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Impact of pre-existing subclinical depressive symptoms on the mental health of older adults during the COVID-19-related confinements: assessment of moderating factors including meditation training

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The COVID-19 pandemic significantly challenged mental health of populations worldwide. We aimed to assess changes in mental health of cognitively unimpaired (CU) older adults with pre-existing subclinical depressive symptoms during pandemic-related confinements, and the factors that could modulate these changes. CU older adults with (DepS, n = 53) and without (NoDepS, n = 47) pre-existing subclinical depressive symptoms (defined using the Geriatric Depression Scale at baseline) from the Age-Well randomized controlled trial (NCT02977819) were included – for whom data at baseline, post-intervention visits and during the two national confinements were available. The 18-month meditation or non-native language training intervention was completed before the pandemic. DepS, compared to NoDepS, had higher levels of depressive and anxiety symptoms at all assessments, including confinements. DepS had a greater increase in anxiety than NoDepS between the two confinements, and this increase was associated with greater ruminative brooding at baseline, but was not moderated by the meditation training intervention or by meditation practice during confinements. Pre-existing subclinical depressive symptoms in older adults contribute to mental health deterioration during confinements, with rumination being the main factor involved – stressing the need to treat these symptoms.

Keywords Depressive symptoms, Anxiety symptoms, Older adults, COVID-19 pandemic, Meditation

The COVID-19 pandemic required the implementation of unprecedented confinement and social/physical distancing measures, which significantly affected societies, especially their mental health and well-being[1,2]. Older adults were at greater risk for severe complications after COVID-19 infection, and thus were more exposed to virus-related stressors and more likely to be isolated[1]. Despite this vulnerability, early reports showed that anxiety and depressive symptoms were less prevalent in older adults than in younger adults during the pandemic[3–6]—although a significant increase in these symptoms was also reported in older adults[5,7,8]. Notably, anxiety and

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depressive symptoms often co-occur[9,10], particularly in older adults, where comorbidity rates are high. Focusing research on this specific population was all the more relevant as the increase in psychoaffective symptoms, even at a subclinical level, as well as the living conditions to which they were exposed (i.e., social isolation, reduced physical and cognitive activity), are known to have major consequences in older adulthood, such as an increased risk of comorbidities, clinical anxiety and depressive disorders, cognitive decline and dementia[11–20].

"Subclinical depressive symptoms", also called subsyndromal or subthreshold depression, refers to depressive symptoms that do not meet the diagnostic criteria for major depression, i.e., that are rated below a determined threshold for clinically-relevant depression and stand within a low or subclinical range on depression scales[21,22]. In a previous study, we notably showed in two independent samples that cognitively unimpaired (CU) older adults with subclinical depressive symptoms had lower brain integrity, including hippocampal atrophy[23]—strengthening the need to consider subclinical depressive symptoms as relevant in older adults, and even more in the context of the COVID-19 pandemic. Individuals with a pre-existing clinical depressive disorder have been found to be at greater risk of mental health deterioration during the confinements[24–27]; however, little is known about those with a subclinical level of depressive symptoms. In this context, it seems crucial to better characterize older adults who could be most vulnerable to mental health deterioration during the confinements, and the underlying mechanisms, in order to promote appropriate care/intervention for these individuals if similar situations recur.

Among non-pharmacological interventions, mental training through meditation practice[28,29]—targeting emotional and attentional regulation and stress reduction – might notably address this need. Meditation-based interventions have been shown to be particularly effective in reducing clinical and subclinical levels of depressive and anxiety symptoms in young and middle-aged adults[30–34], with similar effects observed in the few studies conducted in older adults[28,35–40]. Additionally, meditation training was found to have beneficial effects on cognition especially in older adults[41], as well as on brain structure and function[29,42,43] in regions involved in emotional, attentional, and interoceptive processes, most of which are significantly altered in aging and dementia[28,44]. Compared to other possible interventions, meditation seems particularly suited for those with subclinical psychoaffective symptoms because it teaches emotion regulation techniques that can be applied autonomously whenever needed, fostering long-term emotional self-management, and it is accessible, within everyone's reach, without the need for professional support. Furthermore, previous studies have shown that meditation can directly reduce biological stress markers[45], offering a more targeted physiological impact compared to other interventions. Overall, these findings suggest that meditation practice appears to positively impact various crucial domains in aging (i.e., mental health, cognition, and brain integrity), making it a promising intervention for addressing the multifaceted challenges associated with aging, especially during a pandemic.

Our goal was to assess changes in mental health across the COVID-19-related confinements in CU older adults with pre-existing subclinical depressive symptoms, compared to those without pre-existing symptoms. We also aimed to investigate the underlying psychological mechanisms (i.e., ruminative brooding, worry, emotion regulation abilities, and cognitive defusion) that may predict mental health deterioration. Finally, we also evaluated whether an 18-month meditation intervention completed before the pandemic (compared to active and passive control groups), as well as meditation practice during both confinements, moderated the mental health changes between participants with and without pre-existing depressive symptoms during the pandemic confinements. We hypothesized that CU older adults with pre-existing subclinical depressive symptoms would have lower psychoaffective health (i.e., higher depressive and anxiety symptoms) – compared to those without pre-existing symptoms – across the pandemic confinements, and that this poorer mental health could be associated with negative psychological processes (i.e., higher ruminative brooding and/or worry, lower emotion regulation abilities and/or cognitive defusion) and moderated by meditation practice before and during the pandemic.

Materials and methods

Participants and study design

We included CU older adults from the Age-Well randomized controlled trial of the Medit-Ageing European project, sponsored by the French National Institute of Health and Medical Research (INSERM). The design of the trial has been fully described elsewhere[44,46]. Participants were recruited from the general population. Main eligibility criteria included being: a native French speaker, aged at least 65 years, retired for at least one year, educated for at least 7 years and showing performance within the normal range for their age and educational level on standardized cognitive tests (see Tables 1 and 2 in the Age-Well protocol paper[46] for details). Participants had no evidence of a major neurological or psychiatric disorder, chronic disease or acute unstable illness, history of cerebrovascular disease, and no current or recent medication that may interfere with cognitive functioning (including antidepressants and anxiolytics). Notably, the absence of major depression was assessed using a clinician-administered questionnaire, the Montgomery-Åsberg Depression Rating Scale (MADRS)[47], with a cut-off value of 6 (participants with MADRS > 6, indicating mild to major depressive disorder, were excluded). All participants provided written informed consent prior to the examinations, and the Age-Well randomized clinical trial was approved by the ethics committee (Comité de Protection des Personnes Nord-Ouest III, Caen, France; trial registration number: EudraCT: 2016-002441-36; date of first registration: 30/11/2016; IDRCB: 2016-A01767-44; ClinicalTrials.gov Identifier: NCT02977819).

Out of 157 participants who attended a screening visit, 137 were randomly assigned to three groups: one group with a meditation training (intervention group), one group with a structurally matched non-native language training (English learning = active control group), and one group with no intervention (passive control group). The 18-month intervention period started just after randomization, and participants had a post-intervention visit at the end of the intervention[44,46]. Two participants were excluded from all secondary analyses by the Trial Steering Committee for not meeting eligibility criteria (i.e., history of head trauma and amyotrophic

Age-Well Cohort (n = 100)	NoDepS Group (n = 47)	DepS Group (n = 53)	Between-group comparisons		
			p-value	T, F or χ^2 value	Mean difference [95% CI]
Baseline					
Demographic data					
Sex, Female, n (%)	23 (49)	36 (68)	*0.09*[a]	*2.97*	
Age, years (Range)	70.26 ± 4.20 (65–84)	68.34 ± 3.02 (65–77)	**0.01**[b]	**-2.64**	**-1.92 [-3.36 to -0.48]**
Education, years (Range)	13.28 ± 3.08 (7–22)	13.32 ± 3.03 (7–20)	0.94[b]	0.07	0.04 [-1.17 to 1.26]
Global cognition					
MMSE (Range)	29.06 ± 0.92 (26–30)	29.13 ± 1.14 (26–30)	0.75[b]	0.33	0.07 [-0.35 to 0.48]
Psychoaffective variables					
GDS (Range)	0.00 ± 0.00 (0–0)	2.23 ± 1.87 (1–11)	NA		
STAI-A (Range)	26.21 ± 4.92 (20–42)	29.19 ± 6.12 (20–46)	**0.013**[c]	**6.36**	**2.95 [0.63 to 5.27]**
Psychological processes					
RRS brooding (Range)	7.53 ± 2.01 (5–15)	8.83 ± 2.52 (5–16)	**0.014**[c]	**6.23**	**1.22 [0.25 to 2.18]**
PSWQ (Range)	38.85 ± 10.20 (20–58)	45.08 ± 12.75 (24–70)	**0.019**[c]	**5.65**	**5.82 [0.96 to 10.69]**
ERQ Cognitive reappraisal (Range)	29.92 ± 6.15 (15–40)	29.32 ± 5.77 (6–40)	0.494[c]	0.47	-0.87 [-3.38 to 1.64]
ERQ Expressive suppression (Range)	17.00 ± 5.51 (4–28)	17.02 ± 4.97 (4–28)	0.545[c]	0.37	0.67 [-1.51 to 2.84]
DDS Cognitive defusion (Range)	36.06 ± 6.04 (19–48)	32.55 ± 5.30 (19–43)	**0.007**[c]	**7.49**	**-3.25 [-5.61 to -0.89]**
Post-intervention					
Psychoaffective variables					
GDS (Range)	1.00 ± 1.23 (0–4)	2.28 ± 2.03 (0–8)	**< 0.001**[c]	**12.05**	**1.28 [0.55 to 2.01]**
STAI-A (Range)	26.49 ± 6.36 (20–51)	30.13 ± 6.78 (20–53)	**0.011**[c]	**6.75**	**3.67 [0.87 to 6.48]**
Confinement 1					
Psychoaffective variables					
DASS Depression (Range)	2.36 ± 3.10 (0–12)	4.87 ± 5.46 (0–25)	**0.008**[c]	**7.37**	**2.65 [0.71 to 4.59]**
STAI-A (Range)	32.32 ± 7.65 (20–54)	37.23 ± 10.52 (20–67)	**0.026**[c]	**5.09**	**4.53 [0.54 to 8.52]**
Confinement 2					
Psychoaffective variables					
DASS Depression (Range)	3.68 ± 5.33 (0–20)	7.42 ± 7.36 (0–35)	**0.013**[c]	**6.37**	**3.51 [0.75 to 6.26]**
STAI-A (Range)	32.55 ± 10.24 (20–61)	40.38 ± 11.44 (20–64)	**0.002**[c]	**10.41**	**7.56 [2.91 to 12.21]**

Table 1. Participants' characteristics and between-group comparisons for each visit. Data are presented as mean ± standard deviation of participants, unless otherwise indicated. Between-group differences were assessed using, [a]χ^2 tests for categorical variables, [b]Student's t-tests, or [c]ANCOVA adjusted for age, sex, and education (as well as intervention group for post-intervention and confinement time points) for continuous variables. Values in bold correspond to significant p-values ($p < 0.05$) and values in italics correspond to trends ($0.05 < p < 0.1$). N, Sample size; NoDepS, Group without pre-existing subclinical depressive symptoms; DepS, Group with pre-existing subclinical depressive symptoms; MMSE, Mini-Mental State Examination; GDS, Geriatric Depression Scale; STAI-A, State-Trait Anxiety Inventory form Y-A; DASS Depression, Depression Anxiety and Stress Scale – Depression subscale; RRS brooding, Rumination Response Scale – Brooding subscale; PSWQ, Penn State Worry Questionnaire; ERQ, Emotion Regulation Questionnaire – Cognitive Reappraisal and Expressive suppression subscales; DDS, Drexel Defusion Scale; NA, Not applicable.

lateral sclerosis diagnosis during the intervention period [with a likely subclinical state at inclusion]). One non-study related death (i.e., myocardial infarction) was reported during the intervention period before the post-intervention visit (data not included), and one participant revealed to have not followed their allocated arm (randomized to no intervention but attended non-native language training, he was therefore analyzed within the non-native language training arm). Baseline, interventions and post-intervention visits were all completed before the COVID-19 pandemic (between 22th November 2016 and 6th February 2020).

Interventions

The meditation and non-native language training interventions are fully detailed in Chételat et al., 2022[44]. Briefly, both interventions were matched in terms of course length, class time, home activities, and teacher expertise. Both involved 2-h weekly sessions, daily home practice (at least 20 min), and a 5-h intensive practice day. Participants were encouraged not to engage in the activities of the other group(s). Detailed manuals outlining each intervention's procedures were prepared before the study. The meditation program, designed specifically for this study, was based on secular mindfulness, loving-kindness, and compassion meditations. The non-native language intervention consisted of English language exercises focused on comprehension, writing, and speaking. Passive control group participants maintained their usual habits.

	Within-group changes across time points			Between-group comparisons for each time point	Overall Interaction effect
	NoDepS	DepS		DepS versus NoDepS	Time x Group
	Estimate (SE) P	Estimate (SE) P		Estimate (SE) P	*P*
Anxiety symptoms (STAI-A)					**0.026**
Baseline to Post-intervention	0.36 (1.28) 0.992	1.01 (1.21) 0.840	Baseline	2.87 (1.74) 0.100	
Baseline to C1	**6.25 (1.35) < .0001**	**8.10 (1.28) < .0001**	Post-intervention	**3.52 (1.74) 0.044**	
Baseline to C2	**6.49 (1.39) < .0001**	**11.27 (1.33) < .0001**	C1	**4.73 (1.74) 0.007**	
Post-intervention to C1	**5.88 (1.25) < .0001**	**7.09 (1.18) < .0001**	C2	**7.65 (1.74) < .0001**	
Post-intervention to C2	**6.13 (1.27) < .0001**	**10.26 (1.20) < .0001**			
C1 to C2	0.25 (1.24) 0.997	**3.16 (1.17) 0.037**			
Depressive symptoms (DASS Depression)					0.204
C1 to C2	*1.32 (0.71) 0.066*	**2.54 (0.67) 0.0002**	C1	**2.49 (1.19) 0.038**	
			C2	**3.72 (1.19) 0.002**	

Table 2. Post-hoc statistical summary of the changes in anxiety and depressive symptoms within the groups across time points and between groups for each time point. Linear mixed-effect models were adjusted for age, sex, education and intervention group, with a statistical significance set to $p < 0.05$. Post-hoc analyses comparing the estimated marginal means were adjusted for multiple comparisons. For within-group changes, positive estimate values represent an increase in anxiety and/or depressive symptoms across time. For between-group comparisons, positive estimate values represent higher anxiety and/or depressive symptoms in the DepS group compared to the NoDepS group for each time points. Values in bold correspond to significant p-values ($p < 0.05$) and values in italic correspond to trends ($0.05 < p < 0.1$). NoDepS, Group without pre-existing subclinical depressive symptoms; DepS, Group with pre-existing subclinical depressive symptoms; P, p-value; SE, Standard Error; STAI-A, State-Trait Anxiety Inventory form Y-A; DASS Depression, Depression Anxiety and Stress Scale – Depression subscale; C1, Confinement 1; C2, Confinement 2.

COVID-19 follow-up assessments

Participants then completed the COVID-19 follow-up assessments, which corresponded to the first (C1, from 17th March to 11th May 2020, date for sending out online questionnaires: 22th April 2020) and the second (C2, from 30th October to 15th December 2020, date for sending out online questionnaires: 23th November 2020) national confinement periods that occurred in France during the pandemic. Thirty-four participants who did not complete the first and/or second confinement assessments were excluded from our analyses. A total of 100 participants were therefore included (See Fig. 1 for the detailed inclusion process).

Assessment of subclinical depressive symptoms and classification of participants at baseline

In this study, we were specifically interested in the presence of pre-existing subclinical depressive symptoms before the onset of the COVID-19 pandemic—which was assessed using the 15-item version of the Geriatric Depression Scale (GDS) during the Age-Well baseline visit. This self-reported binary response questionnaire ranges from 0 to 15, with a higher score indicating more depressive symptoms[48,49]. As in our previous study[23], we split participants into having subclinical depressive symptoms (DepS; GDS > 0, n = 53) or not (NoDepS; GDS = 0, n = 47) based on GDS scores at baseline. Of note, the GDS was also administered at the post-intervention visit, but not at the COVID-19 follow-up assessments.

Assessment of psychoaffective health across time

Depressive symptoms during pandemic-related confinements

During the confinements, self-reported depressive symptoms were obtained from the full 42-item Depression Anxiety and Stress Scale (DASS)[50], with scores from the 14-item depression subscale (scores range from 0 to 42). Each item is rated on a 4-point Likert-type scale, ranging from 0 (*Did not apply to me at all—Never*) to 3 (*Applied to me very much, or most of the time – Almost always*). Higher scores indicate greater depressive symptoms. This scale was not administered at baseline, nor post-intervention.

Anxiety symptoms before and during pandemic-related confinements

For all assessments, self-reported state anxiety symptoms were obtained from the 20-item Spielberger State-Trait Anxiety Inventory form Y-A (STAI-A) (scores range from 20 to 80)[51]. Each item is rated on a 4-point Likert-type scale, ranging from 1 (*No*) to 4 (*Yes*), to indicate the extent to which the respondent felt that way at the time of the evaluation. Higher scores indicate greater anxiety symptoms. At baseline and post-intervention follow-up visits, we used the mean of the STAI-A scores reported before the magnetic resonance imaging (MRI) examinations (n = 2) and during the first neuropsychological session.

Assessment of psychological processes at baseline

Ruminative brooding

Self-reported ruminative brooding (i.e., repetitive passive and judgmental thoughts about one's mood) was obtained from the 5-item brooding subscale (scores range from 5 to 20) of the 22-item Rumination Response

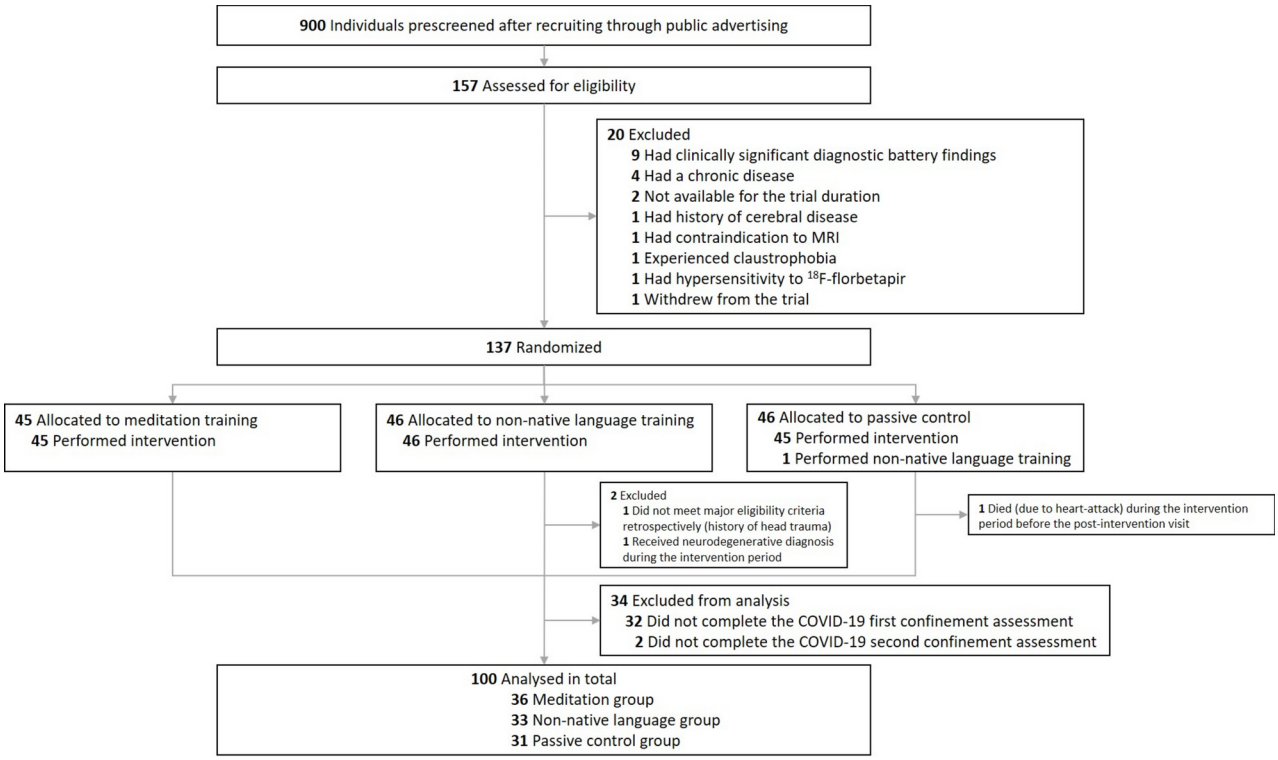

Fig. 1. **Flow diagram of the inclusion process.** *MRI* Magnetic Resonance Imaging.

Scale (RRS)[52]. Each item is rated on a 4-point Likert-type scale, ranging from 1 (*Almost never*) to 4 (*Almost always*). Higher scores indicate greater ruminative brooding. One participant had no available data for this questionnaire.

Worry
Self-reported worry was obtained from the 16-item Penn State Worry Questionnaire (PSWQ) (scores range from 16 to 80)[53]. Each item is rated on a 5-point Likert-type scale, ranging from 1 (*Very typical of me*) to 5 (*Not at all typical of me*). Higher scores indicate greater worry.

Emotion regulation abilities
The Emotion Regulation Questionnaire (ERQ) consists of 10 items that evaluate the tendency to regulate emotions through two strategies, resulting in two distinct subscales: cognitive reappraisal (i.e., changing one's way of thinking in an emotional situation, scores range from 6 to 42) or expressive suppression (i.e., inhibiting one's expressive behaviour in an emotional situation, scores range from 4 to 28)[54]. Each item is rated on a 7-point Likert-type scale, ranging from 1 (*Strongly disagree*) to 7 (*Strongly agree*). Higher scores indicate greater cognitive reappraisal or expressive suppression.

Cognitive defusion
The Drexel Defusion Scale (DDS) consists of 10 items that evaluate the extent to which individuals can defuse from difficult internal experiences (i.e., their ability to achieve psychological distance from one's thoughts and feelings) in a specific situation (scores range from 0 to 50)[55]. Each item is rated on a 6-point Likert-type scale, ranging from 0 (*Not at all*) to 5 (*Very much*). Higher scores indicate greater cognitive defusion.

Assessment of meditation practice and self-perceived benefit across confinements
Participants who underwent the meditation training intervention completed before the pandemic were asked to report whether they continued practicing meditation on their own during the first and the second confinement. For those who meditated, the assessment included average frequency of practice (number of sessions per week) and average duration per session (minutes). The self-perceived benefit of meditation practice was also evaluated using a 7-point Likert-type scale, ranging from 0 (*No benefit*) to 7 (*Very beneficial*).

Statistical analyses

Between-group comparisons at baseline, post-intervention and COVID-19 follow-up assessments
Group differences between participants with and without pre-existing subclinical depressive symptoms for demographic and global cognitive functioning at baseline were assessed using Student's t-tests for continuous variables and χ^2 tests for categorical variables, with statistical significance set to $p < 0.05$. Between-group differences in depressive and anxiety symptoms at each time-point, as well as baseline differences in psychological

processes, were assessed using analyses of covariance (ANCOVA) corrected for age, sex and education, as well as intervention group for post-intervention and confinement assessments, with statistical significance set to $p < 0.05$.

Impact of COVID-19 confinements on psychoaffective health of participants with and without pre-existing subclinical depressive symptoms: longitudinal analyses

Longitudinal data were analyzed using linear mixed-effect models (with the *lme4* package[56] in RStudio version 1.4.1106) to evaluate the change in depressive and anxiety symptoms across assessments between participants with and without pre-existing subclinical depressive symptoms.

As depressive symptoms were not assessed with the DASS scale before the confinements, only the impact of the confinement repetition (i.e., no comparison with pre-COVID-19 scores) on depressive symptoms between participants with and without pre-existing depressive symptoms was assessed.

Longitudinal models included all main effects, as well as the interaction between **Time** (categorical variable, i.e., C1 and C2 for depressive symptoms or Baseline, Post-intervention, C1 and C2 for anxiety symptoms) and **Group of participants** (categorical variable, i.e., DepS versus NoDepS) and were adjusted for age, sex, education and intervention group (i.e., meditation training, non-native language training and no intervention). Post-hoc analyses comparing the estimated marginal means using the *emmeans* package[57] in RStudio were adjusted for multiple comparisons. The significance level was set at $p < 0.05$ for all statistical analyses.

Results

Participants' characteristics at baseline and post-intervention follow-up visits

Demographic data, cognitive performance, psychoaffective, and psychological processes variables for each group, as well as between-group differences, are reported in Table 1.

Participants with subclinical depressive symptoms were younger and tended to have a higher proportion of women compared to participants without symptoms. The two groups did not differ in any other demographic or cognitive variables.

Participants with subclinical depressive symptoms at baseline had higher anxiety, ruminative brooding and worry levels, as well as lower cognitive defusion, compared to participants without subclinical depressive symptoms. At the post-intervention follow-up visit, participants with pre-existing subclinical depressive symptoms had higher depressive and anxiety symptoms compared to those without pre-existing symptoms (Table 1).

Between-group differences in psychoaffective variables during confinements

Participants with pre-existing subclinical depressive symptoms had higher anxiety and depressive symptoms during the first and the second confinement compared to those without pre-existing subclinical depressive symptoms (Table 1).

Longitudinal analyses

Firstly, we found a main effect of **Time** (all time points considered) and **Group** (DepS versus NoDepS) on anxiety symptoms ($p < 0.001$ and $p = 0.007$, respectively), as well as an interaction between **Time** and **Group** ($p = 0.026$) (Fig. 2 and Table 2). Post-hoc analyses showed that higher anxiety symptoms were observed during the confinements (C1 and C2) compared to the baseline and post-intervention visits (all between-time points comparisons, $p < 0.0001$) regardless of the group of participants (DepS versus NoDepS). Moreover, the DepS group reported higher anxiety symptoms at all time points compared to the NoDepS group, except at baseline (Baseline, $p = 0.100$; post-intervention, $p = 0.044$; C1, $p = 0.007$; C2, $p < 0.0001$). Lastly, anxiety symptoms increased in the second confinement (C2) compared to the first confinement (C1) in the DepS group ($p = 0.037$) but not in the NoDepS group ($p = 0.997$).

Secondly, we found a main effect of **Time** (C1 versus C2) and **Group** (DepS versus NoDepS) on depressive symptoms ($p = 0.0001$ and $p = 0.036$, respectively), with no interaction between **Time** and **Group** ($p = 0.204$) (Fig. 3 and Table 2). Post-hoc analyses showed that higher depressive symptoms were observed during the second confinement (C2) compared to the first one (C1) in the DepS group ($p = 0.0002$) and tended to be higher in the NoDepS group (0.066). Moreover, the DepS group had higher depressive symptoms than the NoDepS group in the first and the second confinement ($p = 0.038$ and $p = 0.002$, respectively).

Complementary analyses: factors associated with greater anxiety increase from confinement 1 to confinement 2 in participants with pre-existing subclinical depressive symptoms

As we found that the increase in anxiety symptoms from the first to the second confinement was higher in the DepS than in the NoDepS group, we performed additional analyses to assess i) whether we could identify pre-existing psychological processes (i.e., ruminative brooding, worry, emotion regulation abilities, and cognitive defusion) that would be associated with this disproportionate anxiety increase; and ii) whether the meditation training intervention completed before the pandemic (in the context of the Age-Well randomized control trial), as well as meditation practice during both confinements (i.e., frequency per week, duration per session, and self-perceived benefit) moderated this effect. For these analyses, the change in anxiety symptoms between the first and the second confinement was expressed as a percentage increase and was calculated as follows: [((C2 score – C1 score)/C1 score) × 100].

A forward stepwise linear regression analysis was performed to select, for the percentage increase in anxiety symptoms between the first and the second confinement in the DepS group, the most predictive psychological processes at baseline, including ruminative brooding, worry, emotion regulation strategies (i.e., cognitive reappraisal and expressive suppression), and cognitive defusion. Demographics (i.e., age, sex, and education)

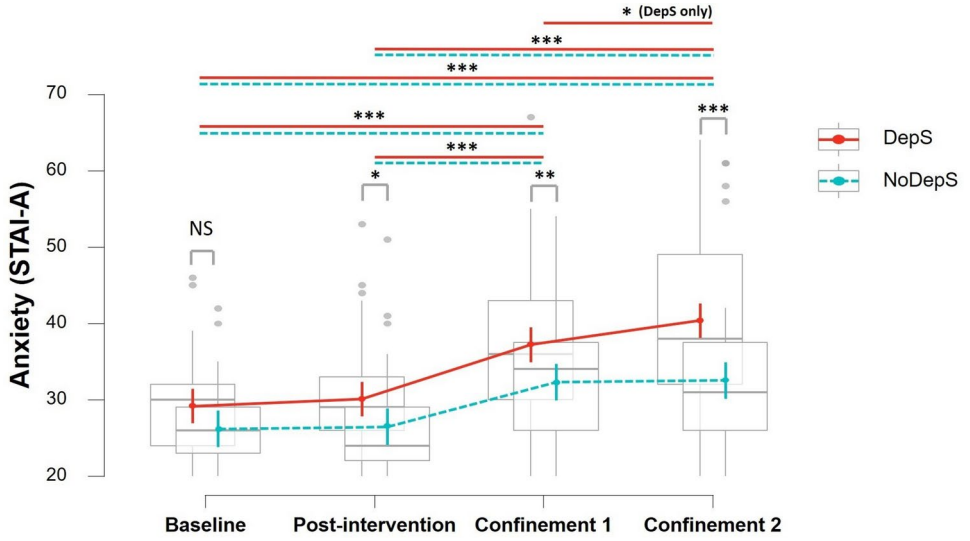

Fig. 2. Graph illustrating the evolution of anxiety symptoms over time in participants with (red solid line) and without (blue dotted line) pre-existing subclinical depressive symptoms. Linear mixed-effect model was adjusted for age, sex, education, and intervention group, with a statistical significance set to $p < 0.05$ (*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$). The main effect of **Time** (all time points considered) and **Group** (DepS versus NoDepS) on anxiety symptoms were significant ($p < 0.001$ and $p = 0.007$, respectively), as well as the interaction between **Time** and **Group** ($p = 0.026$). Post-hoc analyses comparing the estimated marginal means were adjusted for multiple comparisons. NoDepS, Group without pre-existing depressive symptoms; DepS, Group with pre-existing subclinical depressive symptoms; STAI-A, State-Trait Anxiety Inventory form Y-A; NS, Not Significant.

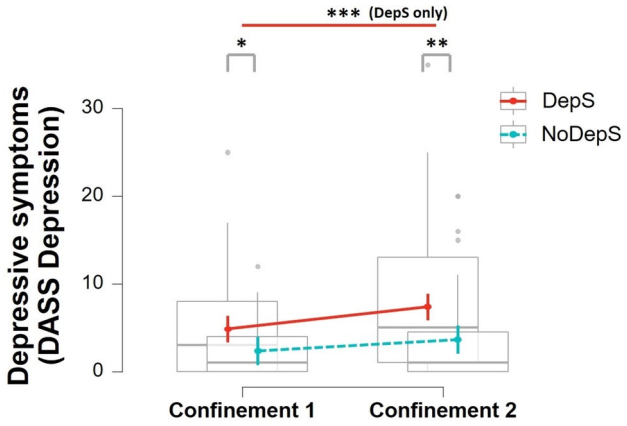

Fig. 3. Graph illustrating the evolution of depressive symptoms during confinements in participants with (red solid line) and without (blue dotted line) pre-existing subclinical depressive symptoms. Linear mixed effect model was adjusted for age, sex, education, and intervention group, with a statistical significance set to $p < 0.05$ (*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$). The main effect of **Time** (C1 and C2) and **Group** (DepS versus NoDepS) on depressive symptoms were significant ($p = 0.0001$ and $p = 0.036$, respectively), with no interaction between **Time** and **Group** ($p = 0.204$). Post-hoc analyses comparing the estimated marginal means were adjusted for multiple comparisons. NoDepS, Group without pre-existing depressive symptoms; DepS, Group with pre-existing subclinical depressive symptoms; DASS Depression, Depression Anxiety and Stress Scale – Depression subscale.

as well as intervention group were controlled for by forcing their inclusion into the model ("step 0"). The significance level was set at $p < 0.05$. This regression analysis was performed using the *stepwise* function (https://rubin.msu.domains/code/stepwise_demo.nb.html) and the *stats* package in RStudio (R Core Team, 2019).

An ANCOVA was performed to assess the effect of the intervention group (completed before the COVID-19 pandemic) on the change in anxiety symptoms in the DepS group (Meditation training, $n = 23$; Non-native language training, $n = 15$ and No intervention, $n = 15$) – adjusted for age, sex, and education.

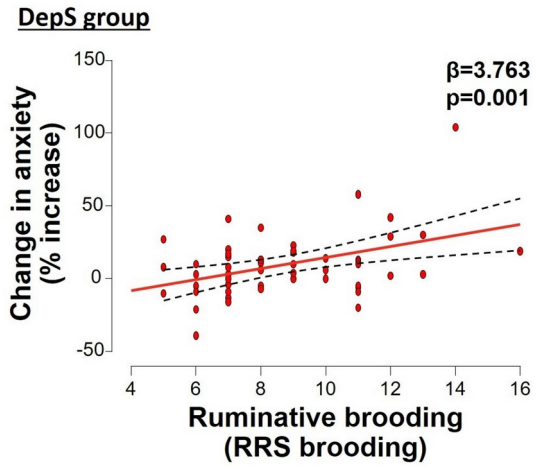

Fig. 4. Associations between the change in anxiety symptoms (percentage increase between the first and the second confinement) and baseline ruminative brooding in participants with pre-existing depressive symptoms. Reported statistics were obtained from a forward stepwise linear regression adjusted for age, sex, education, and intervention group. Raw values are plotted and confidence intervals (95%) are represented by the dotted line. DepS, Group with pre-existing subclinical depressive symptoms; RRS brooding, Rumination Response Scale – Brooding subscale.

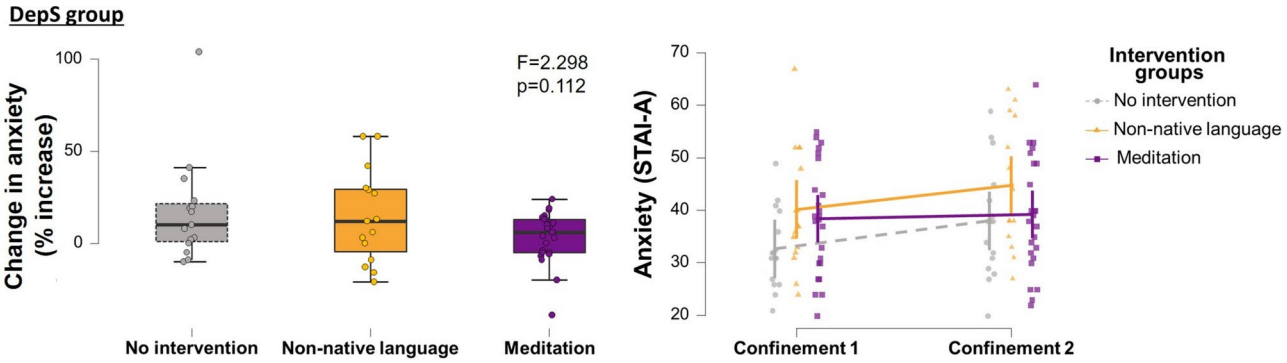

Fig. 5. Box-plots of the change in anxiety symptoms (percentage increase between the first and the second confinement) (left panel) and the evolution of anxiety symptoms during the first and the second confinement (right panel) according to the groups of intervention (No intervention in grey, Non-native language training in orange and Meditation training in violet) in participants with pre-existing subclinical depressive symptoms. ANCOVA was adjusted for age, sex, and education with a statistical significance set to $p < 0.05$. DepS, Group with pre-existing subclinical depressive symptoms.

Multiple regression models were conducted to assess the association between the percentage increase in anxiety symptoms between the first and the second confinements and the frequency per week, duration per session, and self-perceived benefit of meditation practice during each confinement in DepS who underwent the meditation training intervention – adjusted for age, sex, and education.

In the DepS group, among the psychological processes investigated, only higher baseline ruminative brooding emerged as a significant predictor, showing a positive association with the percentage increase in anxiety symptoms between the first and the second confinement ($\beta = 3.763$ $p = 0.001$) (Fig. 4).

In the DepS group, no significant main effect of the intervention group was observed regarding the change in anxiety symptoms with confinement repetition ($F = 2.298$ $p = 0.112$) (Fig. 5).

In the meditation training group, 18/23 (78.3%) of DepS participants reported practicing meditation during confinement 1 (mean frequency: 5.0 ± 2.1 sessions per week; mean duration: 16.7 ± 7.7 min per session; mean self-perceived benefit score: 5.7 ± 1.1) and 17/23 (73.9%) during confinement 2 (mean frequency: 6.6 ± 3.5 sessions per week; mean duration: 15.0 ± 8.5 min per session; mean self-perceive benefit score: 5.4 ± 1.2). Meditation practice of these participants during both confinements, including the frequency per week (C1, $\beta = -1.444$ $p = 0.472$; C2, $\beta = 0.293$ $p = 0.849$) and the duration per session (C1, $\beta = 0.371$ $p = 0.514$; C2, $\beta = 0.584$ $p = 0.262$), was not associated with the change in anxiety symptoms with confinement repetition. Similarly, the self-perceived benefit of meditation practice (C1, $\beta = 4.085$ $p = 0.276$; C2, $\beta = 3.805$ $p = 0.283$) was not associated with this change in anxiety symptoms.

Discussion

This study showed that CU older adults with pre-existing subclinical depressive symptoms had lower mental health during the COVID-19-related confinements, with higher levels of depressive and anxiety symptoms. More specifically, anxiety symptoms increased with confinement repetition only in participants with pre-exiting subclinical depressive symptoms, and this increase was associated with higher levels of ruminative brooding at baseline. Finally, meditation training before the pandemic or meditation practice during both confinements did not moderate the change in anxiety symptoms over the pandemic confinements.

The higher level of anxiety in older adults with subclinical depressive symptoms compared to those without depressive symptoms, both before and during the pandemic, is consistent with studies showing that anxiety symptoms are frequently observed in patients with late-life depression[9,10]. Moreover, the pandemic had an effect on anxiety symptoms in all individuals, but those with pre-existing subclinical depressive symptoms were more affected by its duration – since their anxiety symptoms increased with the repetition of confinements. This result could reflect the fact that these individuals tended to dwell on past negative events (e.g., of the first confinement), which amplified their anxiety during the second confinement. These results indicate that older adults with pre-existing subclinical depressive symptoms were less resilient to the multiple stressors experienced during the pandemic compared to individuals without pre-existing symptoms – consistent with what has been previously reported in clinical mental disorders[24–27]. Older adults with subclinical depressive symptoms thus represent a population highly vulnerable to mental health deterioration. As the presence of depressive symptoms, even at subclinical levels, could have deleterious consequences in older adults (i.e., increased risk of clinical depressive disorder, comorbidity including anxiety symptoms, mortality and dementia)[11–16,58], there is a need to monitor and treat these depressive symptoms in this population.

Ruminative brooding was associated with increased anxiety symptoms from the first to the second confinement, making it an important psychological process to target through mental health interventions in individuals at risk of depression. Higher levels of ruminative brooding were already present in individuals with subclinical depressive symptoms at baseline, which is consistent with previous works highlighting that rumination is frequently experienced by patients with clinical depressive disorder and is thought to play a role in the depressive symptomatology[59]. Indeed, higher levels of rumination have been linked to the onset, severity and duration of depressive episodes, as well as an increased risk of relapse in depressive patients in remission[59–61]. Interestingly, the brain substrates of subclinical depressive symptoms identified in our previous study[23] involved regions of the default mode network (DMN) (i.e., the precuneus/cingulate posterior, medial prefrontal and temporoparietal cortex and the hippocampus), which is also associated with rumination processes[62,63]. Changes in this network's activation and functional connectivity have been observed in late-life depression and are thought to be associated with a dysregulation of mental content in favor of negative thoughts and ruminations[64].

In young and middle-aged adults, meditation-based interventions have been shown to reduce depressive and anxiety symptoms in individuals with[30–32] or without[33,34] mental disorders – making it a promising practice for improving mental health. While preliminary research in older adults showed encouraging results indicating a similar impact of meditation on psychoaffective symptoms[28,35–40], the results need to be confirmed as the studies are scarce and had limitations (i.e., small sample size, short duration of intervention, lack of active and/or passive control groups). Although our study addressed some of these limitations, the 18-month meditation intervention that was completed before the pandemic, as well as meditation practice during both confinements, did not mitigate the pandemic's impact on the anxiety symptoms of these older adults. Given that only 23 participants with subclinical depressive symptoms underwent the meditation training and that, of those, only 18 (C1) and 17 (C2) continued practicing meditation during confinements, the sample may have been too small to detect an effect. A power analysis for ANCOVA using G*Power software[65] indicated that, with 80% power, an observed effect size of $f = 0.313$, and three covariates; 34 participants per intervention group would be required to detect a significant effect at $p < 0.05$. Alternatively, it would have been necessary to maintain meditation practice in a more formal way during confinement (e.g., guided lessons with an instructor) to really benefit from its effects. In addition, our population was enriched with healthy, highly educated and very active participants, which may also limit the potential for intervention-related improvements in mental health. Further investigations are needed to better understand whether and how psychological interventions could moderate the influence of major stressors, such as the pandemic and the associated confinement, on mental health in older adults.

The main strength of the study was to provide a greater insight on mental health during the COVID-19 pandemic and its determinants in a well-characterized sample of CU older adults with and without subclinical depressive symptoms. Repeated longitudinal assessments allowed us to follow the evolution of mental health before and during the pandemic, as well as to evaluate the effect of baseline psychological processes and meditation practice via a randomized controlled trial design. However, the use of self-report questionnaires for assessing psychoaffective factors is a limitation; as it is subjective, the measure could be biased by demand characteristics, awareness and introspective ability. Yet, we previously found a link between subclinical depressive symptoms assessed using the same questionnaire (GDS; with the same cut-off value used to split participants) and neurodegeneration biomarkers, both in our sample and in a completely independent sample (ADNI), which suggests that this measure is relatively reliable[23]. Furthermore, the fact that depressive symptoms were not evaluated with the same questionnaire before and during the confinements prevented us from assessing the direct impact of confinements on depressive symptoms. Moreover, thirty-four participants did not complete the first and/or second confinement assessments (reason not collected) and were excluded from the analyses, which may have impacted the findings due to the potential dropout of those most severely affected. Of note, after performing linear mixed-effect models to evaluate the change in depressive and anxiety symptoms across assessments, including all available data for all 135 participants (i.e., all available data at baseline, post-intervention, and confinement assessments), we found that the results remained consistent with the initial

findings. All analyses were also repeated when adjusting for psychotropic medications (3 participants have taken antidepressants and/or anxiolytics), and the findings remained the same.

Overall, our study highlights that CU older adults with subclinical depressive symptoms were particularly vulnerable to the mental health effects of the COVID-19 pandemic and its repeated confinements. More particularly, pre-existing subclinical depressive symptoms were associated with lower mental health during the COVID-19-related confinements, including higher levels of depressive and anxiety symptoms, and an increase in anxiety symptoms with the repetition of confinements. This increase was associated with higher ruminative brooding at baseline but was not moderated by meditation training before the pandemic or meditation practice during both confinements. Future planning to manage mental health in older adults with subclinical depressive symptoms, especially during stressful events such as the pandemic, needs prioritization and could involve interventions targeting these psychoaffective factors and their determinants to limit their negative consequences.

Data availability

Data and code are made available on request following a formal data sharing agreement and approval by the consortium and executive committee (https://silversantestudy.eu/2020/09/25/data-sharing). The Material can be mobilized, under the conditions and modalities defined in the Medit-Ageing Charter by any research team belonging to an Academic, for carrying out a scientific research project relating to the scientific theme of mental health and well-being in older people. The Material may also be mobilized by non-academic third parties, under conditions, in particular financial, which will be established by separate agreement between Inserm and by the said third party. Data sharing policies described in the Medit-Ageing charter are in compliance with our ethics approval and guidelines from our funding body. The data has been presented orally at the GREPACO conference (May 22–23, 2023, Louvain-la-Neuve, Belgium).

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References

1. Holmes, E. A. et al. Multidisciplinary research priorities for the COVID-19 pandemic: A call for action for mental health science. *Lancet Psychiatry* **7**, 547–560 (2020).
2. Benke, C., Autenrieth, L. K., Asselmann, E. & Pané-Farré, C. A. Lockdown, quarantine measures, and social distancing: Associations with depression, anxiety and distress at the beginning of the COVID-19 pandemic among adults from Germany. *Psychiatry Res.* **293**, 113462 (2020).
3. Bäuerle, A. et al. Increased generalized anxiety, depression and distress during the COVID-19 pandemic: A cross-sectional study in Germany. *J. Public Health (Oxf.)* https://doi.org/10.1093/pubmed/fdaa106 (2020).
4. Benke, C., Autenrieth, L. K., Asselmann, E. & Pané-Farré, C. A. Stay-at-home orders due to the COVID-19 pandemic are associated with elevated depression and anxiety in younger, but not older adults: Results from a nationwide community sample of adults from Germany. *Psychol. Med.* **52**, 3739–3740 (2022).
5. Ettman, C. K. et al. Prevalence of depression symptoms in US adults before and during the COVID-19 pandemic. *JAMA Netw. Open* **3**, e2019686 (2020).
6. González-Sanguino, C. et al. Mental health consequences during the initial stage of the 2020 Coronavirus pandemic (COVID-19) in Spain. *Brain Behav. Immun.* **87**, 172–176 (2020).
7. Briggs, R., McDowell, C. P., De Looze, C., Kenny, R. A. & Ward, M. Depressive symptoms among older adults pre- and post-COVID-19 pandemic. *J. Am. Med. Dir. Assoc.* **22**, 2251–2257 (2021).
8. Klaus, F. et al. Increase in depression and anxiety symptoms and stable levels of compassion among older adults from before to during the COVID-19 pandemic. *Am. J. Geriatr. Psychiatry* **29**, S53–S54 (2021).
9. Beekman, A. T. et al. Anxiety and depression in later life: Co-occurrence and communality of risk factors. *Am. J. Psychiatry* **157**, 89–95 (2000).
10. Diefenbach, G. J. & Goethe, J. Clinical interventions for late-life anxious depression. *Clin. Interv. Aging* **1**, 41–50 (2006).
11. Wilson, R. S. et al. Depressive symptoms, cognitive decline, and risk of AD in older persons. *Neurology* **59**, 364–370 (2002).
12. Lyness, J. M. et al. The clinical significance of subsyndromal depression in older primary care patients. *Am. J. Geriatr. Psychiatry* **15**, 214–223 (2007).
13. Meeks, T. W., Vahia, I. V., Lavretsky, H., Kulkarni, G. & Jeste, D. V. A tune in "a minor" can "b major": A review of epidemiology, illness course, and public health implications of subthreshold depression in older adults. *J. Affect. Disord.* **129**, 126–142 (2011).
14. Ezzati, A., Katz, M. J., Derby, C. A., Zimmerman, M. E. & Lipton, R. B. Depressive symptoms predict incident dementia in a community sample of older adults: Results from the Einstein Aging Study. *J. Geriatr. Psychiatry Neurol.* **32**, 97–103 (2019).
15. Livingston, G. et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *Lancet* **396**, 413–446 (2020).
16. Jeuring, H. W., Huisman, M., Comijs, H. C., Stek, M. L. & Beekman, A. T. F. The long-term outcome of subthreshold depression in later life. *Psychol. Med.* **46**, 2855–2865 (2016).
17. Zhang, Z. et al. Associations of subsyndromal symptomatic depression with cognitive decline and brain atrophy in elderly individuals without dementia: A longitudinal study. *J. Affect. Disord.* **274**, 262–268 (2020).
18. Petkus, A. J. et al. Anxiety is associated with increased risk of dementia in older Swedish twins. *Alzheimers Dement.* **12**, 399–406 (2016).
19. Santabárbara, J. et al. Clinically relevant anxiety and risk of Alzheimer's disease in an elderly community sample: 4.5 years of follow-up. *J. Affect. Disord.* **250**, 16–20 (2019).
20. Tales, A. & Basoudan, N. Anxiety in old age and dementia—Implications for clinical and research practice. *Neuropsychiatry* **6**, 142–148 (2016).
21. Rodríguez, M. R., Nuevo, R., Chatterji, S. & Ayuso-Mateos, J. L. Definitions and factors associated with subthreshold depressive conditions: A systematic review. *BMC Psychiatry* **12**, 181 (2012).
22. Donovan, N. J. et al. Depressive symptoms and biomarkers of Alzheimer's disease in cognitively normal older adults. *J. Alzheimers Dis.* **46**, 63–73 (2015).
23. Touron, E. et al. Depressive symptoms in cognitively unimpaired older adults are associated with lower structural and functional integrity in a frontolimbic network. *Mol. Psychiatry* https://doi.org/10.1038/s41380-022-01772-8 (2022).
24. Robillard, R. et al. Emerging New Psychiatric Symptoms and the Worsening of Pre-existing Mental Disorders during the COVID-19 Pandemic: A Canadian Multisite Study: Nouveaux symptômes psychiatriques émergents et détérioration des troubles mentaux préexistants durant la pandémie de la COVID-19: une étude canadienne multisite. *Can. J. Psychiatry* **66**, 815–826 (2021).

25. Gobbi, S. *et al.* Worsening of Preexisting Psychiatric Conditions During the COVID-19 Pandemic. *Frontiers in Psychiatry* **11**, (2020).
26. Neelam, K., Duddu, V., Anyim, N., Neelam, J. & Lewis, S. Pandemics and pre-existing mental illness: A systematic review and meta-analysis. *Brain Behav. Immun. Health* **10**, 100177 (2020).
27. Benke, C., Asselmann, E., Entringer, T. M. & Pané-Farré, C. A. The role of pre-pandemic depression for changes in depression, anxiety, and loneliness during the COVID-19 pandemic: Results from a longitudinal probability sample of adults from Germany. *Eur. Psychiatry* **65**, e76 (2022).
28. Lutz, A. et al. The protective effect of mindfulness and compassion meditation practices on ageing: Hypotheses, models and experimental implementation. *Ageing Res. Rev.* **72**, 101495. https://doi.org/10.1016/j.arr.2021.101495 (2021).
29. Tang, Y.-Y., Hölzel, B. K. & Posner, M. I. The neuroscience of mindfulness meditation. *Nat. Rev. Neurosci.* **16**, 213–225 (2015).
30. Hoge, E. A. et al. Mindfulness-based stress reduction vs escitalopram for the treatment of adults with anxiety disorders: A randomized clinical trial. *JAMA Psychiat.* https://doi.org/10.1001/jamapsychiatry.2022.3679 (2022).
31. Hofmann, S. G., Sawyer, A. T., Witt, A. A. & Oh, D. The effect of mindfulness-based therapy on anxiety and depression: A meta-analytic review. *J. Consult. Clin. Psychol.* **78**, 169–183 (2010).
32. Reangsing, C., Lauderman, C. & Schneider, J. K. Effects of mindfulness meditation intervention on depressive symptoms in emerging adults: A systematic review and meta-analysis. *J. Integr. Complement. Med.* **28**, 6–24 (2022).
33. Kallapiran, K., Koo, S., Kirubakaran, R. & Hancock, K. Review: Effectiveness of mindfulness in improving mental health symptoms of children and adolescents: A meta-analysis. *Child Adolesc. Mental Health* **20**, 182–194 (2015).
34. Hilton, L. et al. Mindfulness meditation for chronic pain: Systematic review and meta-analysis. *Ann. Behav. Med.* **51**, 199–213 (2017).
35. Reangsing, C., Rittiwong, T. & Schneider, J. K. Effects of mindfulness meditation interventions on depression in older adults: A meta-analysis. *Aging Ment. Health* **25**, 1181–1190 (2021).
36. Young, L. A. & Baime, M. J. Mindfulness-based stress reduction: Effect on emotional distress in older adults. *Complement. Health Pract. Rev.* **15**, 59–64 (2010).
37. Kishita, N., Takei, Y. & Stewart, I. A meta-analysis of third wave mindfulness-based cognitive behavioral therapies for older people. *Int. J. Geriatr. Psychiatry* **32**, 1352–1361 (2017).
38. Li, S. Y. H. & Bressington, D. The effects of mindfulness-based stress reduction on depression, anxiety, and stress in older adults: A systematic review and meta-analysis. *Int. J. Ment. Health Nurs.* **28**, 635–656 (2019).
39. Liu, Z., Chen, Q. & Sun, Y. Mindfulness training for psychological stress in family caregivers of persons with dementia: A systematic review and meta-analysis of randomized controlled trials. *CIA* **12**, 1521–1529 (2017).
40. Zoogman, S., Goldberg, S. B., Hoyt, W. T. & Miller, L. Mindfulness interventions with youth: A meta-analysis. *Mindfulness* **6**, 290–302 (2015).
41. Whitfield, T. et al. The effect of mindfulness-based programs on cognitive function in adults: A systematic review and meta-analysis. *Neuropsychol. Rev.* **32**, 677–702 (2022).
42. Fox, K. C. R. et al. Is meditation associated with altered brain structure? A systematic review and meta-analysis of morphometric neuroimaging in meditation practitioners. *Neurosci. Biobehav. Rev.* **43**, 48–73 (2014).
43. Fox, K. C. R. et al. Functional neuroanatomy of meditation: A review and meta-analysis of 78 functional neuroimaging investigations. *Neurosci. Biobehav. Rev.* **65**, 208–228 (2016).
44. Chételat, G. et al. Effect of an 18-month meditation training on regional brain volume and perfusion in older adults: The age-well randomized clinical trial. *JAMA Neurol.* **79**, 1165–1174 (2022).
45. Pascoe, M. C., Thompson, D. R., Jenkins, Z. M. & Ski, C. F. Mindfulness mediates the physiological markers of stress: Systematic review and meta-analysis. *J. Psychiatr. Res.* **95**, 156–178 (2017).
46. Poisnel, G. et al. The Age-Well randomized controlled trial of the Medit-Ageing European project: Effect of meditation or foreign language training on brain and mental health in older adults. *Alzheimers Dement. (N Y)* **4**, 714–723 (2018).
47. Montgomery, S. A. & Asberg, M. A new depression scale designed to be sensitive to change. *Br. J. Psychiatry* **134**, 382–389 (1979).
48. Sheikh, J. I. & Yesavage, J. A. Geriatric Depression Scale (GDS): Recent evidence and development of a shorter version. *Clin. Gerontol. J. Aging Mental Health* **5**, 165–173 (1986).
49. Wancata, J., Alexandrowicz, R., Marquart, B., Weiss, M. & Friedrich, F. The criterion validity of the Geriatric Depression Scale: A systematic review. *Acta Psychiatr. Scand.* **114**, 398–410 (2006).
50. Lovibond, S. H., Lovibond, P. F., & Psychology Foundation of Australia. *Manual for the Depression Anxiety Stress Scales*. (Psychology Foundation of Australia, Sydney, N.S.W., 1995).
51. Spielberger, C. D., Gorsuch, R. L. & Lushene, R. E. *Manual for the State-Trait Anxiety Inventory*. (1970).
52. Treynor, W., Gonzalez, R. & Nolen-Hoeksema, S. Rumination reconsidered: A psychometric analysis. *Cogn. Ther. Res.* **27**, 247–259 (2003).
53. Meyer, T. J., Miller, M. L., Metzger, R. L. & Borkovec, T. D. Development and validation of the Penn State Worry Questionnaire. *Behav. Res. Ther.* **28**, 487–495 (1990).
54. Gross, J. J. & John, O. P. Individual differences in two emotion regulation processes: Implications for affect, relationships, and well-being. *J. Pers. Soc. Psychol.* **85**, 348–362 (2003).
55. Forman, E. M. et al. The Drexel defusion scale: A new measure of experiential distancing. *J. Contextual Behav. Sci.* **1**, 55–65 (2012).
56. Bates, D., Mächler, M., Bolker, B. & Walker, S. Fitting linear mixed-effects models using lme4. *J. Stat. Softw.* **67**, 1–48 (2015).
57. Lenth, R. V. *et al.* emmeans: Estimated Marginal Means, aka Least-Squares Means. (2023).
58. Braam, A. W. et al. Depression, subthreshold depression and comorbid anxiety symptoms in older Europeans: Results from the EURODEP concerted action. *J. Affect. Disord.* **155**, 266–272 (2014).
59. Nolen-Hoeksema, S., Wisco, B. E. & Lyubomirsky, S. Rethinking rumination. *Perspect. Psychol. Sci.* **3**, 400–424 (2008).
60. Michl, L. C., McLaughlin, K. A., Shepherd, K. & Nolen-Hoeksema, S. Rumination as a mechanism linking stressful life events to symptoms of depression and anxiety: Longitudinal evidence in early adolescents and adults. *J. Abnorm. Psychol.* **122**, 339–352 (2013).
61. Figueroa, C. A. et al. Cognitive reactivity versus dysfunctional cognitions and the prediction of relapse in recurrent major depressive disorder. *J. Clin. Psychiatry* **76**, 3195 (2015).
62. Andrews-Hanna, J. R., Smallwood, J. & Spreng, R. N. The default network and self-generated thought: Component processes, dynamic control, and clinical relevance. *Ann. N. Y. Acad. Sci.* **1316**, 29–52 (2014).
63. Makovac, E., Fagioli, S., Rae, C. L., Critchley, H. D. & Ottaviani, C. Can't get it off my brain: Meta-analysis of neuroimaging studies on perseverative cognition. *Psychiatry Res. Neuroimag.* **295**, 111020 (2020).
64. Alexopoulos, G. S. et al. Functional connectivity in the cognitive control network and the default mode network in late-life depression. *J. Affect. Disord.* **139**, 56–65 (2012).
65. Faul, F., Erdfelder, E., Lang, A.-G. & Buchner, A. G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav. Res. Methods* **39**, 175–191 (2007).

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Author contributions

Dr Chételat had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: ET, NLM, GC. Acquisition, analysis, or interpretation of data: ET, JG, LP, MD, OH, FM, SF, DV, VDLS, GP, NLM, GC. Drafting of the manuscript: ET. Critical revision of the manuscript for important intellectual content: ET, JG, LP, MD, OH, FM, SF, DV, VDLS, GP, NLM, GC. Statistical analysis: ET. Obtained funding: ET, GP, NLM, GC. Administrative, technical, or material support: FM, SV, DV, GP. Supervision: NLM, GC. Other–Principal investigators: GC, VDLS (MD, principal investigator).

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Declarations

Competing interests

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Additional information

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