

White matter tracts alterations underpinning reward and conflict processing

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Abstract

Background

Reinforcement sensitivity theory (RST) is proposed as a neurobiological system that eventually led to emotion and motivation-based constructs of personality. Traditionally segmented into the behavioral activation system (BAS) and the behavioral inhibition system (BIS), RST is commonly used to describe personality and behavior. Although there have been studies linking gray matter alterations with BIS/BAS subscales, the role of white matter (WM) integrity is yet controversial. We aimed to investigate the specific WM tracts associated with BIS/BAS scores.

Methods

224 healthy participants (mean age=39.14 ± 20.23, 80 (35.7%) females) were evaluated using the BIS/BAS questionnaire from the LEMON database. Diffusion MRI connectometry (dMRI) was used to investigate the WM correlates of BIS/BAS subscales. Multiple regression models with the covariates of age and gender were fitted to address the correlation of local connectomes with BIS/BAS components.

Results

dMRI connectometry revealed that the QA value of the splenium of the corpus callosum, right cerebellum, middle cerebellar peduncle, and superior cerebellar peduncle, had a significant negative correlation with each BIS/BAS subscale. In contrast, the QA value in the body of the corpus callosum, left cingulum, and right cingulum showed a positive correlation with BIS/BAS subscales.

Conclusion

The integrity of WM in certain tracts may contribute to behavioral activation and inhibition. This finding expands the findings on the neural networks associated with risk-taking and reward-seeking behaviors.

Introduction

Reinforcement sensitivity theory (RST) aims to provide a neurobiological understanding of motivation, emotion, and learning and has been subsequently translated into a framework of personality traits (Gray 1978). RST was initially proposed for examining anxiety and identifying its associated neural underpinnings. Evidence of individual differences in the functioning of these systems eventually led to motivation and emotion-based theory of personality. The original theory proposed two neurobiological systems including the behavioral approach system (BAS) modulating appetitive motivation and the behavioral inhibition system (BIS) modulating aversive motivation. The BAS was sensitive to conditioned reward and related to trait impulsivity. The BIS was sensitive to conditioned aversive and high-intensity stimuli and associated with trait anxiety (Standen et al. 2022). BAS and BIS are therefore two aspects of an approach to describing personality and behavior (Gray 1982). BAS is correlated with cues of reward and the high scores of its subscales are related to measures of extraversion (Carver and White 1994).

Individuals with substance use, attention deficit hyperactivity disorder, bipolar and conduct disorder show higher BAS scores (Franken and Muris 2006; Alloy et al. 2009; Bijttebier et al. 2009). The BIS is correlated with cues of punishment and negative aspects of a goal. Individuals with high scores of BIS are more susceptible to experiencing anxiety (Carver and White 1994) and studies have found that higher BIS scores are related to shyness as a result of anxiety (Ran et al. 2018). Hence, these studies suggest a strong association between BIS/BAS and psychopathologies.

Previous studies have indicated correlations between gray matter (GM) matrices and BIS/BAS scores. One study using structural MRI data, investigating the volume of the hippocampus and amygdala in pathological gambling and its relationship with BIS/BAS scores, reported a correlation between BIS scores of pathological gambling subjects and left amygdala and hippocampal volumes (Rahman et al. 2014). Sensitivity to Punishment scores was positively correlated with GM volumes in the amygdala and hippocampal formation while Sensitivity to Reward scores was negatively correlated with GM volumes in the dorsal striatum and right superior frontal gyrus in another work (Barrós-Loscertales et al. 2006). EEG findings have also suggested a connection between the right executive control network and the BIS, and a connection between the left executive control network and the BAS (Sutton and Davidson 1997; Eddington et al. 2007; Siltan et al. 2011). Conclusively, BAS scores can be related to areas involved in motivation, including mesolimbic and mesocortical pathways including orbital areas of the prefrontal cortex (McClure et al. 2004; Hahn et al. 2009; Simon et al. 2010; Clithero et al. 2011). BAS scores are also associated with areas activated when exposed to fear stimuli, including the hippocampus/parahippocampal cortex and amygdala (Mathews et al. 2004). The relationship between the BIS score and the volume of the right hemisphere areas was of a converse nature with higher BIS scores showing in persons with lower volumes in these areas (Shinagawa et al. 2015). Personality traits that are related to BIS are positively correlated with activity in the amygdala, hippocampus, posterior cingulate cortex, medial hypothalamus, and dorsal prefrontal cortex which activates in response to conflict (Kennis et al. 2013).

More recent investigations on structural properties of WM and behavioral traits in healthy individuals have revealed controversial findings, where some studies have explored the association between WM microstructure and individual differences in reward sensitivity (Bjørnebekk et al. 2012; Xu et al. 2012), while some others were conducted on task-based reward processing (Camara et al. 2010; Samanez-Larkin et al. 2012; Park et al. 2021). In a previous study on WM integrity and measures of BIS/BAS using diffusion tensor imaging (DTI), scores on the Fun-Seeking subscale of the BAS positively correlated with fractional anisotropy (FA) in the left corona radiata and adjacent superior longitudinal fasciculus, and with mean diffusivity (MD) in the left inferior longitudinal fasciculus and inferior frontooccipital fasciculus after controlling for age, gender, and education. While scores on BAS-D and BAS-RR did not show significant correlations with values of any DTI parameters (Xu et al. 2012) even though previous studies reported scores on reward sensitivity negatively correlated with GM values in the striatum and prefrontal cortex (Barros-Loscertales et al. 2006; Gardini et al. 2009). A previous fMRI study on personality differences reported a significant correlation between BAS scores and task-related activity in the lateral prefrontal cortex, anterior cingulate, and parietal cortex while performing a cognitive control

task (Gray et al. 2005). Moreover, functional imaging studies reported that BAS scores correlated positively with reactivity in the left hippocampus/parahippocampal area and insula while HPs viewed erotic and disgusting pictures, respectively (Reuter et al. 2004).

Although there have been many studies linking gray matter (GM) alterations with BIS/BAS scales, the role of white matter (WM) integrity was only scarcely investigated. Research suggested high reward sensitivity and in particular, the BAS-fun subscale reflecting the tendency to seek novel potentially rewarding experiences was related to increased WM metrics within corona radiate and superior longitudinal fasciculus (high FA values), but with lower WM coherence in the inferior fronto-occipital fasciculus and inferior longitudinal fasciculus (high MD values). (Xu et al. 2012). Another study investigating the associations between different WM properties and reward-based performance modulation indicated that WM properties in the corpus callosum, right uncinate fasciculus, left ventral cingulum, and accumbens/ventral striatum tracts were inversely related to reward-triggered performance benefits manifested with faster reaction times. Moreover, smaller WM property values in the corpus callosum, uncinate fasciculus, and accumbens/ventral striatum tracts were associated with higher scores on the BIS scale, reflecting greater sensitivity to potential punishment. An association was also found between functional hemodynamic activity in the ventral striatum and WM microstructure. This study indicated a contradiction regarding the finding that reward-based behavioral benefits are related to lower measures of WM tracts with studies linking higher WM metrics to superior cognitive performance. This research suggested higher susceptibility to motivationally relevant stimuli, which is in line with the current and previous studies reporting inverse relationships between WM properties and motivational traits (Park et al. 2021).

DTI is a promising method that can assess the integrity of the WM by measuring water molecule diffusion in axons (Alexander et al. 2007). Various DTI matrices, particularly FA, were formerly vastly used to investigate the microstructure of cognitive performances and certain psychiatric manifestations (Mayeli et al. 2018). Diffusion magnetic resonance imaging (dMRI) connectometry as an innovative analytical technique enables the evaluation of the WM integrity and exploring the microstructural alteration associated with a variable of interest in whole brain analysis (Yeh et al. 2016). Using water diffusion density instead of diffusion velocity used in DTI is considered to be more accurate, giving dMRI enhanced spatial resolution to characterize WM tracts in areas with kissing or crossing fibers (Yeh et al. 2011). Moreover, dMRI connectometry uses the concept of the local connectome to track patterns of the local connectivity in the fiber pathways instead of merely finding global connectivity patterns at either end, and it identifies the pathways subcomponents that express significant associations with the variable of interest (Yeh et al. 2016). In connectometry, SDF is then converted to a new variable, quantitative anisotropy (QA), which is a density-based index used for further analyses (Yeh et al. 2013a). QA and SDF are used to extract fiber tracts, compute between-group differences analysis, or evaluate the diffusion density association with a variable of interest. Eventually, dMRI connectometry possess significant reduction in false negative results, higher spatial resolution, and lower susceptibility to partial volume effect of connectometry compared to conventional DTI tractography. QA is also less sensitive to the partial volume effect and is a more accurate index for fiber tracking (Yeh et al. 2013b).

Considering the exceptional properties of dMRI connectometry and the abovementioned mixed findings suggest necessitates further clarification of the potential relationship between WM microstructural properties and reward-related processes. To the best of our knowledge, our work is the first to investigate the WM properties underlying behavioral activation and inhabitation using QA with a considerable sample size. We aimed to examine the relationship between Carver and White BIS/BAS questionnaire scores and WM integrity measures, using correlations to address the associations of local connectomes with BIS/BAS components with the covariates of age and gender using QA, as a more accurate fiber-tracking measure.

Materials And Methods

Overview

DTI is an advanced magnetic resonance imaging (MRI) technique that is based on the measurement of the diffusion of water molecules. It provides detailed information about tissue microstructure such as fiber orientation, axonal density, and degree of myelination. Diffusion MRI measures the density of water diffusion through different directions of a voxel. Thus, making it possible to visualize the tract pathways that are associated with our study variables which are the BIS/BAS scales.

Study data

In the current study, we obtained the data from Leipzig Study for Mind-Body-Emotion Interactions (LEMON) dataset. The LEMON study was carried out in four phases between 2013 to 2015 to study mind-body-emotion interactions (Babayán et al. 2019). Participants were recruited via advertisement, leaflets, and information events at the University of Leipzig. Participants were evaluated for exclusion criteria on day 0 of the event in a telephone interview. Participants with uncontrolled hypertension, cardiovascular disease, psychiatric conditions requiring inpatient treatment for longer than 2 weeks within the last 10 years, history of neurological disease (multiple sclerosis, stroke, brain tumor, etc.), and malignant conditions, some particular drug usage (amphetamines, cannabis, opiates, benzodiazepine), any MRI contraindications and also enrollment in any scientific study for the past 10 years were excluded from the study. A total of 227 German-speaking individuals participated and met the eligibility criteria for further evaluation. The participants were asked to complete a 5-day survey, and all enrolled participants were asked to complete: (1) four fMRI and one structural scan in one session; (2) a battery of personality questionnaires; and (3) a set of cognitive and creativity-related tasks. The BIS/BAS questionnaire was completed on the second day of the study.

Participants

Of the 227 individuals in the LEMON study, 225 completed the BIS/BAS questionnaire and were recruited in the study. The study was put through following the World Medical Association Declaration of Helsinki revised in 1989 and approved by the Ethics Committee of the University of Leipzig (Reference Number: 154/13-ff).

BIS/BAS Scale

BIS/BAS scales were developed based on the RST proposed by J. A. Gray (1981, 1982) (Gray 1978; Carver and White 1994). The German version of the BIS/BAS was used to measure the reactivity of the behavioral activation and inhibition, and the approach system in response to reward or punishment. The questionnaire consists of 24 items to measure 3 BAS subscales and one BIS subscale. The BAS subscales include Drive, Reward Responsiveness, and Fun-seeking. BAS Drive (BAS-D) measures the motivation to follow one's goals and four items contribute to this score. BAS Reward Responsiveness (BAS-RR) measures the sensitivity to pleasant reinforcers in the environment and four items contribute to this score. BAS Fun-Seeking (BAS-F) measures the motivation to find novel rewards spontaneously and five items contribute to this score. 7 items contribute to the BIS, which are contributed to the tendency for people to avoid negative outcomes. There are also four fillers in this questionnaire. The items are rated on a 4-point Likert-type response format ranging from 1 (doesn't apply at all) to 4 (completely applies to me) (Strobel et al. 2001).

Image Acquisition and Data Analysis

MRI were obtained using a 3 Tesla scanner (MAGNETOM Verio, Siemens Healthcare GmbH, Erlangen, Germany) and a 32-channel head coil in addition to a multi-band accelerated sequence merged with an in-plane GRAPPA (TR = 7,000 ms, TE = 80 ms, bandwidth = 1,502 Hz/Px, field of view = 220 × 220 mm², GRAPPA acceleration factor = 2, and voxel size = 1.7 × 1.7 × 1.7 mm³) to collect DTI.

The ExploreDTI toolbox was utilized to carry out preprocessing steps (head motion, eddy current distortions, and susceptibility artifacts because of the magnetic field in homogeneity correction) (Leemans et al. 2009). Diffusion data were reconstructed within Montreal Neuroimaging Initiative (MNI) space, using q-space diffeomorphic reconstruction to obtain the Spin Diffusion Function (SDF; the main component of diffusion connectometry) (Yeh et al. 2011). Subsequently, a diffusion sampling length ratio of 1.25 was used.

Diffusion metrics associated with subscales of BIS/BAS were analyzed through diffusion MRI (dMRI) connectometry (Yeh et al. 2016). A multiple regression model was performed to evaluate these subscales. Age and handedness were taken into account in all the analyses to adjust for possible confounding effects. A T-score threshold of 2.5 was defined to delineate local connectomes. A deterministic fiber tracking algorithm was used to estimate WM tracts (Yeh et al. 2013b). After normalization, topology-informed pruning was undertaken to prevent false-positive tracking. Tracks were generated from bootstrap resampling, and a length threshold of 20 voxel distance was utilized to highlight tracks. The seeding number for each permutation testing was set to 100000. A total of 2000 randomized permutations were employed to the group label to obtain the null distribution of track lengths to estimate the false discovery rate (FDR). Lastly, structural connectivity was assessed using QA, which gives a measure of the peak density of water diffusion along the main axes of WM fibers. Higher QA reflects higher structural connectivity and WM microstructural integrity.

Results

Table 1 illustrates the demographic information of 224 participants who underwent this study. The mean age of the study population was 39.14 ± 20.23 years, 144 (64.3%) were male, 200 (88.9%) were right-handed, and 69 (30.7%) were single (Table 1).

Table 1
Demographics of study population (N = 224)

Age		39.14 ± 20.23
Gender	Male	144 (64.3%)
	Female	80 (35.7%)
Handedness	Right-Handed	200 (88.9%)
	Left-Handed	21 (9.3%)
	Ambidextrous	4 (1.8%)
Education Level*	0	1 (0.4%)
	1	7 (3.1%)
	2	41 (18.2%)
	3	175 (77.8%)
Data are presented as mean ± standard deviation or number (percentage)		
*Education Level: 1: elementary school (Hauptschule), 2: secondary modern (Realschule), 3: intermediate modern secondary school/high school (Gymnasium)		

Table 2 shows descriptive BIS/BAS scores and a quantitative comparison based on gender. BAS sub scores regarding the drive, fun-seeking, and reward responsiveness were 11.99 ± 2.07 , 12.26 ± 1.67 , and 16.93 ± 1.95 , respectively, and the BIS score was 19.83 ± 3.10 . Among these, only the BIS score showed a significant difference between the male and female groups (Table 2).

Table 2
BIS/BAS scores based on gender

BIS/BAS Scores	Total	Male	Female	p-value
BAS Drive	11.99 (2.07)	11.95 (2.13)	12.08 (1.96)	0.665
BAS Fun-seeking	12.26 (1.67)	12.32 (1.66)	12.14 (1.68)	0.445
BAS Reward Responsiveness	16.93 (1.95)	16.87 (1.89)	17.04 (2.06)	0.545
BIS	19.83 (3.10)	19.47 (3.10)	20.47 (3.03)	0.022
Data are presented as mean (standard deviation)				

Table 3 shows WM tracts associated with BIS/BAS subscales using QA. The connectometry analysis found splenium of the corpus callosum, right cerebellum, middle cerebellar peduncle, and superior cerebellar peduncle showing negative correlation with BAS-D (FDR = 0.042265), and also found the body of corpus callosum, left cingulum and right cingulum showing positive correlation with BAS-D (FDR = 0.033117). The connectometry analysis also indicated that splenium of the corpus callosum, right cerebellum, and middle cerebellar peduncle negatively correlated with BAS-F (FDR = 0.052641), and the body of corpus callosum, left cingulum, and right cingulum positively correlated with BAS-F (FDR = 0.041446). Additionally, the splenium of the corpus callosum, right cerebellum, middle cerebellar peduncle, and superior cerebellar peduncle showed a negative correlation with BAS-RR (FDR = 0.033739). Regarding BIS score, our results indicated that splenium of the corpus callosum, right cerebellum, middle cerebellar peduncle, and superior cerebellar peduncle negatively correlated with BIS (FDR = 0.049389) and body of corpus callosum, left cingulum, and right cingulum positively correlated with BIS (FDR = 0.055305) (Table 3).

Table 3
White matter integrity using quantitative anisotropy associations with BIS/BAS subscales

White Matter Tracts		
BIS/BAS	Positive	Negative
BAS Drive	Body of corpus callosum	Splenium of corpus callosum
	Left cingulum	Right cerebellum
	Right cingulum	Middle cerebellar peduncle Superior cerebellar peduncle
FDR	0.033117	0.042265
BAS Fun-seeking	Body of corpus callosum	Splenium of corpus callosum
	Left cingulum	Right cerebellum
	Right cingulum	Middle cerebellar peduncle
FDR	0.041446	0.052641
BAS Reward Responsiveness	None	Splenium of corpus callosum Right cerebellum Middle cerebellar peduncle Superior cerebellar peduncle
FDR	None	0.033739
BIS	Body of corpus callosum	Splenium of corpus callosum
	Left cingulum	Right cerebellum
	Right cingulum	Middle cerebellar peduncle Superior cerebellar peduncle
FDR	0.055305	0.049389
FDR: False Discovery Rate		

Discussion

The present study aimed to investigate the association of WM integrity using QA to trait reward responsiveness, impulsivity, drive, and inhibition evaluated with the BIS/BAS questionnaire in healthy individuals. To the best of our knowledge, this is the first dMRI connectometry study to explore brain structures associated with individual differences in personality measures linked to reward responsiveness, impulsivity, drive, and inhibition. QA approach to examining WM integrity benefits several

advantages compared to other DTI models, which include being able to take into account multiple fiber populations within a voxel and taking away the ambiguities of crossing fibers while suppressing partial volume effects with free water and grey matter, and enabling the distinction between microscopic and macroscopic features (Yeh et al. 2013b).

As the present study is the first to utilize QA to examine the link between WM integrity and behavior, the fact that our results are in line with the previous studies lends further support for an association between WM microstructural properties and reward-related behavioral modulations. The implications of these findings will be discussed below.

Our results revealed that the microstructural integrity of the splenium of the corpus callosum is negatively correlated with BAS-D, BAS-F, BAS-RR, and BIS, whereas, the body of the corpus callosum showed a trend towards a positive correlation with BAS-D, BAS-F, and BIS. Therefore, participants with a higher level of reward-seeking traits who are more influenced by novelty and reward to pursue a goal, displayed a higher level of QA in the body of the corpus callosum, however, there is an inverse relationship between reward-seeking traits and QA in the splenium of the corpus callosum. Additionally, participants with more sensitivity to negative aspects of a goal showed a higher level of QA in the body of the corpus callosum and a lower one in the splenium of the corpus callosum. Some previous studies on the relationship between WM microstructure and social reward dependence using DTI measures observed either reduced FA values or increased MD values in individuals with reward-seeking traits in the striatum and multiple frontal regions (Bjørnebekk et al. 2012; Xu et al. 2012). These findings are also in line with high scores in psychometric impulsivity measures, indicating that alterations in the microstructural properties in the corpus callosum affect reward sensitivity (Peper et al. 2013; Sackett et al. 2019), although impulsivity is not directly measured by BIS/BAS.

Moreover, in a recent study aiming to investigate potential associations between WM tracts and performance in a reward-cuing task, a significant reduction in the WM properties value in the corpus callosum in participants who responded faster in the rewarded trial was observed (Park et al. 2021). Based on this task-based study, behavioral facilitation seems to be related to a reduced number of axons across the width of the anterior portion of the corpus callosum. Besides, various studies on alcohol and drug addiction have suggested reduced integrity of the corpus callosum (Kim et al. 2009; Liu et al. 2010). As using QA allows for more specific results, our results on corpus callosum add more details to previous findings on the association between WM integrity and behavioral and motivational traits.

According to our results, the microstructural integrity of either right and left cingulum was positively correlated with BAS-D, BAS-F, and BIS. These results indicate that individuals with higher reward sensitivity are associated with higher integrity in both the right and left cingulum, and individuals with more sensitivity to negative aspects of a goal showed a higher level of QA in these properties. The cingulum bundles connect the cingulate cortex with other limbic areas (Pandya et al. 1981). Since the anterior cingulate and prefrontal cortex have inhibitory effects on limbic areas, more cortical inhibition over limbic areas may lead to behavioral activation and inhibition (Etkin et al. 2011).

In a study, reduced FA values in frontally distributed regions in participants with reward dependency personality traits were observed (Bjørnebekk et al. 2012). In another, similar associations in three uncinate fasciculus, ventral cingulum, and accumbo-frontal tracts were found (Park et al. 2021). According to the previous findings of positive correlations between BIS scores and GM volumes of hippocampus and amygdala (Barrós-Loscertales et al. 2006), better integrity of WM connecting limbic regions would correlate with higher BIS scores. Similarly, BIS score positively correlated to higher integrity in both left and right cingulum bundles in our study. However, some studies did not show significant correlations between BIS scores and any DTI parameters (Xu et al. 2012).

Movement-related structures showing a correlation with BIS/BAS scores were the cerebellum and cerebellar peduncles. Regarding the cerebellum, our results showed a negative correlation between the right cerebellum and each BIS/BAS subscale. The QA value of the middle cerebellar peduncle was negatively associated with BAS-D, BAS-F, BAS-RR, and BIS, and similarly, the QA value of the superior cerebellar peduncle was also negatively associated with BAS-D, BAS-F, and BIS. These results show that individuals with higher reward sensitivity and individuals with more sensitivity to negative aspects of a goal are associated with higher integrity in these tracts. Previously, the cerebellum was only known for involvement in the movement and maintenance of balance and posture, however, recent studies have also suggested that cerebellar tracts to other regions including the prefrontal cortex and posterior parietal cortices might play further cognitive functions and emotion regulation other than movement (Strick et al. 2009). Although studies suggested that stimulating the superior peduncle increases negative feelings in patients (Nashold and Slaughter 1969), in a more recent study, repetitive transcranial magnetic stimulation of the cerebellum mood enhancement was seen (Ferrucci et al. 2012), hence, the results are contradictory. Inconsistent with our finding, a previous study has shown an association between the left middle cerebellum peduncle and anxiety and depression, which indicated a positive correlation between BIS score and this cerebellum peduncle integrity (Hamdy et al. 2022). Again, our results on the cerebellum add more details to previous findings on the association between WM integrity and behavioral and motivational traits due to performing QA analysis. However, the cerebellum's role in behavioral traits is still unknown and controversial, and further studies focused on these regions are warranted.

Conclusion

The present study was the first to employ QA to investigate the underlying WM tracts involved in self-control modulations, reward-related behaviors, and personality traits. As significant correlations between DTI QA in the body and splenium of the corpus callosum, left and right cingulum and cerebellum projectories, and scores of the BIS/BAS subscales were observed, the present study provides evidence showing that the integrity of WM in these brain regions may contribute to behavioral activation and inhibition. This finding expands the previous findings on the neural networks associated with risk-taking and reward-seeking behavior of earlier studies, however, future studies are warranted to increase our knowledge of the areas implicated in individual personality differences. Eventually, it is to be noted that we used the initial version of BIS and BAS, developed based on the original RST, as it was available on LEMON data. Recent updates have suggested that distinguishing between BIS and fight-flight-freeze

system (FFFS) would possess a better psychometric measurement, and future studies are required to consider this distinction (Heym et al. 2008).

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Figures

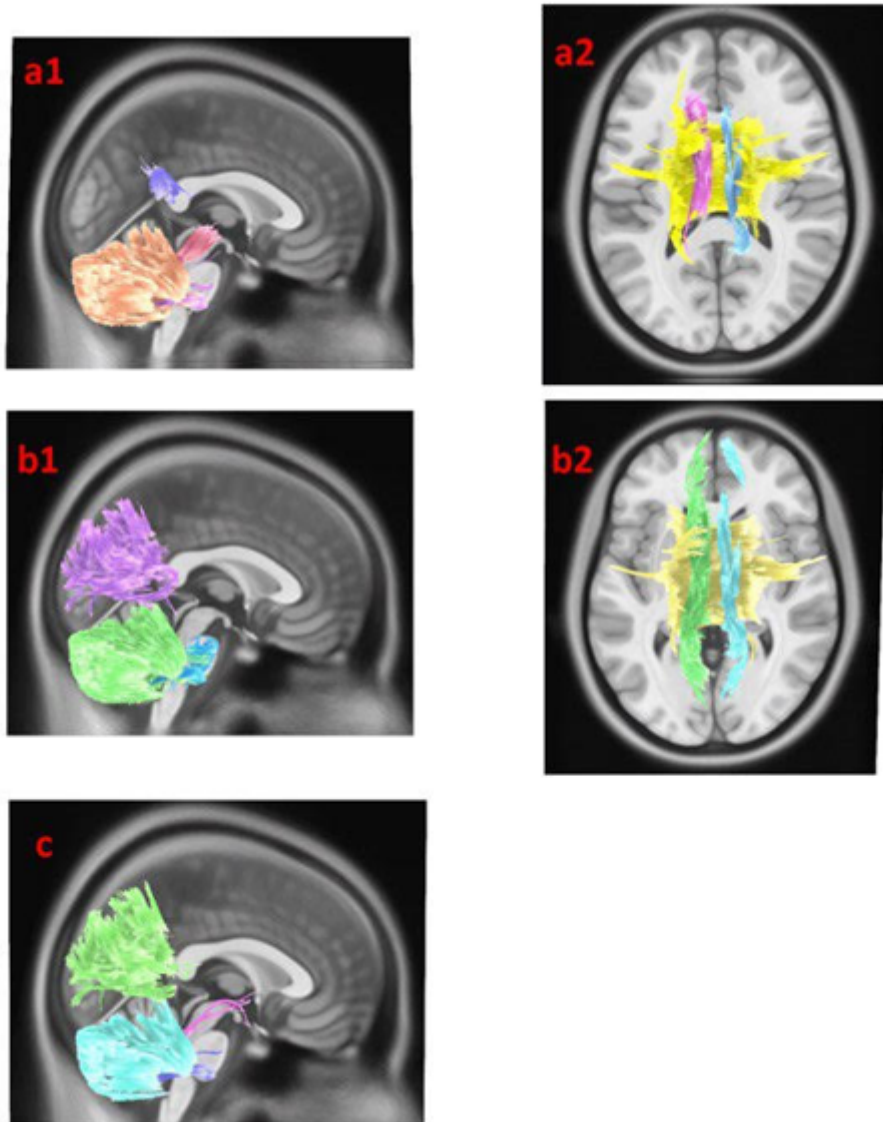


Figure 1

White matter tracts with significant associations with BIS BAS scores