



Neuroanatomy of Deep Brain Stimulation: modulation of multiple brain networks.

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Maladie de Parkinson: un diagnostic clinique

1. Bradykinésie
2. Tremblement de repos (4-6 Hz)
3. Rigidité (roue dentée)
4. (Altération des réflexes posturaux)
5. (Réponse à la levodopa)



2/3 minimum

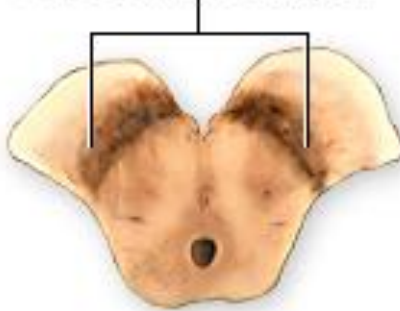
Les symptômes cardinaux sont en lien avec perte de dopamine



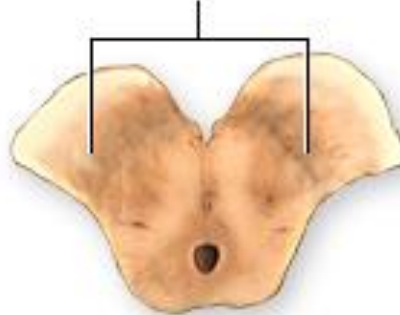
Cut section
of the midbrain
where a portion
of the substantia
nigra is visible



Substantia nigra



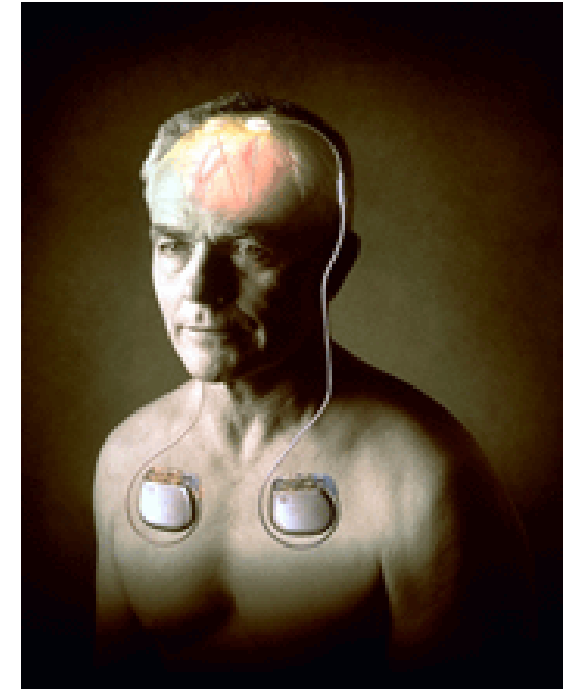
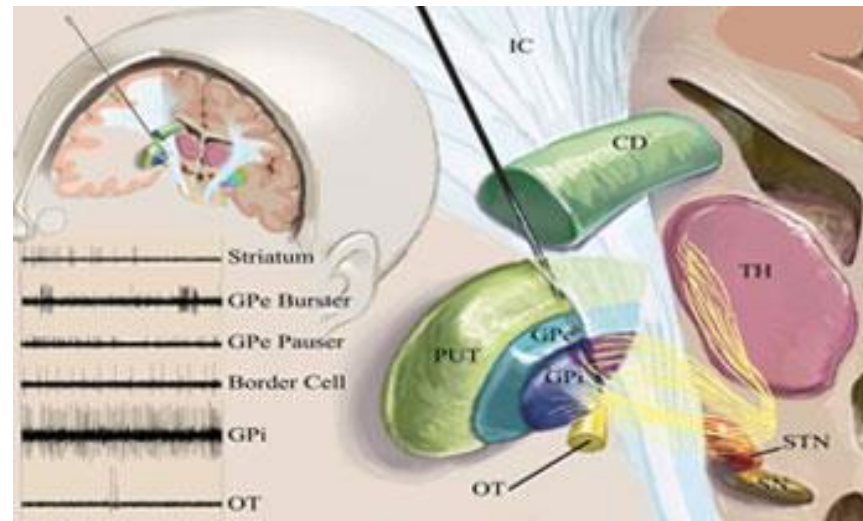
Diminished substantia
nigra as seen in
Parkinson's disease

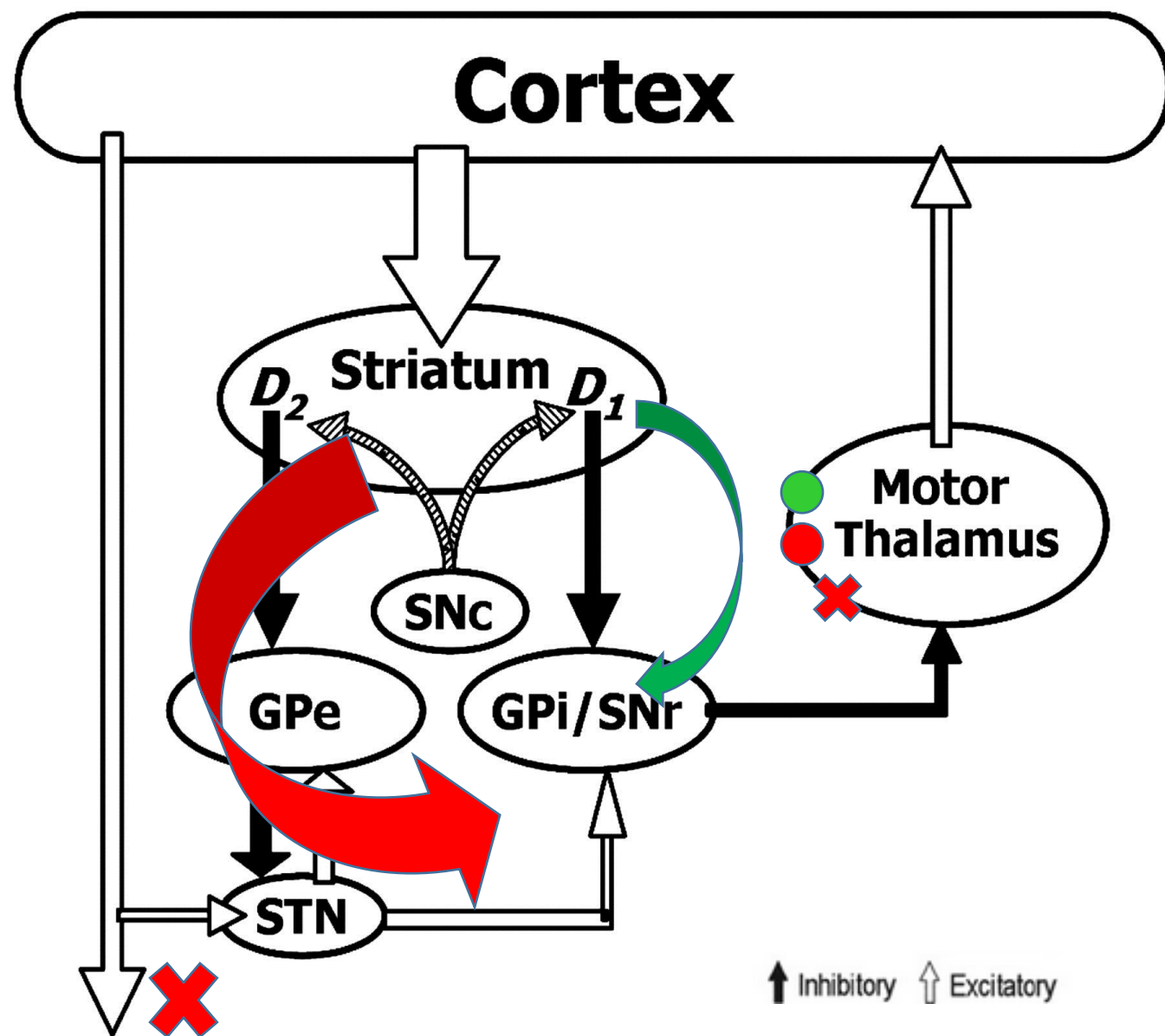
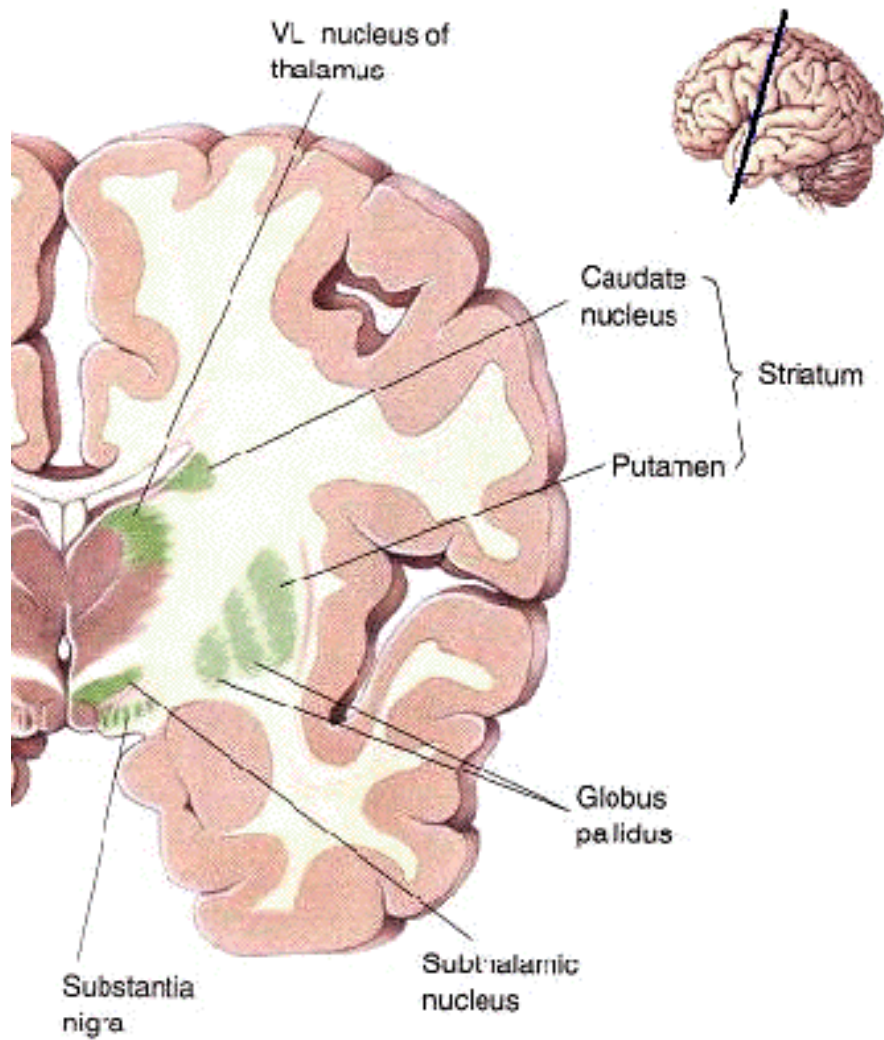


ADAM.



STIMULATION CEREBRALE PROFONDE



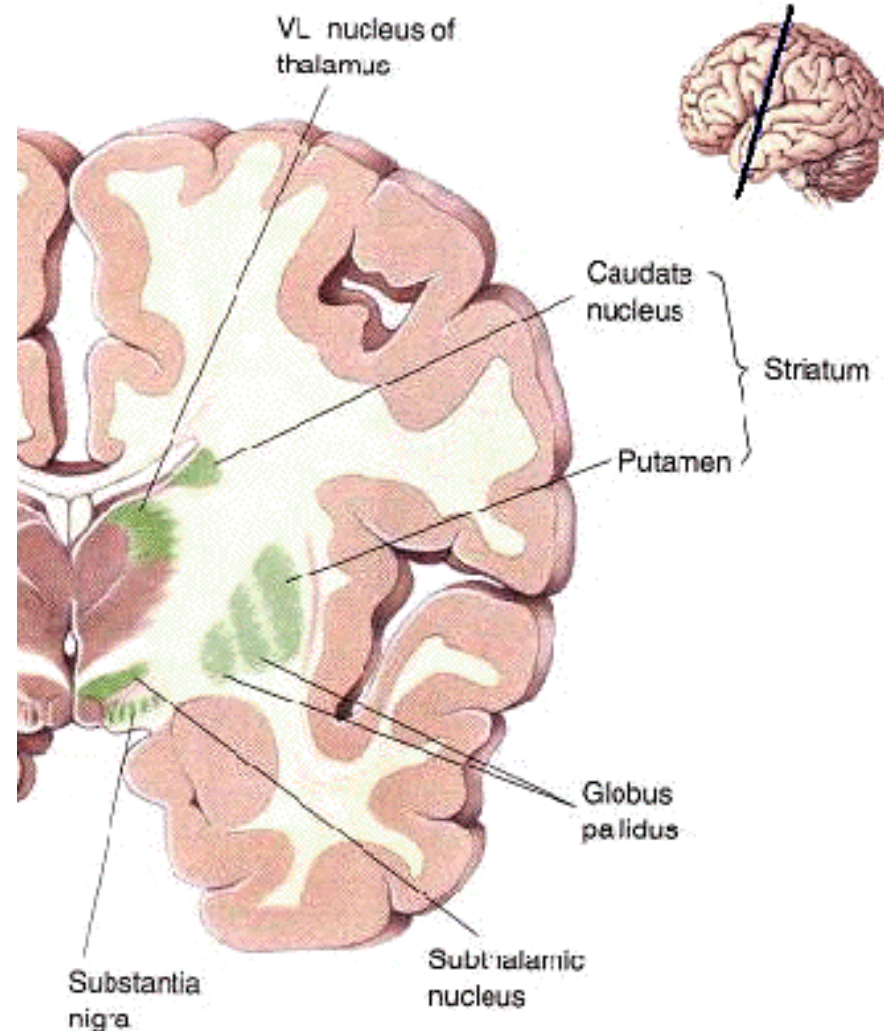


Effets de la stimulation cérébrale profonde

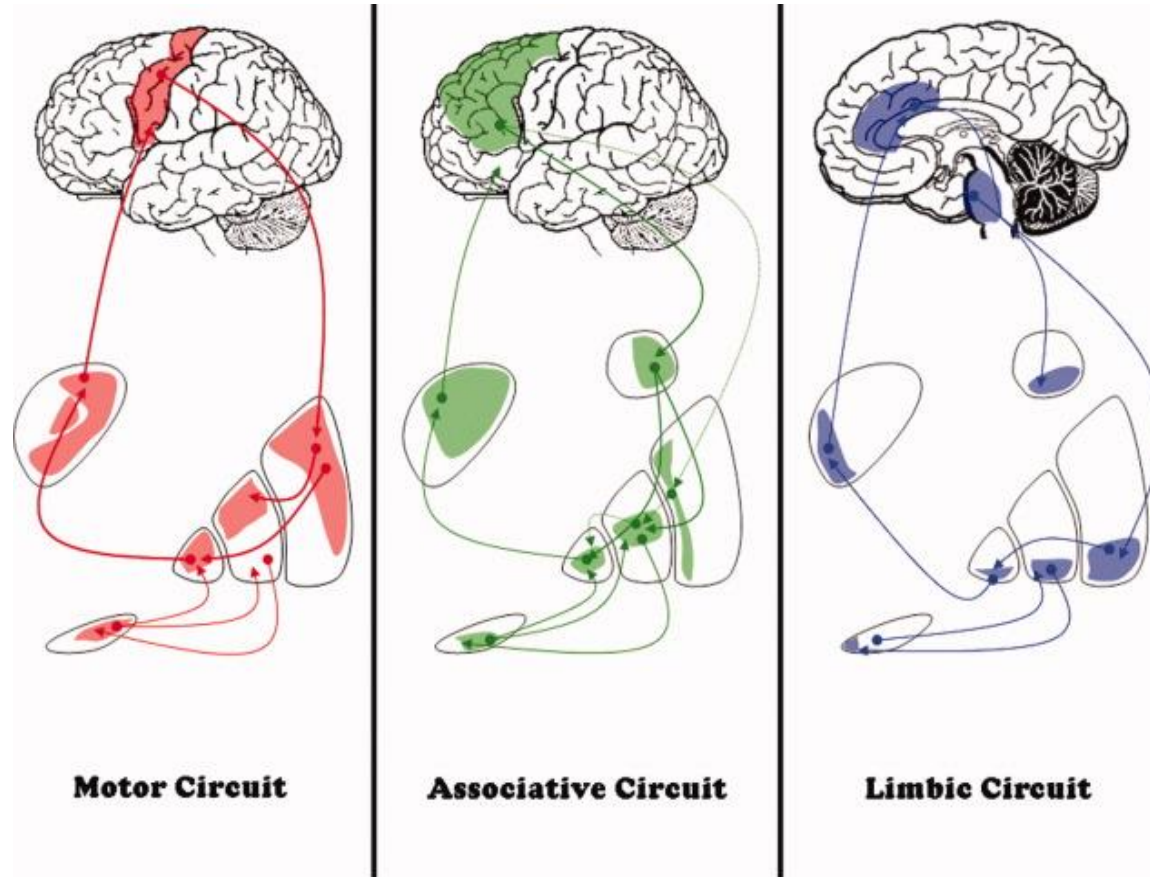


Basal ganglia consist of 5 nuclei

- Caudate
- Putamen
- Globus Pallidus
- STN
- Substantia nigra



Parallel loops

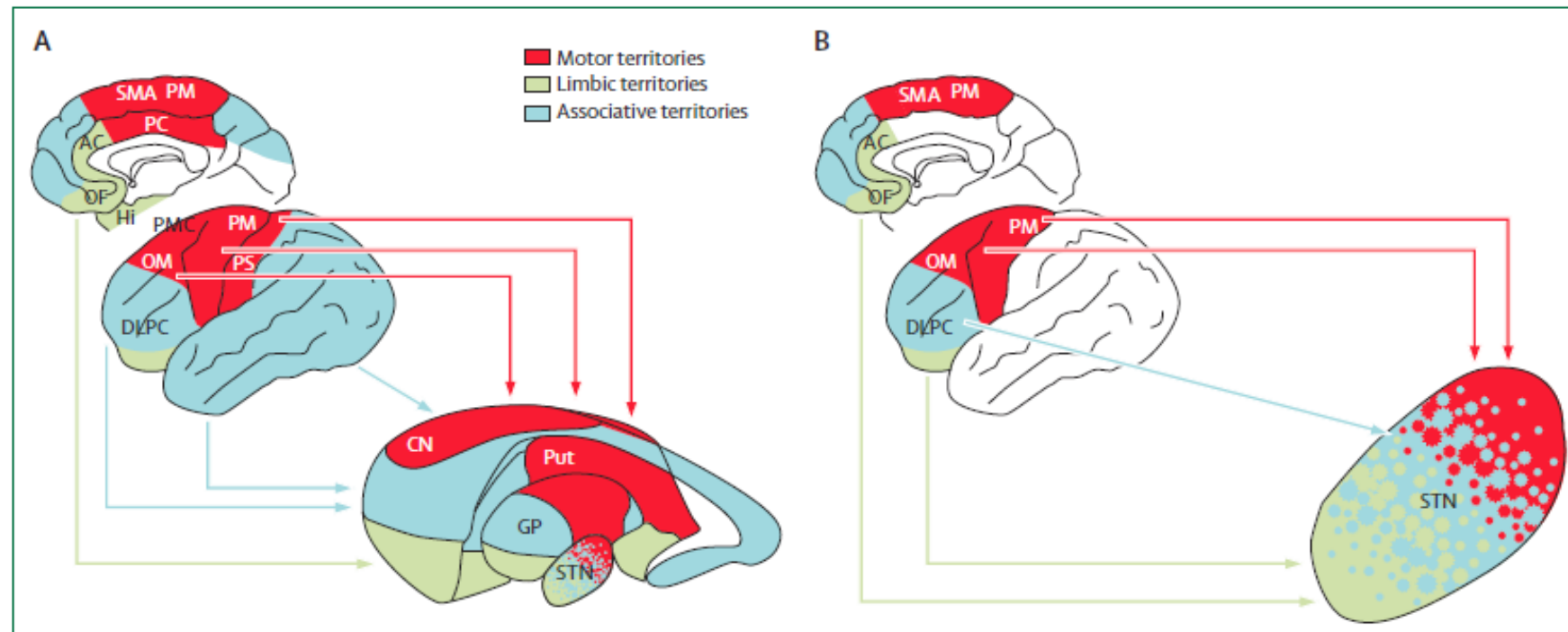


Selemon & Goldman-Rakic, 1985 JNeurosci
Parent & Hazrati, 1995 Brain Rev Res
Alexander et al., 1990 Prog Brain Res

DBS: cognitive and psychiatric undesired effects

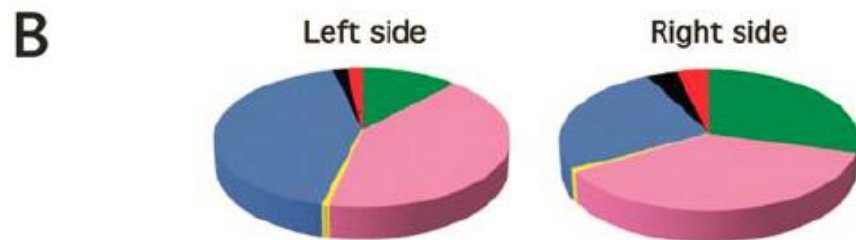
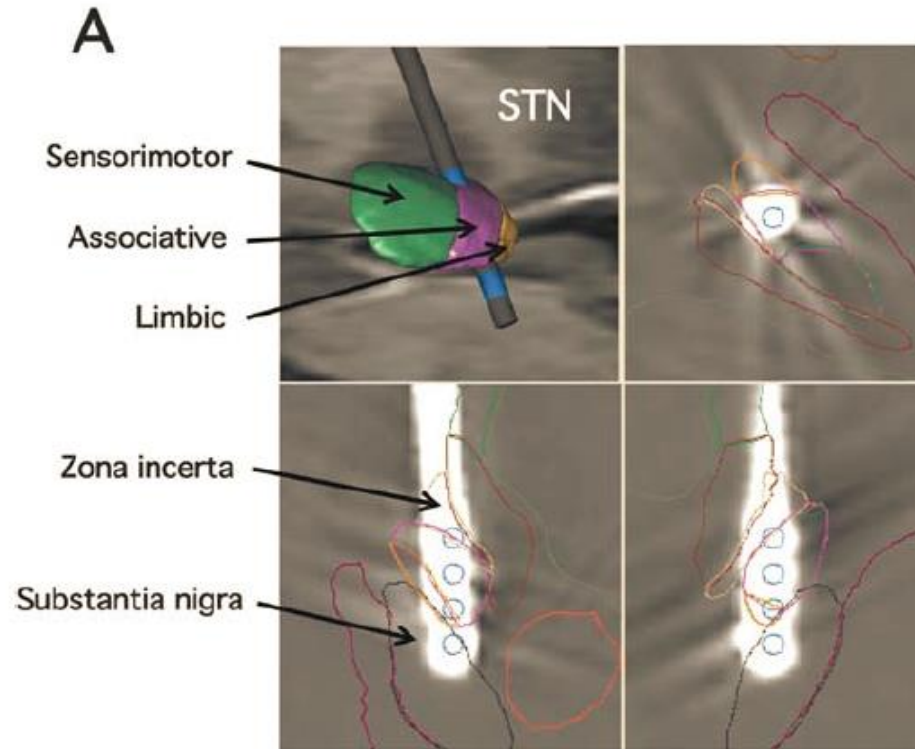
- Depression (Okun *et al.*, 2009; Witt *et al.*, 2012)
- Impulsivity (Cavanagh *et al.*, 2011; Frank *et al.*, 2007)
- Emotional lability (Krack *et al.*, 2001; Odekerken *et al.*, 2012)
- Hypomanic /manic episodes induction (Chopra *et al.*, 2012; Kulisevsky *et al.*, 2002; Mallet *et al.*, 2007; Ulla *et al.*, 2011; Welter *et al.*, 2014).

- The localisation of the stimulating contact seems to be the main factor underlying appearance of side effects.
- Multiple STN functional subareas.

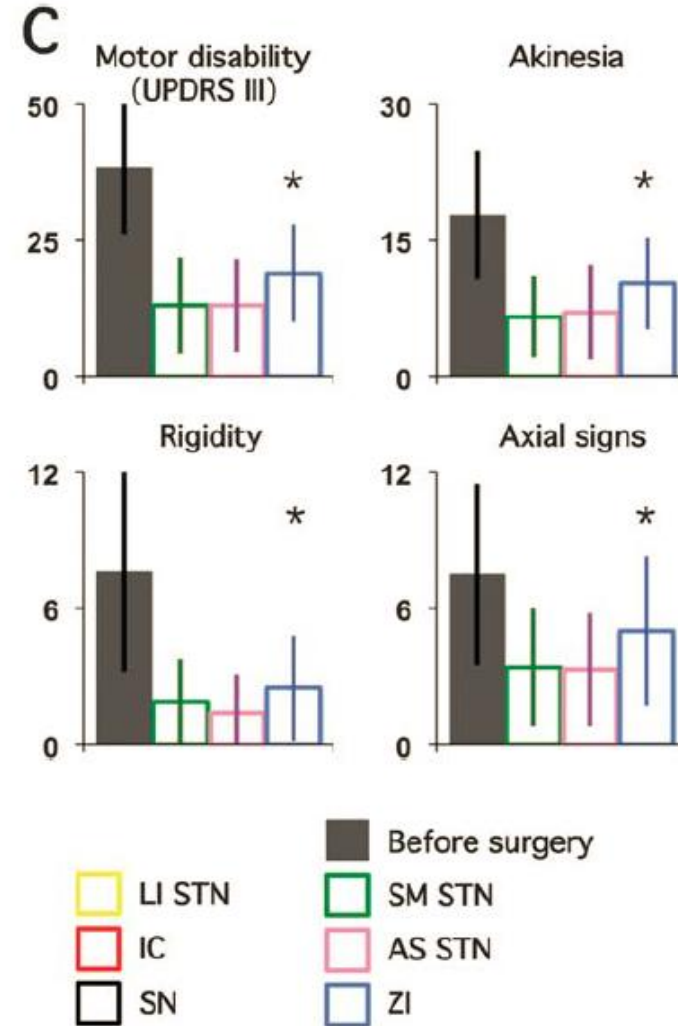


Castrioto et al, 2014

Sensory-motor, dorso-lateral STN preferred target



262 patients.



Welters et al., Neurology 2014

Manic/hypomanic manifestations

Clinical correlates:

- Young onset
- Male gender
- Monopolar stimulation
- Voltage
- **Ventromedial electrode location**
 - **Switch to more dorsal contact often dramatically reduce symptoms**

(Herzog et al., 2003; Coenen VA, 2009, Mandat et al, 2006; Raucher-Chene Det al., 2008; Kulisevsky et al, 2002; Ulla M et al., 2010; Tsai S et al., 2007, Chopra et al., 2012, Welter et al, 2014).

Main Aim

Study the connectivity characteristics differentiating neighbouring contacts, possibly underlying undesired psychiatric side effects.

Study Outline

LFP

Localisation of milestone contact most close to the electrophysiological source of beta oscillations (= Contacts B)

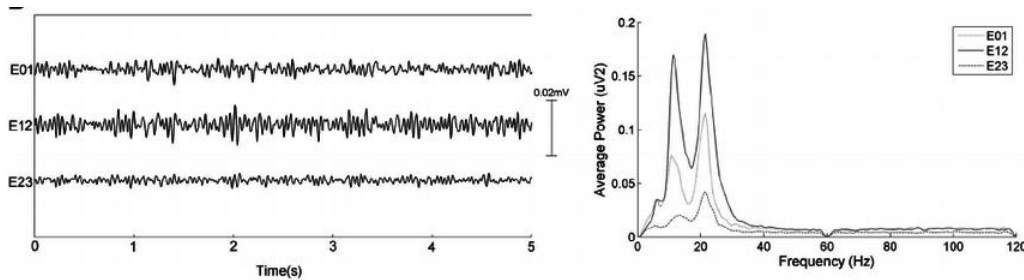
DTI

Connectivity study of
Contacts B (=beta),
Contacts V (= ventral to beta)
Contacts D (= dorsal to beta)

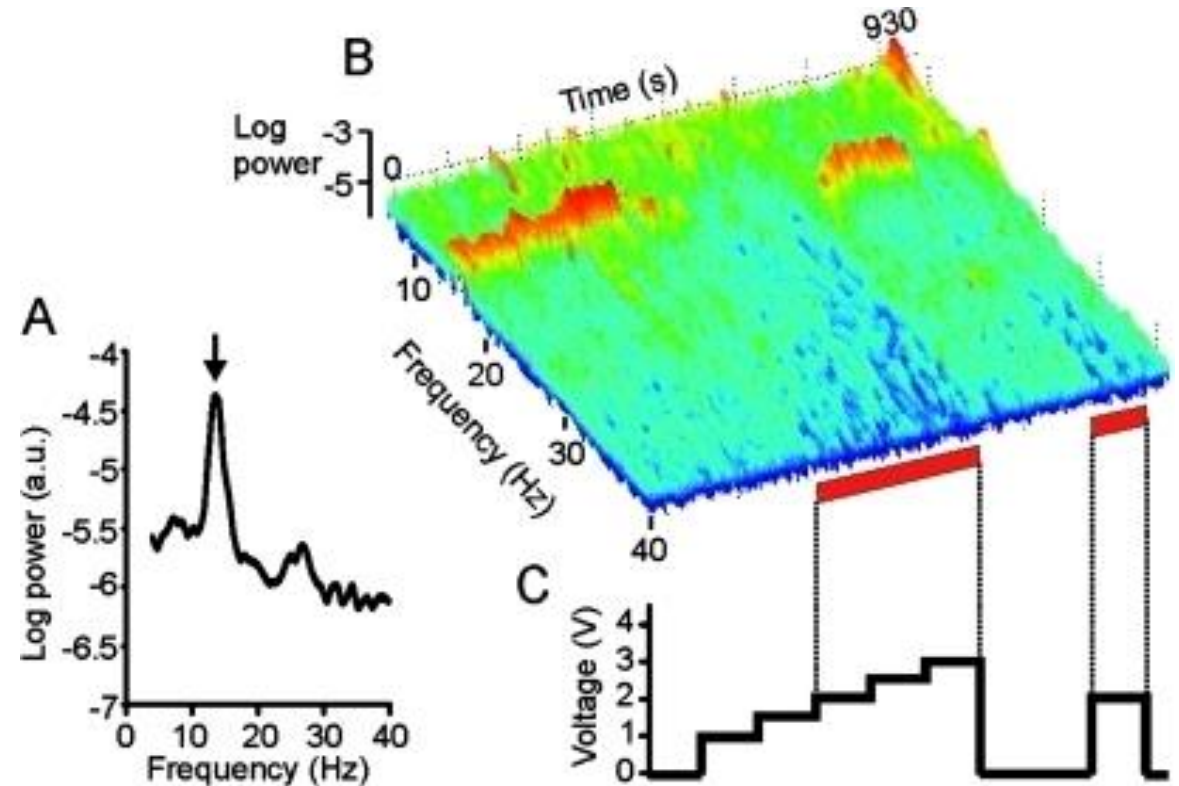
Local Field Potentials



LEAD-DBS



Abosch et al., 2012



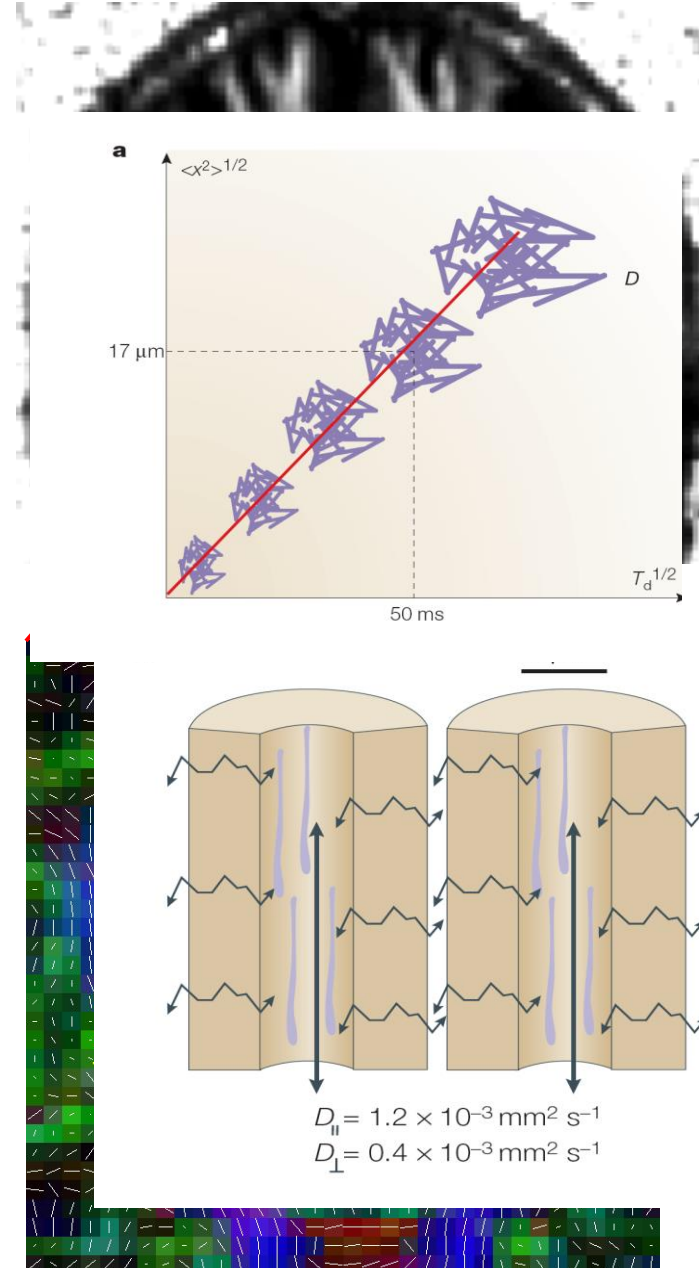
Eusebio et al., JNNP 2010

Diffusion-weighted imaging

- Physics
 - Random movement of molecules due to thermal energy
 - Parallel organization of white matter tracts hinders diffusion
 - Fractional Anisotropy – index of white matter fibre integrity

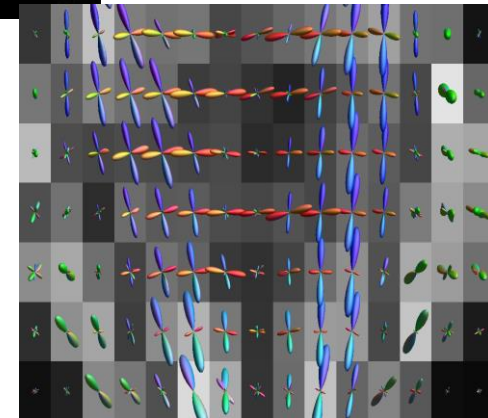
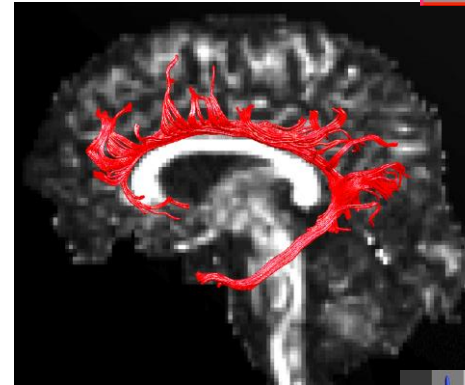
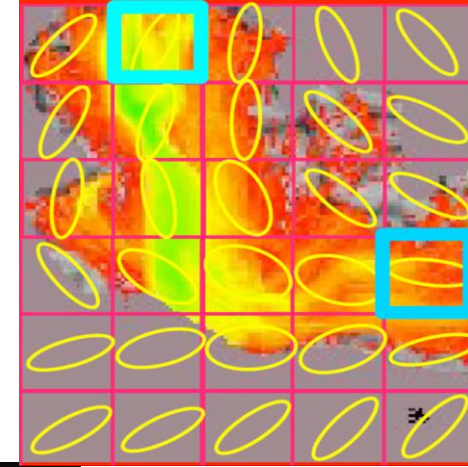
Basser et al., 1994 Biophys J

Pierpaoli et al., 1996 Radiology

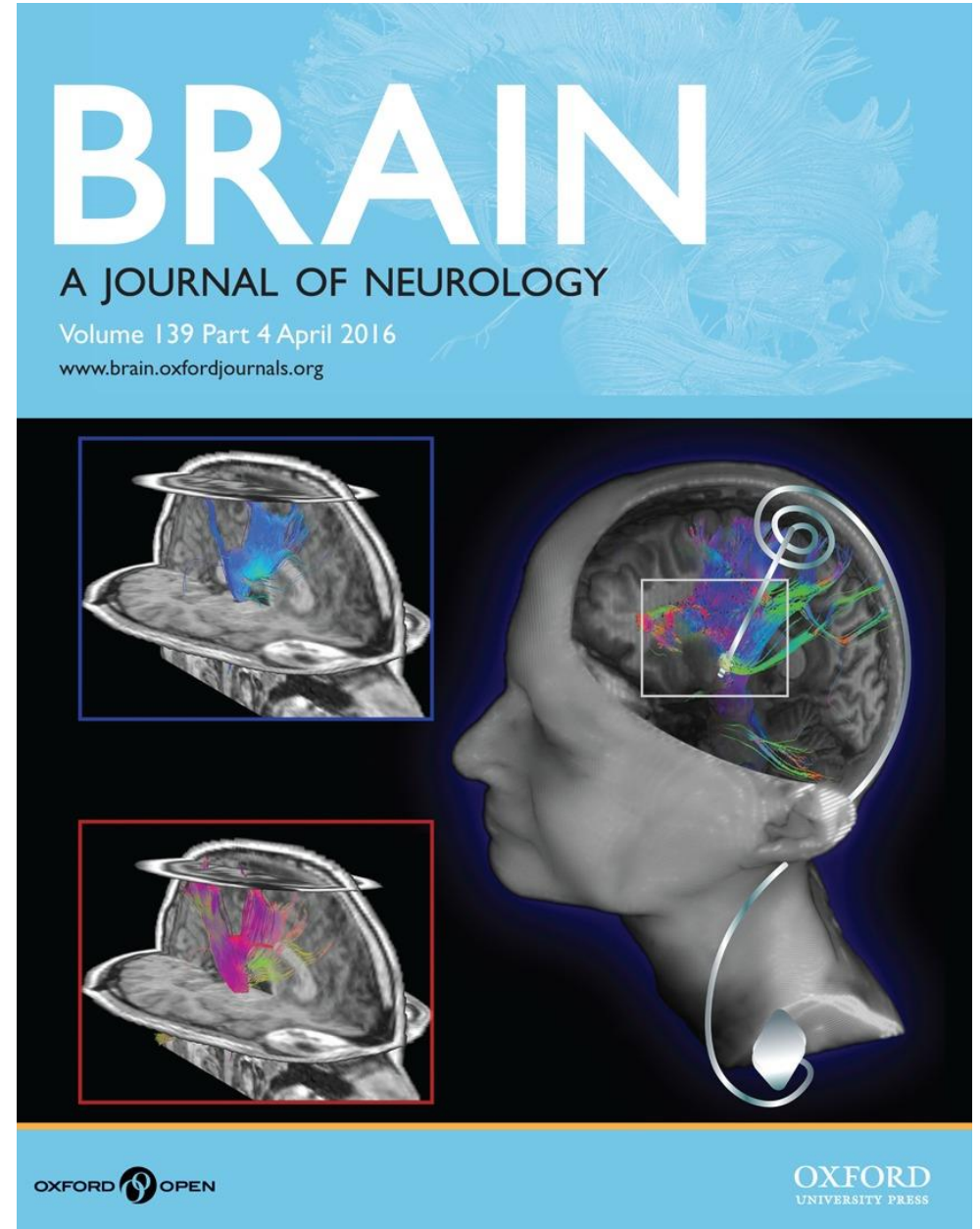
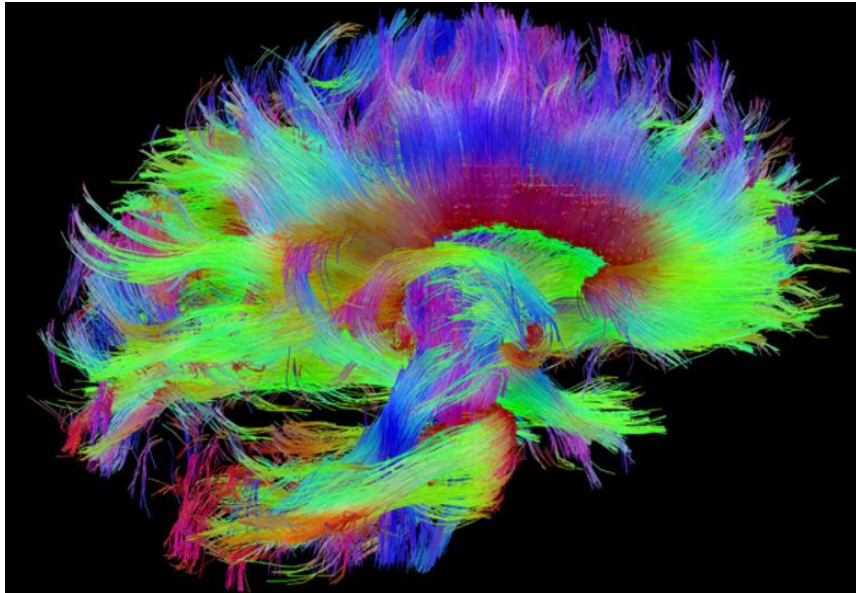


Probabilistic tractography

- Methods
 - Multi-tensor models
 - Spherical deconvolution
 - Quantitative representation of anatomical connectivity strength



Diffusion Tensor Imaging



Contact connectivity study across subjects

Challenges:

- STN dimensions (average 173 mm³)
- STN variability in shape and size
- Accuracy of electrode implantation

Identification of a “milestone” contact

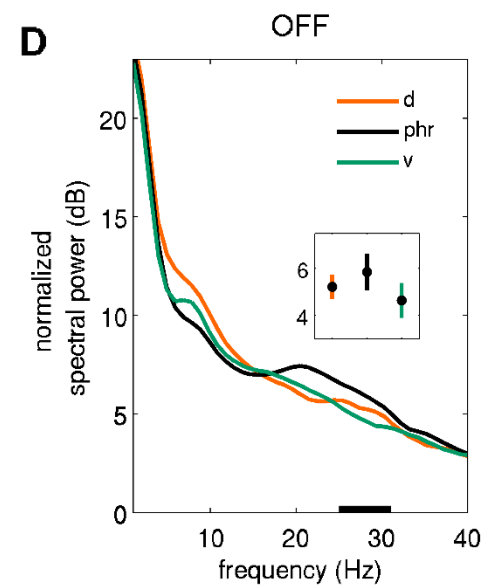
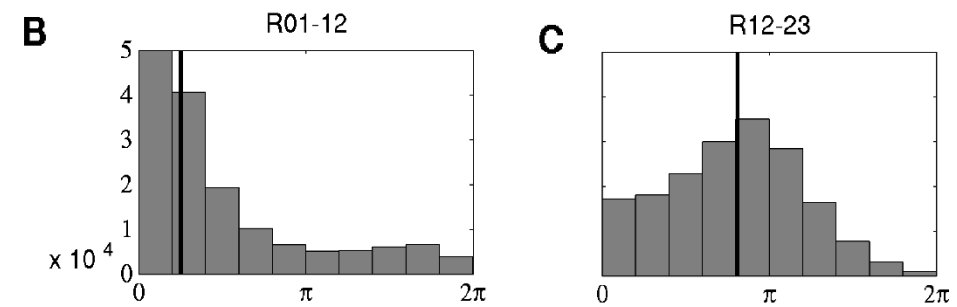
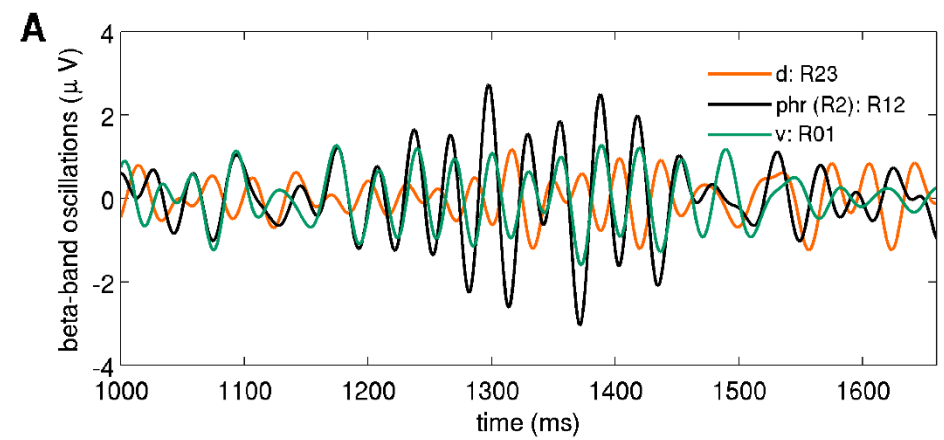
Electrophysiological activity

STN subareas are characterised by typical electrophysiological activity

- Beta oscillations are consistently observed in the dorso-lateral STN (Kühn *et al.*, 2006, Weinberger *et al.*, 2006; Zaidel *et al.*, 2010)
- Beta spectral power is substantially and consistently reduced after the intake of levodopa along with clinical improvement (Hammond *et al.*, 2007; Kühn *et al.*, 2006).
- Beta activity could be considered as the electrophysiological signature of the posterior-dorsal STN in Parkinson's Disease, a region significantly overlapping with the sensori-motor subdivision (Zaidel *et al.*, 2010).

Methods

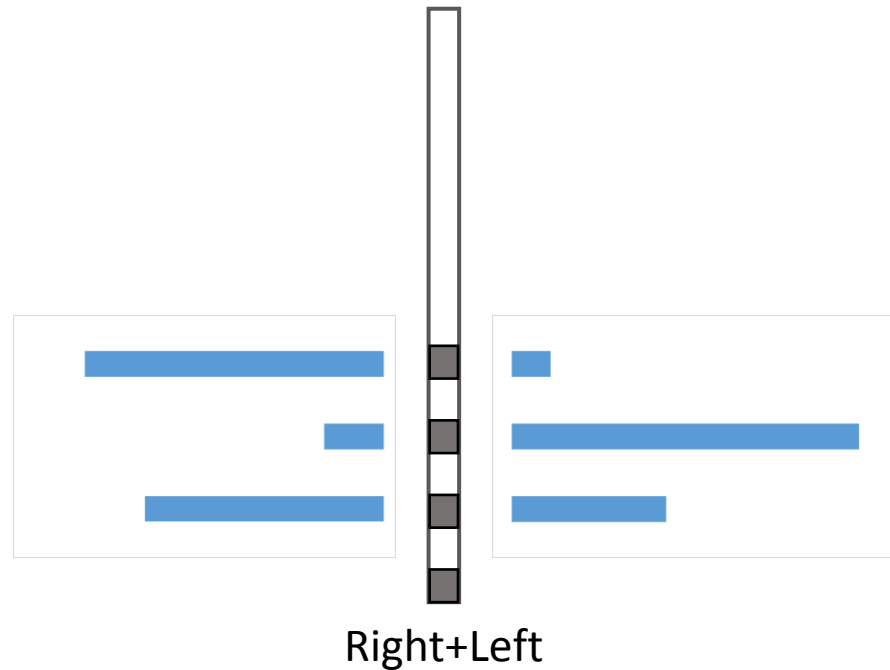
- 10 PD patients, operated for DBS of the STN
- Rest recording from macroelectrode contact pairs in the first 72 hours after operation (OFF and ON)
- DTI whole brain acquisition, high resolution (1,7 isotropic)
- Segmentation of MT maps used for non –linear registration to MNI space



Results: contacts most close to Beta source

Chosen for stimulation

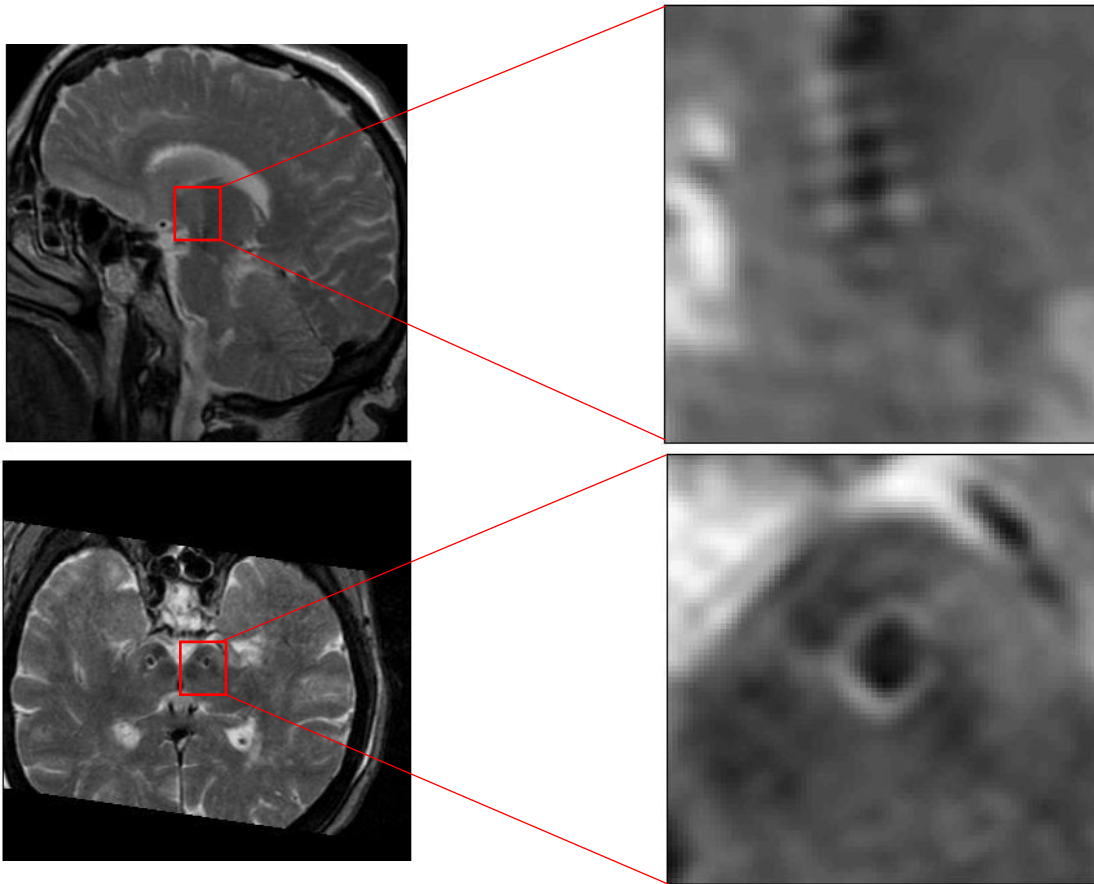
10 times in most dorsal contact
2 second dorsal
8 second ventral
0 most ventral



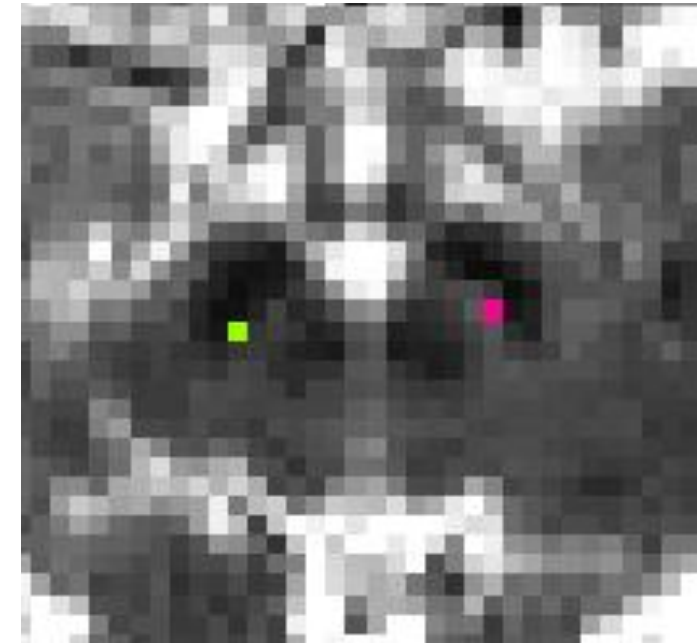
Source of Beta Oscillations

1 times in most dorsal contact
9 second dorsal
4 second ventral
0 most ventral

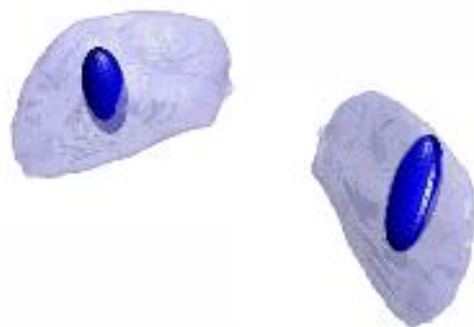
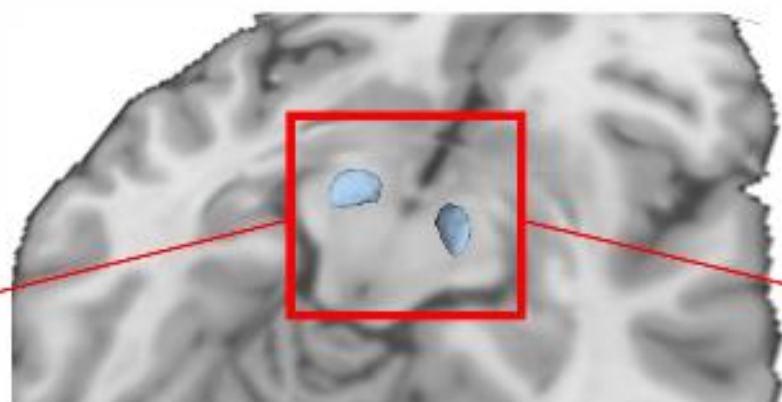
Identification of contacts artifacts: Manual identification of contacts artefact coordinates in diffusion space



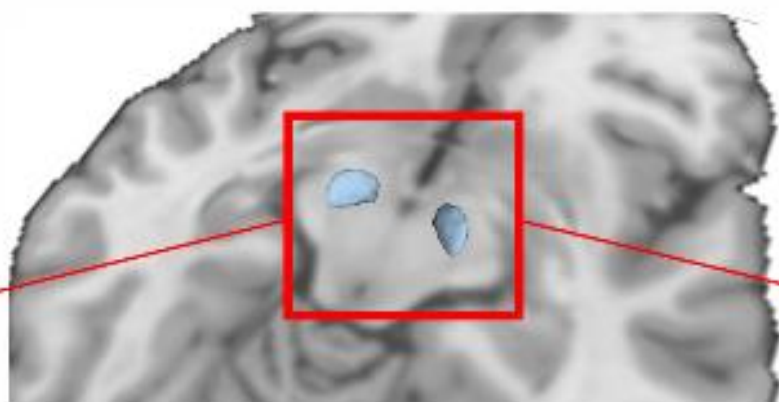
Postop T2



Preop. mean B0



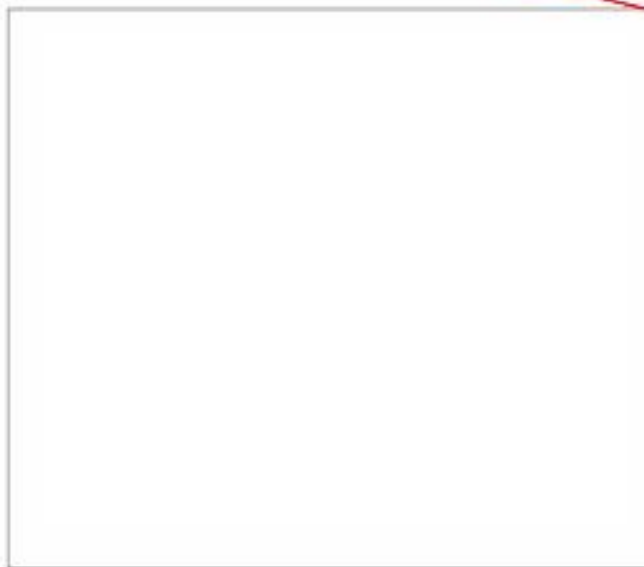
Contacts B

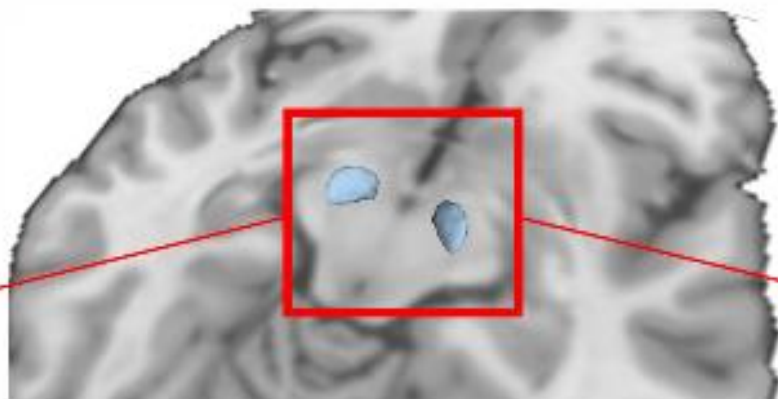


Contacts D



Contacts B





Contacts D

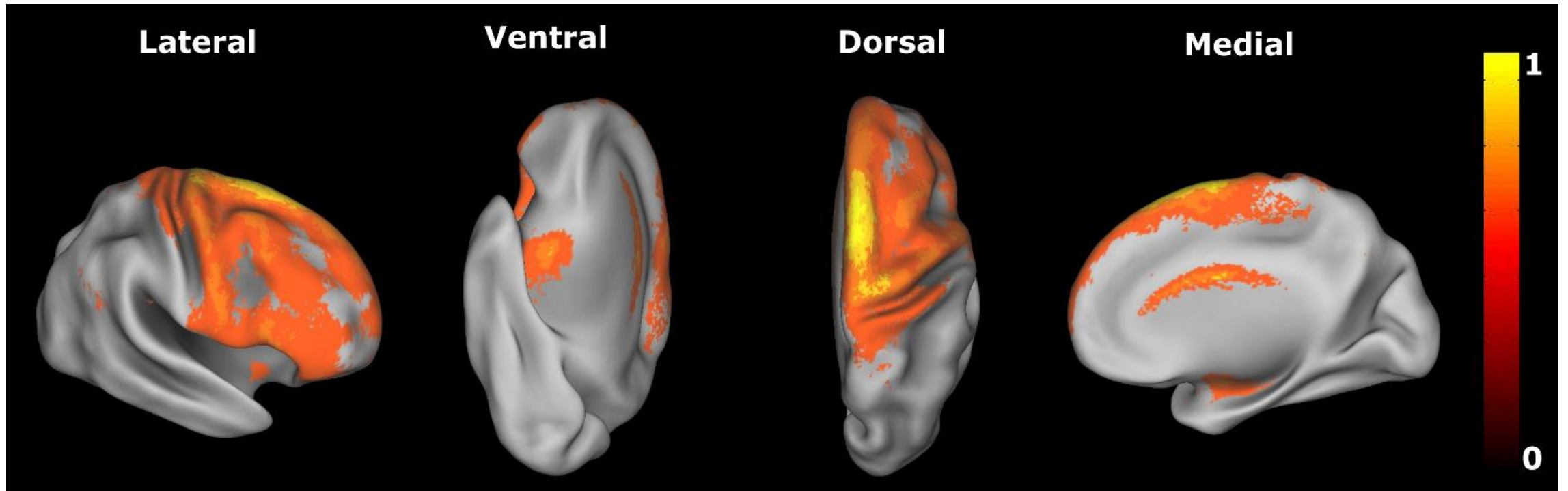


Contacts B

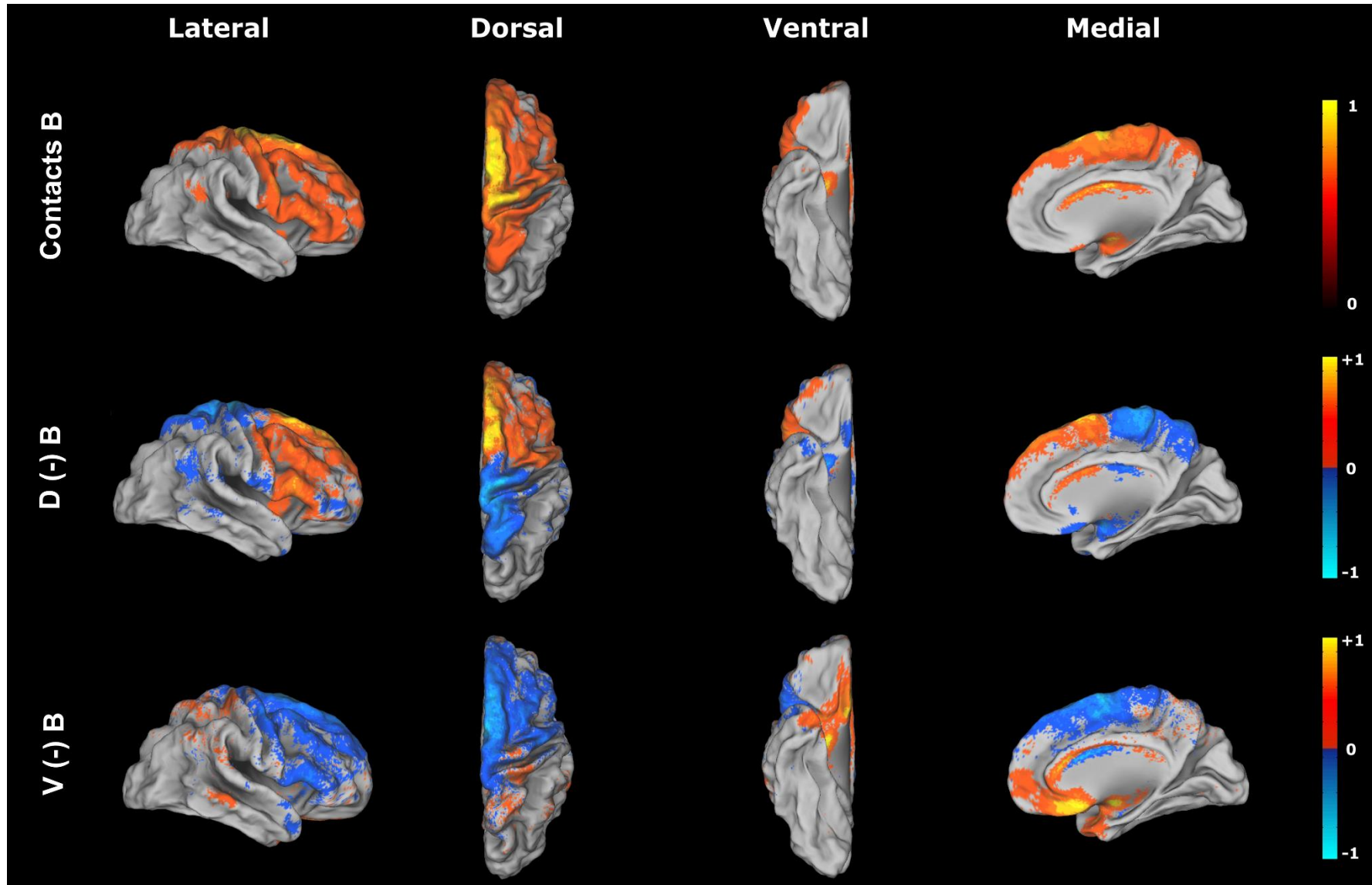


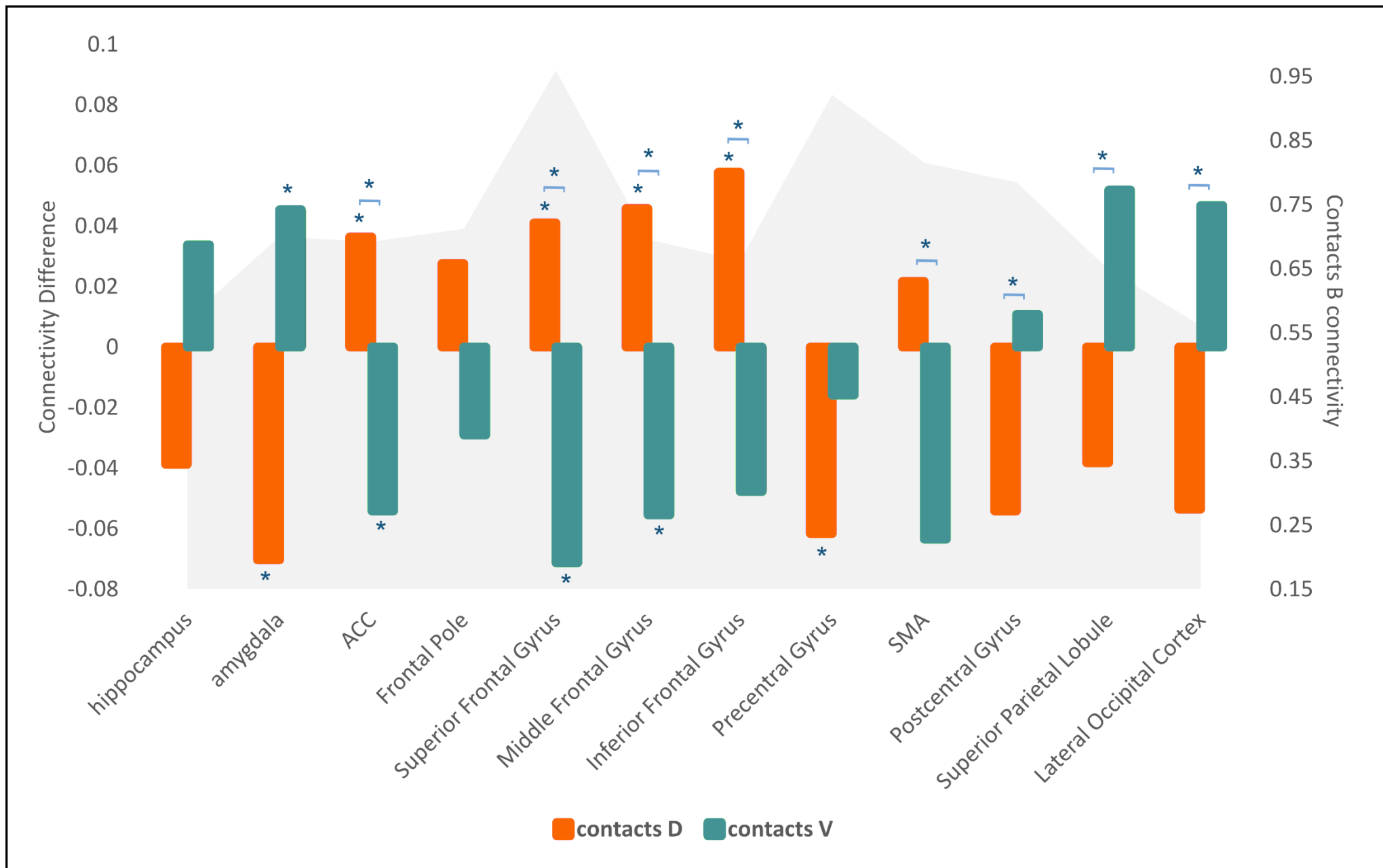
Contacts V

Beta Network



Connectivity variation across contacts





Conclusions

- The source of beta activity in the STN lies in the postero-dorsal STN
- A beta connectivity network includes motor, associative, and limbic cortical regions
- Connectivity to limbic structures might underlie psychiatric side effects of more ventral contacts.



Thank you