GOF did not index learning quality, but rather reflected the degree to which learning trajectories were constrained or stereotyped.

To characterize gross demographic associations with learning-curve conformity, GOF was initially examined using linear regression models including age, sex, and strain as predictors. In this model, age was positively associated with GOF (unstandardized $B = 0.019$, $SE = 8.163E-4$, $t = 22.726$, $p < 0.001$; Figure 3B). Sex showed a marginal effect, with males tending towards lower GOF than females ($B = -0.054$, $SE = 0.028$, $t = -1.922$, $p = 0.055$). Strain effects were substantial and systematic: relative to F344 (reference strain), both FBN ($B = -0.363$, $SE = 0.030$, $t = -12.100$, $p < 0.001$) and LE rats ($B = -0.758$, $SE = 0.016$, $t = -46.973$, $p < 0.001$) exhibited lower GOF, corresponding to a step-wise decrease in learning-curve conformity from F344 to FBN to LE. Notably, these strain differences paralleled those observed for rate of spatial learning, with FBN and LE rats also exhibiting lower EARC than F344 rats. This parallel pattern indicates that group differences in GOF primarily reflected differences in rate of spatial learning rather than independent biological effects on learning variability.

Because GOF was strongly structured by rate of spatial learning, with both its mean and variance dependent on the EARC, a conditional analysis was performed to determine whether age-related differences in learning dynamics were present beyond differences in overall performance. GOF was therefore regressed on both EARC and age. This model was significant ($F(2, 5275) = 1089.163$, $p < 0.001$) and explained approximately 29.2% of the variance in GOF ($R^2 = 0.292$). While EARC remained a strong positive predictor of GOF ($B = 0.521$, $SE = 0.011$, $t = 45.416$, $p < 0.001$), the relationship between age and GOF reversed

after accounting for rate of spatial learning, with age emerging as a significant negative predictor of GOF ($B = -0.009$ per month, $SE = 9E-4$, $t = -10.454$, $p < 0.001$). The partial regression (added-variable) plot (Figure 3C) illustrates this relationship, showing the effect of age on GOF after accounting for rate of spatial learning (EARC). In practical terms, at comparable levels of learning rate, older animals exhibited greater trial-to-trial variability and less smooth improvement across training trials. This effect suggests that age-related differences in learning-curve conformity may reflect an additional feature of behavior beyond overall rate of acquisition, although the specific behavioral or cognitive mechanisms underlying this pattern cannot be determined from the present data.

3.3. Inter-individual variability in rate of spatial learning

Inter-individual variability (IIV) in rate of spatial learning was quantified as the absolute residuals from the demographic-adjusted EARC model. A linear regression model including age, sex, strain, and their interaction was significant ($F(6, 5271) = 54.303$, $p < 0.001$, $R^2 = 0.058$). IIV increased significantly with age in the F344 (reference) strain ($B = 0.006$ per month, $SE = 0.001$, $t = 4.389$, $p < 0.001$), with positive age-related trends observed across all strains (Figure 4A). Relative to F344, LE rats exhibited lower baseline IIV ($B = -0.108$, $SE = 0.029$, $t = -3.752$, $p < 0.001$), while FBN rats did not differ significantly ($B = -0.077$, $SE = 0.053$, $t = -1.468$, $p = 0.142$). The age $\times$ strain interaction was significant for LE ($B = 0.006$, $SE = 0.002$, $t = 3.572$, $p < 0.001$), indicating a steeper age-related increase in variability compared to F344, whereas the interaction for FBN was not significant ($B = 0.003$, $SE = 0.003$, $t = 1.164$, $p = 0.244$; Figure 4B). Sex was not significantly associated with IIV ($B = -0.033$, $SE = 0.022$, $t = -1.545$, $p = 0.122$).

4. Discussion

A central challenge in the study of cognitive aging in rodent models is the absence of a coordinated, collaborative framework for integrating behavioral data across laboratories. While large-scale, shared datasets have become standard in studies of human cognitive aging and Alzheimer's disease (Ellis et al., 2009; Mueller et al., 2005; Sudlow et al., 2015; Weiner et al., 2017), behavioral data in animal research are typically generated and analyzed within individual laboratories, limiting comparability and reuse. As a result, differences in protocol, scaling, and analytic approach constrain the ability to perform

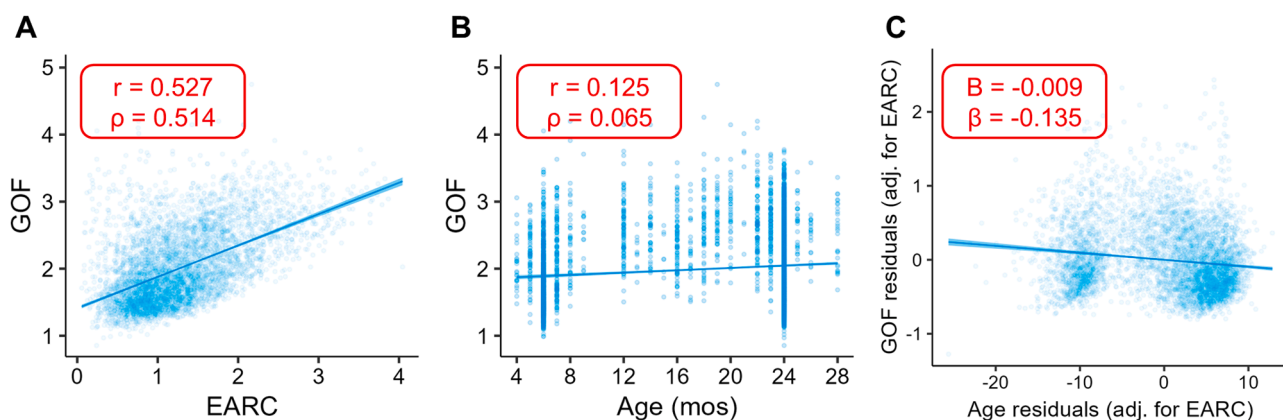


Fig. 3. Relationships between goodness of fit, age, and EARC. A. Relationship between goodness of fit (GOF) and rate of spatial learning (EARC). Each point represents an individual subject. The solid line indicates the line of best fit, with shaded area representing the standard error (SE). Correlation coefficients are shown for both Pearson (r) and Spearman (ρ) analyses. B. Relationship between GOF and age (months). Each point represents an individual subject. The solid line indicates the line of best fit, with shaded area representing the standard error (SE). Correlation coefficients are shown for both Pearson (r) and Spearman (ρ) analyses. C. Partial regression (added-variable) plot illustrating the relationship between age and GOF after accounting for rate of spatial learning (EARC). The x-axis represents residualized age (adjusted for EARC), and the y-axis represents residualized GOF. The solid line indicates the line of best fit, with shaded area representing the standard error (SE). Regression coefficients are reported as unstandardized B and standardized β .

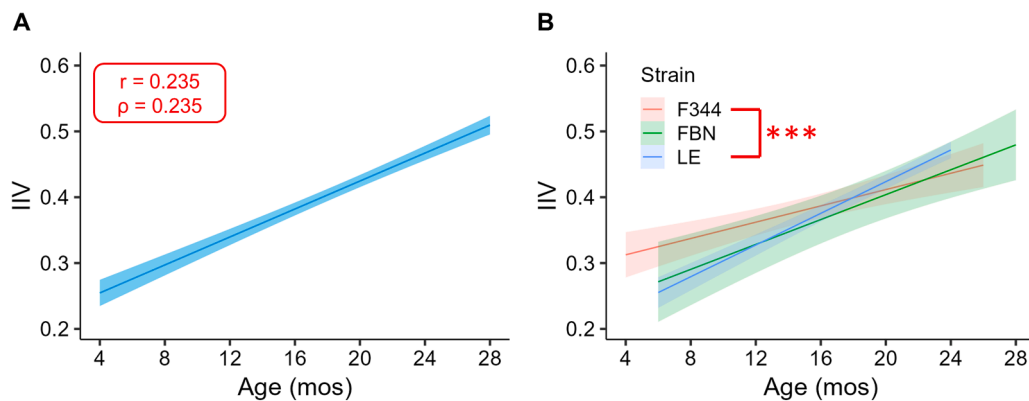


Fig. 4. Age-related changes in inter-individual variability and strain-specific effects. **A.** Relationship between inter-individual variability (IIV) in rate of spatial learning and age (months) across the full cohort. The solid line indicates the line of best fit, with shaded area representing the standard error (SE). Correlation coefficients are shown for both Pearson (r) and Spearman (ρ) analyses. **B.** IIV as a function of age stratified by strain. Separate lines represent best fit for each strain (F344, FBN, LE), with shaded SE, illustrating the interaction between age and strain (*** $p < 0.001$, F344 vs LE).

cross-study, individual-level analyses. The present work addresses this limitation through both the construction of a shared behavioral data repository and the development of an analytical framework demonstrating that cross-laboratory heterogeneity can be accommodated rather than eliminated. By combining normalization in both training and performance domains with model-based characterization of learning trajectories, trial-level data from independent studies can be transformed into a common quantitative space without requiring retrospective harmonization of experimental design. This approach enables extraction of comparable individual-level metrics from datasets that were not originally intended to be analyzed together, establishing a practical framework for large-scale behavioral integration.

The empirical findings validate this framework by demonstrating that biologically meaningful signal is preserved despite substantial heterogeneity in strain, protocol, and laboratory context. The error accumulation rate coefficient (EARC), a parameter indexing the rate at which animals reduce cumulative spatial error across training, showed a robust positive association with age across more than 5000 animals, indicating an age-associated decline in the rate of spatial learning. This pattern is consistent with findings from human cognitive aging research demonstrating slower rates of acquisition and attenuated practice-related gains with advancing age, despite preserved capacity for learning (Hertzog et al., 2008; Salthouse, 2019). This relationship persisted after accounting for non-spatial performance (cue latency) and demographic covariates (strain, sex), indicating that the association between age and EARC persists after accounting for available measures of non-spatial performance. However, because other potential age-related non-cognitive influences were not uniformly documented across all contributing datasets, these analyses cannot completely exclude contributions from generalized performance factors (Bevilacqua et al., 2026). The recovery of this canonical aging effect under conditions of pooled, non-uniform data provides strong evidence that the normalization and modeling approach retains features of hippocampus-dependent learning while mitigating inter-study variability. Consistent with this interpretation, laboratory-specific age effects were examined within the F344 subset, the only strain represented across three laboratories. Although the age-related association varied somewhat among laboratories, the estimated age slope remained positive in all three cohorts. These findings indicate that the harmonization framework recovers a directionally consistent relationship between age and spatial learning across independent laboratory implementations, while accommodating laboratory-specific differences in effect size.

Beyond capturing age-related differences in overall rate of spatial learning, the modeling framework reveals structure in behavior that is not accessible through conventional summary measures. The asymmetric relationship between EARC and goodness of fit (GOF) indicates

that rate of spatial learning constrains the form of learning trajectories: poorer learners exhibit highly stereotyped, model-conforming behavior, whereas better learners show greater dispersion in trajectory shape, consistent with more flexible or exploratory search behavior. When this dependency is accounted for, the relationship between age and GOF reverses, with advancing age associated with reduced GOF, indicating reduced learning-curve conformity and greater variability in trial-to-trial performance independent of overall rate of spatial learning. This dissociation suggests that aging influences not only the rate of acquisition but also the stability of performance across trials, potentially reflecting differences in strategy use, attentional demands, or other factors influencing behavioral expression of learning (Barnes et al., 1997; Burke and Barnes, 2006; Foster, 2012; Gallagher et al., 1993). Conceptually, this distinction separates how well an animal learns from how consistently performance unfolds across training, indicating that age-related impairment reflects not only reduced learning capacity but also changes the organization of behavior over time.

A similar distinction emerges for inter-individual variability (IIV). By defining variability as absolute residuals from a demographic-adjusted EARC model, IIV reflects deviation from expected performance given age and other covariates, rather than raw dispersion. Within this framework, variability increases systematically with age, with additional modulation by strain. This pattern aligns with the view that variability is a defining feature of cognitive aging rather than a statistical byproduct (Hultsch et al., 2002; MacDonald et al., 2006). Importantly, increased IIV captures both individuals with pronounced impairment and those whose performance remains comparable to younger animals, consistent with the coexistence of vulnerability and relative preservation within aged populations—a pattern also observed in human aging and central to frameworks of cognitive reserve and resilience (Stern et al., 2023). This framing situates variability as a tractable target for identifying factors associated with preserved function. The ability to quantify such deviations at scale creates opportunities to link behavioral heterogeneity to underlying biological mechanisms.

The scale and composition of the dataset also allow more constrained interpretation of demographic effects. Although the sample was not balanced by design, no meaningful sex differences were observed in rate of spatial learning across a large cohort, suggesting that age-related trajectories in this task are broadly similar between males and females within the conditions and sex representation currently captured by IDCARD (Faghihi et al., 2026; Koh et al., 2022). Although the female cohort was substantially smaller than the male cohort and unevenly represented across contributing datasets, the present analyses nevertheless included a substantial number of females and did not identify a meaningful sex effect under these sampling conditions. These findings

should therefore be interpreted within the context of the current dataset composition. Further, strain differences were also evident in baseline performance and in age-related changes in variability, but these are more appropriately interpreted as modest differences in trajectory and dispersion rather than as evidence favoring a particular strain as a model of aging. Age-associated decline in spatial learning and increasing heterogeneity were observed across the cohort, reinforcing the importance of considering both central tendency and variability when selecting for, and interpreting behavioral data from, animal models.

More broadly, the significance of this work lies not in the identification of a novel behavioral phenomenon, but in demonstrating that behavioral neuroscience in animal models can support the same class of large-scale, integrative analyses that have transformed human cognitive aging research. By enabling pooled individual-level analysis without requiring prospective harmonization, this framework makes it possible to leverage existing data to address questions that are inaccessible within single studies, including the simultaneous characterization of rate of spatial learning, trajectory structure, and inter-individual variability across thousands of subjects. In this context, the present analysis serves as a proof-of-principle that such integration is both feasible and informative.

Several considerations define the scope of the present work and its interpretation. The current analyses were necessarily limited to the datasets presently represented within the ID-CARD repository, including three commonly used wild-type rat strains with complete hidden-platform acquisition data. Accordingly, the biological findings should be interpreted within the context of the current collaborative resource rather than as a comprehensive characterization of cognitive aging across all rodent models. Similarly, harmonization was demonstrated using a single, well-established proximity-based measure of spatial learning, although the repository includes additional behavioral measures that will support future comparative analyses as the resource expands. Finally, because laboratory, strain, and training protocol were closely associated within the available datasets, laboratory-specific effects could not be interpreted independently in the pooled analyses. These considerations do not diminish the principal contribution of the present study, which is to demonstrate that heterogeneous behavioral datasets can be harmonized to recover robust, biologically meaningful relationships across independent studies. Rather, they define the current scope of a collaborative resource that is designed to expand through continued community participation.

An important implication is that this type of resource creates a foundation for more explicit investigation of variability in aging trajectories, including those related to maintenance, reserve, and resilience. While the present analyses are cross-sectional, the ability to quantify individual differences relative to expected performance provides a framework that can be extended to longitudinal designs (McQuail et al., 2020), which are essential for distinguishing preserved function from delayed decline and for identifying predictors of divergent aging trajectories. Continued expansion of shared behavioral datasets, coupled with longitudinal sampling and integration with biological measures, has the potential to substantially improve mechanistic understanding of cognitive aging while increasing rigor, reproducibility, and translational relevance.

CRedit authorship contribution statement

Shannon J. Moore: Writing – review & editing, Resources, Conceptualization. **Jeffrey M. Long:** Writing – review & editing, Resources, Conceptualization. **Joseph A. McQuail:** Writing – review & editing, Writing – original draft, Supervision, Resources, Methodology, Investigation, Formal analysis, Conceptualization. **Peter R. Rapp:** Writing – review & editing, Resources, Conceptualization. **Thomas C. Foster:** Writing – review & editing, Resources, Conceptualization. **John F. Disterhoft:** Writing – review & editing, Resources, Conceptualization. **Catherine C. Kaczorowski:** Writing – review & editing, Resources,

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Ethics Statement

All experimental procedures involving animals were approved by the Institutional Animal Care and Use Committees at the respective institutions and were conducted in accordance with National Institutes of Health guidelines for the care and use of laboratory animals.

Verification

This manuscript is original, has not been published previously, and is not under consideration for publication elsewhere. All authors have approved the manuscript and agree with its submission. All authors meet authorship criteria. All applicable institutional and national guidelines for the care and use of animals were followed and approved by the appropriate ethics committees. The authors declare that any competing interests have been disclosed. Funding sources are fully reported in the manuscript.

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Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used ChatGPT (OpenAI) to assist with language editing and refinement of figure descriptions and legends. After using this tool, the authors reviewed and edited all content as needed and take full responsibility for the content of the published article.

Declaration of Competing Interest

The authors declare no competing interests.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.neurobiolaging.2026.09.003](https://doi.org/10.1016/j.neurobiolaging.2026.09.003).

Data Availability

Aggregated and trial-level behavioral datasets are available through the ID-CARD framework at GitHub and the R&R Collaboratory website (<https://reserveandresilience.com/animal-cohorts/>). The analysis-ready dataset generated for the present study after application of the inclusion criteria and preprocessing described in the Methods is available from the corresponding author upon reasonable request.

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