

## Cognitive changes and emotional heart rate variability dynamics in subjective cognitive decline: An exploratory longitudinal neuropsychophysiological study

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### ABSTRACT

Subjective cognitive decline (SCD) is increasingly recognised as a potential preclinical stage of Alzheimer's disease, yet the physiological mechanisms underlying its progression remain poorly understood. This longitudinal study examined whether heart rate variability (HRV), a non-invasive marker of autonomic nervous system regulation, could serve as an early psychophysiological indicator of cognitive vulnerability in older adults with SCD.

Twenty-one participants meeting established SCD criteria completed two identical experimental sessions approximately 12 months apart. Each session included comprehensive neuropsychological testing and continuous HRV recording during exposure to emotionally evocative images from the International Affective Picture System, presented in a temporally extended and affectively rich paradigm known as an "affective storm".

At the group level, no significant changes in cognitive performance or HRV indices were observed over time. However, analyses of individual change scores revealed that longitudinal variations in HRV, particularly in indices reflecting parasympathetic tone and overall autonomic flexibility, were selectively and consistently associated with performance in global cognition, verbal fluency, and visuospatial working memory.

These findings suggest that dynamic autonomic responses to emotional stimulation may reflect subtle physiological correlates of cognitive functioning, even in the absence of overt cognitive decline. The observed associations are consistent with neurovisceral integration models, and support the potential utility of HRV as a sensitive, non-invasive marker of early cognitive trajectories in ageing.

In conclusion, HRV may offer unique insights into the complex interaction between emotional reactivity and cognitive resilience in older adults with SCD, opening promising avenues for early screening and intervention.

### 1. Introduction

Cognitive complaints are common among older adults, and often prompt neurological evaluation. When these complaints occur without objective impairments on standardised neuropsychological tests, the condition is classified as subjective cognitive decline (SCD), defined as a

self-perceived decline in cognitive abilities without measurable deficits (Jessen et al., 2014, 2020; Molinuevo et al., 2017). SCD is increasingly recognised as a heterogeneous condition with diverse aetiologies, not all of which are neurodegenerative.

Recent evidence suggests that SCD, particularly when accompanied by "SCD-plus" features, may indicate a preclinical stage of Alzheimer's

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disease (AD) or mild cognitive impairment (MCI), providing a critical window for early detection and preventive intervention (Jessen et al., 2014; Molinuevo et al., 2017).

While extensive research has focused on pathological risk factors for AD, including cardiovascular and metabolic diseases and lifestyle factors (Livingston et al., 2020; Niotis et al., 2024), less is known about protective or compensatory mechanisms, such as cognitive reserve and physiological resilience, which support emotional regulation and healthy cognitive ageing (Amanzio, Cipriani, Bartoli, et al., 2023, Amanzio, Cipriani, Canessa, et al., 2023; Pappalettera et al., 2024; Stern et al., 2020; Turrini et al., 2023).

Despite their potential, longitudinal studies integrating neuropsychological and physiological data remain limited. A growing body of evidence links cognitive ageing with autonomic nervous system (ANS) function (Alrosan et al., 2024). In particular, heart rate variability (HRV) - the beat-to-beat variation in heart rate - has emerged as a sensitive, non-invasive biomarker of autonomic regulation (Olivieri et al., 2024). HRV reflects the dynamic interplay between the sympathetic and parasympathetic branches of the ANS, and is considered a marker of physiological flexibility and resilience (Shaffer & Ginsberg, 2017). Decreased HRV has been associated not only with cardiovascular risk but also with poorer cognitive performance, executive dysfunction, and emotional dysregulation (Kim et al., 2018; Thayer et al., 2009). The potential link between low HRV and cognitive function involves several factors and mechanisms.

Arterial stiffness, impaired baroreflex sensitivity, and microvascular damage may deteriorate white-matter integrity in bundles underlying executive performance (Tarumi et al., 2015). Chronic sympathetic dominance or vagal withdrawal reduces cerebral perfusion and neuroplasticity (Agorastos et al., 2023), while reduced cerebral perfusion may impair dynamic regulation of brain blood flow (neurovascular coupling: Scarsoglio & Ridolfi, 2021). Dysregulated stress responses can damage hippocampal and prefrontal circuits (Lupien et al., 2009), eventually resulting in increased inflammatory response (e.g., IL-6, CRP) and accelerated neurodegeneration (Lampert et al., 2008; Marsland et al., 2007).

The neurovisceral integration model (Smith et al., 2017; Thayer et al., 2009) provides a theoretical framework linking HRV to cognitive and emotional self-regulation, implicating a central autonomic network that includes the medial prefrontal cortex, anterior cingulate cortex, insula, and amygdala, all involved in autonomic control and higher-order cognition (Grol & De Raedt, 2020). Notably, changes in HRV may precede overt cognitive decline, making it a potential early indicator of neurodegenerative processes (Pham et al., 2021).

The emotional aspect of autonomic reactivity can be assessed using dimensional models of affect, which characterise emotions along valence (positive - negative) and arousal (low - high) axes (Russell, 2003). The International Affective Picture System (IAPS) provides standardised emotionally evocative images widely used to elicit autonomic responses such as HRV and skin conductance (Bradley & Lang, 2007; Codispoti et al., 2001; Lang et al., 1997). Older adults tend to rate negative stimuli as more arousing than younger individuals (Grühn & Scheibe, 2008), indicating age-related changes in emotional reactivity.

Despite this background, no longitudinal studies have examined the interplay between HRV, emotion, and cognitive change in SCD. To address this gap, we used an IAPS-based "affective storm" paradigm (Borghesi et al., 2024; Simoncini et al., 2024), a dynamic sequence of emotionally varied images, to probe HRV responses in older adults with SCD at two time points approximately 12 months apart.

We aimed to determine whether changes in HRV, measured during emotionally evocative stimulation, are associated with individual trajectories of cognitive performance in older adults with SCD. Specifically, we investigated whether longitudinal variations in HRV indices, reflecting autonomic flexibility and regulation, correlate with changes in cognitive performance. We hypothesised that individual differences in HRV dynamics would relate to cognitive trajectories, highlighting

HRV as a sensitive biomarker of early neurophysiological changes in SCD. Additionally, we explored potential associations between HRV changes and mood or health status, in order to characterise the broader affective and physical context of autonomic regulation in SCD. This longitudinal approach, integrating neuropsychological and physiological data, aims to elucidate subtle early markers of cognitive vulnerability, and supports the utility of HRV during emotional challenges as a non-invasive tool to monitor neuropsychophysiological ageing processes in at-risk populations.

## 2. Methods

### 2.1. Participants

From March 2023 to September 2024, 60 healthy older adults were invited to participate in a longitudinal neuropsychophysiological study examining the relationship between changes in cognitive performance, mood state, physical health, and autonomic emotional reactivity to emotionally evocative visual stimuli from the IAPS database.

Participants were classified as healthy older adults according to the criteria defined by the World Health Organization (2025). Eligibility required full functional autonomy, operationalised as the maximum score on the Instrumental Activities of Daily Living Scale (iADL: Lawton & Brody, 1969), and consistent right-handedness throughout life.

Participants were excluded if they had a history of neurological or psychiatric disorders, were currently using psychotropic medication, or showed objective cognitive impairment, including MCI as defined by Petersen and Negash (2008), or a score below 24 on the Mini-Mental State Examination (MMSE: Folstein et al., 1975). Participants were also excluded if they met criteria for physical frailty, as defined by the phenotypic model of Fried et al. (2001).

An a priori power analysis was conducted using G\*Power 3.1 (statistical test: Correlation - Bivariate normal model). The analysis was performed under the exact distribution, assuming a two-tailed test, an expected medium-to-large association ( $\rho = 0.55$ ) under  $H_1$ , a significance level of  $\alpha = 0.05$ , and a desired power of  $1 - \beta = 0.70$ . Under these parameters ( $\rho_0 = 0$ ), the required sample size was  $N = 19$  participants, with critical correlation values ranging from  $r = -0.4555$  to  $r = 0.4555$  and an actual power of 0.7201. A recent experimental study used a similar design, integrating HRV analysis with IAPS-based emotional elicitation in a small sample ( $N = 20$ ), and reported robust associations ( $\geq 0.4$ ) between HRV parameters and affective responses, supporting the adequacy of the present sample size and analytic approach (Cittadini et al., 2023). Furthermore, the present sample size is comparable to that of previous HRV studies conducted in SCD and MCI populations (Albinet et al., 2010; Grässler et al., 2023; Kim et al., 2018).

A final sample of 21 participants (14 women, 7 men) who met all inclusion criteria completed the full study protocol at two identical time points, approximately 12 months apart. The decision to use a 12-month follow-up period was based on established methodological recommendations in the SCD literature. Specifically, Jessen et al. (2014, 2020, 2023) identified annual re-evaluation as the standard and appropriate interval for longitudinal monitoring in individuals with SCD, as it enables the detection of subtle but potentially meaningful cognitive and physiological changes while maintaining feasibility and participant retention. In line with this consideration, some studies (e.g., Chipi et al., 2018; Maffoni et al., 2022) have adopted this approach, supporting the relevance of a 12-month follow-up interval for assessing within-person changes in both subjective and objective markers of early cognitive vulnerability.

The study was conducted at the Observation Laboratory of the Department of Psychology and the Psychophysiological Laboratory of Human Science and Technologies at the University of Turin. Ethical approval was granted by the University of Turin Ethics Committee (Protocol Nos. 0442042 and 0211867), and all procedures complied with the ethical standards outlined in the Declaration of Helsinki. Before

enrolment, each participant provided written informed consent in accordance with study procedures.

## 2.2. Neuropsychophysiological evaluation

Data were collected between April 2023 and February 2025. To minimise participant fatigue and maintain high-quality data acquisition, the overall evaluation was divided into two sessions scheduled within the same week.

The physiological assessment, including HRV recording and the emotional stimulation protocol, was conducted in a single session lasting approximately 45 min.

The neuropsychological evaluation was conducted in a separate session, scheduled to last approximately 45 min. If participants could not complete the full cognitive battery within this time, they were given a 15-minute rest break to aid recovery and relaxation. The assessment then resumed and was completed on the same day, with up to an additional 45 min allowed, depending on the participant's pace and comfort.

This split-session design aimed to reduce physical and mental fatigue while ensuring that both physiological and cognitive assessments were conducted under optimal conditions.

## 2.3. Neuropsychological assessment

The neuropsychological test battery was designed to assess three domains: cognitive performance, mood state, and physical health.

Global cognitive performance was assessed using the Addenbrooke's Cognitive Examination - Revised (ACE-R: Mioshi et al., 2006), which includes the MMSE and consists of subscales for orientation and attention, memory, verbal fluency, language, and visuospatial abilities. At baseline, SCD was assessed using the Jessen criteria (Jessen et al., 2020) and the Cognitive Function Instrument (CFI: Chipi et al., 2018), which includes both self and partner reports. At follow-up, executive functions were assessed using the Montreal Cognitive Assessment (MoCA: Conti et al., 2015), the Trail Making Test (TMT, parts A and B: Giovagnoli et al., 1996), and phonemic and semantic fluency tasks (Carlesimo et al., 2008; Spinnler & Tognoni, 1987). Other cognitive domains were assessed using the following instruments: attention with the Attentional Matrices (Spinnler & Tognoni, 1987); long-term memory with the Rey Auditory Verbal Learning Test (RAVLT: Carlesimo et al., 2008); short-term memory with the Digit Span (Orsini et al., 1987) and the Corsi Block Tapping Test (Spinnler & Tognoni, 1987); and speech comprehension with the Token Test (De Renzi & Vignolo, 1962).

Mood state was assessed using the Apathy Evaluation Scale (AES: Marin, 1996), the Beck Depression Inventory (BDI: Beck et al., 1988), and the Hamilton Rating Scale for Anxiety (HARS: Hamilton, 1959).

Physical frailty was assessed using the phenotypic model (Fried et al., 2001) based on five criteria: unintentional weight loss, decreased grip strength, self-reported fatigue, decreased walking speed, and low physical activity. Participants were categorised as robust (0 criteria), prefrail (1–2), or frail ( $\geq 3$ ).

Data on multimorbidity were collected using the Cumulative Illness Rating Scale (CIRS: Linn et al., 1968).

Each of these instruments provides standardised cut-off scores derived from Italian normative samples, which are widely used in clinical and research settings in Italy.

## 2.4. IAPS stimuli and experimental procedure

To measure emotional reactivity, participants were passively exposed to 156 IAPS images (see Supplementary Table S1 for descriptions and identification numbers) over a 26-minute period (i.e., one image every 10 s). Images were preselected based on arousal and valence ratings, with scores above 6 indicating high arousal or positive valence, and scores below 4 indicating low arousal or negative valence.

Previous research (e.g., Kommula et al., 2023) has confirmed the validity of these thresholds in older adults.

The preselected images were categorised into four affective quadrants: A. high arousal, negative valence; B. high arousal, positive valence; C. low arousal, negative valence; D. low arousal, positive valence (Fig. 1).

The final stimulus set comprised 50, 48, 46, and 12 pictures from quadrants A, B, C, and D, respectively, divided into 13 blocks of 12 pictures each. Both the order of images within each block, and the order of blocks, were individually randomised across participants.

The task consisted of passive observation, with participants instructed to simply look at the pictures without performing any explicit cognitive task. This emotionally dense and temporally extended sequence of stimuli is referred to as an “affective storm” - a dynamic period of fluctuating autonomic activation elicited by sustained exposure to diverse affective content - designed to capture fine-grained HRV changes reflecting emotional reactivity and autonomic flexibility (Borghesi et al., 2024; Simoncini et al., 2024).

Experimental sessions were conducted in a quiet room with controlled temperature and no unexpected external stimuli. Two phases, each lasting 2 min, preceded and followed the visual stimulation. During these periods, participants were asked to remain still and breathe naturally while focusing on a white fixation cross on a black background.

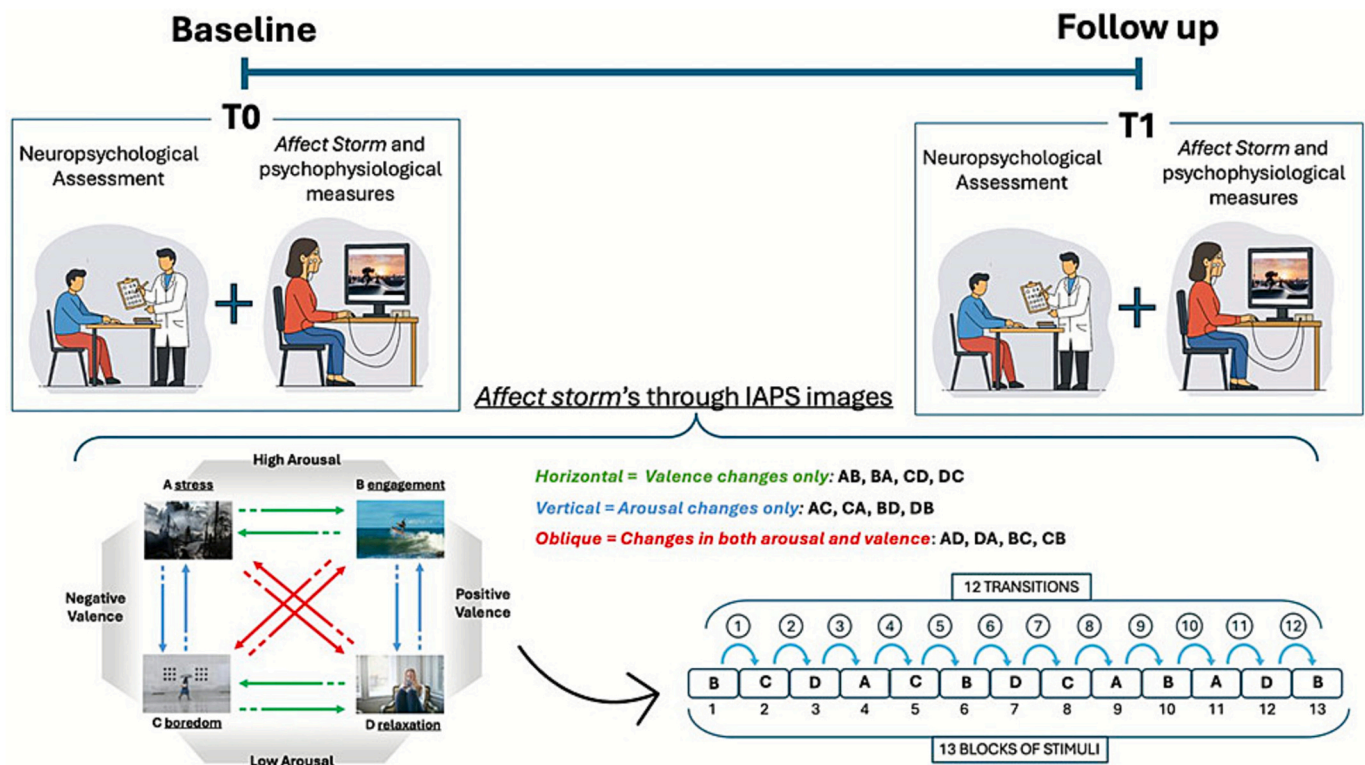
## 2.5. Acquisition and processing of psychophysiological data

Autonomic responses were continuously recorded using the Nexus 10 system (Mind Media, Netherlands) at a sampling rate of 1024 Hz. Cardiovascular activity was measured with photoplethysmographic blood volume pulse sensors placed on participants' fingers. Data collection comprised three phases: a pre-task resting phase (relaxation), the 26-minute emotional stimulation task (the “affective storm”), and a post-task recovery phase. The post-task recovery phase served as a control condition, providing baseline autonomic measures following emotional stimulation. This enabled comparison of HRV indices during active emotional processing with those recorded during recovery, isolating task-specific autonomic responses from residual or baseline fluctuations.

Signal processing and HRV analyses were performed offline in MATLAB R2022b. Artefacts and missing data segments were corrected using linear interpolation. A 50 Hz notch filter was applied to remove power line interference, and the Pan-Tompkins algorithm was used to extract inter-beat intervals. The resulting R-R interval (RR) series was interpolated and detrended at 4 Hz before feature extraction.

HRV indices were calculated in accordance with guidelines from the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (Electrophysiology, 1996). Time-domain measures included the root mean square of successive differences (RMSSD), reflecting short-term parasympathetic activity; the standard deviation of normal-to-normal intervals (SDNN), representing overall HRV; and standard deviation of heart rate (SD HR), indicating beat-to-beat variability in beats per minute. Frequency-domain analysis provided the low frequency (LF) to high frequency (HF) ratio, a marker of sympathovagal balance. Non-linear dynamics were assessed using Poincaré plot indices: the standard deviation perpendicular to the line of identity (SD1), associated with parasympathetic modulation, and standard deviation along the line of identity (SD2), indexing overall autonomic variability.

Change scores ( $\Delta T1$  vs  $T0$ ) for each HRV index were calculated for each participant. Correlations between HRV changes and fluctuations in cognitive performance, mood, and physical health were then analyzed to investigate the potential of HRV as a psychophysiological marker of early cognitive vulnerability.



**Fig. 1.** Experimental design and model of emotional transition. The protocol includes two assessment time points (baseline, T0, and follow-up, T1), combining neuropsychological tests with psychophysiological responses to an affective stimulation task using IAPS images. Emotional transitions are categorised based on changes in valence (horizontal), arousal (vertical) or both dimensions (oblique).

## 2.6. HRV during the affective storm

HRV was continuously recorded throughout the IAPS-based affective stimulation phase - referred to as the “affective storm” - during which participants passively viewed a sequence of emotionally evocative images designed to elicit sustained and dynamic autonomic responses across valence and arousal dimensions. Although the entire stimulation lasted 26 min, it comprised 13 rapid emotional transitions, each inducing a brief and distinct emotional state.

Given the dynamic and rapidly shifting nature of these emotional states, we computed mean HRV values over the entire stimulation period rather than for individual emotional segments. This approach balances ecological validity, capturing the complexity and dynamism of real-life emotional experiences, with physiological precision.

While classical guidelines for HRV analysis recommend stable 5-minute intervals within homogeneous physiological states (Electrophysiology, 1996), recent methodological advances support continuous HRV sampling in emotionally rich and dynamic contexts to better capture autonomic adaptability over time (Laborde et al., 2017).

HRV analyses included traditional time-domain indices (SDNN, RMSSD), nonlinear indices (SD1, SD2), and frequency-domain measures focusing on low-frequency (LF: 0.04–0.15 Hz) and high-frequency (HF: 0.15–0.4 Hz) components. Consistent with both classical and contemporary interpretations (Electrophysiology, 1996; Shaffer & Ginsberg, 2017), HF power was considered a reliable marker of parasympathetic (vagal) activity, whereas LF power was interpreted cautiously due to its mixed sympathetic and parasympathetic influences, especially in emotionally or cognitively demanding contexts.

The LF/HF ratio served as a composite index of sympathovagal balance, acknowledging ongoing debates about its interpretation as a direct marker of sympathetic versus parasympathetic dominance (Laborde et al., 2017; Shaffer & Ginsberg, 2017). In this study, the LF/HF ratio was conceptualised primarily as a proxy for autonomic

adaptability, consistent with the broader aim of linking physiological flexibility to cognitive performance and emotional functioning.

This baseline HRV profile during the affective storm provided the data input for subsequent analyses, with delta scores ( $\Delta T1-T0$ ) for each HRV index representing individual changes across time points. These delta scores were correlated with changes in cognitive and affective measures, including global cognition, mood, and subjective cognitive complaints. This approach allowed us to test whether individual differences in autonomic regulation during emotional stimulation could serve as early psychophysiological markers of cognitive resilience or vulnerability in older adults with SCD (see Fig. 1).

## 2.7. Statistical analysis

All statistical analyses were conducted using Jamovi (version 2.2.5.0) and RStudio (version 4.3.2). Normality of each variable was assessed by visual inspection of histograms and Q-Q plots, as well as by examining skewness and kurtosis values. The Shapiro-Wilk test was used for formal normality testing.

Due to violations of normality assumptions in several variables, non-parametric Wilcoxon signed-rank tests were used to examine within-subject changes over time (T0 vs T1) in cognitive, affective, and physical health measures.

To investigate associations between changes in neuropsychological performance and autonomic reactivity during emotional stimulation, as indexed by HRV parameters, a Spearman's rank correlation matrix was computed. For each correlation coefficient ( $\rho$ ), 95% confidence intervals were calculated to assess estimated precision.

Partial correlations controlling for age, gender and educational level were also computed to evaluate their potential confounding effects on the observed associations.

All tests were two-tailed, with statistical significance set at  $p < 0.05$ . Correction for multiple comparisons was applied using the

Benjamini–Hochberg (BH) False Discovery Rate (FDR) procedure (Benjamini & Hochberg, 1995), controlling the expected proportion of false discoveries at  $\alpha = 0.05$ . Statistical significance was assessed using the original step-up formulation of the Benjamini–Hochberg test, comparing each ordered  $p$ -value to its corresponding rank-dependent critical value  $(i \div m)\alpha$ . The largest  $p$ -value satisfying this criterion was identified, and all tests with smaller or equal  $p$ -values were considered statistically significant.

### 3. Results

#### 3.1. Neuropsychological, emotional, physical and health profile

Descriptive statistics for cognitive, affective, physical, and health variables at baseline and follow-up are presented in Table 1. As several variables violated normality assumptions, as determined by visual inspection and formal testing, non-parametric tests were used in subsequent analyses.

##### 3.1.1. Demographic characteristics and cognitive performance over time

The final sample consisted of 21 healthy older adults (14 women, 7 men; mean age: 72.33 years, mean education: 12.95 years). At baseline, all participants met the SCD criteria according to Jessen et al. (2020) and were classified using the CFI. Despite subjective cognitive complaints, performance on standardised cognitive measures, including the ACE-R, MMSE, and other neuropsychological tests, remained within the normal range, thus excluding MCI.

At follow-up, approximately 12 months later, most participants still met the SCD criteria, with no significant group-level decline in global cognitive functioning. Only two participants showed signs of objective cognitive impairment, indicated by below-threshold scores on the delayed recall subtest of the RAVLT, consistent with normative age-related variability.

Paired-sample comparisons revealed no statistically significant changes in cognitive performance between T0 and T1 after FDR correction for multiple comparisons, indicating relative cognitive stability during the observation period (see Supplementary Table S2).

##### 3.1.2. Mood and health status

At baseline, approximately 40% of participants scored above the clinical threshold on both the AES and BDI, indicating depressive or apathetic symptoms, while about 20% exceeded the HARS cutoff for anxiety.

At the 12-month follow-up, roughly one-third of the sample still scored above the threshold on the AES and BDI, and approximately 24% remained above the threshold on the HARS.

Despite these proportions, no statistically significant longitudinal changes were observed in mood symptoms or physical health indicators (i.e., CIRS) after FDR correction (see Supplementary Table S2).

Throughout the study, no participant met the criteria for physical frailty.

These results suggest overall stability in emotional and physical health across the two assessment points.

**Table 1**

Demographic and neuropsychological characteristics of study participants at baseline and follow-up.

	Baseline			Follow-up			Cut-off
	N	M	SD	N	M	SD	
<i>Demographic characteristics</i>							
Subjects	21			21			
Gender [women/men]	14/7			14/7			
Age [years]		72.33	5.02		73.43	5.10	
Education [years]		12.95	3.80		12.95	3.80	
<i>Neuropsychological assessment</i>							
Mini Mental State Examination		29.33	1.02		28.81	1.17	$\geq 23.8$
Addenbrooke's Cognitive Examination - Revised version		94.24	3.13		93.29	4.70	$\geq 79$ (<75 years old); $\geq 60$ (>75 years old)
Montreal Cognitive Assessment		25.52	2.62		25.14	2.57	$\geq 17.363$
Cognitive Function Instrument							
Self-report		5.00	1.88		3.98	1.86	
Partner-report		3.85	1.70		2.90	2.04	
Self-partner		1.15	2.06		1.07	1.62	
Rey Auditory Verbal Learning Test							
15 instant words		41.43	7.52		43.24	8.60	$\geq 28.53$
15 delayed words		8.48	3.20		8.29	3.96	$\geq 4.69$
Digit span forward		6.00	0.84		6.38	0.97	$\geq 4.26$
Corsi Block Tapping Test		4.95	0.86		5.05	1.12	$\geq 3.46$
Phonemic fluency		44.90	9.19		45.52	12.41	$\geq 17.35$
Semantic fluency		27.57	5.21		25.98	5.99	$\geq 7.25$
Token Test		33.74	1.87		33.90	1.76	$\geq 29$
Trail Making Test - part A		50.31	12.75		47.86	15.61	$\leq 94$
Trail Making Test - part B		101.09	26.70		106.57	41.27	$\leq 283$
Trail Making Test B-A		50.81	20.52		58.71	32.87	$\leq 187$
<i>Neuropsychiatric assessment</i>							
Apathy Evaluation Scale		13.70	4.45		13.95	5.65	$\leq 14$
Beck Depression Inventory		9.40	4.43		8.00	4.80	$\leq 9$
Hamilton Rating Scale for Anxiety		10.90	5.23		10.00	5.25	$\leq 14$
<i>Health status</i>							
Cumulative Illness Rating Scale							
Severity index		1.46	0.24		1.48	0.19	
Comorbidity index		2.00	1.18		1.90	1.09	

Note. N, number. M, mean. SD, standard deviation.

### 3.2. Descriptive profile of HRV indices at baseline and follow-up

To characterise the autonomic profile of the sample, descriptive statistics for key HRV parameters were examined at baseline and follow-up. These measures reflect distinct aspects of autonomic nervous system regulation. Time-domain indices such as SDNN, RMSSD, and SD HR track overall heart rate variability and short-term parasympathetic activity. Mean RR interval and mean HR provide information on average cardiac cycle length and resting heart rate, respectively, offering insights into basal cardiovascular function.

Total power autoregressive (TOTpow\_AR), a frequency-domain metric, represents total autonomic power and serves as a global index of autonomic responsiveness. Nonlinear indices, including SD1 and SD2, capture the complexity of beat-to-beat HR fluctuations, with SD1 mainly reflecting parasympathetic modulation, and SD2 indexing both sympathetic and parasympathetic influences.

Visual inspection and formal normality tests indicated that several HRV variables deviated from a normal distribution. Consequently, Wilcoxon signed-rank tests were applied to evaluate longitudinal changes between T0 and T1.

No statistically significant differences were found in any HRV parameter over the 12-month interval. These results remained consistent after FDR correction for multiple comparisons, suggesting stable autonomic function throughout the follow-up period (see Supplementary Table S3).

### 3.3. Heart rate variability and its relationship with cognitive changes

To determine whether longitudinal variations in autonomic functioning were associated with cognitive trajectories, Spearman's rank-order correlations were calculated between delta scores ( $\Delta = T1-T0$ ) of neuropsychological measures and HRV indices.

Table 2 presents FDR-corrected results. Fig. 2 illustrates the significant associations after FDR correction based on raw (non-partial) correlation analyses.

Two significant associations were identified between changes in visuospatial working memory ( $\Delta\_CORSI$ ) and cardiac parameters.  $\Delta\_CORSI$  was negatively correlated with changes in mean HR and positively correlated with changes in mean RR interval, both of which remained significant after FDR correction.

For global cognitive performance, changes in ACE-R total score ( $\Delta\_ACE-R$ ) were positively correlated with several HRV indices, including  $\Delta\_SDNN$ ,  $\Delta\_SD\_HR$ ,  $\Delta\_TOT\ pow\_AR$ ,  $\Delta\_RMSSD$ ,  $\Delta\_SD1$ , and  $\Delta\_SD2$ . All these correlations survived FDR correction.

However, the robustness of these effects varied across indices. In particular, although the correlation between  $\Delta\_ACE-R$  and  $\Delta\_SD1$  survived BH FDR correction in the bivariate analyses, its 95% confidence interval included zero.

A further significant positive correlation was also observed between

changes in verbal fluency ( $\Delta\_ACE-R\_F$ ) and  $\Delta\_SD\_HR$ , which remained significant after FDR correction.

All detailed statistics, including Spearman's rho, *p*-values, BH critical values, and confidence intervals, are provided in Table 2.

Given the absence of a priori hypotheses regarding sex differences, exploratory correlation analyses stratified by gender were conducted and are reported separately for descriptive purposes. These results are presented for completeness in the Supplementary material (see Supplementary Tables S4 and S5) but are considered ancillary to the main analyses, as they are difficult to interpret due to the unbalanced sample composition (14 females vs 7 males) and the consequently limited statistical power for reliable between-gender comparisons.

To further assess the robustness of the observed associations, partial correlation analyses were conducted while controlling for age and educational level (see Table 3). After adjustment for these covariates, the previously observed associations largely remained statistically significant following FDR correction. Specifically, significant partial correlations were observed between  $\Delta\_CORSI$  and both  $\Delta\_MEAN\_HR$  and  $\Delta\_MEAN\_RR$ , as well as between  $\Delta\_ACE-R$  and multiple HRV indices, including  $\Delta\_SDNN$ ,  $\Delta\_TOT\ pow\_AR$ ,  $\Delta\_RMSSD$ ,  $\Delta\_SD\_HR$ , and  $\Delta\_SD2$ . In addition, a significant association between changes in verbal fluency ( $\Delta\_ACE-R\_F$ ) and  $\Delta\_SD\_HR$  was also retained.

Notably, after adjustment for age and educational level, the association between  $\Delta\_ACE-R$  and  $\Delta\_SD1$  remained statistically significant and was characterised by a 95% confidence interval that no longer included zero, indicating increased precision relative to the unadjusted analysis.

## 4. Discussion

This exploratory longitudinal study examined whether autonomic regulation, as measured by HRV during emotionally evocative stimulation, is associated with subtle cognitive changes in older adults with SCD.

Although cognitive performance, mood, and autonomic indices remained stable at the group level over 12 months, analyses of individual difference scores revealed selective associations between longitudinal variations in HRV, particularly indices reflecting parasympathetic modulation, and performance in global cognition, visuospatial working memory, and verbal fluency. Notably, the strength and robustness of these associations varied across analytical steps, emphasising the importance of statistical correction and covariate adjustment when interpreting psychophysiological markers in preclinical populations.

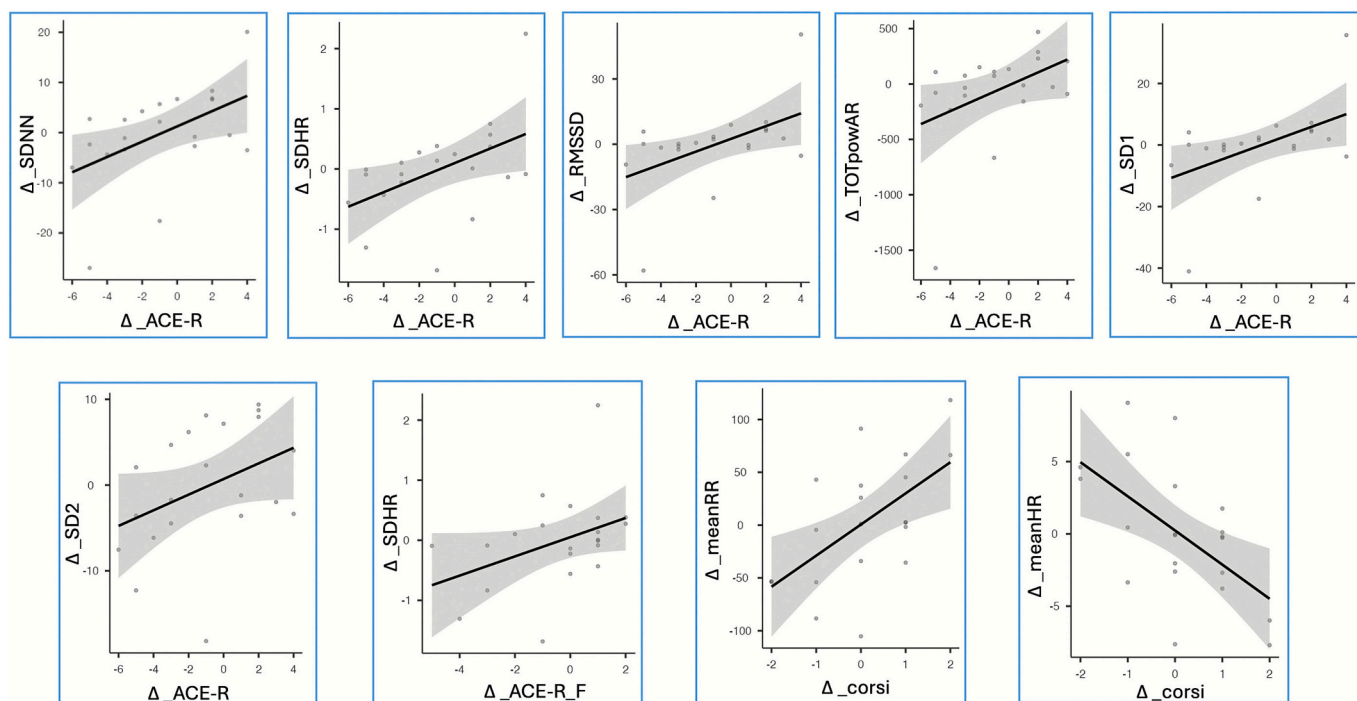
Ageing is accompanied by biological processes that may progressively compromise cognitive function, including structural and functional brain changes, vascular alterations, and neurochemical dysregulation (DeCarli, 2003; Murman, 2015). In parallel, cardiac vagal activity tends to decrease with advancing age (Bertson et al., 1997), potentially reducing the organism's capacity to respond flexibly to

**Table 2**

Correlations between changes in cognitive variables and heart rate variability indices including Spearman's rho ( $\rho$ ), *p*-value, and 95% confidence intervals.

$\Delta$ neuropsychological tests	$\Delta$ psychophysiological measures	rho	<i>p</i> -Value	CI lower	CI upper	BH critical value	BH adjusted <i>p</i> -value	Significant
$\Delta\_CORSI$	$\Delta\_MEAN\_HR$	-0.592	0.004	-0.831	-0.188	0.0056	0.02250	Yes
$\Delta\_CORSI$	$\Delta\_MEAN\_RR$	0.587	0.005	0.215	0.837	0.0111	0.02250	Yes
$\Delta\_ACE-R$	$\Delta\_SDNN$	0.505	0.019	0.088	0.818	0.0166	0.03700	Yes
$\Delta\_ACE-R$	$\Delta\_SD\_HR$	0.503	0.020	0.092	0.802	0.0222	0.03700	Yes
$\Delta\_ACE-R$	$\Delta\_TOT\ pow\_AR$	0.493	0.023	0.064	0.771	0.0278	0.03700	Yes
$\Delta\_ACE-R$	$\Delta\_RMSSD$	0.473	0.030	0.010	0.820	0.0333	0.03700	Yes
$\Delta\_ACE-R$	$\Delta\_SD1$	0.473	0.030	-0.019	0.801	0.0388	0.03700	Yes
$\Delta\_ACE-R$	$\Delta\_SD2$	0.463	0.034	0.076	0.767	0.0444	0.03700	Yes
$\Delta\_ACE-R\_F$	$\Delta\_SD\_HR$	0.457	0.037	0.068	0.733	0.0500	0.03700	Yes

Note.  $\Delta$ , delta scores (baseline – follow-up); CI, confidence intervals; BH, Benjamini-Hochberg; Corsi, Corsi Block Tapping Test; ACE-R, Addenbrooke's Cognitive Examination - Revised version; ACE-R\_F, ACE-R verbal fluency; HR, heart rate; RR, R-R interval; SDNN, standard deviation of normal-to-normal intervals; SD\_HR, standard deviation of HR; TOTpow\_AR, total power - autoregressive; RMSSD, root mean square of successive differences; SD1, Poincaré plot standard deviation perpendicular to the line of identity; SD2, Poincaré plot standard deviation along the line of identity.



**Fig. 2.** Scatterplots of significant Spearman correlations based on the raw data. ACE-R, Addenbrooke's Cognitive Examination – Revised version. ACE-R\_F, ACE-R verbal fluency. Corsi, Corsi Block Tapping Test. HR, heart rate; RR, R-R interval; SDNN, standard deviation of normal-to-normal intervals; SD\_HR, standard deviation of HR; TOTpow\_AR, total power - autoregressive; RMSSD, root mean square of successive differences; SD1, Poincaré plot standard deviation perpendicular to the line of identity; SD2, Poincaré plot standard deviation along the line of identity.

**Table 3**

Partial correlations between changes in cognitive variables and heart rate variability indices including Spearman's rho ( $\rho$ ),  $p$ -value, and 95% confidence intervals controlling for age and educational level.

$\Delta$ neuropsychological tests	$\Delta$ psychophysiological measures	rho	$p$ -Value	CI lower	CI upper	BH critical value	BH adjusted $p$ -value	Significant
$\Delta$ _CORSI	$\Delta$ _MEAN_HR	-0.571	0.011	-0.843	-0.135	0.0055	0.0360	Yes
$\Delta$ _CORSI	$\Delta$ _MEAN_RR	0.584	0.012	0.101	0.846	0.0111	0.0360	Yes
$\Delta$ _ACE-R	$\Delta$ _SDNN	0.533	0.019	0.084	0.825	0.0166	0.0360	Yes
$\Delta$ _ACE-R	$\Delta$ _TOTpow_AR	0.530	0.020	0.064	0.789	0.0222	0.0360	Yes
$\Delta$ _ACE-R	$\Delta$ _SD1	0.508	0.026	0.069	0.783	0.0277	0.0360	Yes
$\Delta$ _ACE-R	$\Delta$ _RMSSD	0.508	0.026	0.044	0.789	0.0333	0.0360	Yes
$\Delta$ _ACE-R	$\Delta$ _SD_HR	0.505	0.028	0.054	0.828	0.0388	0.0360	Yes
$\Delta$ _ACE-R_F	$\Delta$ _SD_HR	0.483	0.036	0.006	0.788	0.0444	0.0405	Yes
$\Delta$ _ACE-R	$\Delta$ _SD2	0.467	0.044	0.014	0.790	0.0500	0.0440	Yes

Note.  $\Delta$ , delta scores (baseline – follow-up); CI, confidence intervals; BH, Benjamini–Hochberg; Corsi, Corsi Block Tapping Test; ACE-R\_F, ACE-R verbal fluency; ACE-R, Addenbrooke's Cognitive Examination – Revised version; HR, heart rate; SD\_HR, standard deviation of heart rate; SD2, Poincaré plot standard deviation along the line of identity; RMSSD, root mean square of successive differences; SD1, Poincaré plot standard deviation perpendicular the line of identity; SDNN, Standard Deviation of Normal-to-Normal Intervals; RR, R-R Interval; TOTpow\_AR, total power – autoregressive.

environmental and emotional demands. In this context, the present findings therefore suggest that interindividual variability in autonomic regulation during emotionally evocative stimulation may be meaningfully related to cognitive performance, even when no overt cognitive decline is detectable at the group level. This interpretation is consistent with accumulating evidence indicating that autonomic regulation plays a role in sustaining cognitive performance in ageing, with HRV emerging as a sensitive physiological correlate of this relationship (Forte et al., 2019).

From a theoretical perspective, the observed associations can be interpreted within the framework of the Neurovisceral Integration Model (Porges, 1995; Thayer et al., 2010; Thayer & Lane, 2000, 2009), which conceptualises HRV as an index of the functional integrity of a distributed cortico-subcortical network supporting autonomic regulation, emotional processing, and executive control. This network includes prefrontal regions that are critically involved in higher-order cognition and are known to be vulnerable to age-related changes (Ellis & Thayer,

2010; Thayer et al., 2012). In this framework, greater vagally-mediated HRV during emotional stimulation may reflect more efficient prefrontal inhibitory control over subcortical and brainstem regions, thereby supporting adaptive emotional and cognitive regulation. The present results extend this model by suggesting that individual differences in such regulatory efficiency are associated with cognitive performance in older adults with SCD, particularly in cognitively demanding domains.

The present findings build on previous evidence linking HRV to neuropsychological, affective and age-related factors (Almeida-Santos et al., 2016; Fatisson et al., 2016; Jandackova et al., 2016), and support the view that individual differences in autonomic reactivity, particularly in emotionally salient contexts, may be meaningfully associated with cognitive trajectories in SCD. Although group-level measures of cognition and emotional state remained stable over time, interindividual variability in HRV change scores was selectively related to cognitive outcomes, reinforcing the importance of longitudinal approaches that focus on individual differences when investigating early cognitive

vulnerability.

From an interpretative standpoint, the pattern of associations observed suggests that indices reflecting parasympathetic engagement and overall autonomic flexibility may be particularly informative in the context of early cognitive vulnerability.

Measures capturing global autonomic regulation appear to provide stable associations with cognitive performance when relevant demographic factors are taken into account. In this regard, differences in robustness observed in unadjusted analyses highlight the importance of analytic context and underscore the need to control for relevant covariates when interpreting psychophysiological-cognitive associations. This observation is consistent with previous work indicating that broader measures of autonomic flexibility may better capture the functional integrity of the central autonomic network in older adults (Forte et al., 2019; Jandackova et al., 2016).

Visuospatial working memory emerged as one of the cognitive domains most consistently associated with autonomic regulation. Working memory relies heavily on prefrontal inhibitory mechanisms, which are known to be sensitive to age-related changes (Arnsten & Goldman-Rakic, 1998; Borella et al., 2008; Goldman-Rakic, 1998; Verhaeghen & Cerella, 2002). In this context, greater parasympathetic modulation during emotional stimulation may indicate more efficient central autonomic regulation, supporting the maintenance of visuospatial working memory performance over time despite subjective cognitive complaints.

More broadly, these findings are consistent with previous evidence linking vagally mediated HRV to global cognition, executive functioning, and language abilities in older adults, both in normative ageing and in populations at increased risk of cognitive decline (Almeida-Santos et al., 2016; Forte et al., 2019; Thayer et al., 2009). Together, the results support the view that HRV reflects the regulatory efficiency of the central autonomic network underlying higher-order cognitive functions (Smith et al., 2017; Thayer et al., 2009).

At the same time, the results highlight the value of adopting multi-metric approaches when investigating HRV-cognition relationships, as complementary indices may capture partially distinct aspects of autonomic regulation. When appropriate statistical controls are applied, convergent patterns across indices can provide robust evidence for psychophysiological-cognitive associations in preclinical populations.

Altogether, the present results provide further support for autonomic dysfunction as a potential mechanism linking early neurobiological vulnerability to cognitive variability in ageing. Parasympathetic dysregulation has been reported in mild cognitive impairment and linked to early alterations in the central autonomic network (Collins et al., 2012). Autonomic imbalance is also associated with vascular risk factors (La Rovere et al., 1998; Tsuji et al., 1996), which increase the risk of dementia (Launer, 2005), and stress-related dysregulation may further contribute to cognitive decline in later life (Qiu et al., 2003; Vergheze et al., 2003). These mechanisms are particularly relevant for SCD, a condition characterised by self-perceived cognitive deterioration in the absence of objective impairment but associated with an increased risk of subsequent cognitive decline and dementia (Mitchell et al., 2014; Nicolini et al., 2024; Sidenkova et al., 2023).

A number of methodological limitations should be acknowledged. The relatively small sample size limits the generalisability of the findings and, despite a priori power estimation, statistical adjustment for age and educational level, and correction for multiple comparisons using FDR, constrains the reliable examination of subgroup-specific or interaction effects. In addition, although this study did not include a separate control group, it is important to note that participants with SCD are, by definition, cognitively unimpaired and typically fall within the normative range of healthy ageing. For this reason, the inclusion of a distinct control group was not considered essential in this exploratory framework. Finally, HRV variability was assessed in a laboratory setting, which may limit ecological validity. Future studies could benefit from ambulatory autonomic monitoring using wearable devices, combined with ecologically valid emotional paradigms (e.g., Sampaolo et al.,

2025) and multimodal neuroimaging, to better characterise early autonomic and cognitive vulnerability.

Despite these limitations, a notable strength of the present study is the use of an emotionally evocative and dynamic stimulation paradigm to elicit autonomic responses. Unlike most previous investigations, which focused on resting-state HRV, this approach was designed to increase sensitivity to interindividual differences in autonomic reactivity by exposing participants to rapidly changing emotional stimuli. Emotional contexts place greater regulatory demands on the central autonomic network, and may therefore reveal subtle vulnerabilities that remain undetectable under resting conditions. The present findings provide preliminary support for task-evoked HRV as a sensitive psychophysiological marker of early cognitive variability, extending previous work on emotional and autonomic regulation in healthy ageing (Amanzio, Cipriani, Bartoli, et al., 2023; Amanzio, Cipriani, Canessa, et al., 2023; Cipriani et al., 2025).

In conclusion, this study provides preliminary longitudinal evidence linking individual differences in HRV change scores to variations in cognitive performance in older adults with SCD. Although no group-level decline in cognitive or autonomic functioning was observed over time, domain-specific associations, particularly involving visuospatial working memory and verbal fluency, underscore the relevance of parasympathetic regulation and autonomic flexibility. These findings highlight the importance of focusing on individual trajectories rather than group averages in preclinical populations, where subtle physiological changes may precede overt cognitive decline and could inform early, personalised interventions targeting autonomic and emotional regulation to support cognitive resilience.

#### CRediT authorship contribution statement

**Giuseppina Elena Cipriani:** Writing – review & editing, Investigation, Data curation. **Francesca Borghesi:** Writing – review & editing, Formal analysis, Data curation. **Pietro Cipresso:** Writing – review & editing, Formal analysis, Data curation. **Nicola Canessa:** Writing – review & editing, Formal analysis, Data curation. **Sara Molfese:** Writing – review & editing, Investigation, Data curation. **Cristiano Manco:** Writing – review & editing, Investigation, Data curation. **Alice Chirico:** Formal analysis, Data curation. **Gloria Simoncini:** Formal analysis, Data curation. **Matteo Anselmino:** Writing – review & editing, Formal analysis, Data curation. **Martina Amanzio:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Funding acquisition, Formal analysis, Conceptualization.

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#### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.actpsy.2026.106308>.

#### Data availability

The data sets generated and/or analyzed in this study are available upon request from the corresponding author.

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