



Neuroscientific Report on Quantitative MRI Volumetrics and Diffusion Tensor Imaging

Client: [REDACTED]
DOB: [REDACTED]
Gender: Female
Date of Exam: 11/19/2018
Date of Report: 12/04/2018
Report By: Jeffrey David Lewine, Ph.D.

Background (from self-report notes):

[REDACTED] is a 27 year old female who self-reports involvement in a motor vehicle accident in July of 2018, with brief loss-of-consciousness. Currently, she self-reports numerous symptoms, including headaches, dizziness, confusion, visual difficulties, memory problems, changes in personality and behavior, sleeplessness, depression and fatigue.

Technical Details:

Magnetic Resonance Imaging data were collected at Doctors Imaging in Metairie, LA. Data were collected using a Siemens 3.0 Tesla TRIO system. Employed imaging sequences included a T1-weighted 3D volumetric acquisition, T2 and FLAIR sequences, susceptibility weighted imaging (SWI) and diffusion tensor imaging (DTI).

Quantitative volumetric and DTI analyses were performed by Dr. Jeffrey David Lewine, Ph.D. and his colleagues at MINDSET. For quantitative volumetric analyses, Dr. Lewine and his team used standardized, objective, and automated procedures in which regional brain volumes were calculated for 112 brain regions defined by the TD-Brodmann and AAL Atlases. These volumetric measures were scaled by total intracranial volume to correct for head size. Fractional Anisotropy (FA) was used as the core metric for integrity of white matter axonal pathways in DTI analyses. Standardized, automated, and objective procedures were also used to extract DTI-based FA values from 48 fiber tract regions using the Johns Hopkins University white matter atlas.

Volumetric and FA values from [REDACTED] were statistically evaluated with respect to volumetric and FA values derived from all sex and age-range (+/- 10 years) matched neuro-typical control subjects within a larger database of >1000 subjects that is maintained by the MINDSET Consulting Group in Albuquerque, New Mexico. The MINDSET data were collected on a 3.0 Tesla system belonging to the Mind Research Network. All neurotypical subjects were without history of neurological or psychiatric disease or injury, TBI, substance abuse, learning disability or developmental disability. A total of 227 matched control datasets were identified for volumetric evaluation, with 227 datasets identified for FA evaluation. All datasets (control and [REDACTED]) were obtained on the same type of scanner (a Siemens 3T TRIO), using identical pulse sequences and parameters, and processed using identical software algorithms and procedures.

The appendix document **NOLA-Appendix-I-MRI** provides a brief overview of basic neurobiology, conceptual and technical details on MRI volumetric and diffusion tensor imaging procedures, and how this information is used in the forensic evaluation of traumatic brain injury cases.

Volumetric Findings:

As shown in Figure 1, volumetric analyses conducted individually on 112 brain regions for [REDACTED] revealed 2 regions to show atypically low volumes ($p < 0.05$). Three isolated regions revealed atypically increased brain volumes. Given the number of multiple comparisons ($N=112$), there is an expectation that even a subject without any history of neurological/psychiatric disease or injury will show a handful of brain regions with ‘false positive’ identification as abnormal. To address this issue of false positives during multiple comparisons, a Benjamini-Hochberg correction was applied with a False Discovery Rate of 25%. Following this correction, **NONE** of the brain regions that were identified as having abnormal volume upon isolated individual testing were still considered to be statistically abnormal.

Figure 2 provides a spatial display of the brain regions with abnormal volumes at the level of individual testing. Table 1 provides a description of the functions of evaluated brain regions.

Diffusion Tensor Imaging Findings

As show in Figure 3, [REDACTED] demonstrates abnormal ($p < 0.05$) FA values in 8 fiber tract regions as evaluated individually, in isolation. Five regions showed atypically low FA values (the pontine crossing tracts, the left corticospinal tract, the left medial lemniscus, the left posterior limb of the internal capsule, and the right cingulum [hippocampus]). Three tracts showed atypically high FA values (the fornix [column and body], right cingulum [cingulate gyrus], and the left tapetum). Table 2 provides information on the statistical evaluation of each individual tract. Scatter plots showing the data from [REDACTED] with respect to 454 neurotypical female subjects in the MRN database are provided in the appendix document: **NOLA-Appendix-II-Scatter-Plots-[REDACTED]**. Table 3 summarizes connectivity and functional information on the various fiber tract regions. Additional information on the various fiber tracts in provided in the appendix document: **NOLA-Appendix-I-MRI**.

Given the number of multiple comparisons ($N=48$), there is an expectation that some tracts may be falsely identified as abnormal even for neurotypical subjects. To address this issue, the data were additionally evaluated using a Benjamini-Hochberg correction for multiple comparisons, with a false discovery rate of 25%. Following correction for multiple comparisons, FA abnormalities for the pontine crossing tracts [low], right corticospinal tract [low], fornix [high], right cingulum [high] and left tapetum [high] were still considered to be statistically significant.

Low FA values are indicative of a disruption of the integrity of the white matter pathways, and are believed to be a reflection of extracellular edema, demyelination, and/or axonal fiber loss. Possible causes for high FA include a failure of developmental pruning, and/or disease/injury related intracellular cytogenic edema, neuroinflammation with microglial activation, astrogliosis and/or compensatory reorganization. High FA is most

common during the sub-acute phase following traumatic brain injury (<6 months), whereas low FA is most common during the chronic period (>6 months) after injury. However, low FA values can be seen acutely, and in some cases, high FA persists into the chronic period.

Impression and Conclusions:

This is a mildly abnormal set of MRI evaluations.

Volumetric analyses are mostly within normal limits, despite a handful of brain regions with atypically high or low volume. Given the number of regions evaluated, none of the brain areas identified as atypical on individual, isolated evaluation were still considered to be statistically aberrant following correction for multiple comparisons. In considering these observations, it is important to note that the sensitivity of even quantitative volumetric assessment to mild TBI is only about 60%, even in the chronic period. In this particular case, it is important to additionally note that [REDACTED] is less than 6 months post-injury. Available research suggests that brain volume loss following mild TBI may not be detectable until more than 1 year after incident. Repeat MRI at a later date may therefore be of value, especially if clinical symptoms persist. Given the overall situation, whereas the present volumetric data do not explicitly support the presence of mild TBI, they also do not strongly weigh against the possibility that [REDACTED] has a mild TBI.

DTI data for [REDACTED] were somewhat more abnormal, with two fiber tracts showing significantly low FA and three showing high FA, even after correction for multiple comparisons. The data indicate white matter abnormalities and are of a spatial profile that could be TBI-related injury. In considering these observations, it is important to note that quantitative MRI and DTI analyses are not stand-alone diagnostic tests for traumatic brain injury. They are part of a multifactorial evaluation of possible neurobiological consequences of head trauma.

Careful review of these imaging findings in the context of [REDACTED]'s developmental profile, medical history, timeline of symptom development, and additional radiological, neurological, neuropsychological, and/or psychiatric evaluations may help to further clarify the etiology of her current clinical status.

This report has been prepared by:



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David J. Robinson, R.T. Technical Director

Patient

DOB: [REDACTED]
Gender: Female
Date of Exam: 11/19/2018

Review and Comment

I have supervised the DTI DiCOM data acquisition process performed onsite at Doctors Imaging and reviewed the Mindset Volumetric/DTI analysis; and confirm that the MRI protocols as well as the applied analytic tools were methodically utilized as designed. I accept the final DTI and Volumetric ZScores as statistically appropriate.

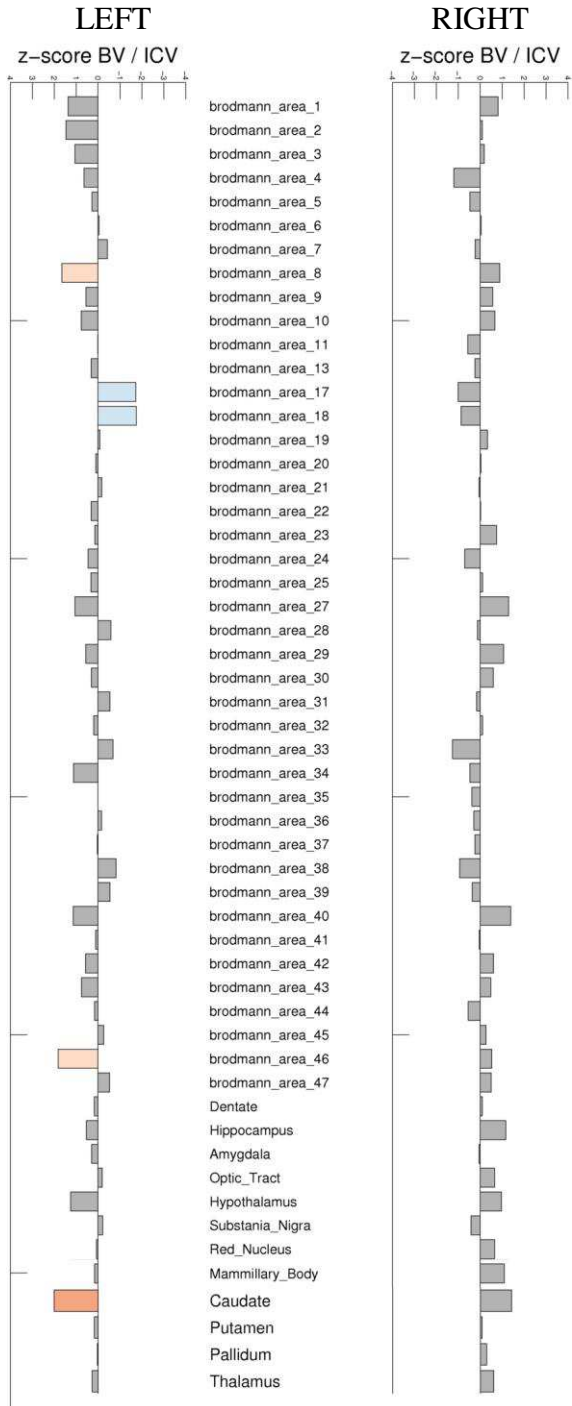
Edward L. Soll, M.D.
Certified, American Board of Radiology 1973 Radiologist, Doctors Imaging
Director, The Concussion Group

Review and Comment

I have reviewed the Mindset Volumetric/DTI analysis and accept the final DTI and Volumetric ZScores as statistically appropriate.

David D. Silvestri, M.D.
Certified, American Board of Radiology 1998
Medical Director, Doctors Imaging Radiologist,
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Figure 1: ██████████
**Z-scores for Regional Brain Volumes,
Scaled by Total Intracranial Volume**



Region-of-interest volumetric analyses

Data are shown as normalized Z-scores based on comparison with a sex and age-range (+/- 10 years) matched group of 227 neuro-typical subjects.

At the level of individual isolated analyses:

Gray bars show regions that do not deviate significantly from normal.

Regions where the bar is red have abnormally high volumes ($p < 0.05$).

Regions where the bar is blue have abnormally low volumes ($p < 0.05$).



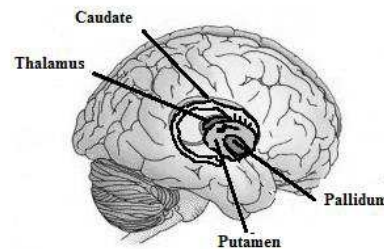
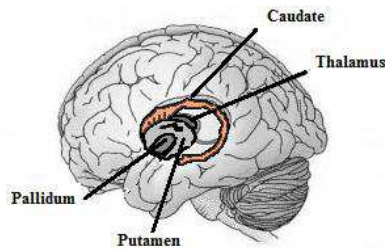
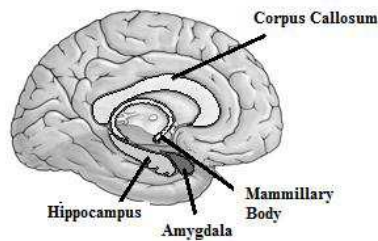
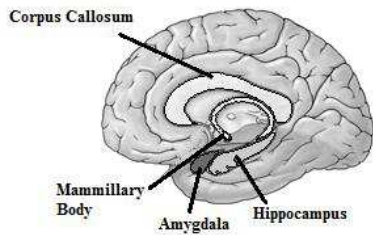
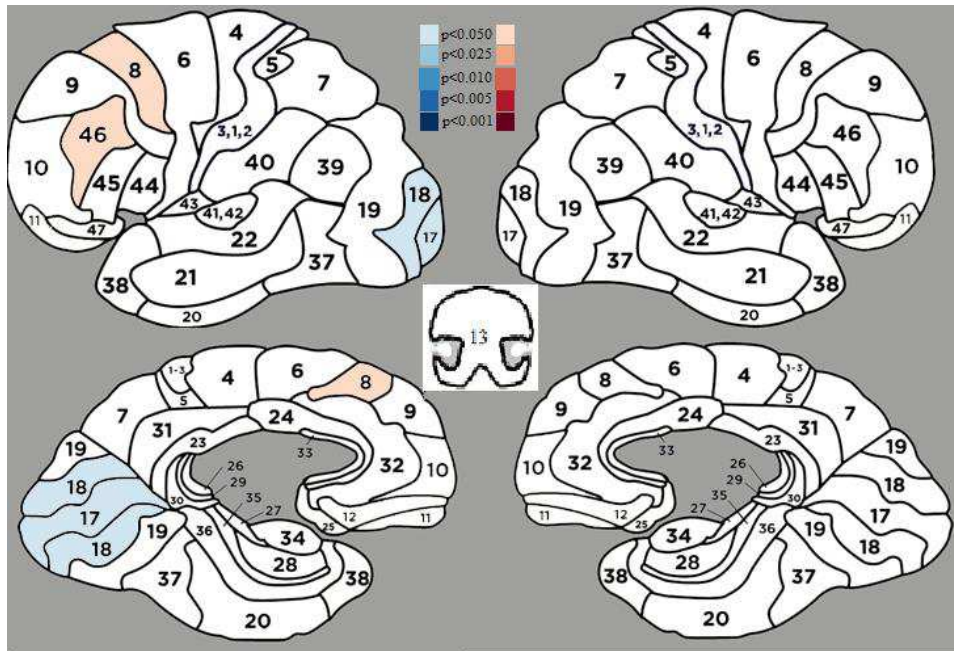
For ██████████, isolated evaluation of individual brain regions reveals 2 regions with atypically low brain volumes, and 3 regions with atypically high volumes.

However, only observations with an * survive correction for multiple comparisons.

Following correction for multiple comparisons, **NONE** of the regions identified as abnormal at the isolated individual level are still considered to be abnormal from a statistical perspective.

Figure 2: [REDACTED] - Brain Regions with Abnormal Volumes on Individual Evaluation

For [REDACTED], NONE of the regions are still considered to be statistically abnormal after correction for multiple comparisons.



white/gray – volume within normal limits
red – high volume
blue – low volume

Table 1: [REDACTED]

Regions-of-Interest with Abnormal Volumes on Individual Evaluation

For [REDACTED], NONE of the regions are still considered to be statistically abnormal after correction for multiple comparisons.

Area		General Location	Supported Functions
Brodman 1,2,3	L/R	Primary somatosensory cortex	Tactile sensation
Brodman 4	L/R	Primary motor cortex	Motor control
Brodman 5	L/R	Somatosensory association cortex	Tactile object recognition
Brodman 6	L/R	Premotor and Supplementary motor cortex	Control of proximal and trunk muscles; Motor sequencing
Brodman 7	L/R	Somatosensory association cortex	Visuo-spatial processing; Praxic abilities
Brodman 8	L	Frontal eye fields	Planning of complex movements, control of eye movements
Brodman 9	L/R	Dorsolateral Prefrontal Cortex	Executive Function, Working Memory
Brodman 10	L/R	Anterior Prefrontal Cortex	Strategic Planning, Cognitive Branching
Brodman 11	L/R	Orbital Frontal Cortex	Behavioral/Emotional Regulation, Behavioral Inhibition
Brodman 13	L/R	Insula	Social emotions, multimodal sensory processing, salience
Brodman 17	L	Primary Visual Cortex	Basic Vision
Brodman 18	L	Secondary Visual Cortex	Shape recognition, visual attention
Brodman 19	L/R	Association Visual Cortex	Visual-spatial processing, visual motion, face and word processing (R/L)
Brodman 20	L/R	Inferior Temporal Gyrus	High-level visual information processing and recognition memory
Brodman 21	L/R	Middle Temporal Gyrus	Complex auditory processing and language
Brodman 22	L/R	Superior Temporal Gyrus	Auditory processing, Receptive Language (Wernicke's area)
Brodman 23	L/R	Posterior Cingulate Cortex	Emotion and Memory, Intrinsic Control
Brodman 24	L/R	Anterior Cingulate Cortex	Behavioral Control, Reward Based Decision Making, Social Evaluation
Brodman 25	L/R	Subgenual Ventromedial Prefrontal Cortex	Decision making, emotion, social behavior
Brodman 27	L/R	Periform Cortex	Olfaction
Brodman 28	L/R	Ventral Entorhinal Cortex	Short-term memory
Brodman 29	L/R	Retrosplenial Cingulate Cortex	Emotion and Memory, Intrinsic Control
Brodman 30	L/R	Part of Cingulate Cortex	Emotion and Memory, Intrinsic Control
Brodman 31	L/R	Dorsal Posterior Cingulate Cortex	Emotion and Memory, Intrinsic Control
Brodman 32	L/R	Dorsal Anterior Cingulate Cortex	Behavioral Control, Reward Based Decision Making, Social Evaluation
Brodman 33	L/R	Part of the Anterior Cingulate Cortex	Behavioral Control, Reward Based Decision Making, Social Evaluation
Brodman 34	L/R	Dorsal Entorhinal Cortex/Parahippocampal Gyrus	Short-term memory
Brodman 35	L/R	Perirhinal Cortex	Short-term memory
Brodman 36	L/R	Ectorhinal Area	Short-term memory
Brodman 37	L/R	Fusiform Gyrus	Word recognition (L) / Face Processing (R)
Brodman 38	L/R	Temporopolar Regions	Memory, Language
Brodman 39	L/R	Angular Gyrus	Language, reading, mathematics, attention
Brodman 40	L/R	Supramarginal Gyrus	Spatial perception, phonological choices
Brodman 41	L/R	Primary Auditory Cortex	Basic Hearing
Brodman 42	L/R	Auditory Cortex	Auditory processing
Brodman 43	L/R	Primary Gustatory Cortex	Taste
Brodman 44	L/R	Pars opercularis, inferior frontal gyrus, part of Broca's area	Expressive Language
Brodman 45	L/R	Pars triangularis, inferior frontal gyrus, part of Broca's area	Expressive Language
Brodman 46	L	Dorsolateral Prefrontal Cortex	Executive Function, Working Memory
Brodman 47	L/R	Pars orbitalis, inferior frontal gyrus	Syntax
Dentate	L/R	Part of the Hippocampus	Short-term Memory
Hippocampus	L/R	Medial Temporal Lobe	Short-term Memory
Amygdala	L/R	Medial Temporal Lobe	Emotion
Optic Tract	L/R		Post-chiasm Fibers, Contralateral Visual Field
Hypothalamus	L/R		Regulates autonomic functions, pituitary, hunger, sleep
Substantia Nigra	L/R		Dopaminergic motor control
Red Nucleus	L/R		Motor Coordination
Mammillary Body	L/R		Memory
Anterior Commissure	L/R		Interconnects L/R temporal lobes
Corpus Callosum	L/R		Interconnects L/R hemisphere
Caudate	L	Part of the Basal Ganglia	Regulates movement
Putamen	L/R	Part of the Basal Ganglia	Regulates movement
Pallidum	L/R	Part of the Basal Ganglia	Regulates movement
Thalamus	L/R		Sensory, Motor, Emotional and Cognitive Functioning

Low volumes may reflect perturbation of early developmental processes, malnutrition, toxic stress, toxic exposures, or more commonly neurological/psychiatric disease and/or brain injury.

High volumes may reflect perturbation of early developmental pruning, enhanced skill development, brain injury related edema and/or compensatory reactions to damage in other areas.

Figure 3: [REDACTED]
Z-scores for FA Values

FA Values for Fiber Tract Regions

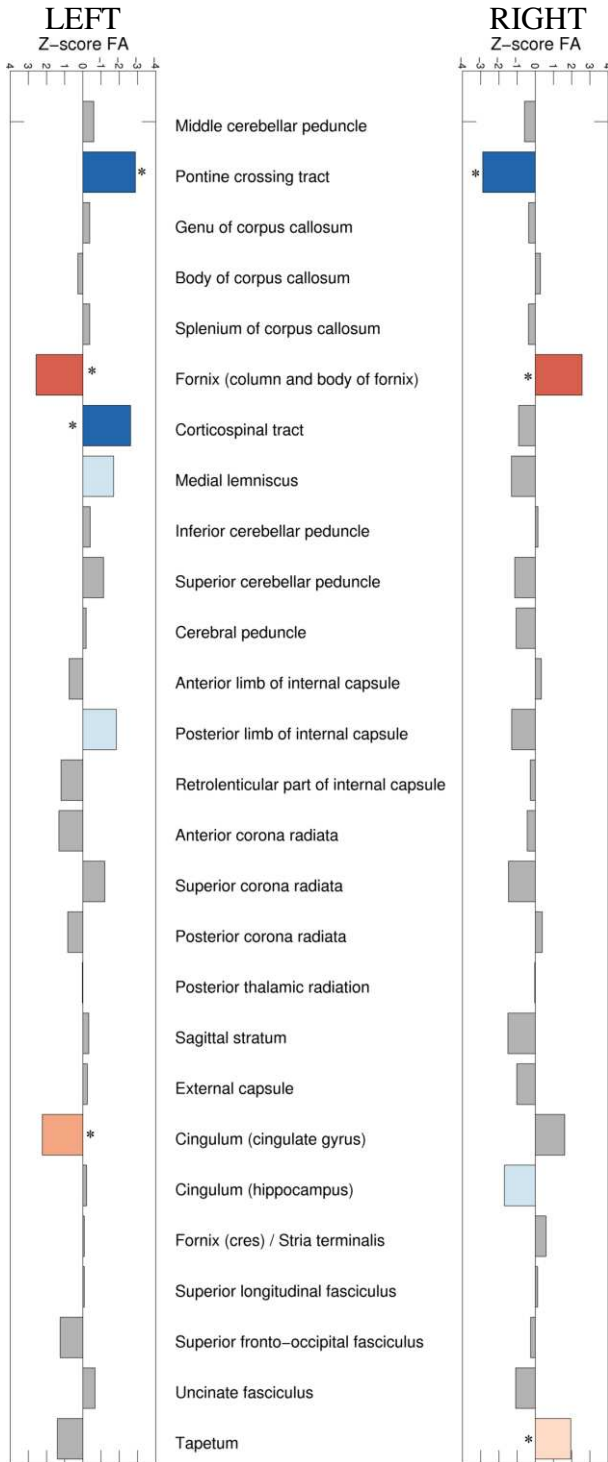
Data are shown as normalized Z-scores based on comparison with a sex and age-range (+/- 10 years) matched group of 227 neuro-typical subjects.

At the level of individual isolated analyses:

Gray bars show tract regions that do not deviate significantly from normal.

Tract regions where the bar is red have abnormally high FA values ($p < 0.05$).

Tract regions where the bar is blue have abnormally low FA values ($p < 0.05$).



For [REDACTED], isolated evaluation of individual fiber tract regions reveals 3 tracts with atypically low FA, and 5 tracts with atypically high FA values.

However, only observations with an * survive correction for multiple comparisons.

Following correction for multiple comparisons, there remain 2 tracts with significantly low FA and 3 with significantly high FA.

The first 6 tracts are at the midline and without separable left/right components. Identical values are plotted on the left and right sides.

Table 2 - [REDACTED], FA Values

#	Regions	Client	Database	Stdev	Z-score
1	Middle cerebellar peduncle	0.438	0.447	0.016	-0.593
2 *	Pontine crossing tract (a part of MCP)	0.347	0.429	0.028	-2.884
3	Genu of corpus callosum	0.636	0.643	0.019	-0.367
4	Body of corpus callosum	0.692	0.683	0.029	0.279
5	Splenium of corpus callosum	0.746	0.753	0.017	-0.373
6 *	Fornix (column and body of fornix)	0.544	0.405	0.054	2.570
7	Corticospinal tract R	0.404	0.429	0.028	-0.912
8 *	Corticospinal tract L	0.373	0.445	0.027	-2.613
9	Medial lemniscus R	0.509	0.539	0.023	-1.304
10	Medial lemniscus L	0.502	0.544	0.025	-1.681
11	Inferior cerebellar peduncle R	0.417	0.414	0.025	0.145
12	Inferior cerebellar peduncle L	0.404	0.414	0.025	-0.400
13	Superior cerebellar peduncle R	0.502	0.533	0.027	-1.128
14	Superior cerebellar peduncle L	0.484	0.513	0.025	-1.131
15	Cerebral peduncle R	0.617	0.637	0.020	-1.054
16	Cerebral peduncle L	0.648	0.651	0.019	-0.173
17	Anterior limb of internal capsule R	0.532	0.526	0.018	0.335
18	Anterior limb of internal capsule L	0.541	0.527	0.018	0.764
19	Posterior limb of internal capsule R	0.570	0.592	0.017	-1.294
20	Posterior limb of internal capsule L	0.575	0.607	0.017	-1.831
21	Retrolecticular part of internal capsule R	0.546	0.552	0.022	-0.275
22	Retrolecticular part of internal capsule L	0.614	0.587	0.023	1.206
23	Anterior corona radiata R	0.422	0.433	0.025	-0.444
24	Anterior corona radiata L	0.456	0.424	0.024	1.316
25	Superior corona radiata R	0.428	0.458	0.021	-1.471
26	Superior corona radiata L	0.447	0.473	0.021	-1.202
27	Posterior corona radiata R	0.455	0.446	0.024	0.384
28	Posterior corona radiata L	0.461	0.441	0.024	0.841
29	Posterior thalamic radiation R	0.557	0.558	0.028	-0.030
30	Posterior thalamic radiation L	0.543	0.542	0.026	0.033
31	Sagittal stratum R	0.470	0.504	0.023	-1.501
32	Sagittal stratum L	0.476	0.483	0.022	-0.322
33	External capsule R	0.368	0.386	0.017	-1.023
34	External capsule L	0.412	0.417	0.020	-0.241
35	Cingulum (cingulate gyrus) R	0.491	0.445	0.028	1.622
36 *	Cingulum (cingulate gyrus) L	0.546	0.489	0.025	2.235
37	Cingulum (hippocampus) R	0.321	0.363	0.025	-1.698
38	Cingulum (hippocampus) L	0.361	0.367	0.028	-0.200
39	Fornix (cres) / Stria terminalis R	0.468	0.455	0.023	0.587
40	Fornix (cres) / Stria terminalis L	0.503	0.505	0.026	-0.071
41	Superior longitudinal fasciculus R	0.440	0.437	0.021	0.124
42	Superior longitudinal fasciculus L	0.453	0.455	0.022	-0.075
43	Superior fronto-occipital fasciculus R	0.450	0.456	0.026	-0.253
44	Superior fronto-occipital fasciculus L	0.486	0.448	0.030	1.246
45	Uncinate fasciculus R	0.398	0.429	0.028	-1.084
46	Uncinate fasciculus L	0.420	0.439	0.028	-0.667
47	Tapetum R	0.443	0.379	0.032	1.949
48	Tapetum L	0.354	0.312	0.030	1.409

Client FA value abnormally high, p<0.05 (isolated, individual testing)
Client FA value abnormally low, p<0.05 (isolated, individual testing)
* indicates survival of correction for multiple comparisons

Table 3: [REDACTED]
Fiber Tract Regions of Interest With Abnormal FA Values

JHU White Matter Atlas Fiber Tract Regions		Connections	Supported Functions
Middle Cerebral Peduncle	Midline	Interconnects Cerebellum and Pons	Initiation and Timing of Volitional Movement
Pontine Crossing Tracts *	Midline	Interconnects Pons and Contralateral Cerebellum	Coordination of Movement
Genu of the Corpus Callosum	Midline	Interconnects Right and Left Anterior Frontal Lobes	Interhemispheric Integration of Executive Functions
Body of the Corpus Callosum	Midline	Interconnects Right and Left Posterior Frontal Lobes Interconnects Right and Left Parietal Lobes	Interhemispheric integration of Motor and Somatosensory Functions
Splenium of the Corpus Callosum	Midline	Interconnects Right and Left Occipital Lobes	Interhemispheric Integration of Visual Functions
Fornix *	Midline	Interconnects the Hippocampus and Mammillary Bodies	Short-Term Memory
Corticospinal Tracts *	L	Connects Primary Motor Cortex with Contralateral Spinal Motor Neurons	Motor Control of the Contralateral Side of the Body
Medial Lemniscus	L	Connects Dorsal Column Nuclei with the Contralateral Thalamus (VPL)	Somatosensory Perception of the Contralateral Side of the Body
Inferior Cerebellar Peduncles	R/L	Connects Spinal Cord and the Medulla to the Cerebellum	Posture, Balance, and Coordination
Superior Cerebellar Peduncles	R/L	Interconnects Cerebellum to Pons and Midbrain	Motor Coordination and Balance
Cerebellar Peduncles	R/L	Interconnects Cerebellum with the Thalamus and Motor Cortex	Motor Control
Anterior Limb of the Internal Capsule	R	Contains Fibers Interconnecting the Thalamus and Frontal Lobe; Lentiform and Caudate Nuclei; Cortex and Corpus Striatum	Motor Control; Higher Cognitive Function
Posterior Limb of the Internal Capsule	R/L	Contains Fibers Interconnecting Motor Areas with the Brainstem; Midbrain and the Thalamus, Occipital Lobes, and Temporal Lobes	Visual-Spatial Processing, Visual Motion, Face and Word Processing (R/L)
Retrolenticular Part of the Internal Capsule	R/L	Interconnects Thalamus and Occipital Cortex	Visual Processing
Anterior Corona Radiata	R/L	Contains Descending and Ascending Fibers Related to Cortex – especially for the Frontal Lobes	Higher Cognitive Function
Superior Corona Radiata	R/L	Contains Descending and Ascending Fibers Related to Cortex – especially for the Motor Cortex	Motor Control
Posterior Corona Radiata	R/L	Contains Descending and Ascending Fibers Related to Cortex – especially for the Parietal Lobes	Attentional Control, Somatosensory Function
Posterior Thalamic Radiation	R	Interconnects Thalamus and Cortex	Visual and Auditory Function
Sagittal Stratum	R/L	Interconnects Thalamus with Occipital, Parietal, Temporal and Cingulate Cortices	Visual, Auditory, and Cognitive Function
External Capsule	R/L	Contains Cortico-Cortical Association Fibers for Occipital, Temporal, Parietal, and Cingulate Cortices	Cognitive Processing
Cingulum (cingulate cortex) *	L	Interconnects Cingulate and Pre-Frontal Cortices	Cognitive Processing and Decision Making
Cingulum (hippocampus)	R	Interconnects Cingulate and Entorhinal Cortices	Memory, Emotional Processing
Fornix (cres) and Stria Terminalis	R/L	Interconnects Hippocampus and Mammillary Bodies; Amygdala with the Septal Region and Hypothalamus	Memory, Emotional Processing, Fear Response
Superior Longitudinal Fasciculus	R/L	Interconnects the Front and Back of the Cerebrum, Including Frontal, Parietal, Occipital, and Cingulate Areas	Higher Cortical Functions
Superior Fronto-Occipital Fasciculus	R	Interconnects the Frontal Lobe with the Occipital and Parietal Lobes	Spatial Awareness
Uncinate Fasciculus	R	Interconnects Hippocampus and Amygdala with Orbital Frontal Cortex	Memory, Emotional Processing
Tapetum *	R	Contains Commissural Fibers Interconnecting Right and Left Temporal Lobes	Interhemispheric Integration for Auditory Processing

Client FA value abnormally high, p<0.05 (isolated, individual testing)
Client FA value abnormally low, p<0.05 (isolated, individual testing)
* indicates survival of correction for multiple comparisons