

Chapter 2

Neural Circuits Affected by Deep Brain Stimulation for the Treatment of Psychiatric Disorders

Suzanne N. Haber and Benjamin D. Greenberg

Abbreviations

AC	Anterior commissure
ACC	Anterior cingulate cortex
dACC	Dorsal anterior cingulate cortex
DBS	Deep brain stimulation
MD	Major depression
OCD	Obsessive–compulsive disorder
OFC	Orbitofrontal cortex
PFC	Prefrontal cortex
SCGwm	Subgenual cingulate gyrus white matter
VC	Ventral anterior internal capsule
vmPFC	Ventromedial prefrontal cortex
vPFC	Ventral prefrontal cortex
VS	Ventral striatum

2.1 Introduction

Although the pathophysiology of obsessive–compulsive disorder (OCD) and major depression (MD) remains incompletely understood, converging lines of evidence point to abnormalities in the anterior cingulate cortex (ACC) and orbitofrontal

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cortex (OFC)–basal ganglia circuit. Collectively, these brain regions are involved in various aspects of incentive-based learning and good decision-making skills (Chase et al. 2008; Rudebeck et al. 2008; Haber and Knutson 2010). They are also associated with sadness and pathological risk-taking (Mayberg 2007; Chamberlain et al. 2008). Changes in activity in the OFC and ACC associated with OCD and MD are accentuated during provocation of symptoms, but the activity often returns to near normal following successful treatment, either pharmacological or cognitive behavioral, or surgical therapies. Moreover, regional activity in OFC (for OCD) or ACC (for MD) predicts the subsequent response to treatment with medication or behavioral therapy (McGuire et al. 1994; Rauch et al. 1994; Mayberg 2003; Yucel et al. 2007; Greenberg et al. 2010a). Taken together, the data suggest that abnormalities in OFC/ACC–basal ganglia–thalamus circuitry are central to the pathophysiology of OCD and MD and are consistent with the classic targets for ablative neurosurgical therapies. Indeed, stereotactic neurosurgical lesions in the ventral anterior internal capsule (VC), the ACC, or the subcaudate white matter, both of which interrupt these circuits, are effective in the treatment of refractory OCD and depression.

Deep brain stimulation (DBS), a standard treatment for otherwise refractory movement disorders, such as Parkinson's disease (Vitek 2002), is currently being investigated for the treatment of severe mental health disorders, in particular, medication-resistant MD and OCD (Nuttin et al. 2003; Mayberg et al. 2005; Greenberg et al. 2008). Patients appropriate for neurosurgical intervention for OCD and MD exhibit a high degree of severity and functional impairment despite aggressive sustained efforts with conventional treatments, and thus represent very small subsets of OCD or MD patient populations. DBS targets for the treatment of OCD and MD are centered in structures that interrupt subcomponents of the ACC or OFC networks, including their connections to the ventral striatum (VS), the thalamus, and closely connected brainstem regions, (McFarland and Haber 2002; Mayberg et al. 2005; Haber et al. 2006; Cecconi et al. 2008; Greenberg et al. 2010a). Two promising targets are located within white matter tracts. One is centered in the ventral part of the anterior limb of the internal capsule (VC/VS), extending caudally into the VS (nucleus accumbens), at the border of the anterior commissure (AC). The second site is located in the subgenual cingulate gyrus white matter (SCGwm) in the ventromedial prefrontal cortex (vmPFC). Two other targets are centered within the grey matter, one in the nucleus accumbens, overlapping the VC/VS target, the other in the subthalamic nucleus (Mallet et al. 2008; Denys et al. 2010).

The mechanisms of action for DBS are not well understood and the specific pathways affected by DBS at these sites remain unknown. Moreover, regardless of the site or disorder treated, the effectiveness of DBS differs between patients. Small differences in specific electrode placement likely play a critical role in clinical outcomes, as is true for all clinical applications of DBS in movement disorders. This emphasizes the importance of understanding more precisely which part(s) of the OFC/ACC–basal ganglia neural network plays a central role in the

effects of DBS for the treatment of OCD and MD (Greenberg et al. 2010b; Mayberg 2007; Lehman et al. 2011).

2.2 The Anterior Cingulate and Orbital Prefrontal Cortices

The ACC and OFC are complex and heterogeneous regions, each of which is further divided into specific cortical areas: the ACC includes areas 24, 25, and 32; the orbital cortex is divided into areas 11, 12, 13, and 14 (Brodmann 1909; Fuster 2001). Several homologies have been developed based primarily on cytoarchitectonics between monkey and human prefrontal cortical areas (for a review, see Ongur and Price 2000). Although imaging studies cannot distinguish between these relatively small cortical divisions, functional studies have defined three main regions (Petrides et al. 2002; O'Doherty et al. 2003; Rushworth et al. 2007; Rudebeck et al. 2008): the vmPFC, OFC, and dorsal ACC (dACC). The vmPFC includes areas 10, 11/14, 25, and 32. The OFC includes areas 13, 12, and parts of 11, and the dACC is area 24. Since the main targets for DBS treatment of psychiatric disease focus on connections of the vmPFC and OFC, this chapter will address these specifically. Collectively the vmPFC and OFC are referred to as the ventral prefrontal cortex (vPFC).

Overall vPFC fibers reach cortical targets primarily via the uncinate fasciculus and extreme capsule. The uncinate fasciculus occupies the ventral plate of the vPFC and connects the prefrontal cortex (PFC) with the temporal lobe (Schmahmann and Pandya 2006; Petrides and Pandya 2007). The extreme capsule lies between the insula and the claustrum, and carries association fibers between the frontal, temporal, and parietal cortex. vmPFC and OFC projections to subcortical regions travel primarily in the internal and external capsules. Subcortical fibers pass through the external capsule to the ventral anterior limb of the internal capsule (Beever and Horsley 1890; Schmahmann and Pandya 2006; Petrides and Pandya 2007). Although these major PFC pathways are well defined, less is known about the organization of vPFC fibers within them. Of particular importance is determining how fibers from the vmPFC and OFC are segmented within these bundles, and the rules can be used to determine their trajectories. This information is fundamental for predicting where specific fibers should travel, and, thus for a more precise identification of the specific connections within a white matter bundle that are affected by DBS.

2.3 Organization of Pathways from Different vPFC Regions

All vPFC axons enter the uncinate fasciculus immediately adjacent to their cortical region. Within the uncinate fasciculus, fibers from each injection site split into separate bundles, each of which contains subsets of axons that travel in different

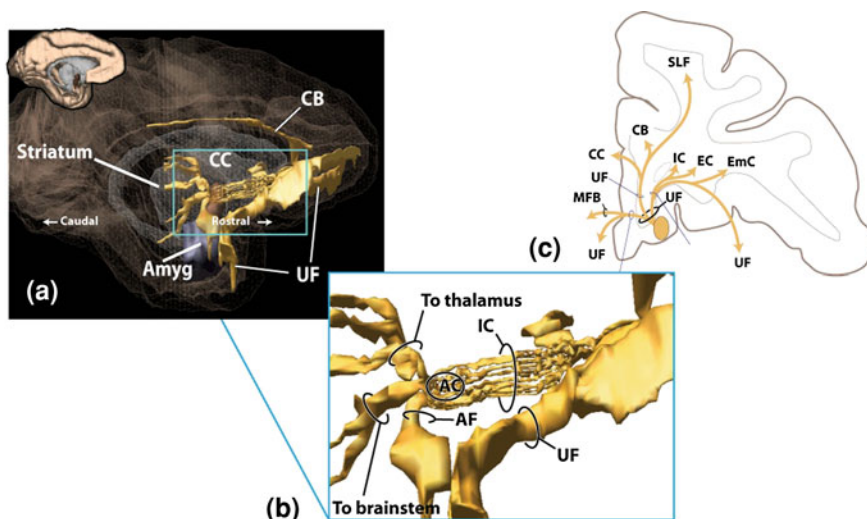


Fig. 2.1 Medial orbital fiber pathways. Illustration of how different bundles separate from the injections site as they enter the white matter. Note fibers divide into medial, dorsal, and lateral pathways. *a* Three-dimensional rendering of a lateral view of a sagittal plane. *b* Inset to better visualize the separation of fiber bundles. External and extreme capsule pathways have been removed for clarity. *AC* indicates the location of the AC. Note axons traveling through the internal capsule divide into dorsal thalamic fibers and ventral brainstem axons. *AF* ventral amygdalofugal pathway, *Amyg* amygdala, *CB* cingulum bundle, *CC* corpus callosum, *EC* external capsule, *EmC* extreme capsule, *IC* internal capsule, *MFB* medial forebrain bundle, *MLF* middle longitudinal fasciculus, *SLF* superior longitudinal fasciculus, *UF* uncinate fasciculus

white matter tracts, the specifics of which depend on the cortical location of origin (Fig. 2.1). Axons from all vPFC areas travel in the uncinate fasciculus, corpus callosum, cingulum bundle, superior longitudinal fasciculus, internal capsule, external capsule, and extreme capsule. In addition, fibers from specific vPFC regions also travel in the middle longitudinal fasciculus, ventral amygdalofugal pathway, stria terminalis, and the medial forebrain bundle. Most axons pass through the external capsule initially, before breaking into separate subcortical bundles, including those that travel to the striatum, or enter the internal capsule. The uncinate fasciculus and the internal capsule are the main fiber bundles that connect the vPFC to cortical and subcortical regions, respectively.

Although the uncinate fasciculus is known for its vmPFC–temporal lobe connection (Schmahmann and Pandya 2006; Petrides and Pandya 2007), these frontotemporal axons do not form a distinct bundle within the ventral plate of the vPFC. Rather, fibers from each cortical region travel through the uncinate fasciculus to connect distal regions of the vPFC. vPFC axons also use this bundle as a channel to enter other white matter tracts, including the corpus callosum, cingulum bundle, and superior longitudinal fasciculus. Thus, the uncinate fasciculus contains three components, connections between the vPFC and temporal lobe, connections between distal parts of vPFC regions, and as a conduit to other

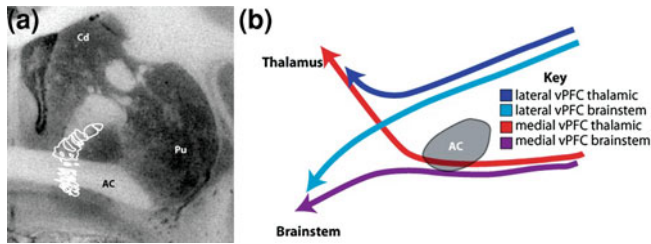


Fig. 2.2 Photomicrograph and schematics of vmPFC and lateral orbitofrontal cortex (OFC) pathways through the internal capsule (parasagittal plane). **a** Fibers passing through the internal capsule travel dorsal to, embedded within, and ventral to the anterior commissure. **b** The different positions of thalamic versus brainstem fibers of the vmPFC (red and purple) and the lateral OFC (dark blue and light blue) entering and traveling through the internal capsule. Brainstem fibers (purple and light blue) travel ventral to thalamic fibers (red and dark blue). AC anterior commissure, Cd caudate nucleus, Pu putamen, vPFC ventral prefrontal cortex

fiber bundles (Dejerine 1895; Nauta 1964; Lehman et al. 2011). These three components are intertwined within the vPFC (Fig. 2.1).

Axons from the vPFC occupy the most ventral part of the rostral anterior limb of the internal capsule. The internal capsule has been classically defined as the dorsal nucleus accumbens and AC (Dejerine 1895; Schmahmann and Pandya 2006). However, a significant proportion of the descending vPFC fibers travel in white matter fasciculi embedded within the nucleus accumbens and AC (Fig. 2.2a). Thus, these fasciculi, which can be seen in human histological preparations (Dejerine 1895), constitute an integral part of the internal capsule and carry descending vPFC internal capsule fibers (Fig. 2.3b). The vPFC fibers within the internal capsule are organized according to their destination. In particular, thalamic internal capsule fibers from each cortical region travel dorsal to their brainstem axons (Lehman et al. 2011) (Fig. 2.2b).

The medial/lateral position within the vPFC dictates both the route that fibers take to enter major white matter tracts and the position they take within some of those tracts (Lehman et al. 2011). The medial vPFC fibers enter the internal capsule (and striatum) ventrally, directly through the subcaudate white matter, and move dorsally in the internal capsule as they travel caudally (Fig. 2.3a, b). In contrast, the lateral vPFC fibers enter the internal capsule from a lateral and dorsal position and move ventrally through the internal capsule as they travel posteriorly (Fig. 2.3c, d). This results in an organization in which fibers from medial areas travel ventral to axons from lateral vPFC regions (Fig. 2.3a). Thus, fibers are stacked in the internal capsule with the vmPFC axons ventral or embedded within the AC and the lateral OFC regions positioned dorsal to the AC. This topography is maintained (albeit with a great deal of compression) as they enter the inferior thalamic peduncle.

Superimposed on this topographic organization is the arrangement of thalamic axons that travel dorsal to brainstem axons from the same cortical area. This creates a complex convergence between thalamic and brainstem fibers from different vPFC

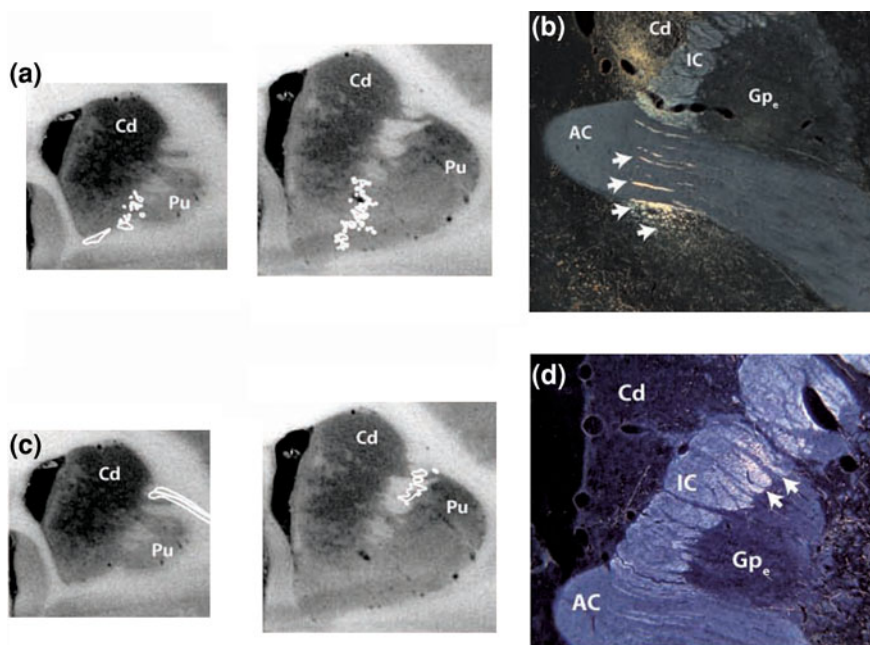


Fig. 2.3 Schematics and photomicrographs of ventral prefrontal cortex (vPFC) fibers through the internal capsule. **a, b** Fibers from the vmPFC enter ventrally and move dorsally as they travel caudally. **c, d** Fibers from the lateral OFC enter dorsally and move ventrally as they travel caudally. AC anterior commissure, Cd caudate nucleus, GP globus pallidus, IC internal capsule, Pu putamen

regions. For example, medial PFC brainstem fibers are embedded within the VS; the fibers that pass through the AC travel to the thalamus. In contrast, axons that terminate in the brainstem from more lateral vPFC regions travel within the AC, whereas those that lie dorsal to the AC terminate in the thalamus. Thus, within the AC region of the internal capsule, axons from thalamic fibers from the vmPFC travel with brainstem fibers from more lateral parts of vPFC (see Fig. 2.2b). The most lateral vPFC fibers all travel dorsal to the AC. Taken together, the medial/lateral origin of vPFC fibers coupled with their thalamic versus brainstem organization, positions thalamic internal capsule fibers from medial vPFC regions with those that terminate in the brainstem that arise from more lateral vPFC areas. These results imply that DBS at various internal capsule locations affects combinations of thalamic and brainstem vPFC fibers from different vPFC regions.

2.4 Deep Brain Stimulation Sites: What Gets Stimulated?

To estimate the most likely set of fibers involved at the different DBS contacts, we used the fiber trajectories outlined from non-human-primate experiments with representations of electrodes used in humans for the DBS targets adjusted for size

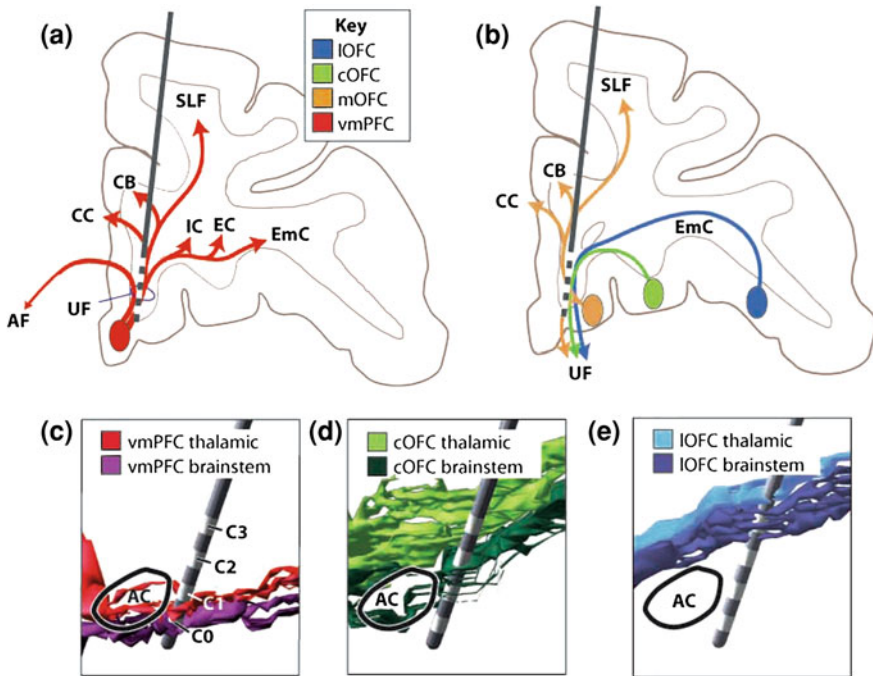


Fig. 2.4 Modeled deep brain stimulation electrodes at the SCGwm and ventral anterior internal capsule/ventral striatum (VC/VS) targets. **a** The SCGwm target involves all fibers from cortical areas adjacent to the electrode, including descending projections. **b** The SCGwm target also involves other vPFC fibers that pass through the site, including axons from lateral vPFC regions traveling medially, and those from medial OFC areas traveling dorsally. **c–e** Sagittal view of specific vPFC bundles traveling in the internal capsule with an electrode representation embedded at the VC/VS site. Each contact captures a different set of thalamic and/or brainstem fibers. *AF* ventral amygdalofugal bundle, *AC* anterior commissure, *C0* contact 0, *C1* contact 1, *C2* contact 2, *C3* contact 3, *CB* cingulum bundle, *CC* corpus callosum, *cOFC* central orbital prefrontal cortex, *EC* external capsule, *EmC* extreme capsule, *IC* internal capsule, *IOFC* lateral orbital cortex, *mOFC* medial orbital cortex, *SLF* superior longitudinal fasciculus, *UF* uncinate fasciculus, *vmPFC* ventral medial prefrontal cortex

(40 % of human dimensions) (Lehman et al. 2011). The most effective SCGwm contacts (1 and 2) are at the border between the subgenual cingulate gyrus and the inferior rostral gyrus (Hamani et al. 2009). Contact 1 is within the inferior rostral gyrus, contact 2 is within the subgenual cingulate gyrus, and contracts 0 and 3 are ventral and dorsal, respectively. Thus, at this site, contacts 0–2 will involve (1) all connections from vmPFC areas adjacent to the electrode contacts (both cortical and subcortical projections) (Fig. 2.4a); (2) uncinate fasciculus fibers from nonadjacent vmPFC and medial OFC as they travel medially to other vPFC areas and/or enter the medial forebrain bundle; (3) a subset of central OFC fibers traveling medially to innervate medial PFC areas (Fig. 2.4b); (4) a subset of anterior vmPFC and medial OFC fibers on route to the corpus callosum through

the uncinate fasciculus; and (5) axons traveling from the contralateral vmPFC and medial OFC (not illustrated). Contact 3 involves primarily fibers in the corpus callosum. In addition, this site captures a subset of fibers traveling from the medial OFC and posterior central OFC to the cingulum bundle and superior longitudinal fasciculus.

The VC/VS electrode is implanted at an angle, positioning contact 0 most posteriorly. Each contact activates a different subset of corticothalamic and brainstem fibers (Fig. 2.4c–f). Axons from the vmPFC pass through contact 0, most traveling to the brainstem, with few traveling to the thalamus (Fig. 2.4c). In contrast, contact 1 captures fibers from the vmPFC traveling to the thalamus, but not those traveling to the brainstem. Contact 1 involves some central OFC brainstem axons, but few thalamic OFC fibers (Fig. 2.4d). Contact 2 captures central OFC brainstem fibers, whereas contact 3 captures both brainstem and thalamic central OFC fibers and brainstem fibers from the lateral OFC (Fig. 2.4d, e).

Finally, contact 0 at the nucleus accumbens site is placed in the shell of the VS and contact 1 is placed in the core. In contrast to the subgenual cingulate gyrus and VC/VS, stimulation of the two ventral contacts is located primarily in gray matter, but within corticostriatal fibers. Contacts 2 and 3 are within the VC and likely involve cortical connections similar to those described above for the VC/VS target.

The effectiveness of DBS for the treatment of depression at the SCGwm and VC/VS (white matter) sites has not been directly compared in a randomized study for patient selection and other variables. Nonetheless, both sites have shown promising initial efficacies in open-label trials in over 50 % of otherwise intractable patients (Malone et al. 2009; Kennedy et al. 2011; Greenberg et al. 2010a, b). Stimulation at the SCGwm site captures all cortical and subcortical projections from the area surrounding each contact site. However, it also captures fibers from nonadjacent cortical areas passing through the target, both corticocortical and corticosubcortical connections. In contrast, neither the VS nor the VC/VS site directly involves corticocortical fibers. However, each contact in the VC/VS region involves a different combination of thalamic and/or brainstem bundles. DBS at all three of the different stimulation targets will capture subsets of fibers that include both thalamic and brainstem fiber projections from prefrontal cortical regions. Thus, an important part of the clinical effectiveness of DBS is likely to require a combination of thalamic and brainstem fibers. Interestingly, there can be notable differences in fibers likely to be modulated by DBS within a given surgical target. This is in accord with accumulating clinical experience suggesting, as in DBS in the subthalamic nucleus for the treatment of Parkinson's disease, activation of even adjacent stimulation contacts may be associated with very different clinical effects.

Thus, the rules fibers use to reach their targets provides an important guide for understanding the relationship between specific contact stimulation and the functional connectivities likely to be involved at each contact, providing insight into behavioral and therapeutic effects of DBS.

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References

- Beevor CE, Horsley V (1890) An experimental investigation into the arrangement of the excitable fibres of the internal capsule of the Bonnet Monkey (*Macacus sinicus*). *Philos Trans Royal Soc Biol Sci* 181:49–88
- Brodmann K (1909) *Vergleichende Lokalisationslehre der Grosshirnrinde*. J.A. Barth, Leipzig
- Ceccconi JP, Lopes AC, Duran FL, Santos LC, Hoexter MQ, Gentil AF, Canteras MM, Castro CC, Noren G, Greenberg BD, Rauch SL, Busatto GF, Miguel EC (2008) Gamma ventral capsulotomy for treatment of resistant obsessive-compulsive disorder: a structural MRI pilot prospective study. *Neurosci Lett* 447:138–142
- Chamberlain SR, Menzies L, Hampshire A, Suckling J, Fineberg NA, del Campo N, Aitken M, Craig K, Owen AM, Bullmore ET, Robbins TW, Sahakian BJ (2008) Orbitofrontal dysfunction in patients with obsessive-compulsive disorder and their unaffected relatives. *Science* 321:421–422
- Chase HW, Clark L, Myers CE, Gluck MA, Sahakian BJ, Bullmore ET, Robbins TW (2008) The role of the orbitofrontal cortex in human discrimination learning. *Neuropsychologia* 46:1326–1337
- Dejerine J (1895) *Anatomie des centres nerveux*. Rueff, Paris
- Denys D, Mantione M, Figeet M, van den Munckhof P, Koerselman F, Westenberg H, Bosch A, Schuurman R (2010) Deep brain stimulation of the nucleus accumbens for treatment-refractory obsessive-compulsive disorder. *Arch Gen Psychiatry* 67:1061–1068
- Fuster JM (2001) The prefrontal cortex—an update: time is of the essence. *Neuron* 30:319–333
- Greenberg BD, Askland KD, Carpenter LL (2008) The evolution of deep brain stimulation for neuropsychiatric disorders. *Front Biosci* 13:4638–4648
- Greenberg BD, Rauch SL, Haber SN (2010a) Invasive circuitry-based neurotherapeutics: stereotactic ablation and deep brain stimulation for OCD. *Neuropsychopharmacology* 35:317–336
- Greenberg BD, Gabriels LA, Malone DA Jr, Rezai AR, Friehs GM, Okun MS, Shapira NA, Foote KD, Cosyns PR, Kubu CS, Malloy PF, Salloway SP, Giftakis JE, Rise MT, Machado AG, Baker KB, Stypulkowski PH, Goodman WK, Rasmussen SA, Nuttin BJ (2010b) Deep brain stimulation of the ventral internal capsule/ventral striatum for obsessive-compulsive disorder: worldwide experience. *Mol Psychiatry* 15:64–79
- Haber SN, Knutson B (2010) The reward circuit: linking primate anatomy and human imaging. *Neuropsychopharmacology* 35:4–26
- Haber SN, Kim KS, Mailly P, Calzavara R (2006) Reward-related cortical inputs define a large striatal region in primates that interface with associative cortical inputs, providing a substrate for incentive-based learning. *J Neurosci* 26:8368–8376
- Hamani C, Mayberg H, Snyder B, Giacobbe P, Kennedy S, Lozano AM (2009) Deep brain stimulation of the subcallosal cingulate gyrus for depression: anatomical location of active contacts in clinical responders and a suggested guideline for targeting. *J Neurosurg* 111:1209–1215
- Kennedy SH, Giacobbe P, Rizvi SJ, Placenza FM, Nishikawa Y, Mayberg HS, Lozano AM (2011) Deep brain stimulation for treatment-resistant depression: follow-up after 3 to 6 years. *Am J Psychiatry*
- Lehman JF, Greenberg BD, McIntyre CC, Rasmussen SA, Haber SN (2011) Rules ventral prefrontal cortical axons use to reach their targets: implications for diffusion tensor imaging tractography and deep brain stimulation for psychiatric illness. *J Neurosci* 31:10392–10402
- Mallet L et al (2008) Subthalamic nucleus stimulation in severe obsessive-compulsive disorder. *N Engl J Med* 359:2121–2134
- Malone DA Jr, Dougherty DD, Rezai AR, Carpenter LL, Friehs GM, Eskandar EN, Rauch SL, Rasmussen SA, Machado AG, Kubu CS, Tyrka AR, Price LH, Stypulkowski PH, Giftakis JE, Rise MT, Malloy PF, Salloway SP, Greenberg BD (2009) Deep brain stimulation of the ventral capsule/ventral striatum for treatment-resistant depression. *Biol Psychiatry* 65:267–275
- Mayberg HS (2003) Positron emission tomography imaging in depression: a neural systems perspective. *Neuroimaging Clin N Am* 13:805–815

- Mayberg HS (2007) Defining the neural circuitry of depression: toward a new nosology with therapeutic implications. *Biol Psychiatry* 61:729–730
- Mayberg HS, Lozano AM, Voon V, McNeely HE, Seminowicz D, Hamani C, Schwab JM, Kennedy SH (2005) Deep brain stimulation for treatment-resistant depression. *Neuron* 45:651–660
- McFarland NR, Haber SN (2002) Thalamic relay nuclei of the basal ganglia form both reciprocal and nonreciprocal cortical connections, linking multiple frontal cortical areas. *J Neurosci* 22:8117–8132
- McGuire PK, Bench CJ, Frith CD, Marks IM, Frackowiak RS, Dolan RJ (1994) Functional anatomy of obsessive-compulsive phenomena. *Br J Psychiatry* 164:459–468
- Nauta W (1964) Some efferent connections of the prefrontal cortex in the monkey. In: Waren J, Akert K (eds) *The frontal granular cortex and behavior*. McGraw-Hill, New York, pp 397–409
- Nuttin BJ, Gabriels LA, Cosyns PR, Meyerson BA, Andriewitch S, Snaert SG, Maes AF, Dupont PJ, Gybels JM, Gielen F, Demeulemeester HG (2003) Long-term electrical capsular stimulation in patients with obsessive-compulsive disorder. *Neurosurgery* 52:1263–1272; discussion 1272–1264
- O'Doherty J, Critchley H, Deichmann R, Dolan RJ (2003) Dissociating valence of outcome from behavioral control in human orbital and ventral prefrontal cortices. *J Neurosci* 23:7931–7939
- Ongur D, Price JL (2000) The organization of networks within the orbital and medial prefrontal cortex of rats, monkeys and humans. *Cereb Cortex* 10:206–219
- Petrides M, Pandya DN (2007) Efferent association pathways from the rostral prefrontal cortex in the macaque monkey. *J Neurosci* 27:11573–11586
- Petrides M, Alivisatos B, Frey S (2002) Differential activation of the human orbital, mid-ventrolateral, and mid-dorsolateral prefrontal cortex during the processing of visual stimuli. *Proc Natl Acad Sci U S A* 99:5649–5654
- Rauch SL, Jenike MA, Alpert NM, Baer L, Breiter HC, Savage CR, Fischman AJ (1994) Regional cerebral blood flow measured during symptom provocation in obsessive-compulsive disorder using oxygen 15-labeled carbon dioxide and positron emission tomography. *Arch Gen Psychiatry* 51:62–70
- Rudebeck PH, Bannerman DM, Rushworth MF (2008) The contribution of distinct subregions of the ventromedial frontal cortex to emotion, social behavior, and decision making. *Cogn Affect Behav Neurosci* 8:485–497
- Rushworth MF, Behrens TE, Rudebeck PH, Walton ME (2007) Contrasting roles for cingulate and orbitofrontal cortex in decisions and social behaviour. *Trends Cogn Sci* 11:168–176
- Schmahmann J, Pandya D (2006) *Fiber pathways of the brain*. Oxford University Press, New York
- Vitek JL (2002) Mechanisms of deep brain stimulation: excitation or inhibition. *Mov Disord* 17:S69–S72
- Yucel M, Harrison BJ, Wood SJ, Fornito A, Wellard RM, Pujol J, Clarke K, Phillips ML, Kyrios M, Velakoulis D, Pantelis C (2007) Functional and biochemical alterations of the medial frontal cortex in obsessive-compulsive disorder. *Arch Gen Psychiatry* 64:946–955

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