

PET Neuroimaging Data Harmonization

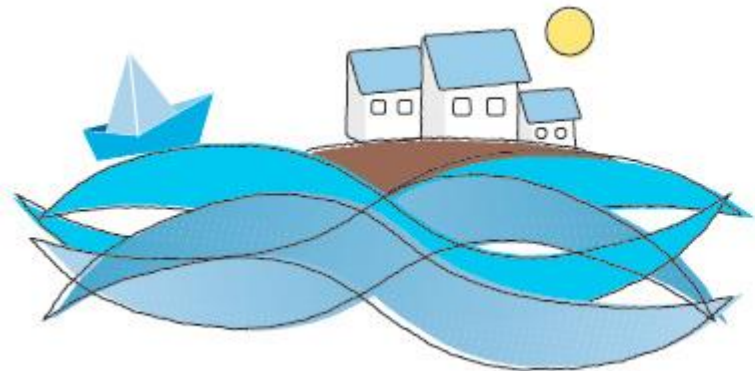
Gitte Moos Knudsen, Professor.
Neurobiology Research Unit, Rigshospitalet and University
of Copenhagen, Denmark



Rigshospitalet

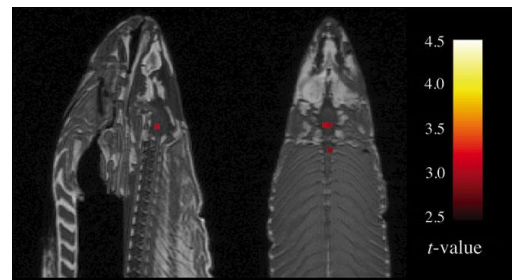
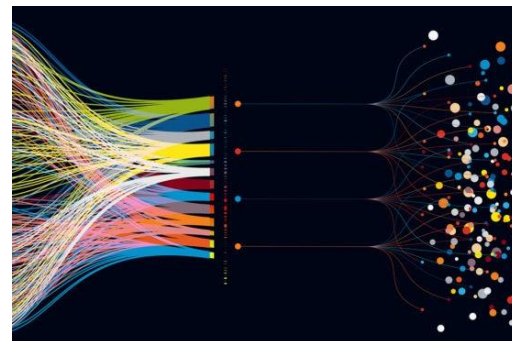


Mediterranean
Thematic Workshops
in Advanced Molecular Imaging



The reproducibility crisis in neuroscience

- Data
 - Insufficient power
 - Noise
- Analysis
 - Highly flexible processing workflows with multiple decision trees
 - Unreported assumptions
 - Insufficient statistics
- Biased reporting



PUBLISHED JUNE 3, 2020 IN RESEARCH, MEDICINE

STUDIES OF BRAIN ACTIVITY AREN'T AS USEFUL AS SCIENTISTS THOUGHT

Duke researcher questions 15 years of his own work with a reexamination of functional MRI data

The German National Research Data Infrastructure in Neuroscience (NFDI-Neuro)

74%

Data re-used from public repositories might help me to answer my research question

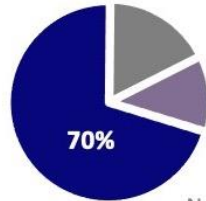
N=131



70%

Sharing my research data could help others to answer their own research questions

N=131



I would share (more of) my data if I had better data management

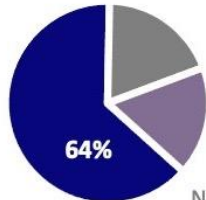
N=115



Fully or rather agree

Undecided

Fully or rather disagree

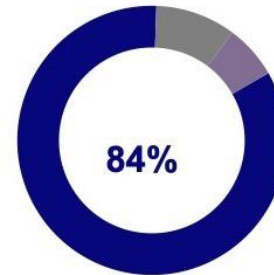


I would have more collaborative projects if I had better data management

N=121



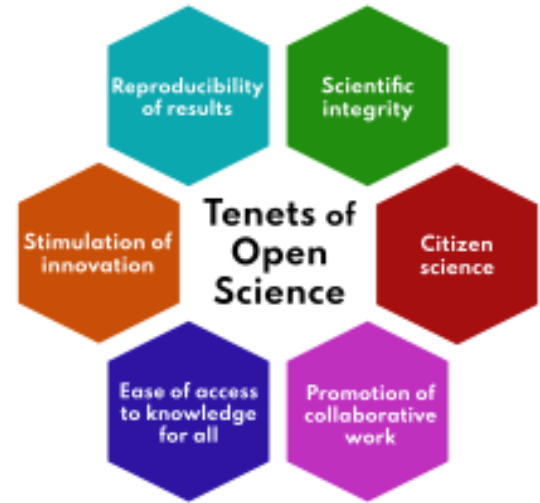
Applying research data management increases the quality of my research output



N=124

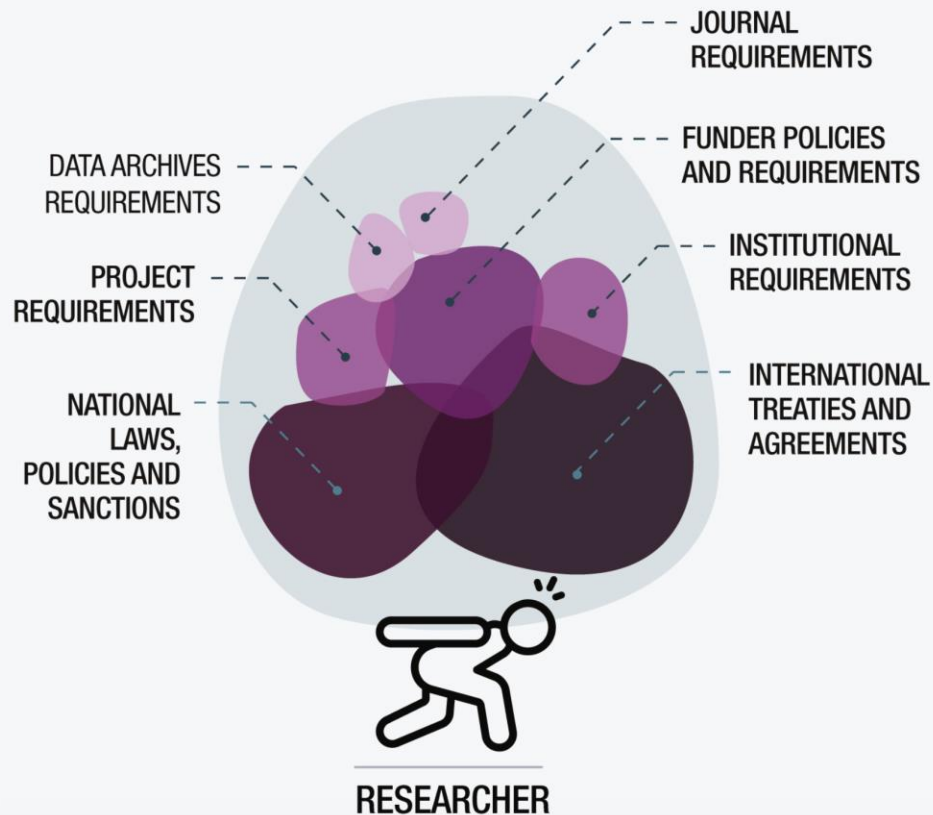
Barriers for Open Science

- (1) are due to lack of data and metadata standards,
- (2) of community adopted provenance tracking methods,
- (3) of research data management literacy,
- (4) of required time and resources for proper research data management, and
- (5) of a privacy preserving research infrastructure for sensitive data.

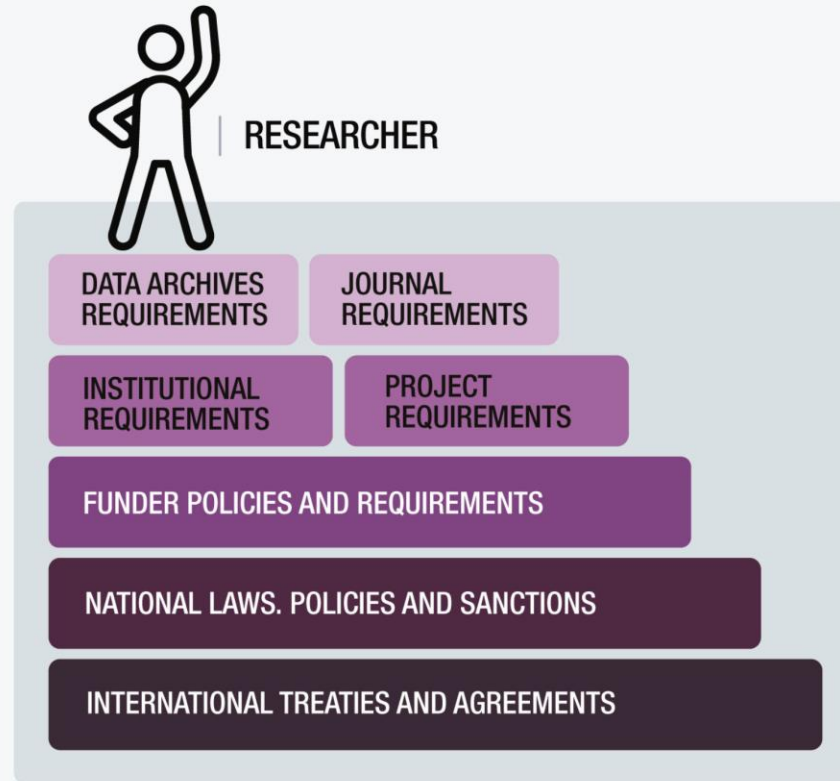


! **PLUS:**
Better citation rates for open access
articles and research data

BURDENS OF REGULATORY OVERSIGHT



INTERNATIONAL DATA GOVERNANCE



Example of brain PET data sharing

Neuroticism Associates with Cerebral in Vivo Serotonin Transporter Binding Differently in Males and Females

Lauri Tuominen, MD, PhD; Jouko Miettunen, PhD; Dara M. Cannon, PhD; Wayne C Drevets, MD; Vibe G. Frokjaer, MD, PhD; Jussi Hirvonen, MD, PhD; Masanori Ichise, MD, PhD; Peter S. Jensen, MSc; Liisa Keltikangas-Järvinen, PhD; Jacqueline M. Klaver, PhD; Gitte M. Knudsen, MD, PhD; Akihiro Takano, MD, PhD; Tetsuya Suhara, MD, PhD; Jarmo Hietala, MD, PhD

Data from four different PET centers to address whether neuroticism is related to serotonin transporter binding in vivo. The data includes thalamic and striatal serotonin transporter BP_{ND} values and personality scores from 91 healthy males and 56 healthy females.

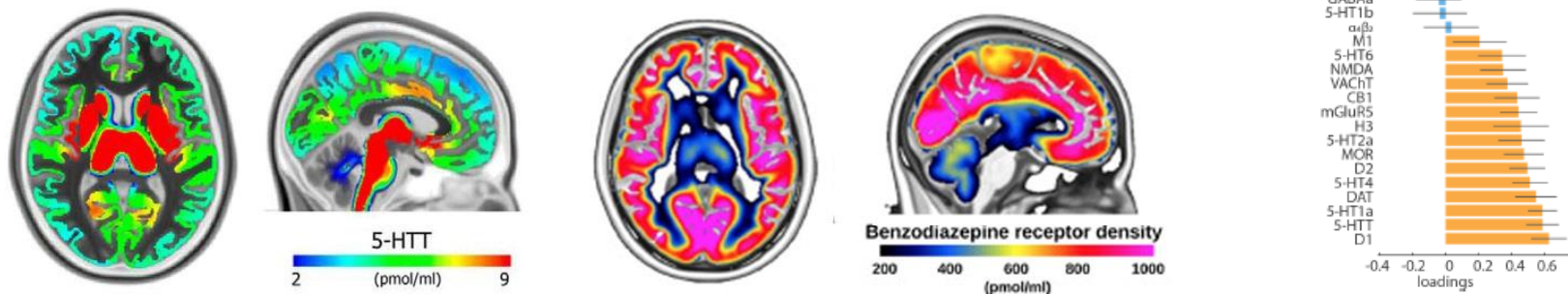
Center	N (M/F)	Age	Neuroticism ^a	Questionnaire	Tracer	Serotonin transporter BP_{ND}	
						Thalamus	Striatum
NIRS ¹	31 (31/0)	23.6 ± 2.8	2.1 ± 0.46	NEO-PI-R	[¹¹ C]DASB	1.8 ± 0.29	1.3 ± 0.16
NRU ²	57 (37/20)	35.1 ± 18.0	1.5 ± 0.40	NEO-PI-R	[¹¹ C]DASB	1.8 ± 0.25	1.6 ± 0.18 ^b
NIMH ³	28 (8/20)	36.3 ± 9.1	1.9 ± 0.14	NEO-PI-R	[¹¹ C]DASB	1.7 ± 0.23	1.3 ± 0.17 ^b
TPC ⁴	31 (15/16)	39.1 ± 5.1	1.2 ± 0.76	NEO-FFI	[¹¹ C]MADAM	1.4 ± 0.15	1.1 ± 0.16 ^c

Molecular (and functional) brain atlases

MNI (volume) and FreeSurfer Average (Surface)

Tracer based vs. Target based atlases (multi-sites, multi-tracers harmonization)

How do the different anatomical and functional (fMRI connectivity) atlases match receptor maps?



Beliveau et al, J Neurosci 2017; Norgaard et al, NeuroImage 2021; Hansen et al, Nature Neurosci 2022 (in press).

Standard nomenclature

Journal of Cerebral Blood Flow & Metabolism (2007) 27, 1533–1539

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www.jcbfm.com



Review Article

Consensus nomenclature for *in vivo* imaging of reversibly binding radioligands

Robert B Innis¹, Vincent J Cunningham², Jacques Delforge³, Masahiro Fujita¹, Albert Gjedde⁴, Roger N Gunn⁵, James Holden⁶, Sylvain Houle⁷, Sung-Cheng Huang⁸, Masanori Ichise⁹, Hidehiro Iida¹⁰, Hiroshi Ito¹¹, Yuichi Kimura¹², Robert A Koeppe¹³, Gitte M Knudsen¹⁴, Juhani Knuuti¹⁵, Adriaan A Lammertsma¹⁶, Marc Laruelle², Jean Logan¹⁷, Ralph Paul Maguire¹⁸, Mark A Mintun¹⁹, Evan D Morris²⁰, Ramin Parsey⁹, Julie C Price²¹, Mark Slifstein⁹, Vesna Sossi²², Tetsuya Suhara¹¹, John R Votaw²³, Dean F Wong²⁴ and Richard E Carson²⁵

¹National Institute of Mental Health, Bethesda, Maryland, USA; ²GlaxoSmithKline and Imperial College, London, UK; ³CEA/DSV/SHF, Orsay, France; ⁴University of Aarhus, Aarhus, Denmark; ⁵GlaxoSmithKline and University of Oxford, London, UK; ⁶University of Wisconsin, Madison, Wisconsin, USA; ⁷Centre for Addiction and Mental Health & University of Toronto, Toronto, Ontario, Canada; ⁸UCLA School of Medicine, Los Angeles, California, USA; ⁹Columbia University, New York, New York, USA; ¹⁰National Cardiovascular Center Research Institute, Suita City, Osaka, Japan; ¹¹National Institute of Radiological Sciences, Chiba, Japan; ¹²Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan; ¹³University of Michigan, Ann Arbor, Michigan, USA; ¹⁴Copenhagen University Hospital Rigshospitalet, Copenhagen, Denmark; ¹⁵Turku PET Centre, Turku, Finland; ¹⁶VU University Medical Centre, Amsterdam, The Netherlands; ¹⁷Brookhaven National Laboratory, Upton, New York, USA; ¹⁸Pfizer Global R&D, Groton, Connecticut, USA; ¹⁹Washington University School of Medicine, St Louis, Missouri, USA; ²⁰Indiana University-Purdue University, Indianapolis, Indiana, USA; ²¹University of Pittsburgh, Pittsburgh, Pennsylvania, USA; ²²University of British Columbia, Vancouver, British Columbia, Canada; ²³Emory University, Atlanta, Georgia, USA; ²⁴Johns Hopkins University School of Medicine, Baltimore, Maryland, USA; ²⁵Yale University, New Haven, Connecticut, USA

Consensus on publishing PET experiments

- Replication in science can be improved with standards for reporting and sharing of primary research data

Opinion

Guidelines for the content and format of PET brain data in publications and archives: A consensus paper

Gitte M Knudsen¹, Melanie Ganz¹, Stefan Appelhoff², Ronald Boellaard³, Guy Bormans⁴, Richard E Carson⁵, Ciprian Catana⁶, Doris Doudet⁷, Antony D Gee⁸ , Douglas N Greve⁶, Roger N Gunn⁹, Christer Halldin¹⁰, Peter Herscovitch¹¹, Henry Huang⁵, Sune H Keller¹², Adriaan A Lammertsma³, Rupert Lanzenberger¹³, Jehi-San Liow¹⁴, Talakad G Lohith¹⁵, Mark Lubberink¹⁶, Chul H Lyoo¹⁷, J John Mann¹⁸, Granville J Matheson¹⁰, Thomas E Nichols¹⁹ , Martin Nørgaard¹ , Todd Ogden²⁰, Ramin Parsey²¹, Victor W Pike¹⁴, Julie Price⁶, Gaia Rizzo⁹, Pedro Rosa-Neto^{22,23}, Martin Schain²⁰, Peter JH Scott²⁴, Graham Searle⁹, Mark Slifstein²¹, Tetsuya Suhara²⁵, Peter S Talbot²⁶, Adam Thomas²⁷, Mattia Veronese²⁸, Dean F Wong²⁹, Maqsood Yaqub³, Francesca Zanderigo³⁰, Sami Zoghbi¹⁴ and Robert B Innis¹⁴

JCBFM

Journal of Cerebral Blood Flow & Metabolism
2020, Vol. 40(8) 1576–1585
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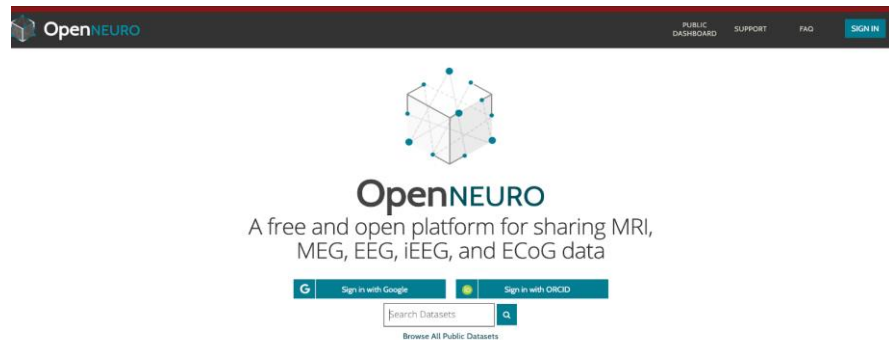


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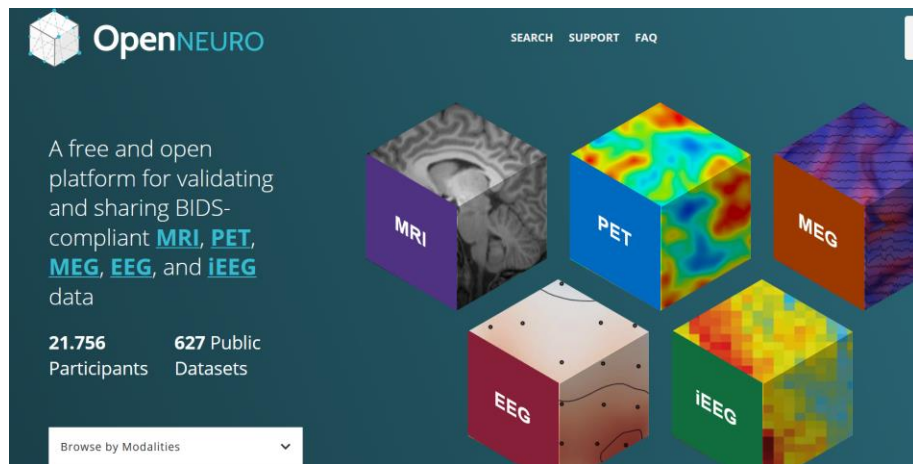
From OpenNeuro ...

- Official repository for BRAIN Initiative
- Part of the Amazon Public Datasets project
- 627 public datasets
- 21.756 subjects / ~16 TB
- 10-20 new dataset uploads per month
- Serving 1000 + downloads/month (almost 20TB of data)
- Over 8K users/month



...to OpenNeuroPET

- Establish PET archive as an extension of OpenNeuro
 - Standard format and content
 - “Best Practices” for pipelines and QC checks
- Educate and seek feedback from the PET user community
- Establish average images of receptor density, connecting to the larger fMRI community



OpenNEURO SEARCH SUPPORT FAQ

A free and open platform for validating and sharing BIDS-compliant [MRI](#), [PET](#), [MEG](#), [EEG](#), and [iEEG](#) data

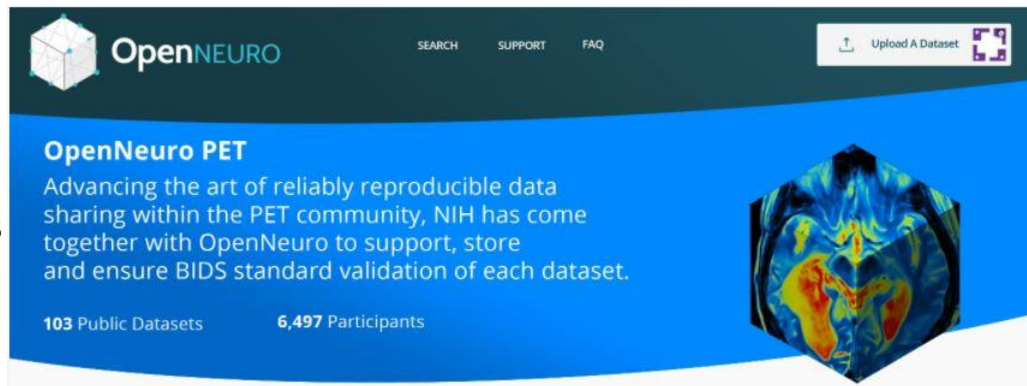
21,756 Participants 627 Public Datasets

Browse by Modalities

MRI PET MEG EEG iEEG

OpenNeuroPET

- Principles
 - Standard format to meaningfully share and combine data
 - Follow Guidelines, include “best practices” for data pipelines, and sample data sets for QC
- Benchmarks of success
 - Number of scans deposited
 - Number of resulting publications
- Community engagement
 - Provide help to sites
 - Integrate with commonly used software
 - Stimulate projects



OpenNeuroPET setup



OpenNeuroPET

PI: Robert Innis

Funding: NIMH via BRAIN Initiative (Brain Research through Advancing Innovative Neurotechnologies)

Duration: Oct 2021 – Sept 2026

Collaborator: NRU, Rigshospitalet; MGH

Consultant: Russell Poldrack (Stanford)



PI: Gitte Moos Knudsen

Funding: Novo Nordisk Foundation (Research Infrastructure program)

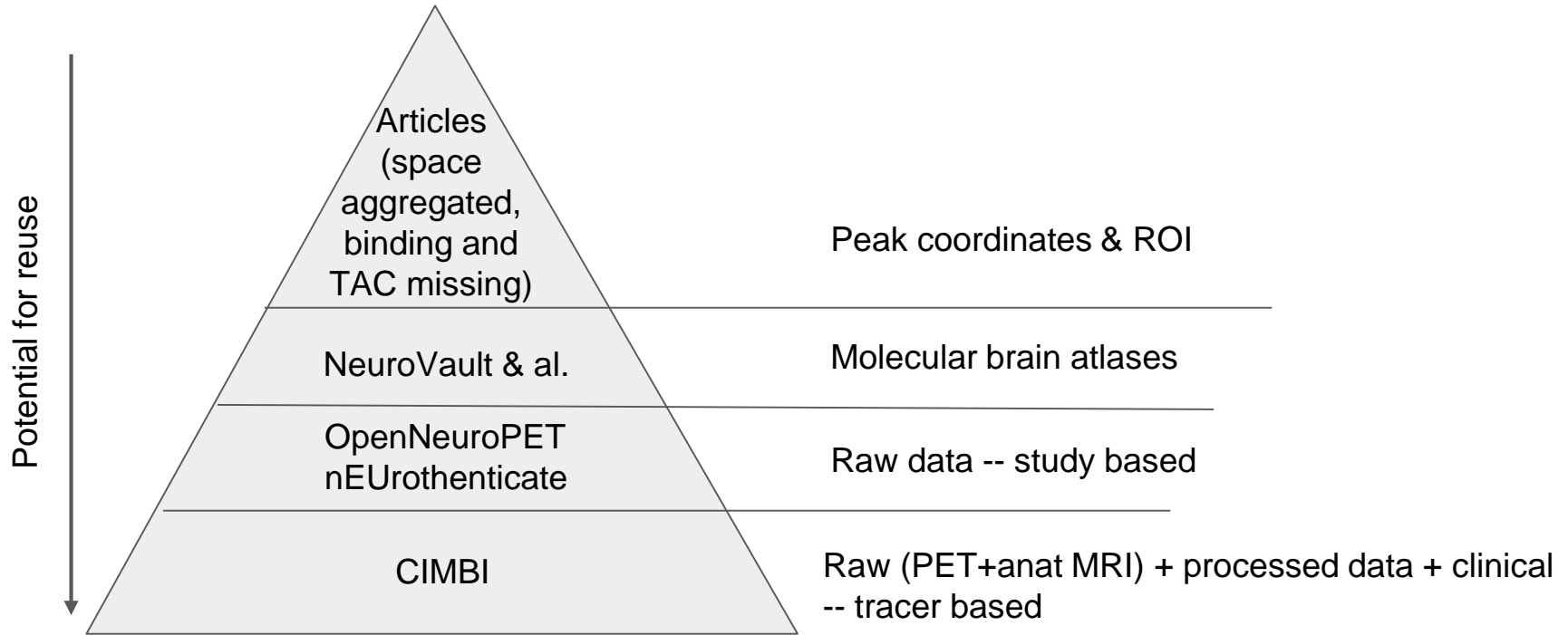
Duration: Jan 2021 – Dec 2025

Collaborator: NIMH; MGH

Consultant: Russell Poldrack (Stanford)



Data scales in neuroimaging (OpenNeuro PET version)



Raw Data harmonization

Opinion

Guidelines for the content and format of PET brain data in publications and archives: A consensus paper

Gitte M Knudsen¹, Melanie Ganz¹, Stefan Appelhoff², Ronald Boellaard³, Guy Bormans⁴, Richard E Carson⁵, Ciprian Catana⁶, Doris Doudet⁷, Antony D Gee⁸ , Douglas N Greve⁶, Roger N Gunn⁹, Christer Halldin¹⁰, Peter Herscovitch¹¹, Henry Huang⁵, Sune H Keller¹², Adriaan A Lammertsma³, Rupert Lanzenberger¹³, Jieh-San Liow¹⁴, Talakad G Lohith¹⁵, Mark Lubberink¹⁶, Chul H Lyoo¹⁷, J John Mann¹⁸, Granville J Matheson¹⁰, Thomas E Nichols¹⁹ , Martin Nørgaard¹ , Todd Ogden²⁰, Ramin Parsey²¹, Victor W Pike¹⁴, Julie Price⁶, Gaia Rizzo⁹, Pedro Rosa-Neto^{22,23}, Martin Schain²⁰, Peter JH Scott²⁴, Graham Searle⁹, Mark Slifstein²¹, Tetsuya Suhara²⁵, Peter S Talbot²⁶, Adam Thomas²⁷, Mattia Veronese²⁸, Dean F Wong²⁹, Maqsood Yaqub³, Francesca Zanderigo³⁰, Sami Zoghbi¹⁴ and Robert B Innis¹⁴

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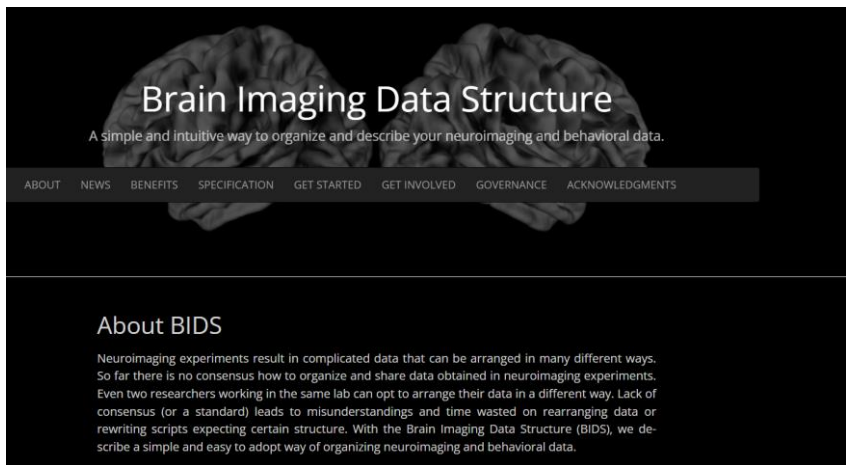
DOI: 10.1177/0271678X20905433

journals.sagepub.com/home/jcbfm



Raw Data harmonization

Use a common, community-based data structure (the way to store data on hard-drives) and naming



<https://bids.neuroimaging.io/>

Comment | [Open Access](#) | [Published: 02 March 2022](#)

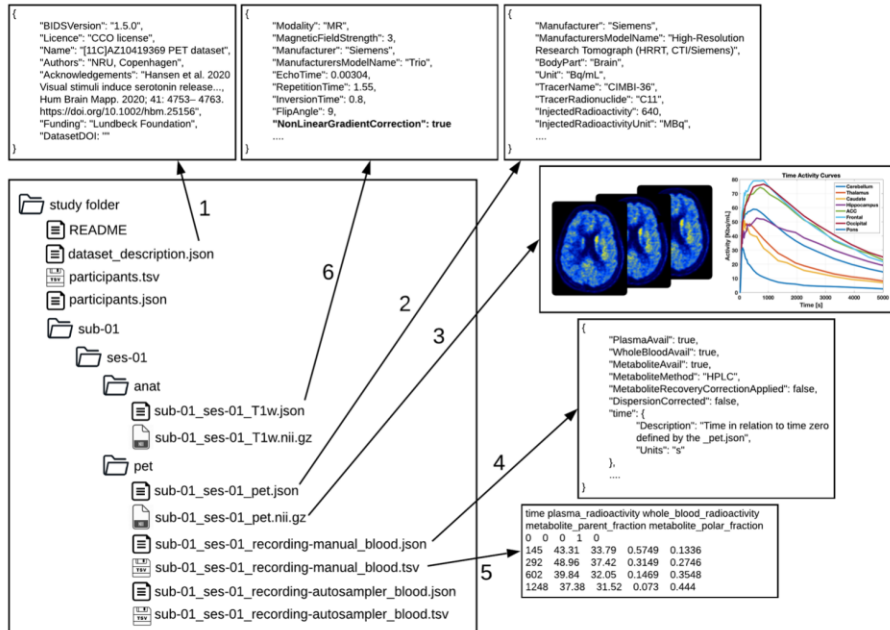
PET-BIDS, an extension to the brain imaging data structure for positron emission tomography

[Martin Norgaard](#), [Granville J. Matheson](#), [Hanne D. Hansen](#), [Adam Thomas](#), [Graham Searle](#), [Gaia Rizzo](#), [Mattia Veronese](#), [Alessio Giacomel](#), [Maqsood Yaqub](#), [Matteo Tonietto](#), [Thomas Funck](#), [Ashley Gillman](#), [Hugo Boniface](#), [Alexandre Routier](#), [Jelle R. Dalenberg](#), [Tobey Betthausen](#), [Franklin Feingold](#), [Christopher J. Markiewicz](#), [Krzysztof J. Gorgolewski](#), [Ross W. Blair](#), [Stefan Appelhoff](#), [Remi Gau](#), [Taylor Salo](#), [Guiomar Niso](#), [Cyril Pernet](#), [Christophe Phillips](#), [Robert Oostenveld](#), [Jean-Dominique Gallezot](#), [Richard E. Carson](#), [Gitte M. Knudsen](#), [Robert B. Innis](#) & [Melanie Ganz](#) 

Scientific Data **9**, Article number: 65 (2022)

Raw Data harmonization

OpenNeuro PET: new library PET2BIDS to curate PET and blood data to BIDS standard (<https://github.com/openneuroPET/PET2BIDS>)






There is a lot of extra information which is not in the image data (ecat or dcm) – all tracer related, the library helps creating all metadata and validates them

Data Processing harmonization

Original Article

JCBFM

Reproducibility of findings in modern PET neuroimaging: insight from the NRM2018 grand challenge

Mattia Veronese^{1,*} , Gaia Rizzo^{2,*}, Martin Belzunce³ , Julia Schubert¹, Graham Searle², Alex Whittington², Ayla Mansur^{2,4} , Joel Dunn^{3,5}, Andrew Reader³ and Roger N Gunn^{2,4}; and the Grand Challenge Participants[#]

Journal of Cerebral Blood Flow & Metabolism
2021, Vol. 41(10) 2778–2796
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Abstract

The reproducibility of findings is a compelling methodological problem that the neuroimaging community is facing these days. The lack of standardized pipelines for image processing, quantification and statistics plays a major role in the variability and interpretation of results, even when the same data are analysed. This problem is well-known in MRI studies, where the indisputable value of the method has been complicated by a number of studies that produce discrepant results. However, any research domain with complex data and flexible analytical procedures can experience a similar lack of reproducibility. In this paper we investigate this issue for brain PET imaging. During the 2018 NeuroReceptor Mapping conference, the brain PET community was challenged with a computational contest involving a simulated neurotransmitter release experiment. Fourteen international teams analysed the same imaging dataset, for which the ground-truth was known. Despite a plurality of methods, the solutions were consistent across participants, although not identical. These results should create awareness that the increased sharing of PET data alone will only be one component of enhancing confidence in neuroimaging results and that it will be important to complement this with full details of the analysis pipelines and procedures that have been used to quantify data.

Data Processing harmonization



HHS Public Access

Author manuscript

Neuroimage. Author manuscript; available in PMC 2020 October 01.

Published in final edited form as:

Neuroimage. 2019 October 01; 199: 466–479. doi:10.1016/j.neuroimage.2019.05.055.

Optimization of Preprocessing Strategies in Positron Emission Tomography (PET) Neuroimaging: A [¹¹C]DASB PET Study

Martin Nørgaard^{1,2}, Melanie Ganz^{1,3}, Claus Svarer¹, Vibe G. Frokjaer¹, Douglas N. Greve⁵, Stephen C. Strother⁴, Gitte M. Knudsen^{1,2,*}

To evaluate the impact of various preprocessing strategies, we systematically examined 384 different pipeline strategies in data from 30 healthy participants scanned twice with the serotonin transporter (5-HTT) radioligand [¹¹C]DASB. Five commonly used preprocessing steps with two to four options were investigated: (1) motion correction (MC) (2) co-registration (3) delineation of volumes of interest (VOI's) (4) partial volume correction (PVC), and (5) kinetic modeling. To quantitatively compare and evaluate the impact of various preprocessing strategies, we used the performance metrics: test-retest bias, within- and between-subject variability, the intraclass-correlation coefficient, and global signal-to-noise ratio. We also performed a power analysis to estimate the required sample size to detect either a 5% or 10% difference in 5-HTT binding as a function of preprocessing pipeline.

The results showed a complex downstream dependency between the various preprocessing steps on the performance metrics. The choice of MC had the most profound effect on 5-HTT binding, prior to the effects caused by PVC and kinetic modeling, and the effects differed across VOI's.

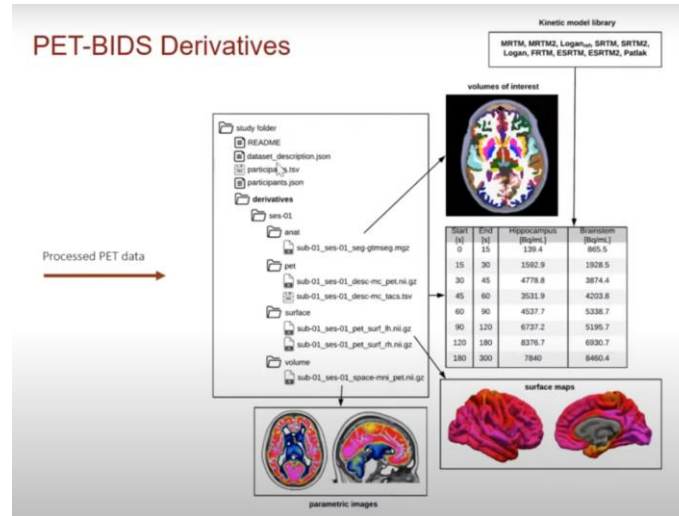
Notably, we observed a negative bias in 5-HTT binding across test and retest in 98% of pipelines, ranging from 0–6% depending on the pipeline. Optimization of the performance metrics revealed a trade-off in within- and between-subject variability at the group-level with opposite effects (i.e. minimization of within-subject variability increased between-subject variability and vice versa).

The sample size required to detect a given effect size was also compromised by the preprocessing strategy, resulting in up to 80% increases in sample size needed to detect a 5% difference in 5-HTT binding.

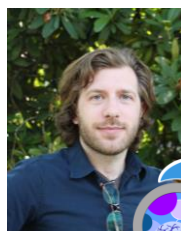
Data Processing harmonization

OpenNeuro PET: development of volume and surface based data analysis pipelines (with/without containerization) to have fully reproducible workflows (https://github.com/openneuropet/PET_pipelines)

BIDS PET preprocessing derivatives: what should be shared, which form, etc .. ([open specification to contribute](#))



Thank you!



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