J Biosci Vol. 43, No. 5, December 2018, pp. 877–886
DOI: 10.1007/s12038-018-9800-3

Trait anxiety and neural efficiency of abstract reasoning: An fMRI investigation

Shilpi Modi, Mukesh Kumar, Sanjeev Nara, Pawan Kumar and Subash Khushu*
Institute of Nuclear Medicine and Allied Sciences (INMAS), Lucknow Road, Timarpur, Delhi 110 054, India

**Corresponding author (Email, skhushu@yahoo.com)*

MS received 16 December 2017; accepted 9 July 2018; published online 28 September 2018

Worries preoccupy the working memory capacity in anxious individuals, thereby affecting their performance during tasks that require efficient attention regulation. According to the attentional control theory (ACT), trait anxiety affects the processing efficiency, i.e. the effort required for task performance, more than the accuracy of task performance. We investigated the relation between trait anxiety and neural response for a reasoning task in healthy subjects. Functional magnetic resonance imaging (fMRI) was carried out on 22 healthy participants and blood oxygenation level dependent (BOLD) contrast estimates were extracted from *a priori* regions of interest (ROIs) that were earlier implicated in reasoning (i.e., bilaterally caudate head, globus pallidus, thalamus, prefrontal cortex [rostral, dorsal and ventral regions], inferior parietal lobule and middle occipital gyrus). Controlling for the effects of age, gender, state anxiety and depressive symptoms, for equivalent levels of task performance, trait anxiety of the participants was found to be associated with an increase in task related BOLD activation in right globus pallidus, left thalamus and left middle occipital gyrus. Our results suggest a reduced processing efficiency for reasoning in high trait anxiety subjects and provides important brain–behaviour relationships with respect to sub-clinical anxiety.

Keywords. Attentional control theory; globus pallidus; STAI; thalamus

1. Introduction

Anxiety can interfere with many dimensions of life, causing a person to be on high alert for potential problems even under the best of circumstances. It is often characterised by behavioral and cognitive consequences such as hyper-responsive amygdale, increased distractibility and attentional bias in favor of threat-related information (Bishop *et al.* 2004; Eysenck *et al.* 2007; Bishop 2008; Berggren and Derakshan 2012). Apart from clinical anxiety, these effects are also present as a personality dimension within the normal population (Eysenck *et al.* 2007). Spielberger's State-Trait Anxiety Inventory (STAI) is a popular measure to assess trait anxiety of individuals (Spielberger 1983). The STAI consists of two scales (20 questions each): Y2, which measures the participants' predisposition to respond anxiously (trait anxiety, a personality dimension), and Y1, which measures how anxious the subject/participant feels at the moment (state). Trait anxiety is a personality dimension and therefore is relatively stable over time. High trait anxiety individuals will experience more intense levels of anxiety than low trait anxiety individuals when subjected to anxiety arousing situations (Spielberger 1983). In contrast, state anxiety is transitory and is a reaction to a threatening situation or stimuli, which generate tension, apprehension and increased physiological response (e.g. increase heart rate) in an anxious person. Both trait and state anxiety have been found to be positively correlated with each other as the intensity of the anxiety felt at a certain situation, i.e. state anxiety, is influenced by the individual's predisposition to anxiety, i.e. trait anxiety. Further, high anxiety trait is particularly prone phenotype for the susceptibility to the adverse effects of stress. It is also a vulnerability factor for the development of various anxiety disorders and depression. Large scale demographic data on anxiety disorders in Indian population is not available. However, according to the reports of Anxiety and Depression Association of America (ADAA), anxiety disorders are the most common mental illness in the US, affecting around 18% of the population costing almost one-third of the country's medical bill (approx. $42 billion a year). Therefore, studying the neural underpinnings of trait anxiety becomes important.

According to the Attentional Control Theory (ACT) proposed by Eysenck *et al.* (2007), anxiety impacts the attentional processes of shifting, inhibition, and updating working memory and might adversely affect the processing efficiency (i.e. accuracy/effort) or response time without significantly affecting the performance effectiveness or accuracy (Eysenck *et al.* 2007). Neuroimaging using functional magnetic resonance imaging (fMRI) provides a measure of

task-related neural activity elicited during cognitive processing (Basten *et al.* 2011). The Blood Oxygenation Level Dependent (BOLD) signal thus serves as an index of neural effort required during task performance with positive BOLD response shown to be related to increased neuronal activity in many earlier studies (Basten *et al.* 2011). An estimate of the efficiency of cognitive processing can be derived by relating the BOLD signal to behavioral performance (Basten *et al.* 2011). Few earlier studies have used fMRI to test the hypotheses of the ACT using color word stroop task (Basten *et al.* 2011), response conflict task (Bishop 2009), or working memory task with distraction (Denkova *et al.* 2010).

According to Englert and Bertrams (2015), worries preoccupy working memory capacity (WMC) in an anxious individual; as a result of which the accessibility of attentional resources required for storing and processing pertinent information in the central executive is reduced. This load on WMC significantly influences the subjects' performance during tasks that require efficient attention regulation such as crisis decision making, performance under pressure, etc. (Englert and Bertrams 2015). Although explored to a lesser extent, fluid reasoning being strongly correlated with WMC is also influenced by trait anxiety. For a series of inferential reasoning tasks, high trait anxiety individuals displayed significantly longer reaction times and lower accuracy scores in comparison to low trait anxious ones (Mayer 1977; Bensi and Giusberti 2007). In a study by Leon and Revelle (1985), the performance of the high trait anxiety group was inferior (both in terms of accuracy and reaction time) to the low trait anxiety group in relaxed condition (non-time-stressed) for an analogical reasoning task. However, in the stressed condition (time-stressed/ego-threatened) they were faster but less accurate. In a study by Bensi and Giusberti (2007), high trait anxiety group displayed a jump-to-conclusion style of decision making, which suggests a tendency to end the task, remove uncertainty and reduce high emotional uneasiness. Few other studies have reported that subjects with high anxiety display comparable performance to that of low anxiety but with an increased response time for reasoning tasks including verbal (Darke 1988), spatial (Markham and Darke 1991) and grammatical (MacLeod and Donnellan 1993; Derakshan and Eysenck 1998) reasoning. However, till date no study has investigated how the neural response while reasoning is modulated by the anxiety trait in healthy participants.

In the present study, we designed an fMRI paradigm for reasoning based on a simple version of the Matrix Reasoning subtest, following an earlier study by Melrose *et al.* (2007). We focused our analyses on regions previously implicated in reasoning. Dorsolateral prefrontal cortex (DLPFC) and regions of the parietal lobe are known to be activated during verbal working memory and visuospatial tasks and hence are also attributed during reasoning (Prabhakaran *et al.* 1997; Christoff *et al.* 2001; Kroger *et al.* 2002). Similarly, rostrolateral PFC (RLPFC) plays an important role in the executive processes of working memory (Prabhakaran *et al.* 1997) and during relational integration (Christoff *et al.* 2001) and is therefore also implicated in reasoning. Melrose *et al.* (2007) showed the involvement of the regions of frontostriatal circuitry in abstract reasoning. We therefore focused our analyses on the following regions previously implicated in reasoning: bilateral DLPFC, RLPFC, VLPFC, inferior parietal lobe, caudate, globus pallidus, thalamus and middle occipital gyrus. We investigated whether the trait anxiety scores of the participants influence the neural response of these ROIs to a reasoning task. Keeping in mind the relation between WMC and reasoning and the reduced processing efficiency hypothesis associated with trait anxiety, we hypothesised an increased neural response in at least a few of the above ROIs as an additional effort by high trait anxious individuals for an equivalent task performance as that of their low trait anxiety counterparts. It was also hypothesized that the neural response for reasoning will be modulated by underlying trait characteristic (reflecting vulnerability to anxiety) of the subjects, even after controlling for their current or state levels of anxiety.

2. Methods

2.1 *Participants*

Twenty-two healthy adults (male – 10, female – 12, mean age – 21.09 years, SD – 1.51 years) were recruited from the authors' home institute using verbal communication explaining the study. The handedness of the participants was assessed using Edinburgh Handedness Inventory (Oldfield 1971). All the participants were right handed. The Hindi version of the Diagnostic Interview for Genetic Studies (DIGS) (version 2) (Deshpande *et al.* 1998) was used to screen the participants for current or past illness. Inclusion criterion included: (1) Participants should be healthy as per Diagnostic Interview of Genetic Studies (DIGS-NIMH1992), (2) Age: 20–30 years, (3) Education up to graduation/ post graduation level. All the experiments were conducted in accordance with the Declaration of Helsinki. All procedures were carried out with the adequate understanding and written consent of the subjects. Formal approval to conduct the experiments described was obtained from Institutional Human Ethics Committee. Participants completed the STAI self-report questionnaires for adults after the fMRI session (Spielberger 1983).

Exclusion criterion included claustrophobia, pregnancy (in case of female subjects), history of any type of substance abuse, stroke, head injury, cardiovascular diseases or hypertension, neurological or psychiatric disorder, any type

of sensory or cognitive impairment. T2-weighted MR images were also assessed for any cortical infarctions. A Beck Depression Inventory (BDI) score above 12 was also an exclusion criterion (Beck *et al.* 1996). None of the subject was on any type of medication. It was ascertained that none of the female subjects were scanned during menstrual/premenstrual period since the hormonal changes in females can result in emotional and physical effects that can aggravate anxiety in them (Sigmon and Schartel 2008).

2.2 *fMRI task paradigm*

A block paradigm based on the study by Melrose *et al.* (2007), with alternating blocks of two conditions: reasoning (activity block) and baseline (control condition) was chosen for the study. The trials in both the conditions consisted of a stimulus phase for 4 s followed by a response phase for 3.5 s. Three pictures were presented simultaneously in one row across the screen during the stimulus phase which was followed by two possible answer choices in the response phase. The subjects' response was recorded using a response grip in each of their hands. The buttons on the left and right were pressed to select the answer on the left and right respectively. During all the trials the phrase 'NEXT?' appeared at the top of the screen.

The stimulus phase consisted of three sequential stimuli in the reasoning trials, whereas in the baseline trials the stimulus phase consisted of the same stimuli in all three positions. The stimulus phase pictures disappeared and two possible answer choices appeared during the response period. In the reasoning condition, the subjects' task was to determine the fourth picture in the sequence (figure 1), while in the baseline condition subject had to perform a matching task by selecting the matching picture between the stimulus and the response phase. The response phase for both the conditions consisted of two answer choices: the correct response and a foil. The line drawings of shapes such as triangles, squares and circles were used as stimuli in the reasoning condition. While designing the stimuli sequences, change along only one visuospatial dimension (size, position, number or shading) was allowed per trial (Carpenter *et al.* 1990; Kroger *et al.* 2002; Melrose *et al.* 2007). The number of trial types that varied across each of the four visuospatial dimensions was kept equal. One of the pictures, either from the presented sequence or a variation along another visuospatial dimension, was used as a foil. A randomly selected stimulus from the reasoning sequences was shown in the baseline trials. Before undergoing the fMRI experiment, all the subjects were thoroughly introduced to the task using sample trials of reasoning and baseline conditions on a laptop.

2.3 *MRI protocol*

Imaging was performed using 3-Tesla whole-body MRI system (Magnetom Skyra, Siemens, Germany) with a 20 channel head and neck coil. The head was supported and immobilized (using foam pads) within the head coil to minimize head movement and gradient noise. Anatomical T1-weighted images were collected using a three-dimensional magnetization-prepared rapid gradient echo (MPRAGE) sequence, with 160 contiguous 1 mm thick

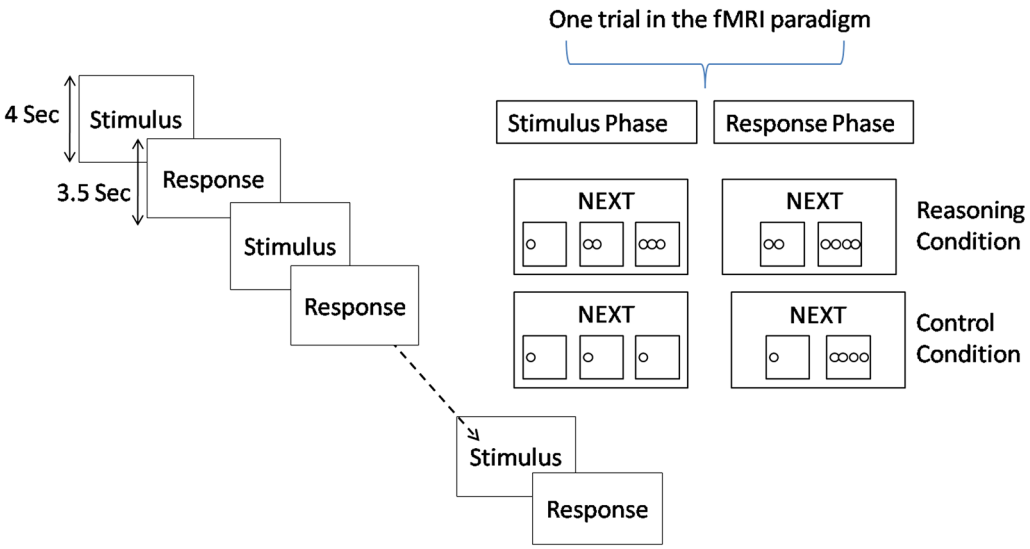

Figure 1. fMRI reasoning task paradigm: Three pictures were presented simultaneously in one row across the screen during the stimulus phase (in both reasoning and control conditions) which was followed by two possible answer choices in the response phase. The participants were cued to determine the next picture in the sequence using the word 'NEXT'.

sagittal slices (echo time [TE]=2.07 ms; repetition time [TR]=1900 ms; field of view [FOV]=256 mm; flip angle=9°; voxel size, 1 × 1 × 1 mm). Functional images were acquired using echo-planar T2*-weighted sequence. Each brain volume consisted of 36 interleaved 3 mm thick slices parallel to AC-PC axis (TE=36 ms; TR=3000 ms; FOV=210 mm; matrix=64×64; flip angle=90°; voxel size=3.28 mm × 3.28 mm × 3 mm).

2.4 *fMRI protocol*

The entire paradigm consisted of two hundred and three sequential image volumes (belonging to six alternating blocks of both the conditions + one additional baseline). The baseline and the reasoning task blocks consisted of 4 and 8 stimuli (and response phases) respectively along with an introductory screen (3 sec) at the beginning of each condition. The duration of each baseline and reasoning block was 33 s and 63 s respectively making the total fMRI acquisition time as10 min and 9 s (total 28 stimuli for baseline condition and 48 stimuli in reasoning condition). NordicActiva and the associated fMRI hardware from NordicNeuroLab were used for stimuli presentation and monitoring the subject's response (accuracy and reaction time) (*http://www.nordicneurolab.com/Products and Solutions/Nordic fMRI solution/index.aspx*).

2.5 *Functional data analysis*

Functional MRI data was processed using SPM8 (Wellcome Department of Cognitive Neurology, London, UK, *http://www.fil.ion.ucl.ac.uk/spm*).The preprocessing steps were carried out as outlined in the manual of SPM8. In brief, fMRI images (after deleting the first baseline block to remove the initial transit signal fluctuations) were first slice time corrected and then they were realigned with each other using first image as the reference image. The translational and rotational movement for all the subjects was within ±1.5 mm or ±1.5° respectively, hence all the 22 participants were included in the analysis. The anatomical image for each participant was co-registered with the mean functional image generated from the realignment step. The registered anatomical images were then segmented to obtain spatial normalization parameters which were subsequently used to normalize the realigned functional images and registered anatomical images to the MNI space. The spatially normalized images were then smoothed with a Gaussian kernel of 6 mm FWHM (full width half maximum). Low frequency signal drift was removed by applying high-pass filter (residual forming matrix with a high-pass filter cut-off period of 128 s (=0.0078 Hz)). The preprocessed data of each subject was analyzed using the General Linear Model (GLM) (Friston and Worksley 2005). Contrast images ('t' statistic map, SPM{t}) were generated for reasoning versus baseline contrast (Family Wise Error (FWE) corrected, $p<0.05$) for each subject. For within group analysis (taking all the subjects together), a one-sample t test was then performed in SPM using the contrast images from the single-subject analyses (FWE corrected, $p<0.05$). The anatomical regions of the activated clusters were determined using SPM Anatomy Toolbox (Eickhoff *et al.* 2005).

2.6 *ROI analysis*

Regions previously implicated in reasoning were taken as *a priori* ROIs (i.e., bilaterally caudate head, thalamus, globus pallidus, RLPFC, DLPFC, VLPFC, inferior parietal lobule, middle occipital gyrus (Broadmann Area(BA) 17/18)). BOLD contrast estimates were extracted from these ROIs (8 mm radius sphere defined on coordinates from Melrose *et al.* (2007) using MarsBaR toolbox of SPM (*http://marsbar.sourceforge.net/*) (see table 1 for coordinates).

Group differences (high vs low trait anxiety) in BOLD contrast estimates of all the ROIs were studied using Multivariate Analysis of COVAriance (MANCOVA). MANCOVA is used to test for significant differences between group when there are more than one dependent variable (BOLD contrast estimates of various ROIs) and where the control of concomitant continuous independent variables i.e.

Table 1. List of *a priori* ROIs and their MNI coordinates

		MNI Coordinates		
Hemisphere	Region	x	y	z
	Subcortical Nuclei			
L	Caudate (head)	−8	14	8
R	Caudate (head)	16	14	6
L	Globus Pallidus	−12	0	−2
R	Globus Pallidus	14	2	−2
L	Thalamus	−10	−8	10
R	Thalamus	22	−30	6
	Frontal Regions			
R	Middle frontal gyrus (RLPFC)	38	60	−4
L	Middle frontal gyrus (RLPFC)	−40	52	−10
R	Middle frontal gyurs (DLPFC)	46	34	18
L	Middle frontal gyrus (DLPFC)	−50	32	26
R	Inferior frontal gyrus (VLPFC)	52	10	34
L	Inferior frontal gyrus (VLPFC)	−42	10	32
	Parietal Regions			
R	Inferior parietal lobule/postcentral gyrus	60	−36	46
L	Inferior parietal lobule	−42	−42	44
	Occipital Regions			
R	Middle occipital gyrus	30	−86	0
L	Middle occipital gyrus	−18	−92	6

MNI: Montreal Neurological Institute.

covariates is required. Covariates are added to reduce error terms and so that the analysis eliminates the covariates' effect on the relationship between the independent grouping variable and the continuous dependent variables. Anxiety group (high trait anxiety (n=12; STAI-Y2 score=40–57) vs low trait anxiety (n=10; STAI-Y2 score=24–39)) and BOLD contrast estimates were analysed in all the regions of interest with MANCOVA in SPSS (version 15.0, SPSS Inc, Chicago, IL, USA). Age, gender, STAI-Y1 (state anxiety) scores and BDI scores were taken as covariates of no interest. Here, state anxiety was partialled out (by adding it as a covariate) to prove the hypothesis that trait anxiety modulates the neural response for reasoning even when the effect of current or state levels of anxiety is negated. Bonferroni correction was applied to adjust for multiple comparisons. Partial correlation analysis between BOLD contrast estimates in all the ROIs and trait anxiety scores of the subjects (n=22) was also carried out with the assumption that there was no correlation between them (Ho=0). Partial correlation was carried out to measure the strength and direction of a linear relationship between two continuous variables (BOLD contrast estimates of various ROIs and trait anxiety scores of the subjects) whilst controlling for the effect of one or more other 'covariates' or 'control' variables. Age, gender, STAI-Y1 scores and BDI scores were taken as covariates. p-Values of ≤ 0.05 were considered to be significant.

3. Results

3.1 *Behavioral data*

None of the participants met criteria for any mental health disorder as assessed by the DIGS. The self-report measures for the subjects are: state anxiety score (STAI-Y1)=37.41±10.8 (range 21–64), trait-anxiety score (STAI-Y2)=41.32±9.40 (range 24–57), BDI=9.23±2.41 (range 3–12). The scores were well within the range defined for healthy population (Kim *et al.* 2011; Spielberger 1983). State and trait anxiety of the subjects was positively correlated with each other (r=0.444, p<0.039, 2-tailed). No gender related differences were obtained in any of the self-report measures (STAI-Y1: males: 37.00±13.18, females: 37.75±8.96, p=0.876; STAI-Y2: males: 41.00±9.27, females: 41.58±9.90, p=0.889; BDI: males: 9.50±2.32, females: 9.08±2.68, p=0.704).

Following the earlier neuroimaging studies on trait anxiety (Bishop *et al.* 2004; Bishop 2008; Basten *et al.* 2011; Basten *et al.* 2012), the subjects were categorised into two groups by median splitting their trait anxiety scores: low trait anxiety group (trait anxiety scores 24–39; mean±SD=33.1±3.75; male – 5, female – 5) and high trait anxiety group (trait anxiety score 40 and above; mean±SD=48.17±6.67; male – 5, female – 7). The two groups differed significantly in their trait anxiety scores (p<0.001). There was no significant difference in the reaction time (Reasoning phase: High trait anxiety group: 1397.8±154.77 ms; low trait anxiety group: 1358.3±172.08 ms; p=0.577 and Baseline phase: High trait anxiety group: 746.28±92.08 ms; low trait anxiety group: 791.99±127.28 ms; p=0.340) and accuracy (Reasoning phase: High trait anxiety group: 80.56±11.80%; low trait anxiety group: 84.17±6.96%; p=0.405 and Baseline phase: High trait anxiety group: 98.81±1.76%; low trait anxiety group: 98.21±2.53%; p=0.523) between the two groups.

3.2 *fMRI*

3.2.1 *Within-group analysis:* Significant activation was obtained bilaterally in superior and middle occipital gyrus, superior and inferior parietal lobule, precentral gyrus, inferior frontal gyrus and left supplementary motor area (see figure 2 and table 2 for details. For illustrative purposes, in figure 2, the activation map is thresholded at p<0.05, False Discovery Rate (FDR) corrected).

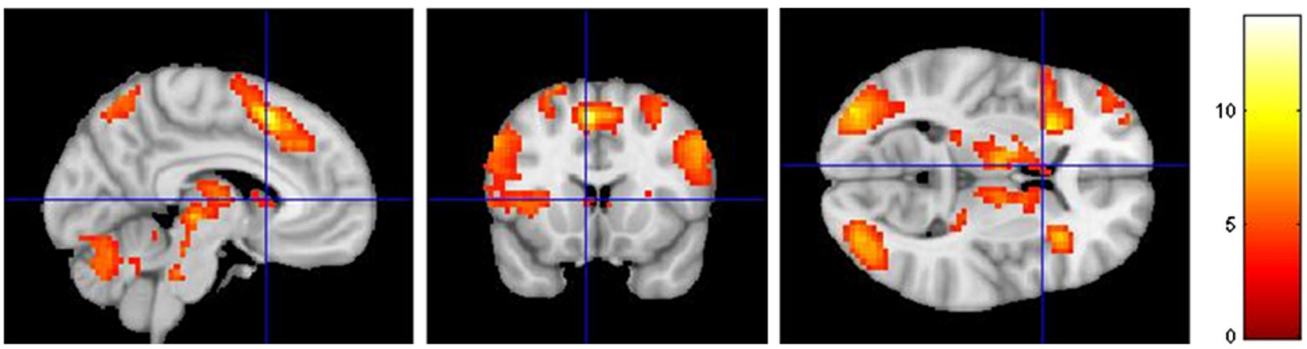

Figure 2. Whole brain activation map for one sample t-test overlaid on MNI152_T1_brain template provided in SPM8. Activation maps are displayed at p<0.05, FDR corrected.

Table 2. Significant regions of activation for Reasoning>Reasoning Control contrast

Hemisphere	Localization of peak voxels	MNI Coordinates of the peak voxel			Z value (peak voxel)	Cluster size (no. of voxels)
L	Inferior parietal lobule	−36	−49	52	6.97	1011
	Superior occipital gyrus	−24	−67	28	6.91	
	Middle occipital gyrus	−30	−76	28	6.62	
R	Middle occipital gyrus	33	−70	31	6.45	849
	Inferior temporal gyrus	48	−55	−11	6.2	
	Fusiform gyrus (hOC4v (V4))	39	−70	−14	6.12	
L	Precentral gyrus (BA 44)	−45	5	40	6.77	115
	Inferior frontal gyrus (p. Opercularis) (BA 44)	−48	8	28	5.61	
	Precentral gyrus (BA 6)	−51	−1	49	5.07	
L	Supplimentary motor area (BA 6)	−6	14	52	6.45	70
L	Superior frontal gyrus (BA 6)	−24	−1	58	6.38	61
	Middle frontal gyrus (BA 6)	−27	8	64	5.39	
R	Inferior frontal gyrus (p. Opercularis)	51	8	22	6.09	58
R	Middle frontal gyrus	30	5	55	5.89	56
	Superior frontal gyrus	33	5	65	5.66	
L	Inferior frontal gyrus (p. Triangularis) (BA 44)	−42	23	28	5.9	52
	Middle frontal gyrus (BA 45)	−45	23	40	5.27	
L	Insula lobe	−30	23	1	6.23	51
L	Thalamus (Th-Temporal)	−9	−13	13	5.45	35
	Thalamus (Th-Prefrontal)	−12	−25	13	5.3	
R	Cerebellum (Lobule VI (Hem))	9	−73	−23	5.49	10

This table able lists significant areas of activation ($p<.05$, FWE corrected across the whole brain, extent threshold 5 voxels)

MNI: Montreal Neurological Institute; BA: Brodmann Area; R: right; L: left.

3.2.2 *ROI analysis:* The overall F statistic (indicating that we are comparing to an F-distribution (F-test)) in MANCOVA showed that the group (high/low trait anxiety) had no significant effect on ROI BOLD signals (Wilk's Lambda=0.038, F (16, 1)=1.565, p=0.564, partial $\eta^{2=}$0.962). The univariate results showed that the contrast estimates of BOLD response in DLPFC (bilaterally) were higher in high trait anxiety group (n=12) as compared to low trait anxiety group (n=10) (right DLPFC: F(1, 16)=4.602, p=0.048, partial $\eta^{2=}$0.223; Left DLPFC: F(1, 16)=7.838, p=0.013, partial $\eta^{2=}$0.329) (see table 3, figure 3a and b). However, the observed power for the analysis (the probability that the test correctly rejects the null hypothesis (H0) when a specific alternative hypothesis (H1) is true) was low (right DLPFC: 0.522 and left DLPFC: 0.748). MANCOVA results have insufficient power (<0.80) to claim that the result obtained is statistically significant.

A significant positive relationship between trait anxiety scores and BOLD contrast estimates was obtained in right globus pallidus (n=22, r=0.453, p<0.030), left thalamus (n=22, r=0.420, p<0.041) and left middle occipital gyrus (n=22, r=0.418, p<0.042) (see figure 4a–c). A trend towards correlation was obtained in left globus pallidus (n=22, r=0.351, p<0.076) and left DLPFC (n=22, r=0.380, p<0.060). Neural activation to performing a reasoning task increased as a function of trait anxiety scores in each of the above regions.

4. Discussion

Ours is one of the few reports that used fMRI to test the processing efficiency of cognitive tasks in relation to the trait anxiety of the subjects. A positive association obtained between BOLD activation (in few of the *a priori* regions of interest) and trait anxiety suggests an increased neural effort required by high trait anxious individuals in order to maintain equivalent level of task performance to that of their low anxiety trait counterparts.

Anxiety is associated with deficits in attentional control and it interferes with the central executive functions such as inhibition and shifting. This has a deleterious effect on the WMC and processing efficiency of high trait anxiety individuals (Eysenck *et al.* 2007; Berggren and Derakshan 2012). Fluid reasoning has also been shown to be strongly correlated with WMC (Chuderski and Necka 2012). In the present fMRI study, we studied the neural activity in *a priori* regions of interest that have been earlier implicated in reasoning. The overall multivariable model was not significant suggesting that the groups (high and low trait anxiety) had a non-significant effect on the ROI BOLD signals. However, univariate analysis suggests an increased BOLD activity in DLPFC (bilaterally) in high anxiety group as compared to low anxiety group (though with insufficient power). On partial correlation analysis, BOLD activity in right globus pallidus, left thalamus and left middle occipital gyrus was

Table 3. BOLD contrast estimates in different ROIs for the high and low trait anxiety groups

	Experimental group				
	High trait anxious Mean (SD)	Low trait anxious Mean (SD)	P value[a]	Observed power[b]	Partial η^2
L Caudate Head	0.168 ± 0.18	0.157 ± 0.29	0.173	0.269	0.113
R Caudate Head	0.110 + 0.18	0.084 + 0.22	0.095	0.384	0.164
R RLPFC	0.311 + 0.25	0.185 + 0.42	0.474	0.106	0.032
L RLPFC	0.355 + 0.39	0.293 + 0.32	0.916	0.051	0.001
R DLPFC	0.482 + 0.36	0.278 + 0.31	0.048	0.522	0.223
L DLPFC	0.524 + 0.25	0.360 + 0.28	0.013	0.748	0.329
R VLPFC	0.829 + 0.42	0.775 + 0.56	0.814	0.056	0.004
L VLPFC	0.686 + 0.22	0.590 + 0.48	0.346	0.150	0.056
R IPL	−0.002 + 0.29	0.009 + 0.36	0.838	0.054	0.003
L IPL	0.845 + 0.48	0.718 + 0.34	0.264	0.193	0.077
R MOG	0.625 + 0.31	0.549 + 0.32	0.278	0.185	0.073
L MOG	0.196 + 0.35	0.161 + 0.32	0.086	0.405	0.173
L Global Pallidus	0.156 + 0.10	0.100 + 0.15	0.264	0.193	0.077
R Global pallidus	0.092 + 0.15	0.043 + 0.15	0.118	0.342	0.146
L Thalamus	0.254 + 0.21	0.195 + 0.11	0.126	0.329	0.140
R Thalamus	0.125 + 0.17	0.143 + 0.11	0.682	0.068	0.011

[a] With age, sex, BDI scores, Y1 scores as covariates of no interest.

[b] Computed using alpha=0.05.

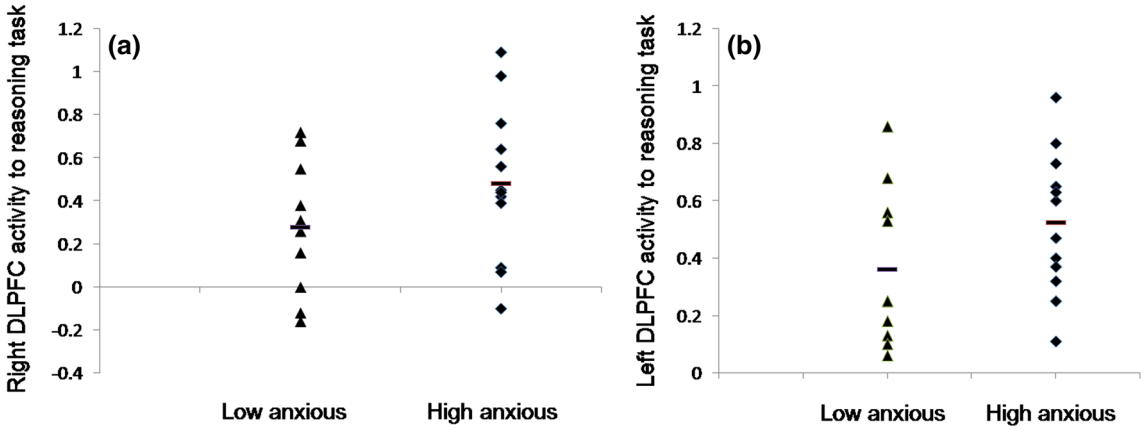

Figure 3. Dorsolateral prefrontal cortex (DLPFC) activity to a reasoning task and anxiety level. Participants were divided into low- and high-trait anxious groups using a median split on STAI trait anxiety scores. DLPFC activity is the contrast estimate for the peak voxel from (**a**) right DLPFC ROI (x, y, z=46, 34 18) and (**b**) left DLPFC ROI (x, y, z=−50, 32 26).

found to be positively related with trait anxiety of the subjects.

DLPFC has been known to play a major role in problem solving and working memory, with its anterior regions being activated in reasoning and problem solving tasks that require branching between multiple goals, exploiting analogous relationships or integration of multiple constraints (Kroger *et al.* 2002). The study by Kroger *et al.* (2002) showed that increasing relational complexity and task difficulty both led to an increased activation in DLPFC. However, anterior left prefrontal cortex was selectively activated with high levels of relational complexity as compared to task difficulty. A trend towards an increased BOLD activity in high trait anxious individuals in our subject group might suggest an increased neural effort required by them for equivalent task performance as that of low trait anxiety individuals, as no difference in the response times or response accuracy between the two groups was obtained.

Further, on correlating the BOLD activity in ROIs with the trait anxiety scores of the subjects, a positive relationship was obtained in right globus pallidus, left thalamus and left middle occipital gyrus. BOLD activity in left DLPFC also showed a positive correlation with trait anxiety levels but with marginal significance. The basal ganglia interact with the frontal cortex through a series of interconnections in the form of multiple parallel loops (Alexander *et al.* 1986). The

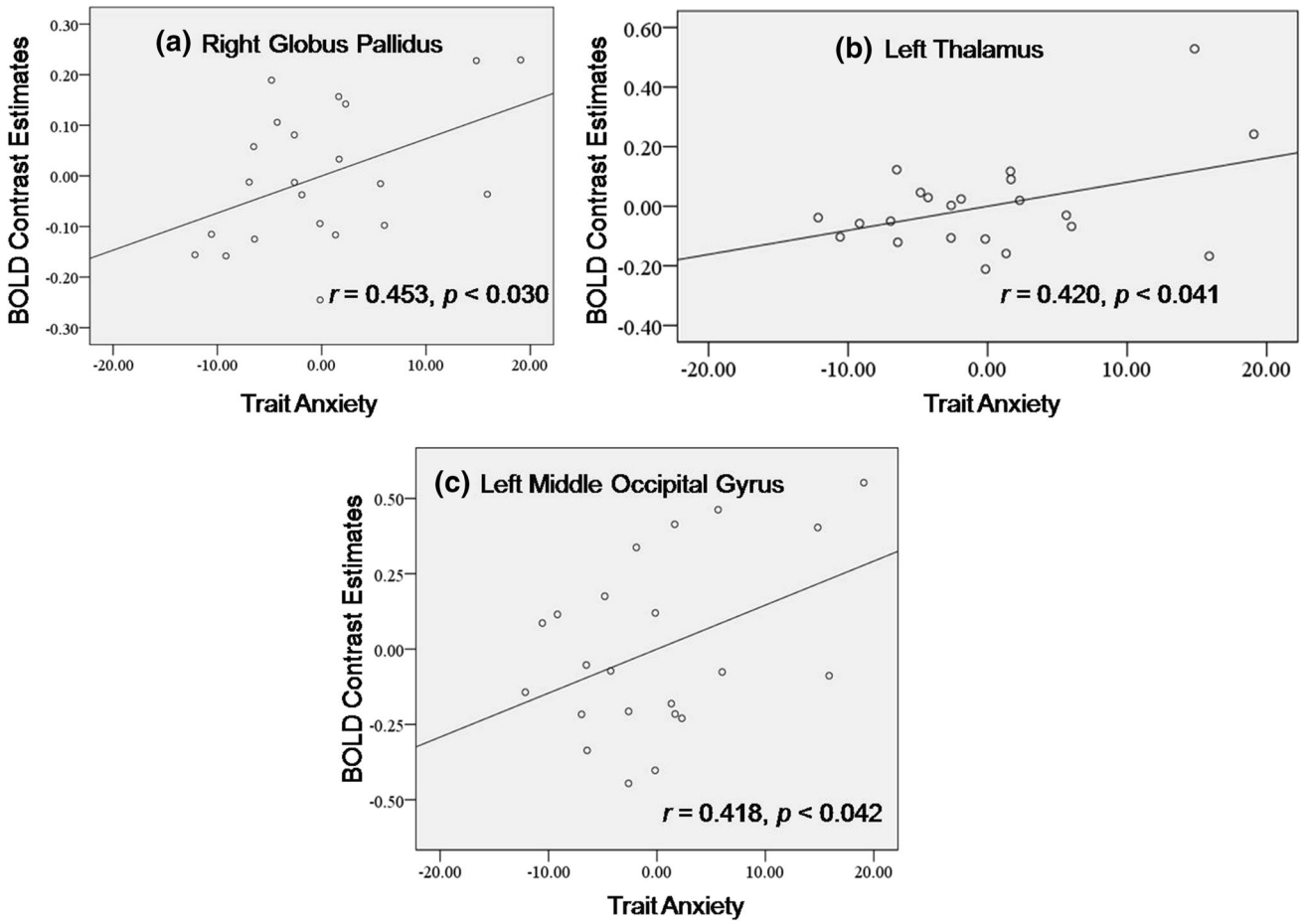

Figure 4. Within the (**a**) right globus pallidus, (**b**) left thalamus and (**c**) left middle occipital gyrus ROIs, the BOLD contrast estimates associated with reasoning vs control contrast showed a positive correlation with participant's trait anxiety. Age, Sex, BDI scores and state anxiety scores were taken as covariates no interest.

individual loops are involved in distinct behavioral functions depending on the cortical areas subserved by these loops (Leisman and Melillo 2013). Basal ganglia seem to play a pivotal role in implicit automation of the serial information processing at the cortical sites. It also acquires and updates information in context of the sequence and thus fascilitates the selection of the most appropriate response (Peigneux *et al.* 2000). It has been earlier shown to be activated during sequencing tasks such as the Serial Reaction Time task and semantic event sequencing task (Tinaz *et al.* 2006; Melrose *et al.* 2007). Therefore, basal ganglia activation might also be associated with reasoning task that involves the detection of a sequence rule. The globus pallidus is the primary output nuclei of the basal ganglia that supports the selective updating of information within working memory (Tinaz *et al.* 2006). The increased activity in globus pallidus in relation to trait anxiety of the subjects might be attributed to the greater effort required for successive updating of the elements of the sequence while performing the experimental task.

Thalamus has been known to be the primary site of relay for the sensory pathways, cerebellar and basal ganglia inputs to the cerebral cortex. Further, thalamus receives a reciprocal connection from the cerebral cortex whereby the cortex can modify thalamic functions. Thalamus subserves various functions such as sensory, motor and limbic functions by means of its various component nuclei. The thalamus mediates frontal–subcortical interactions and thus, is an important part of a functional system involved in executive functions (Tuchscherer *et al.* 2010). In a morphometric study on temporal lobe epilepsy patients it was found that the performance on measures of executive functioning evaluated 4 years later could be significantly predicted by baseline total thalamic volume, thereby showing a close link between thalamic volumes and executive performance. Thalamus is also a key component of the brain circuitry involved in active vision (Wurtz *et al.* 2011). Lateral geniculate nucleus (LGN) which is also called the sensory relay nucleus of the thalamus, transfers the visual information received by the retinal receptors from the outside world to primary visual

cortex (V1 or striate cortex) (Wurtz *et al.* 2011). The internally-generated information that governs the neuronal mechanisms underlying both visual perception and the visual control of movement, reaches the cortex via the higher order thalamic nuclei (Wurtz *et al.* 2011).

The BA 17 has been shown to be activated while performing 'copying' task that required making comparisons among visual images (Ferber *et al.* 2007) and in updating the contents in the working memory (Roth and Courtney 2007). It has also been known to be involved in attention shifting (Makino *et al.* 2004) and selective attention (Hahn *et al.* 2006; Yeh *et al.* 2007). Similarly, extrastriate cortical areas (BA 18) have been widely implicated in reasoning tasks (Jung and Haier 2007). A correlation between scores on Wechsler Scales and the gray matter volume or the cortical thickness in BA18 and BA19 has also been reported (Colom *et al.* 2006; Shaw *et al.* 2006).

Our correlation analysis findings, thus suggest a possibly stronger engagement of sensory pathways as well as visual encoding, visual information analysis and attention systems in high trait anxiety individuals thereby providing a plausible physiological mechanism by which they might exhibit comparable performance as that of low trait anxious individuals. The increased neural activity in the obtained ROIs might subserve a compensatory mechanism for equivalent task performance in high trait anxious individuals.

The findings are in line with an earlier study by Fales *et al.* (2008) that showed stronger task-related activation in a cognitive control network comprising prefrontal and parietal cortical regions for high-anxiety subjects during the performance of a demanding verbal 3-back working memory task although no performance decrements were observed in the subjects. The authors interpreted this study as support for the processing efficiency hypothesis. Similarly, in another study by Basten *et al.* (2011), a stronger task related activation was obtained in high anxious individuals in DLPFC regions while performing an affectively neutral Stroop task. Authors suggested that a general attentional control deficit leads to reduced neural processing efficiency in anxious individuals. Basten *et al.* (2012) further showed that for the manipulation of affectively neutral verbal information held in working memory, high- and low-anxious individuals did not differ in their behavioral performance, yet trait anxiety was positively related to the neural effort (as measured by BOLD signal changes in fMRI) required for task processings.

4.1 *Limitations and conclusion*

Our study also has a few limitations that are listed below. First, the sample size is small, owing to which our results should be considered as preliminary. Future studies with a larger sample size are therefore needed to generalize the findings. Second, the use of a large number of ROIs as dependent variables in MANCOVA might have resulted in the reduced power as obtained. Third, the study would have been further benefited if the personality measures such as neuroticism (using NEO Personality Inventory Revised (NEO-PI-R) questionnaire, Costa and McCrae 1992) were also assessed. However, despite these limitations, this is one of the few published fMRI studies in healthy individuals to assess how trait anxiety modulates the neural responses to a reasoning task. The study, though preliminary, provides newer insight into the physiological mechanisms associated with sub-clinical trait anxiety.

Acknowledgements

This work was supported by DRDO R&D Project No. INM 311 (4.1). The authors declare no competing financial interests. The authors thank Mr. Pawan Kumar for his assistance in data collection.

References

Alexander GE, Delong MR and Strick PL 1986 Parallel organization of functionally segregated circuits linking basal ganglia and cortex. *Annu. Rev. Neurosci*. **9** 357–381

Basten U, Stelzel C and Fiebach CJ 2011 Trait anxiety modulates the neural efficiency of inhibitory control. *J. Cognitive Neurosci*. **23** 3132–3145

Basten U, Stelzel C and Fiebach CJ 2012 Trait anxiety and the neural efficiency of manipulation in working memory. *Cogn. Affect. Behav. Neurosci*. **12** 571–588

Beck AT, Steer RA, and Brown GK 1996 *Beck depression inventory: Manual* 2nd edition (San Antonio, TX: The Psychological Corporation)

Bensi L and Giusberti F 2007 Trait anxiety and reasoning under uncertainty. *Pers. Individ. Dif*. **43** 827–838

Berggren N and Derakshan N 2012 Attentional control deficits in trait anxiety: Why you see them and why you don't. *Biol. Psychol*. **92** 440–446

Bishop SJ 2008 Trait anxiety and impoverished prefrontal control of attention. *Nat. Neurosci*. **12** 92–98

Bishop SJ 2009 Trait anxiety and impoverished prefrontal control of attention. *J. Neurosci*. **24** 10364–10368

Bishop SJ, Duncan J, Brett M and Lawlence AD 2004 Prefrontal cortical function and anxiety: controlling attention to threat related stimuli. *Nat. Neurosci*. **7** 184–188

Carpenter PA, Just MA and Shell P 1990 What one intelligence test measures: a theoretical account of the processing in the Raven Progressive Matrices Test. *Psychol. Rev.* **97** 404–431

Christoff K, Prabhakaran V, Dorfman J, Zhao Z, Kroger JK, Holyoak KJ and Gabrieli JD 2001 Rostrolateral prefrontal cortex involvement in relational integration during reasoning. *NeuroImage* **14** 1136–1149

Chuderski A and Necka E 2012 The contribution of working memory to fluid reasoning: capacity, control, or both? *J. Exp. Psychol. Learn. Mem. Cogn*. **38** 1689–710

Colom R, Jung RE and Haier RJ 2006 Distributed brain sites for the g-factor of intelligence in *Neuroimage* **31** 1359–1365

Costa P and McCrae R 1992 Normal personality assessment in clinical practice: The NEO Personality Inventory. *Psychol. Assessment* **4** 5–13

Darke S 1988 Effects of anxiety on inferential reasoning task performance. *J. Person. Soc. Psychol.* **55** 499–505

Denkova E, Wong G, Dolcos S, Sung K, Wang L, Coupland N and Dolcos F 2010 The impact of anxiety-inducing distraction on cognitive performance: a combined brain imaging and personality investigation. *PLOS One* **5** e14150

Derakshan N and Eysenck MW 1998 Working memory capacity in high trait-anxious and repressor groups. *Cogn. Emot.* **12** 697–713

Deshpande SN, Mathur MNL, Das SK, Bhatia T, Sharma SD and Nimgaonkar VL 1998 A Hindi version of the Diagnostic Interview for Genetic Studies. *Schizophr. Bull.* **24** 489–493

Eickhoff S, Stephan KE, Mohlberg H, Grefkes C, Fink GR and Amunts K 2005 A new SPM toolbox for combining probabilistic cytoarchitectonic maps and functional imaging data. *Neuroimage* **25** 1325–1335

Englert C and Bertrams A 2015 Integrating attentional control theory and the strength model of self-control. *Front. Psychol*. **6** 1–6

Eysenck MW, Derakshan N, Santos R and Calvo MG 2007 Anxiety and cognitive performance: attentional control theory. *Emotion* **7** 336–353

Fales CL, Barch DM, Burgess GC, Schaefer A, Mennin DS, Gray JR and Braver TS 2008 Anxiety and cognitive efficiency: Differential modulation of transient and sustained neural activity during a working memory task. *Cogn. Affect. Behav. Neurosci*. **8** 239–253

Ferber S, Mraz R, Baker N and Graham SJ 2007 Shared and differential neural substrates of copying versus drawing: a functional magnetic resonance imaging study. *Neuroreport* **18** 1089–1093

Friston KJ and Worksley KJ 2005 Analysis of fMRI time series revisited again. *Neuroimage* **2** 173–181

Hahn B, Ross TJ and Stein EA 2006 Neuroanatomical dissociation between bottom-up and top-down processes of visuospatial selective attention. *Neuroimage* **32** 842–853

Jung RE and Haier RJ 2007 The Parieto-Frontal Integration Theory (P-FIT) of intelligence: converging neuroimaging evidence. *Behav. Brain. Sci*. **30** 135–154; discussion 154–187

Kim MJ, Gee DG, Loucks RA, Davis C and Whalen PJ 2011. Anxiety dissociates dorsal and ventral medial prefrontal cortex functional connectivity with the amygdala at rest. *Cereb. Cortex*. **21** 1667–1673

Kroger JK, Sabb FW, Fales CL, Bookheimer SY, Cohen MS and Holyoak KJ 2002 Recruitment of anterior dorsolateral prefrontal cortex in human reasoning: a parametric study of relational complexity. *Cereb. Cortex*. **12** 477–485

Leisman G and Melillo R 2013 The basal ganglia: motor and cognitive relationships in a clinical neurobehavioral context. *Rev. Neurosci* **24** 9–25

Leon MR and Revelle W 1985 The effects of anxiety on analogical reasoning: a test of three theoretical models. *J. Person. Soc. Psychol*. **49** 1302–1315

MacLeod C and Donnellan AM 1993 Individual differences in anxiety and the restriction of working memory capacity. *Person. Individ. Dif*. **15** 163–173

Makino Y, Yokosawa K, Takeda Y and Kumada T 2004 Visual search and memory search engage extensive overlapping cerebral cortices: an fMRI study. *Neuroimage* **23** 525–533

Markham R and Darke S 1991 The effects of anxiety on verbal and spatial task performance. *Aust. J. Psychol*. **43** 107–111

Mayer RE 1977 Problem-solving performance with task overload: Effects of self-pacing and trait anxiety. *Bull. Psychon. Soc*. **9** 283–286

Melrose RJ, Poulin RM and Stern CE 2007 An fMRI investigation of the role of the basal ganglia in reasoning. *Brain. Res*. **1142** 146–158

Oldfield RC 1971 The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia*. **9** 97–113

Peigneux P, Maquet P, Meulemans T, Destrebecqz A, Laureys S, Degueldre C, Delfiore G, Aerts J, Luxen A, Franck G, Van der Linden M and Cleeremans A 2000 Striatum forever, despite sequence learning variability: a random effect analysis of PET data. *Hum. Brain. Mapp*. **10** 179–194

Prabhakaran V, Smith JA, Desmond JE, Glover GH and Gabrieli JD 1997 Neural substrates of fluid reasoning: an fMRI study of neocortical activation during performance of the Raven's Progressive Matrices Test. *Cogn. Psychol*. **33** 43–63

Roth JK and Courtney SM 2007 Neural system for updating object working memory from different sources: sensory stimuli or long-term memory. *Neuroimage* **38** 617–630

Shaw P, Greenstein D, Lerch J, Clasen L, Lenroot R, Gogtay N, Evans A, Rapoport J and Giedd J 2006 Intellectual ability and cortical development in children and adolescents. *Nature* **440** 676–679

Sigmon ST and Schartel JG 2008 Anxiety, anxiety disorders and the menstrual cycle; in *Anxiety in health behaviors and physical illness* (eds) MJ Zvolensky and JAJ Smits (New York: Springer) pp 181–204

Spielberger CD 1983 *Manual for the state-trait anxiety inventory* (Palo Alto, CA: Consulting Psychologists Press)

Tinaz S, Schendan HE, Schon K and Stern CE 2006 Evidence for the importance of basal ganglia output nuclei in semantic event sequencing: an fMRI study. *Brain. Res.* **1067** 239–249

Tuchscherer V, Seidenberg M, Pulsipher D, Lancaster M, Guidotti L and Hermann B 2010 Extrahippocampal integrity in temporal lobe epilepsy and cognition: Thalamus and executive functioning. *Epilep. Behav.* **17** 478–482

Wurtz RH, McAlonan K, Cavanaugh J and Berman RA 2011 Thalamic pathways for active vision. *Trends. Cogn. Sci*. **15** 177–184

Yeh YY, Kuo BC and Liu HL 2007 The neural correlates of attention orienting in visuospatial working memory for detecting feature and conjunction changes. *Brain Res.* **1130** 146–157

Corresponding editor: Anant Bahadur Patel