PET Imaging of Brain Connectivity: Hype or future?

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Symposium

In the last decade, brain connectivity has become a dominant concept in neuroscience. Herewith, functional magnetic resonance imaging (fMRI) has made an essential contribution to the delineation of the human brain connectome. While fMRI measures neural activity through changes in cerebral blood flow, positron emission tomography (PET) captures relevant biological processes in a more direct way, through the measurement of e.g., glucose metabolism, neurotransmission, and pathological protein aggregation. Emerging evidence indicates that PET is also able to provide valuable insights into brain connectivity. This symposium provides an overview of methods and applications of PET-based connectivity modelling in health and disease, highlighting its advantages and limitations. Given an increasing pool of publicly available PET data, the presented concepts might be of interest to the broad community of MRI researchers. We conclude that along with fMRI and diffusion imaging, PET represents a valuable tool for exploration of brain connectivity.

Objective

The symposium positions PET in the fast developing field of brain connectivity.
Specific learning objectives are:
- Learn advantages and limitations of PET-based connectivity modelling, relative to more established MRI-based connectivity indices
- Learn common methods and applications of PET-based connectivity modelling
- Understand how publicly available PET datasets can be used to enrich current studies on structural and functional connectivity

Target Audience

The target audience are researchers in the field of brain connectivity and PET researchers with interest in brain connectivity.

Presentations

Relationships between MRI- and PET-based Measures of Brain Connectivity

Functional magnetic resonance (fMRI) and diffusion weighted imaging (DWI) have so far made a major contribution to characterization of the human brain connectome. These methods enable quantification of so-called functional and structural connectivity, respectively. In contrast to fMRI and DWI, PET data are typically available for analyses as one single image per subject. Thus, PET-based connectivity modelling commonly relies on identification of intersubject covariance patterns at a group level. Still, increasing evidence indicates that these patterns are biologically meaningful, resembling brain networks built from fMRI and DWI data. This talk will provide an overview of the relationships between functional and structural indices of brain connectivity and measures of covariance from [18F]fluorodeoxyglucose (FDG) PET data, so-called metabolic connectivity. Recent data suggest that structural connectivity determines metabolic and functional connectivity to a similar degree. Further, metabolic and functional connectivity overlap only partially, while patterns of intersubject covariance in regional grey matter volume overlap poorly with all other connectivity indices. In summary, FDG-PET measures of brain connectivity are related to the more established functional and structural connectivity measures, but explain an additional unique variance.

Presenter

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Modelling Brain Connectivity Using FDG-PET

“Regions of the brain whose rCMRglc [cerebral metabolic rates of glucose] values are significantly correlated are functionally associated, and the strength of the association is proportional to the magnitude of the correlation coefficient.” This statement from a pioneering study by Horwitz et al. (1984) represents the starting point of what we now define “metabolic connectivity”. Metabolic connectivity is based on PET recordings with the glucose analogue [18F]fluorodeoxyglucose (FDG), an established marker of neural activity. The talk will address methods of metabolic connectivity modelling such as seed correlation, sparse inverse covariance estimation, independent component analysis, and graph theory. Applications of metabolic connectivity in the healthy state and neurological disorders will be presented as well. Finally, we will discuss strengths and weaknesses of metabolic connectivity, with special emphasis on its novel applications, e.g., as a biomarker. In summary, metabolic connectivity is a promising index of brain function that fruitfully extends the repertoire of the neuroimaging tools targeting brain connectivity.

Presenter

Silvia Caminiti, Vita-Salute San Raffaele University Milan, Lombardy, Italy

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Modelling Brain Connectivity using Neurotransmitter PET

Neurotransmitter signaling is a major determinant of neural activity. Thus, computing brain connectivity on the basis of neurotransmitter systems may carry important additional value. This talk will cover different approaches to assess “molecular connectivity” as well as recent examples to study normal brain function and pathological alterations. Neurotransmitters such as dopamine and serotonin are released within the entire brain through known neuronal projections. Using this neuroanatomical information, seed based correlation and graph theory analyses proved to be highly efficient in the characterization of neurotransmitter connectivity. Given perturbations of dopamine and serotonin neurotransmission in a variety of neuropsychiatric disorders, this tool might provide valuable information on disease-specific patterns of connectivity. Another exciting application is the combination of specific neurotransmitter systems with fMRI-based functional connectivity. Publicly available PET datasets promote incorporation of the neurotransmitter information into connectivity analyses, especially in research centers without an on-site PET system. This approach has also important implications for brain disorders and pharmacological interventions. Specifically, it enables to model connectivity while taking into account the influence of particular neurotransmitter binding proteins, which are involved in brain disorders or drug action. Altogether, modelling brain connectivity using neurotransmitter PET provides complementary knowledge that cannot be obtained solely by conventional neuroimaging modalities such as fMRI.

Presenter

Andreas Hahn, Medical University of Vienna, Austria

Modelling Brain Connectivity Using Amyloid and Tau PET

Increasing evidence suggests that pathological accumulation of amyloid-β and tau does not occur in brain regions randomly but follows spatial patterns resembling specific brain networks. Thanks to recent advantages in molecular imaging of proteinopathies, it is now possible to identify these patterns in the living human brain. This talk will describe the spatial patterns associated with amyloid and tau deposition across different stages of Alzheimer’s disease (AD) as well as their relationship with other disease markers such as cognitive function and neural injury. Furthermore, an overview of techniques that can be used to identify these patterns, or networks, in single as well as multi-tracer PET studies will be provided. Finally, I will discuss how graph theory and epidemiological models contribute to definition of the spreading trajectories of amyloid-β and tau within these networks, as a function of the genetic profile. In summary, molecular imaging of proteinopathies provides valuable insights into brain connectivity. This information can be useful in understanding and staging of AD and as well as other proteinopathies.

Presenter

Joana Pereira, Karolinska Institute Stockholm, Sweden