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Abnormal white matter integrity in antipsychotic-naïve first-episode psychosis patients assessed by a DTI principal component analysis

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Abstract

Introduction—Diffusion tensor imaging (DTI) studies in patients with schizophrenia have shown abnormalities in the microstructure of white matter tracts. Specifically, reduced fractional anisotropy (FA) has been described across multiple white matter tracts, in studies that have mainly included patients treated with antipsychotic medications.

Objective—To compare FA in antipsychotic-naïve patients experiencing a first episode of psychosis (FEP) to FA in healthy controls to demonstrate that the variance of FA can be grouped, in a coincidental manner, in four predetermined factors in accordance with a theoretical partition of the white matter tracts, using a principal components analysis (PCA).

Methods—Thirty-five antipsychotic-naïve FEP patients and 35 age- and gender-matched healthy controls underwent DTI at 3T. Analysis was performed using a tract-based spatial statistics (TBSS) method and exploratory PCA.

Results—DTI analysis showed extensive FA reduction in white matter tracts in FEP patients compared with the control group. The PCA grouped the white matter tracts into four factors explaining 66% of the total variance. Comparison of the FA values within each factor highlighted the differences between FEP patients and controls.

Discussion—Our study confirms extensive white matter tracts anomalies in patients with schizophrenia, more specifically, in drug-naïve FEP patients. The results also indicate that a small number of white matter tracts share common FA anomalies that relate to deficit symptoms in FEP patients. Our study adds to a growing body of literature emphasizing the need for treatments targeting white matter function and structure in FEP patients.

Keywords

Diffusion tensor imaging; First-episode psychosis; Schizophrenia; Fractional anisotropy; TBSS; Principal components analysis

1. Introduction

Schizophrenia is a neurodevelopmental disorder in which alterations in brain connectivity have been observed (Friston and Frith, 1995; McGuire and Frith, 1996; Olabi et al., 2011), leading to ineffective communication between brain regions (Seal et al., 2008; Shi et al., 2012). These disturbances in connectivity may be caused by the interaction of biological (Church et al., 2002; Insel, 2010; Weinberger, 1987) and environmental factors during early life (Cannon et al., 2002; Tandon et al., 2008; van Haren et al., 2012), causing developmental brain alterations that predispose an individual to suffer schizophrenia (Singh et al., 2012; Weinberger, 1987).

The changes in microstructure of specific white matter tracts seems to be the anatomical substrate for the disturbances of brain connectivity in schizophrenia (Konrad and Winterer, 2008). This conclusion has been supported by postmortem and genetic studies showing myelin-related alterations (Flynn et al., 2003; Shergill et al., 2000; Yurgelun-Todd et al., 1996), as well as functional imaging studies that demonstrated connectivity abnormalities, specifically between temporo-limbic and prefrontal regions (Meda et al., 2012; Yu et al., 2011).

Diffusion tensor imaging (DTI) is a magnetic resonance imaging (MRI) technique that yields information about white matter microstructure. DTI measures the direction and degree of water diffusion that can be altered by pathologic factors such as demyelination and axonal membrane deterioration (Kubicki et al., 2005a). Fractional anisotropy (FA) is a commonly reported index reflecting white matter microstructure (Basser and Pierpaoli, 1996; Beaulieu, 2002). Several DTI studies have revealed abnormalities in the microstructure of white matter as evidenced by reduced FA in patients with schizophrenia (Ellison-Wright and Bullmore, 2009; Kanaan et al., 2005; Kubicki et al., 2005b; White et al., 2013). In a recent systematic review (Peters and Karlsgodt, 2014) conflicting results were found: some studies have shown no differences between first-episode psychosis (FEP) patients and healthy individuals (Collinson et al., 2014; Kong et al., 2011; Peters et al., 2010), while others have described white matter abnormalities (Cheung et al., 2008; Fitzsimmons et al., 2014; Guo et al., 2012; Lee et al., 2012; Luck et al., 2011; Mandl et al., 2013; Wang et al., 2013a). Some of the factors that might contribute to these results are variability in medication status, symptom history, image analysis, among others (Peters and Karlsgodt, 2014). In order to avoid some confounding variables, studies in antipsychotic-naïve FEP patients are of particular interest. Studies in patients never treated with antipsychotics have shown abnormalities in inferior longitudinal fasciculus (Cheung et al., 2008; Liu et al., 2013), superior longitudinal fasciculus (Filippi et al., 2014; Guo et al., 2012; Mandl et al., 2013), cingulum (Wang et al., 2013b), fornix (Filippi et al., 2014; Guo et al., 2012), internal capsule (Guo et al., 2012), uncinate fasciculus (Mandl et al., 2013), genu and splenium (Cheung et al., 2008; Gasparotti et al., 2009), and occipital-frontal fasciculus (Cheung et al., 2008; Liu et al., 2013).

As presented, some concordance exists in some of the white matter tracts in studies of FEP patients; however, definitive regions have not been confirmed (Wang et al., 2013a). These results could be mediated by heterogeneity of the disease, different methods of image analysis, or statistical analysis. In our study, we examine white matter microstructure in antipsychotic-naïve FEP patients, using DTI with a tract-based spatial statistics (TBSS) method (Smith et al., 2006) and principal components analysis (PCA). We chose this method because region of interest analysis is likely to have more Type II errors (false negatives) than TBSS analysis (Pasternak et al., 2012), and because TBSS also takes into account non-normal distributions of FA in certain brain regions (Smith et al., 2007).

2. Materials and Methods

2.1 Participants

The study was approved by the Ethics and Scientific Committees of the National Institute of Neurology and Neurosurgery of Mexico (INNN). All participants were included in the study after completion of an informed consent procedure in which written consent was obtained.

Thirty-five patients were recruited from the Emergency Room, Neuropsychiatry Department or the Adolescent Program of Neuropsychiatric and Imaging Study (PIENSA) of the INNN during their first non-affective episode of psychosis. For inclusion in the study, subjects were assessed using the Structured Clinical Interview for DSM-IV (First et al., 1997). Psychopathology was assessed using the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987). The patients were antipsychotic-naïve and capable of providing informed consent. Exclusion criteria included concomitant medical or neurological illness, history of head trauma, current substance abuse or history of substance dependence (excluding nicotine), comorbidity with other Axis I disorders, high risk for suicide and psychomotor agitation. The use of other concomitant medications (eg, benzodiazepines, mood stabilizers, and antidepressants) was not allowed before the imaging study. Thirty-five healthy controls matched for age, gender and handedness were also recruited. The control participants were assessed in the same manner as the patients and were excluded if they had a history of psychiatric illness or family history of schizophrenia. All participants were screened for drugs of abuse (cannabis, cocaine, heroin, opioids and benzodiazepines) at the time of inclusion and one hour prior to the neuroimaging studies.

2.2 Image acquisition

MRI studies were acquired on a GE HDxt 3T scanner (GE Healthcare, Waukesha, WI, USA) with an 8-channel head coil (Invivo, Orlando, FL, USA). For each subject, a DTI acquisition, covering the whole brain, was obtained using a diffusion-weighted single-shot echo planar image sequence (DW-EPI) in axial orientation (FOV=256 mm, 60 slices, 128×128 matrix; ASSET factor=2, TR=12000 ms, TE=70 ms, b-value=700 s/mm²; slice thickness=2.6 mm, slice gap=0 mm, 35 non-collinear diffusion directions) and 1 non-DW image.

2.2 Image Analysis

2.2.1 Data preprocessing—Data were preprocessed using the Functional MRI of the Brain Software Library (FSL) (www.fmrib.ox.ac.uk/fsl) (Smith et al., 2004). First, each data set was corrected for eddy currents and head movement using an affine registration to the first volume in the series. Then, non-brain matter was removed from the images using the brain extraction tool. The diffusion tensor for each voxel was estimated by the multivariate linear fitting algorithm. Finally, the FA values were calculated from the eigenvalues of the diffusion tensor matrix.

2.2.2 TBSS analysis—Analysis of FA images was performed by using TBSS, version 1.2. FA maps were normalized to the Montreal Neurological Institute (MNI) standard space. Each map was projected onto a standard mean FA skeleton to create a skeletonized FA map

by thinning the area around the skeleton; this method determined the highest local FA value and assigned this value to the corresponding voxel of the skeleton structure. An FA threshold of 0.2 was chosen for this analysis. Our analysis included 48 white matter fiber tracts, comparable to the approach used in a recent study (Lee et al., 2013) in medicated FEP patients (the description of the 48 included tracts is available in supplementary material).

3. Statistical analysis

The results are presented in terms of means and standard deviations ($\pm$ SD). Demographic and clinical characteristics were compared between the control and FEP groups. Group differences in demographic and clinical variables were explored using χ^2 , Fisher's exact test or independent samples t-tests, as appropriate. The statistical comparisons were carried out with a significance level set at $p < 0.05$. Exploratory partial correlations between tracts with lower FA values changes and clinical measures (PANSS positive, negative and general subscores) were computed using Spearman *rho*. These analyses were restricted to tracts that initially showed a significant group difference between FEP patients and healthy controls.

To evaluate the differences between groups, skeletonized FA data were fed into a voxel-wise statistics analysis (Astrakas and Argyropoulou, 2010; Chung et al., 2008) by using the FSL randomized program software. This analysis uses permutation-based non-parametric inferences within the framework of the general linear model (Nichols and Holmes, 2002). Ten-thousand permutations were used, including full correction for multiple comparisons over space. Two-sample *T*-tests comparing controls and patients were performed for each FA values voxel across the entire brain, with a voxel-wise intensity threshold of $p < 0.05$ (corrected). A second analysis was performed using a cluster-label maps technique based on the Johns Hopkins University (JHU) white matter tractography atlas (Hua et al., 2008) and the International Consortium of Brain Mapping (ICBM) DTI-81 (Mori et al., 2009) white matter labels atlas. This technique evaluates the FA values of 48 default white matter fiber tracts. For this analysis, we also used FSL, and a *T*-test was performed to compare patients and controls. Finally, because the number of variables was large, we decided to use the parcellation proposed by Mori et al (2008), as frame of reference to observe how the variance of the FA is grouped in healthy controls and FEP; the statistical method selected to reduce the dimensionality of the tracts with statistically significant differences between groups, was a PCA for each one of them. A varimax rotation was carried out in order to understand how the variance was described. We used varimax rotation because this method simplifies the interpretation (Bryant and Yarnold, 1995), since each factor represents only a small number of variables. We fixed the threshold at eigenvalues-greater-than-one as the criterion for factor extraction because such analysis is probably most reliable when the number of variables is between 20 and 50 (Hair, 1988). Only those items with communality greater than 0.40, were retained and allocated to factors. We used the Family Wise Error method in order to correct for multiple comparisons, and we applied the Threshold-Free Cluster Enhancement method to find clusters in the data. All statistical analyses were performed using SPSS version 17.

4. Results

4.1 Demographic and clinical characteristics

DSM-IV diagnoses of the FEP patients included in the study were as follows: brief psychotic disorder (n=11), schizophreniform disorder (n=16) and schizophrenia (n=8). The level of education was higher in the control group compared with the FEP group ($t(68)=4.71$, $p<0.001$). The mean duration of untreated psychosis in the FEP group was 25.14 weeks ($SD\pm 27.59$, range 1-104 weeks). The FEP patients and the control group were similar in age, gender, handedness, cannabis use and tobacco use (Table 1). The mean PANSS total score for the FEP group was 97.3 ± 16.1 at the time of MRI scanning.

4.2 Diffusion measures

The results from voxel-based DTI analysis in white matter fiber tracts across the entire brain showed FA reduction in the white matter in FEP patients compared with controls (Figure 1). Similarly, using the JHU and the ICBM-DTI-81 atlases, lower FA values were found in projection, association, commissural, and brain stem tracts in the FEP patients compared with the control group (Table 2, Figure 2). The results of the FA comparisons did not change regardless of whether the educational level was included as a covariate (data not shown).

The results from voxel-based and cluster-label maps analysis were very similar in the regions that showed lower FA values in FEP patients. No significant correlations were found between FA and the age of onset or duration of symptoms. A correlation was found between negative subscores on the PANSS and FA values in the right external capsule ($r=-0.363$, $p=0.03$). However, this correlation was not significant after correction for multiple comparisons.

4.3 Principal component analysis

According to Mori et al (2008) based on diffusion tensor imaging (DTI), the white matter tracts were parceled into four possible groups: projection fibers, association fibers, commissural fibers and brainstem tracts; as a main result, the analysis confirmed that the variance of the FA was properly distributed in four factors that represents the theoretical division of the fibers; there was a corresponding distribution especially in the PCA of the FEP.

4.3.1 Control Group PCA—The FA from the Healthy group was described by four factors (Table 3); however, the fiber groups were not clearly separated. Most of the projection fibers were well described by the first factor. The association fibers were described mostly by the first three factors; therefore, these fibers behavior reveals another subgrouping. The brainstem tracts are represented by the first and fourth factors, describing also another subgrouping.

4.3.2 First episode of psychosis PCA—The FA from the FEP group was clearly described by different factors associated to the fibers groups (Table 4). Also, as an interesting result, the variables of the association fibers and the brainstem tracts were clearly separated and explained by their corresponding factors. The first factor grouped all the

projection fibers variables and the fourth factor grouped all the brainstem tracts, showing a high correlation between each type of fibers and the proposed factors. The association fibers were described by two factors; therefore, these fibers behavior reveals another subgrouping.

4.3.3 First episode of psychosis PCA vs Control Group PCA—The composition of the factors obtained by the rotated PCA was qualitatively different between controls and patients. The total variance included in the control group was 66.2% and in the patient group was 66.5%. In both groups, the factor that described most of the variance corresponded to projection fibers. This means that FA values in the projection fibers have a high correlation between them in contrast with the values located in different factors, showing that there is a group of fibers that, with the DTI technique, behave in a very similar way.

The variance explained by the first factor in the FEP group was 22.9%, and the variance in the control group was 27.1%. In the analysis of the two models, it is clear that the parcellation proposed by Mori et al is more apparent in the PCA of the FEP group than in the PCA of the control group.

As a secondary result, the association fibers seem to reveal a sub segmentation that could be studied in further researches. No correlations were observed between the mean FA for each factor composition and PANSS subscores in FEP patients.

5. Discussion

The results of the present study confirms white matter integrity abnormalities that have already been described in drug-naïve FEP patients (Cheung et al., 2008; Filippi et al., 2014; Guo et al., 2012; Liu et al., 2013; Mandl et al., 2013; Wang et al., 2013b). To the best of our knowledge, our DTI study is the first to investigate at 3T the white matter integrity in drug-naïve FEP patients compared with controls, using TBSS and PCA. Some studies have assessed FEP drug-naïve patients, but have used different image analysis (Mandl et al., 2013; Wang et al., 2013a) or not performed at 3T (Cheung et al., 2008; Filippi et al., 2014; Gasparotti et al., 2009; Mandl et al., 2013). Moreover, our study used a PCA based on functional classification of white tract fibers. The combination of a voxelwise analysis of FA with TBSS has been shown to improve the sensitivity, objectivity and interpretability of the analysis, including multi-subject DTI for group comparison, and has shown more sensitivity than region-of-interest analysis in detecting changes in white matter regions (Focke et al., 2008).

The PCA helped explain the difference in white matter tracts between FEP patients and controls in terms of a limited number of underlying factors. This analysis showed that the factor composition is qualitatively different in patients than in controls. In both groups, the first factor mainly composed by projection fibers, explained most of the variance. In the differences found between them, it can be seen that the parcellation proposed by Mori et al, is most clearly observed in the PCA of the FEP patients. This is evident in the projection fibers and in the fibers of the brain stem, where the FEP model shows a better grouping, in comparison with the model of the control group. Similarly, in the PCA of the FEP, commissural and association fibers are compacted in the factors 2 and 3.

The projection fibers play a key role in the processing, coordination and integration of perceptual inputs and outputs, and a disruption in this connection has been hypothesized to contribute significantly to neuropsychological disturbances seen in schizophrenia (Spoletini et al., 2009). In patients, the second and third factors encompass association and commissural fibers, including temporo-limbic tracts that have been associated with the presence of abulia, anhedonia and apathy in schizophrenia, especially in the early onset of the illness (Fujiwara et al., 2007; Paillere-Martinot et al., 2001). The anomaly within temporo-limbic tracts could also affect heteromodal processing of information, mainly processes such as attention, executive function, mnemonic function and abstraction. Bilateral involvement of the fornix may affect the short-term memory and the formation of new memories, characteristics that have been observed in patients with schizophrenia (Fitzsimmons et al., 2009).

The fourth factor encompasses tracts in the brainstem such as the inferior and superior cerebellar peduncles. The anomalies in the cerebellar peduncles may help explain the higher degree of postural instability in patients with schizophrenia, compared with healthy individuals (Caligiuri and Lohr, 1994; Kent et al., 2012; Marvel et al., 2004). Wang et al (2003) specifically studied the FA of the cerebellar peduncles in patients with schizophrenia and did not find any difference from controls. However, this study included medicated schizophrenia patients, and the sample size was smaller than that used in the current study.

Our study has various limitations. First, we did not include cognitive evaluations; therefore, the relationship between white matter alterations and cognitive performance could not be explored. Second, the groups could not be matched for education; educational levels were higher in the control group than in the FEP group, which is a common observation. Nevertheless, the results did not change whether or not the educational level was included as a covariate in the analysis. Our results, generated using TBSS and a novel statistical analysis, suggest extensive white matter alterations in drug-naïve FEP patients. White matter alterations apparently occur before antipsychotic exposure and during the FEP, before the psychotic illness becomes chronic. Our study adds to a growing body of literature that emphasizes the need for treatments targeting white matter function and structure. Future studies should integrate white matter imaging techniques to help decipher which components of white matter anomalies (i.e., myelin, axon, extracellular matrix) are specifically altered in schizophrenia.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Regions with fractional anisotropy (FA) reduction in first-episode psychosis compared to healthy controls are presented in red. Regions in green represents those showing no difference between controls and patients and are provided as reference. Results are shown overlaid on the Montreal Neurologic Institute template and the mean FA skeleton.

Figure 2.

Fractional anisotropy differences between first-episode psychosis patients and healthy control groups. Results are shown overlaid on the Montreal Neurologic Institute template. For detailed statistics, please refer to Table 2.

Table 1
Demographic and Clinical Characteristics of the Sample

	Control group	FEP group
Age ($\pm$ SD) years	24.54 (6.27)	24.60 (6.24)
Gender (male/female)	22/13	22/13
Education ($\pm$ SD) years	15.09 (3.76)	11.14 (3.21)*
Handedness (right/left)	35/0	35/0
Tobacco (Ever Used)	11/35	11/35
Cannabis (Ever Used)	5/35	6/35
Duration of untreated psychosis ($\pm$ SD) weeks	-----	25.14 (27.59)
PANSS Positive Symptoms	-----	23.03 (4.36)
PANSS Negative Symptoms	-----	24.66 (5.69)
PANSS General Symptoms	-----	49.54 (9.75)

FEP, First-episode psychosis patients; PANSS, Positive and Negative Syndrome Scale.

*
 $p < 0.05$

Table 2
Fractional anisotropy in first episode-psychosis and healthy control groups

Tract	Side	Mean FA		Statistics	
		Control	FEP	T	p
Body of corpus callosum	-	0.583 ± 0.017	0.566 ± 0.029	3.130	0.030
Fornix (column and body of fornix)	-	0.415 ± 0.045	0.383 ± 0.042	3.092	0.003
Inferior cerebellar peduncle	R	0.501 ± 0.022	0.479 ± 0.031	3.431	0.001
Inferior cerebellar peduncle	L	0.506 ± 0.019	0.484 ± 0.029	3.671	<0.0001
Superior cerebellar peduncle	R	0.546 ± 0.028	0.527 ± 0.024	3.177	0.002
Superior cerebellar peduncle	L	0.514 ± 0.025	0.497 ± 0.020	3.067	0.003
Cerebral peduncle	R	0.631 ± 0.023	0.617 ± 0.019	2.820	0.006
Cerebral peduncle	L	0.635 ± 0.020	0.618 ± 0.020	3.714	<0.0001
Anterior limb of internal capsule	R	0.533 ± 0.021	0.522 ± 0.021	2.211	0.030
Anterior limb of internal capsule	L	0.518 ± 0.019	0.508 ± 0.017	2.237	0.029
Retrolenticular part of internal capsule	L	0.561 ± 0.025	0.547 ± 0.023	2.446	0.017
Anterior corona radiata	L	0.432 ± 0.020	0.421 ± 0.021	2.183	0.033
Sagittal stratum (includes inferior longitudinal fasciculus and inferior fronto-occipital fasciculus)	R	0.513 ± 0.023	0.495 ± 0.020	3.617	0.001
Sagittal stratum (includes inferior longitudinal fasciculus and inferior fronto-occipital fasciculus)	L	0.477 ± 0.018	0.462 ± 0.019	3.533	0.001
External capsule	R	0.386 ± 0.015	0.378 ± 0.015	2.260	0.027
External capsule	L	0.396 ± 0.013	0.386 ± 0.014	3.280	0.002
Cingulum (cingulate gyrus)	L	0.486 ± 0.031	0.466 ± 0.032	2.727	0.008
Cingulum (hippocampus)	R	0.386 ± 0.032	0.354 ± 0.026	4.577	<0.0001
Cingulum (hippocampus)	L	0.381 ± 0.029	0.349 ± 0.025	4.990	<0.0001
Fornix / Stria terminalis	L	0.492 ± 0.027	0.477 ± 0.026	2.241	0.028
Superior longitudinal fasciculus	R	0.447 ± 0.020	0.436 ± 0.020	2.172	0.033
Superior longitudinal fasciculus	L	0.438 ± 0.019	0.426 ± 0.017	2.810	0.006

FA, fractional anisotropy; FEP, first episode-psychosis group; R, right; L, left

Table 3
Factor loadings of regional fractional anisotropy in the four-factor model-Varimax in First-episode psychosis patients

Parcelation	Region	Factors			
		1	2	3	4
Projection fibers	Anterior limb of internal capsule L	0.894			
Projection fibers	Cerebral peduncle R	0.618			
Projection fibers	Anterior limb of internal capsule R	0.803			
Projection fibers	Cerebral peduncle L	0.712			
Projection fibers	Anterior corona radiata L	0.592			
Projection fibers	Retro lenticular part of internal capsule L	0.752			
Commissural fibers	Body of corpus callosum		0.451		
Association fibers	External capsule R			0.677	
Association fibers	Cingulum (cingulate gyrus) L			0.715	
Association fibers	Sagittal stratum R		0.659		
Association fibers	Sagittal stratum L		0.768		
Association fibers	Superior longitudinal fasciculus R	0.633			
Association fibers	Superior longitudinal fasciculus L			0.539	
Association fibers	Cingulum (hippocampus) R		0.579		
Association fibers	Cingulum (hippocampus) L		0.649		
Association fibers	Fornix (cres) / Stria terminalis L		0.635		
Association fibers	External capsule L			0.721	
Association fibers	Fornix (column and body of fornix)		0.599		
Brainstem tracts	Inferior cerebellar peduncle R				0.67
Brainstem tracts	Inferior cerebellar peduncle L				0.655
Brainstem tracts	Superior cerebellar peduncle R				0.811
Brainstem tracts	Superior cerebellar peduncle L				0.905
	Eigenvalue	5	3.4	3.2	2.9
	Variance (%)	22.9	15.5	14.7	13.4

R, Right; L, Left.

Table 4
Factor loadings of regional fractional anisotropy in the four-factor model-Varimax in healthy control group

Parcelation	Region	Factors			
		1	2	3	4
Projection fibers	Anterior limb of internal capsule L	0.85			
Projection fibers	Cerebral peduncle R	0.783			
Projection fibers	Anterior limb of internal capsule R	0.757			
Projection fibers	Cerebral peduncle L	0.718			
Projection fibers	Anterior corona radiata L	0.653			
Projection fibers	Retrolenticular part of internal capsule L		0.795		
Commissural fibers	Body of corpus callosum	0.549			
Association fibers	External capsule R	0.727			
Association fibers	Cingulum (cingulate gyrus) L	0.569			
Association fibers	Sagittal stratum R		0.746		
Association fibers	Sagittal stratum L		0.764		
Association fibers	Superior longitudinal fasciculus R		0.55		
Association fibers	Superior longitudinal fasciculus L		0.786		
Association fibers	Cingulum (hippocampus) R			0.863	
Association fibers	Cingulum (hippocampus) L			0.839	
Association fibers	Fornix (cres) / Stria terminalis L			0.561	
Association fibers	External capsule L	NA	NA	NA	NA
Association fibers	Fornix (column and body of fornix)				0.532
Brainstem tracts	Inferior cerebellar peduncle R				0.678
Brainstem tracts	Inferior cerebellar peduncle L				0.679
Brainstem tracts	Superior cerebellar peduncle R	0.63			
Brainstem tracts	Superior cerebellar peduncle L	0.673			
	Eigenvalue	5.7	3.9	2.6	1.8
	Variance (%)	27.1	18.4	12.2	8.5

R, Right; L, Left.