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Anatomo-clinical atlases correlate clinical data and electrode contact coordinates: Application to subthalamic deep brain stimulation

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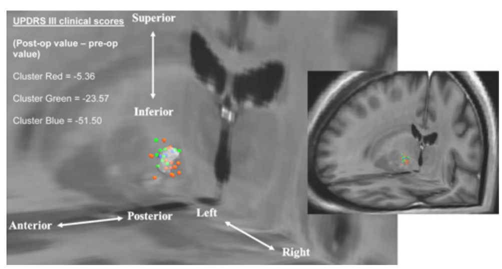
HIGHLIGHTS

- ► Creation of anatomo-clinical atlases for SubThalamic Deep Brain Stimulation.
- ► Atlases enable extraction of representative clusters to determine the optimum site.
- ► Atlases help acquire a better understanding of functional mapping in deep structures.

GRAPHICAL ABSTRACT



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ABSTRACT

For patients suffering from Parkinson's disease with severe movement disorders, functional surgery may be required when medical therapy is not effective. In Deep Brain Stimulation (DBS), electrodes are implanted within the brain to stimulate deep structures such as SubThalamic Nucleus (STN). The quality of patient surgical outcome is generally related to the accuracy of nucleus targeting during surgery. In this paper, we focused on identifying optimum sites for STN DBS by studying symptomatic motor improvement along with neuropsychological side effects. We described successive steps for constructing digital atlases gathering patient's location of electrode contacts automatically segmented from postoperative images, and clinical scores. Three motor and five neuropsychological scores were included in the study. Correlations with active contact locations were carried out using an adapted hierarchical ascendant classification. Such analysis enabled the extraction of representative clusters to determine the optimum site for therapeutic STN DBS. For each clinical score, we built an anatomo-clinical atlas representing its improvement or deterioration in relation with the anatomical location of electrodes and from a population of implanted patients. To the best of our knowledge, we reported for the first time a discrepancy between a very good motor improvement by targeting the postero-superior region of the STN and an inevitable deterioration of the categorical and phonemic fluency in the same region. Such atlases and associated analysis may help better understanding of functional mapping in deep structures and may help pre-operative decision-making process and especially targeting.

1. Introduction

1.1. Background

Parkinson's Disease (PD) is recognized as one of the most common neurological disorders, affecting 1% of people over the age of 60 years. It is the second most prevalent neurodegenerative disorder.

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One of the characters of PD is the apoptosis of the dopamine-rich neurons of the substantia nigra. Major symptoms are indeed characterized by abnormalities of motor functions, several of which predominate, but all do not necessarily occur in all individuals. While these PD-related symptoms can be treated with medical therapy, when it remains ineffective for some patients, a Deep Brain Stimulation (DBS) surgery (Benabid et al., 2000a,b; Krack et al., 2003) might be necessary according to strict patient inclusion criteria. This iterative procedure, initially approved by the Federal Drug Agency in U.S. in 1997 for essential tremor disorders, and in 2002 for PD, has gained much interest over the past decade and is now widely used by a large number of neurosurgical departments. The DBS anatomical target is based on the relief of symptoms and results of previous implantations only. The three major targets chosen by neurosurgeons according to the patients' symptoms are the Caudal part of the Ventro-Lateral thalamic nucleus (VLc), the medial Global Pallidus (GPm) and the Sub-Thalamic Nucleus (STN). Among these three deep brain structures, the STN became the most common target of high-frequency DBS in patients with severe motor disabled symptoms and no cognitive impairment (Benabid et al., 2000a,b; Lang and Lozano, 1998; Hamani et al., 2003; Bardinet et al., 2009; Volkmann et al., 2009).

1.2. Surgical procedure

During routine DBS surgery, two stages are mainly involved: pre-operative planning and the surgery itself. Pre-operative planning is the process of loading pre-operative patient's medical images (such as Computed Tomography and/or Magnetic Resonance Images), registering them together and proposing a 2D and/or 3D visualization interface to define the target localization in the Anterior and Posterior Commissures (AC–PC) plan. Mainly due to contrast and spatial resolutions limitations, the usual DBS targets are not easily visible on the MR images available to the surgeon, even though MRI offers better contrast than other medical imaging techniques (Dormont et al., 2010). Neurosurgeons directly localize the optimal target position on the T2 MR image and choose the trajectory of the electrode on patient's anatomical information. During this step, the additional help of an atlas may be necessary. In practice, experts manually localize AC–PC coordinates, midsagittal points and entry on the MR images of the patient. Finally, coordinates are automatically put in AC–PC space, then computed in a stereotactic coordinates system.

The surgical procedure is then performed under local anaesthesia. The trajectory estimated during planning is implemented with stereotactic frame based or frameless systems and used as an initial position that has to be refined. A few causes of discrepancy between chosen target and the final implant might appear, such as brain shift (Khan et al., 2008; Pallavaram et al., 2009), or patient's anatomical variability. An X-ray control is thus performed intraoperatively to confirm the initial placement and evaluate potential biases. Electrophysiological explorations are also performed to help neurosurgeons refine the placement of active electrode contacts. Similarly, neurologists may test the clinical effects with different settings for each contact to reach optimum placement. Changing frequency, voltage, stimulated contact and electrode trajectory, they reach optimum placement. Lastly, the surgeon anchors the electrode to the skull.

Even though STN DBS has demonstrated its efficiency for motor symptom improvement, questions remain concerning contact location providing the greatest motor improvement while producing the minimal neuropsychological and psychiatric side effects. Indeed, despite satisfactory motor improvements, several studies have reported adverse-events after DBS surgery affecting cognitive functions, emotion or behaviour (Parsons et al., 2006; Temel et al., 2006; Biseul et al., 2005; Dujardin et al., 2004; Houeto et al., 2002). In particular, Brücke et al. (2007), Kühn et al. (2005), Greenhouse et al. (2011), Lhommée et al. (2012) or Mallet et al. (2007) elucidated the role of STN in emotional processing, showing that STN DBS leads to behavioural complications. Similarly, Burrows et al. (2011) were interested in complications of STN DBS around the zona incerta, and York et al. (2009) looked at neuropsychological complications according to electrode location and trajectory. All these results suggest that the STN forms part of a broadly distributed neural network encompassing the associative and limbic circuits. Similarly, Witt et al. (2008) studied neuropsychiatric consequences of STN DBS. Based on this hypothesis, new works have then emerged. For instance, Karachi et al. (2005), or more recently Lambert et al. (2012) supported the hypothesis that the nucleus was separated in three regions: the limbic, associative and motor regions. Similarly, Lenglet et al. (2012) studied the basal ganglia and thalamic connections using high-resolution MR images. As outlined above, one of the major challenges in DBS is the identification of the target, which requires additional information and knowledge for indirect identification of such small structures during the pre-operative stage with the support of digital atlases.

1.3. Atlases

Brain atlases and atlas-based segmentation techniques have been developed to facilitate the accurate targeting of deep brain structures in patients with movement disorders (Schaltenbrand and Wahren, 1977; Talairach and Tournoux, 1988; Chakravarty et al., 2006; Yelnik et al., 2007; Bardinet et al., 2009; Lalys et al., 2009). Some digitized atlases aim at providing information with optimum spatial and intensity resolution, to allow better identification of structures, which is impossible with usual medical imaging techniques only. Histological atlases were thus created (Yelnik et al., 2007; Chakravarty et al., 2006) along with high-resolution MR based atlases (Aubert-Broche et al., 2006; Lalys et al., 2011). Both types of atlas have been successfully introduced in the targeting stage of standard DBS procedures.

The concept of probabilistic functional atlases, built from a population of previous surgical cases, was initially introduced by Nowinski et al. (2003, 2005, 2007). After a step of normalization within a common space, effective contacts are linked to preoperative electrophysiological recordings and clinical scores acquired during the stages of the procedure. Statistical techniques are used to study anatomical or functional variability between patients. Response to stimulation, electro-physiological recordings and clinical scores related to motor or cognitive evolution are all potential data that can be integrated into such atlases. This fusion of clinical and anatomical information allows an understanding of functional organization within deep-brain structures that helps in the identification of the optimal therapy zone for further patients. Finnis et al. (2003) and Guo et al. (2006) proposed probabilistic functional atlases by integrating intra-operative recordings. D'Haese et al. (2005, 2006) and Pallavaram et al. (2008, 2009) proposed a system to automatically predict the optimum target position according to atlases built from retrospective studies. More recently, D'Haese et al. (2010) proposed a fully integrated computer-assisted system called CRAnialVault. The system addresses the issue of data administration between the different stages of the therapy. It permits the centralization of various types of data acquired during the procedure and provides data visualization through data processing tools. A preliminary validation process in a clinical context, from planning to programming, is described and shows that the system provides genuine assistance to the surgical team.

Evaluation of DBS electrode implantation involves significant neurological and psychological follow-up estimated by clinical tests. Resulting clinical scores allow post-operative evaluation of the decrease in motor disorders and possible clinical side effects.