Medical Image Analysis 33 (2016) 122–126

Contents lists available at ScienceDirect

Medical Image Analysis

journal homepage: www.elsevier.com/locate/media

Editorial

Computational brain connectivity mapping: A core health and scientific challenge

1. Introduction

In its reports published in Andlin-Sobocki et al. (2005); Wittchen et al. (2011), the European Brain Council (EBC) investigated the socio-economic impact of brain diseases on European society and concluded that about one third of the burden of all diseases in Europe is due to brain diseases. Every year, over a third of the total EU population suffers from mental disorders and the burden of brain diseases (neurological, neurosurgical and psychiatric diseases together) in Europe is estimated to cost € 798 billion per year. Both EBC reports project that this burden will further increase in the coming decades due to the ageing of the European society and conclude that for now and in the near future there is a very strong societal and economical need for improvement in diagnosis and therapy of brain diseases. They also call for increased efforts in basic and clinical research and strongly advocate the need for new models and computational approaches in neuroscience and neuroimaging to better understand the brain architecture and functioning.

2. Mapping the human brain: a core health ambition of modern science

Mapping the brain architecture and functioning is a core health ambition of the 21st century and one of the greatest challenges of modern science. The human brain is one of the most impressive and complex structures in the known universe. With approximately 85 to 100 billion neurons, the human brain is definitely an object of prodigious complexity. However, more important than the number of neurons is the extraordinary complex brain circuitry formed by the 1.000 trillion possible synaptic connections between the neurons. Since the work of pioneers such as Wernicke and Dejerine, and following Geschwind's revolutionary disconnectionist framework, many important neurological diseases and disorders including Alzheimer's, Schizophrenia, Autism, Brain trauma, Epilepsy and others have been shown to be related to pathological alterations in the connectivity of the brain (Johansen-Berg and Behrens, 2009).

This is why ambitious worldwide scientific efforts to understand the hierarchical, complex, architectural and functional network organization of the brain, are combined to conduct huge data generation projects in the USA (Human Connectome Project[1] and Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative[2] and models integration project in Europe (FET Flagship Human Brain Project[3]. Slightly smaller but equally ambitious complementary initiatives have been launched around the globe such as China's Brain Database to identify clues to tackling brain diseases and disorders, Japan's Brain/MINDS (Brain Mapping by Integrated Neurotechnologies for Disease Studies) project, Israel Brain Technologies, Brain Canada, AusBrain (Australia) to name just a few. These large initiatives and brain research projects differ in scope and detail but all have been developed to federate efforts to improve our understanding of the brain.

Due to the vast amount of complex data to acquire, broad range of scales at which they have to be considered, huge variety of problems to tackle and models to integrate, projects as HCP, HBP, BRAIN etc are only a first step and there is clearly a long way to go to achieve the aims of precisely understanding the structure and functioning of the brain. Although exceptional progress has been obtained for exploring the brain during the past decades, the contribution from the exact sciences in this endeavor is still relatively less than what it should be, not to say insufficient and more appropriate models and robust methods for identifying and characterizing structural and functional brain connectivity are still lacking while very much needed. By providing the right mathematical and computational tools as well as the rigorous methodologies, exact sciences may indeed offer substantial added value for exploring the brain, still terra incognita and last continent remaining to discover. In addition, although various new insights from individual imaging modalities have been obtained for brain diseases, it is very clear that an effective research approach is to use various non-invasive imaging modalities and capitalize on the strengths of each of them to solve the limited view of the brain provided separately by any imaging modality.

3. BCM: Brain Connectivity Mapping

During the last decade, huge progress has been made with non-invasive and in vivo medical imaging technologies, such as diffusion and functional magnetic resonance image (dMRI, fMRI)

[1] http://www.humanconnectomeproject.org
[2] http://www.nih.gov/science/brain
[3] https://www.humanbrainproject.eu

http://dx.doi.org/10.1016/j.media.2016.06.003

(Buxton, 2002) as well as electro and magneto-encephalography (EEG & MEG jointly denoted as M/EEG) to reconstruct the hierarchical complex structural and functional network organization of the brain. Multi-modal imaging, integrating functional (fMRI & M/EEG) with structural (dMRI) descriptions has the potential to yield a detailed picture of brain architecture and dynamics and dramatically improve our understanding of brain connectivities. A broad range of studies have shown links between anatomical and functional whole-brain connectivity. However, there has been limited work on a systematic framework to investigate whole-brain interactions between structure and function.

A large amount of work has already been devoted to joint analysis methods for dMRI and fMRI data, Hence, a significant review study of dMRI and fMRI data fusion methodologies and their applications in cognitive and clinical neurosciences can be found in Zhu et al. (2014). The large amount of relevant literature published on dMRI and fMRI has been estimated to include hundreds of papers (at the date of March 2013) with methods categorized into three classes: fMRI assists dMRI, dMRI assists fMRI, and joint dMRI and fMRI fusion. This interest in combining dMRI and fMRI will certainly continue to grow and I envision that effective multi-modalities fusion will play increasingly important roles in neuroimaging and brain sciences in the years to come. See for instance Castellanos et al. (2013) where clinical applications of the functional connectome are considered with a focus on how resting-state fMRI methods can lead to biomarker identification for brain disorders and to Griffa et al. (2013) where interesting highlights and outlooks of structural connectomics for clinical applications in brain diseases are discussed.

However, if a large amount of work has been devoted to joint analysis methods for dMRI and fMRI data, much less work, not to say none, has been devoted for dMRI and M/EEG. Therefore, to advance our current fragmentary and limited understanding of the brain, and solve the limited view of the brain provided just by one imaging modality, I push forward the idea to map the brain connectivity with new generation of models and well appropriate non-invasive neuro-imaging modalities such as diffusion Magnetic Resonance Imaging (dMRI) & Electro and Magneto-Encephalography (EEG & MEG jointly as M/EEG) methods. At Inria, my research group Athena actively contributes in the field of non-invasive and multimodal brain imaging and has acquired a remarkable joint expertise in the modeling and analysis of dMRI & M/EEG data, which is clearly fundamental to non-invasively examine connections through combinations of functional and anatomical imaging techniques.

During the last decade, my research group has pushed far forward the state-of-the-art in both dMRI & M/EEG, developing new computational models and tools, tackling and solving a set of important and challenging problems to unleash the full power and multivariate information content of dMRI & M/EEG data. Combining the measurements obtained by these two types imaging modalities has the potential of providing a detailed view both in space and time of the functioning brain at a macroscopic level. Capitalizing on the strengths of dMRI & M/EEG and building on the bio-physical and mathematical foundations of our models will bring a remarkable and significant added clinical value to identify and characterize brain connectivity and positively impact brain diseases. In that spirit, I summarize in the sequel some challenges, with a particular emphasis on those related to dMRI, and target areas for the upcoming years and the rationale behind them.

4. Advanced dMRI for structural connectivity

To better understand the brain, it is important first to focus on its structural connectivity and to rely on diffusion MRI (dMRI) which is the unique in vivo and non-invasive technique capable of providing the structural connectivity information and investigating the complex microstructure of the cerebral white matter. Introduced in the mid 80s, dMRI is well adapted to detect, characterize and quantify possible white matter abnormalities of brain tissues that cannot be revealed by standard imaging techniques (Jones, 2011; Johansen-Berg and Behrens, 2009).

To take up the challenge to precisely and accurately recover and characterize the structural brain connectivity and map it with ever-increasing detail and richness, it is important to develop generative and ground-breaking models for the advanced acquisition, processing and analysis of dMRI data. Overall, these last twenty years have seen an explosion of intensive scientific research which has vastly improved and literally changed the face of dMRI. These ground breaking changes range from improved and more powerful gradients, scanner-technology to acquisition, post-processing and reconstruction schemes, resulting in shorter acquisitions and more accurate modeling of the brain-tissues microstructure and connectivity. However, although great improvements have been made in the last twenty years (Assaf et al., 2008; Zhang et al., 2012; Descoteaux et al., 2011; Ozarslan et al., 2013), major improvements are still required primarily to optimally acquire dMRI data, better understand the biophysics of the signal formation, recover invariant and intrinsic microstructure features, identify bio-physically important bio-markers and improve tractography. For short, there is still considerable room for improvement to take dMRI from the benchside to the bedside.

Some recents results and debates in the dMRI community perfectly illustrate this importance and the vital need to develop ground-breaking models for recovering a precise and accurate cerebral connectivity. Indeed, recently, (Wedeen et al., 2012) have analyzed relationships of adjacency and crossing between cerebral fiber pathways in four nonhuman primate species and in humans by using dMRI. Their results suggest that the cerebral fiber pathways adhere to a simple and well organized three-dimensional geometric structure consisting of sheets of fibers that intersect at right angles like Manhattan-like grids. However, this point of view is not totally shared within the community, as pointed out by (Catani et al., 2012) who argue that Wedeen's method is likely to miss fibers crossing at angles less than about 70 degrees. They claim also that this view is clearly biased by the limits of their techniques, and conclude that our brain circuitry is wired more like London's chaotic tangle than Manhattan's organized grid. These results and debates clearly illustrate the challenge and complexity of recovering a precise and accurate cerebral connectivity, and the importance and the vital need to develop accurate and precise computational models and tools to help correctly answer such kind of concerns.

Today, it is well understood that more accurate models and better signal descriptions are necessary to overcome the limitations of these state-of-the-art signal reconstruction and tractography methods. Due to the ambiguities of low dMRI spatial resolution, complexities of the underlying tissue and uncertainties of signal noise, newer and more accurate dMRI models have to be found and developed. In my research group, we have recently contributed to design optimal acquisition schemes for single and multiple q-shell in diffusion MRI (Deriche et al., 2009; Caruyer et al., 2013). In particular, it is our optimal sampling scheme (Caruyer et al., 2013) freely available for download[4] (Caruyer et al., 2013), which has been used in the HCP (Human Connectome Project). We have also exploited the ability of Compressed Sensing to recover the whole 3D dMRI signal and some of its important features from a limited number of samples (Merlet and Deriche, 2013). However, and up to now, in all our acquisitions schemes as well in those developed and used

[4] http://www.emmanuelcaruyer.com/q-space-sampling.php