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Extended Volumetric Analysis based on NeuroQuant® data

Patient:

Location of MRIs:

Date of MRI: 05/03/2012

Date of report:

Region	LH Volume (% of ICV)	%tile rank	RH Volume (% of ICV)	%tile rank	Asymmetry Index %	%tile rank
Whole Brain Parenchyma	35.178%	30.7%	35.975%	39.8%	-2.240%	24.4%
Forebrain Parenchyma	30.367%	30.5%	30.893%	33.8%	-1.719%	40.5%
Cortical Gray Matter	17.208%	98.3%	17.676%	98.7%	-2.681%	21.9%
Cerebral White Matter	11.477%	0.1%*	11.597%	0.1%*	-1.040%	64.3%
Lateral Ventricle	0.908%	43.1%	0.945%	46.3%	-4.004%	39.0%
Inferior Lateral Ventricle	0.059%	16.4%	0.058%	19.2%	1.940%	48.2%
Total CSF	1.113%	45.1%	1.220%	49.9%	-9.147%	35.7%
Caudate	0.240%	35.7%	0.237%	25.5%	0.924%	79.6%
Putamen	0.355%	82.2%	0.325%	69.7%	8.776%	72.4%
Pallidum	0.036%	6.0%	0.053%	21.9%	-38.686%	1.1%*
Thalamus	0.463%	2.4%*	0.369%	0.0%*	22.700%	100.0%*
Amygdala	0.084%	1.5%*	0.087%	5.5%	-3.915%	36.7%
Hippocampus	0.213%	4.7%*	0.229%	11.3%	-7.407%	46.2%
Cerebellum	4.178%	56.5%	4.343%	80.3%	-3.871%	0.6%*
Brain Stem	0.633%	2.1%*	0.738%	4.6%*	-15.415%	36.8%

	L+R Volume (% of ICV)	%tile rank
Whole Brain Parenchyma (L+R)	71.152%	35.1%

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Patient information

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Note: LH = left hemisphere. RH = right hemisphere. %tile = normative percentile. AI = Asymmetry Index.

“---” indicates that the data were unreliable due to segmentation error.

“*” indicates a normative percentile which was statistically and clinically significant, defined as any of the following:

- A parenchymal region $\leq 5^{\text{th}}$ normative percentile, consistent with atrophy
- A ventricular region $\geq 95^{\text{th}}$ normative percentile, consistent with atrophy of the surrounding parenchyma
- Asymmetry index $\leq 2.5^{\text{th}}$ or $\geq 97.5^{\text{th}}$ normative percentile, consistent with atrophy of the smaller structure
- Asymmetry index $\leq 5^{\text{th}}$ or $\geq 95^{\text{th}}$ normative percentile for cases in which there were other unilateral, homodirectional signs of head or brain injury, including:
 - scalp contusions or lacerations
 - cranial fractures
 - unilateral brain abnormalities identified by the attending radiologist which are consistent with or associated with parenchymal atrophy
 - a second asymmetry index $\leq 5^{\text{th}}$ or $\geq 95^{\text{th}}$ normative percentile and homodirectional with the first asymmetry index

Inspection for image segmentation quality: NeuroQuant[®] segmented (color-coded) DICOM images were inspected visually by A.L.O. and D.E.R. The following segmentation errors were identified:

- None

Otherwise, the regions of interest were found to be accurately identified by the NeuroQuant[®] software.

Summary of positive findings: Abnormal volumes consistent with parenchymal atrophy were found in the following regions:

- * The left and right cerebral white matter regions were abnormally small.
- * The left pallidum was abnormally smaller than the right.
- * Both thalami were abnormally small, and the right was abnormally smaller than the left.
- * The left amygdala was abnormally small.
- * The left hippocampus was abnormally small.
- * The left cerebellum was abnormally smaller than the right.
- * The left and right brain stem regions were abnormally small.

Methods for NeuroQuant Extended Analysis

Introduction

NeuroQuant[®] is a commercially available, FDA-approved method for measuring brain volume using MRI data (<http://www.cortechs.net/products/neuroquant.php>). The



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purpose of the NeuroQuant[®] analyses was to test for atrophy of brain parenchymal regions and enlargement of ventricular regions. The published literature strongly supports the idea that, after traumatic brain injury, brain parenchyma atrophies and ventricles enlarge (Bigler 2005; Bigler 2011). Each NeuroQuant[®] analysis compared the patient's data to normal control data. For all NeuroQuant[®] analyses brain region volume was corrected for head size by dividing the brain region volume by intracranial volume and expressing the result as a percentage.

NeuroQuant[®] Standard analysis

The NeuroQuant[®] standard analysis provided measures of 11 brain regions, with 3 of those regions compared to a normal control group. For each of those 3 regions, total volume—that is, combined left and right volumes—were compared to the normal control group.

NeuroQuant[®] Extended analysis

ADNI Normal Control Database

Results from the NeuroQuant standard analysis were used to perform an additional, extended analysis. Normal control data were obtained from a larger group previously studied as part of the Alzheimer's Disease Neuroimaging Initiative (ADNI) (Jack_Jr, Bernstein et al. 2008; Petersen, Aisen et al. 2010; Weiner, Aisen et al. 2010). The ADNI normal control data are publicly available (<http://adni.loni.ucla.edu>).

VIN Normal Control Group

For the present analysis, a subgroup 20 normal control subjects (10 men, 10 women) were chosen from the ADNI database. The IDs and dates of the MRIs were as follows:

ID	Date of MRI
002_S_1261	02/15/07
002_S_1280	02/13/07
011_S_0016	09/27/05
011_S_0022	10/10/05
020_S_1288	03/13/07
023_S_0058	12/12/05
023_S_0926	10/16/06
036_S_0672	07/21/06
037_S_0327	04/19/06
057_S_0934	10/04/06
067_S_0056	11/09/05
073_S_0089	01/26/06
098_S_0172	02/26/06



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099_S_0090	01/11/06
099_S_0534	05/04/06
116_S_1249	03/01/07
128_S_0272	03/22/06
128_S_0522	05/19/06
130_S_0969	10/18/06
133_S_0525	07/10/06

The mean age of the normal controls was 68.3 years (SD 3.6 years; range 60.0-71.5). The standard NeuroQuant[®] analysis was done for each of the normal controls. The results were used to determine means and standard deviations for each of the 11 brain regions, left and right sides, and asymmetry indices.

For the extended analysis, the patient's data from the standard analysis were compared to the data from the normal controls in order to calculate normative percentile ranks (see above).

For further information regarding the use of NeuroQuant, see the appended document "Review of the Evidence Supporting the Use of NeuroQuant[®]."

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