Appendix 1 to Koch S, van Zuiden M, Nawijn L, et al. Decreased uncinate fasciculus tract integrity in male and female PTSD patients: A diffusion tensor imaging study. *J Psychiatry Neurosci* 2017.

Supplementary Methods

Emotional face matching task

The emotional face matching task consisted of three conditions: one visuomotor control condition with scrambled faces (4 blocks), one emotional condition with fearful and angry faces (2 blocks), and one emotional condition with happy and neutral faces (2 blocks)[1]. During each trial (duration 5 seconds), three faces were presented: one face on top (cue) and two faces below (target). Participants had to match the emotion or shape orientation (control blocks) of the cue stimulus with one of the two targets below.

The fMRI images were analyzed with SPM8 (http://fil.ion.ucl.ac.uk/spm/software/spm8). Preprocessing of the fMRI images consisted of realignment, slice-time correction, co-registration to the anatomical scan, segmentation, spatial normalization to the Montreal Neurological Institute (MNI) template, resampling to $2mm^3$ voxels and spatial smoothing with a 5mm full-width half maximum (FWHM) Gaussian kernel. At the first-level, the two emotional conditions were modelled as box-car regressors, convolved with a canonical hemodynamic response function. We included the six realignment parameters to control for movement. A high-pass filter (cut-off 1/200 Hz) was used to remove slow drifts of the signal and the AR(1) process was used to remove temporal autocorrelation. We obtained contrast images for the fearful-angry condition and the happy-neutral condition versus the visuomotor control condition. The contrast images were subsequently entered in a second-level repeated-measures ANOVA with task condition (fearful-angry – happy-neutral) as within-subject factor and group (PTSD – controls) and sex (male – female) as between-subject factors. The covariate medication-order was included to control for possible confounding effects of order in which medication was administered. Only contrast images acquired after placebo administration were used for the current analysis. The female PTSD patient who started using benzodiazepines between the first and second scanning session was excluded from this analysis.

Bibliography

1.   Koch SBJ, van Zuiden M, Nawijn L, et al. Intranasal Oxytocin Administration Dampens Amygdala Reactivity towards Emotional Faces in Male and Female PTSD Patients. *Neuropsychopharmacology* 2016; 41:1495–504.

Supplementary Table S1: Results of the repeated-measures ANOVA's of each tract

	FA values		MD values	
	F(df)	**P-value**	**F(df)**	**P-value**
Uncinate Fasciculus				
Between-subject effects				
Main effect of group	F(1,66) = .130	.719	F(1.67) = 3.037	.086
Main effect of sex *(direction: MD males > females)*	F(1,66) = 5.357	.024	F(1,67) = 6.360	.014*
Group x sex interaction	F(1,66) = 1.209	.276	F(1,67) = .000	.995
Within-subject effects				
Main effect of hemisphere	F(1,66) = .022	.883	F(1,67) = .199	.657
Hemisphere x group interaction (see table notes below for post-hoc tests)	F(1,66) = 1.513	.223	F(1.67) = 7.575	.008*
Hemisphere x sex interaction	F(1,66) = .941	.343	F(1,67) = 1.524	.221
Hemisphere x group x sex interaction	F(1,66) = .789	.378	F(1,67) = .297	.588
Cingulum Bundle				
Between-subject effects				
Main effect of group	F(1,68) = .521	.473	F(1,67) = 0.269	.605
Main effect of sex *(direction: FA males > females)*	F(1.68) = 6.701	.012*	F(1,67) = 5.080	.027
Group x sex interaction	F(1.68) = .779	.380	F(1,67) = 0.878	.352
Within-subject effects				
Main effect of hemisphere	F(1,68) = 2.387	.127	F(1.67) = 0.027	.869
Hemisphere x group interaction	F(1,68) = 2.479	.120	F(1,67) = 0.859	.357
Hemisphere x sex interaction	F(1,69) = 1.673	.200	F(1,67) = 0.154	.696
Hemisphere x group x sex interaction	F(1,69) = .327	.569	F(1,67) = 2.802	.099
Superior longitudinal fasciculus – parietal projections				
Between-subject effects				
Main effect of group	F(1,68) = 2.757	.101	F(1,69) = .328	.569
Main effect of sex (direction: MD females > males)	F(1,68) = 3.865	.053	F(1,69) = 8.897	.004*
Group x sex interaction	F(1,68) = .090	.765	F(1,69) = .037	.848
Within-subject effects				
Main effect of hemisphere (direction: MD left > right)	F(1,68) = .897	.347	F(1,69) = 7.069	.010*
Hemisphere x group interaction	F(1,68) = .620	.434	F(1,69) = .598	.442
Hemisphere x sex interaction	F(1,68) = 1.391	.242	F(1,69) = 3.781	.056
Hemisphere x group x sex interaction	F(1,68) = .017	.897	F(1,69) = .212	.646
Superior longitudinal fasciculus – temporal projections				
Between-subject effects				
Main effect of group	F(1,69) = 2.668	.107	F(1,69) = 1.133	.291
Main effect of sex (direction: MD females > males)	F(1,69) = 1.568	.215	F(1,69) = 6.967	.010*

Supplementary Table S1: Results of the repeated-measures ANOVA's of each tract

	FA values		MD values	
	F(df)	**P-value**	**F(df)**	**P-value**
Group x sex interaction	F(1,69) = .165	.686	F(1,69) = .335	.565
Within-subject effects				
Main effect of hemisphere (direction: MD left > right)	F(1,69) = .166	.685	F(1,69) = 6.874	.011*
Hemisphere x group interaction	F(1,69) = .096	.758	F(1,69) = .742	.392
Hemisphere x sex interaction	F(1,69) = 2.768	.101	F(1,69) = .885	.350
Hemisphere x group x sex interaction	F(1,69) = .948	.334	F(1,69) = .000	1.000

Results of the repeated measures ANOVA's on FA and MD values of the uncinate fasciculus, cingulum bundle and parietal and temporal projections of the superior longitudinal fasciculus (SLF), corrected for age and tract volume. A p-value <.017 was regarded significant for main and interaction effects. df = degrees of freedom; FA = fractional anisotropy; MD = mean diffusivity; * significant at p-corrected <.05 level

Post-hoc test Hemisphere x Group interaction effect MD uncinate fasciculus
One-way ANOVA for each hemisphere with between-subject factors group (PTSD – Control) and sex (male – female):
- Left hemisphere – Main effect of group: F(1,65)=.359, p=.551
- Right hemisphere – Main effect of group: F(1,68)=6.700, p=.012 (direction: PTSD > Controls)

For the post-hoc test of the group x hemisphere interaction effect, a p-value of <.025 was regarded significant.

Supplementary Table S2: Significant results of segment analysis

	FA values		MD values	
	F(df)	**P**	**F(df)**	**P**
Uncinate Fasciculus				
Between-subject effects				
Main effect of sex (direction: FA males > females)	F(1,60) = 7.575	.008*	F(1,60) = 4.596	.036
Within-subject effects				
Main effect of segment (see table notes below for post-hoc tests)	F(2.625, 157.487) = 1.378	.685	F(3.814, 228.852) = 5.076	.001*
Cingulum Bundle				
Within-subject effects				
Main effect of segment (see table notes below for post-hoc tests)	F(2.413, 147.186) = 8.911	<.001*	F(3.338, 213.642) = 4.021	.006*
Superior longitudinal fasciculus – temporal projections				
Between-subject effects				
Main effect of sex (direction: FA males > females)	F(1,61) = 7.404	.008*	F(1,63) = 3.380	.071
Within-subject effects				
Main effect of hemisphere (direction: FA left > right, MD left < right)	F(1,61) = 9.445	.003*	F(1,63) = 469.138	<.001*
Segment x sex interaction (see table notes below for post-hoc tests)	F(3.745, 265.178) = 1.398	.238	F(5.392, 339.721) = 2.938	.010*

Significant results of the repeated measures ANOVA's on FA and MD values of the uncinate fasciculus, cingulum bundle and parietal and temporal projections of the superior longitudinal fasciculus (SLF), corrected for age and tract volume. A p-value of <.011 was regarded significant for all main and interaction effects df = degrees of freedom; FA = fractional anisotropy; MD = mean diffusivity; * significant at p-corrected <.05 level

Post-hoc tests Main effect of Segment (simple contrasts, reference to last segment):
- MD values uncinate fasciculus: lower MD values in the most orbito-frontally located segment (segment #5), compared to the two most temporally located segments (segment #1: p=.001; segment #2: p=.008).
- FA values cingulum bundle: lower FA values in the most anterior located segment (segment #6) compared to the other (more posterior located) segments (segment #1: p=.001; segment #2: p=.001; segment#3: p<.001; segment #4: p<.001; segment #5: p=.030).
- MD values cingulum bundle: higher MD values in most anterior located segment (segment #6) compared to the most posterior located segments (segment #1: p=.007; segment #2: p=.026, segment#3: p=.004; segment #4: p=.0029)

Post-hoc tests Segment x Sex interaction MD values superior longitudinal fasciculus, temporal projections:
- Males - main effect of Segment: F(6,192)=3.237, p=.005)
- Females – main effect of Segment: non-significant (F(6,162, p=.775)

Males - Post-hoc test Main effect of Segment (simple contrast, reference to last segment):
- Lower MD values of the most temporally located segment (segment #7) compared to the two most frontally located segments (segment #1: p=.019; segment #2: p=.027), higher MD values of the most temporally located segment (segment #7) compared to the middle segment (segment #4, p=.049).

Supplementary Figure S1: Design of the emotional face-matching task and task activation
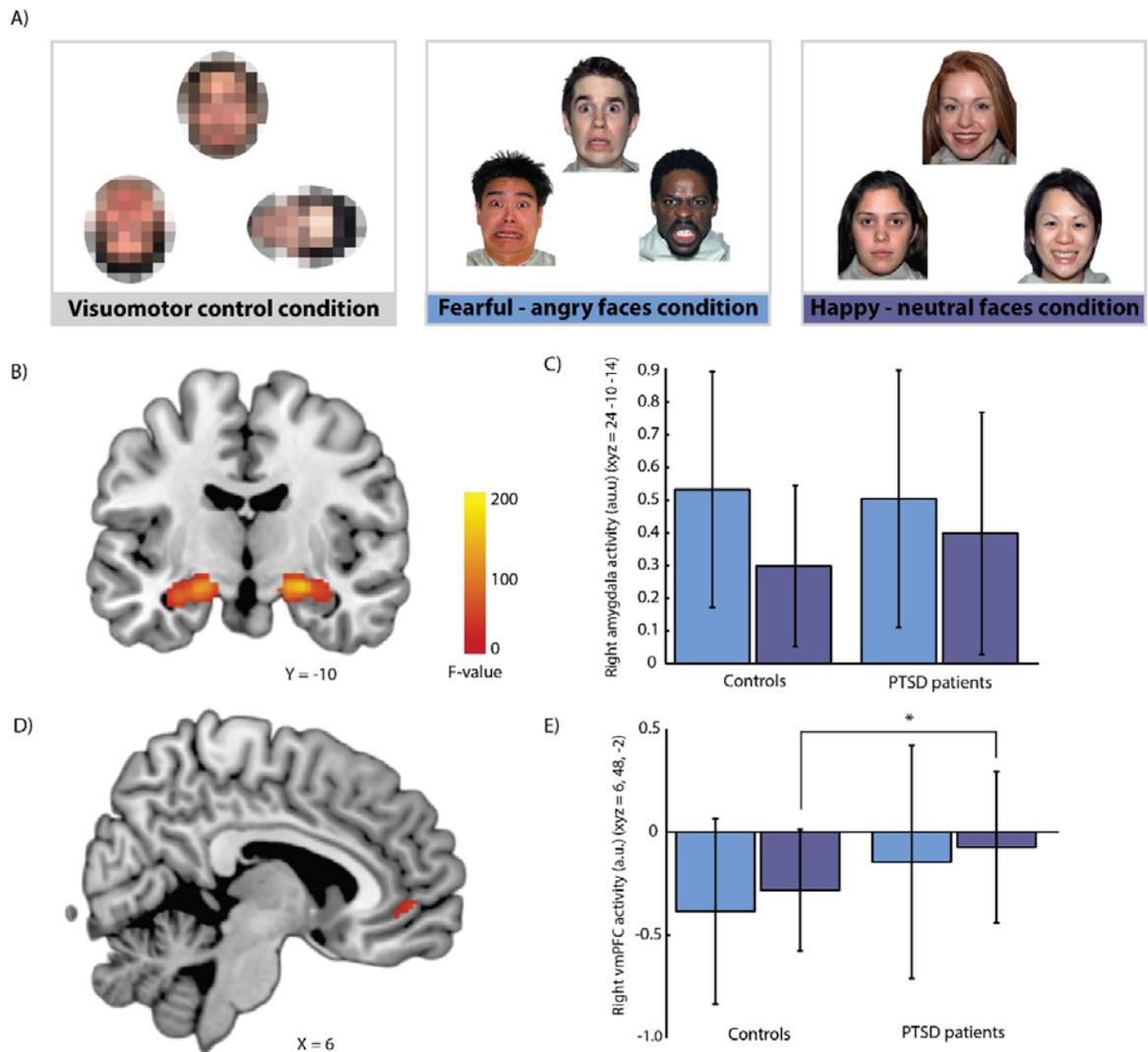
(A) The emotional face-matching task consisted of three conditions: a visuomotor control condition with scrambled faces, one emotion condition with fearful-angry faces (blue) and one emotion condition with happy-neutral faces (purple). Emotion conditions were counterbalanced for sex. Within each trial, cue and target stimuli were always of the same sex. Trials were randomized within each block, and block-order was counterbalanced between task versions (i.e. one task version started with a fearful-angry faces block, whereas the other task version started with a happy-neutral faces block). Task versions were randomized between participants and scanning sessions. **(B)** Bilateral amygdala activation and **(D)** vmPFC deactivation towards emotional faces (fearful-angry and happy-neutral condition combined) vs the visuomotor control condition on a single-subject template image (P_{FWE}<.05 whole-brain corrected). **(C)** Contrast estimates of amygdala activation and **(E)** vmPFC deactivation towards fearful-angry faces (blue) and happy-neutral faces (purple). PTSD patients showed significantly less vmPFC deactivation compared to controls. * p <.05.