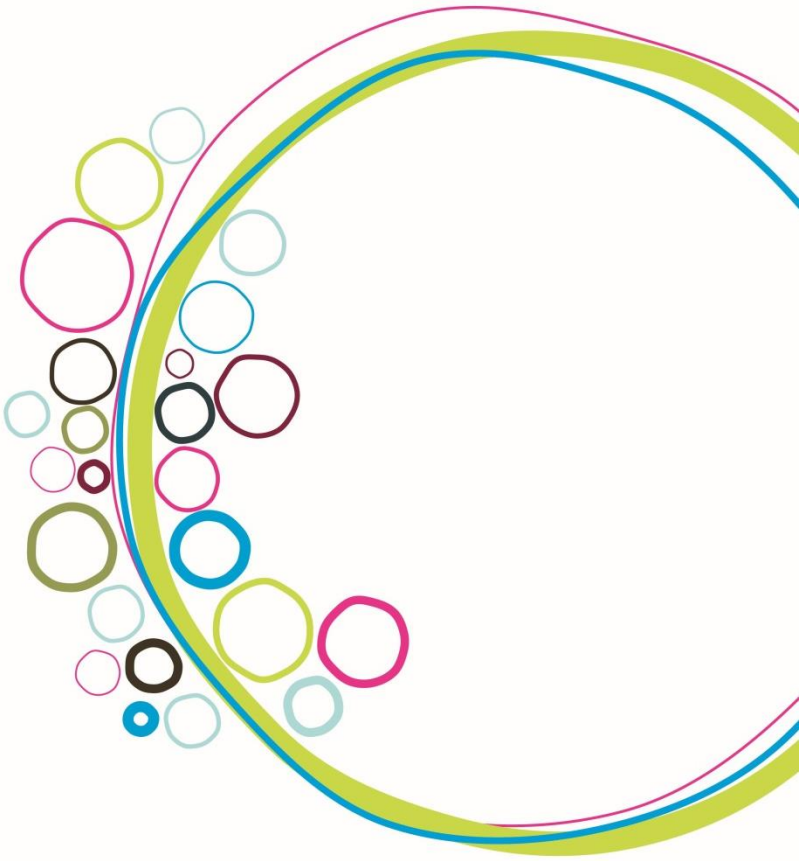

SRA-NED:

HARMONIZATION OF ACQUISITION AND PROCESSING OF BRAIN IMAGING BIOMARKERS FOR NEURODEGENERATIVE DISEASES

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

April 2018

JPND research

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HARMONIZATION OF ACQUISITION AND PROCESSING OF BRAIN IMAGING BIORMARKERS FOR NEURODEGENERATIVE DISEASES: A STRATEGIC RESEARCH AGENDA FOR BEST PRACTICE GUIDELINES (SRA-NED)

JPND 2016 Brain Imaging Working Groups

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Executive Summary

This document is a summary activity report of the European Joint Programme of Neurodegenerative Diseases (JPND) 2016 Brain Imaging Working Group ***"Harmonization of acquisition and processing of brain imaging biormarkers for neurodegenerative diseases: a strategic research agenda for best practice guidelines (SRA-NED)"***.

This initiative was commissioned by the JPND to assess the current state of neuroimaging biomarker harmonization needs of magnetic resonance imaging (MRI), positron emission tomography (PET), single photon emission computerized tomography (SPECT), and electroencephalography (EEG) in the context of large-scale multicenter neurodegenerative studies. To accomplish this goal, we surveyed the expert international community to identify: (1) current barriers for a harmonized use of MRI/PET-SPECT/EEG biomarkers obtained from multicenter studies in neurodegenerative diseases and (2) community driven solutions to overcome these barriers. The full list of the participants who contributed to this project can be found in the project's website: http://www.sra-ned.org/

The survey was completed by 459 participants of the MRI/PET-SPECT/EEG community between February 1 and March 31, 2017 (MRI 53.6% of participants, EEG 30.3%, and PET-SPECT 16.1%). The participants were representative of a strong multidisciplinary community, dominated by research and academia whereas industry and participants from clinical settings were also included. Participants represented also an international community (Europe 75%, North and South America 20%, and Asia, Oceania and Africa 5%). More details about the Survey will be published separately.

The main findings and recommendations resulting from this study are outlined as follows:

- The community that responded to the survey identified the following main barriers, which were also common across the neuroimaging modalities evaluated: (1) lack of updated information and resources to effectively participate in multicenter neurodegenerative studies (77 % MRI, 61% EEG, and 75% PET-SPECT groups); (2) lack of guidelines for the harmonization of data acquisition using state-of-the-art equipment and protocols, biomarker extraction, and statistical modeling; (3) a general tendency of cost underestimation, in particular for software resources as well as for human resources with the relevant expertise, such as for the implementation of multicentric acquisition protocols and

for data analyses; (4) lack of harmonized recommendations resulting from multiple multicentric harmonization efforts.

- To address these general barriers, we recommend that the JPND agenda includes the following action: establish a EU neuroimaging harmonization Working Group, considering MRI/PET-SPECT/EEG neuroimaging modalities, with advisors beyond EU, with commitments that include:

  (1) Develop and maintain an open-access web-based forum that can serve as updated centralized repository of information relevant to multicenter studies in neurodegenerative diseases, generated by this group as well as from other initiatives. This resource should also enable a platform where people can exchange information and discuss new literature findings and recommendations.

  (2) Develop and maintain updated consensus guidelines on the harmonization of neuroimaging MRI/PET-SPECT/EEG acquisition and analyses strategies in multicenter studies in neurodegenerative diseases. Where applicable, these guidelines should relate acquisition strategies with different target derived markers in the context of studying different neurodegenerative diseases using different experimental designs (cross-sectional versus longitudinal studies, observational versus treatment effect studies, etc.).

  (3) Develop and maintain standardized registry for planning and budgeting multicenter neuroimaging projects. This registry should include the comprehensive list of recommendations of aspects that are agreed to be typically essential parts of any successful multicenter study. Such guidelines could be helpful to both researchers preparing grant applications and funding agencies when reviewing project proposals.

  (4) Develop and maintain an updated registry of neuroimaging harmonization efforts that outlines key differences and common aspects of past/ongoing projects. Promote constructive synergies that help cross-reference recommendations and information from relevant multicentric neuroimaging biomarker harmonization projects.

  (5) Promote periodic teaching activities through seminars/workshops/courses on topics relevant to the harmonized use of neuroimaging biomarkers in neurodegenerative diseases. This activity could be synchronized with periodic national and international conference meetings to offer relevant satellite events.

- With specific regards to MRI modality, the JPND agenda may fund the harmonization of multivendor state-of-the-art acquisition protocols for high-spatial resolution anatomical MRI (including quantitative tissue mapping), microstructure and connectivity characterizations from diffusion MRI, as well as high-temporal resolution functional and perfusion MRI neuroimaging. There is a particular need for characterizing test-retest reproducibility errors given the interest in longitudinal studies. In addition, there is a need to develop automated quantitative quality assurance methods specific for the various methodologies in the context of multicenter studies. There is also a need to develop methods that are able to harmonize existing data already acquired without standardized protocols.

- With specific regards to PET-SPECT modalities, the JPND agenda may fund the harmonization of image reconstruction parameters across PET and SPECT vendors as a first necessary step. The action may consider also creating public databases of normal and neurodegenerative disease patients as well as creating centralized analysis platforms.

- With specific regards to the EEG modality, the JPND agenda may fund the harmonization of the recordings and spectral or time-domain analyses of resting state eyes-closed and –open EEG and event-related potentials (especially oddball paradigms), as well as the definition of the best biomarkers for each technique.

The actions here proposed are consistent with current EU legislation developments aimed at allowing secondary use of health data. Such legislation would also lend itself to the secondary use of multicenter neuroimaging data once these data is acquired within a common methodological framework. This therefore suggests that funding for the hereby proposed actions would come timely given the political agenda of health research legislation in the EU.

In conclusion, this JPND initiative produced the largest survey on the barriers and tentative solutions for the harmonized use of neuroimaging MRI/PET-SPECT/EEG techniques for multi-centric clinical studies in neurodegenerative diseases. The Working Group of this initiative transposed those solutions in a tentative agenda for JPND to overcome those barriers. This agenda is also consistent with current EU legislation developments relevant to the use of health data.

Research Outputs

At the time of the final report submission, two research outputs have been generated from this work:

- Jovicich J, Barkhof F, Babiloni C, Herholz K, Mulert C, van Brckel BNM and Frisoni GB; Harmonization of Neuroimaging Biormarkers for Neurodegenerative Diseases: A Survey for Best Practice Guidelines, Alzheimer's Association International Conference, July 16-20, London 2017 (Developing Topic Abstract, P4-526).
- Jovicich J and Frisoni GB, European ADNI, World Wide ADNI Meeting, July 14, London, 2017.

To further increase the visibility of this work, we organized a meeting that brought together the JPND Brain Harmonization working groups and relevant journal editors attending the AAIC London 2017 meeting. Seven from the ten JPND groups could attend, as well as editors from the Journal of Alzheimer's and Dementia and Lancet Neurology. Discussions are ongoing for the preparation of a special issue that presents the whole body of work with summaries from the 10 working groups plus a higher-level paper that integrates and emphasizes the importance of the various harmonization aspects tackled by the different groups.

Acknowledgements

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