Multi-Parametric MRI Protocol for Evaluation of Cognitive Insufficiency, Dementia, and Traumatic Brain Injury (TBI): A Case Series

John L. Sherman, MD[1], Christen F. Kutz, PhD, PA-C[2], Deborah A. York MSN, PMHNP-BC, APRN, CCRA[3], Mitchell S. Szymczak, MS3[4], Laurence J Adams, MD[2]

[1]Colorado Springs Imaging, Colorado Springs CO, [2]Colorado Springs Neurological Associates, Colorado Springs, CO, [3]Salida, CO , [4]Western University of Health Sciences, Pomona, CA

Introduction

- Alzheimer's disease (AD) is the most frequent cause of dementia accounting for 50%–70% of dementia cases.
- Usual considerations include Alzheimer's Disease (AD),Vascular Dementia (VD), Lewy Body Disease (LBD), Frontotemporal Dementia (FTD), and subtypes including Semantic Dementia and Corticobasal Degeneration, Parkinson's Dementia, Parkinson Plus Syndromes, Traumatic Brain Injury, and mixed syndromes.
- Optimal treatment and inclusion in clinical trials requires early and precise diagnosis.
- Amnestic and cognitive complaints can be the harbinger of a devastating degenerative disease that can be difficult to manage and treat, especially when the specific diagnosis is uncertain.
- Typical diagnosis usually occurs later in the disease process and is reliant on the constellation of clinical findings, and increasingly, MRI.
- As early as 2009 it was known that MRI with hippocampal volume measurement and posterior cingulate MRI spectroscopy improved ability to identify patients with prodromal dementia compared to MRI alone.
- Multimodal imaging combines structural (MRI, CT) and molecular imaging (PET, SPECT) and can provide diagnosis using disease specific isotopes and tracers that allow definitive diagnosis.
- MRI alone has progressed to a point where submillimeter resolution and markedly improved tissue contrast is available in most community outpatient and hospital centers.
- Advanced MRI techniques have been developed and studied for years but have not been routinely utilized in clinical outpatient practice

Objectives

Our objective is to test the clinical utility of a multiparametric MRI protocol to advance the diagnosis of degenerative disease by combining MRI structural data with cellular, perfusion, and biochemical information derived from specialized sequences within the scope and timeframe of a single MRI study of standard time and cost.

Methodology

- Selected patients with complex symptomatology were evaluated with Multi-Parametric MRI in a standard clinical outpatient environment. The mpMRI data was summarized at the end of the imaging report and several diagnoses were suggested to the referring clinician.
- All MRI studies were interpreted by JLS and LJA who were not blinded to the symptoms.
- All neurologic exams were performed by LJA.
- All MRI studies were performed on GE 1.5 Tesla MRI machines.
- Multi-Parametric MRI (mpMRI) Technique:
- Standard Sequences
- DWI, T2w FSE, FLAIR, SWAN or GRE T2*w, T1w.
- Specialized Sequences
- SWAN/SWI: extremely sensitive to microbleeds in subcortical vascular dementia and acquired amyloid angiopathy. Cerebral microbleeds are an independent predictor of cognitive impairment.
- MRI Spectroscopy: The literature supports use of MRS in dementia since 1993, especially in the posterior cingulate gyrus foe the evaluation of suspected Alzheimer's disease.
- ASL: Used to assess cerebral blood flow noninvasively by magnetically labeling inflowing blood, using arterial blood as a contrast agent, providing information like FDG-PET and 99mTc-HMPAO SPECT. ASL has found been found to separate individual with mild AD from those with normal cognition with high sensitivity.
- Quantitative volumetric MRI (NeuroQuant®): The technique is an outgrowth of the ADNI (SG)project and initially focused on medial temporal lobe anatomy. NeuroQuant® been used to demonstrate brain atrophy in association with dementia since 2009.

Conclusions

- Readily available advanced MRI techniques (especially quantitative volumetric analysis, NeuroQuant), markedly improves the usefulness of the imaging study when added to the clinical findings. MRI exam time is approximately 45 minutes and patient cost is not significantly increased. Repeat mpMRI exam is often recommended in 9-12 months because it is often important to determine the rate of progression of atrophy, an important parameter use to differentiate mild cognitive insufficiency from early AD and other degenerative disease.
- Future Directions:
- We are beginning to incorporate the addition of diffusion tensor imaging (DTI) to our mpMRI (memory protocol) in our evaluation of selected patients with memory, behavioral, movement and amnestic disorders. In addition, there is an increasing body of literature using resting state fMRI in these patients, and we hope to explore this possibility in our community setting.

Comment

It is increasingly important to accurately diagnose patients with specific disease as therapeutic agents are beginning to be available and patient selection is of utmost importance. Furthermore, earlier diagnosis serves as an impetus to patients and their families to optimize lifestyle changes future planning. A normal mpMRI study is a great relief to those patients whose fear of dementia can act as a strong negative force in their life.

Dementia Patterns

Alzheimer's Dementia
Hippocampal atrophy is the best-established MRI biomarker of AD, usually accompanied by entorhinal cortex atrophy and variable diffuse cortical atrophy. Hippocampal atrophy progresses in rate in AD is over 3.5% per year compared to MCI (1.6%-3.0%).
ASL perfusion show reduced CBF in the posterior cingulate gyri and posterior parietal cortex. ASL can predict cognitive decline and conversion from MCI to dementia.
MR spectroscopy shows an increase in MI/Cr in the initial stages but with AD progression there is decreased NAA/Cr and increased Cho/Cr. MRS changes reflect neuronal loss/dysfunction and gliosis.

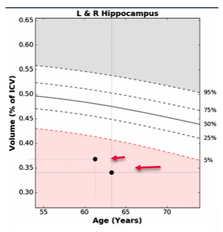
Lewy Body Dementia
A pattern of atrophy of the midbrain, hypothalamus and substantia innominata, with a relative sparing of the hippocampus and temporoparietal cortex. Preserved posterior cingulate perfusion with hypoperfusion on ASL-MRI in the precuneus, cuneus and posterior parieto-occipital cortices. MRS show elevated choline in normal appearing white matter. ASL cannot differentiate AD from Lewy body dementia. Blood flow is markedly reduced in the same area as in AD.

Frontotemporal lobar degeneration
Clinically categorized into 3 subtypes: frontotemporal dementia, semantic dementia, and progressive nonfluent aphasia. Different patterns of atrophy frequently occur centered on right or left temporal or in the frontal lobe. MRS in temporoparietal gray shows more reduced NAA and more elevation of myoinositol than in AD. ASL reveals significant asymmetric perfusion of temporal and frontal lobes with sparing of parietal perfusion.

Vascular Dementia
Excessive white matter and basal ganglia lesions for age, frequently associated with microbleeds. In the context of vascular dementia, microbleeds are mainly thought to result from hypertensive vasculopathy to hypertension. Generalized cortical atrophy without a specific pattern, however there is less pronounced hippocampal atrophy than with AD. ASL shows generalized delayed or decreased perfusion. Posterior cingulate MRS frequently shows reduced NAA, with normal myoinositol and choline. White matter MRS reveals elevated choline compared to normal white matter.

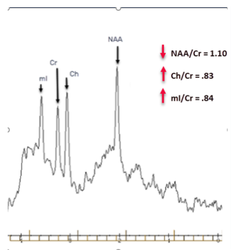
Case Series

Early onset Alzheimer Disease
63 y.o. female with progressive changes in cognitive functions, memory and awareness over two years. Multiparametric MRI (mpMRI) shows hippocampal atrophy and abnormal rate of change over two years. MRS shows typical findings of AD with reduced NAA (reflecting neuronal density) and elevated mI (increased glial activity). ASL shows decreased parietal perfusion similar to a FDG PET scan.

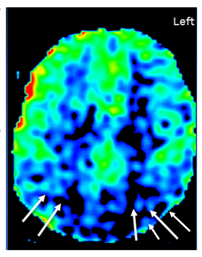


Neuroquant. Hippocampal atrophy > 2 SD below mean.

8% loss of volume per year is more than 4 x normal rate.

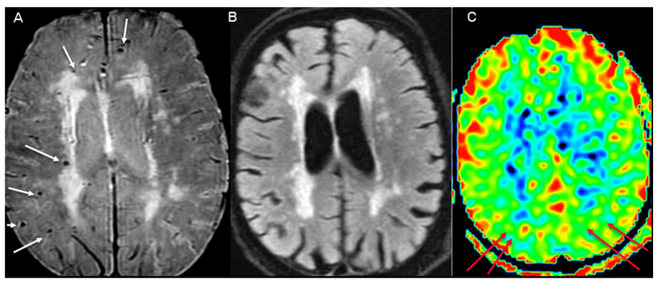


MRS signature findings of reduced NAA and elevated mI



ASL perfusion showing reduced CBF in bilateral posterior parietal lobes L>R (arrows).

Vascular Dementia
78 y.o. male with progressive cognitive insufficiency and amnestic disorder increasing in last month.
Volumetric imaging shows excessive white matter disease burden is 3 SD above the mean. Normal frontal, temporal, parietal and temporal lobes, normal hippocampal and cortical gray matter volume.
MRS shows decreased NAA but normal Ch and mI.
ASL shows normal cortical and posterior cingulate perfusion for age.



A) SWI showing scattered microbleeds (arrows). B) T2w FLAIR showing excessive white matter disease. C) ASL showing normal parietal lobe perfusion (arrows).

Frontotemporal Dementia
73 y.o. male with several years of progressive cognitive difficulty, memory, speech and reading difficulty. Disfluent speech, bradykinesia and dyskinesia. Higher cognitive functions are not as severely affected as would be seen in AD. NeuroQuant study is very abnormal showing a FTD pattern. MRS shows reduced NAA and normal Ch and mI. ASL could not be performed. Ischemic white matter burden was normal for age. Initial diagnosis was Lewy Body dementia but diagnosis after multiparametric MRI is right hemispheric dominant frontotemporal dementia, previously called Picks Disease.

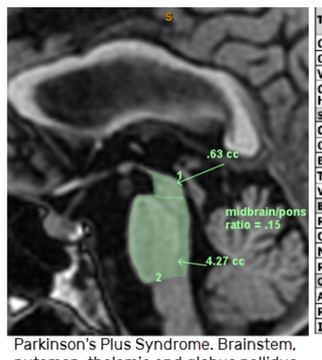
Structure	Total Volume (cm³)	Percentile
Intracranial Volume	1609	-
Whole Brain	1096	1
Forebrain Parenchyma	917	1

Total Volumes	Percentiles		
	Left	Right	Total
Cerebral White Matter	26	1	8
Cortical Gray Matter	4	1	2
Ventricles	97	99	99
Cerebral WM Hypointensities*	62	85	80
Subcortical Structures			
Cerebellar White Matter	99	99	99
Cerebellar Gray Matter	68	91	82
Brainstem	-	-	47
Thalamus	25	1	6
Ventral Diencephalon	76	85	82
Basal Ganglia			
Putamen	1	1	1
Caudate	95	99	99
Nucleus Accumbens	24	16	18
Pallidum	1	1	1
Cingulate	1	4	1
Anterior Cingulate	47	84	74
Posterior Cingulate	1	1	1
Isthmus Cingulate	1	1	1

Cortical Brain Regions	Percentiles		
	Left	Right	Total
Frontal Lobes	1	1	1
Superior Frontal	10	2	4
Middle Frontal	2	1	1
Inferior Frontal	1	1	1
Lateral Orbitofrontal	1	1	1
Medial Orbitofrontal	1	1	1
Paracentral	71	46	62
Primary Motor	11	81	45
Parietal Lobes	22	7	12
Primary Sensory	71	83	80
Medial Parietal	17	3	8
Superior Parietal	68	35	51
Inferior Parietal	23	1	4
Supramarginal	3	8	2
Occipital Lobes	77	87	84
Medial Occipital	96	93	96
Lateral Occipital	41	63	50
Temporal Lobes	3	1	1
Transverse Temporal + Superior Temporal	6	5	4
Posterior Superior Temporal Sulcus	53	10	19
Middle Temporal	7	3	3
Inferior Temporal	5	1	1
Fusiform	9	2	3
Parahippocampal	14	48	27
Entorhinal Cortex	73	13	40
Temporal Pole	7	1	1
Amygdala	38	15	24
Hippocampus	14	1	3

FTD 73 y.o.m
NeuroQuant shows diffuse atrophy with asymmetric sparing of medial temporal lobe structures, motor cortex, cerebellum, brainstem and ventral diencephalon. Cortical atrophy is far more severe than hippocampal atrophy. Note relative parietal lobe and left temporal lobe sparing.

Parkinson's Plus Syndrome (Multisystem Atrophy-PD, MSA-P)
64 y.o. female with diagnosis of Parkinson's disease 5 years ago. Dysmotility, imbalance. Poor response to levodopa. Multiparametric MRI shows atrophy of cortical gray matter, brainstem, thalamus, ventral diencephalon, putamen, globus pallidus, parietal lobes and temporal lobes with hippocampal sparing. MRS shows reduced NAA with normal Ch and mI. ASL shows normal posterior cingulate and hemispheric perfusion. No excess white matter.



Parkinson's Plus Syndrome. Brainstem, putamen, thalamic and globus pallidus atrophy. Abnormal midbrain/pons ratio consistent with multisystem atrophy with Parkinsons (MSA-p)

Total Volumes	Percentiles		
	Left	Right	Total
Cerebral White Matter	71	77	75
Cortical Gray Matter	7	3	5
Ventricles	99	98	99
Cerebral WM Hypointensities*	32	85	76
Subcortical Structures			
Cerebellar White Matter	64	88	79
Cerebellar Gray Matter	71	83	77
Brainstem	-	-	1
Thalamus	1	1	1
Ventral Diencephalon	1	1	1
Basal Ganglia			
Putamen	1	1	1
Caudate	47	67	57
Nucleus Accumbens	24	13	16
Pallidum	1	1	1
Cingulate	36	26	29
Anterior Cingulate	91	65	80
Posterior Cingulate	76	31	57
Isthmus Cingulate	1	3	1

Neuroquant shows atrophy of brainstem, thalami, putamen and other areas.

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