

Author Material

Akdeniz C, Tost H, *et al.* Neuroimaging evidence for a role of neural social stress processing in ethnic minority associated environmental risk

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This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods

Subject recruitment, exclusion criteria, and generalizability of results

In our study, we aimed to reach all individuals suitable for MRI research in a radius of approximately 50 kilometers around the city of Mannheim in southwestern Germany. For this, we used several strategies such as newspaper advertisement, information from local registration offices, flyers, posters, and internet platforms which were broadly distributed or used within this spatial range. All responding subjects were carefully screened for exclusion criteria which included a history of psychiatric or neurological illness, prior psychopharmacological therapy, current hormone therapy, head trauma, and unsuitability for MRI research. The latter criteria exclude individuals with large tattoos or permanent make up, metal implants (e.g., non-removable piercings, large dental implants or braces, contraceptive coils, bone nails or plates, artificial joints, vessel clips), pacemakers, defibrillators, and medication pumps. As custom in neuroimaging research, we further excluded left-handers and individuals age 55 years and older to avoid the confounding of the detected BOLD signals with the effects of altered neurodevelopment or cerebrovascular disease. All subjects received reimbursement for their participation in the study. Since the subjects suitable for this fMRI study come from a preselected pool of individuals, the composition of comparison groups (i.e., majority individuals with German heritage) was carefully balanced so that a wide range of sociodemographic, personality, stress-task related psychological, and task performance variables were comparable to the ethnic minority groups. While these procedures are common in neuroimaging research, and our efforts for a broad recruitment of individuals and careful balancing of samples were high, this implicates that we cannot claim full generalizability our findings to the general population.

Social stress task

Brain function during social stress processing was studied using functional magnetic resonance imaging (fMRI) and a block-designed social stress task (named *ScanSTRESS*) as previously described¹. Consistent with prior work in the field²⁻⁶, we induced acute social stress in the scanner to challenge the neural stress response system and “unmask” functional alterations linked to a chronic stressor and established risk factor for mental health. Briefly, the paradigm consisted of 16 epochs of 60 seconds each with alternating stress performance and control blocks presented in two runs. Each task block was preceded by a five seconds instruction phase and followed by 20 seconds rest period, respectively, summing up to a total task length of 23 minutes for all subjects. In the social stress condition, participants performed, under time pressure, cognitively demanding tasks challenging arithmetic and mental rotation abilities. Time pressure was induced by the visual presentation of a countdown timer, and task difficulty was continuously adapted by adjusting the speed of the displayed timer and the difficulty level to the subjects’ performance. For the induction of social-evaluative stress, a panel of two investigators in lab coats was continuously shown to subjects via video live stream (Figure 1). During the stress condition, the observers faced the participant, kept a serious facial expression, and provided disapproving non-verbal and verbal feedback to the subjects’ performance. In the control condition, participants performed figure and number matching tasks in the absence of time pressure or feedback by the investigators. In a subsample of 81 subjects simultaneous heart rate recordings were obtained using an MRI compatible pulse oximeter. After the scanning session all subjects were thoroughly debriefed.

fMRI control tasks

To examine the relative specificity of our findings to neural stress processing, we studied 24 Turkish second-generation migrants and 24 matched German non-migrants during the performance of two well-established fMRI control tasks as previously described⁷⁻¹² that challenge cognitive and emotional neural circuits but lack an explicit stress component (see eTable 3 for details). The first paradigm was an emotional face matching task, which uses angry and fearful facial expressions to provoke a robust engagement of brain emotional processing circuits including pACC^{7,13}. This experiment was performed to probe for potential group differences in the neural processing of emotionally salient stimuli such as negative facial expressions, an inherent element of many social-evaluative stress experiments, including ours.

The *n*-back task¹⁴ is a working memory experiment that induces robust activation changes mainly in lateral prefrontal cortex, but also dACC¹⁵. This task was included to examine whether differences in the processing of challenging cognitive materials, a frequent component in many social-evaluative stress experiments, related to the observed differences in the neural stress response in migrants. Briefly, in this block-designed task, a series of visual stimuli (numbers one to four) were displayed on a screen in a random order at set locations in a diamond-shaped box [stimulus presentation time: 500 milliseconds (ms), inter-stimulus interval: 1500 ms]. In the 2-back condition, subjects were asked to encode the currently seen number, simultaneously recall the number seen two presentations previously, and respond via an MRI compatible button box with 4 buttons arranged in the same configuration as the stimuli presented on the screen. During the control condition (0-back) subjects were asked to press the button corresponding to the position of the currently seen

number presentation. The task was presented in eight blocks of 30 seconds each, with alternating epochs of 0-back and 2-back conditions (task duration: 4 minutes or 124 whole-brain scans).

Brain function during the implicit processing of negative social-emotional stimuli was studied using fMRI and a well-established emotional face matching task (FMT) as previously described⁷⁻⁹. Briefly, the block-designed task consisted of two experimental conditions: an emotional face matching condition and a control task. In the emotional condition, a trio of faces depicting angry or fearful facial affects was displayed, with one face on the top and two on the bottom of the screen. Emotional stimuli were derived from a standard set of pictures of facial affect¹⁶. Participants were instructed to evaluate the stimuli, and select the face in the bottom row depicting the same individual as the target face on the top by using a left or right button press. In the control condition, subjects were instructed to evaluate trios of simple geometric shapes (circles, vertical, and horizontal ellipses) and select the shape in the bottom row depicting the same shape as the target shape on the top. The task was presented in eight blocks of six trials or 30 seconds each, with alternating epochs of face- and form-matching conditions (task duration: 4 minutes 20 seconds or 130 whole-brain scans).

fMRI data acquisition and preprocessing

All fMRI data were acquired on a 3 Tesla whole-body scanner (Siemens Trio, Erlangen, Germany) using a gradient-echo echo-planar imaging (EPI) sequences. For the social stress task, the following sequence specifications were applied: 32 axial slices, 3 millimeter (mm) slice thickness, 1 mm gap, TR = 2000 ms, TE = 30 ms, 80° flip angle, 192 mm field of view, 64 × 64 matrix. With the exception of a variant slice number (28 axial slices) and slice thickness (4 mm), the same sequence specifications applied for the control tasks. For all tasks, image processing followed previously published procedures^{1,7-12} using standard processing routines in SPM8 (<http://www.fil.ion.ucl.ac.uk/spm/>). Briefly, all images were realigned to the first image of the scan run, spatially normalized into a standard stereotactic space (MNI template), resampled to 3 mm isotropic voxels, and smoothed with a 9-mm full-width at half-maximum (FWHM) Gaussian filter. Additionally, slice timing was applied in control tasks, as well as in the social stress task before functional connectivity analysis.

fMRI activation analyses

For each paradigm and participant, separate linear contrast images of task and control conditions were computed and entered in second-level random-effects analyses as detailed below (stress task: “social stress > control”; *n*-back: “2-back > 0-back”, FMT: “emotional faces > forms”). The main effects of stress induction, associations with salivary cortisol, and the effects of ethnic background on brain activation during social stress processing were examined using general linear models in SPM8 with random-effects group statistics at the second level. Specifically, the main effect of stress induction was examined over all participants using a one-sample *T*-test and a significance threshold of $P < 0.05$ FWE corrected for multiple comparisons across the whole brain. The effects of migration status on brain physiology were examined using *T*-test models with migration status as fixed factors, and age, sex, education, current urbanicity, early urbanicity, and task performance as nuisance covariates. The effects of perceived group discrimination on pACC activation in migrants were examined with a multiple regression model that included the following covariates of no interest: perceived discrimination (self), income, age, sex, education, current urbanicity, and early urbanicity.

To reflect our *a priori* hypothesis derived from previous work¹, significance level for the activation analysis of our social stress task was set to $P < 0.05$ family-wise error (FWE) corrected for multiple comparisons over an *a priori* defined anatomical mask of the rostral ACC derived from the Harvard Oxford Atlas (HO, <http://www.cma.mgh.harvard.edu>). The mask was modified to cover the rostral-ventral affective divisions of the ACC including the areas 24 a-c, 25, 32, and 33 as defined by Bush and colleagues¹⁷, or the areas pgACC and sgACC in the nomenclature used by Etkin and colleagues¹⁸ (total mask volume: 14.661 mm³, maximum extensions in MNI space: x = -18 to 17, y = 18 to 55, z = -12 to 31). Outside this pre-hypothesized ROI findings were considered significant if they passed a significance threshold of $P < 0.05$ FWE corrected for multiple comparisons across the whole brain. The analysis of the fMRI activation data of the control tasks followed the procedures described for the stress experiment. Here, to maximize sensitivity, a nominal significance threshold of $P < 0.05$, uncorrected, was adopted for all regions found to be significant in the analyses of our social stress experiment (i.e., pACC, ventral striatum, frontoinsula cortex, dACC).

Quantification of perceived discrimination

In second-generation migrants, perceived discrimination of the own person (PD_S) and the perceived discrimination of the own ethnic group (PD_G) in German society were evaluated using an adapted version of the discrimination measures detailed in Ruggiero and Taylor¹⁹, a self-rating quantifying the extent of discrimination that migrant individuals experience, and attribute to their variant ethnic background, in German society. Here, PD_S and PD_G were assessed with two questions and corresponding self-ratings on 5-point Likert scales (ranging from 1 = “not-at-all” to 5 = “very much”). The specific questions were “To what extent are you, personally as an

individual with a different ethnic background, discriminated against in Germany?” (for PD_S), and “To what extent are individuals with your ethnic background, as a group, discriminated against in Germany ?” (for PD_G).

Other psychological assessments

Psychometric self-reports were obtained according to previously described ¹ standard procedures and included the quantification of self-esteem (Rosenberg Self-Esteem Scale, RSE ²⁰) and a scale for the assessment of chronic stress (Chronic Stress Screening Scale, CSSS) implemented in the Trier Inventory for the Assessment of Chronic Stress (TICS) ²¹. For multi-dimensional personality assessment, we used a validated 10-item short version of the Big Five Inventory (BFI-10) ²² measuring the following dimensions: neuroticism, extraversion, conscientiousness, agreeableness, and openness to experience. Measures of social support were assessed using the Berlin Social Support Scale (BSSS) ²³. For calculation of social network size, a self-report measure was used that quantifies the total number of individuals with which the participants maintain a regular social contact (criteria: minimum one personal conversation over a period of two weeks). For the assessment of perceived social status in German society, i.e. the individual’s perception of his or her relative social standing relative to other people in German society, we used a previously published ^{24,25} single-item scale presented as a pictorial 10 rung ‘social ladder’, on which participants marked the rung corresponding to their current perceived standing relative to other individuals residing in Germany. Further trait variables were assessed with the German editions of the Fear of Negative Evaluation (FNE) and Self-Monitoring (SM) scales. The FNE scale is a trait measure assessing subjective experiences of anxiety and fear in situations in which the person is negatively evaluated by others ²⁶. The SM scale measures the sensitivity of an individual to situational cues to social appropriateness and the use of these cues for the control of the own behavior and self-presentation in social contexts ^{27,28}. To further control for potential preexisting differences in the experience and handling of performance situations that involve social evaluative feedback, self-ratings for the following trait domains were assessed: sensitivity to criticism, susceptibility to intimidation by authority figures, aggressiveness in competitive situations, susceptibility to intimidation by dominant behavior, fear of failure and negative evaluation in performance situations, and achievement motivation in performance situations. For this, participants were asked to quantify their level of agreement or disagreement with a set of self-describing statements (e.g., “In performance situations, I am more motivated than other individuals to give my best”) on 5-point Likert rating scales. Indices of the urbanization level of the living environment during upbringing (“early-life urbanicity”) and at the time of the study (“current urbanicity”) were calculated as previously detailed [c.f., ¹]. Notably, there are missings in some of the acquired psychological variables. The main reasons for this were the almost four-year long process of our data collection, in which upcoming new findings in the epidemiology and social neuroscience literature motivated us to add additional scales, and the fact that some participants refrained from answering certain items because they could not decide on a definite answer or felt that the items were too personal.

Assessment of stress-task related psychological and hormonal variables

Stress-task related psychometric assessments included a scale for the assessment of subjective emotional responses (SERS) to acute stress ²⁹ as well as questionnaire items quantifying the individuals’ self-ascribed degree of achievement motivation, effort, error monitoring, and intimidation by the investigators during the performance of the stress task on 5-point Likert rating scales (e.g., “To what extent were you intimidated by the negative feedback of the investigators ?”). For quantification of cortisol responses, a total of eight salivary samples per subject were acquired in regular time intervals throughout the stress experiments, i.e., after subject arrival (1 sample), preceding the fMRI procedures (2 samples), immediately after the scan (1 sample), and after leaving the scanner room (4 samples), respectively. Hormonal analyses were performed as detailed elsewhere ^{1,30}. Briefly, salivary cortisol samples were analyzed using time-resolved immunoassays with fluorescence detection. Stress-induced changes in salivary cortisol response (delta cortisol) were calculated from individual peak concentration values and baseline levels and subsequently log-transformed to correct for skewness (Kolmogorov-Smirnov test of log-transformed values: $P > 0.35$).

Analysis of demographical, psychometric and physiological indices

Data analysis was performed using the SPSS Predictive Analytics Software (SPSS 20, IBM Inc., Armonk, New York, USA). Group differences in categorical variables were examined using χ^2 tests. Effects of migration status on continuous variables were examined using ANOVA models and t-tests for independent samples. Effects of group, task condition, and group by task condition interaction effects on heart rate, salivary cortisol and SERS outcome measures were analyzed by means of univariate mixed-effects ANOVA models. Association analyses of the assessed trait- or state variables were performed using partial correlation models in SPSS with extracted contrast estimates from the pACC or dACC masks as dependent variables and age, sex, and education as covariates of no interest.

fMRI connectivity analyses

Based on the observed pACC activation differences during neural social stress processing in our study groups, supplementary functional connectivity analyses were conducted that followed previously published procedures^{1,9,11,13,31}. Briefly, for each participant, first eigenvariates of the seed time series were extracted from 5 mm spheres centered on the pACC hot spot of the activation group comparison (migrants vs. Germans). Then, individual first-level multiple regression models were defined that included the subject-specific pACC time series as regressor of interest, and the following regressors of no interest: (1) the movement parameters from the realignment step, (2) first eigenvariates derived from CSF and white matter masks, and (3) regressors encoding for the block structure of the task conditions (for removal of the task-related variance). During the model estimation step, a high pass filter of 128 seconds, and a first order autoregressive model were applied. The resulting maps consisted of contrast estimates (regression beta) for pACC functional connectivity for each voxel and every subject. These maps were subsequently subjected to the same random-effects group comparison models described for the activation analyses above. Here, we specifically tested whether our study groups displayed differences in the functional connectivity of pACC and dACC, a target region that was motivated by prior evidence highlighting (1) dACC as higher order control area of pACC in fMRI emotion and stress experiments^{13,32,33}, (2) the involvement of dACC in the processing of social experiences such as social exclusion³⁴ and race attitudes³⁵, (3) and the established structural connectivity of pACC with dACC established in a prior tractography study³⁶. The dACC target region was defined by a modified anatomical mask from the Harvard Oxford Atlas (<http://www.cma.mgh.harvard.edu>) covering the caudal-dorsal divisions of ACC, i.e., the areas 24 a'-c' and 32' in the nomenclature by Bush and colleagues¹⁷ or the areas pACC and dACC defined by Etkin and colleagues¹⁸ (total mask volume: 7560 mm³, maximum extensions in MNI space: x = -15 to 17, y = -4 to 33, z = 9 to 31). For connectivity analyses, significance was measured at $P < 0.05$ FWE corrected for multiple comparisons within the dACC mask of interest. Outside this pre-hypothesized ROI findings were considered significant if they passed a significance threshold of $P < 0.05$ FWE corrected for multiple comparisons across the whole brain. The same functional connectivity procedures were also applied to the *n*-back- and face-matching control tasks to probe the relative specificity of the stress-related connectivity findings.

Post-hoc mediation analysis

The potential causal contributions of perceived discrimination to the observed association of perceived chronic social stress and altered pACC-dACC functional connectivity during social stress processing were explored with statistical mediation analysis in a subset of $n = 37$ migrants of mixed ethnicity with all available variables. We used *MEDIATE*³⁷, a structural equation modeling add-on to the SPSS statistical software (SPSS 20, IBM Inc., Armonk, New York, USA). *MEDIATE* allows for the estimation of the indirect effects of a proposed causal variable on an outcome variable through a proposed mediator, thereby controlling for one or more covariates of no interest. Guided by the prior migration-related epidemiological and social neuroscience literature, the following variables were introduced into the model: perceived discrimination of the own ethnic group^{38,39} as proposed causal variable, individual ratings for perceived chronic stress (CSSS) as proposed mediator (motivated by prior accounts on the adverse role of chronic stress in migrants³⁹⁻⁴²), and individual contrast estimates for pACC-dACC functional connectivity (extracted from the dACC target mask) as dependent variable (see eFigure 4). The following subject-specific variables were introduced as covariates of non-interest into the model: age, gender, education as well as migrant density in the neighborhood^{43,44}, social network size^{2,45,46}, perceived social status^{24,47}, and urban upbringing^{1,48}. The last four variables were chosen since they have been previously discussed as social risk and resilience factors for mental health in the literature and may influence the functionality of neural stress circuits. Inferences for significant indirect effects were based on bias-corrected 95% percentile bootstrap confidence intervals based on 10,000 bootstrap samples.

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eTable 1: Details of the sample with heterogeneous ethnic minority background and their German comparison subjects

	Germans	n	%*	Migrants ¹	n	%*	P value
Demographic variables							
Sex: males/females	21/19	40	100	18/22	40	100	0.655
Age: mean (SD), years	23.65 (3.33)	40	100	22.88 (4.40)	40	100	0.377
School education, mean (SD), years	12.55 (1.01)	40	100	12.45 (1.09)	40	100	0.671
Smokers	5	40	100	9	40	100	0.378
Body mass index, mean (SD), kg/m ²	23.32 (3.81)	40	100	23.08 (3.45)	40	100	0.761
Marital status: single/married	27/2	29	72.5	38/2	40	100	1.000
Currently employed	25	40	100	25	40	100	1.000
Household size, mean (SD), individuals	3.55 (3.60)	29	72.5	3.35 (1.89)	40	100	0.764
Household income p. month after tax, mean (SD), €	1890.38 (1424.99)	26	65	1988.80 (1469.70)	40	100	0.789
Current urbanicity, mean (SD)	2.58 (0.64)	40	100	2.68 (0.62)	40	100	0.477
Early-life urbanicity, mean (SD)	33.00 (10.59)	40	100	35.43 (10.19)	40	100	0.300
Relocation frequency until age 15, mean (SD)	0.85 (1.08)	40	100	0.98 (0.95)	40	100	0.583
Density of migrants in the area, mean (SD), %	18.65 (12.40)	40	100	23.18 (12.46)	40	100	0.107
fMRI task performance							
Stress condition, mental calculation, correct responses, mean (SD), %	71.74 (7.20)	40	100	69.83 (7.23)	40	100	0.241
Stress condition, mental rotation, correct responses, mean (SD), %	48.89 (8.16)	40	100	46.28 (8.19)	40	100	0.157
Psychological inventories							
Perceived self-discrimination, mean (SD)	-	-	-	2.38 (1.10)	40	100	-
Perceived group discrimination, mean (SD)	-	-	-	3.55 (1.09)	40	100	-
Social support, mean score, mean (SD)	3.63 (0.66)	35	87.5	3.64 (0.48)	40	100	0.947
Social network size, mean (SD), individuals	18.00 (13.46)	35	87.5	15.59 (13.12)	39	97.5	0.438
Perceived social status in Germany, mean (SD)	6.40 (1.59)	35	87.5	6.36 (1.60)	39	97.5	0.912
<u>Chronic stress, sum score, mean (SD)</u>	<u>13.84 (8.26)</u>	<u>38</u>	<u>95</u>	<u>18.97 (9.87)</u>	<u>39</u>	<u>97.5</u>	<u>0.016</u>
Self-esteem, sum score, mean (SD)	24.76 (4.09)	37	92.5	24.76 (4.51)	38	95	0.995
Self-monitoring, sum score, mean (SD)	12.09 (3.45)	33	82.5	10.57 (3.97)	30	75	0.108
Fear of negative evaluation, sum score, mean (SD)	9.30 (3.07)	33	82.5	9.53 (3.63)	30	75	0.786
Susceptibility to criticism, mean (SD)	3.12 (1.14)	33	82.5	3.37 (1.30)	30	75	0.427
Achievement motivation in performance situations, mean (SD)	2.21 (0.93)	33	82.5	2.30 (1.06)	30	75	0.726
Intimidation by authority figures, mean (SD)	3.27 (1.31)	33	82.5	3.33 (1.18)	30	75	0.848
Competitiveness and aggression in performance situations, mean (SD)	2.79 (0.89)	33	82.5	2.67 (1.27)	30	75	0.666
Intimidation by dominant behavior, mean (SD)	3.58 (1.12)	33	82.5	3.77 (1.22)	30	75	0.520
Anxiety in performance situations, mean (SD)	3.15 (1.28)	33	82.5	2.90 (1.16)	30	75	0.417
Stress-task related psychological variables							
Achievement motivation, mean (SD)	1.42 (0.94)	33	82.5	1.27 (0.69)	30	75	0.454
Motivation to perform well, mean (SD)	1.45 (0.91)	33	82.5	1.37 (0.62)	30	75	0.657
Error monitoring, mean (SD)	1.55 (0.91)	33	82.5	1.27 (0.52)	30	75	0.136
Intimidation by investigators, mean (SD)	2.55 (1.33)	33	82.5	2.37 (1.07)	30	75	0.556

	Germans	n	%*	Migrants¹	n	%*	P value
Stress-task related psychological variables cont.							
SERS-Anxiety, stress vs. control, mean (SD)	0.18 (0.56)	40	100	0.20 (0.62)	40	100	0.850
SERS-Self-related emotions, stress vs. control, mean (SD)	0.42 (0.56)	40	100	0.55 (0.64)	40	100	0.320
SERS-Tense arousal, stress vs. control, mean (SD)	0.05 (0.44)	40	100	0.00 (0.50)	40	100	0.671
Physiological measurements							
Cortisol, post-stress - pre-stress, mean (SD), nmol/l ²	2.16 (0.50)	40	100	2.17 (0.30)	40	100	0.902
Cortisol, post-stress - pre-stress, responder ²	24	40	100	23	40	100	1.000
Heart rate, stress - control, mean (SD), bpm ³	8.74 (5.55)	31	77.5	7.82 (4.69)	35	87.5	0.467
Acceleration in heart rate ⁴ , mean (SD), bpm ³	1.20 (5.10)	30	75	2.13 (3.63)	34	85	0.400

¹ Ethnic parental background: n = 28 Turkish, n = 3 former Yugoslavian, n = 2 Italian, n = 2 Polish, n = 1 Russian, n = 1 Syrian, n = 1 Vietnamese, n = 1 Egyptian, n = 1 Algerian.

² Log-transformed

³ Beats per minute

⁴ Heart rate difference between the delta heart rate of first and second run of the stress experiment (i.e., after additional verbal negative feedback)

* Percentage of individuals with available questionnaire data relative to the total sample

eTable 2: Details of the Turkish and German samples examined by experimenters with balanced ethnical background

	Germans	n	%*	Migrants ¹	n	%*	P value
Demographic variables							
Sex: males/females	9/14	23	100	11/12	23	100	0.767
Age: mean (SD), years	23.35 (2.77)	23	100	22.61 (3.10)	23	100	0.399
School education, mean (SD), years	12.48 (1.31)	23	100	12.48 (1.04)	23	100	1.000
Smokers	4	23	100	3	23	100	1.000
Body mass index, mean (SD), kg/m ²	23.33 (3.56)	23	100	23.15 (3.04)	23	100	0.855
Marital status: single/married	20/3	23	100	23/0	23	100	0.233
Currently employed	14	23	100	16	23	100	0.758
Household size, mean (SD), individuals	2.65 (1.43)	23	100	3.48 (2.04)	23	100	0.119
Household income per month after tax, mean (SD), €	1770.95 (1907.13)	21	91.3	1884.57 (1288.15)	23	100	0.817
Current urbanicity, mean (SD)	2.74 (0.62)	23	100	2.61 (0.66)	23	100	0.492
Early-life urbanicity, mean (SD)	35.59 (9.30)	23	100	34.96 (8.98)	23	100	0.816
Relocation frequency until age 15, mean (SD)	1.13 (1.10)	23	100	0.83 (0.78)	23	100	0.284
Density of migrants in the area, mean (SD), %	21.36 (11.71)	23	100	22.74 (12.75)	23	100	0.703
fMRI task performance							
Stress, mental calculation, mean (SD), % correct	70.32 (7.09)	23	100	69.76 (7.09)	23	100	0.789
Stress, mental rotation, mean (SD), % correct	47.37 (9.45)	23	100	47.99 (8.34)	23	100	0.815
Psychological inventories							
Perceived self-discrimination, mean (SD)		-		2.65 (1.23)	23	100	-
Perceived group discrimination, mean (SD)		-		4.09 (0.79)	23	100	-
Social support, mean score, mean (SD)	3.68 (0.39)	23	100	3.64 (0.51)	23	100	0.776
Social network size, mean (SD), individuals	16.78 (13.08)	23	100	13.41 (8.18)	22	95.7	0.308
Perceived social status in Germany, mean (SD)	6.43 (1.56)	23	100	6.36 (1.84)	22	95.7	0.889
<u>Chronic stress, sum score, mean (SD)</u>	<u>13.05 (5.31)</u>	<u>21</u>	<u>91.3</u>	<u>20.73 (9.83)</u>	<u>22</u>	<u>95.7</u>	<u>0.003</u>
Self-esteem, sum score, mean (SD)	25.09 (2.76)	22	95.7	24.67 (4.53)	21	91.3	0.711
Self-monitoring, sum score, mean (SD)	11.65 (3.22)	17	73.9	10.20 (3.75)	15	65.2	0.249
Fear of negative evaluation, sum score, mean (SD)	8.29 (2.62)	17	73.9	9.00 (3.65)	15	65.2	0.530
Susceptibility to criticism, mean (SD)	3.53 (1.18)	17	73.9	3.67 (1.23)	15	65.2	0.750
Achievement motivation in performance situations, mean (SD)	2.47 (1.33)	17	73.9	2.33 (1.05)	15	65.2	0.750
Intimidation by authority figures, mean (SD)	3.76 (1.09)	17	73.9	3.40 (1.18)	15	65.2	0.372
Competitiveness and aggression in performance situations, mean (SD)	2.59 (1.28)	17	73.9	2.80 (1.21)	15	65.2	0.635
Intimidation by dominant behavior, mean (SD)	3.65 (1.00)	17	73.9	3.93 (1.16)	15	65.2	0.459
Anxiety in performance situations, mean (SD)	3.29 (1.11)	17	73.9	2.87 (1.13)	15	65.2	0.288
BFI-Neuroticism, sum score, mean (SD)	5.43 (1.44)	23	100	5.96 (1.99)	23	100	0.314
BFI-Extraversion, sum score, mean (SD)	7.91 (1.44)	23	100	7.35 (2.27)	23	100	0.320
BFI-Conscientiousness, sum score, mean (SD)	7.26 (1.71)	23	100	6.83 (1.75)	23	100	0.399
BFI-Openness, sum score, mean (SD)	7.35 (1.92)	23	100	7.91 (1.72)	23	100	0.300
BFI-Agreeableness, sum score, mean (SD)	6.74 (1.25)	23	100	6.04 (1.82)	23	100	0.138

	Germans	n	%*	Migrants¹	n	%*	P value
Stress-task related psychological variables							
Achievement motivation, mean (SD)	1.24 (0.44)	17	73.9	1.27 (0.80)	15	65.2	0.890
Motivation to perform well, mean (SD)	1.35 (0.61)	17	73.9	1.40 (0.63)	15	65.2	0.831
Error monitoring, mean (SD)	1.29 (0.47)	17	73.9	1.13 (0.35)	15	65.2	0.279
Intimidation by investigators, mean (SD)	2.53 (1.23)	17	73.9	2.53 (1.06)	15	65.2	0.992
SERS-Anxiety, stress vs. control, mean (SD)	0.11 (0.56)	23	100	0.20 (0.70)	23	100	0.646
SERS-Self-related emotions, stress vs. control, mean (SD)	0.55 (0.62)	23	100	0.55 (0.66)	23	100	1.000
SERS-Tense-arousal, stress vs. control, mean (SD)	-0.04 (0.54)	23	100	-0.09 (0.53)	23	100	0.785
Physiological measurements							
Cortisol, post-stress - pre-stress, mean (SD), nmol/l ²	2.24 (0.30)	22	95.7	2.20 (0.34)	23	100	0.640
Cortisol, post-stress - pre-stress, responder	15	22	95.7	14	23	100	0.758
Heart rate, stress - control, mean (SD), bpm ³	8.63 (6.20)	15	65.2	6.70 (4.37)	20	87	0.314
Acceleration in heart rate ⁴ , mean (SD), bpm ³	2.04 (3.40)	13	56.5	1.78 (3.70)	20	87	0.843

¹ Ethnic parental background: n = 23 Turkish. The Turkish participants are an ethnically homogenous subsample of the ethnically heterogeneous sample given in eTable 1.

² Log-transformed

³ Beats per minute

⁴ Heart rate difference between the delta heart rate of first and second run of the stress experiment (i.e., after additional verbal negative feedback)

* Percentage of individuals with available questionnaire data relative to the total sample

eTable 3: Details of the fMRI control tasks samples

	Germans	n	Migrants¹	n	P value
Demographic variables					
Sex: males/females	11/13	24	13/11	24	0.773
Age: mean (SD), years	23.83 (3.74)	24	23.54 (3.46)	24	0.780
School education, mean (SD), years	12.58 (1.18)	24	12.38 (1.14)	24	0.535
Current urbanicity, mean (SD)	2.83 (0.38)	24	2.79 (0.51)	24	0.750
Early-life urbanicity, mean (SD)	37.21 (7.63)	24	37.63 (8.76)	24	0.861
Relocation frequency until age 15, mean (SD)	0.75 (1.11)	24	0.92 (0.78)	24	0.551
fMRI task performance					
FMT, mean (SD), % correct	99.31 (1.59)	24	99.31 (1.59)	24	1.000
2-back, mean (SD), % correct	84.72 (12.40)	24	83.16 (16.73)	24	0.715

¹ Ethnic parental background: n = 24 Turkish. 62.5 % of the Turkish participants in the fMRI control tasks have also participated in the social stress experiment.