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# Structural brain correlates of resilience to traumatic stress in Dutch police officers

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## ABSTRACT

**Objective:** Neurobiological research has traditionally focused on vulnerability rather than on resilience to severe stress. So far, only a few neuroimaging studies examining resilience have used designs that allow disentangling of the neural correlates of resilience from those related to psychopathology or trauma-exposure. The aim of this study was to identify structural brain correlates of resilience, and their correlations with behavioral measures. **Method:** MRI scanning was performed in three groups of police officers: (1) a resilient group (N = 29; trauma-exposed, no psychopathology), (2) a vulnerable group (N = 33; trauma-exposed, psychopathology), and (3) a control group (N = 19; no trauma, no psychopathology). Using whole brain and region-of-interest approaches, we examined gray matter volume and shapes, and white matter integrity using software tools from the FSL-library.

**Results:** We did not find patterns of gray matter volumes or shape specific for the resilient group. In resilient police officers, we found an increase in structural connectivity in the corticopontine tract. White matter integrity in this location correlated with a coping style of positive reappraisal.

**Conclusions:** Resilient police officers show a specific pattern of increased structural connectivity, which is associated to the use of higher order emotion regulation strategies. Given this finding in an area that has not been implicated in stress-related disorders before, as well as the null findings in areas repeatedly shown to be involved in stress-related disorders, the current study indicates that resilience is not simply the opposite of having psychiatric symptoms, but rather an independent construct.

## 1. Introduction

By virtue of their profession, police officers have a higher chance of experiencing traumatic events compared to the general population. Stringent selection criteria for admission to police academies, including an extensive psychological assessment, exist to safeguard an elevated level of resilience in police officers. Moreover, training methods have been applied to further increase resilience to stress in police forces. Although in some cases experiencing traumatic events may lead to the development of trauma-related disorders like posttraumatic stress disorder (PTSD), major depressive disorders (MDD) and anxiety disorders (Berg et al., 2006, Carlier et al., 1997, Maguen et al., 2009), there is no evidence that police officers suffer from more psychiatric symptomatology compared to individuals without high-risk occupations (van der Velden et al., 2013). This makes the police force an interesting group to study in light of resilience (Marmar et al., 2006).

Despite progress in neuroscience methods, research into the neurobiology of resilience to traumatic stress is still very limited. Information we do have is often based on studies that examine PTSD patients compared to trauma-exposed non-PTSD individuals; for a review see: (van der Werff et al., 2013). With this comparison, however, it remains unclear whether differences found between these two groups are to be attributed to trauma-related symptomatology in the patient group, or to the resilience in the control group. To identify alterations in brain networks associated with resilience, a third group of individuals without traumatic experiences and without psychopathologies should be added to the design. As only a comparison of these three groups can elucidate the specific characteristics of the resilient individuals compared to the other two groups and thus which of the effects are specifically related to resilience.

Structural neuroimaging studies using magnetic resonance imaging (MRI) to study gray matter in trauma-exposed twins and non-trauma-

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exposed co-twins suggest that an increased size of the hippocampus is related to resilience (Gilbertson et al., 2002, Kasai et al., 2008). In addition, neuroimaging studies consistently show reductions in hippocampal volume in stress-related disorders like PTSD and MDD (Bremner et al., 2003, Campbell et al., 2004, Gurvits et al., 1996, Kitayama et al., 2005, O'Doherty et al., 2015, Cardenas et al., 2011), and as a result of hypercortisolism (Starkman et al., 1992, Starkman et al., 1999).

The role of white matter structural connectivity has not yet been studied in the context of resilience. In stress-related disorders, decreases of white matter integrity of the uncinate fasciculus (Cullen et al., 2010, Eluvathingal et al., 2006) and the cingulum bundle (Daniels et al., 2013, Fani et al., 2012) have often been found using diffusion tensor imaging (DTI). The uncinate fasciculus connects parts of the limbic system with the medial prefrontal cortex (mPFC). The mPFC inhibits fear responses and emotional responsiveness mediated by the amygdala (Sotres-Bayon et al., 2004), a process that has been found to be disturbed in stress-related psychiatric disorders, including PTSD (Elzinga and Bremner 2002). However, it remains unclear whether these decreases in white matter integrity are purely associated the PTSD symptomatology or whether an increase of white matter integrity might also be indicative of resilience.

This study examines the gray matter volume and white matter integrity correlates of resilience to traumatic stress in a design with a resilient group, a vulnerable group and a healthy control group. Given the lack of existing data on neurobiological characteristics of resilience we based our hypotheses on the existing literature on stress-related disorders. We hypothesized to find an increase in gray matter volume of the hippocampus in trauma-exposed police officers without a history of psychopathology (the resilient group) compared to both trauma-exposed police officers with a history of psychopathology (the vulnerable group) and trauma non-exposed recruits from the police academy without a history of psychopathology (the control group). We also hypothesized to find an increase in white matter integrity of the uncinate fasciculus and the cingulum, specific for resilient officers. In addition to analyses in these regions-of-interest (ROI), we performed an explorative whole brain analysis to detect structural correlates of resilience outside these a priori defined ROI's. For a better understanding of the results, we will associate these measures of brain structure and structural connectivity with resilience-related behavioral measurements.

## 2. Material and methods

### 2.1. Subjects

Trauma-exposed executive personnel of the Dutch police were recruited through advertisements on the intranet of the Dutch police force. For optimal homogeneity across groups the non-exposed healthy control group, was recruited from the Dutch police academy. A total of 149 subjects signed up and were screened for eligibility. Exclusion criteria for all subjects were: MRI contraindications such as metal implants, heart arrhythmia, claustrophobia and possible pregnancy, a history of neurological or other medical illness with central nervous system sequelae, the use of psychotropic medications other than stable use of SSRI's or infrequent benzodiazepine use (i.e., equivalent to 2 doses of 10 mg of oxazepam 3 times per week as a maximum and refrain from use 48 h before scanning), a history of childhood maltreatment (i.e. < 18 years), a history of psychopathology with onset before work related traumatic events, left-handedness, insufficient knowledge of the Dutch language, and smoking > 5 cigarettes a day on average. 86 subjects were invited to participate in the study. Five subjects were excluded from the study after quality checking the MRI data, due to imaging artifacts in their respective MRI scans. The resulting 81 subjects were divided into three groups based on clinical assessment. The resilient group (N = 29) consisted of individuals who report having experienced traumatic events, and did not fulfill the criteria for any

DSM-IV diagnoses, either current or past. The vulnerable group (N = 33) consisted of individuals who report having experienced traumatic events and fulfilled the criteria for one or more DSM-IV diagnoses, either current or past. Individuals in this group met the criteria for the following diagnoses at least once in their lives, after graduating from the Police Academy: major depressive disorder (n = 27), panic disorder (n = 3), agoraphobia (n = 7), specific phobia (n = 1), social phobia (n = 2), generalized anxiety disorder (n = 2), posttraumatic stress disorder (n = 14), substance abuse (n = 8). The control group (N = 19) consisted of trainees recruited from the police academy who reported no exposure to traumatic experiences and did not meet the criteria for any DSM-IV diagnosis in the present or past. As participants in this group were still in training and the participants in the other groups had already completed their training in the past it was expected that there would be an age difference between the groups, with the control group being younger compared to the other groups. Written informed consent was obtained from all participants before the clinical assessment. The medical ethical committee of the Leiden University Medical Center approved the study protocol.

### 2.2. Behavioral assessment

Past and current DSM-IV axis-1 psychiatric disorders were assessed using the mini-international neuropsychiatric interview (MINI); (van Vliet and de Beurs, 2007).

Severity of depressive symptoms were evaluated using the Montgomery-Asberg Depression Rating Scale (MADRS); (Montgomery and Asberg 1979), and the Inventory of Depression Symptomatology (IDS); (Rush et al., 1996). Severity of anxiety symptoms was assessed using Becks Anxiety Inventory (BAI); (Beck et al., 1988). The Harvard Trauma Questionnaire (HTQ) was used to inquire trauma-related symptom severity (Mollica et al., 1992). The Connor-Davidson Resilience Scale (CD-RISC) was used to assess self-report resilience (Connor and Davidson 2003). The Police Life Events Schedule (PLES) was used to assess the amount of exposure to work-related life events (Carlier et al., 1997). The Cognitive Emotion Regulation Questionnaire (CERQ) was used to assess cognitive coping strategies. This questionnaire consisted of nine subscales which all measure a different coping strategy (Garnefski et al., 2001). Higher scores on these subscales indicate that it is more likely an individual will use that specific cognitive coping strategy in challenging situations. The nine subscales of the CERQ are: (1) Self-blame: referring to thoughts of blaming yourself for what you have experienced; (2) Blaming others: referring to thoughts of putting the blame of what you have experienced on others; (3) Acceptance: referring to thoughts of accepting what you have experienced and resigning yourself to what has happened; (4) Refocus on planning: referring to thinking about what steps to take and how to handle the negative event; (5) Positive refocusing: referring to thinking about joyful and pleasant issues instead of thinking about the actual event; (6) Rumination: referring to thinking about the feelings and thoughts associated with the negative event; (7) Positive reappraisal: referring to thoughts of attaching a positive meaning to the event in terms of personal growth; (8) Putting into perspective: referring to thoughts of playing down the seriousness of the event or emphasizing its relativity when compared to other events; (9) Catastrophizing: referring to thoughts of explicitly emphasizing the terror of an experience (Garnefski et al., 2001).

### 2.3. MRI data acquisition

Images were acquired on a Philips 3T MRI system (Philips Healthcare, Best, The Netherlands; software version 3.2.1). A SENSE-32 channel head coil was used for radio frequency transmission and reception.

For each subject both a high resolution anatomical scan and a DTI scan were acquired. The high resolution anatomical scan was obtained

using a sagittal three-dimensional gradient-echo T1-weighted sequence (repetition time = 9.8 ms, echo time = 4.6 ms, matrix size  $256 \times 256$ , voxel size  $1.17 \times 1.17 \times 1.2$  mm, 140 slices, scan duration 4:56 min).

DTI scans were acquired using a single-shot echo-planar imaging sequence with the following scan parameters: repetition time = 6250 ms, echo time = 70 ms, flip angle =  $90^\circ$ , b-factor =  $1000 \text{ s/mm}^2$ , voxel dimensions =  $2.07 \times 2.12 \times 2.10$  mm, number of slices = 60, and no slice gap. DTI data were acquired along 32 directions, together with a baseline image having no diffusion weighting ( $b = 0$ ). Total DTI scanning time was  $\sim 8$  min.

A neuroradiologist, blinded for the clinical details of the subjects, examined all high resolution anatomical scans. No macroscopic abnormalities were observed.

## 2.4. Gray matter analyses

All MRI analyses were conducted in FSL (FMRIB's Software Library, [www.fmrib.ox.ac.uk/fsl](http://www.fmrib.ox.ac.uk/fsl); (Smith et al., 2004) version 5.0.6). To test our hypothesis that size of the hippocampus is different in resilient individuals we used FSL's Integrated Registration and Segmentation Tool (FIRST) to automatically segment both the left and right hippocampus and construct them as vertexes, which also allows comparisons of shape. This method searches through linear combinations of shape modes of variation for the most probable shape instance given the observed intensities in the T1-weighted image. To test whether there were any between-groups differences in shape of the hippocampus a  $1 \times 3$  ANOVA design was modeled in the general linear model (GLM), with age and gender included as confound regressors, and tested using FSL's Randomise Tool, permutation-based (5000 permutations) non-parametric testing, correcting for multiple comparisons across space. Threshold free cluster enhancement (TFCE) was used for finding clusters in the data and threshold for significance was set at  $p < 0.05$  TFCE corrected.

Because FSL FIRST is not suitable for analyses in cortical areas, the explorative whole brain analysis was performed using a standard voxel-based morphometry approach (VBM) implemented in FSL. In order to correct for local expansion or contraction a modulation step was used. Images were smoothed using an isotropic Gaussian kernel with a sigma of 3 mm.

The groups were compared using a GLM including age and gender as confound regressors. To investigate where the resilient group differentiated from both the vulnerable group and the control group the voxel-wise GLM tested an inversed quadratic model, using permutation-based (5000 permutations) non-parametric testing, correcting for multiple comparisons across space. TFCE was used with thresholds for both the ROI comparison and the whole brain analysis set on  $p < 0.05$  corrected.

## 2.5. Diffusion tensor imaging analyses

DTI data were corrected for distortion and motion artifacts induced by eddy currents or by simple head motions, using affine registration of each diffusion weighted image to the  $b = 0$  reference image. Non-brain tissue was removed using the Brain Extraction Tool. Following, in order to generate individual fractional anisotropy (FA) maps for each participant, the diffusion tensor model was fitted to each voxel using FMRIB's diffusion toolbox (FDT). Tract-based spatial statistics (TBSS) version 1.2 was used for voxelwise analysis of the preprocessed FA data, creating a study-specific FA skeleton using a threshold at an FA value of  $\geq 0.45$  to exclude peripheral tracts and to minimize partial voluming.

To test for regional specific fractional anisotropy alterations, we implemented a ROI-based tract-based spatial statistics. A binary mask encompassing the bilateral uncinate fasciculus and the cingulum was created as a ROI using the Johns Hopkins University White Matter Atlas provided by FSL, with probability set to 15%–100%, and subsequently applied to the mean FA skeleton. The resulting study-specific ROI mask

was used for voxelwise permutation-based ROI analysis.

Using FSL's Randomise Tool, permutation-based inferences with TFCE were carried out for voxelwise analysis of FA data. In both the ROI analysis and the whole brain analysis 5000 random permutations were generated to build up the null distribution of the cluster size statistic, while testing an inversed quadratic model to investigate where the resilient group differentiated from both the vulnerable group and the control group. Age and gender were included in the analysis as confound regressors to correct for between group variances. The resulting statistical maps were corrected for multiple comparisons ( $p < 0.05$ , TFCE corrected).

## 2.6. Post-hoc analyses

To enable further interpretation of the TBSS results a mask was created of the voxels that were found to differ significantly between groups on FA. Along with this mask, information on each individual's axial diffusivity (the 1st eigenvalue), radial diffusivity (the average of the 2nd and 3rd eigenvalues), and mean diffusivity was fed into FSL's Randomise Tool using permutation-based inferences with TFCE.

To assess whether any of the effects are associated with specific emotion regulation styles within the resilient group, correlation analyses were performed using the FA values for structural connectivity, and the scores on the CD-RISC and the nine subscales of the CERQ. Correlation analyses were performed using Pearson's  $r$  or, when data violated assumptions for parametric tests, with Kendall's tau.

## 3. Results

### 3.1. Psychometric data

Demographic and psychometric data are reported in Table 1. As expected, there was an age difference between the resilient group and the control group ( $p < .001$ ), but not between the resilient group and the vulnerable group ( $p = .178$ ). Furthermore, the resilient group reported higher scores on the CD-RISC compared to the vulnerable group ( $p = 0.05$ ), but not compared to the control group ( $p = .261$ ).

Scores on the PLES indicated that the resilient group experienced more work-related life events compared to the control group ( $p < .001$ ), but not compared to the vulnerable group ( $p = .534$ ) validating our selection procedures. One outlier was present in the vulnerable group, reporting 3388 work-related life events. As a member of a vice squad, the subject reported over 3000 cases of exposure to adult sexual abuse; roughly one experience every day for the last 10 years. After omission of this outlier, mean scores of the resilient group and the vulnerable group on number of experienced work-related life events grew even closer ( $p = .671$ ). The vulnerable group reported more trauma-related symptoms on the HTQ compared to the resilient group ( $p = .008$ ), as well as higher depression scores on the IDS ( $p = .008$ ). The average MADRS-score for all the groups was below the norm for residual depressive symptoms (MADRS-score  $< 6$ ), with significantly lower scores in the resilient group compared to the vulnerable group ( $p < 0.01$ ).

With respect to cognitive emotion regulation strategies measured using the CERQ, we found that the resilient group scored lower on the subscale acceptance compared to both the vulnerable group ( $p = .017$ ) and the control group ( $p = .018$ ). In addition, the resilient group scored lower on blaming others ( $p = .024$ ) and catastrophizing ( $p = .001$ ) compared to the vulnerable group.

### 3.2. Gray matter structure results

The shape analysis for both the left ( $p > 0.955$ ) and right ( $p > 0.58$ ) hippocampus did not show significant differences between groups. Information about individual volumes of the left and right hippocampus was extracted and subsequently analyzed using IBM SPSS

**Table 1**  
Demographics and Psychometric data.

|                                | Resilient Group |        | Vulnerable Group |        | Control Group |       | p 1 vs 2          | p 1 vs 3            |
|--------------------------------|-----------------|--------|------------------|--------|---------------|-------|-------------------|---------------------|
|                                | N               |        | N                |        | N             |       |                   |                     |
| N                              | 29              |        | 33               |        | 19            |       |                   |                     |
| Females/Males                  | 10/19           |        | 8/25             |        | 11/8          |       | .413 <sup>a</sup> | .143 <sup>a</sup>   |
|                                | Mean            | SD     | Mean             | SD     | Mean          | SD    | p 1 vs 2          | p 1 vs 3            |
| Age                            | 40.24           | 11.84  | 44.24            | 11.19  | 25.16         | 4.63  | .178 <sup>b</sup> | < .001 <sup>b</sup> |
| IDS                            | 36.10           | 6.97   | 43.67            | 12.55  | 33.37         | 5.70  | .008 <sup>b</sup> | .091 <sup>b</sup>   |
| BAI                            | 24.07           | 2.82   | 26.18            | 6.5    | 24.06         | 2.92  | .246 <sup>b</sup> | .965 <sup>b</sup>   |
| MADRS                          | 1.72            | 2.36   | 5.21             | 7.53   | .21           | .713  | .195 <sup>b</sup> | .001 <sup>b</sup>   |
| CD-RISC                        | 98.96           | 12.06  | 92.09            | 14.24  | 102.63        | 9.75  | .05 <sup>c</sup>  | .261 <sup>c</sup>   |
| HTQ                            | 34.72           | 5.13   | 43.67            | 14.67  | 33.95         | 5.45  | .008 <sup>b</sup> | .619 <sup>b</sup>   |
| PLES (before outlier omission) | 168.39          | 140.25 | 334.28           | 619.52 | 25.95         | 53.94 | .534 <sup>b</sup> | < .001 <sup>b</sup> |
| PLES (after outlier omission)  | 168.39          | 140.25 | 235.77           | 257.20 | 25.95         | 53.94 | .671 <sup>b</sup> | < .001 <sup>b</sup> |
| CERQ: Self-blame               | 7.65            | 2.74   | 8.52             | 3.29   | 8.16          | 2.32  | .308 <sup>b</sup> | .394 <sup>b</sup>   |
| CERQ: Blaming others           | 5.79            | 1.82   | 7.24             | 2.59   | 5.53          | 1.68  | .024 <sup>b</sup> | .703 <sup>b</sup>   |
| CERQ: Acceptance               | 10.38           | 2.93   | 12.30            | 3.19   | 12.80         | 3.34  | .017 <sup>b</sup> | .018 <sup>b</sup>   |
| CERQ: Refocus on planning      | 13.69           | 3.71   | 13.81            | 3.18   | 14.47         | 2.80  | .898 <sup>b</sup> | .503 <sup>b</sup>   |
| CERQ: Positive refocusing      | 11.66           | 4.29   | 11.33            | 3.36   | 12.11         | 3.51  | .742 <sup>c</sup> | .705 <sup>c</sup>   |
| CERQ: Rumination               | 9.93            | 3.91   | 11.94            | 6.75   | 9.31          | 3.38  | .150 <sup>b</sup> | .626 <sup>b</sup>   |
| CERQ: Positive reappraisal     | 14.59           | 3.49   | 14.00            | 3.86   | 15.37         | 3.44  | .723 <sup>b</sup> | .433 <sup>b</sup>   |
| CERQ: Putting into perspective | 11.66           | 4.15   | 11.30            | 3.37   | 13.16         | 3.53  | .714 <sup>c</sup> | .201 <sup>c</sup>   |
| CERQ: Catastrophizing          | 4.76            | 1.33   | 6.45             | 3.03   | 4.84          | 1.21  | .001 <sup>b</sup> | .767 <sup>b</sup>   |

IDS = Inventory of depression symptomatology; BAI = Becks Anxiety Inventory; CD-RISC = Connor-Davidson Resilience Scale; HTQ = Harvard Trauma Questionnaire; MADRS = Montgomery-Asberg Depression Rating Scale; PLES = Police Life Events Schedule; CERQ = Cognitive Emotion Regulation Questionnaire. In bold are all *p*-values considered significant (*p* < .05 0.05).

<sup>a</sup> Chi-Square test.

<sup>b</sup> Mann-Whitney *U* test.

<sup>c</sup> Independent Sample *t*-test.

statistics 20. A  $1 \times 3$  ANCOVA test was used controlling for age and gender, both left ( $p = .955$ ) and right ( $p = .931$ ) hippocampus did not differ in volume between groups. The explorative whole brain VBM testing the inversed quadratic design did not show any significant results in gray matter volume with  $p > 0.57$  for all voxels.

### 3.3. Tract-based spatial statistics

The ROI analysis of the FA values in the bilateral uncinate fasciculus and the cingulum bundle showed no significant inversed quadratic effect (for all voxels:  $p > .77$ , TFCE corrected). The explorative whole brain analyses, however, showed a significant inversed quadratic effect in FA values of the left corticopontine tract starting adjacent to the left putamen, leading up to cortical areas where it bends in the parietal direction ( $p < .05$ , TFCE corrected; Fig. 1). The size of the found effect is  $92 \text{ mm}^3$ , and its peakvoxel coordinates are  $x = -27$ ,  $y = -7$ ,  $z = 19$ .

### 3.4. Post-hoc correlation analyses

Analyses of the axial diffusivity, radial diffusivity, and mean diffusivity revealed that the effect in FA was driven by decreases of radial diffusivity and mean diffusivity (for both:  $p < .001$ ) in the resilient group. The axial diffusivity values did not differ significantly between groups.

To assess whether FA values in the area with significantly increased FA were related to self-report resilience or emotion regulation strategies within the resilient group, the mean FA values from this specific area were extracted and exported to SPSS.

The correlation coefficients of the FA values in the corticopontine tract with the CD-RISC scores and with the nine subscales of the CERQ were examined (Table 2). To correct for multiple comparisons, we applied a Bonferroni correction and adjusted the level of significance to  $p < .005$ . We found a significant correlation between the positive reappraisal subscale of the CERQ and the FA values within the resilient group ( $r = .513$ ,  $p = .004$ ). After controlling for depressive

symptomatology scores (IDS scores) the association between FA values and positive reappraisal in the resilient police officers remained significant ( $\beta = .464$ ,  $p = .009$ ), indicating that depressive symptoms did not mediate this relation.

## 4. Discussion

In this study, we set out to investigate the gray matter structure and structural connectivity characteristics of resilience to traumatic stress in a sample of Dutch police officers. Considering that there is a clear lack of neurobiological studies focusing resilience, our hypotheses were based on previous studies on stress-related psychopathologies. We hypothesized that resilient police officers would be characterized by increased volumes of the hippocampus, and an increase in white matter integrity of the uncinate fasciculus and cingulum bundle. We also performed additional explorative whole brain analyses on both volume and structural connectivity.

Using FSL-FIRST, we found no increases in volume of the hippocampus. In addition, the explorative whole brain analysis we performed using VBM showed no gray matter characteristics specific for resilience. Smaller hippocampi have been found to be associated with stress-related disorders (Bremner et al., 2003, Campbell et al., 2004, Gurvits et al., 1996), and as a result of hypercortisolism (Starkman et al., 1992, Starkman et al., 1999). However, there has been an ongoing debate on whether an increased size of the hippocampus could also be a marker of improved resilience. Our data in this particular cohort do not support such a notion.

With respect to structural connectivity, we did not find increased white matter integrity of the uncinate fasciculus and cingulum in the resilient group. Decreases of white matter integrity in these tracts have repeatedly been found in stress-related disorders. The fact we did not find increases in white matter integrity specific to the resilient group in these areas indicates that increased white matter integrity in these areas does not protect one from the negative effects of trauma exposure. In addition, our explorative whole brain analysis showed increases in white matter integrity of a part of the corticopontine tract, a white

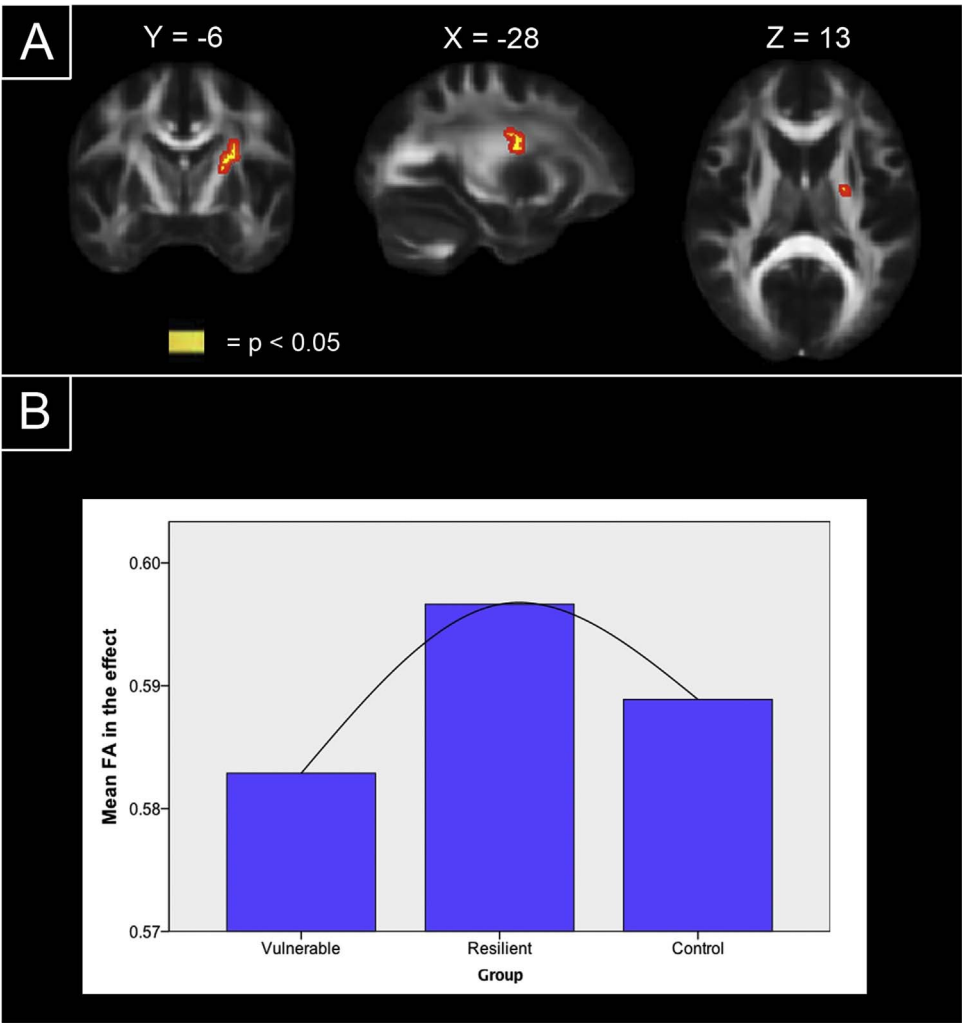


Fig. 1. Structural connectivity specific for resilience.

**Table 2**  
Intercorrelations between structural connectivity and behavioral scales in resilient individuals.

| Scales                         | FA          |               |         |
|--------------------------------|-------------|---------------|---------|
|                                | Pearson's r | Kendall's tau | p       |
| CD-RISC                        | .346        |               | .066    |
| CERQ: Self-blame               | .000        |               | 1.00    |
| CERQ: Blaming others           |             | .058          | .682    |
| CERQ: Acceptance               |             | .327          | .018 *  |
| CERQ: Refocus on planning      | .426        |               | .021 *  |
| CERQ: Positive refocusing      | .429        |               | .020 *  |
| CERQ: Rumination               |             | .186          | .168    |
| CERQ: Positive reappraisal     | .513        |               | .004 ** |
| CERQ: Putting into perspective | .145        |               | .453    |
| CERQ: Catastrophizing          |             | .054          | .716    |

FA = Fractional anisotropy; CD-RISC = Connor-Davidson Resilience Scale; CERQ = Cognitive Emotion Regulation Questionnaire.  
\* =  $p < .05$  (uncorrected); \*\* =  $p < .005$  (bonferroni corrected).

matter tract that has not been implicated in resilience or stress-related disorders before. Given this finding is situated in an area that has not been implicated in stress-related disorders before, as well as the null findings in areas repeatedly shown to be involved in stress-related disorders, the current study indicates that resilience is not simply the opposite of having psychiatric symptoms, but rather an independent construct.

Post-hoc analyses showed that the increased FA in the resilient

group was mostly driven by differences in radial diffusivity and mean diffusivity, and not by differences in axial diffusivity. This pattern of decreases in mean diffusivity and radial diffusivity is an indication of increased myelination of the white matter tract in resilient individuals (Alexander et al., 2007, Song et al., 2005). Increased myelination promotes speed at which impulses travel along the myelinated tract, therefore increasing both structural and functional connectivity between areas connected by these fibers (Hartline 2008). The corticopontine tract is part of the corticopontocerebellar circuitry, and connects the cerebral cortex with the cerebellum, through the pons. Tractography studies show that the corticopontine tract is split into four different fiber tracts, which are named depending on their origin in the cerebral cortex. These are the frontopontine fibers, the parietopontine fibers, the occipitopontine fibers, and the temporopontine fibers (Kamali et al., 2010, Keser et al., 2015). Judging from the location of the finding as well as the way the tract bends into parietal direction (Fig. 1), our finding is situated in the parietopontine fibers. Traditionally, on a functional level the communication between the cerebellum and the cerebral cortex through the corticopontocerebellar tract is linked to the control of action, and specifically the acquisition of motor memory (Brodal and Bjaalie, 1997, Glickstein, 1992, Ramnani, 2006, Stein and Glickstein, 1992). However, it has become clear that this communication is involved in higher order cognitive skills like verbal working memory, and the process of learning cognitive skills (Allen et al., 1997, Fiez et al., 1996, Kim et al., 1994). Our findings suggest that white matter integrity of the tract that connects the cerebral cortex to the cerebellum is involved in resilience to traumatic stress. On a

behavioral level, within the resilient police officers, the white matter integrity within the found effect was associated with an increased skill to positive reappraise problematic situation. This is in line with prior research prospectively linking higher levels of positive emotion before duty related stress exposure to more resilient outcomes (Galatzer-Levy et al., 2013).

Of note, positive reappraisal did not differ between groups, whereas acceptance scores were lower in the resilient group compared to the other two groups. This could indicate a proactive attitude of resilient individuals, and a drive towards a willingness to change negative circumstances rather than accepting them.

There are some limitations to take into account. First, due to our cross-sectional design no causal conclusions can be drawn from the data. We cannot conclude whether the effects in structural and functional connectivity have always been present in the high resilient individuals, or were acquired under influence of severe stressful situations. Second, we did not find effects in the hypothesized ROI's, which were based on studies focusing on psychiatric symptomatology, but only in our whole brain analyses, giving this study an explorative nature.

#### 4.1. Conclusions

To the best of our knowledge this is the first study specifically designed to investigate gray and white matter characteristics of resilience, within a homogenous group of police officers. We found that increased connectivity in the corticopontine tract was associated with resilience police officers, and within this group white matter integrity of the corticopontine tract was related to positive reappraisal behavior in stressful situations.

#### Conflicts of interest

None.

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#### Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.psyneuen.2017.08.019>.

#### References

- Alexander, A.L., Lee, J.E., Lazar, M., Field, A.S., 2007. Diffusion tensor imaging of the brain. *Neurotherapeut. J. Am. Soc. Exp. Neurotherapeut.* 4, 316–329.
- Allen, G., Buxton, R.B., Wong, E.C., Courchesne, E., 1997. Attentional activation of the cerebellum independent of motor involvement. *Science* 275, 1940–1943.
- Beck, A.T., Epstein, N., Brown, G., Steer, R.A., 1988. An inventory for measuring clinical anxiety: psychometric properties. *J. Consult. Clin. Psychol.* 56, 893–897.
- Berg, A.M., Hem, E., Lau, B., Ekeberg, O., 2006. An exploration of job stress and health in the Norwegian police service: a cross sectional study. *J. Occup. Med. Toxicol.* 1, 26.
- Bremner, J.D., Vythilingam, M., Vermetten, E., Southwick, S.M., McGlashan, T., Nazeer, A., Khan, S., Vaccarino, L.V., Soufer, R., Garg, P.K., Ng, C.K., Staib, L.H., Duncan, J.S., Charney, D.S., 2003. MRI and PET study of deficits in hippocampal structure and function in women with childhood sexual abuse and posttraumatic stress disorder. *Am. J. Psych.* 160, 924–932.
- Brodal, P., Bjaalie, J.G., 1997. Salient anatomic features of the cortico-ponto-cerebellar pathway. *Prog. Brain Res.* 114, 227–249.
- Campbell, S., Marriott, M., Nahmias, C., MacQueen, G.M., 2004. Lower hippocampal volume in patients suffering from depression: a meta-analysis. *Am. J. Psych.* 161, 598–607.
- Cardenas, V.A., Samuelson, K., Lenoci, M., Studholme, C., Neylan, T.C., Marmar, C.R., Schuff, N., Weiner, M.W., 2011. Changes in brain anatomy during the course of posttraumatic stress disorder. *Psychiat. Res.* 193, 93–100.
- Carlier, I.V., Lamberts, R.D., Gersons, B.P., 1997. Risk factors for posttraumatic stress symptomatology in police officers: a prospective analysis. *J. Nervous Mental Dis.* 185, 498–506.
- Connor, K.M., Davidson, J.R., 2003. Development of a new resilience scale: the Connor-Davidson Resilience Scale (CD-RISC). *Depress. Anxiety* 18, 76–82.
- Cullen, K.R., Klimes-Dougan, B., Muetzel, R., Mueller, B.A., Camchong, J., Hour, A., Kurma, S., Lim, K.O., 2010. Altered white matter microstructure in adolescents with major depression: a preliminary study. *J. Am. Acad. Child Adolesc. Psych.* 49 (173–83 e1).
- Daniels, J.K., Lamke, J.P., Gaebler, M., Walter, H., Scheel, M., 2013. White matter integrity and its relationship to PTSD and childhood trauma: a systematic review and meta-analysis. *Depress. Anxiety* 30, 207–216.
- Eluvathingal, T.J., Chugani, H.T., Behen, M.E., Juhász, C., Muzik, O., Maqbool, M., Chugani, D.C., Makki, M., 2006. Abnormal brain connectivity in children after early severe socioemotional deprivation: a diffusion tensor imaging study. *Pediatrics* 117, 2093–2100.
- Elzinga, B.M., Bremner, J.D., 2002. Are the neural substrates of memory the final common pathway in posttraumatic stress disorder (PTSD)? *J. Affect. Disord.* 70, 1–17.
- Fani, N., King, T.Z., Jovanovic, T., Glover, E.M., Bradley, B., Choi, K., Ely, T., Gutman, D.A., Ressler, K.J., 2012. White matter integrity in highly traumatized adults with and without post-traumatic stress disorder. *Neuropsychopharmacol.: Off. Public. Amer. College Neuropsychopharmacol.* 37, 2740–2746.
- Fiez, J.A., Raife, E.A., Balota, D.A., Schwarz, J.P., Raichle, M.E., Petersen, S.E., 1996. A positron emission tomography study of the short-term maintenance of verbal information. *J. Neurosci.* 16, 808–822.
- Galatzer-Levy, I.R., Brown, A.D., Henn-Haase, C., Metzler, T.J., Neylan, T.C., Marmar, C.R., 2013. Positive and negative emotion prospectively predict trajectories of resilience and distress among high-exposure police officers. *Emotion* 13, 545–553.
- Garnefski, N., Kraaij, V., Spinhoven, P., 2001. Negative life events, cognitive emotion regulation and emotional problems. *Personality Individual Diff.* 30, 1311–1327.
- Gilbertson, M.W., Shenton, M.E., Ciszewski, A., Kasai, K., Lasko, N.B., Orr, S.P., Pitman, R.K., 2002. Smaller hippocampal volume predicts pathologic vulnerability to psychological trauma. *Nat. Neurosci.* 5, 1242–1247.
- Glickstein, M., 1992. The cerebellum and motor learning. *Curr. Opin. Neurobiol.* 2, 802–806.
- Gurvits, T.V., Shenton, M.E., Hokama, H., Ohta, H., Lasko, N.B., Gilbertson, M.W., Orr, S.P., Kikinis, R., Jolesz, F.A., McCarley, R.W., Pitman, R.K., 1996. Magnetic resonance imaging study of hippocampal volume in chronic, combat-related posttraumatic stress disorder. *Biol. Psychiatry* 40, 1091–1099.
- Hartline, D.K., 2008. What is myelin? *Neuron Glia Biol.* 4, 153–163.
- Kamali, A., Kramer, L.A., Frye, R.E., Butler, I.J., Hasan, K.M., 2010. Diffusion tensor tractography of the human brain cortico-ponto-cerebellar pathways: a quantitative preliminary study. *J. Magn. Reson. Imaging* 32, 809–817.
- Kasai, K., Yamasue, H., Gilbertson, M.W., Shenton, M.E., Rauch, S.L., Pitman, R.K., 2008. Evidence for acquired pregenual anterior cingulate gray matter loss from a twin study of combat-related posttraumatic stress disorder. *Biol. Psychiatry* 63, 550–556.
- Keser, Z., Hasan, K.M., Mwangi, B.I., Kamali, A., Ucsik-Keser, F.E., Riascos, R.F., Yozbatiran, N., Francisco, G.E., Narayana, P.A., 2015. Diffusion tensor imaging of the human cerebellar pathways and their interplay with cerebral macrostructure. *Front. Neuroanat.* 9, 41.
- Kim, S.G., Ugurbil, K., Strick, P.L., 1994. Activation of a cerebellar output nucleus during cognitive processing. *Science* 265, 949–951.
- Kitayama, N., Vaccarino, V., Kutner, M., Weiss, P., Bremner, J.D., 2005. Magnetic resonance imaging (MRI) measurement of hippocampal volume in posttraumatic stress disorder: a meta-analysis. *J. Affect. Disord.* 88, 79–86.
- Maguen, S., Metzler, T.J., McCaslin, S.E., Inslicht, S.S., Henn-Haase, C., Neylan, T.C., Marmar, C.R., 2009. Routine work environment stress and PTSD symptoms in police officers. *J. Nervous Mental Dis.* 197, 754–760.
- Marmar, C.R., McCaslin, S.E., Metzler, T.J., Best, S., Weiss, D.S., Fagan, J., Liberman, A., Pole, N., Otte, C., Yehuda, R., Mohr, D., Neylan, T., 2006. Predictors of posttraumatic stress in police and other first responders. *Ann. N. Y. Acad. Sci.* 1071, 1–18.
- Mollica, R.F., Caspi-Yavin, Y., Bollini, P., Truong, T., Tor, S., Lavelle, J., 1992. The Harvard Trauma Questionnaire Validating a cross-cultural instrument for measuring torture, trauma, and posttraumatic stress disorder in Indochinese refugees. *J. Nervous Mental Dis.* 180, 111–116.
- Montgomery, S.A., Asberg, M., 1979. A new depression scale designed to be sensitive to change. *Br. J. Psych.: J. Mental Sci.* 134, 382–389.
- O'Doherty, D.C., Chitty, K.M., Saddiqui, S., Bennett, M.R., Lagopoulos, J., 2015. A systematic review and meta-analysis of magnetic resonance imaging measurement of structural volumes in posttraumatic stress disorder. *Psychiatry Res.* 232, 1–33.
- Ramrani, N., 2006. The primate cortico-cerebellar system: anatomy and function. *Nat. Rev. Neurosci.* 7, 511–522.
- Rush, A.J., Gullion, C.M., Basco, M.R., Jarrett, R.B., Trivedi, M.H., 1996. The inventory of depressive symptomatology (IDS): psychometric properties. *Psychol. Med.* 26, 477–486.
- Smith, S.M., Jenkinson, M., Woolrich, M.W., Beckmann, C.F., Behrens, T.E., Johansen-Berg, H., Bannister, P.R., De Luca, M., Drobnjak, I., Flitney, D.E., Niaz, R.K., Saunders, J., Vickers, J., Zhang, Y., De Stefano, N., Brady, J.M., Matthews, P.M., 2004. Advances in functional and structural MR image analysis and implementation as FSL. *Neuroimage* 23 (Suppl 1), S208–19.
- Song, S.K., Yoshino, J., Le, T.Q., Lin, S.J., Sun, S.W., Cross, A.H., Armstrong, R.C., 2005. Demyelination increases radial diffusivity in corpus callosum of mouse brain. *Neuroimage* 26, 132–140.
- Sotres-Bayon, F., Bush, D.E., LeDoux, J.E., 2004. Emotional perseveration: an update on

- prefrontal-amygdala interactions in fear extinction. *Learning Memory* 11, 525–535.
- Starkman, M.N., Gebarski, S.S., Berent, S., Scheingart, D.E., 1992. Hippocampal formation volume, memory dysfunction, and cortisol levels in patients with Cushing's syndrome. *Biol. Psychiatry* 32, 756–765.
- Starkman, M.N., Giordani, B., Gebarski, S.S., Berent, S., Schork, M.A., Scheingart, D.E., 1999. Decrease in cortisol reverses human hippocampal atrophy following treatment of Cushing's disease. *Biol. Psych.* 46, 1595–1602.
- Stein, J.F., Glickstein, M., 1992. Role of the cerebellum in visual guidance of movement. *Physiol. Rev.* 72, 967–1017.
- van Vliet, I.M., de Beurs, E., 2007. The MINI-International Neuropsychiatric Interview: a brief structured diagnostic psychiatric interview for DSM-IV en ICD-10 psychiatric disorders. *Tijdschrift voor psychiatrie* 49, 393–397.
- van der Velden, P.G., Rademaker, A.R., Vermetten, E., Portengen, M.A., Yzermans, J.C., Grievink, L., 2013. Police officers: a high-risk group for the development of mental health disturbances? A cohort study. *BMJ Open* 3.
- van der Werff, S.J., van den Berg, S.M., Pannekoek, J.N., Elzinga, B.M., van der Wee, N.J., 2013. Neuroimaging resilience to stress: a review. *Front. Behav. Neurosci.* 7, 39.