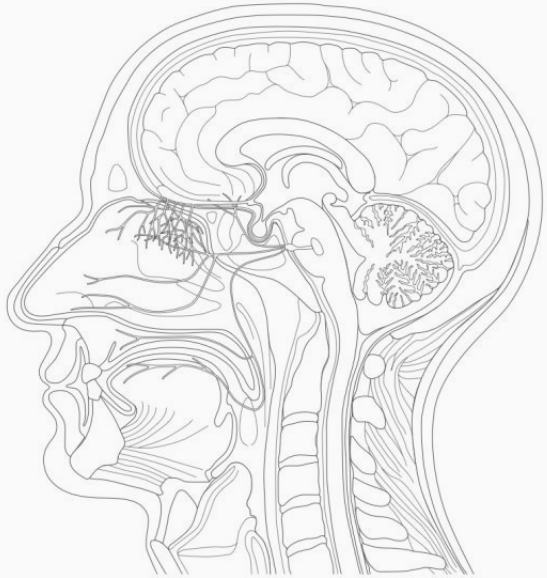
Homework - Academic Year 2024/2025

Investigating TSPO PET imaging lateralization in healthy individuals



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Rationale in brief: TSPO PET imaging

Neuroinflammatory processes are essential cellular and molecular mechanisms aimed to guarantee the homeostasis of the central nervous system (CNS).

Positron emission tomography (PET) imaging of the mitochondrial 18kDa translocator protein (TSPO) represents the most widely adopted technique for imaging neuroinflammation. Alterations in brain TSPO density have been observed in vivo using TSPO PET imaging in various conditions, including schizophrenia, depression, Alzheimer's disease, Parkinson's disease, multiple sclerosis, chronic pain, stroke, peripheral inflammation, and other conditions. Despite its signal complexity and lack of cellular specificity, TSPO PET imaging remains the most reliable and valuable tool for in vivo studying brain inflammation in humans, and hundreds of publications support the use of TSPO PET imaging in experimental medicine studies.

Rationale in brief: TSPO PET imaging

As a standard, regional TSPO PET imaging analysis typically combines tracer activity from left and right hemisphere together (i.e. Whole cerebellum).

Only few studies separately report information for the left and right regions (i.e Left cerebellum vs Right cerebellum)

This approach is based on the assumption that there are negligible aterality differences in the immune organisation of the brain.

The rationale of this homework is to understand whether this approach might have an impact on the TSPO PET results accuracy and interpretation.

Rationale in brief: neuroimmune response and laterality

However, there is evidence for hemispheric asymmetries of immunological brain function[1]. For instance, higher production of interleukines IL-1β and IL-6 in the right than in the left hemisphere have been reported in mice[2]. In humans, resections in the language-dominant hemisphere due to epilepsy reduced lymphocytes, total T cells, and helper T cells in the blood, while resections in the non-dominant hemisphere had the opposite effect[3].

Some References

1. Stoyanov Z, Decheva L, Pashalieva I, et al. Brain asymmetry, immunity, handedness. Central European Journal of Medicine 2012; 2. Shen Y-Q, Hébert G, Moze E, et al. Asymmetrical distribution of brain interleukin-6 depends on lateralization in mice. Neuroimmunomodulation 2005; 3. Meador KJ, Loring DW, Ray PG, et al. Role of cerebral lateralization in control of immune processes in humans. Annals of Neurology: Official Journal of the American Neurological Association and the Child Neurology Society 2004; 55: 840-844.

Outline of the homework

- The aim of the homework is to prepare a technical report that explores the value of right vs left lateralization of TSPO brain PET imaging. This would be important to inform future neuroimaging studies on the validity of combining left and right hemisphere data when running the analysis

- **RESEARCH QUESTIONS:**

  By using the dataset provided, this report should address the following questions:

  1) Is there any laterality in TSPO brain PET imaging?
  - What is the magnitude of this laterality across brain regions? Does TSPO laterality follow the same pattern of structural laterality, as measured by brain regional volume?

  2) What are the main confounding factors affecting TSPO brain PET imaging laterality?
  - Please explore the presence of any association between covariates of no interest (age, sex, weights) and TSPO brain PET laterality

Exam questions (what I expect to see in the report)

- **Background**
  - To introduce the **rationale** of investing brain TSPO brain PET imaging laterality.
  - To introduce the **aims** and **study hypothesis** (if any)

- Specifically, the main points to cover:
  - What are there the evidences for lateralise immune function?
  - What are the evidences for TSPO brain PET left-right asymmetry?

Exam questions (what I expect to see in the report)

- **Material and Methods**

Dataset

- 72 healthy controls acquired with [11C]PBR28 PET imaging as described in Maccioni et al 2025 (REF)
- Please refer to the paper section "Dataset 1. KCL [11C]PBR28 scans"

IMPORTANT NOTE – READ CAREFULLY. Before starting any relevant analysis, please consider the data quality by investigating the presence of outliers and/or missing data. In those cases where data are not compliant reasonable data quality criteria, take action to correct them.

- Some parameters of interests
  - Vt = Volume of distribution, it is used as proxy of TSPO density (ml/cm^3)
  - Vol – Volume, regional volume (mm^3)
  - Genotype (MAB,HAB) indicate the individual TSPO polymorphism

Exam questions (what I expect to see in the report)

- **Material and Methods**

Research methods

- Provide a description of the methodology used to answer the research questions.
- Provide an extensive and motivated description of statistical analysis plan, including the metrics used to assess the biomarker performances
- Suggestion: please use a laterality/Asymmetry index as (right – left) / (right+left). This parameter has been already proposed in other context in literature (see Kaasinen 2016)

Exam questions (what I expect to see in the report)

- **Results**
  - A clear and concise description of the statistical results providing answers to the research questions
  - A sensitivity analysis of the results to covariates, group matching and data quality (e.g. missing data, data miss-balance)

- **Discussion**
  - Direct answers to the research questions and critical comments of the main results
  - An overview of the limitations of the study
  - A list of possible suggestions to improve the study in case someone will repeat it in future

Deliverables

Expected deliverables (i.e. what you have to submit) consist in

- A technical report (pdf file)
- A zip folder with all the code and software used to process the data and ancillary files (make sure it contains all the information for re-using it)

SUBMISSION RULES

- Max Four members per group [choose your team wisely]
- Submission date: Sunday 2nd June at midnight

Marking: PROJECT REPORT MARKING GRID file

Element	Content	Maximum Mark
Abstract (Max 1/2 page)	• Summary of the work presented in the report • Clarity of writing • Shows awareness of the limitations and significance of the work	10
Visual Graphical Abstract (Max 1 page)	• Summary of the work presented in the report	20 (extra)
Background (Max 2 page)	• Clarity of statement of aims and hypothesis to be tested • Range and appropriateness of background material and/or references • Clarity of writing including presentation and organisation of material • Analysis and summary of background material	15
Materials & Methods (Max 3 page)	• Correct description of materials and their sources (e.g. study sample etc.) • Clarity of description of methods and appropriate level of detail such that someone else could repeat the experiments or study • Correct statistical planning	15
Results (Max 3 page)	• Results or data presented in a logical order and containing all the relevant information • Presentation of data including appropriate use of graphs/illustrations such as micro photographs with appropriate figure legends or statistical analysis with correct labelling in each case • Clarity of written description and of experimental work and results • Correct interpretation of findings	30
Discussion (Max 2 page)	• Quality of conclusions drawn from the data • Comparison with the literature where appropriate, and appropriate referencing • Analysis and insight • Discussion of future work	15
Figures/Tables (Max 5 elements)	• Correct presentation • Quality and quantity • Relevance	5
References (Max 1 page)	• Correct presentation • Quality and quantity • Relevance and recency	5
Code	• Clarity of the code and presentation • Reproducibility	5

Read carefully!!!