

Connectome Analysis of the Nucleus Accumbens: Refining Radiosurgical Targeting for Addictive Disorders

WSSFN 2025 Interim Meeting. Abstract 0169

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How to Cite: Contreras López WO, Chang J, Gonzalo Párraga R, Torres Monterrosa J, Merlos Salazar L. Connectome Analysis of the Nucleus Accumbens: Refining Radiosurgical Targeting for Addictive Disorders: WSSFN 2025 Interim Meeting. Abstract 0169. *NeuroTarget*. 2025;19(2):150-1.

Abstract

Introduction: Addictions pose a major global health and socioeconomic challenge. Treatment strategies include pharmacological interventions, deep brain stimulation, and ablative procedures. Stereotactic radiosurgery (SRS) has emerged as a noninvasive, precise option for addiction management. Understanding the anatomy and connectivity of the nucleus accumbens (NAc) is key to refining radiosurgical targets and improving outcomes.

Method: Diffusion tensor imaging from 3T and 1.5T MRI scanners was obtained in five healthy subjects using T1 and T2 sequences. Images were fused with autosegmentation of the NAc, ventral tegmental area (VTA), amygdala, hippocampus, hypothalamus, and periventricular gray (PVG). The insula, medial/lateral orbitofrontal cortex, and dorsolateral prefrontal cortex were manually drawn. Connectivity to the NAc was visually assessed with fractional anisotropy thresholds (20–10). The five densest fiber tracts guided target selection, aligned to the anterior–posterior commissure, and transferred to Gamma Plan for radiosurgical planning.

Results: The strongest connections were between the medial orbitofrontal cortex (mOFC), hypothalamus, VTA, PVG, and amygdala with the NAc. The mOFC–NAc and hippocampus–NAc tracts were the most and least robust, respectively. Derived stereotactic coordinates supported connectome-based targeting, proposing a 90 Gy dose to the NAc shell and aligning the 20 Gy isodose for neuromodulation. The right and left NAc received > 20 Gy in 75.2% and 55.6% of their volumes, while the optic apparatus received ≤ 5.4 Gy (Dmax).

Discussion: The NAc, within the ventral striatum, integrates limbic, cognitive, and motor inputs regulating reward and motivation. Its shell and core subregions differ functionally, with the shell showing dense dopaminergic input from the

VTA and high sensitivity to reinforcement stimuli. Chronic substance exposure induces neuroplastic changes underlying compulsive behaviors, making the NAc shell a rational neurosurgical target. DBS, radiofrequency ablation, and SRS have yielded variable but promising results in refractory opioid and alcohol dependence. Advances in diffusion imaging now enable precise mapping of NAc connectivity and subregion-specific targeting. High-dose (up to 90 Gy) LINAC-based radiosurgery has shown safety and potential for radiomodulation, highlighting the therapeutic promise of anatomically informed, connectivity-guided interventions.

Conclusions: Addiction remains a pervasive disorder with high relapse rates despite medical and behavioral therapies. Radiosurgery, a time-tested and safe functional technique, may offer a new treatment alternative. Connectivity-based SRS using commercial planning software allows visualization and autosegmentation of key NAc connections, supporting patient-specific, circuit-informed targeting in addiction neuromodulation.

References

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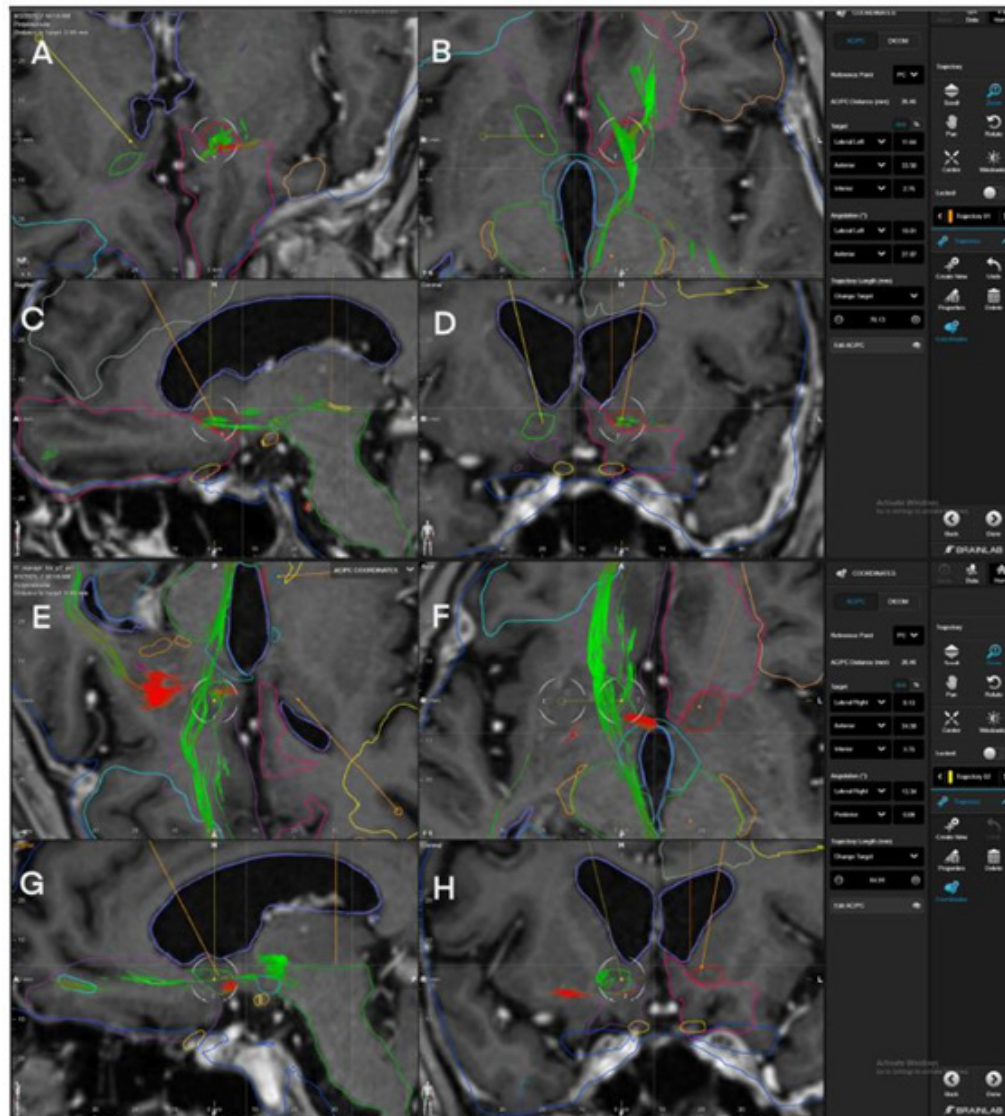


Figure 1. Bilateral trajectories targeting the highest-density fiber bundles crossing the nucleus accumbens (NAc). Axial, sagittal, coronal, and superior views of the left (A–D) and right (E–H) trajectories show fibers connecting the medial orbitofrontal cortex, amygdala, hypothalamus, ventral tegmental area, and periaqueductal gray with the NAc, particularly its ventromedial “shell.” Images were generated using BrainLab Elements (BrainLab, Munich, Germany).