Aus der Klinik für Neurologie
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DISSERTATION

Toward Connectomic Deep Brain Stimulation

zur Erlangung des akademischen Grades

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Inhaltsverzeichnis

1. Abstract (deutsch)

Die tiefe Hirnstimulation (THS) stellt eine etablierte und hocheffektive Therapieoption bei Morbus Parkinson, Dystonie und essentiellem Tremor dar. In der Vergangenheit wurden die klinischen Resultate der Therapie vor allem auf lokale Effekte im Bereich des Zielgebiets der Elektrode zurückgeführt. Diese Ansicht gilt heute nur als Teilantwort auf die Frage des Wirkmechanismus der THS. Vielmehr geht man von additiven Effekten aus, die sich aufgrund der funktionellen und strukturellen Konnektivität des Zielgebiets auf Bereiche des gesamten Gehirns, namentlich eine sog. Kortex-Basalganglien-Zerebellum-Schleife, auswirken. Die Analyse der Gesamthirnkonnektivität ist innerhalb der sogenannten neurowissenschaftlichen Konnektomforschung angesiedelt. Ziel der drei Studien dieser Doktorarbeit ist die Etablierung eines Software-Frameworks, welches die beiden Wissenschaftsbereiche – THS und Konnektomforschung – miteinander verbindet, um in zukünftigen Studien konnektombasierte THS-Forschung zu ermöglichen.

Die drei Studien hatten folgendes zum Ziel: In der ersten Arbeit (*Horn et al. 2013*) erfolgte die Analyse der kombinierten strukturellen und funktionellen Ganzhirnkonnektivität zwischen vierzigtausend Bildpunkten der grauen Substanz des Gehirns bei neunzehn gesunden Probanden. Mittels dieses neuartigen Analysekonzepts konnte gezeigt werden, dass sich die strukturelle und funktionelle Konnektivität bei Gesunden am stärksten innerhalb von Regionen des sogenannten *default mode networks* überlappt. In der zweiten Studie (*Horn et al. 2016*) wurde auf Basis von diffusionsgewichteter MRT-Daten ein strukturelles Gruppenkonnektom von 169 gesunden Probanden berechnet. Dieser neuartige Datensatz ermöglicht die Berechnung von Fasertraktographieresultaten innerhalb des stereotaktischen Normalraums. Schließlich wurde in der dritten Arbeit (*Horn et al. 2015*) eine Software entwickelt, die i) die exakte Lokalisation von THS-Elektroden auf der Basis von postoperativer MRT/CT-Bildgebung ermöglicht und ii) die Analysekonzepte der ersten beiden Studien in ein gemeinsames Softwarekonzept integriert. Diese Software wurde als *open source* unter dem Namen '*Lead DBS*' veröffentlicht und ermöglicht die Durchführung von Studien im Kontext von THS, konnektombasierter Neurowissenschaft und einer Kombination der Kontexte.

2. Abstract (englisch)

Deep brain stimulation (DBS) is an established and highly efficacious treatment option in idiopathic Parkinson's disease, dystonia and essential tremor. In the past, the clinical effects of DBS were explained as local effects within the target structure of the DBS electrode. Nowadays, this concept is only considered part of the explanation of the mechanism of action of DBS. Rather, the concept has been extended by additive effects mediated via structural and functional connectivity of the target area to different other areas of the whole brain, namely the so-called cortex basal ganglia cerebellar loop. The analysis of whole brain connectivity is a discipline of the so-called connectomic neuroscience. The goal of the three studies that make up this dissertation was the establishment of a software-framework which combines the two fields of research – DBS and connectomic neuroscience – to allow for connectomic DBS research in future studies.

The aims of the three studies were as follows: In the first study (*Horn et al. 2013*), a combined structural-functional whole brain connectivity analysis between forty-thousand points within the gray matter of the brain was performed in 19 healthy subjects. Using this novel observer-independent approach, it could be shown that regions forming part of the so-called *default mode network* exhibit the highest similarity in their structural and functional connectivity to the rest of the brain. In the second study (*Horn et al. 2016*), a structural group connectome was estimated by using diffusion-weighted data from 169 subjects. This novel dataset allows estimating fiber tracking results within a standardized stereotactic space. Last, in the third study (*Horn et al. 2015*), a software package was developed that i) can be used to exactly localize DBS electrodes based on postoperative CT-/MR-Imaging and ii) integrates the methods and data estimated in the first two studies into a joint analysis framework. This software package was released as open source to the scientific community under the name of '*Lead DBS*' and facilitates studies in the fields of DBS, connectomic neuroscience and a combination of both.

3. Zusammenfassung

3.1. Introduction

(i) Background

Functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI) are well-established techniques to non-invasively assess functional (Friston 2011) and structural (Basser et al. 1994) connectivity between distinct regions in the human brain. Using these methods, after parcellating the brain into small units, the inter-connectivity between each and every region of tghe brain can be computed. This results in the concept of the *connectome,* a structural description of the elements forming the human brain and the connections among them (Sporns et al. 2005; Hagmann 2005). The connectome framework makes it possible to formally characterize and analyze connectivity-changes that have widespread effects across the whole brain in health (Hagmann 2005; Honey et al. 2009) and disease (Skudlarski et al. 2010) by using graph-theoretical methods (Rubinov & Sporns 2010).

The mathematical analysis of this 'wiring diagram' of the brain can help to gain insight into the pathophysiology and mechanism of action of neuronal diseases (Varoquaux & Craddock 2013; Friston & Frith 1995; Carbon & Eidelberg 2009). Movement disorders such as Parkinson's Disease (PD) or dystonia are associated with abnormalities in their structural and functional connectivity between regions forming loops between the basal ganglia, the cerebellum and the cortex (Carbon & Eidelberg 2009; Wu et al. 2009; Hacker et al. 2012; Helmich et al. 2010).

As a consequence of the connectome framework and it's promising potential in movement disorders, the concept of *connectomic surgery* has been proposed recently in a perspective article (Henderson 2012). The concept may be seen as an extension to deep brain stimulation (DBS) and involves the definition of more effective and patient-specific DBS electrode placements by means of whole-brain connectivity analyses. These advances may improve the clinical outcome of patients and reduce the occurrence rate of adverse effects in the future.

Already, DBS represents a well-accepted treatment option in movement disorders such as PD and dystonia, leading to significant improvements in motor symptoms and quality of life (Kupsch et al. 2006; Mueller et al. 2008). Initially, DBS was thought to solely inhibit target regions (Breit et al. 2004), but it is now generally accepted that it may influence widespread areas of the brain (Dostrovsky & Lozano 2002; Johnson et al. 2008; Montgomery & Gale 2008; Hauptmann & Tass 2010). Such network effects have been empirically detected by fMRI (McIntyre & Hahn 2010) and cortical electrode recordings (Henderson et al. 2010). Given this fact, and since robust predictive factors for the success of DBS have not yet been found, connectomic studies seem promising in improving therapy, or even predicting clinical outcome before surgery.

As a consequence of the local effects of DBS, electrode placement is crucial for a beneficial outcome, even more so in patients with unilateral PD or segmental/focal dystonia. In this sense, connectivity information might help to refine target locations (Berman et al. 2007; Coenen et al. 2009; Bello et al. 2010; Leclercq et al. 2010). DBS-induced side effects such as dysarthria and bradykinesia may occur after surgery, which are also often explained by an inadvertent stimulation of fiber bundles that traverse alongside the stimulated tissue, the so-called 'volume of tissue activated' (VAT; Butson et al. 2007, Vitek 2002). As a result, single-site tractographical data has already been successfully used to avoid complications (Berman et al. 2007; Coenen et al. 2009; Bello et al. 2010; Leclercq et al. 2010).
This thesis is composed of three studies that provide a foundation to perform connectomic studies within the field of DBS research. Although two studies deal with connectome analyses in healthy subjects and the third study deals with 'non-connectomic' research within the field of DBS, methods and results of all three studies were incorporated into the software-package *Lead DBS* that will allow carrying out 'Connectomic DBS' studies in the near future. The software itself has been released as an open source tool as part of this thesis and is now freely available to the scientific community.

(ii) Aim of the studies

The aim of the studies was to establish a methodological framework for connectomic analyses in the context of deep brain stimulation. Both fields of study – connectomic analyses and deep brain stimulation – require a substantial amount of expertise and methodological skills. Until now, to the best of our knowledge, no software package is available that covers both fields of study and focuses on the combination of DBS with connectomics. The final goal of the three studies that led to this dissertation was to establish such a framework and an accompanying software package. The result was published as the software *Lead DBS* and its first extension *Lead Connectome* online under www.lead-dbs.org. To gather the necessary expertise in both fields of study, in a first step, a connectomic analysis-framework was established in two consecutive studies that focused on i) the combined analysis of structural and functional connectivity and ii) on the estimation of a structural-functional group connectome in MNI space. In parallel, the second aim was covered by a third study that aimed at precisely locating DBS electrode placement based on postoperative magnetic resonance or computed tomography imaging. This last study laid the groundwork for *Lead DBS*, whereas the methodology established in the first two studies was integrated into *Lead DBS* via the extension *Lead Connectome*. Methodologies from both fields of study are now freely available to the broader scientific community in a seamlessly integrated software package that is based on the MATLAB programming environment (the Mathworks, MA, USA).
The ultimate hope is that a better understanding of movement disorders and their treatment can be gained by providing accurate, state-of-the-art methodology and by making it freely available.

3.2. Methods

Methods will be discussed separately for the connectomic (Horn & Blankenburg 2016; Horn et al. 2013) **studies and the DBS** (Horn & Kühn 2015) **study:**

(i) Horn et al. 2013 & 2016:

In *Horn et al. 2013*, structural, T1-weighted MRI data as well as fMRI and dMRI data was acquired from 19 healthy subjects. fMRI data was acquired with subjects at rest, i.e. can be considered as resting-state fMRI (rs-fMRI) data. In the second study (*Horn et al. 2016*), similar data was obtained from a community sample of 169 subjects freely available on the internet (http://fcon_1000.projects.nitrc.org/indi/enhanced/).

In both studies, the structural and functional connectivity between approximately fourty-thousand small regions in the gray matter of the brain was estimated. A single region's functional and structural connectivity to the rest of the brain was estimated and compared by correlating the respective whole-brain connectivity vectors. Thus, a single value for each region was gained which was termed the structure-function agreement index. By mapping the values of this index back to the gray matter of the brain for each spatial position, regions that exhibit a global similarity in their structural and functional connectivity to other brain regions could be highlighted.

In *Horn et al. 2016*, the focus lay on estimating a structural group connectome of anatomical fiber tracts within a standardized stereotactic space. To do so, dMRI based fiber tracts were estimated for each subject's diffusion MRI data by applying a global fiber reconstruction approach (Reisert et al. 2011). Using a modern diffeomorphic image registration algorithm (DARTEL; Ashburner 2007), the spatial positions of fiber tracts were warped into standard space. The estimated group connectome was evaluated for its data quality in four consecutive ways. First, by comparison to the JHU white-matter atlas (Bürgel et al. 2006). Fiber tracts defined by this atlas were isolated from the group connectome and compared to the JHU tracts by visual inspection. Second, a more quantitative comparative analysis to the Oxford thalamic connectivity atlas (Behrens et al. 2003) was performed. Here results from the original study that showed distinct connectivity between subparts of the thalamus and distinct cortical regions of the brain were replicated. Third, results from a study that analyzed structural connectivity between functional zones of the 'default mode network' (Greicius et al. 2009) were reproduced. Lastly, as a whole-brain connectivity analysis, results from two graph-theoretical studies were reproduced, namely a study by (Nijhuis et al. 2013) which analyzed graph theoretical estimates based on pure structural connectivity and main results from the *Horn et al. 2013* study.

(ii) Horn et al. 2015

In *Horn et al. 2015*, a toolbox that can be used to localize deep brain stimulation electrodes based on post-operative images of DBS patients was developed and evaluated scientifically. In total, fifty

patients that underwent DBS surgery were analyzed in this study. Details of surgical and postoperative imaging protocols varied for some subgroups of patients, since the goal was to analyze the generalizability of the toolbox (see table 1 in original publication for patient demographics and target regions of DBS surgery). Postoperative imaging for each patient was available either in form of T2-weighted MRIs, CT-scans or both of the former.

Postoperative CT-scans were co-registered to preoperative MRIs using BRAINSFit software as implemented in 3DSlicer 4 (http://www.slicer.org). Postoperative MRI scans were co-registered to preoperative MRIs using SPM8 (http://www.fil.ion.ucl.ac.uk/spm/software/spm8/). Both pre- and postoperative images were then warped into standard space by using the normalization parameters estimated based on the preoperative imaging following the approach of (Schönecker et al. 2009).

3.3. Results

Results will be discussed separately for the three studies.

(i) Horn et al. 2013:

Results of *Horn et al. 2013* are grouped around the finding that regions forming part of the default mode network (DMN) show the highest similarity in their structural and functional connectivity to the rest of the brain. This could be shown by using two different fiber tracking approaches (probabilistic tractography and a novel global tracking approach referred to as *Gibbs' tracking;* Reisert et al. 2011) and two estimations of functional connectivity (marginal correlations and partial correlations). The results of the two structural connectivity estimates predominantly differed in the medial prefrontal cortex. The Gibbs' tracking approach showed high (see fig. 4 in original publication) and statistically significant (fig. 2 in original publication) structure-function overlap in this region whereas the probabilistic tracking approach found lower (fig. 4) and statistically insignificant (fig. 2) structure-function overlap here. This was also shown by direct mass-univariate pairwise t-tests performed between the two modalities (fig. 3 in original publication). Results for functional connectivity estimated using full and partial correlations did not differ significantly.

To quantitatively assess the similarity between the results and the DMN, results were spatially correlated to a template of the DMN (Garrity et al. 2007). See table 3 in the original publication for specific Pearson's R values. For all combinations of methods, R-values ranked around 0.3 which is a high value given the voxel-wise nature of the comparisons across all areas of the brain.

(ii) Horn et al. 2016:

The main result of *Horn et al., 2016* was the establishment of a structural group connectome in standardized stereotactic (MNI) space. Several analyses were performed to evaluate the connectome. First, comparisons to the JHU white-matter atlas (Bürgel et al. 1999) were performed qualitatively by visual inspection (see fig. 4 and S2 of the original publication for a direct synopsis). Fiber tracts isolated from the group connectome using masks from the JHU atlas traversed in the expected anatomical directions (see color coded representations mapping x/y/z to red/green/blue in original figures). Second, a more quantitative analysis aimed at reproducing the results from (Behrens et al. 2003) using the group connectome. Here, the thalamus was parcellated into seven functional zones based on its connectivity to distinct anatomical regions (tagged as prefrontal, temporal, sensory, primary motor, premotor, occipital and posterior parietal) regions. See figure 5 in the original publication for a direct comparison of results from (Behrens et al. 2003) and this study. Despite the different methodology used in the two studies (probabilistic tractography in Behrens et al. 2003 and the global Gibbs' tracking algorithm in this study), the overall parcellation results of the thalamus were strikingly similar in both studies. Third, a reproduction from a study by Greicius and

colleagues (2009) which aimed to assess structural connectivity between areas forming part of the default mode network yielded results similar to the original study. As in the study by Greicius and colleagues, fiber-tracts connecting posterior cingulate cortex (PCC) and medial prefrontal cortex (MPFC; blue tracts in Fig. 6 of *Horn et al. 2016*, top left panel) as well as precuneus and medial temporal lobes (MTL; orange tracts) were identified. Again, as in the original study, fibers from the MTL entered more caudally, i.e. into the putative retrosplenial portion of the PCC/RSC, whereas fibers from the MPFC entered more rostrally, i.e. into the PCC proper. Lastly, graph-theoretical estimates yielded similar results to the *Horn et al. 2013* study and a study carried out by Nijhuis and colleagues (2013). Both in terms of centrality of whole-brain structural connectivity and in terms of the global structure-function agreement index (see above chapter), brain patterns were largely similar to the ones estimated in the original studies (see figure 6 bottom two panels of *Horn et al. 2016* for a direct synopsis).

(iii) Horn et al. 2015:

Figure 1 graphically visualizes the main result of this third study. In summary, 98.3% of 120 electrode trajectories were identified by the algorithm (referred to as *TRAC* in the original publication) of the toolbox. 16 trajectories were analyzed twice, once based on postoperative MRI, once based on CT imaging. Furthermore, the second algorithm (*CORE* in original publication) identified the correct height of electrode contacts alongside the trajectories in 69.2% of cases. This latter result is not as important, since the toolbox provides a tool to manually localize electrode contacts once the trajectory has been identified.

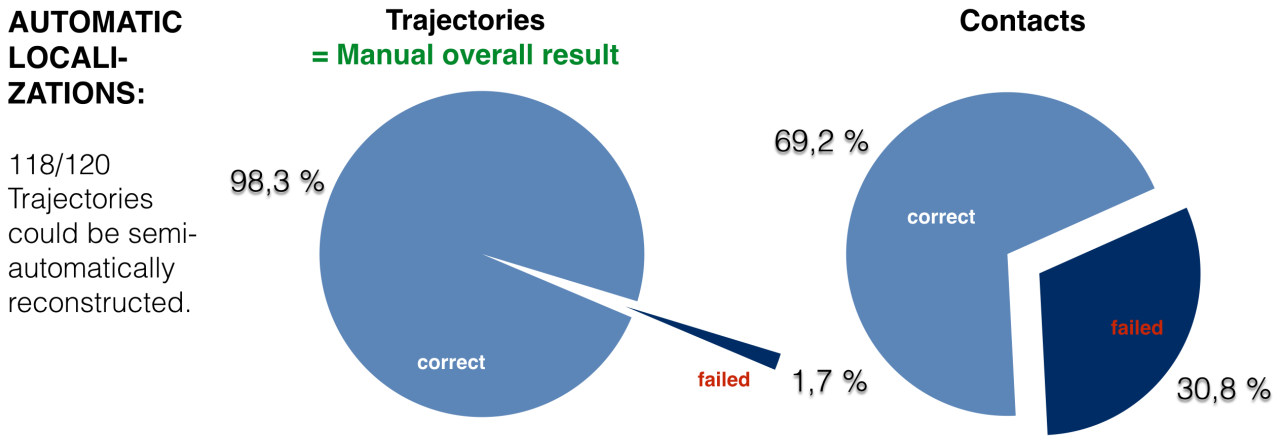

Figure 1: Results of electrode localization attempts. The toolbox automatically reconstructed 98.3% of lead trajectories and 69.2% of electrode contacts. By combining the automatic 'pre-localization' with a follow-up manual refinement of localizations, this leads to an overall success rate of 98.3%.

As a secondary result, contact placement based on the two postoperative imaging modalities (MR/CT) were compared in patients that received both after surgery (n=8). The estimated Pearson's R-

values between MR- and CT-based reconstructions ranked above 0.9. In summary, the evaluation of the toolbox was positive in terms of its generalizability and modality-independence.

3.4. Discussion

In the following section, results from the three studies are discussed and set into context of the scientific literature with special focus on their contribution to the software package *Lead DBS* (also see figure 2 for a graphical summary).

In *Horn et al., 2015*, the main *Lead DBS* toolbox was developed and evaluated. The two core algorithms of the electrode reconstruction part of the software showed high robustness and electrode contacts could be reconstructed in 119/120 cases in a semi-automated fashion. *Lead DBS* allows for single-subject and group studies of DBS electrode placements, simulations of stimulations (by modeling the volume of activated tissue) and comprises structural-functional connectomic analyses methods (fiber tracking and analysis of resting-state functional connectivity measures based on fMRI data). The usefulness of the toolbox has already been shown in several electrophysiological (Neumann et al. 2015; Barow et al. 2014; Schroll et al. 2015; Herrojo Ruiz et al. 2013; Hohlefeld et al. 2015; Merkl et al. 2015) and clinical (Brücke et al. 2014) studies. Here, the localization of electrodes was performed to verify that all contacts were located within the subcortical target structure or to exclude contacts from the analysis if they lay outside the structure. After the publication of the software package as an open source tool, it was downloaded more than five hundred times from within DBS centers on all continents at the time of writing. Similar software that is able to localize DBS electrodes based on postoperative imaging is available from various sources in varying states of development. The following potentially non-exhaustive list shall give an overview on alternatives to *Lead DBS*. Namely, three commercial applications are being or have been developed (*Optivise – now discontinued –* and *SureTune* by Medtronic, Minneapolis, MN, USA; *GUIDE* by Boston Scientific, Marlborough, MA, USA). None of the three software packages are commercially available to the public at the time of writing. However, they are all being evaluated in DBS centers all over the world at present. Apart from that, a software package formerly freely available called *CiceroneDBS* (Miocinovic et al. 2007; *discontinued*) served as the basis of the software *GUIDE*. A software package called *PyDBS* has been developed at the Université de Rennes 1 and is available for partners of the *ACouStiC*-Project at the time of writing (D'Albis et al. 2014). A further piece of software called *Virtual Patient* has been developed at the Martinos Center for Biomedical Imaging at Massachusets General Hospital in Boston, USA (Bonmassar et al. 2014). This software is still in the development stage and the first methodological study focused on ex-vivo high resolution MRI of a single hemisphere. At the time of writing, no download/landing page of the project is available, thus the software is not openly available to the community at present. Finally, a software pipeline called *DBSproc* has lately been integrated into the AFNI MRI analysis software package (http://afni.nimh.nih.gov/afni; Lauro et al. 2015). To the best of our knowledge, this package is the only openly available alternative to Lead-DBS at the time of writing. Like *Lead DBS*, it

consists of functionality that cover CT/MR fusion, MR normalization, electrode localization as well as modeling VATs and VAT-based tractography.

In *Horn et al., 2013*, we showed that the combined analysis of whole-brain structural and functional connectivity metrics is a promising tool to analyze the brain of healthy subjects. As mentioned in the introduction, other researchers have applied similar frameworks to clinical populations (Skudlarski et al. 2010) that yielded an observer-independent assessment of structural and functional changes in connectivity that are linked to a certain disease. Already, researchers have shown that movement disorders may also be characterized by their structural and functional connectivity when compared to healthy controls (Carbon & Eidelberg 2009; Wu et al. 2009; Hacker et al. 2012; Helmich et al. 2010). However, these studies applied 'local' point-to-point connectivity assessments that may only capture effects based on a priori selections of regions of interests. In combination with the other studies that form part of this thesis, the novel analysis framework will help to gain an observer-independent view on structural and functional connectivity differences between patients suffering from movement disorders and healthy controls in future studies. The methodology of this joint structure-function analysis framework was fed into *Lead DBS* in terms of its first extension *Lead Connectome* in 2015.

Results of this novel analysis framework were not only confirmed and refined in *Horn et al. 2016* on the basis of a larger group of subjects. The main goal of this second study was to establish a structural group connectome in standard stereotactic space which forms a second substantial basis to perform connectomic analyses in the context of DBS. This group fiber set enables researchers to perform fiber-tracking (in terms of a post-hoc fiber selection) directly within the stereotactic standard space. In the context of *Lead DBS*, it offers the possibility of an ad hoc estimation of connectivity from the volume of stimulated tissue to other brain regions. The data quality of the group connectome was evaluated by reproducing main results from five studies (Behrens et al. 2003; Horn et al. 2013; Greicius et al. 2009; Bürgel et al. 1999; Nijhuis et al. 2013) and all results were achieved directly within standard space. The combination of these reproductions covers both qualitative and quantitative, both local and global, both structurally and functionally motivated analyses. Thus, one can say that the group connectome portrays a largely precise estimate of the inner structural connectivity of the human brain. In medical studies in which subject-specific dMRI is not available and cannot be acquired, a standardized connectome such as the one presented here might help to gain at least some canonical insight into the inner architecture of the brain if the interpretation of results is done carefully. In the present context, patients that underwent deep-brain-stimulation (DBS) surgery are subject to a very limited signal absorption rate (SAR) level if the implanted electrodes and stimulators are certified for use in the MR scanner at all. On the other hand, especially in DBS, fiber tracking results connecting the precisely located electrode contacts with the rest of the brain have shown interesting new insights that may help to better understand the mechanism of action of DBS and to characterize the profile of clinical effects and side effects in

single patients (Butson et al. 2006; Coenen, Allert, et al. 2011; Coenen et al. 2012; Coenen, Mädler, et al. 2011). Thus, in this context, a standardized group connectome may be of particular importance.

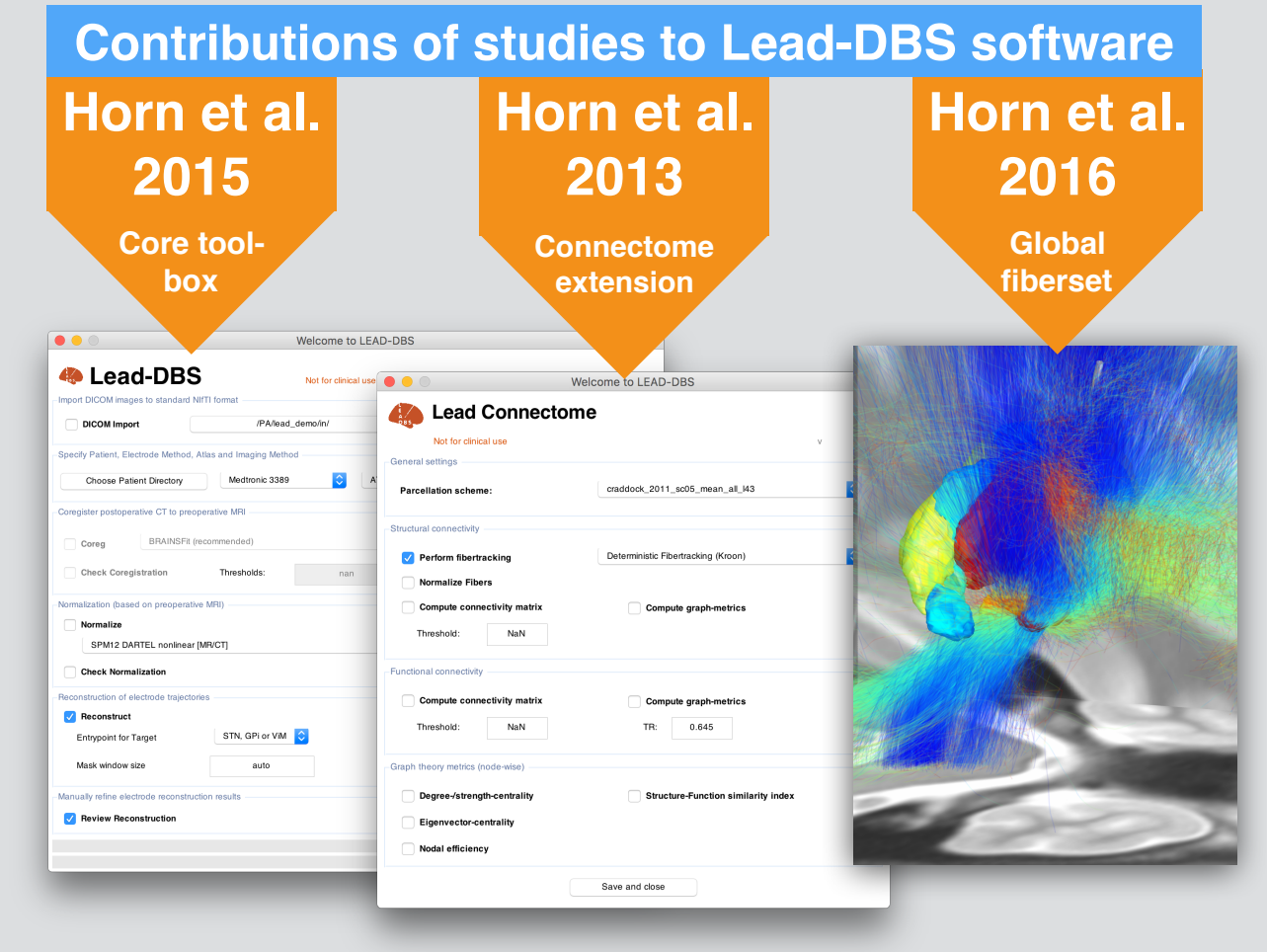

Figure 2: Contributions of the three studies to the software package *Lead DBS*. In *Horn et al. 2015*, the core software was developed. Methodology from *Horn et al. 2013* was later on incorporated into the connectome part of the software. Lastly, the structural group connectome estimated in *Horn et al. 2016* was incorporated into *Lead DBS* to allow for structural connectivity estimates that connect the DBS electrode contacts to other regions of the brain.

In combination, the novel connectomic structure-function analysis framework that was established in *Horn et al. 2013* and refined in *Horn et al. 2016*, as well as the methodology to exactly localize DBS electrodes in *Horn et al. 2015* may serve as the methodological foundation of a 'connectomic deep brain stimulation' framework in the future.

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4. Eidesstattliche Versicherung

„Ich, Andreas Horn, versichere an Eides statt durch meine eigenhändige Unterschrift, dass ich die vorgelegte Dissertation mit dem Thema: ‚Toward Connectomic Deep Brain Stimulation' selbstständig und ohne nicht offengelegte Hilfe Dritter verfasst und keine anderen als die angegebenen Quellen und Hilfsmittel genutzt habe.

Alle Stellen, die wörtlich oder dem Sinne nach auf Publikationen oder Vorträgen anderer Autoren beruhen, sind als solche in korrekter Zitierung (siehe „Uniform Requirements for Manuscripts (URM)" des ICMJE -www.icmje.org) kenntlich gemacht. Die Abschnitte zu Methodik (insbesondere praktische Arbeiten, Laborbestimmungen, statistische Aufarbeitung) und Resultaten (insbesondere Abbildungen, Graphiken und Tabellen) entsprechen den URM (s.o) und werden von mir verantwortet.

Meine Anteile an den ausgewählten Publikationen entsprechen denen, die in der untenstehenden gemeinsamen Erklärung mit dem/der Betreuer/in, angegeben sind. Sämtliche Publikationen, die aus dieser Dissertation hervorgegangen sind und bei denen ich Autor bin, entsprechen den URM (s.o) und werden von mir verantwortet.

Die Bedeutung dieser eidesstattlichen Versicherung und die strafrechtlichen Folgen einer unwahren eidesstattlichen Versicherung (§156,161 des Strafgesetzbuches) sind mir bekannt und bewusst."

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Datum Unterschrift

5. Anteilserklärung an den erfolgten Publikationen

Andreas Horn trug in angegebenem Anteil zu den folgenden Publikationen bei:

Publikation 1: Horn, A., Ostwald, D., Reisert, M., & Blankenburg, F. The structural-functional connectome and the default mode network of the human brain. NeuroImage (2013)
Beitrag im Einzelnen: Durchführung der Experimente, Auswertung der Ergebnisse, Schreiben des Manuskriptes

Publikation 2: Horn, A., & Kühn, A. A. Lead-DBS: A toolbox for deep brain stimulation electrode localizations and visualizations. NeuroImage (2015)
Beitrag im Einzelnen: Entwurf der Studie, Auswertung der Ergebnisse, Schreiben des Manuskriptes

Publikation 3: Horn, A., & Blankenburg, F. Toward a standardized structural–functional group connectome in MNI space. NeuroImage (2016).
Beitrag im Einzelnen: Entwurf der Studie, Auswertung der Ergebnisse, Schreiben des Manuskriptes

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(Prof. Dr. med. A. Kühn)
Berlin, den 14. Dezember 2016

6. Druckexemplare der ausgewählten Publikationen

Im Folgenden sind Druckexemplare der publizierten Originalarbeiten in die Dissertation eingebunden.

Druckexemplar der Originalpublikation 1

Horn, A., Ostwald, D., Reisert, M., & Blankenburg, F. (2013). The structural-functional connectome and the default mode network of the human brain., 102, 142–151.

DOI / Weblink:

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Druckexemplar der Originalpublikation 2

Horn, A., & Kühn, A. A. (2015). Lead-DBS: A toolbox for deep brain stimulation electrode localizations and visualizations, 107, 127–135.

DOI / Weblink:

http://doi.org/10.1016/j.neuroimage.2014.12.002

Druckexemplar der Originalpublikation 3

Horn, A., & Blankenburg, F. (2016). Toward a standardized structural-functional group connectome in MNI space. NeuroImage, 124(Pt A), 310–322.

DOI / Weblink:

http://doi.org/10.1016/j.neuroimage.2015.08.048

7. Lebenslauf

Mein Lebenslauf wird aus datenschutzrechtlichen Gründen in der elektronischen Version meiner Arbeit nicht veröffentlicht.

Mein Lebenslauf wird aus datenschutzrechtlichen Gründen in der elektronischen Version meiner Arbeit nicht veröffentlicht

8. Liste der eigenen Publikationen in chronologischer Reihenfolge

Horn, A. (2012) DTI-Fibre-Tracking funktioneller Netzwerke der Sprach- und Musik Verarbeitung. *Inaugural Dissertation, Universität Freiburg*

Horn, A., Ostwald, D., Reisert, M., & Blankenburg, F. (2013). The structural-functional connectome and the default mode network of the human brain. *NeuroImage (IF: 6.1)*, 102, 142–151. http://doi.org/10.1016/j.neuroimage.2013.09.069

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