

How are neuroticism and depression related to the psychophysiological stress response to acute stress in healthy older people?



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HIGHLIGHTS

- We studied how depression and neuroticism affect to the stress response in older people.
- Neuroticism was not related to the psychophysiological stress response.
- Depression was related to higher cortisol and lower heart rate response to stress.
- Our results confirm the adverse effects of depression on stress response.

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ABSTRACT

Neuroticism and depressive symptomatology have been related to a heightened and diminished physiological stress response, which may partly explain their negative relationship with health and wellbeing. Identifying factors that may increase disease vulnerability is especially relevant in older people, whose physiological systems decline. With this in mind, we investigated the influence of neuroticism and depression on the psychophysiological stress response in healthy older people (from 55 to 76 years old). A total of 36 volunteers were exposed to a stressful task (Trier Social Stress Test, TSST), while 35 volunteers performed a control non-stressful task. The physiological stress response was assessed through measures of cortisol, alpha-amylase, heart rate (HR). Our results showed that, neuroticism was not related to physiological stress response. However, depression was related to higher cortisol response and lower HR reactivity in the stress condition. In summary, emotional states such as depressive mood seem to amplify the cortisol stress response and reduce the cardiovascular response, whereas more stable dispositions such as neuroticism did not affect stress response in older people. These findings confirm, in healthy older people, the adverse effects of depression, acting on different subsystems of the stress response.

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1. Introduction

Throughout life, people are exposed to a wide range of circumstances that can be experienced as stressful. Some of these situations are related to psychosocial stimuli that induce physiological and psychological changes that can damage long-term health [40].

Stress exposure involves the activation of the autonomic nervous system (ANS) and the hypothalamic–pituitary–adrenal axis (HPA). Physical and/or psychological stress events first affect the autonomic nervous system (ANS) [92], increasing the influence of the sympathetic branch in young and older people [4,5]. This activity can be observed through Heart Rate (HR) (for review: [78,80]), and through salivary alpha-amylase (sAA) (for review see: [66]). When coping with stress,

young and older people show an increase in HR and sAA [4,22,58,59,67,87]. Furthermore, to cope with the situation, the HPA axis is activated, triggering a sharp increase in cortisol levels [21,47].

Recent investigations have suggested that the dysregulation of the stress response, i.e. the dissociation between the ANS and HPA systems, would be associated with a greater number of health problems [2]. In fact, a coordinated response by both systems is considered more adaptive than uncoordinated functioning [6]. Previous research has employed several ways to examine the associations between these two systems [2,24,31,32], with Ali and Pruessner [2] highlighting the relevance of studying their interaction through the ratio of the two salivary biomarkers, cortisol and alpha-amylase.

Aging involves changes in the ability to regulate the systems involved in the stress response, leading to a poorer control of HPA and autonomic regulation [49,57,61]. These changes can be reflected in physiological disruptions in the ability to respond to stress. In fact, previous studies report that older people show higher sympathetic and

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cortisol response to stress [4,61]. Additionally, there is a large body of evidence about the influence of stable and non-stable psychological factors on the stress response [16], and on wellbeing and life satisfaction over the years [29]. Given that this would lead to health consequences in later life [48], studying the moderating variables in the stress response is especially relevant in older people.

One of the most important variables affecting the stress response is neuroticism, which has been considered a basic personality dimension that involves emotional lability and over-responsiveness to stimuli [25]. Higher neuroticism has been associated with increased emotional reactivity to stressors [9,83] and heightened perception of stressful events [19,90]. Neuroticism seems to increase the vulnerability to mental and physical diseases because people with more neuroticism usually show higher reactivity and are less capable of mitigating problematic events and experiences [9,48,83,84]. However, the link between neuroticism and the stress response in advanced stages of the life cycle is still not completely understood [48]. In young people, some studies have shown no relationship between neuroticism and autonomic or cortisol responses in stressful situations [37,42–45,73,88,95], while others have reported that neuroticism is related to higher autonomic response and lower cortisol release after stress [39,41,60,64,74,79]. To the best of our knowledge, only one study [8] has analyzed the middle-aged population (55–59 years old), showing that neuroticism is related to blunted autonomic and cortisol reactivity to stressful situations. However, no previous studies have been carried out with older people, increasing the need to test this relationship in aging.

In addition to neuroticism, other state dimensions have been related to the stress response. Thus, depression has also shown an important effect on the stress response. On the one hand, studies in a clinical population showed a higher cortisol response to stress in depressed women with and without a history of childhood abuse [34,35]. On the other hand, previous studies [12,56,69] showed lower cortisol release in depressed and remitted depression patients compared to healthy participants under stress conditions, regardless of sex. Other studies suggested different patterns depending on sex, with women showing an increased cortisol response to stress [17] and men showing a decreased peak percentage of change [17,86]. These results coincide with Brooks and Robles [11], who observed that healthy young men with high depression showed lower cortisol responses to psychosocial stress. Nevertheless, Young, Lopez, Murphy-Weinberg, Watson and Akil [97] showed elevated baseline cortisol, but normal stress response, in adult depressed patients exposed to the TSST. In sum, depressive symptoms seem to have a different effect on the cortisol response depending on sex and symptomatology severity.

Regarding autonomic function, depression has been related to higher sympathetic activity in response to stress [33,34,53]. However, other studies have reported negative associations between depression and HR and/or blood pressure reactivity to stress [12,13,23,69,71,98], or no relationship between depression and HR [55]. Except for the Carroll et al. [13] and Burke et al. [12] studies, which had large mixed samples of young, adult and older people, all the studies mentioned above explored the effect of depressive symptomatology on the ANS and HPA axis in young people, adults or middle-aged people. In older people, lower cardiovascular reactivity to stress has been reported in patients with coronary artery disease with high scores on depression [99]. Thus, further research in older people is needed to understand more in depth the pathways through which depression affects physiological adjustment to stress in this period of life.

Apart from a physiological change, coping with a stressor involves psychological changes. People exposed to stress experience it as a negative experience [3], with increases in anxiety [91], stress perception [81], and negative mood [28,96]. Some studies reported that neuroticism predicts higher negative affect and lower positive affect after a stressful task or negative mood induction in young people [30,50,51,70]. However, to the best of our knowledge, no previous research has studied this relationship in older people, highlighting the need to

explore it in this population due to age-related changes in emotional regulation [14].

Taking into account the impact of age [57,61] and psychological factors such as neuroticism and depression in the HPA and ANS stress response (e.g. [33–35,41,60,64]), the aim of the present study was to investigate the effects of these psychological factors on the psychophysiological response to stress and non-stress in a healthy older population from an integrative perspective, including several measures of different systems in order to more closely examine this relationship. Based on previous literature [4,21,100], we expected to find a higher response in these main systems involved in the stress response (HR, sAA and cortisol) in older people exposed to a stress situation compared to those exposed to a non-stress situation. Moreover, considering the literature on healthy middle-aged and older people [8,13,69,99], we expected neuroticism and depression to be related to a blunted physiological stress response. We also explored the relationship between neuroticism and depression, and the dysregulation of the HPA and ANS response, using the approach employed by Ali and Pruessner [2], in order to improve our comprehension of the effects of neuroticism and depression in the coordination of these two systems in healthy older people facing stress. Finally, we studied the relationship of neuroticism and depression with negative or positive affect after stress or non-stress exposure in older people. Previous results showed that both adult and middle-aged people with high neuroticism and depressed people perceived the stressful task as more stressful, difficult and demanding [8,69,71]. Therefore, we expected higher negative affect and anxiety after stress in people with higher neuroticism and depression [30,50,51,70].

2. Material and methods

2.1. Participants

A total of 71 participants from 55 to 76 years old were recruited using informative advertisements. Participants were randomly assigned to two conditions: 36 to the stress condition (16 men) and 35 to the non-stress condition (17 men). The exclusion criteria were: smoking more than 10 cigarettes a day, consuming alcohol or other drugs of abuse, having had surgery under general anesthesia during the past year, severe vision or hearing problems, presence of severe cardiovascular disease, illness that involves a disturbance of the HPA, and neurological or psychiatric disorders. In addition, participants were excluded if they took drugs related to cognitive or emotional function, psychotropic substances, beta-blockers, benzodiazepines, asthma medication, or drugs capable of influencing HPA function such as glucocorticoids. All the female participants were postmenopausal, and none of them were receiving hormonal replacement therapy. Subjects were contacted by telephone and invited to participate in the study.

The study was carried out according to the Declaration of Helsinki, and the Ethics Committee of the University approved the protocol. All participants received verbal and written information about the study and signed an informed consent. At the end of the study, the participants received a gift worth 15€.

2.2. Procedure

The participants were invited to two sessions on two consecutive days. The first session consisted of a neuropsychological assessment (results published in [65]). In this report we focus on the results from the second session, which took 1 h and 30 min to complete and was always carried out in the afternoon between 16 h and 20 h. Participants were asked to sleep as long as usual, refrain from heavy activity the day before, and not consume alcohol since the night before. Additionally, they were instructed to drink only water and not eat, smoke or take any stimulants 2 h prior to both sessions.

The protocol started with a 30-min introduction phase to allow the participants to adapt to the laboratory setting. In this phase, the heart

rate recording system was placed on the participant, the first saliva sample for cortisol and sAA was provided, and state anxiety and positive and negative affect were assessed. After the introduction phase, participants were exposed to a stress task or non-stress task, and a saliva sample was collected during exposure to the task. Immediately after the task, state anxiety and positive and negative affect were assessed again. Finally, subjects had 45 min to recover while they answered several questionnaires. During the recovery period, saliva samples were collected every 10 min from the termination of the task. The participants completed personality (EPQ-RS) and depression (BDI) questionnaires.

2.2.1. Stress condition

The participants were exposed to a standardized psychosocial stressor (Trier Social Stress Test – TSST, [46,101]) that is able to provoke cortisol, sAA and cardiovascular responses in older people [4,65]. The participants performed a 5-min free speech task (job interview) and a 5-min arithmetic task (serial subtraction), both in front of a committee composed of a man and a woman. They remained standing at a distance of 1.5 m from the committee in a room where a video camera and a microphone were clearly visible. The committee member of the opposite sex engaged in all the interactions with participants: (i) ask a set of standardized questions about the participant's characteristics if he/she did not use up the 5 min of free speech; (ii) and interrupt and urge the participant to start the subtraction again after each mistake in the arithmetic task. The participants were informed that the task was recorded in order to analyze their performance later. Thus, the TSST is a social-evaluative stress task whose main stress source stems from lack of control and being evaluated by others (committee).

2.2.2. Non-stress condition

An ad hoc laboratory task was designed following Kudielka et al.'s [46] criteria, in order to make it similar to the stress condition in physical global activity and mental workload, except for the lack of evaluative threat and uncontrollability, the main stress-producing components of the TSST [21]. This task consisted of free speech and an arithmetic task without an audience. For the free speech, the participants talked aloud for 5 min about a neutral non-emotional experience, while the arithmetic task consisted of counting by five aloud. Before the task, the participants were informed that they would not be recorded, and their performance would not be evaluated later. None of the stressful elements were present (video camera, microphone and committee). This control task has been used in previous studies (see [36,65]) and can be considered a nonsocial-evaluative stress task.

2.3. Physiological measurements

2.3.1. Heart rate (HR)

It was continuously recorded in the stress and non-stress conditions using a Polar®RS800cx watch (Polar CIC, USA). This device comprises a chest belt placed on the solar plexus and a Polar watch. The Polar watch records R–R intervals with a sampling frequency of 1000 Hz, providing a time resolution of 1 ms for each R–R interval. After eliminating the artifacts, the HR means were computed using the software Kubios Analyses (Biomedical Signal Analysis Group, University of Kuopio, Finland). We analyzed HR in periods of 5 min. We selected minutes 7–12 (baseline) as the baseline, minutes 35–40 (free speech), and minutes 43–48 (arithmetic task) to measure the response to the stress or non-stress task, and minutes 50–55 (recovery) to measure the capability to recover baseline levels after the tasks. All the minutes mentioned above were measured from the beginning of the session.

2.3.2. Salivary stress markers

The participants provided 7 saliva samples using salivettes (Sarstedt, Nümbrecht, Germany) to measure cortisol and sAA levels during the session. The timing of the saliva sampling was 15 min before the onset of the stress or non-stress task (–15), between the speech and

arithmetic tasks (+5), 5 min after the stress or non-stress task (+15), and then in periods of 10 min until the end of the experimental session (+25, +35, +45 and +55 min). Both cortisol and sAA were analyzed from the same saliva samples, and so the time points were identical.

2.3.2.1. Cortisol. Samples were centrifuged at 3000 rpm for 5 min, resulting in a clear supernatant of low viscosity that was frozen at –80 °C until the analysis took place. The samples were analyzed by a competitive solid phase radio immune assay (tube-coated), using the commercial kit Spectria Cortisol RIA (cat. Nu 06,119) from Orion Diagnostica (Espoo, Finland). All the samples were analyzed in the same trial, assay sensibility was 0.8 nmol/L, and the inter- and intra-assay variation coefficients were all below 10%.

2.3.2.2. Alpha-amylase. sAA was measured by an enzyme kinetic method according to the protocol specified in Rohleder et al. [68] using a commercial kit analysis of sAA (Cat. No. 1-1902, 1-1902-5) by Salimetrics (USA). All the samples from the same individual were analyzed in the same run, the inter- and intra-assay variation was about 10%, and test sensitivity was 0.4 U/ml.

2.4. Psychological measurements

2.4.1. Eysenck personality questionnaire-revised [25]

To obtain the scores for neuroticism, we used the Spanish version of the Eysenck Personality Questionnaire-Revised, short form (EPQ-RS) [26]. The EPQ-RS contains a total of 48 items to which participants are asked to respond “yes” or “no”. The questionnaire provides four factors: psychoticism, extraversion, neuroticism and lie. The alpha values for the Spanish version range from 0.65 to 0.82 for men, and from 0.67 to 0.82 for women, and the correlations among scales are below 0.16 for men and 0.22 for women [26]. In our study, we focused only on neuroticism. Of the 48 items, 12 of them measured neuroticism (e.g. “Do you often worry about things you should not have done or said?” or “Are you an irritable person?”).

2.4.2. Beck depression inventory (BDI) [7]

The Spanish version of the BDI is used to assess depressive symptomatology. It is a 21-item questionnaire scored from 0 to 3 [18]. It measures cognitive, somatic and behavioral symptoms of depression in the previous two months, with high scores indicating more severe depression. This questionnaire showed good internal consistency ($\alpha = 0.91$) and good construct validity.

2.4.3. Positive and negative affect (PANAS)

They were evaluated by the Spanish version [72] of the PANAS (Positive and Negative Affect Scale - PANAS; [94]). This 20-item questionnaire assesses affect according to two dimensions: Positive affect (PA) and Negative affect (NA), with 10 items measuring each of them (*interested, upset excited, scared*, etc.). Participants gave their answers based on how they felt at that particular moment, just after and just before the stress or non-stress task. They responded using a 5-point Likert scale ranging from 1 (not at all) to 5 (extremely). The Spanish version of the PANAS has high internal consistency [72], with a Cronbach's alpha for PA ranging from 0.87 to 0.89, and for NA from 0.89 to 0.91.

2.4.4. State anxiety

The Spanish version [77] of the State-Trait Anxiety Inventory (STAI) [76], with a Cronbach's alpha ranging from 0.90 to 0.93 [77], consists of two scales containing 20 items each, rated on 4-point scales (1–*Not at all* to 4–*Very*), to measure individual differences related to the trait and state anxiety constructs. For this study, we only used the state scale values.

2.5. Statistical analyses

One-way ANOVAs were performed to investigate condition and sex differences on demographic, anthropometric and psychological tests (neuroticism and depression), with condition (stress vs. non-stress) and sex (men vs. women) as between-subject factors.

Given that salivary cortisol and sAA did not show normal distributions, they were square root transformed. To investigate the stress response, we performed ANCOVAs and ANOVAs for repeated measures with condition as between-subject factor and time (for PA, NA and state anxiety: pre-task and post-task; for HR: habituation, stress/non-stress task -average of the speech and arithmetic- and recovery; for sAA: -15, +5 and +15; and for cortisol: -15, +5, +15, +25, +35, +45 and +55 min) as a within-subject factor. Sex was introduced as a covariate for cortisol analyses to control for its effect on the physiological stress response. Moreover, baseline levels for HR ($p = 0.037$) and cortisol ($p = 0.053$) were different in the stress and non-stress conditions; thus, they were added as covariates. Based on Ali and Pruessner [2], we calculated the COAg ($AUC_{gCORTISOL}/AUC_{gSAA}$) and AOCg ($AUC_{gSAA}/AUC_{gCORTISOL}$) ratios to obtain two possible markers of physiological stress dysregulation. Regarding HR response, $HR_{reactivity}$ (average for the speech and arithmetic stress or non-stress task minus habituation period) and $HR_{recovery}$ (recovery period minus habituation period) indexes were calculated. For psychological response, we calculated the change for PA, NA and state anxiety (ΔPA , ΔNA , $\Delta Anxiety$: post-task minus pre-task).

Correlation analyses were performed between neuroticism and depression, with psychological (PA, NA and anxiety change) and physiological response to stress (COAg, AOCg and HR reactivity and recovery indexes) split by condition. To test the relationships between neuroticism and depression and autonomic and endocrine responses to stress or non-stress, we performed a moderation regression analysis. Neuroticism and depression were set as predictors of COAg, AOCg and HR reactivity and recovery indexes. Moreover, we analyzed the relationship between neuroticism and depression and COAg, AOCg, and HR reactivity and recovery indexes, but taking into account the condition as a moderator variable (neuroticism \times condition and depression \times condition interactions). We established sex, age, BMI and SES as covariates due to their effect on cardiovascular [52,57], cortisol and sAA responses [4,15,85]. Except for sex (men = 0, women = 1) and condition (stress = 0, non-stress = 1), all variables were z-transformed prior to their entry in the analysis to facilitate the interpretation of first-order terms.

One woman in the non-stress condition was excluded because her cortisol concentrations differed more than 3 S.D. from the sample mean.

We used the Greenhouse–Geisser procedure when the requirement of sphericity in the repeated-measures ANOVAs was violated. Post hoc planned comparisons were performed using the Bonferroni adjustments for the p -values < 0.05 . All p -values reported are two-tailed, and the level of significance was marked at $p < 0.05$. When not otherwise specified, results shown are means \pm standard error of means (SEM). We used SPSS 19.0 to perform the statistical analyses.

3. Results

3.1. Preliminary analyses

The mean age of the sample was 64.20 years (from 56 to 76 years old), and 52.9% of the participants had an educational level beyond high school. Participants showed a medium subjective socioeconomic status (SES) ($M = 5.51$, $SEM = 0.130$) and normal body mass index (BMI) ($M = 26.901$, $SEM = 0.396$). There were no significant differences between conditions and sex on age, SES or educational level (all $p > 0.359$). BMI did not differ between conditions ($F_{(1,69)} = 0.466$, $p = 0.497$), but men showed a higher BMI than women ($F_{(1,69)} =$

4.376 , $p = 0.040$). Finally, there were no condition or sex differences for depression and neuroticism (all $p > 0.090$) (Table 1).

3.2. Physiological response

3.2.1. HR

Significant effects of condition ($F_{(1,66)} = 35.178$, $p < 0.001$) and the interaction between time and condition ($F_{(1,66)} = 21.199$, $p < 0.001$) were found. Post hoc analyses showed higher HR in the stress condition during the exposure to stress and after it than in the non-stress condition (all $p < 0.001$) (see Fig. 1).

3.2.2. Cortisol

The repeated-measures ANCOVA showed a main effect of condition ($F_{(1,66)} = 33.337$, $p < 0.001$), and the interaction between condition and time ($F_{(2,265, 149.510)} = 20.195$, $p < 0.001$). The time factor approached significance ($F_{(2,265, 149.510)} = 2.790$, $p = 0.058$). Post hoc analyses showed higher cortisol concentrations in the stress condition than in the non-stress condition in all post-task samples (+5, +15, +25, +35, +45 and +55) (all $p < 0.016$) (Fig. 1).

3.2.3. sAA

The ANOVA for repeated-measures showed a main effect of time ($F_{(1,742, 282.101)} = 23.755$, $p < 0.001$) and the interaction between time and condition ($F_{(1,742, 282.101)} = 3.377$, $p = 0.044$). The condition effect was not significant ($F_{(1,69)} = 0.049$, $p = 0.825$) (Fig. 1). Post hoc analyses showed that both the stress and non-stress conditions increased sAA from -15 to +5 (both $p < 0.001$); however, the stress condition maintained its sAA values high at +15 (-15 to +15: $p = 0.004$), while the non-stress condition rapidly recovered its baseline values (-15 to +15: $p > 0.99$).

3.3. Psychological response

3.3.1. State anxiety

The repeated measures ANCOVA showed a main effect of condition ($F_{(1,68)} = 4.957$, $p = 0.029$) and the interaction between time and condition ($F_{(1,68)} = 19.034$, $p < 0.001$), but time was not significant ($F_{(1,68)} = 0.001$, $p = 0.970$). Post hoc analyses showed a significant increase in state anxiety only in the stress condition ($p < 0.001$), but not in the non-stress condition ($p = 0.608$). Higher state anxiety was found after the task in the stress group compared to the non-stress group ($p = 0.001$), but there were no significant differences before the task ($p = 0.999$).

3.3.2. Positive and negative affect

The repeated measures ANCOVA did not show effects of time, condition or the interaction between time and condition (all $p > 0.104$) on positive affect. Regarding negative affect, ANCOVA showed a significant effect of the time-condition interaction ($F_{(1,68)} = 21.344$, $p < 0.001$). Condition approached significance ($F_{(1,68)} = 3.750$, $p = 0.057$), but time was not significant ($F_{(1,68)} = 0.068$, $p = 0.795$). Post hoc analyses showed a significant increase in negative affect only in the stress condition ($p < 0.001$), but not in the non-stress condition ($p = 0.189$). There was higher state anxiety after stress in the stress group compared to the non-stress group ($p = 0.002$), but there were no significant differences before stress ($p = 0.952$).

3.4. Correlation analyses

3.4.1. Neuroticism

Correlation analyses showed that neuroticism was marginally related to lower AOCg ($r = -0.329$, $p = 0.054$). No other significant relationships were found related to neuroticism in the stress or non-stress conditions (see Table 2).

Table 1
Mean values (SEM) of age, socioeconomic status (SES, [1]), body mass index (BMI), depression (BDI) and neuroticism for the men and women exposed to stress, non-stress and the total sample.

	Total (n = 71)			Stress (n = 36)			Non-stress (n = 35)		
	Total	Men	Women	Total	Men	Women	Total	Men	Women
Age	64.20 (0.495)	64.12 (0.784)	64.27 (0.633)	64.66 (0.697)	64.94 (1.043)	64.42 (0.959)	63.74 (0.705)	63.35 (1.163)	64.11 (0.844)
SES	5.51 (0.130)	5.61 (0.208)	5.42 (0.161)	5.46 (0.180)	5.69 (0.299)	5.26 (0.214)	5.56 (0.190)	5.53 (0.298)	5.59 (0.243)
BMI	26.901 (0.396)	27.770 (0.465)	26.146 (0.599)	27.16 (0.604)	27.53 (0.771)	26.88 (0.909)	26.62 (0.514)	27.99 (0.557)	25.332 (0.742)
BDI	4.96 (0.504)	4.06 (0.684)	5.74 (0.714)	4.53 (0.686)	4.06 (1.160)	4.90 (0.833)	5.40 (0.742)	4.06 (0.793)	6.67 (1.177)
Neuroticism	4.01 (0.204)	4.18 (0.284)	3.86 (0.293)	3.91 (0.297)	3.75 (0.382)	4.05 (0.449)	4.11 (0.283)	4.59 (0.403)	3.67 (0.379)

3.4.2. Depression

Correlation analyses showed that depression was related to COAg ($r = 0.354$, $p = 0.034$) in the stress condition and to HR_{Recovery} ($r = 0.405$, $p = 0.018$) in the non-stress condition. No other significant relationships were found related to depression in the stress or non-stress condition (see Table 2).

3.5. Moderation analyses

3.5.1. Neuroticism

There were no significant direct relationships or relationships moderated by condition between neuroticism and HR_{Reactivity}, HR_{Recovery}, AOCg or COAg, (all $p > 0.198$).

3.5.2. Depression

Regardless of the condition, higher scores on depression were directly related to higher COAg ($p = 0.017$), but not to AOCg ($p = 0.237$). The interaction between depression and condition was significant for COAg ($p = 0.010$), but not for AOCg ($p = 0.884$) (see Table 3). Post hoc analyses showed that higher scores on depression were positively related to higher COAg only in the stress condition ($p = 0.017$) (see Fig. 2), but not in the non-stress condition ($p = 0.333$), which is an indicator of physiological stress dysregulation, showing a predominance of cortisol response over sympathetic response (see Table 3). Regarding HR, depression was negatively related to HR_{Reactivity}, regardless of condition ($p = 0.029$), and marginally positively related to HR_{Recovery} ($p = 0.064$). Post hoc analyses showed that depression was negatively related to HR_{Reactivity} in the stress condition ($p = 0.029$) (see Fig. 2), but not in the non-stress condition ($p = 0.203$) (see Table 4). No significant relationships were found in the post hoc analyses for HR_{Recovery} (all $p > 0.127$).

4. Discussion

The main purpose of the present study was to analyze the effects of neuroticism and depression on the psychophysiological response of healthy older people exposed to stress or non-stress. As we expected,

higher response of HR, sAA and cortisol was found in those participants exposed to stress, compared to those exposed to a non-stress condition. We also observed that neuroticism was not related to the psychophysiological stress response. A positive relationship was found between depression and COAg in the stress condition, which is an indicator of physiological stress dysregulation. However, no associations were found between depression and cortisol and sAA response in the non-stress condition. Finally, depression was related to a blunted HR response.

Agreeing with previous research, we observed higher HR, sAA and cortisol release in the stress condition than in the non-stress condition [4,21,47,61]. Additionally, as previous studies showed, we observed an increase in NA and anxiety after stress exposure [28,91,96].

Our results showed that neuroticism was not related to the stress response or recovery after TSST. These results coincide with previous studies in young people that found no effect of neuroticism on autonomic function [37,38,42,43] or on the cortisol response to stress [44, 45,73,88,95]. In contrast to this, some studies have found that neuroticism was related to higher cardiovascular and cortisol reactivity in young people [39,41,74], and to a worse return to baseline after exposure to stress in middle-aged people [8]. We have to take into account that, in the present research, we studied healthy older people with scores around the mean. This restricted range may limit the effect of this trait in stressful situations because neuroticism's effect on ANS lability has been observed in stressful events, especially in the case of extreme neuroticism scores [27].

Regarding depression, our results showed a positive relationship between depression scores and higher COAg in the high stress condition, which is an indicator of a dysregulation of the HPA and ANS response. These results agree with previous studies that showed heightened total cortisol release in response to stress in depressed people [17,34, 35], while others have related depression to a blunted cortisol response [11,56,86], or did not find a relationship [97]. Our results did not reveal any significant relationship with AOCg, i.e. predominance of sAA release over cortisol variations. Ali and Pruessner [2] showed higher levels of AOCg in people with higher depression scores in a mixed sample (healthy and with early life adversities), and they highlighted AOCg as

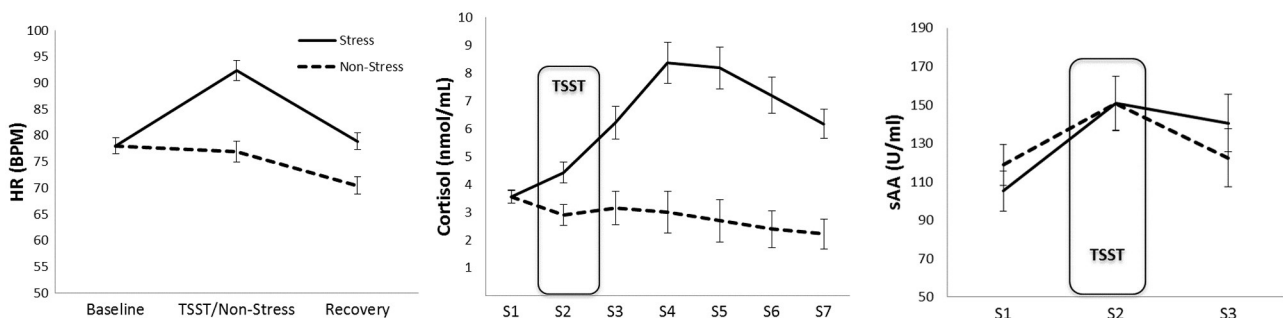


Fig. 1. Mean values and \pm SEM of the physiological response to the stress and non-stress tasks in HR, cortisol and alpha-amylase.

Table 2

Correlation analyses between neuroticism and depression and psychophysiological response to stress and non-stress exposure (psychological: change of PA, NA, state anxiety; physiological: HR reactivity and recovery indexes, and AOCg and COAg).

	Neuroticism		Depression	
	Stress	Non-stress	Stress	Non-stress
ΔPA	$r = -0.064, p = 0.714$	$r = 0.299, p = 0.081$	$r = 0.418, p = 0.139$	$r = 0.085, p = 0.629$
ΔNA	$r = 0.121, p = 0.490$	$r = -0.014, p = 0.938$	$r = 0.343, p = 0.163$	$r = 0.213, p = 0.216$
ΔAnxiety	$r = -0.035, p = 0.841$	$r = -0.136, p = 0.435$	$r = -0.006, p = 0.974$	$r = 0.229, p = 0.187$
HR _{Reactivity}	$r = 0.048, p = 0.784$	$r = 0.161, p = 0.363$	$r = -0.275, p = 0.105$	$r = 0.282, p = 0.106$
HR _{Recovery}	$r = 0.125, p = 0.474$	$r = -0.039, p = 0.827$	$r = -0.003, p = 0.985$	$r = 0.405, p = \mathbf{0.018}$
AOCg	$r = 0.063, p = 0.718$	$r = -0.329, p = \mathbf{0.054}$	$r = -0.189, p = 0.271$	$r = -0.165, p = 0.344$
COAg	$r = 0.096, p = 0.583$	$r = 0.280, p = 0.104$	$r = 0.354, p = \mathbf{0.034}$	$r = -0.189, p = 0.276$

ΔPA = post-task PA minus pre-task PA; ΔNA = post-task NA minus pre-task NA; ΔAnxiety = post-task state anxiety minus pre-task state anxiety.
 $p < .05$ are marked in bold.

the best indicator of stress system dysregulations in a population with early life adversities. However, given the closer relationship between depression and the HPA axis (for review see [93]) than between depression and sAA, we consider that COAg could be a better indicator, at least for healthy older people. A decrease in the HPA regulation capability appears, even before the symptomatic phase of depression, which suggests that HPA dysregulation precedes depression [102]. In fact, an increased cortisol release in response to high stress and low stress predicts an increase in depressive symptomatology [56]. Thus, our results extend the knowledge about the effects of depressive symptomatology on the physiological stress response in the healthy older population.

Interestingly, our results showed that depression was related to a blunted cardiovascular response to stress, which partially confirms our results obtained through COAg, showing a predominance of the HPA response over ANS. As in our findings, previous studies showed a decreased cardiovascular response in young [98], adult or middle-aged [69,71], and older people with depression [99], as well as in large age samples [12,13]. These results agree with [99], who argued that a blunted cardiovascular response in older depressed people would be

due to a decrease in the sensitivity and density of adrenergic receptors. Along these lines, Ehrental et al. [23] showed altered cardiovascular adaptability to stress in depressed people. By contrast, Matthews et al. [55] showed no relationship between depression and parasympathetic shifts in a healthy population, and other studies have shown a greater parasympathetic decrease in people with more depressive symptoms

Table 3

Moderation analyses where depression scores predict COAg and AOCg moderating by condition with 95% confidence intervals ($n = 70$).

	β	SE	t	p	CI
Model:					
AdjR ² = 0.273, ΔR ² = 0.087, F(1,60) = 7.176, p = 0.010					
Constant	0.351	0.200	1.756	0.084	[-0.049, 0.752]
Sex	-0.598	0.234	-2.552	0.013	[-1.066, -0.129]
Age (Z)	-0.172	0.117	-1.467	0.148	[-0.406, 0.062]
SES (Z)	0.018	0.118	0.155	0.877	[-0.218, 0.255]
BMI (Z)	0.148	0.121	1.224	0.226	[-0.094, 0.390]
BDI (Z _x)	0.423	0.172	2.456	0.017	[0.078, 0.768]
Condition (M)	-0.079	0.221	-0.356	0.723	[-0.521, 0.364]
BDI × condition (Z _x M)	-0.664	0.248	-2.679	0.010	[-1.159, -0.168]
Effect BDI on COAg					
Stress condition	0.423	0.172	2.456	0.017	[0.078, 0.768]
Non-stress condition	-0.241	0.174	-1.384	0.172	[-0.589, 0.107]
Model:					
AdjR ² = 0.185, ΔR ² < 0.001, F(1,60) = 0.021, p = 0.884					
Constant	-0.307	0.212	-1.447	0.153	[-0.731, 0.117]
Sex	0.565	0.248	2.276	0.026	[0.068, 1.061]
Age (Z)	0.124	0.124	1.002	0.321	[-0.124, 0.372]
SES (Z)	-0.102	0.125	-0.813	0.420	[-0.353, 0.149]
BMI (Z)	-0.172	0.128	-1.341	0.185	[-0.428, 0.084]
BDI (Z _x)	-0.218	0.183	-1.196	0.237	[-0.584, 0.147]
Condition (M)	0.026	0.234	0.112	0.911	[-0.442, 0.495]
Neuroticism × Condition (Z _x M)	0.038	0.263	0.146	0.884	[-0.487, 0.564]
Effect BDI on AOCg					
Stress condition	-0.218	0.183	-1.198	0.237	[-0.549, 0.189]
Non-stress condition	-0.180	0.184	-0.976	0.333	[-0.549, 0.189]

$p < .05$ are marked in bold.

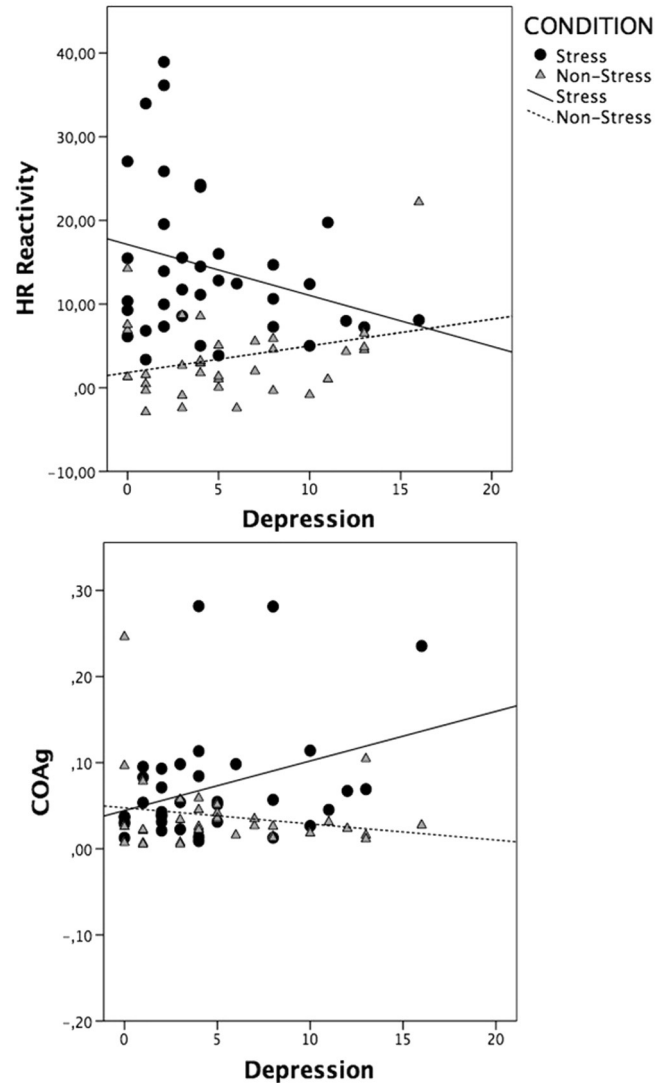


Fig. 2. Scatter plots of direct relationship with depression as predictor of HR reactivity and COAg, all of them without covariates.

Table 4
Moderation analyses where depression scores predict HR_{Reactivity} and HR_{Recovery} moderating by condition with 95% confidence intervals ($n = 70$).

	β	SE	t	p	CI
Model:					
AdjR ² = 0.439, $\Delta R^2 = 0.058$, $F(1,60) = 6.160$, $p = 0.016$					
Constant	0.672	0.177	3.797	< 0.001	[0.318, 1.027]
Sex	-0.242	0.210	-1.153	0.253	[-0.663, 0.178]
Age (Z)	0.019	0.103	0.183	0.856	[-0.187, 0.224]
SES (Z)	0.057	0.105	0.544	0.588	[-0.153, 0.268]
BMI (Z)	0.086	0.108	0.800	0.427	[-0.129, 0.301]
Depression (Z_x)	-0.337	0.151	-2.237	0.029	[-0.639, -0.036]
Condition (M)	-1.157	0.193	-5.985	< 0.001	[-1.544, -0.770]
Depression \times condition ($Z_x M$)	0.528	0.213	2.482	0.016	[0.103, 0.954]
Effect depression on					
HR _{Reactivity}					
Stress condition	-0.337	0.151	-2.237	0.029	[-0.639, -0.036]
Non-stress condition	0.191	0.149	1.286	0.203	[-0.106, 0.489]
Model:					
AdjR ² = 0.392, $\Delta R^2 = 0.036$, $F(1,60) = 3.573$, $p = 0.064$					
Constant	0.490	0.185	2.648	0.010	[0.120, 0.861]
Sex	-0.139	0.220	-0.631	0.530	[-0.578, 0.301]
Age (Z)	0.318	0.107	2.966	0.004	[0.104, 0.533]
SES (Z)	0.062	0.110	0.560	0.577	[-0.158, 0.282]
BMI (Z)	0.192	0.113	1.711	0.092	[-0.033, 0.418]
Depression (Z_x)	-0.180	0.158	-1.142	0.258	[-0.495, 0.135]
Condition (M)	-0.902	0.202	-4.460	< 0.001	[-1.306, -0.497]
Depression \times condition ($Z_x M$)	0.421	0.223	1.890	0.064	[-0.025, 0.866]
Effect depression on					
HR _{Recovery}					
Stress condition	-0.180	0.158	-1.142	0.258	[-0.495, 0.135]
Non-stress condition	0.241	0.155	1.549	0.127	[-0.070, 0.552]

$p < .05$ are marked in bold.

([53]) and a greater sympathetic response in healthy people with higher depressive symptomatology [33] or in depressed women with a previous history of childhood abuse [34]. However, we have to take into account that healthy older people are characterized by showing a flattened sympathetic response [13,49]. It is possible that the effects of age on cardiovascular function [49,57] would be exacerbated by depression symptoms [99].

Surprisingly, we did not find a significant effect of neuroticism or depression on state anxiety or negative or positive affect changes after the task in older people. There is a large body of evidence of the relationship between neuroticism and negative mood in young people ([30,51,70]; 1989). In this line, previous studies [10,69,71] showed that depression could facilitate a heightened negative perception of a stressor in young, adult and middle-aged people. In our results, neuroticism and depression were not associated with stress- and non-stress-related changes in negative mood. We think age is an important factor to take into account because it may affect this relationship. The socioemotional selectivity theory argues that the perception of positive and negative emotions and its regulation is age dependent [14]. In fact, older people experience less negative emotions and improve their emotional regulation with age [14]. Considering this explanation, and the fact that the population explored is non-clinical, we conclude that the improved emotional regulation in healthy older people may affect the relationships among neuroticism, depression, state anxiety and negative affect.

Finally, the present study has some limitations. First, the sample used is a healthy population; thus, we cannot extrapolate our conclusions to the clinical population, although the study of a sub-clinical population can help us to clarify the pathogenesis of affective disorders [11]. Moreover, a confounding effect of some unmeasured variable can never be completely ruled out [20]. Nevertheless, we tried to statistically account for an extensive range of potential confounders and carry out a conservative sample selection. Consequently, the number of participants was low, which limits the generalization of the results of our study, but the strict control of confounding factors provides a

homogeneous healthy sample that allows us to observe the relationships among the variables more clearly. Moreover, our focus on older people extends previous knowledge explored only in young populations or poorly in older people. Finally, the study of behavioral responses and their relationship with neuroticism and the psychobiological response could be of interest in future studies on this topic, given the relevance of behavior in understanding coping strategies to deal with stressors [63,75,89].

In sum, in the present study we contributed to increasing the knowledge about the relationship between neuroticism, depression and the physiological stress response in older people, identifying a possible indicator of HPA and ANS response dysregulation in this population.

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