

Tractography-Guided Multitarget DBS with Multiple Independent Current Control Combining Linear and Directional Electrodes in Resistant Depression and Anxiety

WSSFN 2025 Interim Meeting. Abstract 0167

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How to Cite: Contreras López WO, Millán Giraldo PA, Moreno Guerra N, Rosales JE. Tractography-Guided Multitarget DBS with Multiple Independent Current Control Combining Linear and Directional Electrodes in Resistant Depression and Anxiety: WSSFN 2025 Interim Meeting. Abstract 0167. *NeuroTarget*. 2025;19(2):146-7.

Abstract

Introduction: Treatment-resistant depression (TRD) is a chronic and severe form of major depressive disorder with limited therapeutic options. One-third of TRD patients fail to respond to pharmacological and psychotherapeutic interventions. Deep Brain Stimulation (DBS) is a promising therapy for TRD patients, but its clinical results have been highly variable in multiple studies focused on single target interventions, suggesting suboptimal targeting of the circuits implicated in TRD. Connectomics approaches have emerged to enable an individualized planning of symptom-specific circuits targeting in TRD with promising results. We report a case of Multitarget DBS involving six neural tract including subgenual cingulate cortex, Brodmann area 25 (SGC25) and anterior limb of the internal capsule (ALIC) with distal extension toward the nucleus accumbens (NAc) stimulation.

Clinical description: A 34-year-old woman presented with a chronic psychiatric history dating back to age 10, when she developed disordered eating behaviors, bulimia nervosa type 1 and later anorexia nervosa at 15 years managed with limited success. Over the ensuing years, she experienced recurrent major depressive episodes, generalized anxiety disorder, panic attacks, social phobia, and agoraphobia. Despite multiple evidence-based psychiatric interventions—including cognitive behavioral therapy and sequential pharmacotherapy with selective and multiple serotonin reuptake inhibitors and serotonin–norepinephrine reuptake inhibitors—her symptoms remained refractory or transient improvement. At evaluation, affective lability, anhedonia, hopelessness, and intrusive anxiety are presented persistently. Given the TRD diagnostic, a multidisciplinary team recommended an innovative multitarget DBS approach using Multiple Independent current control (MICC).

Discussion: This case illustrates the potential of simultaneous modulation of interconnected affective and cognitive circuits implicated in TRD. The ALIC-NAc target was selected to precisely modulate anxiety and reward-related networks,

while the SGC25 was chosen to engage affective regulation pathways including medial forebrain bundle (MFB), dorsal longitudinal fasciculus (DLF), and anterior thalamic radiation (ATR), all described with antidepressant effect in DBS for TRD. MICC technology enabled tailored stimulation according to TRD individual evolution explaining the observed multidomain symptomatic improvement across scales. At four-month follow-up, Hamilton Depression Rating Scale (HDRS-17) scores improved by 65%, Montgomery–Åsberg Depression Rating Scale (MADRS) by 70%, with additional improvement in Beck inventory depression and anxiety scales (BDI and BAI).

Conclusions: This novel single-case study supports the feasibility and clinical benefit of multitarget MICC-DBS guided by connectomics in TRD. Individualized modulation of SGC25 and ALIC-NAc may improve cognitive and anxiety predominant symptoms in TRD patients. Further studies are needed to replicate these findings in a well-selected cohort of TRD patients to validate the individualized multitarget MICC-DBS modulation and its progressive capacity to improve symptoms in TRD. Coronal postoperative MRI with tractography overlay demonstrating bilateral multitarget DBS electrode trajectories. Directional Cartesia™ leads were placed in the SGC25, while linear Vercise™ leads traversed the ALIC with distal contacts in the NAc. Patient-specific tractography highlights key white matter pathways: MFB (blue), ATR (green), and DLF (red), confirming engagement of fronto-limbic and reward circuits relevant to depression and anxiety modulation. (Figure 1).

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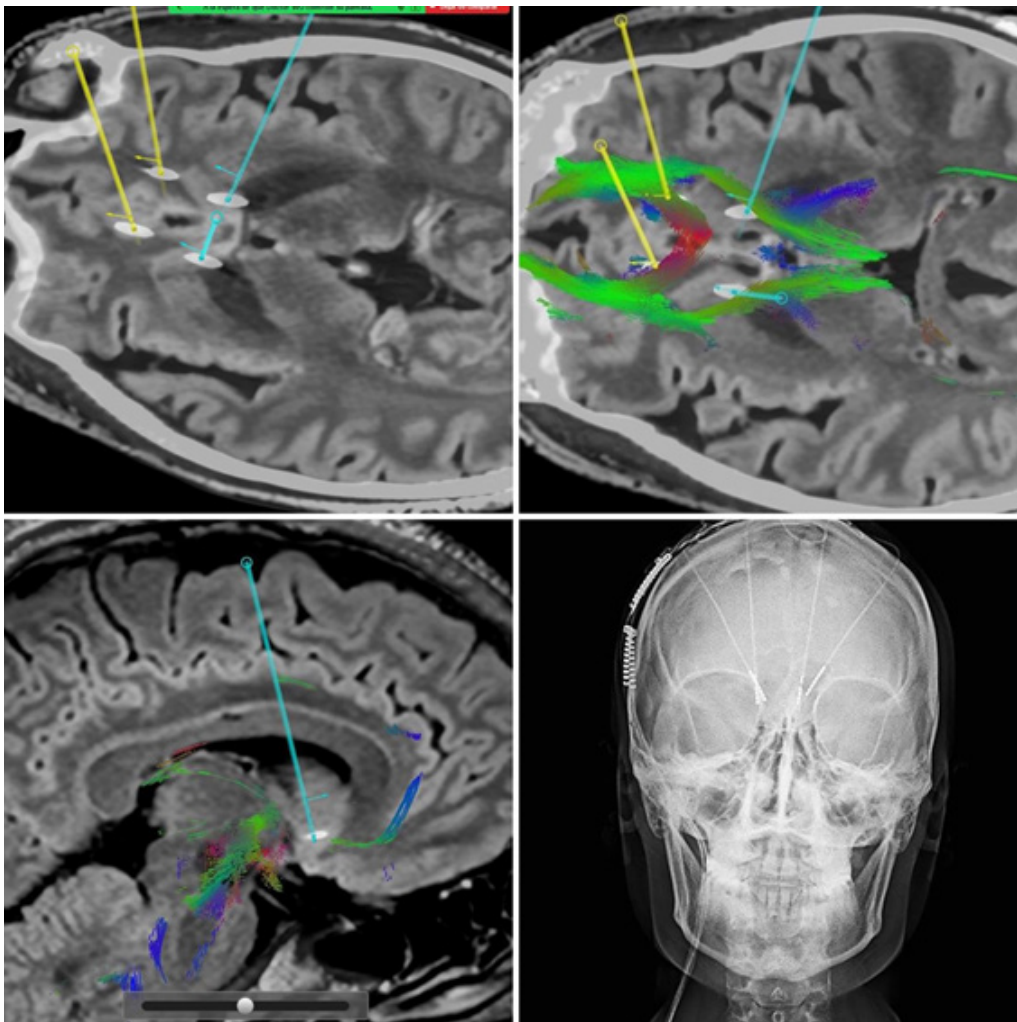


Figure 1. Patient-specific tractography highlights key white matter pathways: MFB (blue), ATR (green), and DLF (red), confirming engagement of fronto-limbic and reward circuits relevant to depression and anxiety modulation.