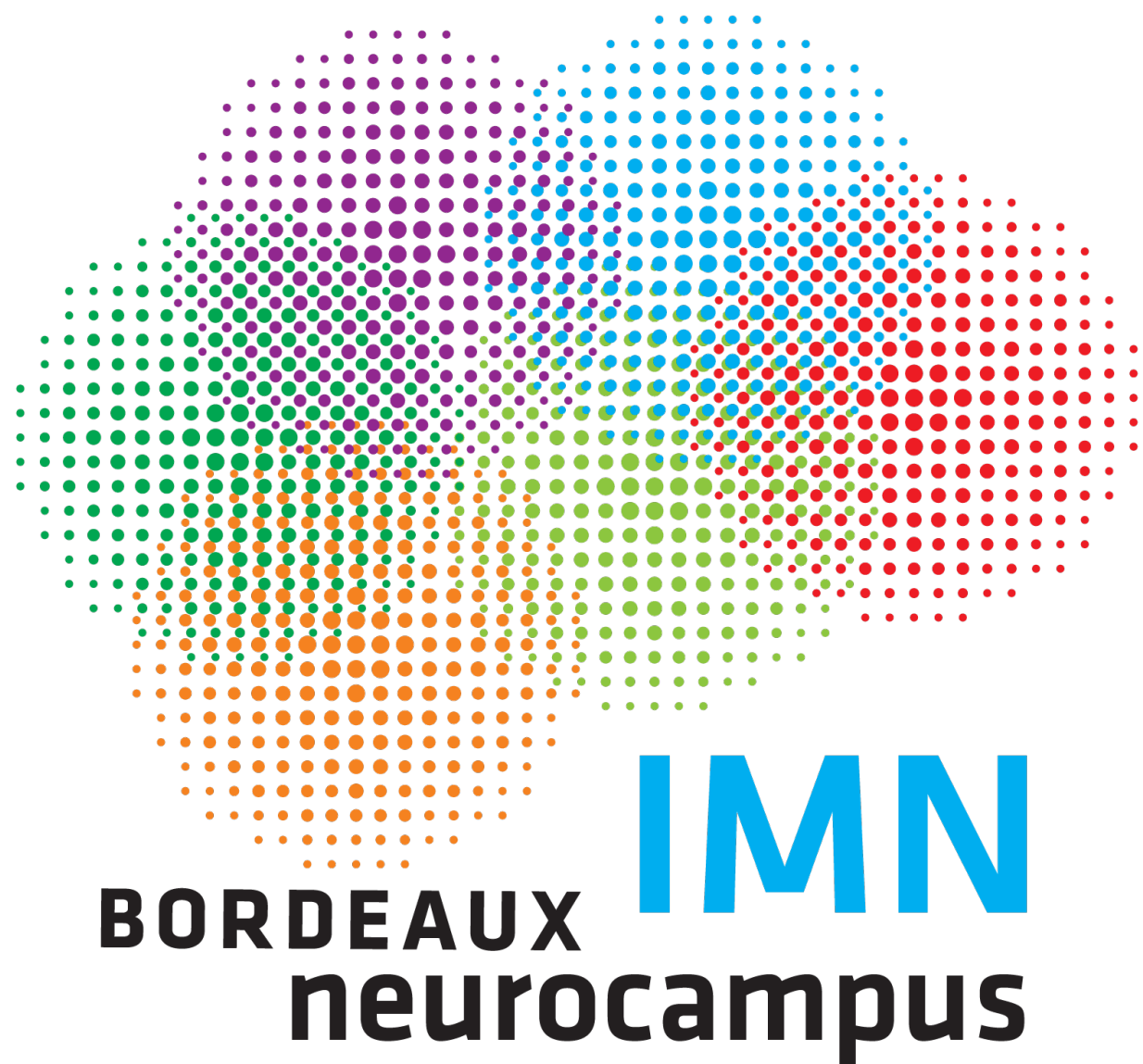


The Biological Scaling Of Alzheimer's Disease Neuropathological Changes Across Primate Species

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INTRODUCTION

Alzheimer's Disease (AD) is often seen as human-specific, yet many studies have found amyloid plaques, neuritic plaques, and NFTs in other species, especially non-human primates (NHPs).

In comparative anatomy, **allometry** refers to the co-variation of traits across species, where proportions, shapes and functions of organs change with body size as a whole. Developmental biology explains such allometric patterns by differences in the rate or duration of developmental process. When it comes to stages of life history, common sense often assumes strict conservation of proportions as exemplified by the widespread belief that the age of a cat should be multiplied by 7 to determine its “human-equivalent” age.

However, the age-related occurrence of **AD neuropathological changes (ADNC)** in non-human primates (NHPs) and their comparison with humans has not been formally studied. Moreover, **a conceptual framework for interpreting the spontaneous occurrence of ADNC in NHPs has yet to be established.**

Analyzing the scaling of amyloid plaques, neuritic plaques, and NFTs in NHPs may shed light on the biology of sporadic AD.

Method

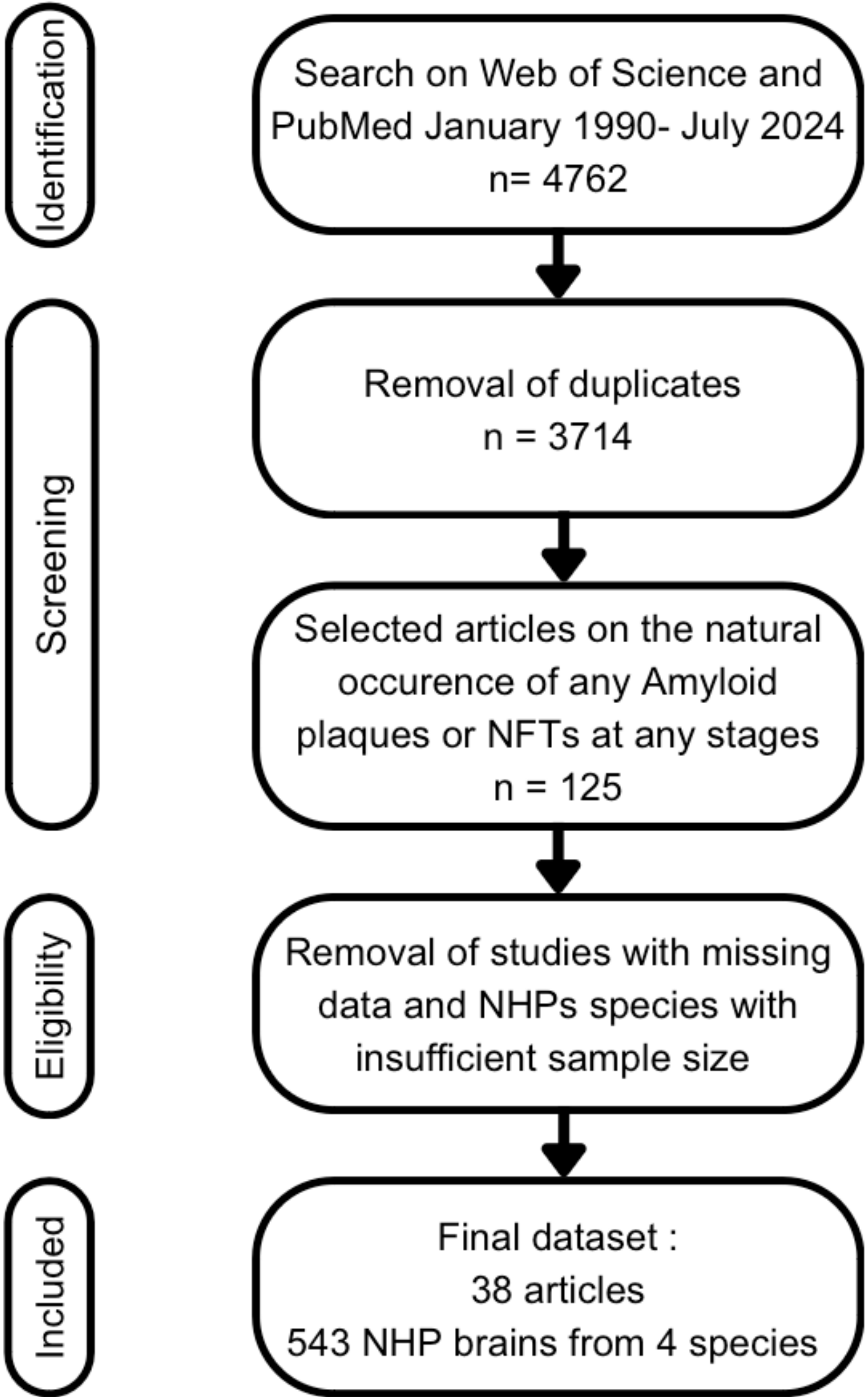


Fig. 2 Flow chart of the study selection for systematic review. A literature search in **PubMed** and **Web of Science** was performed for **56 NHP species**. The search was completed with a generic search for the same keywords associated with “non-human primate” OR “ape”. Titles and abstracts were reviewed to select observational studies reporting the search for **both naturally occurring amyloid and tau lesions**. Final analyses were based on a selection of species for which we had at least **n brains by decades**.

Results

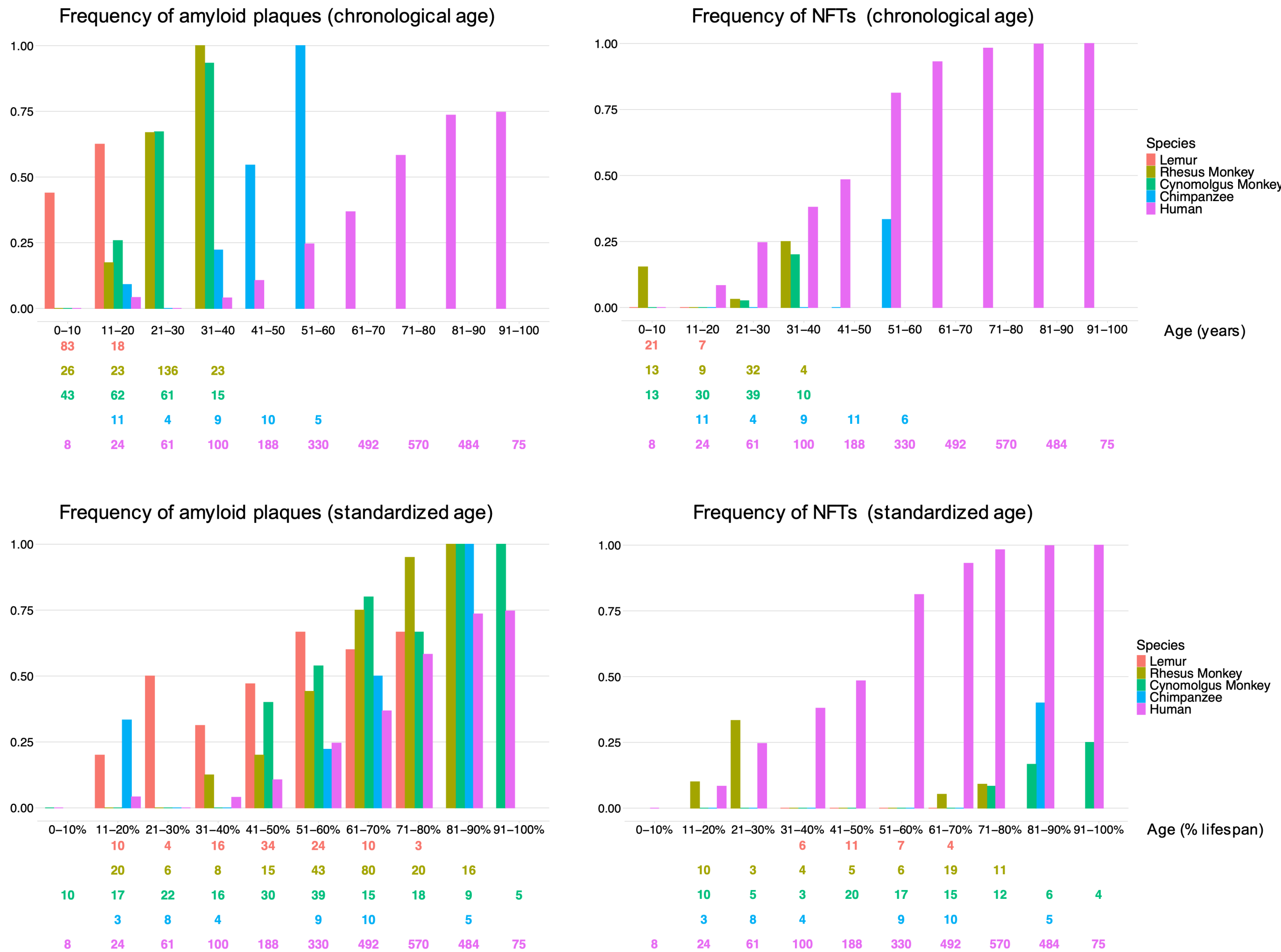


Fig. 3 Chronological (age in years) and standardized (relative to the maximum longevity of each species) frequencies of amyloid plaques and NFTs in lemurs, cynomolgus monkeys, rhesus monkeys, chimpanzees and humans. The number of individuals (n) studied for each species and each age group is indicated below each diagram

	Amyloid plaques Model 1 (Time)	Amyloid plaques Model 2 (Time/Maximum lifespan)	Neurofibrillary tangles Model 1 (Time)	Neurofibrillary tangles Model 2 (Time/Maximum lifespan)
Humans	Ref	Ref	Ref	Ref
Chimpanzees Log(OR) [95% CI]	2.6 [1.7; 3.5]	0.7 [-0.13; 1.5]	-3.0 [-4.8; -1.7]	-7.0 0 [-9.5; -5.2]
Rhesus monkeys Log(OR) [95% CI]	6.0 [4.7; 7.5]	1.3 [0.9; 1.7]	-1.8 [-3.3; -0.8]	-7.6 0 [-9.8; -6.0]
Cynomolgus monkeys Log(OR) [95% CI]	5.9 [4.7; 7.5]	1.4 [1.0; 1.7]	-0.7 [-1.8; 0.2]	-5.0 0 [-6.2; -4.1]
Lemurs Log(OR) [95% CI]	8.7 [7.2; 11.0]	2.0 [1.5; 2.5]	-19 [-1439; 202]	-22 0 [-778; 104]

Table 1 Logistic regression of the frequency of amyloid plaques and neurofibrillary tangles across time and species. Two models were used for both amyloid plaques and neurofibrillary tangles, considering either chronological age (**Model 1: Time**) or age normalized to the species' maximum lifespan (**Model 2: Time/Maximum Lifespan**)

Isometry & Chronometry

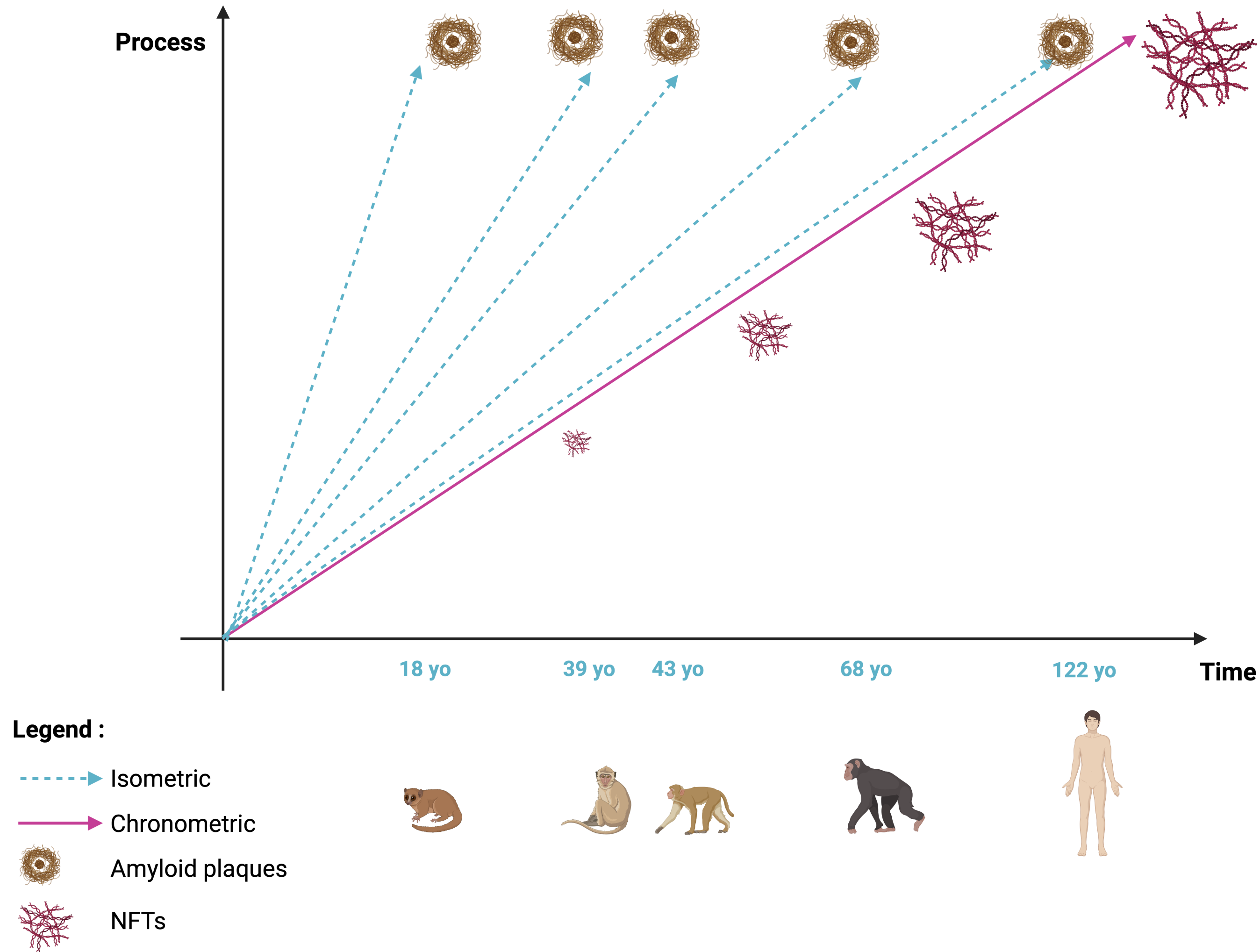


Fig. 4 Isometric and chronometric relationship Isometry refers to a **stricter relationship of proportionality**, in which a phenomenon retains the same relative position in the life history of different species. Conversely, chronometry makes it possible to identify phenomena that appear to **progress over a certain absolute period of time, irrespective of the overall rate of the life cycle.**

CONCLUSION

The presence of **amyloid plaques seems to follow an isometric (proportional) pattern** whereas **NFTs seem to maintain similar duration across species regardless of lifespan**, which stands at odds with the amyloid cascade hypothesis.

PARTENAIRES

