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Citation for final published version:

Koller, Kristin , Hatton, Christopher M, Rogers, Robert D and Rafal, Robert D 2019. Stria terminalis microstructure in humans predicts variability in orienting toward threat. European Journal of Neuroscience 50 (11) , pp. 3804-3813. 10.1111/ejn.14504

Publishers page: https://doi.org/10.1111/ejn.14504

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Stria terminalis microstructure in humans predicts variability in orienting toward threat

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Conflict of interest statement:

The authors declare that no financial or commercial conflicts of interest were present in the conduction of this research.

Data accessibility statement:

Data for this study is not archived in a publicly available repository.

Author contributions:

K.K. and R.D. Rafal developed conception and design of research; K.K. and R. D. Rafal performed experiments; K.K., R.D. Rafal, R.D. Rogers and C.M.H analysed data; K.K., R.D. Rafal, C.M.H. and R.D. Rogers interpreted results of experiments; K.K. and R.D. Rafal prepared figures; K.K., R.D. Rafal, R.D. Rogers and C.M.H. edited and revised manuscript; K.K., R.D. Rafal, R.D. Rogers and C.M.H. approved final version of manuscript.

Abstract

Current concepts of the extended amygdala posit that basolateral to central amygdala projections mediate fear-conditioned autonomic alerting, whereas projections to the bed nucleus of the stria terminalis mediate sustained anxiety. Using DTI tractography in humans, we show that microstructure of the stria terminali correlate with an orienting bias toward threat in a saccade decision task, providing the first evidence that this circuit supports decisions guiding evaluation of threatening stimuli.

Keywords: DTI, Tractography, Amygdala, Saccades, Threat, Orienting, Stria Terminalis, Bed Nucleus of the Stria Terminali.

Abbreviations: BNST (bed nucleus of the stria terminalis), DTI (diffusion tensor imaging), FA (fractional anisotropy), SOA (stimulus onset asynchrony), ST (stria terminalis).

Introduction

Converging evidence in rodent and non-human primate studies have shown two major outputs of the amygdala, and suggest that they serve different functions in transmitting information about threatening stimuli: (i) a projection to the central nucleus of the amygdala, critical in linking aversive cues to phasic fear-conditioned arousal, mediated by the autonomic nervous system; and (ii) projections to the bed nucleus of the stria terminalis (BNST), via the stria terminalis, mediating tonic states manifest as anxiety (Fox et al., 2015; Walker et al., 2003). For example, lesions of the central nucleus abolish fear-potentiated startle responses (Hitchcock and Davis, 1986), as do its projections to the brainstem via the caudal (but not rostral) ventral amygdalofugal pathway (Hitchcock and Davis, 1991); whereas, lesion of the bed nucleus of the stria terminalis have no effect on fear potentiated startle (Hitchcock and

Davis, 1991). By contrast, in a rodent model of anxiety that exploits the anxiogenic effects of exposure to bright light, Walker and Davis (1997) showed that the augmented startle response in light (compared to dark) was abolished by lesions of the BNST. Moreover, they reported a double dissociation between the involvement of the BNST and the central nucleus of the amygdala between fear-potentiated startle and enhanced startle from anxiogenesis induced by light exposure. Specifically, lesions of the BNST had no effect on fear-potentiated startle, but abolished enhanced startle from light exposure; whereas the central nucleus of the amygdala abolished fear-potentiated startle, but had no effect on light-enhanced startle. A similar double dissociation was demonstrated by Walker, Toufexis and Davis in a rodent model that exploited the anxiogenic effects of intraventricular infusion of corticotropin releasing factor (Walker et al., 2003, Figure 3, p.202).

BNST lesions also prevent sensitisation to repeated foot shocks. Whereas in unlesioned animals, the startle response increases over time on repeated exposure to foot shock, long-term sensitisation to repeated foot shock does not occur in BNST lesioned animals (Gewirtz, McNish and Davis, 1998). Based on the cumulative literature dissociating the effects of BNST from central amygdala inactivation, Walker and Davis (1997) have proposed that the BNST is not critical for eliciting startle responses, but rather sensitised the organism to orient toward threat by modulating "a sustained state of defensive preparedness". In this framework, the BNST mediates long-duration (tonic) responses whereas the central nucleus mediates phasic, autonomic responses on detecting threatening or aversive stimuli. Consistent with this account, they noted that light-enhancement effects on startle amplitude build up over time, and decline gradually over time, after the bright light is extinguished. Walker, Toufexis and Davis (2003) have suggested that the tonic, sustained responses mediated by the BNST be referred to as 'anxiety' and the phasic responses mediated by the central nucleus of the amygdala be referred to as 'fear'.

Amygdalofugal projections to the BNST are transmitted via two pathways: The ventral amygdalofugal pathway (a component of the ansa peduncularis), and the stria terminalis. In humans, Kim and Whalen (2009) performed voxelwise analyses regressing amygdala BOLD activation elicited by fearful faces against fractional anisotropy (FA) images derived from DTI. The purpose was to identify voxels in white matter whose microstructure (indexed by fractional anisotropy) was predicted by BOLD activation elicited by fearful faces. The results demonstrated that FA of connections between the amygdala and the ventromedial prefrontal cortex via the ventral amygdolofugal tract was predicted by BOLD activation of the amygdala. By contrast, BOLD activation of the amygdala did not predict FA of voxels in the stria terminalis.

Most experimental models typically involve either a single threatening or non-threatening stimulus presented on each trial, and evocation of fear is inferred from phasic, automatic responses by the autonomic system (Bar-Haim et al., 2007). The current DTI study provides the first evidence that amygdala projections to the BNST, via the stria terminalis, are involved in orienting to threat. Our starting point is a framework advanced originally by Posner and Boise (1971) who posited two separate, isolable components of attentional orienting: alertness and selectivity. We tested the hypothesis that projections from the amygdala to the BNST, via the stria terminalis, convey information that influences *selective* responses to potential threat mediating flee or fight; approach or withdraw responses. We used probabilistic DTI to 'virtually' dissect amygdala innervation via the stria terminalis to the BNST in humans. We then tested associations between the microstructure (fractional anisotropy) of these connections and a bias to orient toward threat in a novel saccade decision task in which the emotional valence of the stimuli was not task relevant.

Method

Participants

Nineteen neurologically healthy humans (9 male, age range 18-47 years) participated. All participants were screened for trait anxiety measured by the State-Trait Anxiety Inventory (Spielberger, 1983) to ensure exclusion of individuals with extreme scores. Bangor University's Ethics Review Committee ethically approved the study, and all participants provided written consent, prior to study commencement. Methodology outlined below correspond with the virtual dissection of stria terminalis and MRI protocol as reported by Rafal et al. (2015) and the temporal order judgement saccade decision task as reported by Koller, Rafal, Platt and Mitchell (2018).

Diffusion Tensor Imaging Tractography

Magnetic Resonance scanner. A Phillips 3 Tesla Achieva magnetic resonance (MR) scanner at the Bangor Imaging Unit at Bangor University was used to acquire T1-weighted anatomical and diffusion weighted images.

T1 anatomical scans. High resolution multi-echo T1 weighted images (0.7x0.7x0.7mm isotropic voxel resolution) were acquired using an MPRAGE (magnetization prepared gradient echo) sequence.

DTI scans. DWI-EP (diffusion weighted imaging – echo planar) images were collected at 2x2x2mm with the following parameters: b-values = 0 (averaged four volumes) and 2000, b-directions = 61, slices = 76, section thickness = 2mm, TR = 2 s, TE = 35ms.

Data pre-processing. Following data acquisition, the image files for the DTI data and the structural T1 scans were manually converted from DICOM format into NIfTI with dcm2nii (http://www.sph.sc.edu/comd/rorden/mricron/). Subsequent data pre-processing was carried

out using the FSL-FDT toolbox (Behrens et al., 2003; Behrens, Berg, Jbabdi, Rushworth and Woolrich, 2007; http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/). Diffusion weighted images were corrected for eddy currents and head motion using affine registration to the first b-zero volume. This was carried out to prevent approximate stretches and shears created in the diffusion weighted images that may have been induced by eddy currents in the gradient coils (Behrens et al., 2007). Following eddy current correction, diffusion tensor models were fitted at each voxel using the DTI-FIT tool in FSL. Diffusion parameters were calculated using the Markov Chain Monte Carlo sampling method. The DTI data was then prepared for probabilistic tractography via the BEDPOSTX tool in FSL's FDT toolbox. Probabilistic tracking was carried out using the PROBTRACKX tool in FSL's FDT toolbox. Prior to running the BEDPOSTX process, the non-diffusion brain image was extracted from the skull (using the FSL brain extraction tool (BET)), and a brain mask was formed. Anatomical T1-weighted scans were brain extracted using the BET-tool, and were registered to the B0 diffusion brain image, using FSL's FLIRT tool. Masks were drawn based on anatomical landmarks in each participant's individual non-diffusion T1-registered brain using FSLView.

DTI tractography of stria terminalis. Stria terminalis virtual dissection with probabilistic DTI tractography was implemented as previously described (Rafal et al., 2015). Masks employed for virtual dissection with DTI tractography of the stria terminalis were implemented using the FSL-FDT toolbox (Behrens et al., 2007). Tracts were generated from an amygdala seed mask (Fig. 1a, shown in blue) with the use of a waypoint mask drawn on the stria terminalis along its trajectory adjacent to the lateral ventricle between the body of the caudate and the anterior nucleus of the thalamus (Fig. 1a, shown in yellow), and with the use of a target and termination mask in the bed nucleus of the stria terminalis (Fig. 1a and 1b, shown in red). The fornix and the anterior commissure were landmarks for drawing the BNST mask. The BNST mask was drawn over the hypothalamic grey matter lateral to the fornix above and below the anterior

commissure. The stria terminalis mask was drawn on a sagittal section where it is clearly visible as a white stripe between two grey matter structures: the caudate nucleus and the anterior nucleus of the thalamus.

A total of 19 participants took part in the current experiment (including the human participants previously reported as the "Second Group" (Rafal et al., 2015). In some participants, (eight) small exclusions were required to prevent streamlines reaching regions that do not form connections between the BNST and the amygdala via the stria terminalis. Regions included parts of the fornix, a mid-sagittal slice, part of the frontal lobe and a small anterior region between the amygdala and BNST. All voxels of resultant tracts were thresholded so that only voxels containing at least 10% of the maximum number of traces were included in the final tract for each participant. In the majority of participants (17 participants in left and right hemispheres), stria terminalis dissections that were achieved with the amygdala as the seed, the stria terminalis mask as the mid-waypoint mask, and the BNST as the final way-endpoint and termination mask, demonstrated the most consistent stria terminalis streamlines. In some cases where streamlines consistent with the known topography of the stria terminalis tracts were not obtained via the above-mentioned dissection order, the tract was traced in both directions (BNST as seed mask and amygdala as seed mask), and the resultant overlapping voxels between the two tracts were used for calculation of fractional anisotropy values (left hemisphere of 2 participants, and the right hemisphere of 2 participants). In one participant in the right hemisphere, the dissection in the opposite order (BNST as seed, stria terminalis and amygdala as waypoints and amygdala as termination mask) produced a streamline most consistent with the known anatomy of the stria terminalis, and was used for FA calculation.

Temporal order saccade decision task

A threatening and a non-threatening visual stimulus was presented at the same eccentricity in opposite visual fields during each trial of the saccade decision task. The threatening stimulus appeared 53ms before the non-threatening stimulus on 33% of the trials, 53ms after the non-threatening stimulus on 33% of the trials and simultaneously on the remainder of the trials. Stimulus picture pairs matched for luminance (e.g. a snake preparing to strike paired with a bunny) were selected from the International Affective Picture Scale (Lang, Bradley and Cuthbert, 2008). Participants were instructed that one stimulus always appeared first, to ignore the picture content and to saccade from central fixation toward whichever stimulus appeared first (Fig. 2). An Eyelink1000® device recorded saccade latency and direction under monocular viewing conditions. Participant bias towards threat was tested as the percentage of saccadic choices toward threat made on trials of all SOAs. Individual saccadic threat bias was regressed against stria terminalis microstructure measures (FA) with a multi-level binomial model.

Results

Virtual dissection of stria terminalis

Virtual dissection of the stria terminalis was demonstrated in all 19 human participants (bilaterally in 18 participants and unilaterally in the right hemisphere of 1 subject). Consistent with previous DTI findings (Krüger et al., 2015; Avery et al., 2014; Rafal et al., 2015), the stria terminalis emerged from the amygdala, traversing above the lateral ventricle's temporal horn before running along the lateral border of the caudate nucleus tail to the caudo-thalamic groove in the wall of the lateral ventricle, and then descended through the diencephalon to enter the BNST. Figure 3 presents the trajectory of the stria terminalis demonstrated via a composite tract formed from tracts from all participants, aligned to a common brain space. The colour

scale represents the proportion of participants through which the streamline passed through the same voxels. The image represents both the variability in the trajectory and the size of the streamlines across participants.

Stria terminalis structural connectivity as predictor of selective orienting to threat

As reported previously for the behavioural data in this experiment (Koller et. al, 2018), the saccade decision task showed only a small bias (Median = 52%, SD = 2.79, ranging from 44% to 62%) toward the threatening stimulus on trials in which the two stimuli appeared simultaneously. This bias to orient toward threat, computed as the percentage of saccadic choices toward threat made on all trials across three SOAs (simultaneous, left picture first, right picture first), was not statistically significant ($t(18) = 1.47$, $p = .16$ (two-tailed)). The purpose of the Koller *et al*. (2018) study, however, was to test the hypothesis that the retino-tectal tract transmitted visual signals that elicited an orienting response toward threat. The hypothesis predicted that there would be a larger orienting bias toward threat on trials when the threatening stimulus was in the temporal compared to the nasal hemifield. The prediction of a naso-temporal asymmetry was based on cumulative evidence that the colliculus receives more crossed than uncrossed fibres from the retina, whereas there are an equal proportion of crossed and uncrossed fibres from the retina to the lateral geniculate nucleus (See van Koningsbruggen, Rafal and Koller, 2017 for a review). This prediction was confirmed by demonstrating a reliable orienting bias toward threat when the threatening stimulus was in the temporal hemifield (beta =0.27, S.E. =0.04, Z score = 7.16, $p < 0.0001$, Table 1, p.82); and that the bias toward threat was larger when the stimulus appeared in the temporal compared to the nasal hemifield ($F[1,19]= 3.84$, $p = 0.04$) at all SOAs (See Koller et al. (2018), Figure 4, p. 82).

The current research examined the contributions of the stria terminalis in orienting toward threat. The stria terminalis carries projections from the amygdala, which receives visual

afferents from both extra-geniculate pathways and from striate and extrastriate cortices, to the BNST. Therefore, the analyses correlating microstructure of the stria terminalis with threat bias included all trials averaged across trials when the threatening picture was in either the temporal or nasal hemifield. Although the mean threat bias thus computed was quite variable across participants and, overall resulted in only a weak, and statistically unreliable threat bias effect for the group, our purpose was to test whether this variability in threat bias across participants was predicted by the connectivity of the stria terminalis.

The mean stria terminalis FA was collapsed across left and right hemispheres for each participant (no significant differences between left and right hemispheres were reported ($t(17) = 1.47$, $p = .16$ (two-tailed), $M = .01$, $SD = .04$). Binomial regression analyses, with random intercepts fitted for each participant, demonstrated that individual bias scores toward threat stimuli was strongly associated with mean stria terminalis FA across individuals (see Table 1 and Fig. 4). In order to test for gender differences, gender was added as an additional predictor to the model, however no main effect of gender was observed (β .03, SE = .04, Z = .72, p =.47).

Comparison of face versus non-face stimuli

To investigate the potential driving effect of face stimuli on threat bias, stimulus pairs in which one of the stimuli conveyed a face shape (stimulus pairs 1, 5, 6, and 9, see supplementary Figure 1 with list of image pairs) were separated from stimulus pairs that did not. Multi-level binomial regression analyses demonstrated that a bias to threat was greater for picture pairs that did not include a face stimulus (β -.11, SE = .04, Z = -2.76, p <.006).

Trait anxiety as predictor of threat bias

The sample, which included no individuals with a diagnosis of generalized anxiety disorder, produced a broad range of trait anxiety scores (22-54, Mean = 38.56, SD = 9.5). A multi-level

binomial regression was conducted to test whether, in addition to stria terminalis FA, trait anxiety also predicted bias to threat stimuli. Results demonstrated that only stria terminalis FA was a significant predictor of threat bias (Table 2). No significant correlations were observed between stria terminalis FA and trait anxiety ($r = .09$, $p = .73$)

Discussion

Evidence in rodent and non-human primates suggest two basolateral outputs of the amygdala that potentially serve dissociable roles in transmitting 'threatening' information; a projection to the central nucleus of the amygdala elicits phasic startle and fear-conditioned autonomic arousal in response to threat signals; and another projection to the bed nucleus of the stria terminalis (BNST) that mediates tonic states of defensive preparedness that can be manifest as anxiety (Fox et al., 2015, Walker et al., 2003).

To our knowledge, it has not yet been determined whether anxiogenesis modulated by the BNST is dependent upon amygdala efferents transmitted by the ventral amygdalofugal pathway, or by the stria terminalis, or both. The BNST has previously been shown to be involved in threat monitoring using visual stimuli (Somerville et al. 2010, 2013; Alvarez et al. 2011). However, the amygdalofugal efferents transmitted via the BNST via the stria terminalis have not been shown previously to be involved in rapid, phasic responding to fear evoking stimuli. Our study is the first ST-BNST study to show associations with response to fear stimuli and we provide novel evidence that projections from the amygdala to the BNST, via the stria terminalis, support the processing of and selective responding to individual fear-evoking stimuli.

We recently reported data, from the same participants reported here, that microstructure (measured with FA derived from virtual dissections with probabilistic DTI tractography) of a subcortical pathway connecting the superior colliculus and the amygdala, via the pulvinar nucleus of the thalamus, predicted a saccadic bias to threat on the same temporal order decision

task (Koller et al., 2018). This pathway traverses above the temporal horn of the lateral ventricle and we have previously shown that it is anatomically separate from the stria terminalis projection in humans and monkeys and, in humans, is medial to it (Rafal et al., 2015).

The experiment was conducted with monocular viewing. Although, there was not, overall, a statistically reliable bias to orient toward threat, there was a bias to orient toward threat specifically when the threatening stimulus in a pair was presented in the temporal hemifield. This observation suggested that at least some of the visual signals transmitted from the superior colliculus to the amygdala (via the pulvinar) derived from direct retino-tectal projections from the retina to the colliculus. The pathway from the pulvinar connects to the lateral amygdala. The current research shows that the variability in saccadic bias toward threat is supported by amygdalofugal projections via the stria terminalis to the BNST. The anatomy of the stria terminalis demonstrated in this study is consistent with its known topography, and with that reported in previous DTI studies in humans (Avery et al., 2014; Krüger et al., 2015; Kamali et al., 2016) and monkeys (Rafal et al. 2015; Oler et al. 2017). The stria terminalis traverses above the temporal horn of the lateral ventricle before arcing along the lateral border of the tail of the caudate nucleus and the caudo-thalamic groove in the wall of the lateral ventricle between the caudate nucleus and the superior border of the anterior thalamic nucleus, prior to descending through the diencephalon to the region of the bed nucleus of the stria terminalis (De Olmos and Ingram, 1972). It should be noted that previous virtual dissections of the stria terminalis with DTI (Avery et al., 2014; Krüger et al., 2015; Kamali et al., 2016) sought to demonstrate all connections between the amygdala and the BNST (including both the stria terminalis and ventral pathways (ventral amygdalofugal tract)) between the amygdala and BNST. By contrast, our study sought to isolate only the stria terminalis. Therefore, in our virtual dissections, we employed exclusion masks to exclude the amygdalofugal tract. This was done for two reasons. First, our goal was specifically to examine the function of the stria

terminalis. Secondly, although Kamali,et al. (2016) have shown that it is possible to virtually dissect the amygdalofugal pathway with DTI tractography, the fibre bundle containing the amygalofugal pathway also contains amygdalopetal projections from the BNST to the amygdala (Nieuwenhuys, Voogd, and Van Huijzen, 2007). As is always the case with virtual dissections, caution is necessary in ascribing anatomical veracity to streamlines demonstrated via the technique of DTI tractography. Tractography can demonstrate spurious connectivity that does not correspond to actual anatomical structure. The current research not only replicates previous tractographic demonstrations (Avery et al., 2014; Krüger et al., 2015) of a putative stria terminalis tract, but confirms the anatomical veracity of the virtual dissection by demonstrating a functional role in responding to threatening visual signals.

It must be noted that the bias effect to orient toward threat measured with the saccade decision task was small and, for the group as a whole, was not statistically reliable (when averaged across trials in which threat was presented in both temporal and nasal hemifields). The participant with the strongest bias oriented toward threat, on simultaneous trials, on only 62% of trials. One reason for the weak effect may have been because the stimulus pairs also included faces, which have been shown to capture attention (Langton, Law, Burton and Schweinberger, 2008). In three of the four pairs in which one of stimuli contained a face, the face was competing with a threatening stimulus in the opposite visual field. Our analysis demonstrated a larger bias to threat for stimuli that did not contain a face within the presented stimulus pairs.

Although the threat bias effect was small, the purpose of this research was to determine whether individual variability in connectivity of the stria terminalis predicted a propensity for attentional capture by threatening stimuli under task conditions where the emotional valence of competing stimuli was irrelevant. The results show that individuals with the strongest stria

terminalis connectivity exhibited a greater propensity to have their attention captured by a threatening stimulus.

Our results showed no association between trait anxiety and either threat bias, or stria terminalis microstructure (FA). As reviewed in the Introduction, it has been established that the effects of experimental manipulations that heighten preparedness for threat are modulated by amygdala outputs to the BNST. It might, therefore, be expected that individuals with higher levels of trait anxiety might have stronger stria terminalis connectivity. There is no evidence in our data that this was the case. It has not, to our knowledge, been established whether the anxiogenic functions of the BNST are dependent upon afferents from the amygdala that are transmitted via the stria terminalis or via the ventral amygdalofugal pathway. One possibility is that the role of the BNST in anxiogenesis is dependent upon amygdalar projections via the ventral amygdalofugal tract, and that the role of the BNST in selective orienting toward threat is dependent upon amygdalar projections via the stria terminalis. This account would be consistent with the dissociation between trait anxiety and threat orienting bias observed in the current experiment.

It might be expected that individuals with higher trait anxiety would have a stronger bias to orient toward threat. Although our sample included a broad range of trait anxiety (excluding individuals with generalized anxiety disorder), our data provided no evidence that higher levels of trait anxiety were associated with a stronger bias to orient toward threat. Attentional bias to consciously perceived threat has been shown with a variety of experimental paradigms (see Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg and Van Ijzendoorn, 2007 for review). However, threat bias to stimuli outside awareness has also been shown across various anxious populations, but not in non-anxious individuals. Furthermore, Mogg et al. (2000) reported that compared with normal controls and individuals with depressive disorder,

individuals with generalised anxiety disorder (GAD) were more likely to look first at and quicker to shift gaze toward threatening compared to neutral faces.

Conclusions

Our results provide the first evidence that stria terminalis projections from the amygdala to the BNST support the processing of individual fear-evoking stimuli, and specifically in regulating selective orienting response toward threat. The framework suggested by these observations posits a specific role of basolateral amygdala projections to the central amygdala nucleus in detecting threat, whereas projections to the BNST via the stria terminalis play a role in evaluation of potential threats. The role of the BNST in selective orienting toward threat appears to be independent of its role in anxiogenesis. It is tentatively suggested that the function of the BNST in anxiogenesis may be modulated by amygdalar efferents in the ventral amygdalofugal pathway.

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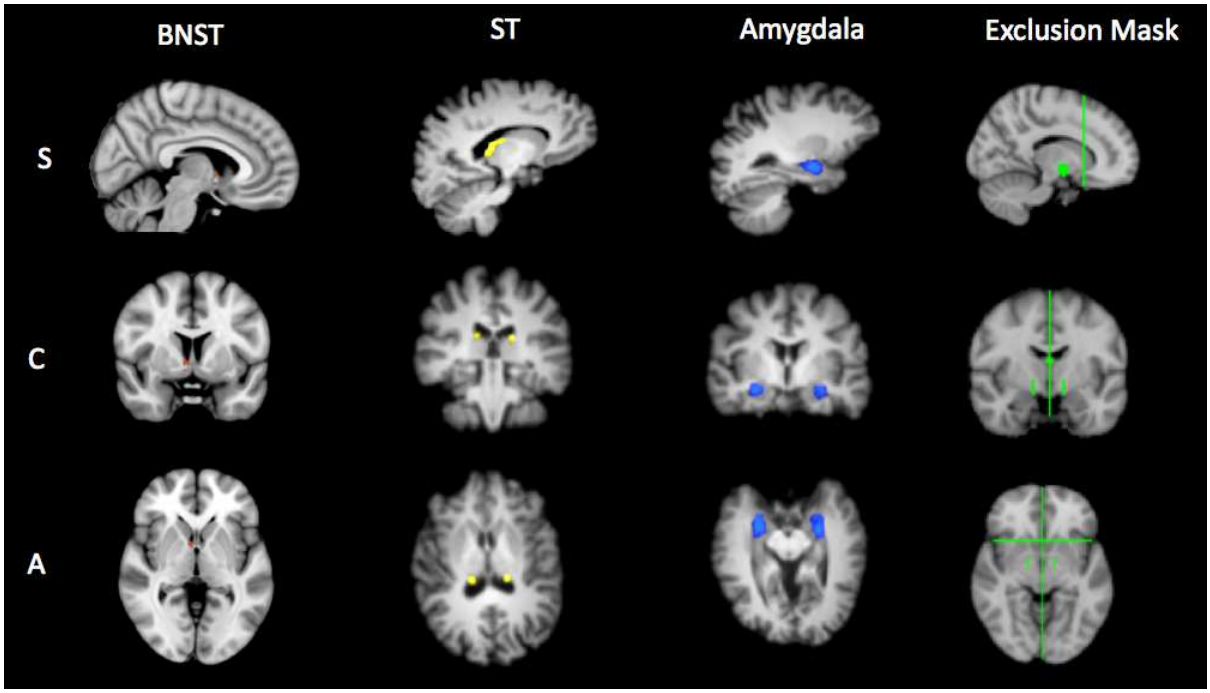

Fig. 1a. Masks employed during virtual dissection of the stria terminalis with probabilistic DTI tractography. Tracts were generated from an amygdala seed mask (shown in blue) with

the use of a waypoint mask drawn on the stria terminalis along its trajectory adjacent to the lateral ventricle between the body of the caudate and the anterior nucleus of the thalamus (shown in yellow), and with the use of a target and termination mask in the bed nucleus of the stria terminalis (shown in red). Regions of exclusion are presented in green. Masks are presented in the saggital (top row), coronal (middle row) and axial (bottom row) views. S = saggital, C = coronal, A = axial.

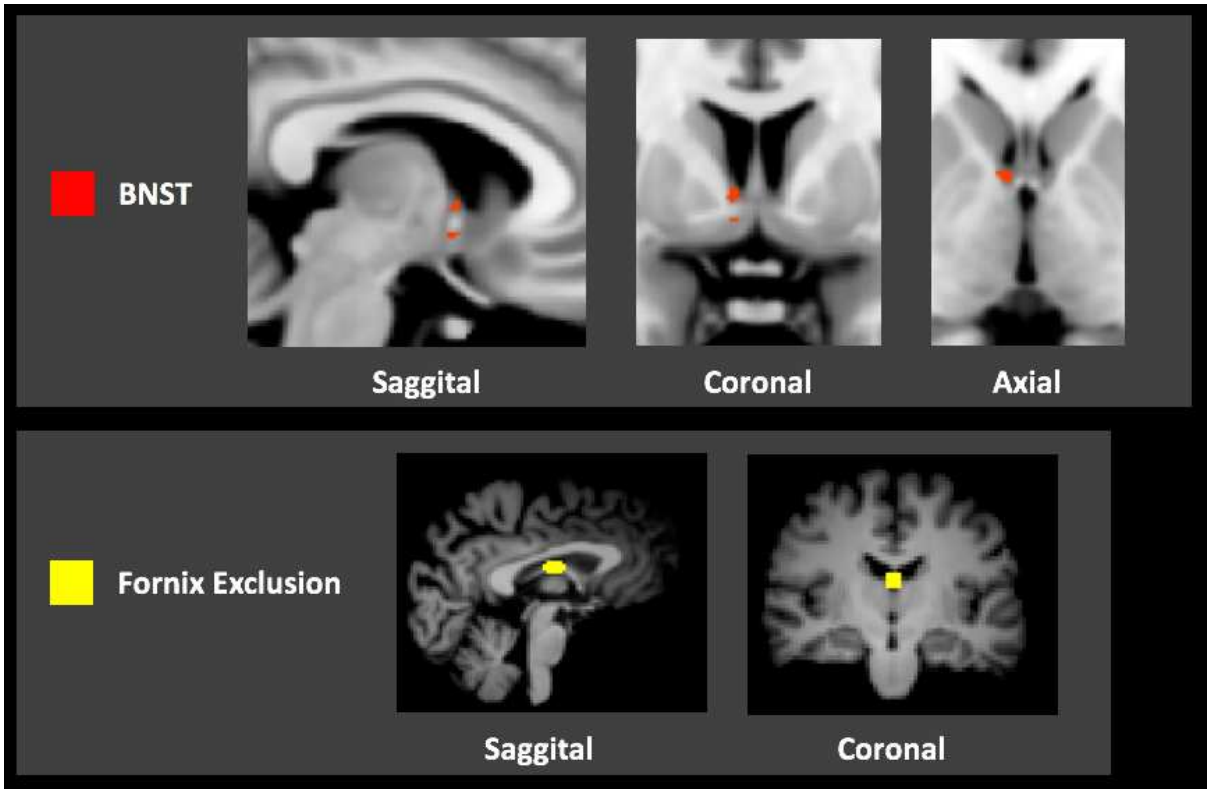

Fig. 1b. Close up views of bed nucleus of the stria terminalis mask (red) in saggital, coronal and axial planes; fornix exclusion mask (green) in saggital and coronal views.

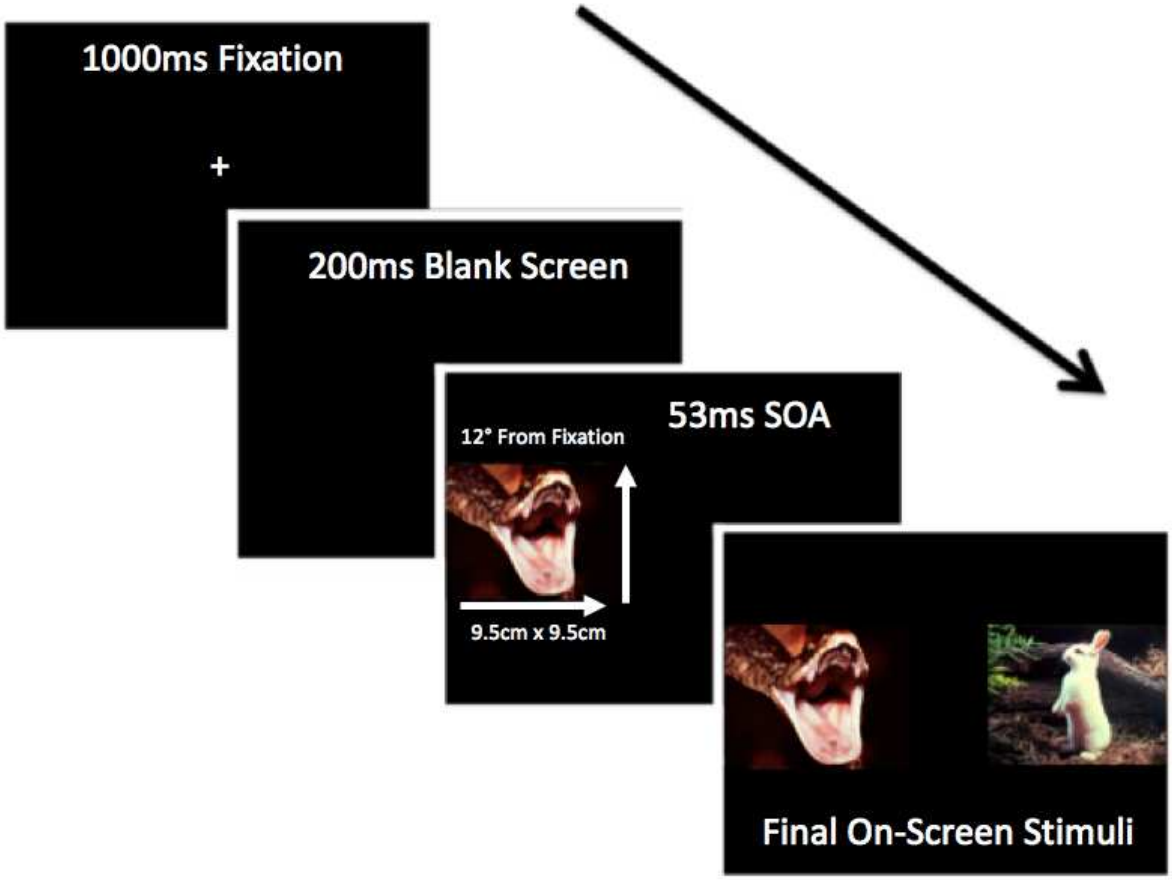

Fig. 2. Example of a typical trial sequence during the temporal order saccade decision task. Trials were preceded by an inter-trail interval of 1000ms (not shown).

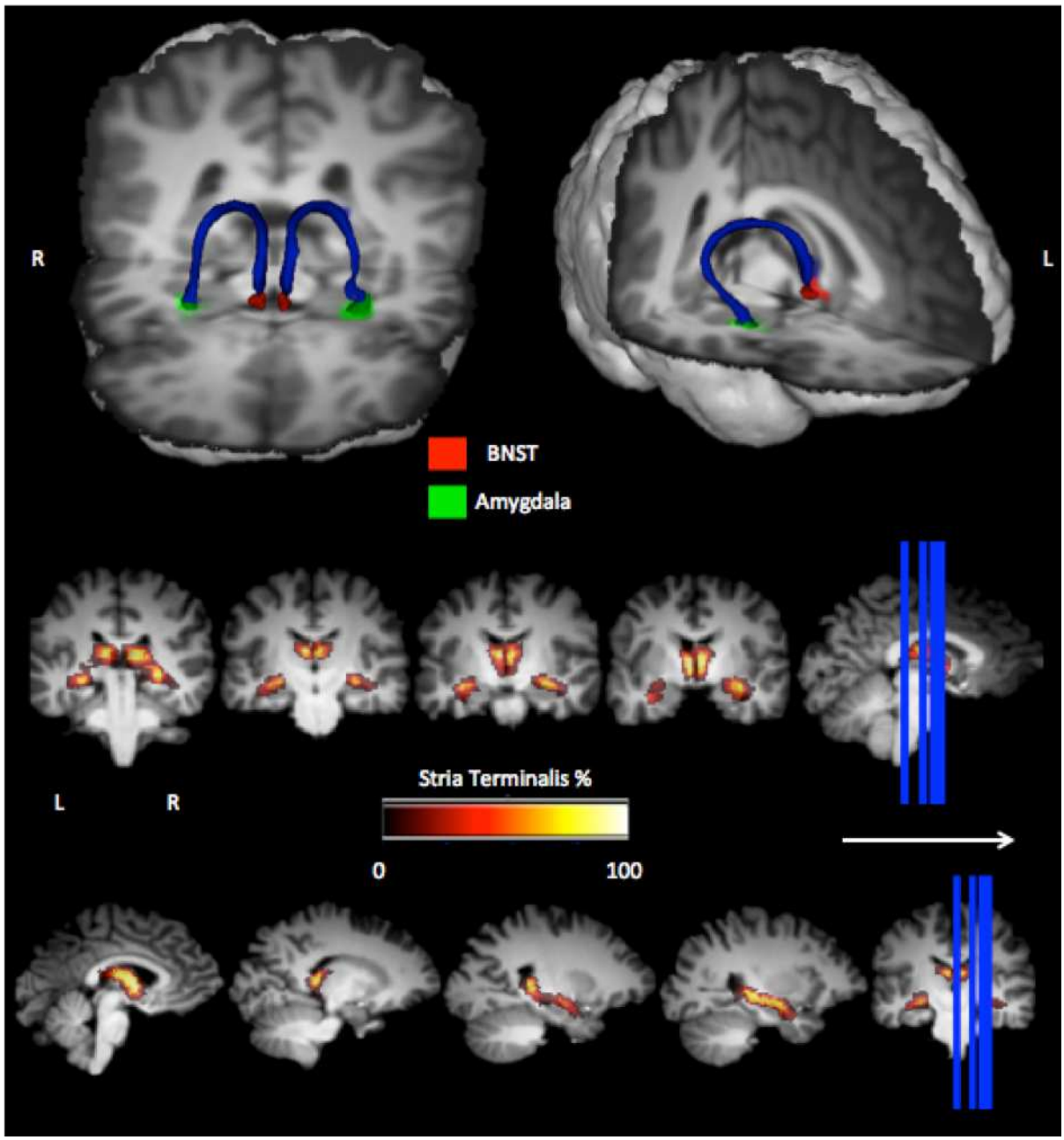

Fig. 3. Probabilistic tractography of the stria terminalis in the healthy human brain (N=19). Top: Composite 3D reconstruction (shown in blue, thresholded) of connection between the bed nucleus of the stria terminalis (shown in red) and the amygdala (shown in green), composited of tracts from each participant registered to a common brain space. Coronal (middle) and sagittal (bottom) slices demonstrate the unthresholded composite streamline for all participants with a colour scale indicating the proportion of participants in whom the streamline passed through the same voxels.

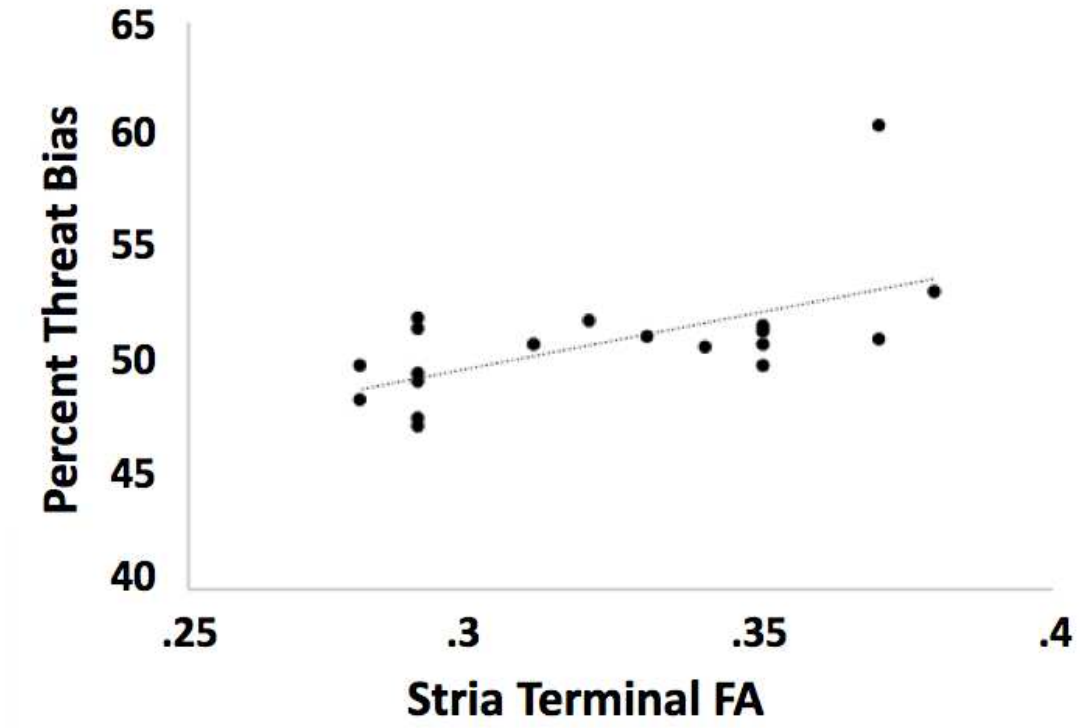

Fig. 4. Microstructure of stria terminalis (FA) as predictor of bias to threatening stimuli (r = .59, p =.008, slope = 49.98).

Table 1. Microstructure of stria terminalis as predictor of bias to threat

	β	*SE*	*Z-score*	*p*
Threat Bias (Intercept)	-0.49	0.2	-2.44	0.015
Stria Terminalis FA	1.62	0.62	2.63	<0.009

Table 2. Trait anxiety and microstructure of stria terminalis as predictors of bias to threat

	β	*SE*	*t*	*p*
Threat Bias				
	-2.56	1.11	-2.31	0.02
Stria Terminalis FA				
	8.23	3.6	2.29	0.02
Trait Anxiety				
	0.05	0.03	1.89	0.06