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Stressed-out stress systems: dysregulated stress-systems in the pathophysiology of stress-related disorders

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Chapter 6

Cortical thickness in Dutch police officers: an examination of factors associated with resilience

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Abstract

Previous neuroimaging studies on resilience have generally compared resilience and psychopathology after stress exposure, which does not allow for conclusions regarding correlates specific to resilience. The aim of the present study was to investigate resilience-specific correlates in cortical thickness and/or cortical surface area and their correlations with psychometric measurements, using a three-group design that included a non–trauma-exposed control group in order to disentangle effects related to resilience from those related to psychopathology. Structural magnetic resonance imaging scans were acquired from 82 Dutch police officers. Participants were categorized into resilient (n = 31; trauma exposure, no psychopathology), vulnerable (n = 32; trauma exposure, psychopathology), and control groups (n = 19; no trauma exposure, no psychopathology). Specific regions of interest (ROIs) were identified based on previous studies that found the rostral and caudal anterior cingulate cortex (ACC) to be implicated in trauma-related psychopathology. Cortical thickness and surface area of the ROIs—the rostral and caudal ACC—and of the whole brain were examined. No significant differences in cortical thickness or surface area were found between the resilient group and other groups in the ROI and whole-brain analyses. Thus, the results of the present study provide no evidence of an association between resilience to traumatic stress and measures of thickness and surface area in cortical regions of the brain in a sample of Dutch police officers.

Introduction

Due to the nature of their work, police officers and other first responders, such as firefighters, are more likely to experience traumatic events when compared to other occupational groups (Maguen et al., 2009). Although exposure to traumatic events can predispose an individual to developing psychopathology, there is no evidence that police officers suffer from more stress- related psychopathology compared to occupations that are not considered high risk; thus, one may hypothesize that police officers show resilience (Skogstad et al., 2013; van der Velden et al., 2013).
Resilience to traumatic stress can be defined as a dynamic process that enables an individual to positively adapt to and recover from a traumatic stressful event (Katz et al., 2009; Wu et al., 2013). The neural circuitry of resilience is postulated to overlap with the brain circuitry involved in emotion and stress regulation, including the limbic network (i.e., the amygdala and the hippocampus; van der Werff, van den Berg, Pannekoek, Elzinga, & van der Wee, 2013). It is thought that resilient individuals, through structural and/or functional alternations in parts of the limbic network, are more capable of upregulating their emotions and having top-down control over emotional attention, reflecting increased emotion regulation capacities (see for review, van der Werff et al., 2013). In addition, trait resilience (i.e., low neuroticism, high extraversion, and high conscientiousness) is known to be linked to the neurocircuitry involved in emotion and stress regulation (Daniels et al., 2012). Furthermore, when comparing individuals with low and high trait resilience, those with high trait resilience have been found to show higher levels of recovery and more rapid recovery of insula activity when anticipating and recovering from stress, thereby linking high trait resilience to a brain pattern that reflects efficient arousal modulation and emotional reappraisal (Waugh, Wager, Fredrickson, Noll, & Taylor, 2008). However, aside from the many studies on the neurobiology of stress-related disorders, such as posttraumatic stress disorder (PTSD), major depressive disorder (MDD), and anxiety disorders, relatively few studies have examined the neurobiology of resilience to traumatic stress. Clearly, a better understanding of the neurobiology of resilience to traumatic stress is of importance to foster improvement of treatment and prevention (Yamasue et al., 2003).

Various neuroimaging studies have identified structural abnormalities in patients with stress-related disorders. In individuals with PTSD, smaller volumes of gray matter have been found for the anterior cingulate cortex (ACC) and medial prefrontal cortex (mPFC; Kasai et al., 2008; Rauch, Shin, & Phelps, 2006; Villarreal et al., 2002; Woodward et al., 2006; Yamasue et al., 2003; J. Zhang et al., 2011). These

brain structures are part of emotion and pain processing networks (Etkin, Egner, & Kalisch, 2011; Phelps, 2004). In addition, smaller gray matter volumes for these brain structures also have been observed in MDD patients (Zhao et al., 2017).

In the context of resilience, however, findings regarding gray matter volume are inconsistent. For example, relative to PTSD patients, smaller volumes of the frontal and occipital regions have been found in resilient individuals (Fennema-Notestine, Stein, Kennedy, Archibald, & Jernigan, 2002). In contrast, a previous study on resilience to traumatic stress, which employed a three-group design that included a non–trauma-exposed control group, did not find any resilience-specific gray matter volume patterns based on the use of a whole-brain voxel-based morphometry (VBM) approach with analysis of the volume and shape of the hippocampus (van der Werff, Elzinga, Smit, & van der Wee, 2017).

Gray matter volume is determined by two independent genetic measures of cortical structures, cortical thickness and cortical surface area, which have distinct developmental trajectories (Wierenga, Langon, Oranje, & Durston, 2014; Winkler et al., 2010). Cortical thickness is thought to reflect dendritic arborization and pruning, whereas surface area may reflect folding and gyrification (Huttenlocher 1990; Rakic 2009). Therefore, changes in cortical thickness or surface area are related to different underlying biological processes (Ecker, Bookheimer, & Murphy, 2015). Thus, it is possible that, although there may not be specific patterns of gray matter volume related to resilience, one or both of the components of gray matter—cortical thickness and cortical surface area—could be implicated in resilience to traumatic stress. For example, a recent study of a sample of healthy individuals showed that a lower level of resilience was associated with a lower cortical thickness in the lateral occipital cortex, the fusiform gyrus, the inferior parietal cortex as well as the middle and inferior temporal cortex (Kahl, Wagner, de la Cruz, Kö hler, & Schultz, 2018). The results of several studies have suggested that cortical volume is influenced more by cortical surface area than by cortical thickness (Im et al., 2008; Winkler et al., 2010; Zhao et al., 2017). Notably, in the context of resilience, only a few studies, all of which have employed a two-group design, have reported on cortical measures, and the findings have focused predominantly on cortical thickness rather than cortical surface area and volume (Dickie, Brunet, Akerib, & Armony, 2013; Milad et al., 2005; K. Zhang et al., 2016).

To date, current models and hypotheses regarding resilience have been based mostly on studies of stress-related psychopathology that show an inconsistent pattern

(Hu et al., 2018; Katz et al., 2009; Rutter, 2012; Schmaal et al., 2017). For example, a large study investigating MDD in adults found no differences in cortical surface area between individuals with MDD and controls (Schmaal et al., 2017), whereas a previous study of individuals with a high risk for developing PTSD suggested that reduced left rostral ACC surface area might serve as a potential biomarker for PTSD risk (Hu et al., 2018).

In contrast to the inconsistent pattern for cortical surface area, cortical thickness, and in particular lower cortical thickness, has been more systematically reported in studies of stress-related psychopathology. For example, in a sample of patients with MDD, cortical thinning was found in the temporal and frontal regions (Schmaal et al., 2017). Similarly, in a sample of patients with PTSD, cortical thinning was found mainly in the frontal and temporal gyri (Geuze et al., 2008; Sussman, Pang, Jetly, Dunkley, & Taylor, 2016). Interestingly, higher cortical thickness is thought to be a potential marker of more positive treatment outcomes. For example, a thicker cingulate gyrus has been found to be a marker for potential PTSD recovery, and a thicker right caudal ACC has been associated with better symptom improvement in patients with MDD (Dickie et al., 2013; K. Zhang et al., 2016). In addition, higher cortical thickness of the ventral mPFC has been associated with extinction retention (Milad et al., 2005). Together, these results suggest that cortical thickness of the frontal regions, particularly the ACC and mPFC, may be associated with resilience to traumatic stress.

Thus far, most studies that have investigated resilience to traumatic stress have used a two-group design in which both groups consist of individuals who have been exposed to trauma—one group with psychopathology (i.e., patients) and one group with-out (i.e., trauma controls). Although such studies have been successful in detecting differences between these two groups, this design makes it impossible to distinguish whether the observed effects are related to psychopathology in the patient group or to resilience-specific factors in the trauma-exposed control group. In order to disentangle the differences between resilience and vulnerability to traumatic stress, the inclusion of a third group of individuals who have not been exposed to trauma and who are without psychopathology is needed to allow conclusions regarding resilience-specific correlates (van der Werff et al., 2013).

The aim of the present study, therefore, was to identify resilience-specific characteristics of cortical thickness and cortical surface area in resilient Dutch police officers, using a three- group design consisting of resilient (RES; trauma-exposed,

no psychopathology), vulnerable (VUL; trauma-exposed with psychopathology), and control (CON; non–trauma exposed, no psychopathology) groups. The existing literature has shown that the ACC, an important hub in emotion-regulating circuitry, is associated with psychopathology (Kasai et al., 2008; Rauch et al., 2006; Villarreal et al., 2002; Woodward et al., 2006; Yamasue et al., 2003; J. Zhang et al., 2011). In addition, an animal study that studied resilience in the context of early life stress exposure, an inoculation effect was associated with an increase in ventromedial prefrontal cortical volumes (Katz et al., 2009). Hence, we hypothesized that an increase in ACC volume would be specific to resilience. We also hypothesized that there would be a greater cortical thickness and larger cortical surface area of the ACC in the RES group relative to the other two groups. In addition, we hypothesized that the resilience-specific differences in cortical thickness and cortical surface would correlate with specific coping strategies. Furthermore, to detect possible changes in cortical thickness and cortical surface area outside of our a priori defined region of interest, we also performed an exploratory whole-brain analysis.

Methods

Participants and Procedure

Trauma-exposed executive Dutch police officers and non–trauma-exposed recruits from the police academy were recruited (van der Werff et al., 2017). A total of 149 participants were recruited using advertisements on the internal communication platform of the Dutch police. Eligible participants met the following inclusion criteria: age above 18 years, completed or attending the Dutch Police academy program, right-handed, and sufficient command of the Dutch language. Individuals were excluded upon the following exclusion criteria: (a) magnetic resonance imaging (MRI) contradictions, such as metal implants, heart arrhythmia, claustrophobia, or pregnancy; (b) history of neurological illness; (c) history of psychopathology with onset before work-related traumatic events; (d) use of psychotropic medications other than stable use of selective serotonin reuptake inhibitors or infrequent benzodiazepine use; (e) maltreated during childhood (i.e., before 18 years of age); and (f) smoking an average more than five cigarettes per day. There were 67 potential participants who did not meet the inclusion criteria and were excluded from the study. Of the remaining 82 participants, three groups could be distinguished: RES (n = 31), VUL (n = 32), CON (n = 19). The RES group consisted of police officers who experienced multiple work-related traumatic events but did not develop stress-related disorders (past or present). The VUL group consisted of police officers who had experienced multiple work-related traumatic events and

subsequently developed a stress-related psychopathology. The CON group were undergraduates at the police academy and were still in training; these participants had little to no experience in the field and were therefore naive with regard to work-related traumatic experiences. All participants provided written, informed consent and all procedures were approved by the relevant medical ethical committee (van der Werff et al., 2017). The study was designed and conducted in accordance with principles of the declaration of Helsinki.

Measures

Axis I psychiatric disorders. The Mini-International Neuropsychiatric Interview (M.I.N.I.; Sheehan et al., 1997) is an interview used to assess the presence of the most common Axis 1 psychiatric disorders according to criteria in the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)* and 10th revision of the *International Classification of Diseases (ICD-10*; van Vliet & de Beurs, 2007). The M.I.N.I. has demonstrated good validity and reliability.

Depression. The Montgomery-Asberg Depression Rating Scale (MADRS) is a 10-item diagnostic questionnaire used to measure the severity of depressive episodes in patients with mood disorders (Fantino & Moore, 2009; Montgomery & As- berg, 1979). The symptoms are rated on a scale of 0 (*not at all*) to 6 (*definitely*). The total score classifies the patients by level depressive symptom severity, with 0–6 representing normal or absent symptoms, and 7–19 for mild, 20–34 for moderate, and 35–60 for severe symptoms. The Dutch version of this inven- tory has demonstrated good internal consistency. In the current sample, Cronbach's alpha was .88.

The Inventory of Depression Symptomatology (IDS) is a 28- item, self-report questionnaire that measures the presence and severity of depression symptoms. The symptoms are rated on a scale of 0 (*absence of pathology*) to 3 (*severe pathology*). The total score is obtained by summing the ratings of the items and ranges from 0 to 84. Cronbach's alpha values ranging from .76 to .94 have been reported ranged from .76 to .94 (Rush, Gullion, Basco, Jarrett, & Trivedi, 1996). In the current sample, Cronbach's alpha was .87.

Anxiety. The Beck Anxiety Inventory (BAI; Beck, Epstein, Brown, & Steer, 1988) was administered to assess the severity of anxiety symptoms. The BAI consists of 21 questions regarding anxiety symptoms during the past week, scores ranging from 0 (*not at all*) to 3 (*severely*). The total score ranges from 0 to 63, with a score of

0–7 classified as minimal anxiety, 8–15 as mild anxiety, 16–25 as moderate anxiety, and 30–63 as severe anxiety. The Cronbach's alpha value for the Dutch version of this inventory was found to be .82 (Bosccher, Koning, & Van, 1986). In the current sample, Cronbach's alpha was .85.

Work-related life events. The degree of exposure to work-related life events was evaluated using the Police Life Events Schedule (PLES; Carlier, Lamberts, & Gersons, 1997). The PLES is a 42-item measure of the type and number of traumatic incidents experienced by police officers and the degree to which officers felt threatened, anxious, and helpless at each of the incidents. Respondents score items on a scale of 0 (*none*) to 5 (*extreme*). The incidents are categorized as being sad/depressing or violent. The PLES has demonstrated a Cronbach's alpha value of .87 (Carlier & Gersons, 1992). In the current sample, Cronbach's alpha was .94.

Posttraumatic symptoms. The Harvard Trauma Questionnaire (HTQ) was used to evaluate the variety of trauma and the severity of the corresponding emotions. This questionnaire consists of 30 items that respondents score on a scale of 1 (*not at all*) to 4 (*extremely*). The Cronbach's alpha value has been reported as .95 in previous studies (Mollica et al., 1992). In the current sample, Cronbach's alpha was .95.

Resilience. The Connor–Davidson Resilience Scale (CD- RISC) comprises 25 items, each rated on a 5-point scale of 0 (*not at all true*) to 4 (*true nearly all of the time*), with higher scores reflecting a higher level of resilience. The scale features items related to developing strategy with a clear goal or aim, action orientation, strong self- esteem/confidence, adaptability when coping with change, social problem-solving skills, humor in the face of stress, strengthening effect of stress, taking on responsibilities for dealing with stress, secure/stable affectional bonds, and previous experiences of success and achievement, among others (Connor & Davidson, 2003). The full scale has demonstrated a Cronbach's alpha value for internal consistency of .89 (Connor & Davidson, 2003). In the current sample, Cronbach's alpha was .93.

Coping strategies. The Cognitive Emotion Regulation Questionnaire (CERQ; Garnefski, Kraaij, & Spinhoven, 2001) was used to measure different cognitive coping strategies implemented by the participants. Cognitive emotion regulation strategies were measured on a scale of 1 (*almost never*) to 5 (*al- most always*). The CERQ distinguishes between nine different cognitive emotion regulation strategies: self-blame, blaming others, acceptance, refocus on planning, positive refocusing, rumination, positive reappraisal, putting into perspective, and catastrophizing.

Individual subscale scores were obtained by summing the scores of the particular subscale, with subscale scores ranging from 4 to 20. In the current sample, the Cronbach's alpha values for the subscales ranged from .74 to .84.
Brain analysis. Structural MRIs were acquired using a Philips 3T MRI system (Philips Healthcare; Best, The Netherlands; Version 3.2.1) equipped with a SENSE32 channel head coil. Anatomical images were obtained using sagittal 3D gradient-echo T1-weighted sequence (repetition time = 9.8 ms, echo time = 4.6 ms, matrix size 256 × 256, voxel size 1.17 × 1.17 × 1.2 mm, 140 slices, scan duration: 4:56 min). For each participant, high-resolution anatomical images were examined for macroscopic abnormalities; examinations were performed by a neuroradiologist who was blinded to the clinical details of each participant. However, no such abnormalities were detected.

Data Analysis
Cortical parcellations of 68 cortical gray matter regions (34 regions in each cerebral hemisphere) were performed using FreeSurfer (Version 5.3.0). In addition, two whole-hemisphere measures were extracted using FreeSurfer. ENIGMA's quality assurance protocol was performed before analyses. The segmentations of all 68 cortical gray matter regions and the two whole-hemisphere measures were followed by a statistical outlier assessment and visually inspected by three independent researchers for segmentation errors. A participant was considered a statistical outlier if their volume was measured to be greater than 2.698 standard deviations away from the global mean. For each participant who was marked as a statistical outlier, the segmentation was reinspected in order to verify that it was properly segmented. If a participant was a statistical outlier but was properly segmented, the data were kept in the analysis. Otherwise, the participant's data were removed. No segmentation errors occurred.

All statistical analyses were executed with IBM SPSS (Version 24; IBM Corp., 2016). Assumptions of normal distribution of data and homogeneity of variances were tested using the Kolmogorov–Smirnov test and Levene's test, respectively. Cortical regions that violated these assumptions were analyzed using the nonparametric Quade's test. Analyses of covariance (ANCOVAs) were performed to examine group differences in cortical thickness and cortical surface area in the regions of interests (ROIs; i.e., the rostral and caudal ACC). Sex and intracranial volume (ICV) were included in the model as covariates to adjust for between-group differences.

To examine resilience-specific differences (i.e., a between-group difference present

in the RES vs. VUL comparison as well as in the RES vs. CON comparison), ANCOVAs were first performed to compare the RES group with the VUL group. Only the regions that were significantly different in this first comparison were further investigated using ANCOVAs to compare the RES versus CON group. Given the absence of a significant difference between the RES and the VUL groups, no further analyses were performed between the RES and CON group, as any difference found would not be specific to resilience. Similarly, an exploratory whole-brain analysis (70 measures; 68 cortical regions and two whole-hemisphere measures) was performed using ANCOVA. All comparisons were followed by a false discovery rate (FDR) correction to adjust for multiple comparisons. The FDR was set at 5% for all measures.

Correlation analyses were planned within the RES group to evaluate whether emotional cognitive coping strategies (i.e., CERQ) and levels of resilience (i.e., CD-RISC) were associated with cortical thickness parameters in areas where a resilience-specific pattern was found. For parametric data, the correlation analyses were carried out using Pearson's *r*, whereas for non- parametric data, both Kendall's tau and Spearman's rho were reported. In addition, a Bonferroni correction was applied to the correlation analyses for correction of multiple comparisons. All *p* values reported are one-tailed.

Results

Demographic and psychometric data can be found in Table 1. No significant differences were found between the RES group and the VUL or CON group regarding ICV, BAI score, or CD-RISC score. There were no age differences between the RES and VUL groups, $p = .277$, whereas a significant age difference was found between the RES and CON groups, $p < .001$. This age difference was expected, given that the participants in the CON group were undergraduates in the police academy. Furthermore, a significant difference in sex ratio was found between the RES and CON groups, $p = .033$. The RES group differed significantly in IDS score from both the VUL, $p = .013$, and CON groups, $p = .017$, with lower and higher depression scores, respectively. The CON group reported significantly lower scores, $p = .006$, on the MADRS when compared to the RES group. The HTQ scores for the RES group were significantly lower than those in the VUL group, $p = .010$, but did not differ from the CON group, $p = .159$. Moreover, PLES scores for the RES group were significantly higher than those for the CON group, $p < .001$, but did not differ from the VUL group after exclusion of a VUL-group outlier who re- ported 3,388 work-related life events, $p = .709$; this confirmed that both the RES and VUL groups were exposed

to considerably more work-related traumatic events compared to the CON group. In the context of cognitive emotion regulation, the RES group scored lower on the Blaming Others, $p = .026$, and Catastrophizing subscales, $p = .003$, compared to the VUL group. Furthermore, the RES group scored lower on the Acceptance subscale in comparison to both the CON, $p = .018$, and VUL groups, $p = .011$.

Table 1. Demographics and Psychometric Data of the Resilient, Vulnerable, and Control Groups.

Variable	Resilient Group ($n = 31$)[a]		Vulnerable Group ($n = 32$)[a]		Control Group ($n = 19$)[a]		Resilient vs. Vulnerable	Resilient vs. Control
	M	*SD*	*M*	*SD*	*M*	*SD*	*p*	*p*
Sex (female vs. male)[a]							.524[b]	.033[b]
Age (years)	40.68	11.67	43.75	11.00	25.32	4.61	.277[c]	<.001[c]
Intercranial volume	1,665,573.23	159,671.28	1,654,354.69	182,705.28	1,656,935.26	124,794.49	.858[c]	.944[c]
Assessment score								
IDS	36.39	6.82	43.94	12.65	32.58	5.32	.013[c]	.017[c]
BAI	24.00	2.73	26.31	6.56	23.94	3.0	.183[c]	.841[c]
MADRS	1.61	2.32	5.19	7.64	0.26	0.73	.168[c]	.006[c]
CD-RISC	98.23	11.92	92.25	14.44	103.89	9.57	.079[d]	.086[d]
HTQ	34.84	5.05	43.91	14.93	33.68	5.52	.010[c]	.159[c]
PLES (outlier included)	166.61	144.65	330.31	621.26	27.53	53.60	.564[c]	<.001[c]
PLES (outlier omitted)	166.61	144.65	231.68	277.73	27.53	53.60	.709[c]	<.001[c]
CERQ: Self-Blame	7.55	2.68	8.59	3.32	7.95	2.32	.211[c]	.449[c]
CERQ: Blaming others	5.74	1.79	7.16	2.58	5.42	1.71	.026[c]	.575[c]
CERQ: Acceptance	10.42	2.84	12.44	3.14	12.68	3.30	.011[c]	.018[c]
CERQ: Refocus on Planning	13.58	3.62	13.94	3.15	14.26	2.75	.678[d]	.484[d]
CERQ: Positive Refocusing	11.45	4.22	11.41	3.39	11.74	3.66	.963[d]	.809[d]
CERQ: Rumination	10.06	3.82	12.06	6.82	8.79	3.39	.183[c]	.248[c]
CERQ: Positive Reappraisal	14.55	3.41	14.16	3.81	15.37	3.44	.934[c]	.387[c]
CERQ: Putting Into Perspective	11.71	4.02	11.31	3.42	13.05	3.54	.674[d]	.236[d]
CERQ: Catastrophizing	4.87	1.50	6.34	3.01	4.74	1.19	.003[c]	.811[c]

Note. IDS = inventory of depression symptomatology; BAI = Beck Anxiety Inventory; MADRS = Montgomery-Asberg Depression Rating Scale; CD-RISC = Connor–Davidson Resilience Scale; HTQ = Harvard Trauma Questionnaire; PLES = Police Life Events Schedule; CERQ = Cognitive Emotion Regulation Questionnaire.
[a]Resilient group: $n = 10$ women, $n = 21$ men; Vulnerable group: $n = 8$ women, $n = 24$ men; Control group: $n = 12$ women, $n = 7$ men. [b]Chi-square test. [c]Mann-Whitney *U* test. [d]ndependent-samples *t* test.

Table 2 displays the mean between-group differences for cortical thickness and surface area in the ROIs (i.e., rostral and caudal ACC). These values were not significant. Because we found no significant differences between the measures for participants in the RES and VUL groups regarding the ROI analysis, we did not perform ANCOVAs to calculate the difference between the RES and CON groups.

Table 2. Cortical Thickness and Surface Area of the Rostral and Caudal Anterior Cingulate Cortex (ACC) for the Resilient and Vulnerable Groups.

Brain Hemisphere and Region	Comparison	*M* Difference	95% CI	*p*
Cortical Thickness				
Right				
Caudal ACC	RES > VUL	0.01	[−0.10, 0.11]	.901[a]
Rostral ACC	RES > VUL	0.07	[−0.05, 0.18]	.250[a]
Left				
Caudal ACC	RES > VUL	0.01	[−0.10, 0.12]	.896[a]
Rostral ACC	RES > VUL	0.06	[−0.50, 0.17]	.276[a]
Surface Area				
Right				
Caudal ACC	RES > VUL	3.46	[−92.20, 99.11]	.943[a]
Rostral ACC	RES > VUL	21.08	[−40.57, 82.74]	.497[a]
Left				
Caudal ACC	RES < VUL	−42.62	[−112.17, 26.92]	.225[a]
Rostral ACC	RES < VUL	−19.93	[−86.03, 46.18]	.549[a]

Note. *p* values are uncorrected. ACC = anterior cingulate cortex; RES = resilient group; VUL = vulnerable group.
[a]Analysis of covariance (ANCOVA).

Table 3 shows further exploratory whole-brain analysis differences at the uncorrected level between the RES and VUL groups. Significantly higher cortical thickness was found at the uncorrected $p < .05$ level in the participants in the RES group relative to those in the VUL group in the left fusiform, ^{M}difference = 0.08, 95% CI [0.03, 0.14], $p = .004$, $d = 0.8$; right pars opercularis, ^{M}difference = 0.103, 95% CI [0.03, 0.18], $p = .010$, $d = 0.7$; right lateral orbitofrontal cortex, ^{M}difference = 0.016, 95% CI [0.02, 0.16], $p = .016$, $d = 0.5$; left superior frontal cortex, ^{M}difference = 0.08, 95% CI [0.004, 0.16], $p = .040$, $d = 0.5$; and right caudal middle frontal cortex, ^{M}difference = 0.072, 95% CI [0.001, 0.14], $p = .048$, $d = 0.5$. After adjusting for multiple testing, no significant differences in cortical thickness between the participants in the RES and VUL groups remained.

Table 3. Cortical Thickness and Surface Area in an Exploratory Whole-Breain Analysis.

	Resilient vs. Vulnerable					Resilient vs. Control
Brain Hemisphere and Region	Comparison	*M* Difference	95% CI	*p*	*d*	*p*
Cortical Thickness						
Right						
Pars opercularis	RES > VUL	0.103	[0.03, 0.18]	.010[a]	0.7	.052
Lateral OFC	RES > VUL	0.090	[0.02, 0.16]	.016[a]	0.5	.068
Caudal MFC	RES > VUL	0.072	[0.001, 0.14]	.048[a]	0.5	.606
Left						
Fusiform	RES > VUL	0.080	[0.03, 0.14]	.004[a]	0.8	.081
SFC	RES > VUL	0.080	[0.004, 0.16]	.040[a]	0.5	.417
Surface Area						
Right						
Pars opercularis	RES > VUL	149.86	[23.32, 276.39]	.021[a]	0.6	.315
Left						
Pars orbitalis	RES < VUL	−35.96	[−65.86, −6.07]	.019[a]	0.5	.323

Note. *p* values are uncorrected. OFC = orbitofrontal cortex; MFC = middle frontal cortex; SFC = superior frontal cortex.
[a]Analysis of covariance (ANCOVA).

Furthermore, uncorrected significant differences between participants in the RES and VUL groups were found for the surface area of the left pars orbitalis, ^{M}difference = −35.96, 95% CI [−65.86, −6.07], p = .019, d = 0.6; and right pars triangularis, ^{M}difference = 149.86, 95% CI [23.32, 276.39], p = .021, d = 0.5. However, after adjusting for multiple testing, no significant differences in cortical thickness and surface area remained between these groups. In addition, analyses examining these regions in participants in the RES and CON groups also did not show any differences. In sum, no resilience-specific differences remained significant after FDR correction to the whole brain analysis.

Discussion

The results of the present study provide no evidence for a relation between resilience to traumatic stress and thickness and surface area measures in cortical regions of the brain in a sample consisting of resilient and vulnerable Dutch police officers, as well as a group of controls from the police academy. We hypothesized that participants in the RES group would have a higher cortical thickness compared to those in the VUL and CON groups, specifically in ACC regions. Contrary to our hypothesis, we did not find any resilience-specific differences in cortical thickness or surface area in the two ACC regions nor in other regions in the brain, either at the corrected and uncorrected statistical levels. A previous structural imaging study that used a VBM and diffusion tensor imaging approach (van der Werff et al., 2017) also did not observe abnormalities in gray matter volume, but the results of that study showed a resilience-specific white matter integrity pattern. Preliminary results of a resting- state functional MRI study in the same cohort also seems to point toward

the role of connectivity rather than gray matter structure concerning resilience.

The results of the present study appear to be at odds with prior studies on resilience. There may be a number of reasons for this. First, the discrepancy between our study and prior resilience studies could be attributed to significant differences in study design. Most studies have used two-group design instead of a three-group design that includes a non–trauma-exposed control group and, hence, these studies have not been able to identify resilience-specific findings. It is thus possible that prior findings should not be attributed to resilience specifically. Second, due to our focus on resilience in police officers, we may have selected a population of individuals who already have high levels of baseline resilience due to self-selection and screening, with the implication that we have studied especially highly resilient participants.

Although the three-group design and the sample of police officers are strengths of our study, our study also has some potential limitations. The relatively small sample size might have inflated Type II errors in the whole-brain analyses. Also, participants in the CON group were significantly younger than those in the VUL and RES groups, as they consisted of undergraduates in the police academy. Furthermore, we did not include a fourth group of unexposed controls with no police affiliation, which would have enabled us to make inferences regarding the characteristics of baseline resilience in police officers. We used a robust standard Freesurfer pipeline for the cortical segmentation, but is has been noted (Paus et al., 1996; Yucel et al., 2001) that the segmentation of regions with more natural anatomical variation can be unreliable, leading to inaccuracies in the segmentation of, for example, the paracingulate gyrus and the surrounding region. In addition, use of the predefined segmentations in FreeSurfer limited the analyses to a set of regions that may not cover all regions relevant in resilience. Finally, the operationalization of resilience used in this study does not encompass the dynamic and multidimensional nature of resilience; rather, it was based on static measures of outcome.

In conclusion, this study provides no evidence for a relation between resilience to traumatic stress and thickness and surface area measures in cortical regions of the brain in a large sample of Dutch police officers. Questions about the role of cortical surface area and thickness in the context of resilience remain and should be further investigated, preferably using longitudinal designs, and future research may also benefit from more detailed vertex-based analytic approaches to examine cortical thickness.

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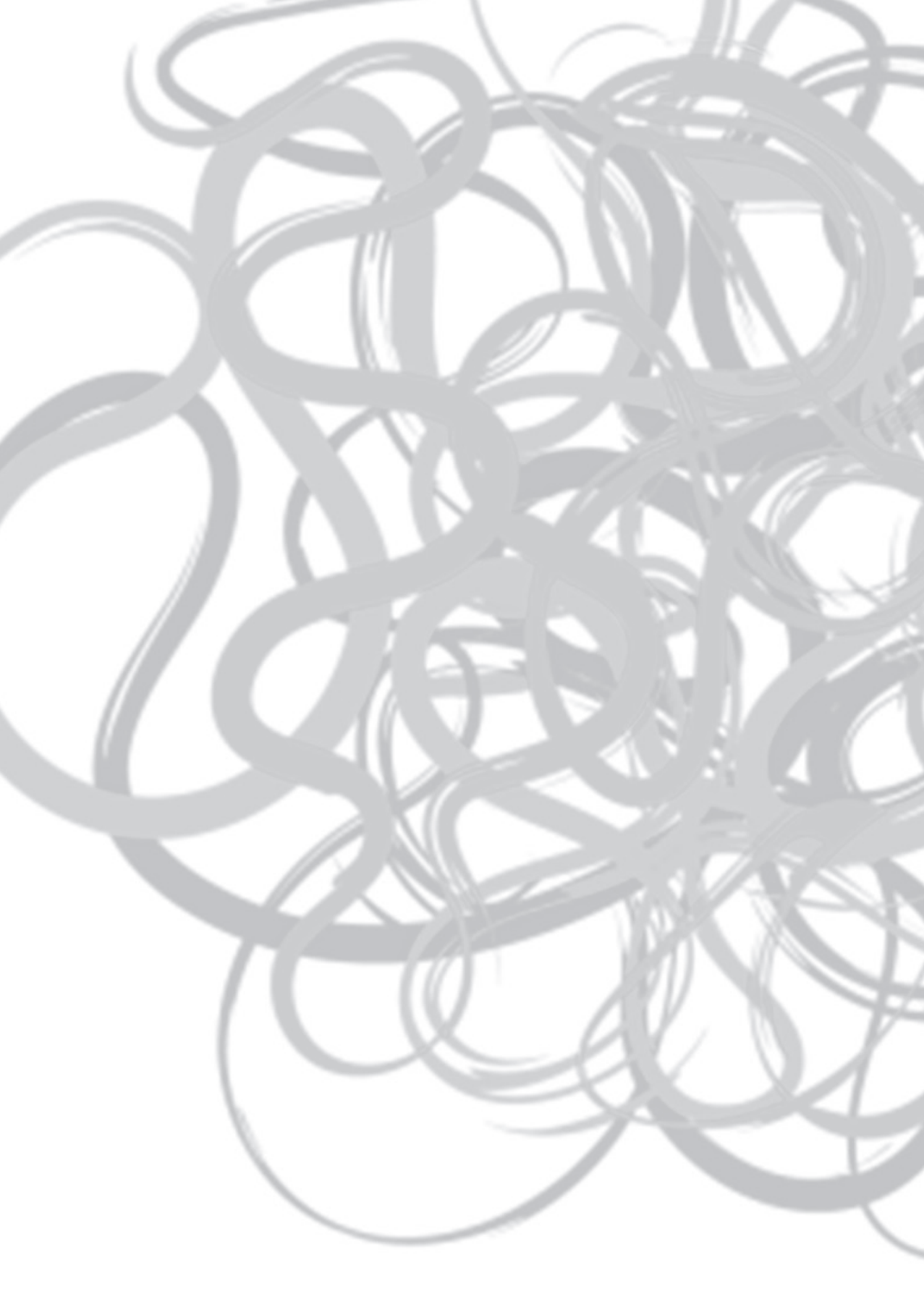
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