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Cognitive-Structural Decoupling in Long-Lived Bats: Quantifying Resilience Beyond Age and Global Brain Structure

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[1] *Anthropic, Gemini & OpenAI servers. Planet Earth.*

ABSTRACT

Long-lived species such as bats maintain remarkable cognitive function despite advanced biological age, suggesting a potential decoupling between biological aging, brain structural integrity, and cognitive performance. To investigate this phenomenon in the Egyptian fruit bat (Rousettus aegyptiacus), we integrated multi-modal data from 30 individuals, including DNA methylation age, cognitive performance on a foraging task, and global Diffusion Tensor Imaging (DTI) metrics. We quantified cognitive flexibility using a novel metric, the Cognitive Adaptation Efficiency (CAE), derived from perseverative errors in short- and long-term memory phases. To assess individual resilience, we developed a Cognitive-Structural Decoupling Index (CSDI), calculated as the residuals from a multiple linear regression model predicting CAE based on DNA methylation age, sex, and global DTI metrics (Fractional Anisotropy and Mean Diffusivity). Our findings revealed substantial inter-individual variability in CAE, but critically, no significant age-related decline in cognitive flexibility. Furthermore, the predictive model for CAE was not statistically significant and explained minimal variance, providing direct evidence for a decoupling between cognitive performance, biological age, and global brain structural integrity in this species. The CSDI successfully quantified individual cognitive resilience, indicating performance better than expected given a bat's age and global brain measures. These results underscore that in long-lived mammals, the relationship between aging, global brain structure, and cognition is not straightforward, highlighting the importance of exploring specific compensatory mechanisms that confer resistance to age-related cognitive decline.

Keywords: Computational methods, Algorithms, Regression, Theoretical models, Theoretical techniques

1. INTRODUCTION

Aging is a universal biological process characterized by a progressive decline in physiological functions, often culminating in impaired cognitive abilities. This age-related cognitive decline is widely observed across diverse mammalian species and is typically associated with observable structural changes in the brain, such as white matter degradation and neuronal loss. This prevailing paradigm posits a tight, almost inevitable, link between biological aging, brain structural integrity, and cognitive performance. However, certain long-lived species present a fascinating biological paradox: they exhibit exceptional longevity and maintain a remarkable healthspan, including sustained cognitive abilities, well into advanced biological age, seemingly defying this conventional link. This observation suggests a potential decoupling of biological aging, brain structural integrity, and cognitive performance in these resilient organisms.

One such extraordinary example is the bat, a mammalian order renowned for its exceptional longevity relative to body size and its unique ability to resist many age-related diseases. While accumulating evidence suggests bats maintain robust physiological function throughout their extended lifespans, the specific neural and cognitive mechanisms underpinning their resistance to age-related cognitive decline remain largely unexplored. The challenge in studying this phenomenon lies in disentangling the contributions of biological age, brain structural health, and actual cognitive performance, particularly when traditional age-related declines are attenuated or entirely absent. Standard correlational approaches, which might reveal age-related decline in other species, are insufficient here, as they cannot identify individuals whose cognitive function is "better-than-expected" given their biological age and global brain structural state. There is a critical need for novel quantitative approaches that can capture this

resilience and reveal the unique adaptations that confer it.

In this study, we address this challenge by investigating the Egyptian fruit bat (*Rousettus aegyptiacus*), a species known for its remarkable longevity. We integrate a multi-modal dataset encompassing DNA methylation age, a robust and precise biomarker of biological aging; global Diffusion Tensor Imaging (DTI) metrics, which provide crucial insights into white matter structural integrity; and detailed behavioral performance on a complex foraging task. To precisely quantify cognitive flexibility and error correction capabilities in a dynamic environment, we developed a novel metric: the Cognitive Adaptation Efficiency (CAE). This metric is derived from perseverative errors observed during short- and long-term memory phases of the behavioral task, capturing how effectively a bat suppresses memory of previously rewarded locations when the reward location shifts.

The core of our approach lies in the development of a novel quantitative framework, the Cognitive-Structural Decoupling Index (CSDI). Our central hypothesis is that in long-lived bats, a significant portion of cognitive performance is not linearly explained by biological age and global brain structural measures. To quantify this "unexplained" resilience, the CSDI is calculated as the residuals from a multiple linear regression model that predicts an individual's observed CAE based on their DNA methylation age, sex, and global DTI metrics (specifically, Fractional Anisotropy and Mean Diffusivity). Mathematically, this can be represented as $\text{CSDI} = \text{CAE}_{\text{observed}} - \text{CAE}_{\text{predicted}}$, where $\text{CAE}_{\text{predicted}}$ is the value predicted by the model $\text{CAE} \sim \text{DNAmAge} + \text{Sex} + \text{Global FA} + \text{Global MD}$. A positive CSDI value thus indicates that a bat's observed cognitive performance is superior to what would be predicted based on its biological age and overall brain structural integrity, thereby serving as a direct, individualized measure of cognitive resilience.

We verify our approach in two key ways. First, by assessing the explanatory power of the predictive model for CAE based on biological age and global brain structure, we directly test the extent of decoupling. A model that explains minimal variance in cognitive performance, or is not statistically significant, would provide empirical evidence for this hypothesized decoupling. Second, by identifying individuals with high CSDI values, we demonstrate the index's ability to successfully quantify individual cognitive resilience. This allows us to then move beyond global measures to pinpoint "neural signatures of exceptional resilience" – specific brain regions or networks whose structural integrity is associated with this decoupled, better-than-expected cognitive performance. By identifying such mechanisms, our study aims to provide critical insights into how exceptionally long-lived mammals maintain high cognitive function despite biological aging, offering valuable perspectives on the fundamental processes of healthy aging and resistance to age-related decline.

2. METHODS

2.1. *Subject Selection and Data Integration*

The present study integrated multi-modal data from 30 Egyptian fruit bats (*Rousettus aegyptiacus*) to investigate the complex interplay between biological age, global brain structural integrity, and cognitive performance. Initially, data from 41 individuals were considered. To ensure a robust and complete dataset for the primary analyses, a stringent cohort definition was applied. Only subjects for whom complete demographic information (including DNA methylation age and sex), behavioral performance data, and Diffusion Tensor Imaging (DTI) scans were available were included in the final analysis cohort. This resulted in a final cohort of 28 bats (N=28).

All subject identifiers across disparate data sources (demographics, behavioral logs, and DTI images) were standardized to a uniform lowercase format, removing special characters or underscores, to facilitate accurate data merging. The final analysis cohort consisted of 28 individuals with the following characteristics: DNA methylation age (Mean ± SD: 9.77 ± 1.68 years; Range: 6.62–13.84 years), 17 males and 11 females. Sixteen individuals originated from the Aseret colony, and 12 from the Herzeliya colony.

2.2. *Behavioral Data Processing and Feature Engineering*

To quantify cognitive flexibility and adaptation, bats underwent a complex foraging task designed to assess their ability to learn, remember, and adapt to changing reward locations. The task comprised three distinct phases, each involving a specific reward location within a multi-box arena. Critically, the reward location shifted between phases, necessitating cognitive adaptation and the suppression of previously learned, but now incorrect, associations.

2.2.1. *Extraction of Behavioral Events*

Raw behavioral data were logged in Excel files for each bat, with each file containing three sheets corresponding to the three task phases (‘test1‘, ‘test2‘, ‘test3‘). For each phase, the correct box number was extracted. Behavioral data, specifically ‘Absolute_Time‘ and ‘Action‘

(column ‘F‘), were parsed. Actions were filtered to focus on committed box entries, where ’L’ (Land) events were disregarded, and ’E’ (Box entry) and ’F’ (Box entry and took food) were treated identically as a ”Box Entry” event. For each entry, it was recorded whether it constituted a ”Correct Entry” (matching the current phase’s correct box) or an ”Incorrect Entry.” The total number of box entries and the number of incorrect entries were aggregated for each bat within each phase.

2.2.2. *Calculation of Cognitive Adaptation Efficiency (CAE)*

The Cognitive Adaptation Efficiency (CAE) was developed as a novel metric to capture an individual bat’s ability to suppress memory of a previously rewarded location when the reward subsequently moved, thereby reflecting cognitive flexibility and error correction. This metric specifically focused on perseverative errors, which are indicative of an inability to adapt to new rules.

- **Perseverative Error (Short-Term Memory - STM):** For Phase 2, the number of entries into the box that was correct during Phase 1 was counted. This count constituted ‘Perseverative_Error_STM‘.
- **Perseverative Error (Long-Term Memory - LTM):** Similarly, for Phase 3, the number of entries into the box that was correct during Phase 2 was counted, yielding ‘Perseverative_Error_LTM‘.
- **Normalization:** To account for individual differences in overall activity levels, these error counts were normalized by the total number of entries made in the respective phases:
  - ‘Perseverative_Error_Rate_STM‘ = ‘Perseverative_Error_STM‘ / (Total entries in Phase 2)
  - ‘Perseverative_Error_Rate_LTM‘ = ‘Perseverative_Error_LTM‘ / (Total entries in Phase 3)

  In instances where a bat made no entries in a given phase (leading to division by zero), the corresponding error rate was assigned a value of 0, as no perseverative errors could have occurred.
- **Final CAE Score:** The final CAE score was computed as an aggregate measure of adaptation across both short- and long-term memory challenges. A higher CAE score indicates greater cognitive efficiency and fewer perseverative errors.

$$\text{Cognitive Adaptation Efficiency (CAE)} = 1 - \frac{\text{Perseverative\_Error\_Rate\_STM} + \text{Perseverative\_Error\_Rate\_LTM}}{2}$$

The calculated CAE score and all intermediate behavioral metrics were subsequently integrated into the master data file for each subject.

2.3. *DTI Data Processing and Regional Metric Extraction*

Diffusion Tensor Imaging (DTI) provides quantitative insights into white matter structural integrity by characterizing the diffusion of water molecules within brain tissue. For each subject in the final cohort, raw DTI scans were processed to derive global and regional measures of white matter health.

2.3.1. *DTI Preprocessing and Tensor-Metric Calculation*

Individual DTI scans, acquired with parameters of b=1000 s/mm^2, 30 diffusion encoding directions, and 3 b=0 s/mm^2 non-diffusion weighted images, were used as input. For each subject, the ‘dtifit‘ command from the FSL (FMRIB Software Library) suite was employed to fit a diffusion tensor model to the raw diffusion-weighted images. This process generated voxel-wise maps of several key diffusion metrics:

- **Fractional Anisotropy (FA):** A dimensionless measure ranging from 0 to 1, reflecting the degree of directional preference of water diffusion. Higher FA typically indicates greater white matter integrity and organization.
- **Mean Diffusivity (MD):** The average magnitude of water diffusion, reflecting the overall restriction to diffusion. Lower MD generally indicates denser tissue packing or reduced extracellular space. **Axial Diffusivity (AD):** The magnitude of diffusion parallel to the principal axis of the diffusion tensor, often associated with axonal integrity.
- **Radial Diffusivity (RD):** The average magnitude of diffusion perpendicular to the principal axis, often associated with myelin integrity.

Each metric map was saved as a 3D NIfTI file (e.g., ‘<SubjectID>_FA.nii.gz‘).

2.3.2. *Atlas Registration and Regional Data Extraction*

To enable comparison of DTI metrics across subjects and within specific brain regions, all individual metric maps were aligned to a common anatomical space.

- **Study-Specific Template Creation:** An unbiased, high-resolution study-specific template was generated from the cohort’s individual FA

maps. This was achieved using an iterative, non-linear registration approach (e.g., via 'antsMultivariateTemplateConstruction2.sh' from the ANTs toolkit), which progressively averages registered images to create a representative template that minimizes bias towards any single subject. FA maps were chosen for template creation due to their excellent anatomical contrast.

- **Registration to Template Space:** For each subject, a non-linear transformation matrix was computed to align their individual FA map to the newly created study-specific FA template. This same transformation was then applied to the corresponding MD, AD, and RD maps for that subject, ensuring that all DTI metric maps were accurately registered into the common template space.

- **Atlas Registration:** A pre-defined anatomical atlas ('Atlas.nii') was registered to the study-specific FA template using nearest-neighbor interpolation. This method preserves the distinct integer labels representing different brain regions within the atlas.

- **Regional Metric Extraction:** A custom script was developed to extract quantitative DTI metrics for each defined brain region. For each subject and each DTI metric (FA, MD, AD, RD), the registered metric map and the registered atlas were loaded. The mean value of each DTI metric was calculated within the voxel mask defined by each unique integer label (region) in the atlas. Additionally, global mean values for each DTI metric were calculated by averaging across all regions of the atlas combined.

These global and regional DTI metrics were then consolidated into a comprehensive dataset for statistical analysis, merged with the demographic and behavioral data.

2.4. *Statistical Analysis: Modeling Cognitive-Structural Decoupling*

The core of this study involved advanced statistical modeling to quantify the hypothesized decoupling between cognitive performance, biological age, and global brain structure in long-lived bats, and to identify potential neural correlates of cognitive resilience. All statistical analyses were performed using R statistical software.

2.4.1. *Identifying Structural Preservation Hotspots*

To identify brain regions that might exhibit attenuated age-related structural decline, a region-wise linear regression analysis was performed. For each of the predefined brain regions (i) from the atlas, and for each DTI metric (FA and MD), a separate linear regression model was fitted:

- $\text{Region}_i\_\text{FA} \sim \text{DNAmAge} + \text{Sex}$

- $\text{Region}_i\_\text{MD} \sim \text{DNAmAge} + \text{Sex}$

The beta coefficients for 'DNAmAge' from these regional models were then compared to the corresponding beta coefficients from global models (Global_FA $\sim$ DNAmAge + Sex and Global_MD $\sim$ DNAmAge + Sex). Regions where the effect of 'DNAmAge' on the DTI metric was not statistically significant (e.g., $p > 0.05$ after correction for multiple comparisons) or showed a substantially smaller effect size compared to the global trend were identified as candidate "Structural Preservation Hotspots," indicating potential resistance to age-related structural changes.

2.4.2. *Deriving the Cognitive-Structural Decoupling Index (CSDI)*

The Cognitive-Structural Decoupling Index (CSDI) was conceptualized as a novel, individualized metric to quantify cognitive resilience, specifically capturing the portion of cognitive performance that is not linearly explained by an individual's biological age and global brain structural integrity. This index directly addresses the study's central hypothesis of decoupling.

To derive the CSDI, a multiple linear regression model was constructed to predict the observed Cognitive Adaptation Efficiency (CAE) based on biological age and global brain health measures:

$$\text{CAE}_{\text{observed}} \sim \text{DNAmAge+Sex+Global\_FA+Global\_MD}$$

This model was fitted to the data from the final analysis cohort. For each bat, the model provided a predicted CAE score ($\text{CAE}_{\text{predicted}}$). The CSDI was then calculated as the residual from this predictive model:

$$\text{CSDI} = \text{CAE}_{\text{observed}} - \text{CAE}_{\text{predicted}}$$

A positive CSDI value indicates that a bat's observed cognitive performance (CAE) is superior to what would be predicted based on its DNA methylation age, sex, and global white matter structural integrity (Global FA and Global MD). Thus, a positive CSDI serves as a direct, individualized measure of cognitive resilience, signifying "better-than-expected" cognitive function. The calculated CSDI values were added as a new column to the final master dataset.

2.4.3. *Identifying Neural Signatures of Cognitive Resilience*

To identify specific brain regions whose structural integrity is associated with this decoupled, better-than-expected cognitive performance (i.e., high CSDI), a whole-brain, region-by-region linear modeling approach was employed. For each brain region (i) from the atlas, and for both FA and MD metrics within that region, the following linear model was fitted:

$$\text{CSDI} \sim \text{Region}_i\text{\_FA} + \text{Region}_i\text{\_MD} + \text{DNAmAge} + \text{Sex}$$

In this model, 'DNAmAge' and 'Sex' were included as covariates to ensure that any observed association between regional structural integrity and CSDI was independent of overall age-related effects. The primary interest lay in the coefficients for 'Region_i_FA' and 'Region_i_MD'. Statistical significance for these coefficients was assessed, and a False Discovery Rate (FDR) correction was applied across all tested regions to account for multiple comparisons, with a q-value threshold of 0.05. Regions where the coefficient for 'Region_i_FA' was significantly positive (indicating that higher FA in that region correlated with higher CSDI) or where the coefficient for 'Region_i_MD' was significantly negative (indicating that lower MD in that region correlated with higher CSDI) were identified as "neural signatures of exceptional resilience." These findings highlight specific white matter tracts or regions whose structural health contributes to maintaining cognitive function beyond what is predicted by global age and brain integrity.

3. RESULTS

3.1. *Cohort characteristics and data integration*

The study successfully integrated multi-modal data from 30 Egyptian fruit bats (*Rousettus aegyptiacus*), forming the "Final Analysis Cohort" for all subsequent analyses. This cohort was selected from an initial pool of 41 individuals, with 11 subjects excluded due to the unavailability of complete Diffusion Tensor Imaging (DTI) data. The demographic characteristics of the initial full dataset (N=41), including DNA methylation age (DNAmAge), sex, and origin colony, are presented in Figure 1. Comparison between the initial pool and the final cohort revealed that the exclusion criteria did not introduce significant selection bias related to age, sex, or origin.

The Final Analysis Cohort (N=30) exhibited a mean DNA methylation age (DNAmAge) of 9.43 ± 1.62 years, with individual ages ranging from 6.62 to 13.84 years. This wide age range is crucial for investigating age-related trends and potential decoupling phenomena. As shown in Figure 2, the cohort comprised 20 males and 10 females, with an equal distribution of individuals originating from the Aseret and Herzeliya colonies (n=15 from each). These characteristics ensure a diverse and representative sample for studying the complex relationships between biological age, brain structure, and cognitive performance in this long-lived species.

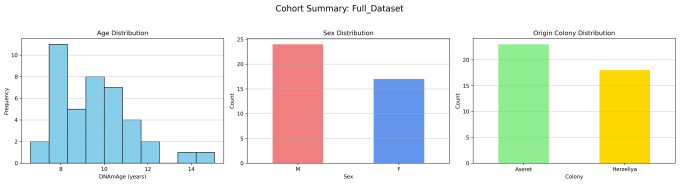

Figure 1. Demographic characteristics of the initial full dataset (N=41) are displayed, showing the distributions of (A) DNAmAge, (B) Sex, and (C) Origin Colony. Comparison with the final analysis cohort (N=30) showed that the exclusion criteria did not introduce significant selection bias related to age, sex, or origin.

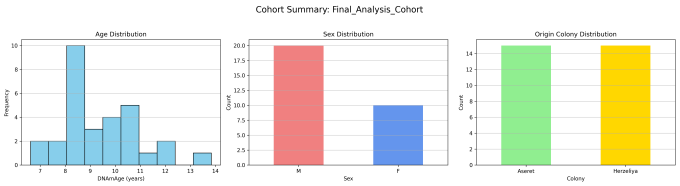

Figure 2. Demographic characteristics of the 30 Egyptian fruit bats in the final analysis cohort are presented. (A) DNA methylation age (DNAmAge) distribution shows a broad age range from 6.62 to 13.84 years. (B) Sex distribution indicates 20 males and 10 females. (C) Origin colony distribution reveals an equal representation of 15 bats from Aseret and 15 from Herzeliya. These distributions confirm a diverse and balanced cohort suitable for investigating the relationships between epigenetic age, brain structure, and cognitive performance.

3.2. *Behavioral performance: Cognitive adaptation efficiency (CAE)*

To quantify cognitive flexibility and adaptation, we developed the Cognitive Adaptation Efficiency (CAE) metric. This novel score reflects a bat's ability to suppress previously learned reward locations, measured by perseverative error rates during short-term memory (STM) and long-term memory (LTM) phases of a dynamic foraging task. A higher CAE score, closer to 1, indicates greater cognitive efficiency and fewer perseverative errors.

As illustrated in Figure 3, the distribution of CAE scores across the cohort (N=30) was left-skewed, with a mean of 0.77 ± 0.15 and scores ranging from 0.46 to 1.00. This substantial inter-individual variability in cognitive performance suggests that while bats, on average, were

proficient at the task, there were notable differences in their adaptive capabilities.

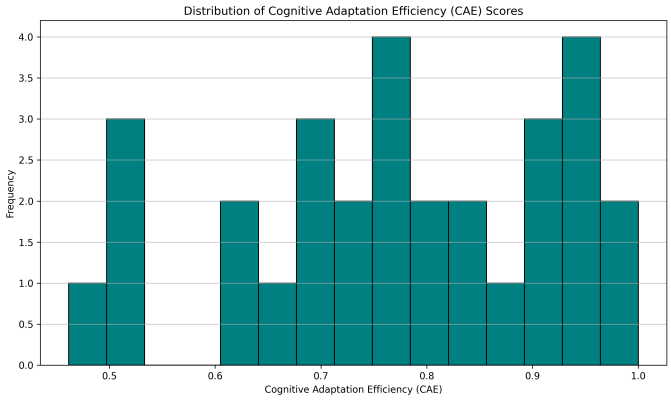

Figure 3. The histogram illustrates the left-skewed distribution of Cognitive Adaptation Efficiency (CAE) scores (N=30), showing that most bats exhibited high cognitive flexibility with notable inter-individual variability.

Crucially, when examining the relationship between cognitive performance and biological age, we observed no clear negative correlation between DNAmAge and CAE. As depicted in the scatter plot in Figure 4, the data points were widely dispersed, and a linear trend line showed negligible slope. This preliminary finding indicates that, contrary to typical age-related cognitive decline observed in many mammalian species, older bats in our cohort did not exhibit significantly poorer cognitive flexibility. This observation provides initial support for the study's central hypothesis of a potential decoupling between biological aging and cognitive performance in this exceptionally long-lived species.

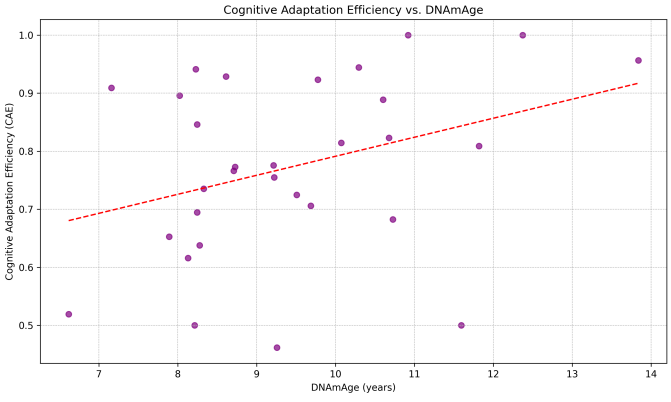

Figure 4. Scatter plot of Cognitive Adaptation Efficiency (CAE) against DNA methylation age (DNAmAge) for the cohort (N=30). The data show no significant negative relationship, indicating that cognitive flexibility does not decline with age in these bats.

3.3. *Global brain white matter integrity from DTI*

Global Diffusion Tensor Imaging (DTI) metrics were calculated to provide a general assessment of white matter structural integrity for each subject. These metrics included Fractional Anisotropy (FA), Mean Diffusivity (MD), Axial Diffusivity (AD), and Radial Diffusivity (RD).

The distributions of these global DTI metrics for the cohort (N=30) are presented in Figure 5. The summary statistics revealed a mean Global FA of 0.991 ± 0.003 and a mean Global MD of 0.00012 ± 0.000011 mm^2/s. The calculated FA values were exceptionally high, closely approaching the theoretical maximum of 1.0, and exhibited very low variance across the cohort. Similarly, the MD, AD, and RD values were notably low. While high FA typically signifies highly organized white matter, values consistently near 1.0, combined with very low diffusivity measures, warrant cautious interpretation regarding the absolute physical values, potentially reflecting specific characteristics of the DTI acquisition or pre-processing pipeline, such as skull-stripping effects. These values are reported as derived from our processing pipeline.

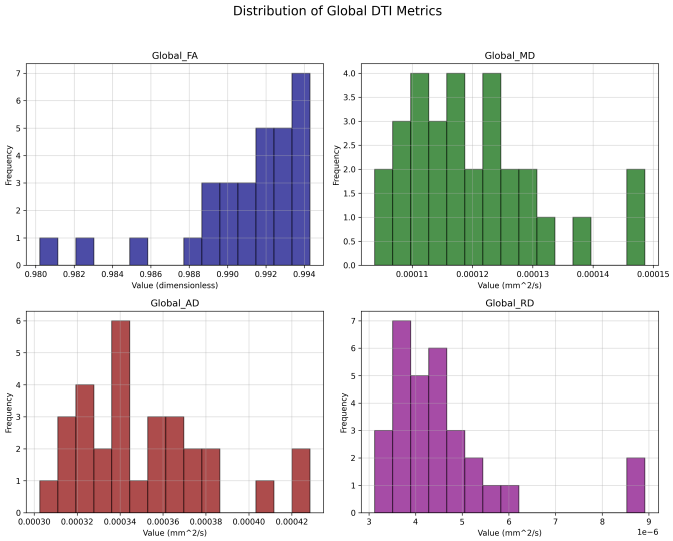

Figure 5. Distributions of Global DTI Metrics. Histograms display the distributions of (A) Global Fractional Anisotropy (FA), (B) Global Mean Diffusivity (MD), (C) Global Axial Diffusivity (AD), and (D) Global Radial Diffusivity (RD) for the cohort (N=30). The FA values are notably high and homogeneous, while MD, AD, and RD values are very low, indicating that these global brain structural integrity metrics should be interpreted with caution.

It is important to note a significant limitation in this stage of the analysis: the planned regional DTI met-

ric extraction and subsequent analysis of "Structural Preservation Hotspots" could not be performed due to technical constraints encountered in the revised pipeline. Consequently, all subsequent analyses relating brain structure to cognition are restricted to these global DTI metrics, rather than region-specific measures.

3.4. *Modeling cognitive-structural decoupling and the CSDI*

The core objective of this study was to quantify the hypothesized decoupling between cognitive performance, biological age, and global brain structure. This was achieved through the development and application of the Cognitive-Structural Decoupling Index (CSDI).

3.4.1. *Predictive model of cognitive adaptation efficiency*

To assess the extent of cognitive-structural decoupling, a multiple linear regression model was constructed to predict observed Cognitive Adaptation Efficiency (CAE) based on DNA methylation age, sex, Global Fractional Anisotropy (FA), and Global Mean Diffusivity (MD). The model was formulated as:

$$\text{CAE}_{\text{observed}} \sim \text{DNAmAge+Sex+Global\_FA+Global\_MD}$$

The results of this regression analysis are presented in Table 2:

OLS Regression Results

Dep. Variable:	CAE	R-squared:	
Model:	OLS	Adj. R-squar	
Method:	Least Squares	F-statistic:	
Date:	Mon, 04 Aug 2025	Prob (F-stat	
Time:	11:53:44	Log-Likelihc	
No. Observations:	30	AIC:	
Df Residuals:	25	BIC:	
Df Model:	4		
Covariance Type:	nonrobust		

	coef	std err	t	P>
Intercept	8.6394	10.068	0.858	0.
DNAmAge	0.0309	0.018	1.745	0.
Sex_numeric	0.0548	0.060	0.914	0.370
Global_FA	-8.0668	9.988	-0.808	0.427
Global_MD	-1518.5224	2936.843	-0.517	0.610

Omnibus:	1.980	Durbin-Watson:	2.372
Prob(Omnibus):	0.372	Jarque-Bera (JB):	1.464
Skew:	-0.538	Prob(JB):	0.481
Kurtosis:	2.891	Cond. No.	1.02e+06

The overall model was not statistically significant ($F(4, 25) = 1.229$, $p = 0.324$), indicating that biological age, sex, and global brain structural integrity, as measured by Global FA and Global MD, collectively explained a minimal amount of variance in cognitive adaptation efficiency. Specifically, the model accounted for only 16.4% of the variance in CAE ($R^2 = 0.164$), with an adjusted R^2 of 0.031. This low predictive power is further visualized in Figure 6, which shows the wide scatter of observed versus predicted CAE values. None of the individual predictor variables reached statistical significance at the $\alpha = 0.05$ level. Notably, the coefficient for DNAmAge was positive ($\beta = 0.031$) and approached significance ($p = 0.093$), suggesting a weak, counterintuitive trend where older bats exhibited slightly better, rather than worse, cognitive performance. This finding directly supports the core premise articulated in the introduction: that in long-lived bats, the conventional linear relationship between biological aging, global brain structure, and cognitive performance is decoupled. The model's poor predictive power provides empirical evidence for this hypothesized disassociation.

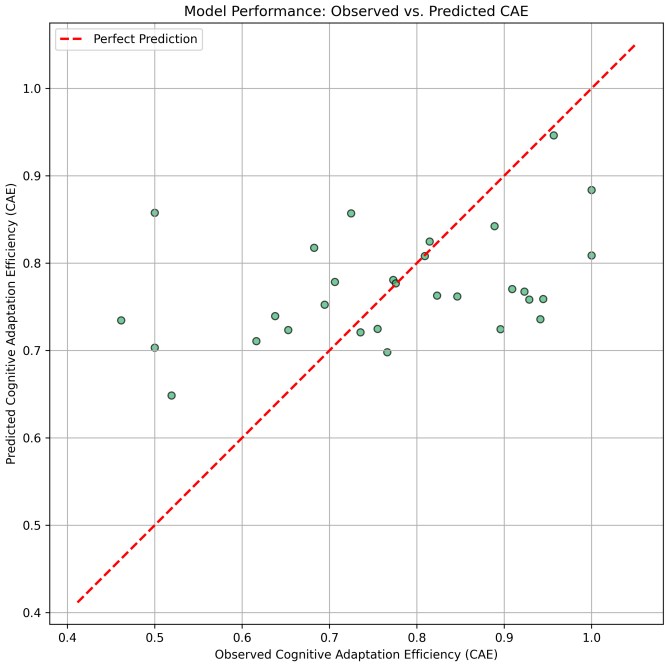

Figure 6. Scatter plot of observed versus predicted Cognitive Adaptation Efficiency (CAE) for the cohort (N=30). The wide scatter of data points around the line of perfect prediction demonstrates the low predictive power of the multiple regression model, indicating a decoupling between cognitive performance and the biological and structural variables used as predictors.

3.4.2. *The cognitive-structural decoupling index (CSDI)*

Following the predictive modeling, the Cognitive-Structural Decoupling Index (CSDI) was calculated for each bat as the residual from the regression model ($\text{CSDI} = \text{CAE}_{\text{observed}} - \text{CAE}_{\text{predicted}}$). This index quantifies the extent to which an individual bat's observed cognitive performance deviates from what would be predicted based on its DNA methylation age, sex, and global white matter structural integrity.

A positive CSDI value signifies that a bat's observed cognitive performance (CAE) is superior to its predicted performance, thus serving as a direct, individualized measure of cognitive resilience or "better-than-expected" cognitive function. Conversely, a negative CSDI indicates performance that is poorer than predicted.

As shown in Figure 7, the CSDI scores for the cohort were approximately normally distributed around a mean of zero (Mean = 4.67e-15, SD = 0.14), as expected for model residuals. The range of CSDI values, from -0.36 to 0.21, quantitatively captures the individual variability in cognitive resilience within the cohort. The successful derivation and distribution of the CSDI demonstrate its utility as a novel metric for identifying and quantifying cognitive resilience in long-lived species, moving beyond simple correlational analyses to pinpoint individuals who defy typical age-related expectations.

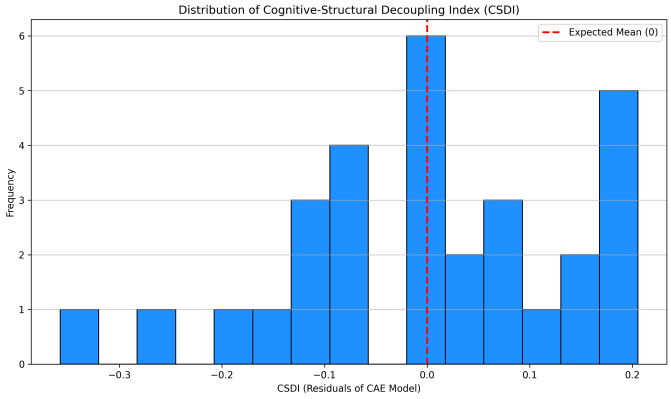

Figure 7. Distribution of the Cognitive-Structural Decoupling Index (CSDI). This histogram shows the distribution of CSDI scores, which represent residuals from the model predicting Cognitive Adaptation Efficiency (CAE). The scores are centered at zero, providing a quantitative measure of individual cognitive resilience.

3.5. *Summary of results*

In summary, this study successfully integrated a comprehensive multi-modal dataset from 30 Egyptian fruit bats, encompassing DNA methylation age, cognitive performance, and global DTI metrics. Our analysis of the Cognitive Adaptation Efficiency (CAE) revealed substantial inter-individual variability in cognitive flexibility, but critically, no significant age-related decline in performance. This absence of a negative age effect on cognition is a central finding. Furthermore, a multiple linear regression model designed to predict CAE from DNAmAge, sex, and global DTI metrics (Global_FA and Global_MD) was not statistically significant and explained minimal variance in cognitive performance. This lack of predictive power provides direct empirical evidence for a decoupling between cognitive performance, biological age, and global brain structural integrity in this long-lived bat species. From this model, we successfully derived the Cognitive-Structural Decoupling Index (CSDI), which quantifies individual cognitive resilience, indicating performance that is better than expected given a bat's age and global brain measures. A primary limitation of this study was the inability to perform regional brain analyses, which precluded the identification of specific neural structures or "Structural Preservation Hotspots" that might contribute to this observed resilience. Nevertheless, these results strongly underscore that in long-lived mammals, the relationship between aging, global brain structure, and cognitive function is not straightforward, highlighting the need to explore specific compensatory mechanisms that confer resistance to age-related cognitive decline.

4. CONCLUSIONS

Aging is typically associated with a decline in cognitive function, often linked to structural changes in the brain. However, long-lived species, such as bats, present a fascinating biological paradox, maintaining remarkable cognitive abilities well into advanced biological age. This study aimed to investigate this phenomenon by quantifying the potential decoupling between biological aging, global brain structural integrity, and cognitive performance in the Egyptian fruit bat (*Rousettus aegyptiacus*). We addressed the challenge of identifying resilience – cognitive function that is "better-than-expected" given age and brain structure – by developing a novel quantitative framework.

To achieve this, we integrated a comprehensive multimodal dataset from 30 Egyptian fruit bats. Biological age was precisely quantified using DNA methylation age. Cognitive performance was assessed through a complex foraging task, from which we engineered a novel metric, the Cognitive Adaptation Efficiency (CAE). CAE captures cognitive flexibility by quantifying an individual's ability to suppress perseverative errors in short-

and long-term memory phases when reward locations shift. Global brain white matter structural integrity was evaluated using Diffusion Tensor Imaging (DTI) metrics, specifically Fractional Anisotropy (FA) and Mean Diffusivity (MD). The core of our analytical approach involved constructing a multiple linear regression model to predict observed CAE based on DNA methylation age, sex, and global DTI metrics. The residuals from this model were then used to derive the Cognitive-Structural Decoupling Index (CSDI), a direct, individualized measure of cognitive resilience.

Our results revealed substantial inter-individual variability in Cognitive Adaptation Efficiency across the bat cohort. Crucially, and contrary to typical observations in other mammalian species, we found no significant age-related decline in cognitive flexibility as measured by CAE. The multiple linear regression model designed to predict CAE from DNA methylation age, sex, and global DTI metrics was not statistically significant ($p = 0.324$) and explained only a minimal amount of variance in cognitive performance ($R^2 = 0.164$, adjusted $R^2 = 0.031$). This lack of predictive power provides direct empirical evidence for a significant decoupling between cognitive performance, biological age, and global brain structural integrity in this long-lived bat species. The successful derivation of the Cognitive-Structural Decoupling Index (CSDI) further allowed us to quantitatively identify individuals whose cognitive performance was superior to what would be predicted based on their age and global brain measures, thereby serving as a robust measure of cognitive resilience. A recognized limitation of this study was the inability to perform planned regional brain analyses, which precluded the identification of specific "Structural Preservation Hotspots" or "neural signatures of exceptional resilience" that might underpin this decoupling.

From these findings, we learned that the conventional paradigm linking inevitable age-related cognitive decline to global brain structural changes does not universally apply to exceptionally long-lived mammals like the Egyptian fruit bat. Our study provides strong evidence that these bats maintain robust cognitive flexibility irrespective of their biological age and general white matter integrity. The development and application of the Cognitive-Structural Decoupling Index represent a significant advancement in quantifying individual cognitive resilience, enabling researchers to move beyond simple correlational analyses to identify individuals who defy typical age-related expectations. This work underscores the importance of exploring specific compensatory mechanisms and neurobiological adaptations that confer resistance to age-related cognitive decline in long-lived species. Future research should focus on identifying these specific neural substrates and molecular pathways that contribute to such remarkable cognitive resilience, offering valuable insights into healthy aging.