Behavioural Brain Research 459 (2024) 114771

Contents lists available at ScienceDirect

Behavioural Brain Research

journal homepage: www.elsevier.com/locate/bbr

Loneliness during the post-confinement period: The significance of social living conditions for stress biomarkers and memory

Daniela Batallas [a], Valerie Rodriguez-Hernandez [a], Vanesa Hidalgo [a,b,*], Alicia Salvador [a,c,**]

[a] Laboratory of Social Cognitive Neuroscience, Department of Psychobiology and IDOCAL, University of Valencia, Valencia, Spain
[b] Department of Psychology and Sociology, Area of Psychobiology, University of Zaragoza, Teruel, Spain
[c] Spanish National Network for Research in Mental Health CIBERSAM, 28029, Spain

ARTICLE INFO

Keywords:
Loneliness
Face-to-face contact
Covid-19
Hair Cortisol
Heart Rate Variability
Memory

ABSTRACT

In the aftermath of the COVID-19 lockdown, concerns about the impact of loneliness and reduced social interactions on mental health have arisen. This study explored the repercussions of post-lockdown social restrictions across psychological (loneliness, perceived stress, and depressive symptoms), biological (hair cortisol and cardiovascular activity), and cognitive dimensions (subjective memory complaints and working, declarative, and prospective memory), with a specific emphasis on perceived loneliness and the living situation. The study included 45 students: 23 (mean age = 25.69 years) in the Alone Group (AG), who experienced significant family changes and international relocation, and 22 (mean age = 25.50 years) in the Not Alone Group (NAG), who maintained their nuclear family and did not move from their home country. We assessed heart rate variability (HRV) before, during, and after immediate memory evaluations using time-domain (the square root of the mean, RMSSD) measures. The analysis revealed no significant group differences in telematic contact with family and friends, perceived stress, or depression. However, the AG participants reported fewer face-to-face interactions and greater perceived loneliness compared to the NAG. Additionally, the AG group exhibited slightly higher hair cortisol levels and worse working memory (WM) and prospective memory (PM) performance. Importantly, no significant associations were observed between memory outcomes and stress biomarkers. However, a significant interaction effect of loneliness in the relationship between hair cortisol levels and PM was found. That is, hair cortisol concentrations were negatively related to PM when participants perceived high and moderate loneliness. This interaction was absent in the working and declarative memory domains. In summary, these findings underscore the intricate interplay between loneliness, cortisol, and memory, emphasizing the need for comprehensive research on the complex mechanisms governing these multifaceted relationships.

1. Introduction

Quarantines produced by the SARS-CoV2 (COVID-19) pandemic globally confined people to their homes, leading to social isolation from approximately March to June 2020. Additionally, even after the lockdowns were lifted, various sanitary measures continued to be enforced worldwide, particularly in public spaces, restricting both individual and community social interactions. Spain, for example, maintained measures such as distancing in crowded spaces, hybrid classes, limited travel, and the mandatory use of face coverings to prevent COVID-19 transmission, among others.

The recent pandemic lockdown has been widely acknowledged as a significant psychosocial stressor [10,15] that has affected and continues to affect emotional, cognitive, and behavioral aspects (i.e., mood, daily habits, social relationships, etc.) that are central to human well-being [48,60]. Furthermore, it is important to note that loneliness and social isolation can have enduring implications for mental and physical health. Indeed, these variables have been associated with a wide range of physical, mental health, and cognitive issues, including psychosocial stress, depression, generalized anxiety, cardiovascular and pulmonary diseases, and even mortality [57,58,8].

Given the inherently stressful circumstances of the COVID-19 pandemic lockdown and the well-established connection between social isolation and cognitive performance found in earlier studies [23,43], it is reasonable to suggest that social isolation may have negatively impacted cognitive functions. Indeed, current research highlights the

* Corresponding author at: Department of Psychology and Sociology, Area of Psychobiology, University of Zaragoza, Teruel, Spain.
** Corresponding author at: Laboratory of Social Cognitive Neuroscience, Department of Psychobiology and IDOCAL, University of Valencia, Valencia, Spain.

https://doi.org/10.1016/j.bbr.2023.114771
Received 11 July 2023; Received in revised form 29 October 2023; Accepted 18 November 2023
Available online 23 November 2023

significance of factors such as living alone, lacking close relationships, and having a limited social network, all of which have been associated with a decline in overall mental well-being, impaired emotional and reasoning self-regulation, and an increased risk of cognitive impairment [25,40,6].

In this context, different types of memory have been extensively studied due to their pivotal role in daily activities [25,70]. Research has primarily focused on working memory (WM) (Ashcraft & Kirk, 2001; [21]), declarative memory [65], and prospective memory (PM) [62]. Notably, during the Covid-19 pandemic, studies shed light on the contrasting effects of confinement and the positive influence of social interaction on memory performance. For instance, Pisano et al. [62] established that the restrictive measures of the pandemic had a negative impact, given that the perceived memory failures of university students coincided with the results of standardized tests highlighting a decrease in both WM and PM. Similarly, Ingram et al. [40] observed that individuals who were living alone demonstrated improved WM performance as opportunities for social contact increased. Although memory has been a predominant focus in the context of the Covid-19 pandemic, the extent of these cognitive deficits has not been definitively established, as discussed in the review by Llana et al. [49].

The precise mechanism by which social isolation or loneliness affects cognitive processes is not well-defined. However, Cacioppo and Hawkley [12] proposed that social isolation may lead to heightened social hypervigilance, characterized by intrusive thoughts, rumination, and stress. This activation could involve neurobiological mechanisms related to the hypothalamic-pituitary-adrenocortical (HPA) axis, resulting in elevated cortisol levels. Cortisol, a well-established hormone in the HPA axis [46,75], may serve as a short-term indicator of loneliness, predicting long-term adverse physical, cognitive, and mental health outcomes [75].

Moreover, some literature on the relationship between basal HPA axis activity and cognitive performance shows that higher cortisol release is related to worse cognitive performance ([30,52]; Ouanes & Popp, 2019), particularly on memory tasks dependent on hippocampal functioning (i.e. DM; [2,36]). Additionally, the hair cortisol measure, an integrated measure of cortisol exposure for up to several months, has been used to explore the relationship between long-term endogenous cortisol levels and cognitive performance (for more details see: [68]). In this context, Pulopulos et al. [63] proposed that individuals with lower long-term cortisol exposure might be more susceptible to the detrimental effects of HPA-axis dysregulation on cognitive processes (working memory and short-term verbal memory). Similarly, some studies have observed adverse connections between hair cortisol levels and cognitive performance, especially verbal memory [24,71]. Although these findings underscore the established value of hair cortisol as a marker of long-term stress and its association with cognitive functions, contradictory outcomes have also emerged in this domain (e.g., [56]), with a significant portion of these studies conducted with older populations [63,69,83]. Thus, further exploration of these variables in young people is warranted.

Another system impacted by physical and psychosocial stress is the Autonomic Nervous System (ANS), often assessed through Heart Rate Variability (HRV), which measures heart rate variation over time [27,80]. It has been suggested that the vagus nerve, part of the parasympathetic system, plays a role in regulating cortisol responses during stress conditions [80]. In this line, a bidirectional interaction between the vagus nerve and the HPA axis supports this connection [55,79], which suggests that individuals with low vagal activity might show poor controlled emotional responses, worse stress adaptation, and impaired cognitive performance [17,64,86]. Moreover, HRV has been linked to cognitive performance, as in the Neurovisceral Integration Model [78], potentially affecting cognitive function due to imbalances in parasympathetic and sympathetic input, which can lead to prolonged and exaggerated autonomous stress responses [17,64,86].

However, studies investigating HRV and cortisol responses during stress often reveal weak or non-significant associations ([13,3,44,50,9]; but see [22]), highlighting the need for additional research in this field.

Based on the above, the aim of this study was to examine how social contact restrictions in the post-pandemic context could affect people at psychological/affective, biological, and cognitive levels, with a focus on the role of perceived loneliness and the living situation. Drawing on the social buffering hypothesis [18], we hypothesized that participants who were not living with their usual nuclear family and had to move from their home country during the restrictive social contact period after the Covid-19 lockdown would exhibit more significant mental, physical, and cognitive health consequences (Hypothesis 1). More precisely, based on previous studies [31,39,48,60], we anticipated that the current living situation would affect loneliness, depression, anxiety, stress, some biological variables (higher cortisol levels and lower heart rate variability during assessments), and cognitive performance. Additionally, we examined the association between biological variables and memory. Moreover, despite the heterogeneity in the previous findings, we expected to find negative relationships between biological factors and memory performance (Hypothesis 2), and a moderator role of loneliness in this association (Hypothesis 3) (See Fig. 1).

2. Materials and methods

2.1. Participants

A final sample of 45 young students between 20 and 33 years old (mean = 25.6 years old, SD = 3.107) participated in the study. They were recruited in person from March to April 2021. All the participants were students at the University of Valencia who were attending the last year of their bachelor's degree or starting a master's degree. All the participants were native Spanish speakers.

The groups were established according to their living situation (living alone far from their home country/or living with others in their home country) during the past 8 months, including the study period. The group that was *living alone* (Alone Group, AG) was composed of 23 participants consisting of a total of 16 women and 7 men with a mean age of 25.70 years (SD=2.721). The inclusion criteria for the AG group were as follows: having to change their family nucleus, having to move from the home country, and having lived alone during the past 8 months. The group that was *living with others* (not alone group, NAG) was composed of 14 women and 8 men with a mean age of 25.50 years (SD=3.529). For the NAG group, the inclusion criteria were: not having changed their family nucleus or moved from the home country, and having lived with relatives, friends, or spouse during the past 8 months, including the study period.

The exclusion criteria used for both groups encompassed the following conditions: the presence of cardiovascular or neuroendocrine abnormalities, a history of neurological or psychiatric disorders, the consumption of more than 10 cigarettes per day, or the excessive use of drugs or alcohol (not exceeding 20 g/day for women and 30 g/day for men). Individuals who reported meeting any of these exclusion criteria in a preliminary telephone interview were not invited to participate in the study. Approximately five participants were excluded from the AG group and 12 from the NAG group. Consequently, no data were collected from these individuals.

2.2. Procedure

Participants who met the inclusion criteria were contacted by telephone and summoned to the University of Valencia to participate in a single evaluation session lasting approximately 55–60 min. The study took place between March and May 2021, when preventive social distancing measures (e.g., hybrid classes, limited travel, no social or mass events, and mandatory use of face masks) were in effect. Participants' well-being was prioritized throughout the protocol. All the necessary preventive measures were taken, such as disinfection, social

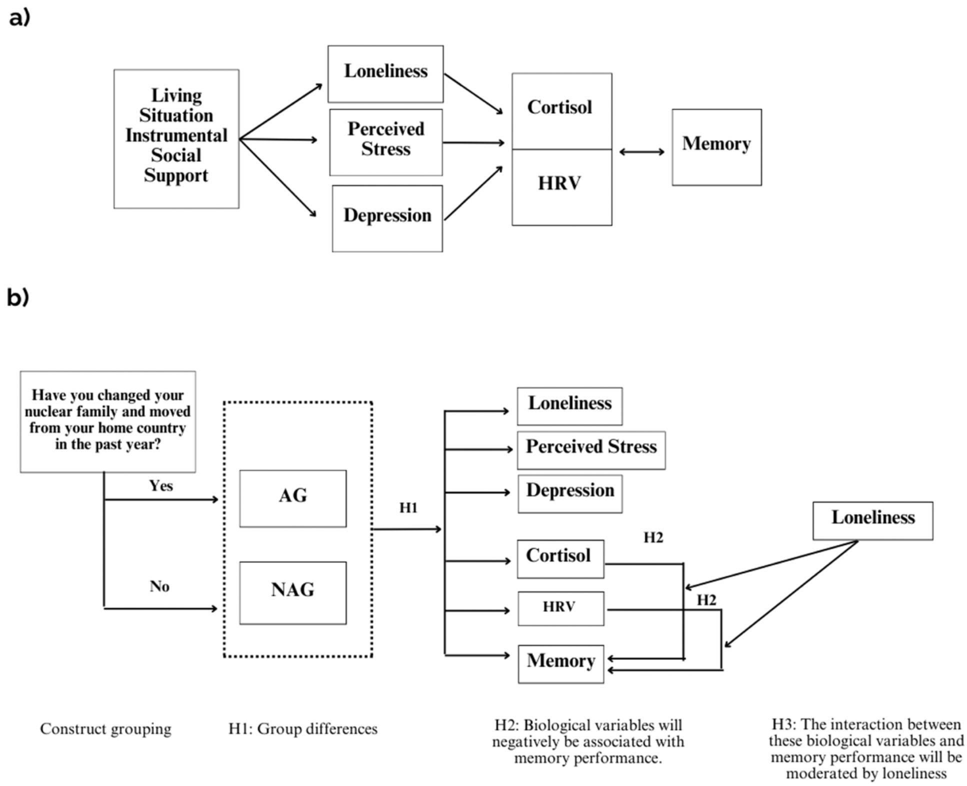

Fig. 1. Conceptual models for the theoretical framework of the hypotheses: (a) Existing literature, suggesting that participants' living situations during the pandemic, whether living alone after relocation or with others, are associated with differences in key variables. It is emphasized that living alone during the pandemic has been linked to increased feelings of loneliness, stress, and depression, reflected in elevated cortisol levels and reduced Heart Rate Variability (HRV). Furthermore, it is posited that these factors may impact memory performance. (b) Framework of the hypotheses: We grouped people into two categories, AG and NAG, based on their living situation. H1: Group differences in psychological, biological and cognitive variables, H2: Correlations between biomarkers and memory performance, H3: We expected that the interaction between the biomarkers and memory performance will be moderated by loneliness.

distancing, obligatory use of masks, etc.

Before the session, participants were told to refrain from smoking, eating, or taking stimulants (e.g., tea or coffee) at least two hours before the session, and to avoid engaging in intense physical activity 24 h before the session. The research protocol was the same for both groups (AG and NAG). All participants received written information about the study and signed an informed consent form to participate in the study, which was conducted in accordance with the Declaration of Helsinki. The Ethics Committee of the University of Valencia approved the study.

The research protocol (see Fig. 2) started with habituation (*pre-tasks* phase) for 10 min to ensure the participant's adaptation to the setting. During this phase, a chest strap for heartbeat detection was placed, and

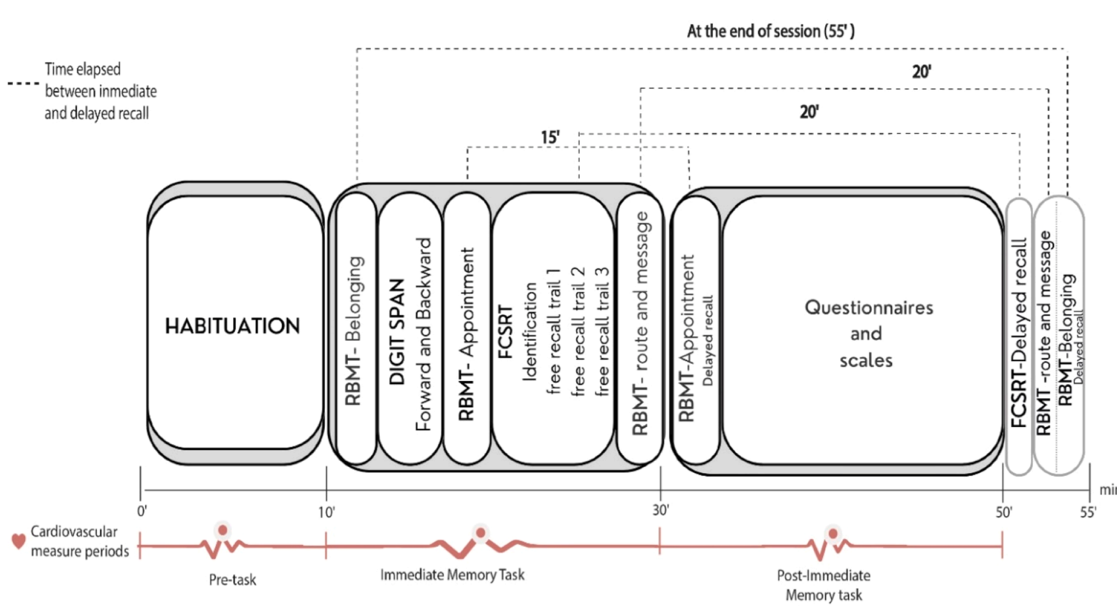

Fig. 2. A representative timeline of the session.

participants did not receive any specific instructions other than to breathe normally, in order to avoid any disturbance in the cardiovascular measurement. Next, the *immediate memory-task* phase, which lasted approximately 20 min, took place, and participants performed the following memory tests or subtests: 1) RBMT-belonging (PM), 2) Digit Span-Forward and Digit Span-Backward (WM), 3) RBMT-Appointment (PM), 4) FCSRT-immediate (DM), and 5) RBMT-route and RBMT-message (PM). During the next phase, the *post-immediate memory task* phase, participants performed the delayed RBMT-Appointment and filled out some psychological questionnaires and scales. After that, participants completed the delayed-free and facilitated recall subtests of the FCSRT, as well as the delayed RBMT-route, RBMT-message, and RBMT-belonging. The cardiovascular recording was continuous throughout the session..

2.3. Questionnaires and psychological scales

2.3.1. Sociodemographic information related to COVID-19 and daily life habits

The questionnaire designed to collect data on socio-demographic variables consisted of three sections: 1) COVID-19 Conditions, which covers symptoms, diagnoses, hospitalization, lingering effects, and the impact on family and friends. The survey also assesses emotional well-being, changes in the living situation, household composition, and pandemic-related stressors. 2) Sociodemographic Characteristics, which allowed us to gather data on various variables of interest, including age, sex, completed education level, alcohol consumption, and cigarette smoking. 3) Lastly, participants responded to a section of questions about their social contact with family and friends, in order to assess their conditions during the study period. This section also included additional questions about aspects related to mobility and social interactions. It began by collecting information about the participant's nationality and then explored experiences of relocation in the past year, requesting details about the type of move and any time zone differences in the case of relocating to another country. Subsequently, the questions delved into aspects of social contact with family and friends, inquiring about the frequency (the average number of hours in a typical week in the past year) and communication methods employed (such as face-to-face, WhatsApp, phone calls). Detailed questions are found in Supplementary Data 1.

2.3.2. Loneliness

Perceived loneliness was assessed with the Spanish adaptation [82] of the revised UCLA loneliness scale (R-UCLA) [67]. This scale contains 20 items rated on a four-point Likert scale ranging from 1 (never) to 4 (often). The total score ranges from 20 (low) to 80 (high). The internal consistency calculated in this study was 0.88.

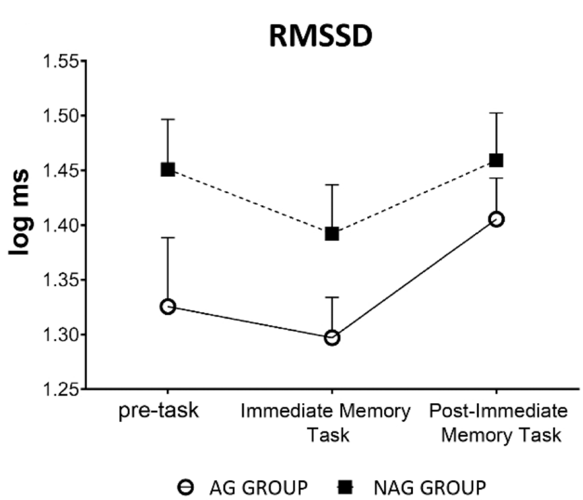

Fig. 3. HRV during pre-task, Immediate memory task, and post-immediate memory task by group. Values are shown as the means + standard error bars. The Y axis represents the log 10 transformed values and the X axis the 3 periods analyzed.

2.3.3. Perceived stress

Perceived stress was assessed with the Spanish version of the 4-item Perceived Stress Scale (PSS-4) [81], which was reduced from the original scale [19]. This scale is designed to measure the degree to which life situations are evaluated as stressful in the past month. The response scale is a five-point Likert-type scale (0 =never, 1 =rarely, 2 =sometimes, 3 = quite often, and 4 = very often). The total score ranges from 0 to 16. Our study showed good internal consistency, with a Cronbach's alpha of 0.85.

2.3.4. Depressive symptoms

Depressive symptoms were measured with the Spanish version [61] of the Beck Depression Inventory-II (BDI-II) [7]. This inventory is composed of 21 items that assess cognitive, somatic, and behavioral symptoms of depression experienced in the past two months. The response scale for each item ranges from 0 to 3, with four possible specific answers for each item (e.g., Mood: I do not feel sad; I feel sad most of the time; I am sad all the time; I am so sad and unhappy that I can't stand it). By directly adding up the score on each item, a total global score can be obtained (from 0 to 63), where higher scores indicate a greater degree of depression. For this study, Cronbach's alpha was 0.94.

2.3.5. Subjective Memory Complaints (SMCs)

SMCs were measured with the Spanish version [51] of the Everyday Life Memory Failure (MFE-30) Questionnaire [77]. This questionnaire contains 30 items that explore SMCs through situations and activities of daily life. Items are rated on a Likert-type scale (0 = never or almost never to 4 = always or almost always). Higher scores indicate more everyday memory failures, with a maximum score of 120. Our study showed good internal consistency, obtaining a Cronbach's alpha of 0.94. In addition, we also used an initial question asking whether or not they had memory problems.

2.4. Memory

2.4.1. Working memory

To measure the participants' working memory performance, the Spanish version of the Digit Span from the Wechsler Memory Scale III (Wechsler, 1997) was administrated. For this study, we used both the Digit Span Forward (DS-Forward) and Digit Span Backward (DS-Backward) subtests.

DS-Forward is a subtest used to measure the spatial component of working memory and attentional processes, whereas DS-Backward is used for the WM executive component [20]. These subtests require participants to repeat a series of numbers of increasing lengths (up to a maximum of 9 digits on the DS-Forward and a maximum of 8 on the DS-Backward). Participants had to repeat the numbers in the same order (DS-Forward) or the reverse order (DS-Backward) of their presentation. For both subtests, each enclosure length was tested twice. After two errors on the same length in each version, the test ends. The maximum possible score on the DS-Forward is 16, whereas for the DS-Backward, it is 14.

2.4.2. Declarative memory

The Spanish adaptation [45] of the Free and Cued Selective Reminding Test (FCSRT; [32]) was used to measure declarative memory performance. The FCSRT measures episodic memory by controlling attention and cognitive processing. The test starts with an identification phase by asking the person to recognize 16 words that belong to a different semantic category. During this phase, the individual is told to identify the 16 words (the participant can only go on to the next phase after identifying all 16 words). There are three recall trial phases, each preceded by 20 s of counting backward to prevent recall from short-term memory. Each recall trial consisted of two parts. First, each subject had up to 2 min to freely recall as many items as possible. Second, aurally presented category cues were provided for items that were not retrieved by free immediate recall. If subjects failed to retrieve the item with the category cue, they were reminded by presenting the cue and the item together. The same recall procedure (freely and cued) is carried out after a 20 min interval during which subjects are required to perform non-verbal tasks. Following Hidalgo et al. [36], we calculated one outcome from this test: (i) Retention Rate percentage of the total number of words recalled after a 30 min delay compared to the total number of words recalled on the first three trials (Delayed Recall/Immediate Recall × 100) (DMI).

2.4.3. *Prospective memory*

To ecologically assess prospective memory, we used four subtests (belonging, appointment, and route and message) from the Rivermead Behavioral Memory Test (RBMT, [85]). The Belonging subtest is a remembering task where the examiner asks for a personal belonging that was hidden somewhere at the beginning of the session (range 0–4 points). The Appointment subtest consists of asking about a future appointment when an alarm rings (range 0–2 points). The route subtest involves remembering a route the examiner had previously shown. The message subtest is part of the route subtest, and it requires the participant to take an envelope and put it in the same place where the examiner put it when demonstrating the route subtest. The route and message subtests measure immediate and delayed recall, and we used both components. The score for both immediate and delayed recall on the route subtest is 5 points each; 1 point is awarded for each place covered in the correct order (range 0–10 points). The message subtest is scored separately; 2 points are awarded if the participant picks up the message instantly and 1 point if he/she leaves it in the correct place. The total score for both immediate and delayed recall ranges from 0 to 6 points. For the analyses, we used the total score on the Prospective Memory Test (PMT), which ranges from 0 to 22 points, using the sum of the raw scores on each subtest.

2.5. *Hair Cortisol*

At the end of the session, three strands of hair samples were carefully cut from the posterior vertex region. Given a general growth rate of 1 cm/month [74], these segments are assumed to reflect hair growth during the four months before the respective sampling points. Due to variability in lengths of strands of hair, only strands of hair (1 ×4 cm segmentation) adjacent to the scalp were analyzed. Hair samples were prepared and analyzed in the laboratory of Prof. Kirschbaum (Department of Psychology, Technische Universität Dresden, Germany). An ultra-performance liquid chromatography–tandem mass spectrometry (UPLC–MS/MS) method was used to examine hair cortisol samples, in line with the protocol by Wang et al. [84].

2.6. *Cardiovascular registry*

Cardiac activity was measured with the Polar watch model RS800cx (PolarCIC, USA). This device has a chest strap for heartbeat detection and transmission and a watch for data storage. The Polar device measures R-R intervals with a sampling rate of 1000 Hz. The obtained data were subsequently analyzed with Kubios Analysis software (Biomedical Signal Analysis Group, University of Kuopio, Finland). The electrocardiogram was visually analyzed, and artifact correction was performed using the "mean" correction option offered directly by the program. Means were analyzed from the middle of the recorded periods, following the recommendations of the Task Force (1996). Hence, we used a 5-minute interval from each of the three periods (pre-tasks, immediate memory task, and post-immediate memory task).

To assess HRV, we employed a time domain variable, specifically, the Root Mean Square of the Successive Differences (RMSSD) value. RMSSD is a reliable measure for capturing the short-term components of HRV, and it represents the square root of the mean of the sum of the squared differences between successive RR intervals. In healthy individuals, RMSSD serves as a robust indicator of vagal tone [42,78]. Importantly, RMSSD is less affected by respiratory influences, compared to high-frequency parameters [37].

2.7. *Statistical analyses*

To characterize the sample and assess the differences between the AG and NAG groups (Hypothesis 1) in the sociodemographic variables, psychological/affective characteristics (loneliness, perceived stress, depression, and SMCs), social interaction characteristics, and cortisol, independent Student's *t*-tests and chi-square were used. In cases of unequal variances, we applied *p*-value corrections based on Levene's test. To assess memory performance, we employed a working memory index (WMI), following the approach of Franz et al. [28]. DS Backward scores were adjusted for DS Forward. To calculate this adjusted index, we performed a one-way ANOVA and included ' DS forward' as a covariate. Then, to compare memory performance between groups, one-way ANOVAs were used, with the following memory outcomes as dependent variables: for working memory, WMI; for declarative memory, the retention rate (DMI); and for prospective memory, the total score (PMT). Effect size was assessed via partial eta-squared values, and the Greenhouse-Geisser correction was applied when the sphericity assumption was not met in the ANOVAs. For multiple comparisons, the False Discovery Rate (FDR) method was used to control for Type I error inflation, and all adjusted *p*-values were reported.

The Kolmogorov-Smirnoff test was used to test the normality of the biological variables. They were not normally distributed, and so they were log-transformed. Because not all the participants provided the hair sample or met the minimum required length, the total sample for this analysis consisted of 19 participants in the AG group (3 men and 16 women) and 12 in the NAG group (3 men and 9 women). In addition, for HRV analysis, the recordings of 1 man and 2 women in the AG group and 1 man in the NAG group had to be excluded due to movement artifacts or insufficient quality of the electrocardiogram signal. Therefore, the total sample for HRV was composed of 20 participants in the AG group (6 men and 14 women) and 21 in the NAG group (7 men and 14 women).

To measure cardiovascular activity during the memory task, a repeated-measures ANOVA was performed with Group (AG vs. NAG) as a between-subjects factor and Period (pre-tasks, immediate and post-immediate memory tasks) as an intra-individual factor. Post-hoc planned comparisons were performed using Bonferroni adjustments for the *p*-values.

To explore possible relationships between memory performance and hair cortisol and cardiovascular measures (Hypothesis 2), Pearson's correlations were calculated using the previously described memory outcomes, hair cortisol levels, and HRV-RMSSD during the memory task.

Finally, we conducted moderation analyses (Hypothesis 3) with cortisol and HRV as the independent variables separately, memory outcomes as the dependent variables, and loneliness as the moderating variable. For this analysis, we utilized PROCESS 3.4 in SPSS (Model 1). PROCESS employs bootstrapped bias-corrected 95% confidence intervals with 5000 bootstrapped samples to determine the significance of the interaction effect in the moderation analysis. When the confidence interval for the interaction effect in the moderation analysis did not include zero, it was interpreted as indicating a significant interaction or indirect effect, following Hayes [35].

The level of significance for all analyses was set at 0.05. All statistical analyses were performed with the statistical program SPSS version 21.0.

3. Results

3.1. Group differences

3.1.1. Sociodemographic and Psychological/affective characteristics

The sociodemographic and psychological/affective characteristics of both groups (described using means and standard deviations) are shown in Table 1. Student's *t*-tests showed no significant differences in age or years of education (all $p > 0.629$). Nor were there significant differences related to having contracted COVID-19, having a family member who died from COVID-19, or any other COVID-19-related questions on the questionnaire (see Supplementary Data 2) (all $p > 0.097$). Moreover, we found no significant differences in perceived stress and depression (both $p > 0.373$).

Although the AG group scored higher on loneliness ($p = 0.018$), the two groups did not exhibit significant differences in the average number of hours in a typical week spent communicating or contacting family ($t(43) = -1.259$, $p = 0.387$) and friends ($t(43) = -0.178$, $p = 0.910$), and they engaged in the same type of contact with family ($\chi 2 = 5.881$, $p = 0.638$) and friends ($\chi 2 = 3.360$, $p = 0.245$) at the telematic level (WhatsApp, Zoom, or similar). However, significant differences were found in face-to-face contact with family ($\chi 2 = 8.696$, $p = 0.018$) and friends ($\chi 2 = 11.761$, $p = 0.018$), with more participants in the NAG group reporting face-to-face contact than in the AG group (see Table 2).

Furthermore, we found a marginal difference in SMCs ($p = 0.056$), given that AG reported more memory complaints. There were also significant differences on the yes/no question about having memory problems ($\chi 2 = 10.672$, $p = 0.002$), with a higher percentage of people in the AG group reporting memory problems (60.9%), compared to 13.6% of the NAG.

3.1.2. Biomarkers

We found marginal differences in the hair cortisol concentrations ($t(29) = 2.426, p = 0.079$), with the AG group showing higher levels than the NAG group.

Analyses of the HRV response pattern during the memory tasks showed that, regarding the RMSSD, the Period factor reached statistical significance (F[2,78]=8.248, $p < 0.001$, $n_p^2 = 0.174$), reflecting lower values during the immediate memory tasks than during the post-immediate memory task period ($p < 0.001$). No significant differences were found between pre-task vs post-immediate memory tasks ($p = 0.306$) and immediate memory tasks ($p = 0.076$). In addition, no significant effects of the Group factor (F[1,39]= 2326, $p = 0.135$, $n_p^2 = 0.056$) or the Group x Period interaction (F[2,78]= 1.402, $p = 0.252$, $n_p^2 = 0.035$) were found.

3.1.3. Memory performance

One-way ANOVAs revealed significant effects of the Group on WM ($F(1,43) = 4.435$, $p < 0.009$, $n_p^2 = 0.286$). Thus, the AG group obtained lower scores than the NAG. Furthermore, a marginal difference was found in PM ($F(1,43) = 20.826$, $p = 0.072$, $n_p^2 = 0.112$). No significant differences were found in DM ($p = 0.262$) (see Table 3).

Table 2
Sample Social interaction characteristics (weekly).

Social interaction characteristics	AG (n = 23)	NAG (n = 22)	p	*Adjusted p*
Hours of communication with family	5.00 (4.112	7.864 (10.073)	0.215	0.352
Hours of communication with friends	6.348 (4.579)	6.636 (6.184)	0.859	0.910
Type of telematic contact maintained with family None Zoom or similar WhatsApp	0(0%) 0(0%) 23(100%)	4(18.2%) 1(4.5%) 17(77.3%)	0.053	0.136
Type of telematic contact maintained with friends None Zoom or similar WhatsApp	0(0%) 0(0%) 23(100%)	3(13.6%) 0(0%) 19(86.4%)	0.109	0.218
Face-To-Face Family Interaction Yes No	1(4.3%) 22(95.7%)	9(40.9%) 13(59.1%)	0.004	0.018*
Face-To-Face Friends Interaction Yes No	0(0%) 23(100%)	9(40.9%) 13(59.1%)	0.001	0.018*

Abbreviations: AG, Along Group; NAG, Not Along Group. *p < 0.05. Weekly: The average number of contact hours in a typical week in the past year

3.2. Relationship between memory performance and biomarkers

We performed Pearson's correlations between memory performance outcomes and biomarkers, but no significant relationships were found (all $p > 0.340$).

3.3. Moderation analyses

Results of the moderation analyses showed a significant interaction effect of loneliness in the relationship between hair cortisol levels and PM ($B = -0.423$, $p = 0.0004$). Hair cortisol concentrations were negatively related to PM when participants scored high ($p = 0.0003$) and moderate ($p = 0.0182$) on loneliness. However, the relationship between cortisol and PM was marginally positive in those participants who scored lower on loneliness ($p = 0.0513$). No interaction effect of loneliness was found in the relationships between cortisol and WM ($p = 0.832$) or DM ($p = 0.536$) (Table 4).

Table 1
Sample characteristics. Mean values (M), Standard Deviations (SD), and Student's *t*-test values.

	AG (n = 23)		NAG (n = 22)		*t* (gl)	*p*	*Adjusted p*
	M	SD	M	SD			
Sociodemographic characteristics							
Age (years)	25.696	2.721	25.500	3.529	0.209(43)	0.836	0.941
Years been in the education system	17.220	1.929	16.59	3.389	0.757(33.008)	0.454	0.584
Alcohol consumption (N° of drinks per week)	1.914	2.466	1.909	1.716	0.006(43)	0.995	0.995
Cigarette consumption (N° of cigarettes per week)	0.174	0.491	0.727	2.251	-1.128(22.911)	0.271	0.375
Psychological/affective characteristics							
Loneliness	38.087	9.657	30.636	5.169	3.246 (33.960)	0.003 *	0.018 *
Perceives stress	6.565	3.883	5.773	3.436	0.724(43)	0.473	0.568
Depression	13.478	10.962	9.818	8.958	1.223(43)	0.228	0.342
SMCs test scores	29.522	17.170	20.182	14.575	1.963(43)	0.056	0.126

Abbreviations: AG, Along Group; NAG, Not Along Group; Subjective Memory Complaints, SMCs. *p < 0.05.

Table 3
Mean values and standard deviations (SD) of memory outcomes and statistics of group comparisons with one-way ANOVAs.

	AG N = 23		NAG N = 22		*F* [1,43]	*p*	*Adjusted p*	η_p^2
	Mean	S.D.	Mean	S.D.				
Working Memory	4.435	1.674	7.091	1.377	16.805	0.001	0.009*	0.286
Declarative Memory	262.032	39.185	245.212	33.857	2.364	0.131	0.236	0.052
Prospective Memory	20.826	1.267	21.636	1.049	5.436	0.024*	0.072	0.112

Abbreviations: AG, Along Group; NAG, Not Along Group. *p < 0.05.

Table 4
Adjusted moderation analyses with cortisol as a predictor and memory as a dependent variables in different values of loneliness.

Dependent variable: working memory

ΔR^2 interaction = 0.001 F= 0.0461, df (1,2)= 1, 26 p = 0.832
LLCI= −0.342 ULCI= 0.421

Loneliness	Effect	SE	*t*	*p*	LLCI	ULCI
27.000	-0.731	1.343	-0.544	0.591	-3.492	2.031
34.000	-0.452	1.071	-0.421	0.677	-2.654	1.751
43.760	-0.626	2.423	-0.026	0.910	-5.043	4.917

Dependent variable: declarative memory
ΔR^2 interaction = 0.014 F= 0.3921, df(1,2)= 1, 27 p = 0.536
LLCI= −6.225 ULCI= 11.693

Loneliness	Effect	SE	*t*	*p*	LLCI	ULCI
27.000	-5.665	31.247	0.181	0.858	-58.450	69.780
34.000	24.803	23.212	1.069	0.295	-22.8259	72.432
43.760	51.487	55.199	0.933	0.360	-61.776	164.749

Dependent variable: Prospective memory
ΔR^2 interaction = 0.312 F= 15.953, df (1,2) = 1, 27 p = 0.0004
LLCI= 0.065 ULCI= 0.338

Loneliness	Effect	SE	*t*	*p*	LLCI	ULCI
27.000	1547	0.759	2.039	0.051	-.0.009	3.104
34.000	-1.417	0.564	-2514	0.0182	-2.5733	-0.2603
43.760	-5549	1340	-4,1405	0.0003	-8299	-2799

Additionally, loneliness did not moderate the relationship between HRV and any type of memory (all $p > 0.179$) (Table 5).

4. Discussion

The present study aimed to explore how social contact restrictions in the post-pandemic context could affect people at psychological/affective, biological, and cognitive levels, with a focus on the role of perceived loneliness and the living situation.

Table 5
Adjusted moderation analyses with HRV as a predictor and memory as a dependent variable in different values of loneliness.

Dependent variable: Working Memory

ΔR^2 interaction = 0.032 F= 1.888, df (1,2)= 1, 36 p = 0.179
LLCI= −0.114 ULCI= 0.594

Loneliness	Effect	SE	*t*	*p*	LLCI	ULCI
26.000	-0.685	2.111	-0.325	0.747	-4.967	3.596
34.000	1.232	1.452	0.849	0.402	-1.712	4.177
41.280	2.978	1.832	-1.625	0.113	-0.739	6.694

Dependent variable: Declarative Memory
ΔR^2 interaction = 0.006 F= 0.248, df (1,2)= 1,37 p = 0.622
LLCI= −9.457 ULCI= 5.728

Loneliness	Effect	SE	*t*	*p*	LLCI	ULCI
26.000	64.474	46.056	1.400	0.170	-28.847	157.794
34.000	49.557	32.181	1.540	0.132	-15.650	114.762
41.280	35.982	40.119	0.897	0.376	-45.308	117.272

Dependent variable: Prospective Memory
ΔR^2 interaction = 0.007 F= 0.323, df (1,2) = 1, 37 p = 0.573
LLCI= −0.296 ULCI= 0.166

Loneliness	Effect	SE	*t*	*p*	LLCI	ULCI
26.000	1.356	1.401	0.968	0.339	-1.482	4.195
34.000	0.839	0.979	0.857	0.397	-1.145	2.822
41.280	0.367	1.220	0.301	0.765	-2.106	2.839

Overall, our results showed that individuals who had changed their nuclear family and were living alone outside their home country for the previous eight months had greater feelings of loneliness, marginally higher hair cortisol levels, and worse working memory and prospective memory performance, compared to individuals who maintained their nuclear family and did not live alone during the previous eight months. Interestingly, although there were no significant differences in telematic communication time with family and friends, there were evident differences in face-to-face communication. Our results suggest that living alone in another country without the usual face-to-face contact with family and friends leads to higher perceived loneliness and worse cognitive performance.

These results replicate what was found by Ingram et al. [40], who showed that performance on cognitive tasks (including memory tasks) was determined by the levels of social isolation of the individuals and improved significantly as the COVID-19 pandemic restrictions were lifted (greater mobility and more social contact). Our results are also consistent with pre-pandemic studies showing that loneliness and social isolation were associated with lower working memory, immediate and delayed recall of verbal fluency, and prospective memory performance, particularly in middle- and older-aged adults [34,47]. Similarly, the results are consistent with research conducted in the older population that concluded that better cognitive functioning was associated with more social support [23,41,43], whereas social isolation showed an inverse pattern [12,57].

To the best of our knowledge, no previous studies have explored the relevance of social support in memory performance specifically in young adults during the pandemic. However, some studies have shown that the situation during the COVID-19 pandemic led to a significant increase in perceived stress, anxiety, and depression that has been negatively linked to cognitive performance [26,5,54]. Indeed, the scores for perceived stress and depression observed in our study, in both the AG and the NAG, align closely with the during-confinement scores documented by Baliyan et al. [4], who reported significant differences between the levels prior to the pandemic and those registered during the pandemic period. There was an increase in perceived stress, anxiety, and depression that was largely attributed to the uncertainty brought about by the restrictions, preventive measures (e.g., quarantines, limited mobility), and, therefore, sudden changes in daily activities, including studies and remote work.

These results align with the social buffering hypothesis [18], which proposes that social relationships have a positive impact on both physical and mental health. Specifically, our findings are in line with a similar study by Hopf et al. [39] during the COVID-19 lockdown, demonstrating that living with others becomes an increasingly important factor in mitigating loneliness. In our study, despite finding no significant differences in any of these perceived psychological factors, significant differences in loneliness and marginal differences in hair cortisol levels were reported. Furthermore, the absence of significant correlations between cortisol and memory outcomes, combined with the significant interaction effect between loneliness and prospective memory in the moderation analysis, suggests that, although cortisol levels alone may not be indicative of memory performance, the interaction with loneliness is a crucial factor that highlights the complex relationship between psychological and physiological factors in memory function, leading us to suggest that both factors are relevant in memory performance.

The stronger negative relationship between cortisol and prospective memory in individuals who report high levels of loneliness indicates a vulnerability in this subgroup. This finding is well-aligned with previous research indicating that chronic stress, reflected by elevated hair cortisol levels, may impact cognitive function, especially during major stressful events (e.g., [29]). Therefore, loneliness might intensify the cognitive effects of stress, possibly due to an increased vulnerability to the harmful effects of stress hormones, as evidenced by the functioning of the hypothalamic-pituitary-adrenal (HPA) axis ([14]; Montuoli, et al., 2019).

Moreover, the weaker but still negative relationship in those with moderate loneliness may indicate a dose-response relationship, where the degree of loneliness corresponds to the strength of the cortisol-prospective memory link. Meanwhile, the marginal significance in the low loneliness group could indicate a resilience to these effects.

The absence of moderating effects of loneliness in the relationships between cortisol and working memory and declarative memory suggests that the observed interaction is specific to prospective memory. It may be related to the unique cognitive processes involved in prospective memory, which is more future-oriented and dependent on self-initiated actions and motivation than the other memory types investigated. In addition, the disruption of established routines during the pandemic led to the emergence of new behavior patterns, potentially affecting prospective memory more profoundly. This specificity underscores the need for further research to explore the underlying mechanisms responsible for this phenomenon, primarily to comprehend the effects of chronic stress on this type of memory, given that the findings in the literature are inconsistent [16,59,76].

Regarding the two groups' cardiovascular responses, it is relevant to note that the physiological status of the participants was not experimentally manipulated with any psychosocial stressor. However, one of the essential components of psychosocial stress is evaluation, and so we consider that the neuropsychological assessment involved a high cognitive demand that required parasympathetic control. Consequently, we hypothesized that participants in the AG group would exhibit lower heart rate variability (HRV). However, we did not find statistically significant differences between the two groups. Nevertheless, during specific periods, our results support the notion that reduced parasympathetic activity may function as a noteworthy biomarker of cognitive performance. This is particularly evident in the resting values, indicating an overall pattern of increased parasympathetic activity following a cognitive challenge [66,73].

However, RMSSD showed no significant negative correlations with memory outcomes or a significant interaction in the moderation analysis. The lack of significant relationships is contrary to previous studies (Giuliano et al., 2017; [33]) in which these measures were associated with better performance on working memory and other cognitive tasks, showing that strong trait-level prefrontal regulatory control buffers individuals' physiological state level. Nevertheless, the correlations between HRV and memory tasks are small and unstable across all studies [11,1,38,72].

This study has some limitations. Although it is known that mental workload may be associated with cardiovascular disease, particularly on cognitive tasks requiring significant effort [53], our assessment was limited to memory performance. Therefore, it would have been interesting to evaluate other functions as well. Additionally, it is important to note that the non-random assignment of our participants in our study, due to ethical and practical considerations, limits our ability to draw causal conclusions. Furthermore, considering the NAG group's position within a spectrum of healthy social contact and interactions in stable situations, future research should take into account perceived social support and the quality of interactions as important factors. Moreover, we did not conduct a power analysis prior to the study, and the sample size could be limiting our statistical power. Therefore, future research could benefit from a larger sample.

In sum, the current study provides novel evidence showing that the lack of close, nearby personal contact, which could serve as instrumental support during the restrictive living conditions associated with the COVID-19 pandemic, was related to worse memory performance (working memory, declarative memory, and prospective memory), and that loneliness played a crucial role in the relationship between cortisol and memory performance. Our findings allow us to understand the intricate relationship between loneliness, cortisol levels, and prospective memory, while highlighting the paramount importance of direct, face-to-face social interactions in memory research. Although cortisol levels alone did not directly correlate with memory outcomes, our study highlights the role of loneliness in the relationship between hair cortisol levels and prospective memory, emphasizing the need to consider both psychological and physiological factors. This research contributes to our understanding of the multifaceted dynamics among these factors, and it underscores the significance of examining individual differences when developing future research and interventions.

This result may contribute to our understanding of the detrimental consequences of social isolation at the cognitive and physiological levels. Additionally, further investigation into the underlying mechanisms that explain the observed interactions is warranted, especially in the context of pandemic-related stressors. Longitudinal studies could help to elucidate the directionality of these relationships and provide insights into potential interventions to mitigate the negative effects of loneliness on memory during challenging times, especially in young people.

CRediT authorship contribution statement

Daniela Batallas: Conceptualization; Methodology; Formal analysis; Investigation; Data curation; Writing-Original Draft. **Valerie Rodriguez-Hernandez**: Methodology; Formal analysis; Investigation; Data curation. **Vanesa Hidalgo**: Conceptualization; Methodology; Resources; Writing-Review and Editing; Supervision; Project administration. **Alicia Salvador**: Conceptualization; Methodology; Resources; Writing-Review and Editing; Supervision; Project administration; Funding acquisition.

Data Availability

Data will be made available on request.

Acknowledgments

The research reported in this study was supported by the Spanish Ministry of Science, Innovation and Universities (PID2020–119406GBI00/AEI/10.13039/501100011033, and FPU 18/03422), and Generalitat Valenciana (PROMETEU 2022, CIPROM/2021/082; R1.07/2022). Moreover, the contribution of V. Hidalgo has been supported by the Gobierno de Aragón (Departamento de Ciencia, Universidad y Sociedad del Conocimiento) under research group S31_23R, and the Universities Ministry and European Union (European Union Next Generation EU, grant for the requalification of the Spanish University System).

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.bbr.2023.114771.

References

[1] L.M. Allan, S.R.J. Kerr, C.G. Ballard, J. Allen, A. Murray, A.T. McLaren, R.A. Kenny, Autonomic function assessed by heart rate variability is normal in Alzheimer's disease and vascular dementia, Dement. Geriatr. Cogn. Disord. 19 (2–3) (2005) 140–144, https://doi.org/10.1159/000082885.

[2] M. Almela, L. van der Meij, V. Hidalgo, C. Villada, A. Salvador, The cortisol awakening response and memory performance in older men and women, Psychoneuroendocrinology 37 (12) (2012) 1929–1940.
[3] M. Altemus, L.S. Redwine, Y.M. Leong, C.A. Frye, S.W. Porges, C.S. Carter, Responses to laboratory psychosocial stress in postpartum women, Psychosom. Med. 63 (5) (2001) 814–821, https://doi.org/10.1097/00006842-200109000-00015.
[4] S. Baliyan, J.M. Cimadevilla, S. de Vidania, M.M. Pulopulos, C. Sandi, C. Venero, Differential susceptibility to the impact of the COVID-19 pandemic on working memory, empathy, and perceived stress: the role of cortisol and resilience, Brain Sci. 11 (3) (2021) 1–21, https://doi.org/10.3390/brainsci11030348.
[5] I.A. Basheti, Q.N. Mhaidat, H.N. Mhaidat, Prevalence of anxiety and depression during COVID-19 pandemic among healthcare students in Jordan and its effect on their learning process: A national survey, PLOS ONE 16 (4) (2021) 1–16, https://doi.org/10.1371/journal.pone.0249716.
[6] R.F. Baumeister, C. Nathan Dewall, N.J. Ciarocco, J.M. Twenge, Social exclusion impairs self-regulation, J. Personal. Soc. Psychol. 88 (4) (2005) 589–604, https://doi.org/10.1037/0022-3514.88.4.589.
[7] Beck, A.T., Steer, R.A., & Brown, G.K. (1996). *BDI-II. Beck Depression Inventory Second Edition. Manual* ({C}TX: & T.P.{C} Corporation. (eds.)).
[8] J. Beller, A. Wagner, Loneliness, social isolation, their synergistic interaction, and mortality, Health Psychol. 37 (9) (2018) 808–813, https://doi.org/10.1037/hea0000605.
[9] J.A. Bosch, E.J. de Geus, D. Carroll, A.D. Goedhart, L.A. Anane, J.J. van Zanten, E. J. Helmerhorst, K.M. Edwards, A general enhancement of autonomic and cortisol responses during social evaluative threat, Psychosom. Med. 71 (8) (2009) 877–885, https://doi.org/10.1097/PSY.0b013e3181baef05.
[10] V.M.E. Bridgland, E.K. Moeck, D.M. Green, T.L. Swain, D.M. Nayda, L.A. Matson, N.P. Hutchison, M.K.T. Takarangi, Why the COVID-19 pandemic is a traumatic stressor, PLoS ONE 16 (1 January) (2021) 1–15, https://doi.org/10.1371/journal.pone.0240146.
[11] A. Britton, A. Singh-Manoux, K. Hnatkova, M. Malik, M.G. Marmot, M. Shipley, The Association between Heart Rate Variability and Cognitive Impairment in Middle-Aged Men and Women, Neuroepidemiology 31 (2) (2008) 115–121, https://doi.org/10.1159/000148257.
[12] J.T. Cacioppo, L.C. Hawkley, Perceived social isolation and cognition, Trends Cogn. Sci. 13 (10) (2009) 447–454, https://doi.org/10.1016/j.tics.2009.06.005.
[13] J.T. Cacioppo, W.B. Malarkey, J.K. Kiecolt-Glaser, B.N. Uchino, S.A. Sgoutas-Emch, J.F. Sheridan, G.G. Berntson, R. Glaser, Heterogeneity in neuroendocrine and immune responses to brief psychological stressors as a function of autonomic cardiac activation, Psychosom. Med. 57 (2) (1995) 154–164, https://doi.org/10.1097/00006842-199503000-00008.
[14] J.T. Cacioppo, L.C. Hawkley, L.E. Crawford, J.M. Ernst, M.H. Burleson, R. B. Kowalewski, W.B. Malarkey, E. Van Cauter, G.G. Berntson, Loneliness and health: potential mechanisms, Psychosom. Med. 64 (3) (2002) 407–417, https://doi.org/10.1097/00006842-200205000-00005.
[15] X. Cai, X. Hu, I.O. Ekumi, J. Wang, Y. An, Z. Li, B. Yuan, Psychological Distress and Its Correlates Among COVID-19 Survivors During Early Convalescence Across Age Groups, Am. J. Geriatr. Psychiatry 28 (10) (2020) 1030–1039, https://doi.org/10.1016/j.jagp.2020.07.003.
[16] J. Chen, Z. Wei, H. Han, L. Jin, C. Xu, D. Dong, J. Lu, G. Wan, Z. Peng, An Effect of Chronic Stress on Prospective Memory via Alteration of Resting-State Hippocampal Subregion Functional Connectivity, Sci. Rep. 9 (1) (2019), 19698, https://doi.org/10.1038/s41598-019-56111-9.
[17] Y. Chida, M. Hamer, Chronic psychosocial factors and acute physiological responses to laboratory-induced stress in healthy populations: A quantitative review of 30 years of investigations, Psychol. Bull. 134 (6) (2008) 829–885, https://doi.org/10.1037/a0013342.
[18] Cohen, S. & McKay, G. In Handbook of Psychology and Health (Volume IV), {C} Chapter{C} 10 (eds Taylor, S. E. et al.) 253–267 (Routledge, 1984).
[19] S. Cohen, T.A. Wills, Stress, Social Support, and the Buffering Hypothesis, Psychol. Bull. 98 (2) (1985) 310–357, https://doi.org/10.1037/0033-2909.98.2.310.
[20] H.M. Conklin, C.E. Curtis, J. Katsanis, W.G. Iacono, Verbal working memory impairment in schizophrenia patients and their first-degree relatives: evidence from the digit span task, Am. J. Psychiatry 157 (2) (2000) 275–277, https://doi.org/10.1176/appi.ajp.157.2.275.
[21] N. Cowan, E.M. Elliott, S.J. Saults, C.C. Morey, S. Mattox, A. Hismjatullina, A.R. A. Conway, On the Capacity of Attention: Its Estimation and Its Role in Working Memory and Cognitive Aptitudes, Cogn. Psychol. 51 (1) (2005) 42, https://doi.org/10.1016/J.COGPSYCH.2004.12.001.
[22] J.A. Doussard-Roosevelt, L.A. Montgomery, S.W. Porges, Short-term stability of physiological measures in kindergarten children: respiratory sinus arrhythmia, heart period, and cortisol, Dev. Psychobiol. 43 (3) (2003) 230–242, https://doi.org/10.1002/dev.10136.
[23] I.E.M. Evans, A. Martyr, R. Collins, C. Brayne, L. Clare, Social Isolation and Cognitive Function in Later Life: A Systematic Review and Meta-Analysis, J. Alzheimer's Dis.: JAD 70 (s1) (2019) S119–S144, https://doi.org/10.3233/JAD-180501.
[24] J.C. Feeney, A.M. O'Halloran, R.A. Kenny, The Association Between Hair Cortisol, Hair Cortisone, and Cognitive Function in a Population-Based Cohort of Older Adults: Results From The Irish Longitudinal Study on Ageing. The journals of gerontology. Series A, Biol. Sci. Med. Sci. 75 (2) (2020) 257–265.
[25] D. Fellman, L. Ritakallio, O. Waris, J. Jylkkä, M. Laine, Beginning of the Pandemic: COVID-19-Elicited Anxiety as a Predictor of Working Memory Performance, Front. Psychol. 11 (November) (2020) 1–13, https://doi.org/10.3389/fpsyg.2020.576466.
[26] E. Fiorenzato, S. Zabberoni, A. Costa, G. Cona, Cognitive and mental health changes and their vulnerability factors related to COVID-19 lockdown in Italy, Plos One 16 (1) (2021), e0246204, https://doi.org/10.1371/journal.pone.0246204.
[27] G. Forte, F. Favieri, M. Casagrande, Heart rate variability and cognitive function: A systematic review, Front. Neurosci. 13 (JUL) (2019) 1–11, https://doi.org/10.3389/fnins.2019.00710.
[28] C.E. Franz, R.C. O'Brien, R.L. Hauger, S.P. Mendoza, M.S. Panizzon, E. Prom-Wormley, L.J. Eaves, K. Jacobson, M.J. Lyons, S. Lupien, D. Hellhammer, H. Xian, W.S. Kremen, Cross-sectional and 35-year longitudinal assessment of salivary cortisol and cognitive functioning: The Vietnam Era Twin Study of Aging, Psychoneuroendocrinology 36 (7) (2011) 1040–1052, https://doi.org/10.1016/j.psyneuen.2011.01.002.
[29] W. Gao, P. Zhong, Q. Xie, H. Wang, J. Jin, H. Deng, Z. Lu, Temporal features of elevated hair cortisol among earthquake survivors, Psychophysiology 51 (4) (2014) 319–326, https://doi.org/10.1111/psyp.12179.
[30] L. Gerritsen, H.C. Comijs, D.J.H. Deeg, B.W.J.H. Penninx, M.I. Geerlings, Salivary cortisol, APOE-ε4 allele and cognitive decline in a prospective study of older persons, Neurobiol. Aging 32 (9) (2011) 1615–1625, https://doi.org/10.1016/J.NEUROBIOLAGING.2009.09.007.
[31] J.M. Groarke, E. Berry, L. Graham-Wisener, P.E. McKenna-Plumley, E. McGlinchey, C. Armour, Loneliness in the UK during the COVID-19 pandemic: Cross-sectional results from the COVID-19 Psychological Wellbeing Study, PloS One 15 (9) (2020), e0239698, https://doi.org/10.1371/journal.pone.0239698.
[32] E. Grober, H. Buschke, Genuine memory deficits in dementia, Dev. Neuropsychol. 3 (1) (1987) 13–36, https://doi.org/10.1080/87565648709540361.
[33] A.L. Hansen, B.H. Johnsen, J.F. Thayer, Vagal influence on working memory and attention, Int. J. Psychophysiol. 48 (3) (2003) 263–274, https://doi.org/10.1016/S0167-8760(03)00073-4.
[34] C. Haslam, T. Cruwys, S.A. Haslam, "The we's have it": Evidence for the distinctive benefits of group engagement in enhancing cognitive health in aging, Soc. Sci. Med. 120 (2014) 57–66, https://doi.org/10.1016/j.socscimed.2014.08.037.
[35] A.F. Hayes, Introduction to Mediation, Moderation, and Conditional Process. Analysis: A Regression-Based Approach, Guilford publications,, New York, NY, 2017.
[36] V. Hidalgo, M. Almela, M.M. Pulopulos, A. Salvador, Memory performance is related to the cortisol awakening response in older people, but not to the diurnal cortisol slope, Psychoneuroendocrinology 71 (2016) 136–146.
[37] L.K. Hill, A. Siebenbrock, Are all measures created equal? Heart rate variability and respiration, Biomed. Sci. Instrum. 45 (2009) 71–76.
[38] J.B. Holzman, D.J. Bridgett, Heart rate variability indices as bio-markers of top-down self-regulatory mechanisms: A meta-analytic review, Neurosci. Biobehav. Rev. 74 (Pt A) (2017) 233–255, https://doi.org/10.1016/j.neubiorev.2016.12.032.
[39] D. Hopf, E. Schneider, C. Aguilar-Raab, D. Scheele, M. Morr, T. Klein, B. Ditzen, M. Eckstein, Loneliness and diurnal cortisol levels during COVID-19 lockdown: the roles of living situation, relationship status and relationship quality, Sci. Rep. 12 (1) (2022), 15076, https://doi.org/10.1038/s41598-022-19224-2.
[40] J. Ingram, C.J. Hand, G. Maciejewski, Social isolation during COVID-19 lockdown impairs cognitive function, Appl. Cogn. Psychol. March (2021) 1–13, https://doi.org/10.1002/acp.3821.
[41] M.E. Kelly, H. Duff, S. Kelly, J.E. McHugh Power, S. Brennan, B.A. Lawlor, D. G. Loughrey, The impact of social activities, social networks, social support and social relationships on the cognitive functioning of healthy older adults: a systematic review, Syst. Rev. 6 (1) (2017), 259, https://doi.org/10.1186/s13643-017-0632-2.
[42] R.E. Kleiger, P.K. Stein, J.T., Jr Bigger, Heart rate variability: measurement and clinical utility, Ann. Noninvasive Electrocardiol.: Off. J. Int. Soc. Holter Noninvasive Electrocardiol., Inc. 10 (1) (2005) 88–101, https://doi.org/10.1111/j.1542-474X.2005.10101.x.
[43] J.S. Kuiper, M. Zuidersma, S.U. Zuidema, J.G.M. Burgerhof, R.P. Stolk, R.C. Oude Voshaar, N. Smidt, Social relationships and cognitive decline: a systematic review and meta-analysis of longitudinal cohort studies, Int. J. Epidemiol. 45 (4) (2016) 1169–1206, https://doi.org/10.1093/ije/dyw089.
[44] R. La Marca, P. Waldvogel, H. Thörn, M. Tripod, P.H. Wirtz, J.C. Pruessner, U. Ehlert, Association between Cold Face Test-induced vagal inhibition and cortisol response to acute stress, Psychophysiology 48 (3) (2011) 420–429, https://doi.org/10.1111/j.1469-8986.2010.01078.x.
[45] E. Labos, S. Trojanowski, C. Ruiz, Free/cued selective reminding test with immediate recall. Verbal Version, Adapt. Norms Span. Lang. *Rev. Neurol. Argent.* 33 (2008) 50–66.
[46] J.C.L. Lai, M.O.Y. Leung, D.Y.H. Lee, Y.W. Lam, K. Berning, Loneliness and Diurnal Salivary Cortisol in Emerging Adults, *Page 1944*, *19*, Int. J. Mol. Sci. 2018 Vol. 19 (7) (2018) 1944, https://doi.org/10.3390/IJMS19071944.
[47] E. Lara, F.F. Caballero, L.A. Rico-Uribe, B. Olaya, J.M. Haro, J.L. Ayuso-Mateos, M. Miret, Are loneliness and social isolation associated with cognitive decline? Int. J. Geriatr. Psychiatry 34 (11) (2019) 1613–1622, https://doi.org/10.1002/gps.5174.
[48] L.Z. Li, S. Wang, Prevalence and predictors of general psychiatric disorders and loneliness during COVID-19 in the United Kingdom, Psychiatry Res. 291 (June) (2020), 113267, https://doi.org/10.1016/j.psychres.2020.113267.
[49] Llana, T., Zorzo, C., Mendez-Lopez, M., & Mendez, M. (2022). Memory alterations after COVID-19 infection: a systematic review. 〈Https://Doi.Org/10.1080/23279095.2022.2123739〉. https://doi.org/10.1080/23279095.2022.2123739.
[50] R.R. Looser, P. Metzenthin, S. Helfricht, B.M. Kudielka, A. Loerbroks, J.F. Thayer, J.E. Fischer, Cortisol is significantly correlated with cardiovascular responses during high levels of stress in critical care personnel, Psychosom. Med. 72 (3) (2010) 281–289, https://doi.org/10.1097/PSY.0b013e3181d35065.

[51] P. Lozoya-Delgado, J.M. Ruiz-Sánchez de León, E.J. Pedrero-Pérez, Validación de un cuestionario de quejas cognitivas para adultos jóvenes: relación entre las quejas subjetivas de memoria, la sintomatología prefrontal y el estrés percibido, Rev. Neurol. 54 (3) (2012) 137–150, https://doi.org/10.33588/rn.5403.2011283.

[52] S.J. Lupien, F. Maheu, M. Tu, A. Fiocco, T.E. Schramek, The effects of stress and stress hormones on human cognition: Implications for the field of brain and cognition, Brain Cogn. 65 (3) (2007) 209–237, https://doi.org/10.1016/J.BANDC.2007.02.007.

[53] A. Luque-Casado, J. Perales, D. Vélez, D. Sanabria, Heart rate variability and cognitive processing: The autonomic response to task demands, Biol. Psychol. 113 (2015), https://doi.org/10.1016/j.biopsycho.2015.11.013.

[54] B.R. Maia, P.C. Dias, Anxiety, depression and stress in university students: The impact of COVID-19, Estud. De. Psicol. (Camp.) 37 (2020) 1–8, https://doi.org/10.1590/1982-0275202037e200067.

[55] E. Makovac, J.F. Thayer, C. Ottaviani, A meta-analysis of non-invasive brain stimulation and autonomic functioning: Implications for brain-heart pathways to cardiovascular disease, Neurosci. Biobehav. Rev. 74 (Pt B) (2017) 330–341, https://doi.org/10.1016/j.neubiorev.2016.05.001.

[56] S.N. McLennan, A. Ihle, S. Steudte-Schmiedgen, C. Kirschbaum, M. Kliegel, Hair cortisol and cognitive performance in working age adults, Psychoneuroendocrinology 67 (2016) 100–103, https://doi.org/10.1016/J.PSYNEUEN.2016.01.029.

[57] T. Montoliu, V. Hidalgo, A. Salvador, The relationship between loneliness and cognition in healthy older men and women: The role of cortisol, Psychoneuroendocrinology 107 (May) (2019) 270–279, https://doi.org/10.1016/j.psyneuen.2019.05.024.

[58] R. Mushtaq, S. Shoib, T. Shah, S. Mushtaq, Relationship between loneliness, psychiatric disorders and physical health ? A review on the psychological aspects of loneliness, WE01-4, J. Clin. Diagn. Res.: JCDR 8 (9) (2014), https://doi.org/10.7860/JCDR/2014/10077.4828.

[59] U.M. Nater, U. Okere, R. Stallkamp, C. Moor, U. Ehlert, M. Kliegel, Psychosocial stress enhances time-based prospective memory in healthy young men, Neurobiol. Learn. Mem. 86 (3) (2006) 344–348, https://doi.org/10.1016/j.nlm.2006.04.006.

[60] J.M. Newby, K. O'Moore, S. Tang, H. Christensen, K. Faasse, Acute mental health responses during the COVID-19 pandemic in Australia, PLoS ONE 15 (7 July) (2020) 1–21, https://doi.org/10.1371/journal.pone.0236562.

[61] Perdig, A.L. (2003). Adaptación española del Inventario para la Depresión de Beck-II (BDI-II): 2. Propiedades psicométricas en población general The spanish adaptation of Beck ' s 2. Psychometric properties in the general. *14*, 249–281.

[62] F. Pisano, G. Torromino, D. Brachi, A. Quadrini, C. Incoccia, P. Marangolo, A standardized prospective memory evaluation of the effects of covid-19 confinement on young students, J. Clin. Med. 10 (17) (2021), https://doi.org/10.3390/jcm10173919.

[63] M.M. Pulopulos, V. Hidalgo, M. Almela, S. Puig-Perez, C. Villada, A. Salvador, Hair cortisol and cognitive performance in healthy older people, Psychoneuroendocrinology 44 (2014) 100–111, https://doi.org/10.1016/J.PSYNEUEN.2014.03.002.

[64] G.A. Reyes del Paso, W. Langewitz, L.J.M. Mulder, A. van Roon, S. Duschek, The utility of low frequency heart rate variability as an index of sympathetic cardiac tone: A review with emphasis on a reanalysis of previous studies, Psychophysiology 50 (5) (2013) 477–487, https://doi.org/10.1111/psyp.12027.

[65] W.J. Riedel, A. Blokland, Declarative Memory, Handb. Exp. Pharmacol. 228 (2015) 215–236, https://doi.org/10.1007/978-3-319-16522-6_7/TABLES/1.

[66] C.M. Roddick, F.S. Chen, Effects of Chronic and State Loneliness on Heart Rate Variability in Women, Ann. Behav. Med. 55 (5) (2021) 460–475, https://doi.org/10.1093/abm/kaaa065.

[67] D. Russell, L.A. Peplau, C.E. Cutrona, The revised UCLA Loneliness Scale: Concurrent and discriminant validity evidence, J. Personal. Soc. Psychol. 39 (3) (1980) 472–480, https://doi.org/10.1037/0022-3514.39.3.472.

[68] E. Russell, G. Koren, M. Rieder, S. Van Uum, Hair cortisol as a biological marker of chronic stress: Current status, future directions and unanswered questions, Psychoneuroendocrinology 37 (5) (2012) 589–601, https://doi.org/10.1016/j.psyneuen.2011.09.009.

[69] N. Saez-Sanz, I. Peralta-Ramirez, R. Gonzalez-Perez, E. Vazquez-Justo, A. Caracuel, Resilience, Stress, and Cortisol Predict Cognitive Performance in Older Adults, Healthc. (Basel, Switz.) 11 (8) (2023) 1072, https://doi.org/10.3390/healthcare11081072.

[70] G. Santangelo, I. Baldassarre, A. Barbaro, N.D. Cavallo, M. Cropano, G. Maggi, R. Nappo, L. Trojano, S. Raimo, Subjective cognitive failures and their psychological correlates in a large Italian sample during quarantine/self-isolation for COVID-19, Neurol. Sci.: Off. J. Ital. Neurol. Soc. Ital. Soc. Clin. Neurophysiol. 42 (7) (2021) 2625–2635, https://doi.org/10.1007/S10072-021-05268-1.

[71] C. Santoso, D. Stuckler, A. Ihle, Investigating longitudinal associations of hair cortisol and cortisone with cognitive functioning and dementia, Sci. Rep. 12 (1) (2022), 20642, https://doi.org/10.1038/s41598-022-25143-z.

[72] A.J. Shah, S. Su, E. Veledar, J.D. Bremner, F.C. Goldstein, R. Lampert, J. Goldberg, V. Vaccarino, Is heart rate variability related to memory performance in middle-aged men? Psychosom. Med. 73 (6) (2011) 475–482, https://doi.org/10.1097/PSY.0b013e3182227d6a.

[73] A.S. Shah, A. Alonso, E.A. Whitsel, E.Z. Soliman, V. Vaccarino, A.J. Shah, Association of psychosocial factors with short-term resting heart rate variability: The atherosclerosis risk in communities study, J. Am. Heart Assoc. 10 (5) (2021) 1–19, https://doi.org/10.1161/JAHA.120.017172.

[74] T. Stalder, C. Kirschbaum, Analysis of cortisol in hair–state of the art and future directions, Brain, Behav., Immun. 26 (7) (2012) 1019–1029, https://doi.org/10.1016/J.BBI.2012.02.002.

[75] A. Steptoe, N. Owen, S.R. Kunz-Ebrecht, L. Brydon, Loneliness and neuroendocrine, cardiovascular, and inflammatory stress responses in middle-aged men and women, Psychoneuroendocrinology 29 (5) (2004) 593–611, https://doi.org/10.1016/S0306-4530(03)00086-6.

[76] Brandon Stewart, Craig Mcfarland, An investigation of the relations between stress and prospective memory, J. Cogn. Psychol. 32 (2020) 1–15, https://doi.org/10.1080/20445911.2020.1724116.

[77] A. Sunderland, J.E. Harris, J. Gleave, Memory failures in everyday life following severe head injury, J. Clin. Exp. Neuropsychol. 6 (2) (1984) 127–142, https://doi.org/10.1080/01688638408401204.

[78] J.F. Thayer, R.D. Lane, A model of neurovisceral integration in emotion regulation and dysregulation, J. Affect. Disord. 61 (3) (2000) 201–216, https://doi.org/10.1016/s0165-0327(00)00338-4.

[79] J.F. Thayer, F. Ahs, M. Fredrikson, J.J., 3rd Sollers, T.D. Wager, A meta-analysis of heart rate variability and neuroimaging studies: implications for heart rate variability as a marker of stress and health, Neurosci. Biobehav. Rev. 36 (2) (2012) 747–756, https://doi.org/10.1016/j.neubiorev.2011.11.009.

[80] Julian F. Thayer, E. Sternberg, Beyond heart rate variability: Vagal regulation of allostatic systems, Ann. N. Y. Acad. Sci. 1088 (2006) 361–372, https://doi.org/10.1196/annals.1366.014.

[81] M.A. Vallejo, L. Vallejo-Slocker, E.G. Fernández-Abascal, G. Mañanes, Determining factors for stress perception assessed with the Perceived Stress Scale (PSS-4) in Spanish and other European samples, Front. Psychol. 9 (JAN) (2018), https://doi.org/10.3389/fpsyg.2018.00037.

[82] A.J. Vázquez, R.J. RULS, Escala de soledad UCLA revisada. Fiabilidad y validez de una versión española, Rev. De. Psicol. De. La Salud 6 (1) (1994) 45–54.

[83] C. Villada, M. González-López, H. Aguilar-Zavala, T. Fernández, Resting EEG, Hair Cortisol and Cognitive Performance in Healthy Older People with Different Perceived Socioeconomic Status, Brain Sci. 10 (9) (2020) 635, https://doi.org/10.3390/brainsci10090635.

[84] X. Wang, J.R. Busch, J. Banner, K. Linnet, S.S. Johansen, Hair testing for cortisol by UPLC–MS/MS in a family: External cross-contamination from use of cortisol cream, Forensic Sci. Int. 305 (2019), https://doi.org/10.1016/j.forsciint.2019.109968.

[85] Wilson, B.A., Cockburn, J. and Baddeley, A. (1985) Rivermead Behavioural Memory Test. Thames Valley Test Company, London.

[86] A. Zeki Al Hazzouri, T. Elfassy, M.R. Carnethon, D.M. Lloyd-Jones, K. Yaffe, Heart Rate Variability and Cognitive Function in Middle-Age Adults: The Coronary Artery Risk Development in Young Adults, Am. J. Hypertens. 31 (1) (2018) 27–34, https://doi.org/10.1093/ajh/hpx125.