PETMETPAT:

HARMONISATION METABOLIC FDG BRAIN PATTERN CHARACTERISTICS

Report of a JPND Working Group on Harmonisation and Alignment in Brain Imaging Methods

April 2018

JPND research

EU Joint Programme – Neurodegenerative Disease Research

Report of JPND project PETMETPAT (Leenders and Boellaard) 22 March 2018.

Joint Programme - Neurodegenerative Disease Research *"Working Groups for Harmonisation and Alignment in Brain Imaging Methods for Neurodegeneration".*
Acronym PETMETPAT.

Supplement 1: Grant proposal (April 2016).

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Introduction:

Many neurodegenerative diseases such as PD are characterized by distinct patterns of relative cerebral glucose metabolism on FDG-PET imaging. Using multivariate spatial covariance analysis methods such as scaled subprofile model and principal component analysis (SSM/PCA), neurodegenerative disease-related metabolic brain patterns can be identified. The degree of pattern expression can be quantified to get a disease-related pattern expression score. The advantage of using such a method is that disease-related pattern expression can often be detected early in prodromal groups before functional changes occur. Additionally, they may be useful for discerning differential diagnoses in early or atypical cases.

The widespread implementation of such SSM/PCA-derived disease-related metabolic brain patterns in multicenter collaborations and clinical practice has been hindered by differences between PET scanners, as well as a lack of standardized imaging and reconstruction protocols. Variations in scanners and image reconstructions have been shown to systematically shift image quality and disease-related pattern scores. One way to resolve this is to use z-scoring to healthy controls. However, many smaller centers are practically-speaking unable to collect their own healthy control cohorts. Additionally, z-scoring to healthy controls has the drawback of potentially introducing additional factors of human variation which could influence pattern expression score comparability between centers; a thorough, large-scale investigation into disease-related pattern score offsets in healthy controls with systematically-differing ages, genders, ethnicities, and other factors has not been done yet.

During the last year the following activities have taken place:

February 2017

Start-up working group meeting Madrid.

JPND Programme – PETMETPAT. Friday 17 and Saturday 18 February 2017. Location: Hospital Universitario HM Puerta del Sur, CINAC, Móstoles – Madrid

Supplement 2: Program of the meeting.

Supplement 3: Summary comments of the Madrid meeting.

Spring 2017:

A survey of the methods used in the participating centers was performed in order to identify the various scanner and reconstruction differences. Participating centers: Århus, Amsterdam, Cologne, Groningen, Ljubljana, Madrid, Milan, Namur, Turku, & Wisconsin

Supplement 4: Template of the survey.

Supplement 5: JPND "PETMETPAT" CENTERS: PRACTICAL REALITY.

An anonymous summary of comments or deviations from standard protocol (from the JPND survey passed out after the Madrid workshop)

Further Actions taken in the course of 2017 and 2018:

a) Phantom studies

Originally the working group planned to have a phantom study done using the Hoffman 3D Brain Phantom in all the participating centers. Unfortunately, the phantom was damaged by the contracted shipping company. Even though it was fully insured, there was no refund achieved. A new phantom had to be ordered (around 10.000,00 EUR) and after surmounting the inevitable administrative hurdles, we at last obtained a new Hoffman 3D Brain Phantom a few weeks ago.

Fortunately Ronald Boellaard and an internship student, Bas de Jong, could in the meantime carry out phantom studies using the Free University (VUmc Amsterdam)'s Hoffman 3D Brain Phantom on a range of Siemens, Philips and

GE scanners in a number of centers. This allowed us to gauge the influence of some of the factors which affect the disease related spatial covariance glucose metabolic brain patterns.

Supplement 6: Bas de Jong's thesis based on the phantom data.

Supplement 7: Abstract for the EANM April 2017.

b) "Sensitivity" paper on the basis of the phantom studies

The first draft of this paper has been written and will soon be submitted.

c) "Position" paper

This paper will shortly be written as a draft and be distributed throughout all the involved JPND PETMETPAT participants for comments as co-authors.

That paper will be based on what has been discussed in Madrid, on the results of the survey, and perhaps also on part of the phantom data.

Next steps:

a) Discussion in Stockholm 23/24th of April 2018

b) Propose actual larger studies?

c) Accreditation system needed? Or post-hoc corrections in reference centers?

d) Expanding towards patient data from the various centers.