Postmortem MRI Microscopy for Teaching Neuroanatomy

Sean Miller MD[1], Julia Goldberg[2], Mary Bruno[1], Arline Faustin, MD[3], Thomas Wisniewski, MD[3], Laura Crandall[4], Orrin Devinsky, MD[5], Timothy Shepherd MD/PhD[1]

NYU Langone Medical Center Departments of Radiology[1], Pathology[3] and Neurology[5], NYU School of Medicine[2] & SUDC Foundation[4]

NYU Langone Health

Introduction

- The small nuclei/internal projections of the brainstem, basal ganglia and thalamus function as important relay stations between the cortex and spinal cord to regulate arousal, motor, sensor and autonomic function.
- Learning this subcortical neuroanatomy is a key, but challenging component of medical student and resident education, especially for trainees interested in neurosurgery, neurology, psychiatry & radiology.
- Current practice is to teach brainstem and thalamic anatomy using histologic-stained sections and surface anatomy [1]. Trainees then must mentally superimpose this conceptual framework onto clinical MRI that lacks sufficient internal detail to directly visualize these structures. We argue this makes it very difficult to retain!

- We have developed a novel postmortem whole brain MRI protocol for an investigation of Sudden Unexplained Death of Childhood (SUDC) that produces exquisite internal contrast in subcortical structures. This protocol can be used for direct visualization of structures when teaching neuroanatomy.

Methods

- After immersion fixation in 4% formaldehyde solution for 2-4 weeks, the whole brain was washed in water for 48 hours, then placed in a custom-built container for an overnight 3-T MRI using a 64 channel head and neck coil (Siemens Healthcare, Erlangen, Germany).
- Washing the brain eliminates T2 shortening effects of fixative [2] thus providing very similar MRI relaxation properties to living brain - this results in high signal-to-noise and reproduces in vivo contrast albeit at much higher spatial resolutions!
- With T2-weighted contrast, dark regions correspond to areas with significant myelination. The contrast recapitulates-myelin stained whole brain sections in teaching atlases [1].

TSE Parameters	Clinical Protocol	Postmortem Protocol
TR	6000 ms	4000 ms
Echo Time	100 ms	55 ms
Echo Train length	18	7
Averages	1	10
Acquisition time (h:min:sec)	1min 38s	2 hrs 30 min
Acquisition matrix	384x252	512x512
Slice thickness (mm)	5	0.8
Voxel size (mm)	0.76x0.57	0.3x0.3
FOV (mm)	220	160

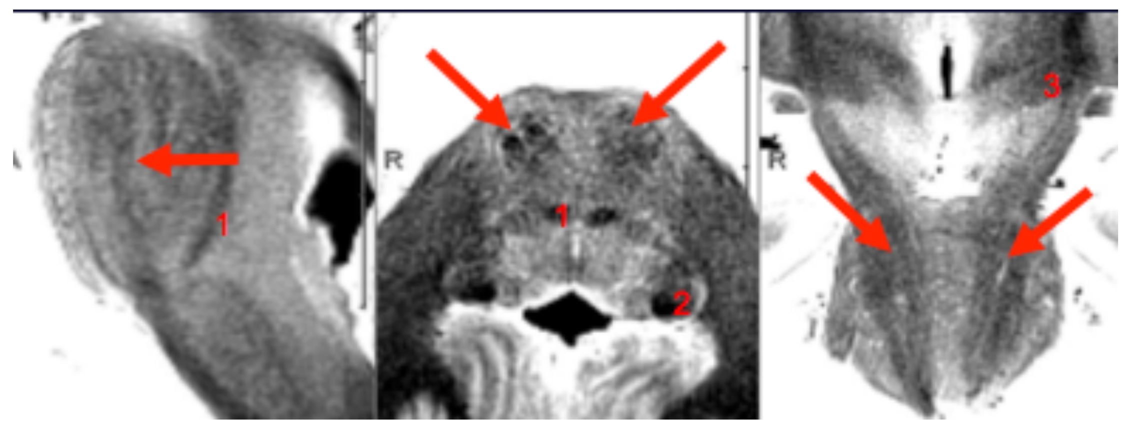

Figure 2: Sagittal, axial and coronal images of the corticospinal tract passing through the basis pontis. This is the major pathway for motor control – it can be hard to appreciate in gross specimens that this tract pivots and varies in relative compaction as it passes through the brainstem. The motor decussation is show below in figure 8. The subthalamic nucleus (3) is a major target for deep brain stimulation in patients with Parkinson's disease. [1 medial leminiscus, 2 = Vestibular nucleus, 3 = Subthalamic nucleus]

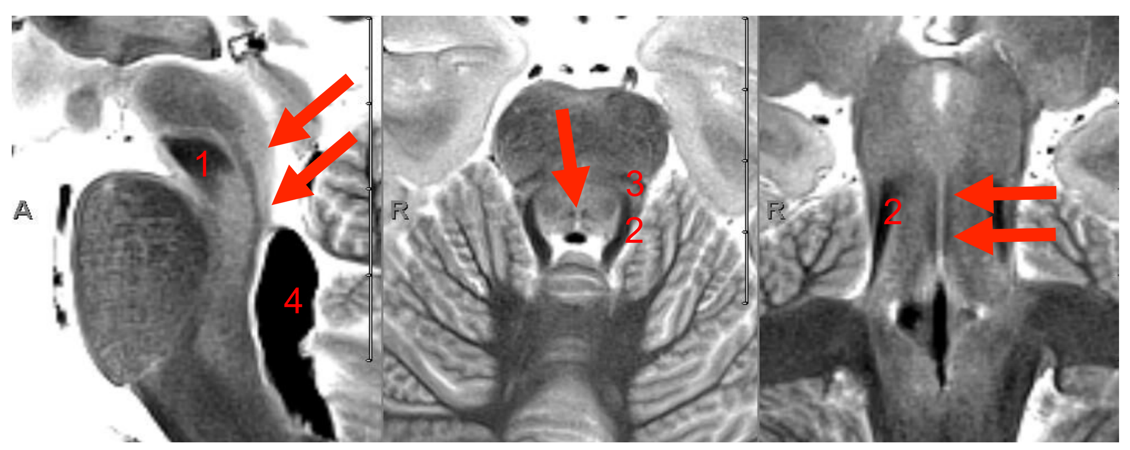

Figure 4: Sagittal, axial and coronal images of the medial longitudinal fasciculus (arrows) which coordinates control of conjugate eye movements. Injury to this structure results in internuclear ophthalmoplegia in patients with multiple sclerosis. [1 brachium conjunctivium, 2 superior cerebellar peduncle, 3 medial leminiscus, 4 air in ventricle associated with postmortem brain]

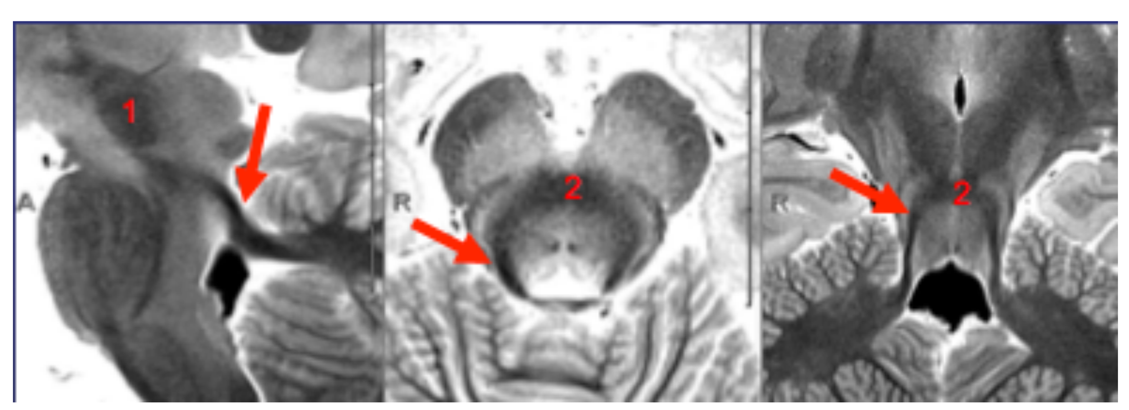

Figure 6: Sagittal, axial and coronal images of the superior cerebellar peduncle (arrows) which represents part of the dentato-rubro-thalamic pathway, the major efferent pathway from the dentate and fastigial nucleus of the cerebellum involved in fine motor coordination. This projection terminates in the red nucleus and the motor thalamus – the latter is a major target of functional neurosurgery for patients with essential tremor or tremor associated with Parkinson's disease. [1 = red nucleus, 2 = brachium conjunctivium]

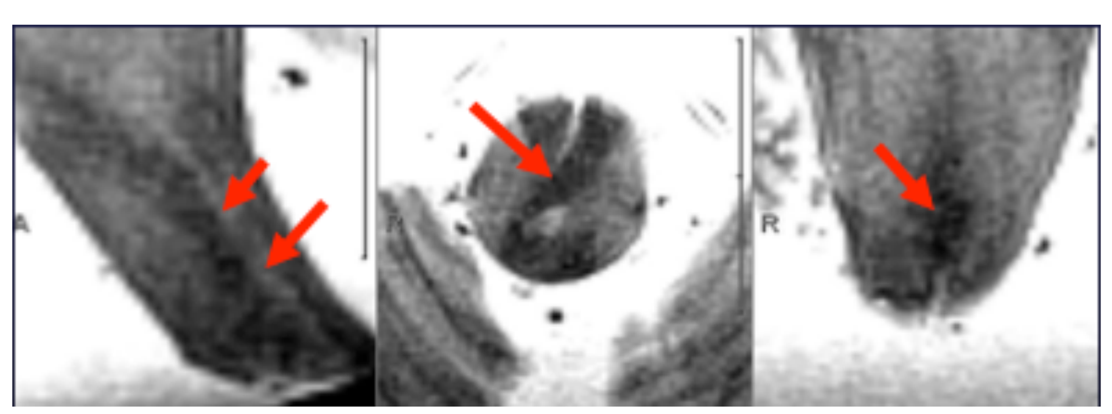

Figure 8: Sagittal, axial and coronal images of the motor decussation in the caudal medulla – here, the corticospinal tract moves dorsally as it crosses the midline to descend in the lateral fasciculus of the spinal cord. The left corticospinal tract decussation (to control right movements, dominant in most individuals) crosses first or more cranially.

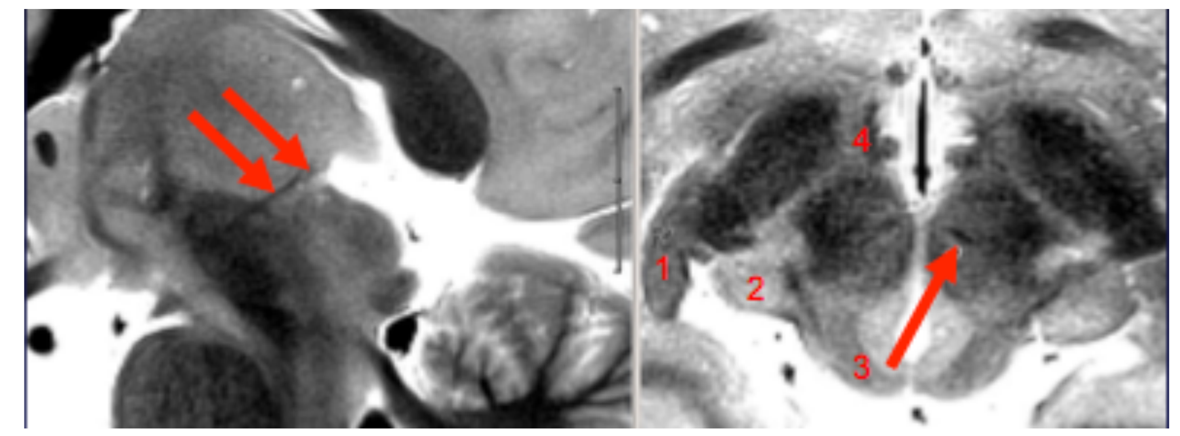

Figure 3: Sagittal and axial images of the habenulopenducular pathway (or retroflexus fasciculus of Meynert) – a compact obliquely oriented pathway that represents the major efferent pathway of the lateral and medial habenula to the ventral tegmental area of the midbrain and interpeduncular nucleus. This may seem obscure, but is major control point for regulating dopamine and serotonin levels in the basal ganglia and other brain regions. This pathway degenerates with chronic drug abuse, whereas overactivity in this pathway has been observed in chronic depression. [1 = optic tract terminating in lateral geniculate nucleus, 2 = medial geniculate nucleus, 3 = superior colliculus, 4 = oculomotor nerve]

Figure 5: Sagittal, axial and coronal images of the ansa lenticularis. The ansa lenticularis and lenticular fasciculus merge to form the thalamic fasciculus. Overall these pallidofugal pathways connect the globus pallidus and thalamus, and plays prominent role in coordination of movements. Recent evidence demonstrates improved clinical outcomes in Parkinson's disease when some fibers of the pallidofugal tracts are traversed by electrode contacts in deep brain stimulation therapy for Parkinson's disease [3].

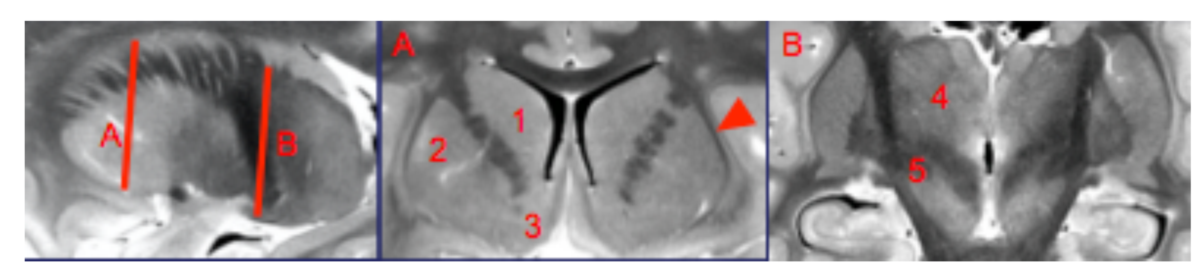

Figure 7: Sagittal and two key coronal images of the internal capsule demonstrating the anterior (A, "ALIC") and posterior limbs (B, "PLIC") help to teach trainees the complex 3-dimensional shape of the internal capsule. The ALIC has a wider, more fanlike projection ventral and superior, the fibers are more variegated in appearance in sagittal and coronal planes, and the two sides form a V-like structure in the coronal plane. The PLIC forms a more compact superior projection, but in the coronal plane demonstrates a pivot at the junction between the midbrain and diencephalon structures such that it has a more vertical, box-like orientation. The subthalamic nucleus is located immediately medial to this pivot in fiber orientation. [Arrowhead = External capsule, 1 = Caudate Nucleus, 2 = Putamen, 3 = Nucleus accumbens, 4 = Thalamus, 5 = Subthalamus]

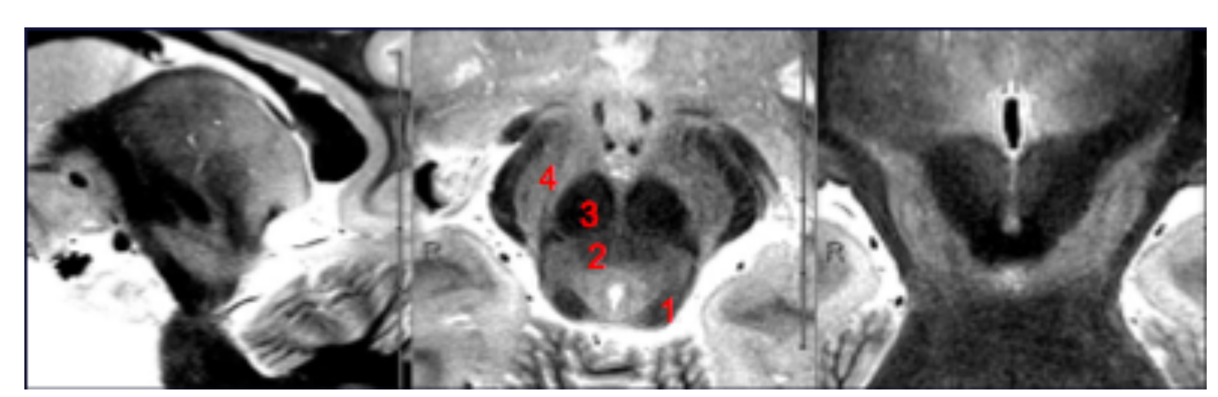

Figure 9: The red nucleus is a rostral midbrain structure that receives input from the dentato-rubrothalamic pathway described above. In combination with the substantia nigra, these structures coordinate motor movement through the extrapyramidal pathway. [1 = Inferior colliculus, 2 = Central tegmental tract, 3 = Red nucleus, 4 = Substantia nigra

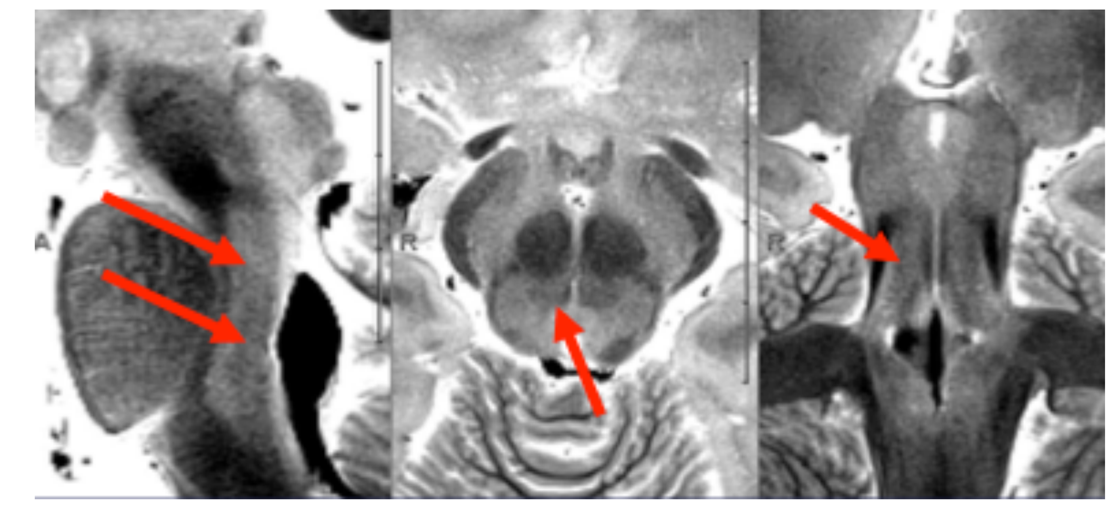

Figure 10: The central tegmental tract (CTT) contains descending fibers from the red nucleus which terminate in the inferior olive. The CTT is a part of the Guillian-Mollaret triangle, which is a series of tracts connecting the red nucleus, inferior olive and dentate nuclei. Pathology associated with these areas is associated with movement disorders, tremors, and myoclonus.

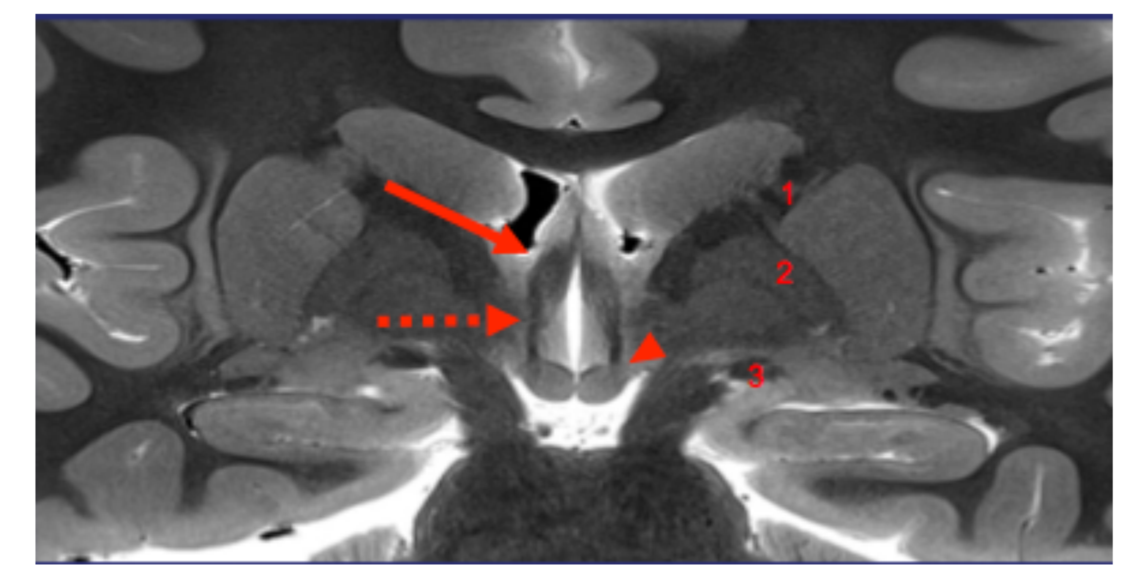

Figure 11: Columns of the fornix (arrow), mammillary bodies and post commissural fibers (arrow head). This image clearly shows that the fornix caliber is reduced below the level of the anterior commissure (dotted arrow) as some of the projections sharply turn dorsally directly into the anterior nucleus of the thalamus. Forniceal fibers originate in the hippocampus before traveling to the mammillary bodies and thalamus via the fornix. [1 = Anterior limb internal capsule, 2 = globus pallidus externa, 3 = optic tract]

Results/Discussion

- Our novel postmortem protocol does not require advanced technical skills, exotic hardware or MRI sequences – it can be used by anyone with approved access to autopsy specimens and a conventional 3-T MRI system.
- Unlike histology, many clinically important subcortical structures can be observed simultaneously in all three planes with dynamic trainee control of the imaging plane position and angle to emphasize spatial relationships.
- Direct visualization of key subcortical nuclei and pathways using a commonly employed clinical modality (MRI) should facilitate both initial learning of the anatomy by trainees and incorporation of that knowledge into clinical practice.
- Further refinement of these sequences may facilitate generating similar contrast in living patients for visualization of pathology and direct functional neurosurgery targeting.

References

1. DE Haines. Neuroanatomy – An atlas of structures, sections and systems. 6th edition. Lippincott Williams & Wilkins; Baltimore, MD 2004. Reproduced Fig. 5-24, pgs 130-131.
2. Shepherd et al. Aldehyde fixative solutions alter the water relaxation and diffusion properties of nervous tissue. Magnetic Resonance Medicine. 2009. 62:26-34.
3. Gallay et al. Human pallidothalamic and cerebellothalamic tracts: anatomical basis for functional sterotactic neurosurgery. Brain Structure and Function. 2008. 212:443-463
4. The senior author appreciates helpful comments and suggestions from Kal Rubinson.