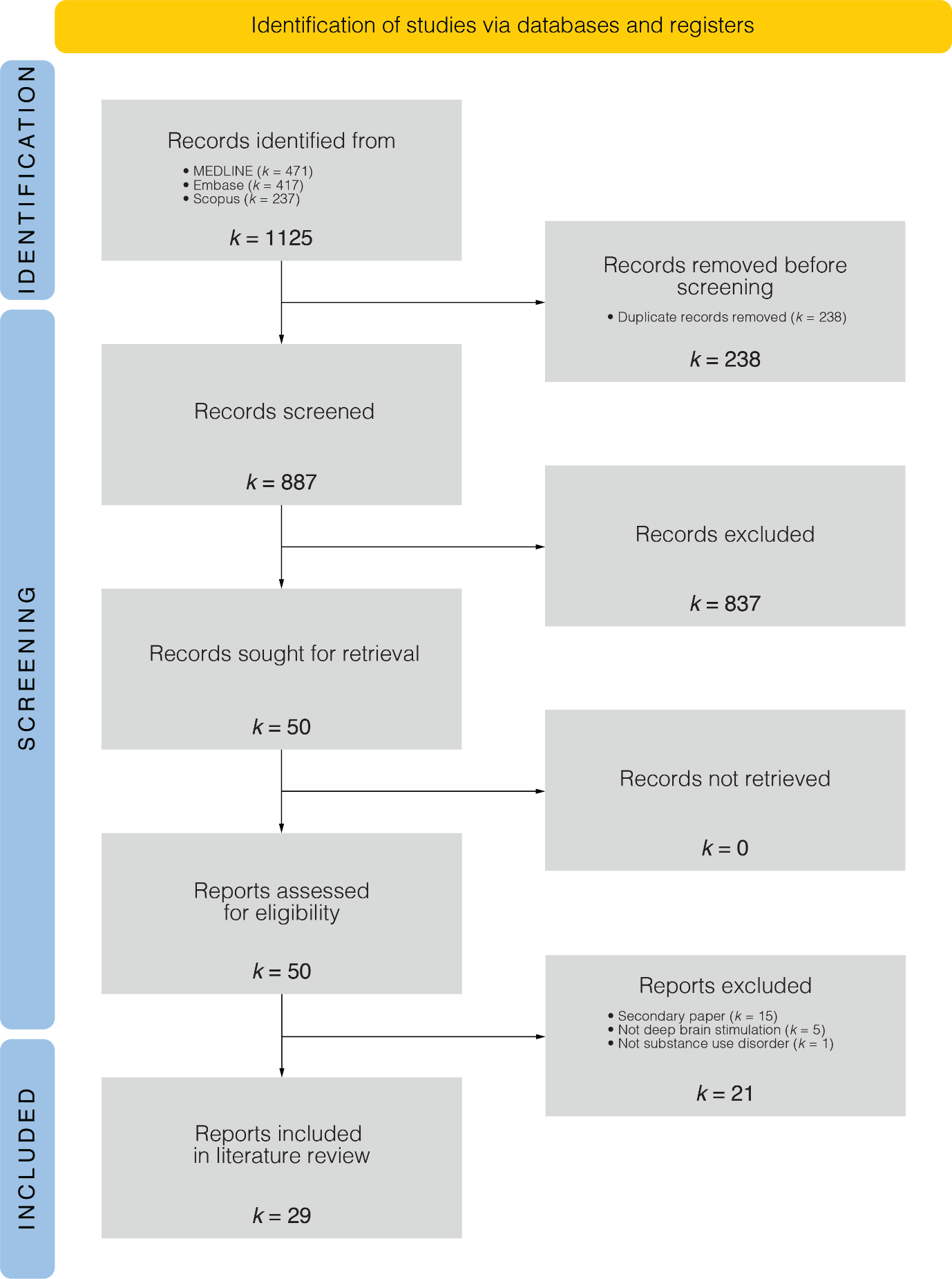
**Supplementary Materials**



Supplementary Figure 1. Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 diagram of literature review of deep brain stimulation for substance use disorder. Two reviewers (AZY and DAH) independently screened titles, abstracts, and full-text article(s) against predefined eligibility criteria, where articles were included if: 1) participants received deep brain stimulation, 2) had substance use disorder (e.g., opioid use disorder, nicotine use disorder, alcohol use disorder, etc.), 3) studies in English, 4) full-text published studies, 5) in humans, and 6) any clinical study (no reviews). Conflicts were resolved by one reviewer (AZY), and if they were not resolved, then by another reviewer (VMT). The databases MEDLINE via Ovid (*k=471*), Embase via Ovid (*k=417*), and Scopus (*k=237*) totalling 1125 articles were searched from their inception to July 24, 2024. After removing duplicates (*k*=238), 842 articles underwent abstract screening, where most were excluded (*k*=837) due to not being deep brain stimulation or substance use disorder. Furthermore, 50 full-text articles were screened, resulting in 29 articles included.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Anxiety** | **Energy** | **Calmness** | **Craving** |
| **Baseline** | 5 | 8 | 8 | 6 |
| L0 | 3 | 8 | 4 | 5 |
| L1 | 10 | 2 | 5 | 2 |
| L2 | 0 | 6 | 10 | 0 |
| L3 | 0 | 10 | 10 | 4 |
| Sham | 2 | 7 | 7 | 5 |
| L4 | 4 | 8 | 9 | 3 |
| L5 | 5 | 2 | 5 | 4 |
| L6 | 6 | 3 | 6 | 6 |
| L7 | 5 | 5 | 4 | 7 |
| R8 | 4 | 6 | 6 | 4 |
| R9 | 3 | 2 | 7 | 6 |
| R10 | 5 | 3 | 5 | 6 |
| R11 | 6 | 5 | 6 | 2 |
| Sham | 2 | 7 | 3 | 4 |
| R12 | 2 | 8 | 9 | 2 |
| R13 | 2 | 10 | 3 | 3 |
| R14 | 5 | 7 | 5 | 5 |
| R15 | 6 | 8 | 2 | 6 |

Supplementary Table 1: Example of monopolar review of deep brain stimulation contacts from second programming session. L: left; and R: right.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Weeks**  **From DBS** | **Illicit**  **Opioid**  **Urinalysis** | **Fentanyl**  **TLFB (g/day)** | **Opioid**  **Craving**  **(0–10)** | **Nicotine Craving**  **(0–10)** | **BSCQ**  **(0–100)** | **PHQ-9**  **(0–27)** | **GAD-7**  **(0–21)** | **QOL**  **(0–100)** |
| Baseline | + | 3.0 | 9 | 10 | 8 | 24 | 21 | 40 |
| 2 | - | 0 | 0 | 10 | 33 | 7 | 5 | 76 |
| 3 | - | 0 | 0 | 5 | 79 | 3 | 0 | 81 |
| 4 | - | 0 | 0 | 5 | 71 | 2 | 0 | 74 |
| 5 | - | 0 | 0 | 7 | 60 | 0 | 0 | 73 |
| 6 | - | 0 | 0 | 5 | 72 | 3 | 1 | 78 |
| 11 | - | 0 | 0 | 5 | 68 | 5 | 5 | 83 |
| 16 | - | 0 | 0 | 0 | 91 | 0 | 0 | 69 |
| 20 | - | 0 | 0 | 5 | 100 | 0 | 0 | 80 |
| 24 | - | 0 | 0 | 3 | 99 | 1 | 2 | 80 |
| 30 | - | 0 | 0 | 3 | 98 | 3 | 0 | 81 |
| 38 | + | 0.2 | 6 | 5 | 33 | 8 | 6 | 49 |
| 43 | + | 0.5 | 7 | 5 | 28 | 10 | 6 | 29 |
| 48 | + | 1.0 | 5 | 5 | 48 | 2 | 1 | 64 |
| ***Post-DBS***  ***Summary*** | ***Σ 11/14 (78.57%)*** | ***μ 0.13***  ***± 0.29*** | ***μ 1.38***  ***± 2.56*** | ***μ 4.85***  ***± 2.18*** | ***μ 67.69***  ***± 24.92*** | ***μ 3.38***  ***± 3.10*** | ***μ 2.00***  ***± 2.42*** | ***μ 70.54***  ***± 14.91*** |

Supplementary Table 2: Patient outcomes. BSCQ: Brief Situational Confidence Questionnaire; DBS: Deep brain stimulation; GAD-7: Generalized Anxiety Disorder 7-item scale; PHQ-9: Patient Health Questionnaire 9-item scale; QOL: Flanagan Quality of Life Scale; and TLFB: timeline follow-back.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **Mean Age** | | **Sample** | **Primary Disorder** | | **Primary SUD** | | **DBS**  **Target** | | **Mean Follow-Up in Months** | | **Abstinence at Mean Follow-Up** | | **Substance**  **Reduction**  **> 50%** | | **Craving Reduction**  **> 50%** | | | **Substance Use Outcome** | | **Other Outcome** | | **DBS Adverse Events** | |
| (2005 Witjas... Azulay)1 | 45.5 | | 2 (2M/0F) | PD | | L-Dopa | | STN | | 24 | | 1/2 | | 2/2 | | 2/2 | | | 1 participant stopped dopaminergic drugs and excessive alcohol consumption with the exception of a brief alcohol relapse. The other participant experienced a 75% reduction in dopaminergic drugs. Both participants experienced cessation of craving and compulsive usage of L-dopa medication. | | Improvements in mood, sociability, quality of life, hypersexuality, and irritability. | | None reported. | |
| (2007 Kuhn... Sturm)2  *• 1 pt in (2009 Kuhn... Sturm)* | 54 | | 1 (1M/0F) | AD | | Alcohol | | NAc | | 12 | | 0/1 | | 1/1 | | 1/1 | | | The participant reduced alcohol consumption from 10+ drinks per day to 1–2. Near cessation of craving for alcohol. | | Anxiety and depression were unchanged. | | None reported. | |
| (2009 Heinze... Münte)3 *• 3 pts in (2009 Müller... Bogerts)* | 37.7 | | 3 (3M/0F) | SUD | | Alcohol | | NAc | | 14 | | 2/3 | | 3/3 | | 3/3 | | | 2/3 participants achieved abstinence, while 1/3 experienced 4 relapses (10 weeks cumulatively) across 16 months postoperatively. Significant to complete reductions in craving across all participants. | | Scalp EEG and LFPs from externalized leads were recorded during cognitive tasks. Action monitoring study using Eriksen Flanker Task found evidence of NAc in goal/directed behaviours. Incentive salience study found LFP modulations when alcohol/related cues were present. | | Hypomania (1). | |
| (2009 Kuhn... Sturm)4 • *1 pt from (2007 Kuhn... Sturm)* | 43.5 | | 10 (7M/3F) | TS (4), OCD (5), AD (1) | | Nicotine | | NAc | | 30 | | 3/10 | | 3/10 | | N/A | | | 3/10 participants (OCD [2] and TS [1]) achieved abstinence from smoking. | | N/A | | None reported. | |
| (2009 Müller... Bogerts)5 *• 3 pts from (2009 Heinze... Münte)*  *• 3 pts in (2013 Voges... Heinz) • 3 pts in (2016 Müller... Bogerts)* | 37.7 | | 3 (3M/0F) | SUD | | Alcohol | | NAc | | 14 | | 2/3 | | 3/3 | | 3/3 | | | 2/3 participants achieved abstinence while 1/3 had 4 relapses (10 weeks cumulatively) in 15 months post/operatively. All 3 participants had notable remarkable reduction of cravings. | | Improvements in depression, anxiety, and quality of life. | | Hypomania (1). | |
| (2010 Mantione... Denys)6 | 47 | | 1 (0M/1F) | OCD | | Nicotine | | NAc | | 24 | | 0/1 | | 1/1 | | 1/1 | | | The participant smoked 35 cigarettes per day up to 10 months postoperatively, where she then remained abstinent for the next 14 months. She no longer experienced cravings for cigarettes. | | Weight loss as well as significant improvements in OCD and depression symptoms. | | None reported. | |
| (2011 Kuhn... Sturm)7 | 69 | | 1 (1M/0F) | SUD | | Alcohol | | NAc | | 12 | | 0/1 | | 1/1 | | 1/1 | | | The participant consumed 200g vodka per day at baseline to occasionally at 8 months and none at 1 year. Craving Believe Questionnaire (0–120) went from 70 at baseline to 5. | | Alcohol Dependence Scale (ADS) and the Obsessive Compulsive Drinking Scale (OCDS) fell below pathological scores. Improvement in cognitive control deficit, as reﬂected in the error/related negativity (ERN) amplitude during psychobehavioural tasks with EEG recordings. | | None reported. | |
| (2011 Zhou... Jiang)8 | 24 | | 1 (1M/0F) | SUD | | Opioids | | NAc | | 72 | | 1/1 | | 1/1 | | N/A | | | The participant reduced substance use from 1–1.5 g heroin per day at baseline to 0 and 40 cigarettes per day to 10. | | Improvement in anxiety, depression, cognition, memory and intelligence quotient. | | Confusion (1), urinary incontinence (1), and weight gain (1). | |
| (2012 Heldmann... Münte)9 | 38 | | 1 (1M/0F) | SUD | | Alcohol | | NAc, BNST, & VP | | 18 | | 1/1 | | 1/1 | | 1/1 | | | The participant was abstinent from alcohol and experienced near complete cessation of craving. | | DBS/ON indicated less risk taking during a gambling task, where simultaneous PET imaging showed activation of the paracingulate cortex in the win situation, whereas hippocampus and precuneous activation in the loss situation, which were not seen in DBS/OFF. | | Hypomania (1). | |
| (2012 Strong... Greenberg)10 | 43 | | 1 (0M/1F) | MDD | | Nicotine | | VC & VS | | N/A | | N/A | | N/A | | N/A | | | The participant smoked <10 cigarettes per day but during 2 periods of DBS interruption (e.g., battery depletion), smoking increased 50% to 200% when DBS stimulation was OFF. Moreover, the participant experienced increased cravings but intense displeasure when smoking. When DBS was ON, smoking rate and pattern returned to baseline. | | During 2 episodes of interrupted DBS, depressive symptoms increased close to MADRS remission threshold (<10) (MADRS of 7 and 10 during episodes 1 and 2, respectively). When DBS resumed, depressive symptoms decreased (MADRS of 5 and 2). | | None reported. | |
| (2012 Valencia-Alfonso... Denys)11 | 47 | | 1 (1M/0F) | SUD | | Opioids | | NAc | | 10 | | 0/1 | | 1/1 | | 1/1 | | | The participant reduced substance use to the weekends for 4 months and then eventually achieved abstinence for more than 6 months, except for a 14/day relapse. Desire and intention scale for drugs went from 33 at baseline to 18. | | Intraoperative recordings demonstrated significant differences in power for drug pictures versus neutral at the dorsal lead contacts (2 and 3). | | None reported. | |
| (2013 Voges... Heinze)12 *• 3 pts from (2009 Müller... Bogerts) • 3 pts in (2016 Müller... Bogerts* | 44 | | 5 (5M/0F) | SUD | | Alcohol | | NAc | | 38 | | 2/5 | | 5/5 | | 5/5 | | | 2 participants were abstinent for over 4 years while the remaining 3 participants experienced considerably reduced frequency and intensity of relapses. All participants reported significant reductions in craving. | | N/A | | Hypomania (1) and lead dislocation (1). | |
| (2014 Kuhn... Sturm)13 *• 2 pts in (2018 Piesker... Kuhn) • 2 pts in (2020 Sildatke... Kuhn) • 2 pts in (2023 Bach... Mann)* | N/A | | 2 (1M/1F) | SUD | | Opioids | | NAc | | 18 | | 0/2 | | 2/2 | | 2/2 | | | Both participants remained abstinent except for 1 single use each. Craving decreased from 10/10 at baseline to 0. | | Significant improvement in craving, depression, and anxiety for both participants. | | Seizure in participant with epileptic history (1) and lead dislocation (1). | |
| (2016 Gonçalves-Ferreira... Teixeira)14 | 36 | | 1 (1M/0F) | SUD | | Cocaine | | NAc, ALIC, & BNST | | 30 | | 0/1 | | 1/1 | | 1/1 | | | Negative urinalysis improved from 12.5% (1/8 tests) at baseline to 56.5% (13/23) at 24 months post/operatively. Craving decreased from 3.4/10 at baseline to 0. | | Y/BOCS improved from 14 at baseline to 4 at 24 months. | | Warmness (1), sweating (1), flushing (1), weight gain (1), decreased libido (1), and occasional metallic taste (1). | |
| (2016 Müller... Bogerts)15 *• 3 pts from (2009 Heinze... Münte) • 3 pts from (2009 Müller... Bogerts) • 3 pts from (2013 Voges... Heinze)* | 43.6 | | 5 (5M/0F) | SUD | | Alcohol | | NAc | | 55.2 | | 2/5 | | 3/5 | | 5/5 | | | 2/5 participants remained abstinent. The remaining 3 participants reported significant reductions in substance use for several years, but 2/3 of these returned to drinking levels similar to baseline. All participants reported the disappearance of cravings though some continued to use. | | Participants reported improved quality of life. | | Hypomania (1) and lead dislocation (1). | |
| (2018 Zhang... Son)16 | 39 | | 1 (1M/0F) | SUD | | Opioids | | VC & VS | | 4.5 | | 0/1 | | 0/1 | | N/A | | | The participant experienced 8 relapses from 3/4 months postoperatively. Decreased cigarette smoking from 140 per week to 20. | | At 1.5 months postoperatively, the participant gained weight, returned to work, and experienced less insomnia. Fatal overdose at 4 months postoperatively. | | Hypomania (1) and impulsivity (1). | |
| (2018 Ge... Gao)17 *• 7 pts from (2019 Chen... Gao)* | 36.7 | | 7 (7M/0F) | SUD | | Opioids | | NAc & ALIC | | 19.9 | | 4/7 | | 4/7 | | 7/7 | | | 4/7 participants remained abstinent for up to 40 months. 2 participants relapsed at 10 and 7 months postoperatively, and 1 participant was lost to follow/up at 3 months. Cravings decreased from on average of 5.71/10 at baseline to 1.71. | | Significant inverse correlation between craving scores and power of theta frequency band of ALIC LFP intraoperative recordings. | | None reported. | |
| (2018 Piesker... Kuhn)18 *• 2 pts from (2014 Kuhn... Sturm) • 4 pts in (2020 Sildatke... Kuhn) • 4 pts in (2023 Bach... Mann)* | 42.6 | | 9 (8M/1F) | SUD | | Opioids and Alcohol | | NAc | | N/A | | N/A | | N/A | | N/A | | | N/A | | Comparing DBS ON and OFF with a 24/hour washout, there were no significant differences in delay discounting tasks. Also, patients with SUD did not differ in their discounting behavior compared to 18 healthy controls. | | None reported. | |
| (2019 Ge... Wang)19 | 43.5 | | 2 (2M/0F) | SUD | | Meth | | NAc & ALIC | | 24 | | 1/2 | | 1/2 | | 1/2 | | | 1 participant remained abstinent, while the other participant relapsed but was found to have misplaced lead after post/operative imaging. The abstinent patient went from 5/10 craving at baseline to 0. | | Weight gain and better quality of life in participant who remained abstinent. | | Insomnia (1), hypomania (1), and (1) teeth grinding at higher voltages. | |
| (2019 Chen... Gao)20 • *7 pts in (2018 Ge... Gao)* | 34 | | 8 (7M/1F) | SUD | | Opioids | | NAc & ALIC | | 36 | | 5/8 | | 5/8 | | 5/8 | | | 5 participants were abstinent for 3+ years, while 2 relapsed after 6 months of abstinence, and was 1 lost to follow/up at 3 months. The degree of cravings was reduced for participants that were abstinent (7.6/10 at baseline to 1.4). | | Abstinent participants experienced improved quality of life, alleviated psychiatric symptoms, PET increase glucose metabolism in brain regions (e.g., inferior frontal gyrus). | | Intracranial hemorrhage with no neurological deficit (1), fever (1), headache (1), insomnia (1), dizziness (1) subjective slight memory decline (1), and agitation/irritability (1). | |
| (2020 Sildatke... Kuhn)21  *• 2 pts from (2014 Kuhn... Sturm)  • 4 pts from (2018 Piesker... Kuhn)  • 4 pts in (2023 Bach... Mann)* | 44.5 | | 4 (4M/0F) | SUD | | Opioids | | NAc | | N/A | | N/A | | N/A | | N/A | | | N/A | | Eriksen flanker task with electrophysiology recordings via externalized leads in the NAc showed that LFP correlated with error processing in 2/4 and subjective error awareness in 3/4. | | None reported. | |
| (2020 Zhang... Sun)22 | 42 | | 1 (1M/0F) | SUD | | Opioids | | NAc | | 24 | | 0/1 | | 1/1 | | 1/1 | | | The participant used opioids once across 24 months and reported marked reduction in craving. | | N/A | | None reported. | |
| (2020 Zhu... Sun)23 | 28 | | 1 (1M/0F) | SUD | | Opioids | | NAc & ALIC | | 12 | | 1/1 | | 1/1 | | 1/1 | | | The participant remained abstinent and reported a significant reduction in craving for all substances. | | Psychiatric and neuropsychological assessments showed significant improvements in depression, anxiety, sleep, quality of life, and most aspects of cognitive functioning. His overall health status was also improved." | | None reported. | |
| (2021 Mahoney... Rezai)24 *• 1 pts in (2023 Rezai... Hodder)* | 30s | | 1 (1M/0F) | SUD | | Opioids | | NAc & ALIC | | 12 | | 1/1 | | 1/1 | | 1/1 | | | Achieved abstinence with a significant decrease in substance craving (53.4/100 at baseline for benzodiazepines to 1.0 and 5.8/100 to 0 for opioids). | | Improvements in sleep, cognition, depression, anxiety, and quality of life. FDG/PET in DBS/ON versus OFF showed increase in the dorsolateral prefrontal and medial premotor cortices and a decrease in the basal ganglia, thalamus, and cerebellum. | | None reported. | |
| (2022 Davidson... Lipsman)25 | 49 | | 6 (4M/2F) | SUD | | Alcohol | | NAc | | 12 | | 0/6 | | 6/6 | | 5/6 | | | All participants reduced alcohol intake by greater than 50%. Across the group, average drinks per day decreased from 10.4 to 2.7, alcohol use disorder identification test (AUDIT) from 35.7 to 11.0, alcohol urge questionnaire (ACQ) from 58.3 to 41.8, alcohol dependency scale (ADS) from 26.0 to 9.0, and obsessive-compulsive drinking scales (OCDS) from 28.7 to 8.3. | | Improvements in depression (HAMD: 15.3 to 11.0) and anxiety symptoms (BAI: 20.3 to 9.3). fMRI BOLD/activation of the dorsal striatum was decreased with DBS turned ON when shown alcohol cues/stimuli compared to neutral images. FDG/PET displayed reduced glucose metabolism in the NAc at 6 months compared to baseline. | | Headache (5), infection (1), hypomania (1), scalp pruritis (1), depressive episode (1), fatigue (1), and unhappy with cosmesis of device (1) | |
| (2023 Bach... Mann)26 *• 2 pts from (2014 Kuhn... Sturm)  • 4 pts from (2018 Piesker... Kuhn)  • 4 pts from (2020 Sildatke... Kuhn)* | 44.2 | | 12 (12M/0F) | SUD | | Alcohol | | NAc | | 18 | | 1/12 | | 3/12 | | 6/12 | | | 1/12 participants achieved abstinence, and 3 participants were classified as responders (i.e., reduction of mean alcohol use by two+ WHO risk drinking levels). The mean reduction alcohol use from baseline was 198.1 grams per day in responders and 43.4 grams per day in non/responders. Across the group, there was a decrease in alcohol craving from 21 to 5.9 (via OCDS). There was a significantly higher number of abstinent days, lower alcohol craving, and anhedonia in the DBS/EARLY ON group 6 months after randomization compared to the DBS/LATE OFF group. | | Reduction in depressive symptoms, anhedonia, and increases in QoL and functioning that were larger in the DBS/EARLY ON compared to the DBS/LATE ON group. | | Decreased libido (2), insomnia (2), erectile dysfunction (1), depressive episode (1), headache (1), premature battery depletion (1), and lack of drive (1). | |
| (2023 Rezai... Hodder)27 *• 1 pt from (2021 Mahoney... Rezai)* | 33.75 | | 4 (4M/0F) | SUD | | Opioids | | NAc & ALIC | | 36 | | 2/4 | | 3/4 | | 3/4 | | | 2/4 participants sustained complete substance abstinence for >1150 and >520 days, and 1 participant experienced post/DBS drug use recurrences with reduced frequency and severity. 3/4 participants experienced significant craving reduction (50%+) across opioids, benzodiazepines, and cannabis. | | Reduction in anxiety and depressive symptoms for 3 participants. 18FDG/PET revealed increased glucose metabolism for 2/3 abstinent patients, with the greatest changes in the dorsolateral prefrontal regions. The DBS system was explanted in 1 participant due to noncompliance with the treatment protocol. | | None reported. | |
| (2023 Vorspan... Mallet)28 | 40s | | 1 (1M/0F) | SUD | | Cocaine | | STN | | 28 | | 0/1 | | 1/1 | | N/A | | | From 7 to 30 months postoperatively, the participant was abstinent from cocaine, other stimulants, opioids, benzodiazepines, and cyamemazine. They were also abstinent from alcohol for 19 months postoperatively and showed low-risk alcohol use 5 months afterward. | | The participant demonstrated improved quality of life and reported the treatment as a success. | | Hypomania (1). | |
| (2024 Li... Ge)29 | 35 | | 6 (6M/0F) | SUD | | Opioids and Alcohol | | NAc & ALIC | | N/A | | N/A | | N/A | | N/A | | | N/A | | Microelectrode recordings (MER) were performed on the right brain, spanning from 15 mm above to 2 mm below NAc and ALIC target site. Most neuron discharges occurred in the NAc, where neurons exhibit the highest firing frequency. Mean firing rate increased when entering the NAc, while decreased when exiting. Neuronal density was relatively lower under general anesthesia versus local. | | None reported. | |
|  |  |  | | |  | |  | |  | |  | |  | |  | |  |  | |  | |  | |

Supplementary Table 3: Findings from a literature review of deep brain stimulation for substance use disorder. AD: Alcohol Dependence; ALIC: Anterior Limb of the Internal Capsule; AUDIT: Alcohol Use Disorder Identification Test; BAI: Beck Anxiety Inventory; BNST: Bed Nucleus of the Stria Terminalis; DBS: Deep Brain Stimulation; EEG: Electroencephalography; ERN: Error-Related Negativity; FDG: Fluorodeoxyglucose; HAMD: Hamilton Depression Rating Scale; L-Dopa: Levodopa; LFP: Local Field Potential; MADRS: Montgomery-Åsberg Depression Rating Scale; MDD: Major Depressive Disorder; MER: Microelectrode Recordings; NAc: Nucleus Accumbens; OCD: Obsessive-Compulsive Disorder; OCDS: Obsessive Compulsive Drinking Scale; PD: Parkinson’s Disease; PET: Positron Emission Tomography; pt: participant; QoL: Quality of Life; SUD: Substance Use Disorder; STN: Subthalamic Nucleus; TS: Tourette Syndrome; VC: Ventral Capsule; VS: Ventral Striatum; and WHO: World Health Organization

**References**

1. Witjas T, Baunez C, Henry JM, et al. Addiction in Parkinson’s disease: impact of subthalamic nucleus deep brain stimulation. *Mov Disord*. 2005;20(8):1052-1055. doi:10.1002/mds.20501

2. Kuhn J, Lenartz D, Huff W, et al. Remission of alcohol dependency following deep brain stimulation of the nucleus accumbens: valuable therapeutic implications? *Journal of Neurology, Neurosurgery &amp; Psychiatry*. 2007;78(10):1152-1153. doi:10.1136/jnnp.2006.113092

3. Heinze HJ, Heldmann M, Voges J, et al. Counteracting incentive sensitization in severe alcohol dependence using deep brain stimulation of the nucleus accumbens: clinical and basic science aspects. *Frontiers in human neuroscience*. 2009;3(101477954):22. doi:10.3389/neuro.09.022.2009

4. Kuhn J, Bauer R, Pohl S, et al. Observations on unaided smoking cessation after deep brain stimulation of the nucleus accumbens. *Eur Addict Res*. 2009;15(4):196-201. doi:10.1159/000228930

5. Müller UJ, Sturm V, Voges J, et al. Successful Treatment of Chronic Resistant Alcoholism by Deep Brain Stimulation of Nucleus Accumbens: First Experience with Three Cases. *Pharmacopsychiatry*. 2009;42(06):288-291. doi:10.1055/s-0029-1233489

6. Mantione M, van de Brink W, Schuurman PR, Denys D. Smoking cessation and weight loss after chronic deep brain stimulation of the nucleus accumbens: therapeutic and research implications: case report. *Neurosurgery*. 2010;66(1):E218; discussion E218. doi:10.1227/01.NEU.0000360570.40339.64

7. Kuhn J, Gründler TOJ, Bauer R, et al. Successful deep brain stimulation of the nucleus accumbens in severe alcohol dependence is associated with changed performance monitoring. *Addiction Biology*. 2011;16(4):620-623. doi:10.1111/j.1369-1600.2011.00337.x

8. Zhou H, Xu J, Jiang J. Deep brain stimulation of nucleus accumbens on heroin-seeking behaviors: a case report. *Biol Psychiatry*. 2011;69(11):e41-42. doi:10.1016/j.biopsych.2011.02.012

9. Heldmann M, Berding G, Voges J, et al. Deep Brain Stimulation of Nucleus Accumbens Region in Alcoholism Affects Reward Processing. Harrison BJ, ed. *PLoS ONE*. 2012;7(5):e36572. doi:10.1371/journal.pone.0036572

10. Strong DR, Haber SN, Tyrka AR, Bernier JA, Rassmussen SA, Greenberg BD. Reversible increase in smoking after withdrawal of ventral capsule/ventral striatum deep brain stimulation in a depressed smoker. *Journal of addiction medicine*. 2012;6(1):94-95. doi:10.1097/ADM.0b013e318240acf5

11. Valencia-Alfonso CE, Luigjes J, Smolders R, et al. Effective Deep Brain Stimulation in Heroin Addiction: A Case Report with Complementary Intracranial Electroencephalogram. *Biological Psychiatry*. 2012;71(8):e35-e37. doi:10.1016/j.biopsych.2011.12.013

12. Voges J, Müller U, Bogerts B, Münte T, Heinze HJ. Deep Brain Stimulation Surgery for Alcohol Addiction. *World Neurosurgery*. 2013;80(3-4):S28.e21-S28.e31. doi:10.1016/j.wneu.2012.07.011

13. Kuhn J, Möller M, Treppmann JF, et al. Deep brain stimulation of the nucleus accumbens and its usefulness in severe opioid addiction. *Mol Psychiatry*. 2014;19(2):145-146. doi:10.1038/mp.2012.196

14. Gonçalves-Ferreira A, do Couto FS, Rainha Campos A, Lucas Neto LP, Gonçalves-Ferreira D, Teixeira J. Deep Brain Stimulation for Refractory Cocaine Dependence. *Biol Psychiatry*. 2016;79(11):e87-89. doi:10.1016/j.biopsych.2015.06.023

15. Müller U, Sturm V, Voges J, et al. Nucleus Accumbens Deep Brain Stimulation for Alcohol Addiction – Safety and Clinical Long-term Results of a Pilot Trial. *Pharmacopsychiatry*. 2016;49(04):170-173. doi:10.1055/s-0042-104507

16. Zhang C, Huang Y, Zheng F, Zeljic K, Pan J, Sun B. Death From Opioid Overdose After Deep Brain Stimulation: A Case Report. *Biological Psychiatry*. 2018;83(1):e9-e10. doi:10.1016/j.biopsych.2017.07.018

17. Ge S, Geng X, Wang X, et al. Oscillatory local field potentials of the nucleus accumbens and the anterior limb of the internal capsule in heroin addicts. *Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology*. 2018;129(6):1242-1253. doi:10.1016/j.clinph.2018.03.008

18. Peisker CB, Schuller T, Peters J, et al. Nucleus Accumbens Deep Brain Stimulation in Patients with Substance Use Disorders and Delay Discounting. *Brain sciences*. 2018;8(2). doi:10.3390/brainsci8020021

19. Ge S, Chen Y, Li N, et al. Deep Brain Stimulation of Nucleus Accumbens for Methamphetamine Addiction: Two Case Reports. *World Neurosurgery*. 2019;122:512-517. doi:10.1016/j.wneu.2018.11.056

20. Chen L, Li N, Ge S, et al. Long-term results after deep brain stimulation of nucleus accumbens and the anterior limb of the internal capsule for preventing heroin relapse: An open-label pilot study. *Brain Stimulation*. 2019;12(1):175-183. doi:10.1016/j.brs.2018.09.006

21. Sildatke E, Schuller T, Grundler TOJ, et al. Error-Related Activity in Striatal Local Field Potentials and Medial Frontal Cortex: Evidence From Patients With Severe Opioid Abuse Disorder. *Frontiers in human neuroscience*. 2020;14(101477954):627564. doi:10.3389/fnhum.2020.627564

22. Zhang C., Li J., Li D., Sun B. Deep brain stimulation removal after successful treatment for heroin addiction. *Australian and New Zealand Journal of Psychiatry*. 2020;54(5):543-544. doi:10.1177/0004867419890671

23. Zhu R, Zhang Y, Wang T, et al. Deep Brain Stimulation of Nucleus Accumbens with Anterior Capsulotomy for Drug Addiction: A Case Report. *Stereotact Funct Neurosurg*. 2020;98(5):345-349. doi:10.1159/000509313

24. Mahoney JJ, Haut MW, Hodder SL, et al. Deep brain stimulation of the nucleus accumbens/ventral capsule for severe and intractable opioid and benzodiazepine use disorder. *Exp Clin Psychopharmacol*. 2021;29(2):210-215. doi:10.1037/pha0000453

25. Davidson B, Giacobbe P, George TP, et al. Deep brain stimulation of the nucleus accumbens in the treatment of severe alcohol use disorder: a phase I pilot trial. *Mol Psychiatry*. 2022;27(10):3992-4000. doi:10.1038/s41380-022-01677-6

26. Bach P, Luderer M, Müller UJ, et al. Deep brain stimulation of the nucleus accumbens in treatment-resistant alcohol use disorder: a double-blind randomized controlled multi-center trial. *Transl Psychiatry*. 2023;13(1):49. doi:10.1038/s41398-023-02337-1

27. Rezai AR, Mahoney JJ, Ranjan M, et al. Safety and feasibility clinical trial of nucleus accumbens deep brain stimulation for treatment-refractory opioid use disorder. *Journal of Neurosurgery*. Published online June 1, 2023:1-9. doi:10.3171/2023.4.JNS23114

28. Vorspan F, Domenech P, Grabli D, et al. A single case report of STN-DBS for severe crack-cocaine dependence: double-blind ON vs. SHAM randomized controlled assessment. *Front Psychiatry*. 2023;14. doi:10.3389/fpsyt.2023.1146492

29. Li W, Li N, Wang X, et al. Microelectrode recording characterization of the nucleus accumbens and the anterior limb of internal capsule in patients with addiction. *Neuroscience Letters*. Published online June 22, 2024:137884. doi:10.1016/j.neulet.2024.137884