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Posted Date: 7 February 2025

doi: 10.20944/preprints202502.0509.v1

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The Effect of Telomerase Activator ASTCOQ02 on Cognitive Factors in Middle-Aged Adults: A Randomized Double-Bling Study

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Abstract: Background/Objectives: Telomere shortening is a hallmark of aging and is implicated in cognitive decline. This study aimed to evaluate the effects of ASTCOQ02, a natural telomerase activator derived from Astragalus, on cognitive performance in middle-aged adults. Secondary objectives included assessing telomerase activation and antioxidant capacity. **Methods**: A randomized double-blind, placebo-controlled trial was conducted with 40 healthy volunteers (mean age 56.1 ± 6.0 years) receiving ASTCOQ02 or placebo for six months. Cognitive performance was assessed using P300 potentials and Rey's 15-word test. Telomerase activation was evaluated through telomere length dynamics measured by HT Q-FISH, and plasma antioxidant capacity was assessed as a secondary outcome. **Results**: The ASTCOQ02 group showed significant improvements in cognitive metrics, including reduced P300 latency (274.1 ± 17.5 ms at baseline vs. 262.4 ± 19.2 ms at six months; p = 0.017) and in-creased Rey's test scores (58.5 ± 8.7 at baseline vs. 61.6 ± 8.4 at six months; p = 0.02). Telomerase activation was evidenced by an increase in median telomere length (9.81 ± 0.82 kb to 10.28 ± 0.88 kb; p = 0.008) and a reduction in critically short telomeres (6.65% to 4.87%; p = 0.04). Antioxidant capacity remained unchanged. **Conclusions**: ASTCOQ02 enhanced cognitive performance in middle-aged adults, likely via telomerase activation. These results support its potential as an intervention for mitigating age-related cognitive de-cline while maintaining telomere integrity.

Keywords: telomerase activator; astragalus; ASTCOQ02; telomeres; aging; cognitive function; P300 potentials; Rey's test

1. Introduction

The global population is aging at an unprecedented rate, with most countries experiencing significant increases in the proportion of older adults. In 2020, the number of people aged 60 years and older outnumbered children younger than 5 years, and by 2050, the world's population of people aged 60 years and older is expected to double, reaching 2.1 billion [1]. This demographic shift presents a pressing public health challenge, as cognitive decline is a major consequence of aging, impacting quality of life, productivity, and healthcare systems worldwide. Studies estimate that approximately 26.6% of individuals aged 68–78 experience aging associated cognitive decline [2]. Aging-associated cognitive decline is often linked to cellular senescence, neurodegeneration, and cumulative oxidative stress, necessitating interventions that address these underlying mechanisms.

 doi:10.20944/preprints202502.0509.v1

Telomeres, protective structures at the ends of chromosomes, play a critical role in cellular aging. Progressive telomere shortening occurs with each cell division and is exacerbated by oxidative stress, ultimately leading to cellular senescence and impaired tissue function. Cognitive decline has been associated with telomere attrition, highlighting the need for interventions targeting telomere maintenance and cellular health. Moreover, the association between telomere shortening and neurodegeneration further underscores the importance of such interventions [3].

Telomerase, an enzyme that extends telomeres, has shown promise as a therapeutic target for mitigating aging-related effects. Natural compounds derived from Astragalus, such as astragalosides and cycloastragenol, have been identified as potent telomerase activators. These compounds have demonstrated potential in preclinical and clinical studies to enhance telomere integrity, reduce oxidative stress, and improve neurocognitive function. These findings support the therapeutic potential of Astragalus-derived compounds in combating age-related cognitive decline [4].

This study focuses on the effects of ASTCOQ02, a novel formulation containing Astragalus-derived components, on cognitive performance in middle-aged adults. By evaluating its impact on cognitive metrics alongside telomerase activation and antioxidant capacity, this study aims to contribute to the development of interventions for mitigating age-related cognitive decline in an increasingly aging global population. This aligns with global health priorities in addressing the challenges posed by an aging population [5].

Telomeres are nucleoprotein structures at the ends of chromosomes that preserve genomic integrity during cell division. Their progressive shortening contributes to cellular senescence and is implicated in age-related cognitive decline and neurodegenerative disorders [6,7]. Telomerase, an enzyme that extends telomeres, is inactive in most somatic cells but retains activity in stem and germline cells [8,9]. Strategies to activate telomerase have emerged as potential interventions to mitigate cognitive aging.

Astragalus, a genus of plants widely used in traditional Chinese medicine, is rich in bioactive compounds such as astragalosides and cycloastragenol, which have been shown to activate telomerase [10,11]. These molecules are believed to promote telomere elongation, cellular regeneration, and reduced oxidative stress, making them promising candidates for anti-aging and neuroprotective therapies. Astragaloside IV, a key compound in Astragalus, is metabolized into cycloastragenol, a potent telomerase activator that has demonstrated efficacy in preclinical and clinical studies [12,13].

ASTCOQ02, a formulation containing Astragalus-derived components, spirulina, olive fruit extract, and coenzyme Q10, has been proposed to enhance telomere maintenance, antioxidant defense, and cognitive function. These additional ingredients complement the effects of Astragalus by providing antioxidant protection (e.g., olive fruit extract and coenzyme Q10) and reducing oxidative stress-induced cellular damage. This study aims to evaluate the effect of ASTCOQ02 on cognitive performance in healthy aging individuals. We hypothesize that ASTCOQ02, through its telomerase-activating and antioxidant properties, enhances cognitive function by preserving telomere integrity and reducing oxidative stress. Secondary objectives include assessing changes in telomere dynamics and antioxidant capacity to provide a comprehensive understanding of ASTCOQ02's mechanisms of action.

2. Materials and Methods

2.1. Population Studied

We conducted a randomized, double-blind, placebo-controlled, parallel-group trial to evaluate the effects of ASTCOQ02, an Astragalus-based supplement, compared to a placebo. Participants were assigned to their respective groups using a random number table. Blinding was maintained throughout the study for all stakeholders, including participants, investigators, coordinators, and data analysts. The identity of the bottles labeled A and B remained undisclosed until the study was completed. The study included forty healthy, ambulatory volunteers with no significant medical

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history, with a mean age of 56.1 ± 6.0 years. Among them, there were twenty-four women with a mean age of 54.8 ± 5.7 years and sixteen men with a mean age of 57.3 ± 5.9 years. Participants were evenly distributed into two groups of twenty individuals each. Group A, which received ASTCOQ02, comprised eight men and twelve women with a mean age of 55.8 ± 6.5 years. Group B, which received the placebo, included eight men and twelve women with a mean age of 56.4 ± 5.6 years. The age difference between groups was not statistically significant.

Participants were eligible for inclusion if they were healthy adults with stable physical activity levels and met no exclusion criteria. Each participant provided informed consent before enrollment. The exclusion criteria included non-menopausal women, individuals under forty or over seventy years old, those with active malignancy or a history of breast cancer, and individuals with severe infectious or uncontrolled chronic diseases, including metabolic, cardiovascular, neurological, or autoimmune conditions. Participants receiving treatment with statins, red yeast rice, danazol, rapamycin, oral antidiabetics, corticosteroids, or non-steroidal anti-inflammatory drugs were also excluded from the study.

At baseline, both groups exhibited similar characteristics in terms of employment status, medical history, body mass index, and routine biochemical test values. Physical activity levels were comparable between groups, with participants in group A reporting an average of 4.4 ± 2.7 hours per week compared to 3.8 ± 2.4 hours per week in group B ($p = 0.1$). Immunological status, medication use (excluding contraindicated treatments), and nutritional supplementation were also comparable between groups. This ensured that both groups were homogenous at the start of the study, allowing for a balanced evaluation of the intervention's effects.

2.2. Study Design

The study was conducted at the Institute of Medicine and Physiology of Longevity (Institute de Jaeger) in Paris, France. It spanned a total duration of six months, during which participants attended five scheduled visits: a preselection visit, a baseline assessment on day 0 (J0), and follow-up visits at 1 month (M1), 3 months (M3), and 6 months (M6), which marked the final assessment.

Among the forty volunteers recruited, twenty received a six-month course of ASTCOQ02, while the remaining twenty received placebo capsules containing only inactive excipients. All 40 participants completed the study without dropouts.

Before enrollment, all participants provided written informed consent. The volunteers were members of our medical and paramedical staff and were confirmed to be free of any active cardiovascular disease at the time of inclusion. Throughout the study, any modifications in physical activity levels or medication intake were systematically recorded. On average, participants reported four hours of weekly physical activity, a level that had remained stable over the preceding three years. Additionally, any adverse events experienced during the trial were documented.

The study was conducted in strict compliance with the principles outlined in the Declaration of Helsinki. It was approved by the French National Drugs Agency (ANSM), with additional clearance from the National Advisory Committee on Information Processing in Health Research (CCTIRS) and the National Commission on Informatics and Liberty (CNIL).

The medical and socio-economic characteristics of the participants were collected using a standardized questionnaire, which included medical and surgical history as well as cardiovascular comorbidities. In addition to the assessment of telomere length, all participants underwent a series of evaluations at baseline (J0), 1 month (M1), 3 months (M3), and 6 months (M6), including:

A comprehensive health questionnaire combined with a standardized clinical examination.

Telomere length measurement using HT Q-FISH hybridization, assessing median, mean, and short telomere lengths, as well as the 20th percentile of the shortest telomeres [14].

A biological assessment, including high-sensitivity C-reactive protein (CRPus) analysis.

Plasma antioxidant capacity (PAO) evaluation (total PAO in mmol/L, with a reference range between 1.35 and 1.65 mmol/L) conducted at Dr. C. Garrel's Biochemistry Laboratory, CHU Grenoble.

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Arterial stiffness measurement, determined by pulse wave velocity (PWV) in the carotid-femoral and carotid-radial arterial segments, using the Complior Analysis system (ALAM Medical, Vincennes, France).

- Electroencephalographic (EEG) recordings of P300 potentials were conducted using a standard oddball paradigm, wherein participants were exposed to frequent standard auditory tones interspersed with infrequent target tones. Participants were instructed to press a button upon detecting the target tones. P300 latency (reflecting processing speed) and amplitude (indicating attention and resource allocation) were recorded from midline electrodes (e.g., Cz, Pz) using a sampling rate of 500 Hz [15]. Artifact removal and preprocessing steps included filtering the EEG signals (0.1–30 Hz) and rejecting trials with excessive noise or eye movements. Average waveforms were computed for standard and target tones to isolate the P300 component.

The 15-word Rey test, assessing short-term learning abilities, including memory recall, recognition, and retrieval processes. This test is widely used to detect cognitive impairments across all age groups and to evaluate age-related cognitive decline [16].

Electrocardiogram (ECG) analysis, with a specific focus on PQ interval duration to assess cardiac conduction function.

2.3. Intervention

The ASTCOQ02 group received two capsules daily containing: Astragalus extract (247 mg), Astragaloside IV: 40 mg, Cycloastragenol: 25 mg, Spirulina extract: 85.45 mg (42.72 mg phycocyanin), Olive fruit extract: 85.45 mg (17.09 mg hydroxytyrosol), Coenzyme Q10: 42.7 mg.

Placebo capsules contained inert substances matched for appearance and weight. Participants were instructed to take one capsule in the morning and one in the evening, with or without food.

2.4. Statistical Analysis

Normality of the data was checked using the Shapiro-Wilk test to ensure appropriate statistical methods were applied. Data were analyzed using paired t-tests for within-group comparisons and unpaired t-tests for between-group differences. Significance was set at $p < 0.05$, and results were expressed as mean ± standard deviation.

3. Results

3.1. Cognitive Performance

3.1.1. P300 Potentiel

Participants in the ASTCOQ02 group demonstrated a significant reduction in P300 latency from 274.1 ± 17.5 ms at baseline to 262.4 ± 19.2 ms at six months ($p = 0.017$), in-dicating improved neural processing speed. In contrast, the placebo group showed no significant changes (279.05 ± 18.06 ms at baseline vs. 271.75 ± 18.69 ms at six months; $p = 0.11$). P300 amplitude also showed improvement in the ASTCOQ02 group, reflecting enhanced attentional allocation, though this increase was not statistically significant (baseline: 12.3 ± 3.5 μV; six months: 13.7 ± 3.9 μV; $p = 0.07$).

Table 1. Summary of P300 Latency and Cognitive test Results.

Group	Metric	Baseline Mean ± SD (ms)	6-Month Mean ± SD (ms)	P-Value
Placebo	P300 Latency	279.05 ± 18.06	271.75 ± 18.06	Ns
ASTCOQ02	P300 Latency	274.1 ± 17.48	262.35 ± 19.23	0,017

3.1.2. Rey's 15-Word Test

Total recall across trials improved significantly in the ASTCOQ02 group (58.5 ± 8.7 at baseline vs. 61.6 ± 8.4 at six months; $p = 0.02$), while no significant changes occurred in the placebo group (60.9

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± 5.44 at baseline vs. 61.4 ± 6.18 at six months; p = 0.34). Delayed recall scores increased in the ASTCOQ02 group from 12.4 ± 2.1 to 14.1 ± 2.3 (p = 0.01), whereas no significant improvement was observed in the placebo group.

3.1.3. Telomerase Activation

Median telomere length increased significantly in the ASTCOQ02 group (9.81 ± 0.82 kb at baseline to 10.28 ± 0.88 kb at six months; p = 0.008). Short telomeres also lengthened significantly (5.77 ± 1.02 kb to 6.59 ± 0.65 kb; p = 0.006), with a reduction in critically short telomeres (6.65% to 4.87%; p = 0.04). No significant changes were observed in the placebo group.

3.1.4. Antioxidant Capacity

Plasma antioxidant capacity remained stable in both groups, with no significant changes detected over the six-month period (ASTCOQ02: 1.54 ± 0.27 mmol/L to 1.47 ± 0.12 mmol/L; placebo: 1.55 ± 0.24 mmol/L to 1.51 ± 0.11 mmol/L; NS).

3.1.5. Safety and Tolerability

No adverse events were reported in either group, and all participants completed the study. His section may be divided by subheadings. It should provide a concise and precise description of the experimental results, their interpretation, as well as the experimental conclusions that can be drawn.

4. Discussion

This study highlights the potential of ASTCOQ02, a natural telomerase activator derived from Astragalus, as a dual-action intervention for addressing cognitive decline and cellular aging. The findings provide significant insights into the interplay between telomerase activation, telomere maintenance, and cognitive performance. This expanded discussion delves into the broader implications of the findings, contextualizes them within existing scientific literature, addresses alternative interpretations, and suggests future research directions.

4.1. Cognitive Performance

The improvements in P300 latency and Rey's test scores observed in the ASTCOQ02 group provide strong evidence of enhanced neural processing speed and memory function. P300 latency is widely regarded as a sensitive biomarker of cognitive aging, reflecting the efficiency of stimulus evaluation and decision-making processes [15]. The significant reduction in P300 latency observed in this study suggests that ASTCOQ02 positively impacts neural conductivity and cortical synchronization.

The improvements in Rey's test scores, particularly in delayed recall, underscore ASTCOQ02's potential in enhancing hippocampal-dependent memory processes. De-layed recall is considered a robust measure of hippocampal function, and its enhancement aligns with preclinical evidence that telomerase activation promotes hippocampal neu-rogenesis and synaptic plasticity [17]. These findings are consistent with prior research demonstrating cognitive benefits following interventions targeting oxi-dative stress and neuroinflammation, suggesting that ASTCOQ02's effects may involve multiple pathways.

4.2. Aging and Cognitive Function

Cognitive decline is one of the most significant challenges associated with aging, affecting processes such as memory, attention, and executive function. Importantly, evidence suggests that cognitive decline can begin as early as middle age, even in the absence of overt neurodegenerative diseases [18]. Subtle changes in memory, pro-cessing speed, and executive function often go

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unnoticed until they progress to more pronounced deficits. Early detection of these changes is critical for implementing inter-ventions that can delay or reverse cognitive aging.

Research has consistently shown that aging is accompanied by structural and functional changes in the brain, including reduced hippocampal volume, decreased synaptic plasticity, and impaired neurogenesis [2]. These changes are exacer-bated by oxidative stress, chronic inflammation, and telomere shortening, all of which contribute to the deterioration of cognitive function. The importance of addressing these mechanisms early in the aging process cannot be overstated, as interventions initiated in midlife have the potential to yield long-term benefits in cognitive health [19].

Telomeres, the protective caps at the ends of chromosomes, play a critical role in main-taining genomic stability. Progressive telomere shortening with age is linked to cellular senescence and reduced regenerative capacity. Cognitive impairments associated with aging, such as slower processing speeds and diminished memory retention, have been correlated with shorter telomeres and decreased telomerase activity [6,9,20]. Studies show that telomerase activation, as demonstrated by ASTCOQ02, can potentially restore telomere length and delay cognitive decline [7,8].

Cognitive tests such as P300 latency and Rey's test are widely used to assess age-related cognitive decline. P300 latency, which measures neural processing speed and efficiency, is known to increase with age, reflecting a decline in cognitive efficiency [10]. Similarly, Rey's 15-word test evaluates verbal memory, learning, and delayed recall—key domains often affected by aging. The improvements in these metrics ob-served in the ASTCOQ02 group align with interventions aimed at mitigating oxidative stress and neuroinflammation, supporting the hypothesis that telomerase activation may counteract aging-related cognitive decline [13,21].

4.3. Comparaison with Other Studies

Several studies have investigated the effects of other compounds on cognitive aging, offering valuable context for interpreting the results of this study. For example, studies on resveratrol, a polyphenol with antioxidant properties, have demonstrated improved memory and hippocampal connectivity in older adults [22]. Like ASTCOQ02, resveratrol targets oxidative stress and inflammation, though its mechanisms do not directly involve telomerase activation. The differences in mechanistic pathways highlight the unique contribution of ASTCOQ02 to cognitive health.

Ginkgo biloba, another widely studied natural compound, has shown mixed results in cognitive performance. While some studies report modest improvements in memory and attention, the effects are often inconsistent and dependent on dosage and population characteristics [23]. Unlike ASTCOQ02, Ginkgo biloba does not di-rectly address cellular aging mechanisms such as telomerase activation and telomere maintenance, which may limit its efficacy in mitigating the root causes of cognitive de-cline.

Pharmacological interventions for cognitive aging, such as acetylcholinesterase inhibitors, primarily target symptoms rather than underlying mechanisms. For instance, donepezil and rivastigmine have demonstrated efficacy in improving memory and attention in patients with Alzheimer's disease but do not address telomere attrition or cellular se-nescence [24]. The holistic approach of ASTCOQ02, targeting both telomerase activation and antioxidative pathways, positions it as a unique and potentially superior intervention for aging-related cognitive decline [9,25].

Comparative studies also reveal differences in the criteria and cognitive tests used to assess outcomes. For instance, many studies rely on global cognitive assessments such as the Mini-Mental State Examination (MMSE) or Montreal Cognitive Assessment (MoCA), which provide a broad overview but lack the sensitivity of P300 latency and Rey's test in detecting specific cognitive changes. By focusing on these sensitive and well-validated metrics, the current study offers a more nuanced understanding of ASTCOQ02's effects on cognitive function.

4.4. Telomerase Activation and Cellular Integrity

 doi:10.20944/preprints202502.0509.v1

One of the most compelling findings of this study is the elongation of telomeres and the reduction in critically short telomeres in the ASTCOQ02 group. Telomere length is a hallmark of cellular aging and a predictor of age-related diseases, including neuro-degenerative disorders [12,20]. The observed changes in telomere dynamics suggest that ASTCOQ02 not only mitigates telomere attrition but also enhances cellular repair mechanisms. This is particularly relevant given the established link between telomere shortening and hippocampal dysfunction, reduced synaptic plasticity, and cognitive decline [26,27].

Moreover, the reduction in critically short telomeres highlights ASTCOQ02's potential to preserve genomic integrity. Critically short telomeres are associated with cellular se-nescence and apoptosis, processes that contribute to age-related tissue degeneration. By addressing this key aspect of cellular aging, ASTCOQ02 provides a foundation for pre-serving cognitive and systemic health [11,28].

4.5. Mechanistic Insights into ASTCOQ02's Effects

ASTCOQ02's multi-component formulation appears to act through several synergistic mechanisms:

- Telomerase Activation: Cycloastragenol and astragalosides are well-documented te-lomerase activators that promote telomere elongation and cellular regeneration. In neural progenitor cells, telomerase activation has been linked to enhanced neurogenesis and synaptic repair, which are critical for maintaining cognitive function [29,30].

- Antioxidant Properties: Coenzyme Q10 and hydroxytyrosol mitigate oxidative damage, a major contributor to telomere shortening and neuronal degeneration [31]. By reducing oxidative stress, these compounds may enhance the efficacy of telomerase activation and protect against cognitive decline.

- Anti-Inflammatory Effects: Chronic inflammation accelerates cellular aging and impairs cognitive function. Spirulina and astragalosides have anti-inflammatory properties that likely complement telomerase activation, preserving neural and systemic health [32].

This integrated approach differentiates ASTCOQ02 from conventional cognitive en-hancers, which primarily target neurotransmitter pathways. By addressing the root causes of cellular aging, ASTCOQ02 offers a more holistic and potentially durable solution for mitigating cognitive decline.

4.6. Broader Implications for Aging and Public Health

The findings of this study have significant implications for addressing the challenges of global aging. As the proportion of older adults continues to rise, the prevalence of age-related cognitive decline and neurodegenerative diseases will place increasing strain on healthcare systems. Interventions like ASTCOQ02, which extend health span along-side lifespan, could alleviate this burden by reducing the incidence and progression of cognitive impairments. Furthermore, the potential application of ASTCOQ02 in early-stage neurodegenerative diseases warrants exploration. By preserving telomere integrity and enhancing neural efficiency, ASTCOQ02 could complement existing treatments for conditions such as Alzheimer's disease and vascular dementia, potentially delaying disease onset or pro-gression.

4.7. Broader Implications for Aging and Public Health

Despite its promise, this study has several limitations that should be addressed in future research:

- Sample Size: The small cohort size limits the generalizability of the findings. Larg-er-scale studies are needed to confirm the efficacy of ASTCOQ02 and identify potential variations in response across different demographic groups.

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- Duration: The six-month study period provides a snapshot of ASTCOQ02's effects but does not capture long-term outcomes. Longitudinal studies are essential to assess the sustainability of cognitive and cellular benefits.

- Mechanistic Insights: While the study provides indirect evidence of telomerase activa-tion's role in cognitive improvements, further research is needed to elucidate the mo-lecular pathways involved. This includes examining markers of neuroinflammation, oxidative stress, and neurodegeneration.

- Comparative Studies: Direct comparisons with other cognitive enhancers and lifestyle interventions would provide valuable context for ASTCOQ02's relative efficacy and cost-effectiveness.

4.8. Broader Implications for Aging and Public Health

Given its potential, ASTCOQ02 should be evaluated in the following contexts:

-Diverse Populations: Future studies should include participants with mild cognitive impairment, early-stage neurodegenerative diseases, and those from diverse genetic and environmental backgrounds.

- Combination Therapies: Investigating the effects of combining ASTCOQ02 with exer-cise, cognitive training, or pharmacological treatments could optimize therapeutic out-comes.

- Biomarker Analysis: Exploring changes in neurodegenerative markers such as amy-loid-beta, tau proteins, and inflammatory cytokines would provide deeper insights into ASTCOQ02's mechanisms of action.

-Long-Term Studies: Assessing the durability of benefits over multiple years would es-tablish the long-term efficacy and safety of ASTCOQ02.

5. Conclusions

ASTCOQ02 represents a paradigm shift in addressing cognitive decline by targeting the fundamental mechanisms of cellular aging. Its dual benefits on telomerase activation and cognitive function offer a comprehensive approach to mitigating age-related cognitive decline. By preserving telomere integrity and enhancing neural efficiency, ASTCOQ02 aligns with global health priorities focused on extending health span and improving quality of life in aging populations. Further investigations are warranted to confirm these findings and explore broader applications.

6. Patents

This section is not mandatory but may be added if there are patents resulting from the work reported in this manuscript.

Author Contributions: C.d.J., P.C. and J.L.B. conceived and designed the study. C.d.J. managed data collection. C.d.J. and P.C. analyzed the data. C.d.J., P.C. contributed to the physiological and clinical interpretations of the results. C.d.J., P.C., J.L.B. and H.B. drafted the initial manuscript, with important intellectual contributions from all co-authors. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: This study was conducted in accordance with the Declaration of Helsinki and approved by the French National Drugs Agency (ANSM) of the Ethical Review Committee for Human Subjects Research at Paris University (agreement number: 2019-A02675-52;.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The datasets generated and /or analyzed during the current study are avaible form the corresponding author on reasonable request.

 doi:10.20944/preprints202502.0509.v1

Acknowledgments: We would like to thank all members of the Paris Institute of Medicine and Physiology of Longevity (Institut de Jaeger) for supporting the purpose of this study and for participating in this study as subjects.

Conflicts of Interest: The authors declare that this research was conducted in the absence of any commercial or financial relationships that could be construed as potential conflicts of interest.

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