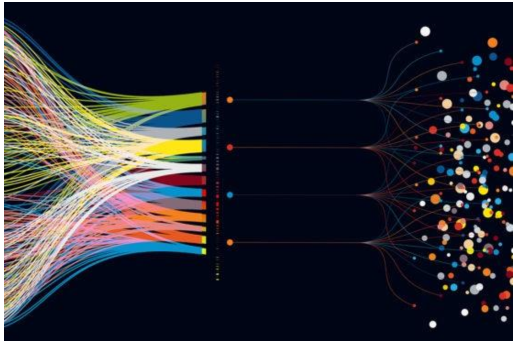
PET Neuroimaging Data Harmonization

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

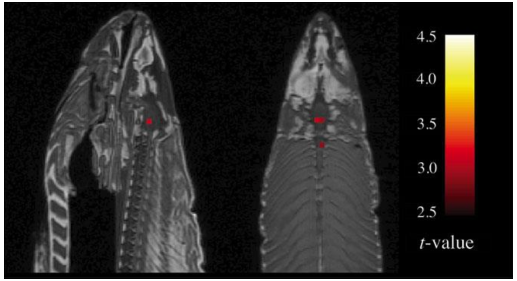
Rigshospitalet

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

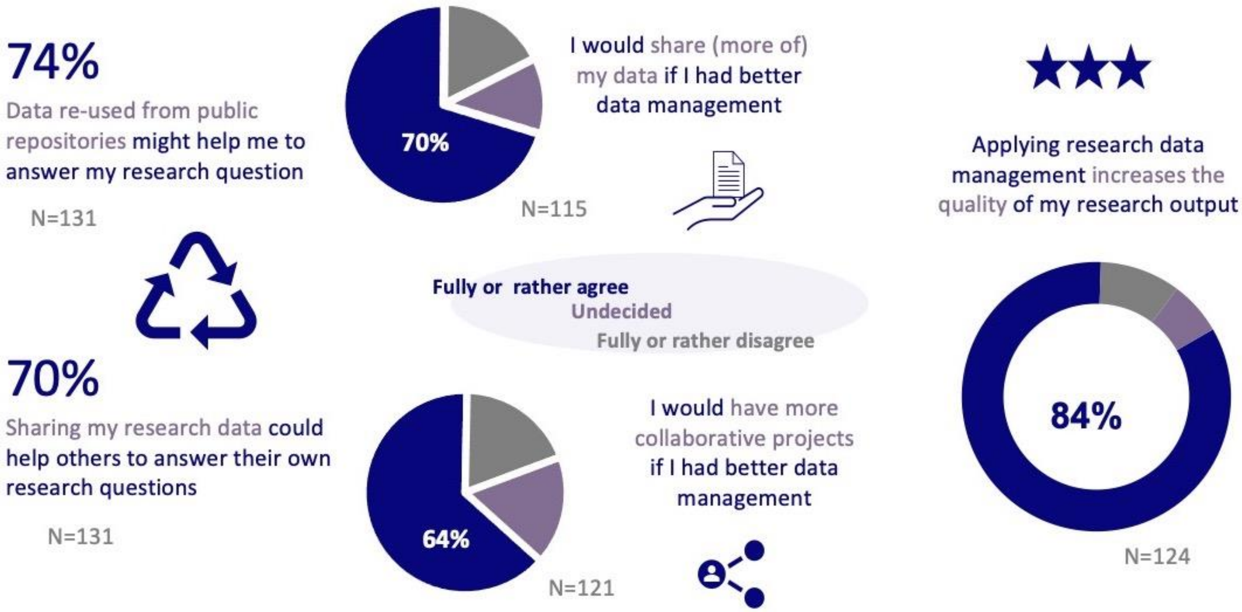


PUBLISHED JUNE 3, 2020 IN RESEARCH, MEDICINE

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

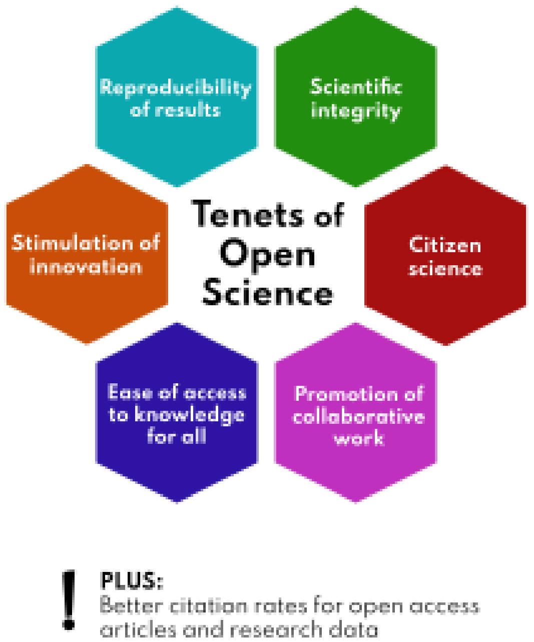
The German National Research Data Infrastructure in Neuroscience (NFDI-Neuro)

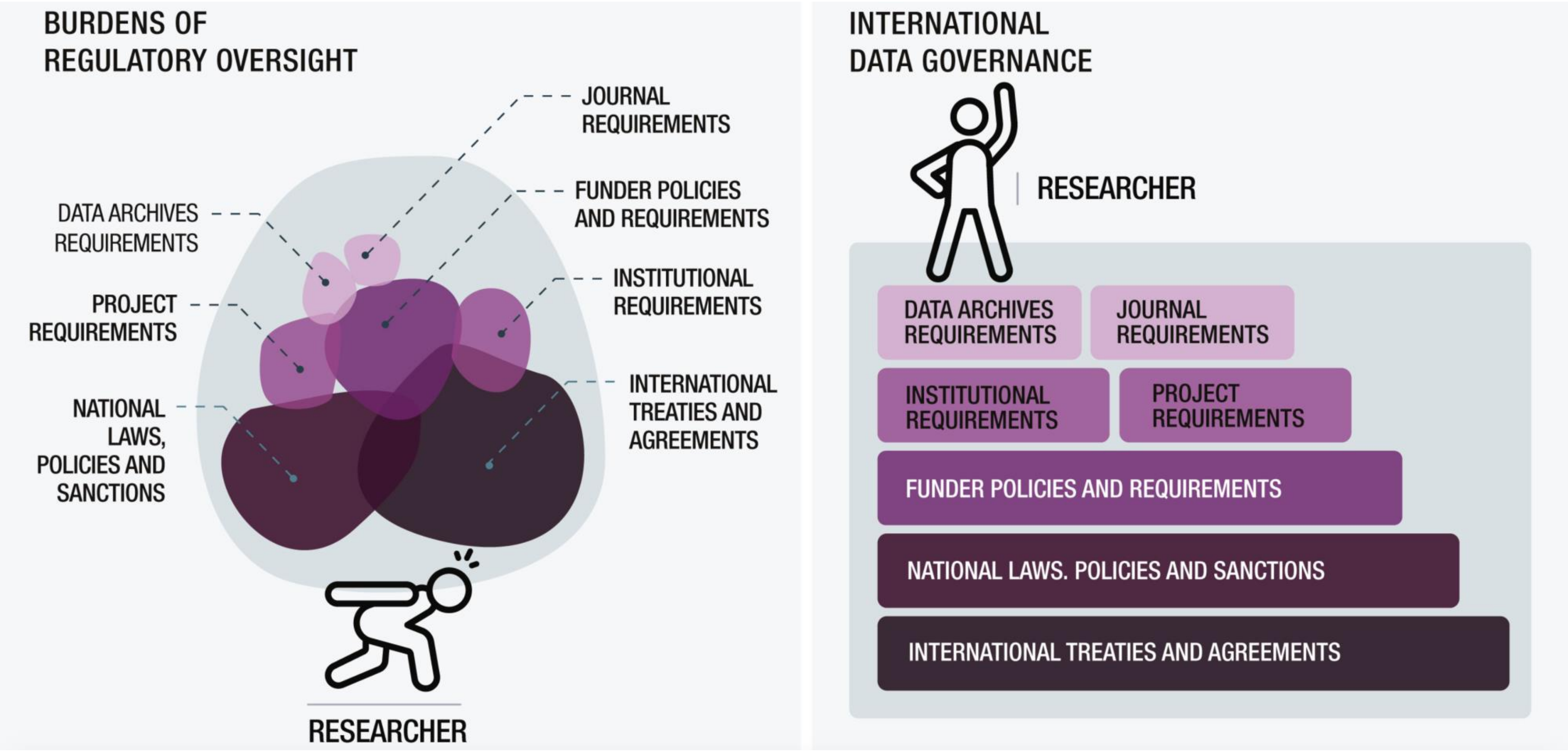


Klingner et al, bioRxiv 2022

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.





Credit: International Brain Initiative

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.

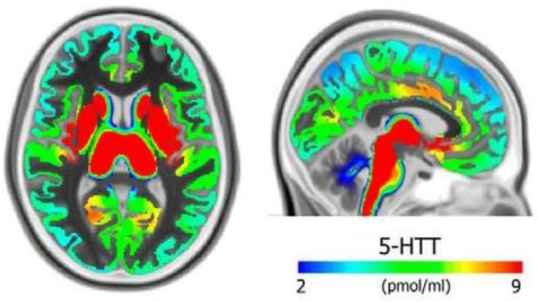
						Serotonin transporter BP_{ND}	
Center	N (M/F)	Age	Neuroticism[a]	Questionnaire	Tracer	Thalamus	Striatum
NIRS[1]	31 (31/0)	23.6 ± 2.8	2.1 ± 0.46	NEO-PI-R	[^{11}C]DASB	1.8 ± 0.29	1.3 ± 0.16
NRU[2]	57 (37/20)	35.1 ± 18.0	1.5 ± 0.40	NEO-PI-R	[^{11}C]DASB	1.8 ± 0.25	1.6 ± 0.18[b]
NIMH[3]	28 (8/20)	36.3 ± 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[b]

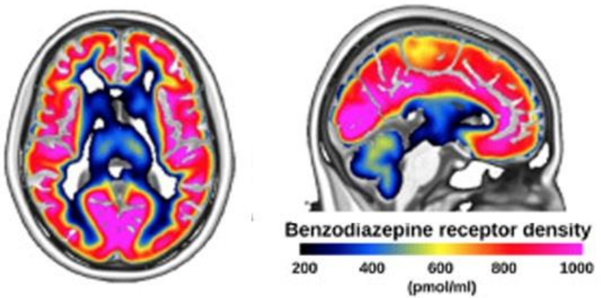
Molecular (and functional) brain atlases

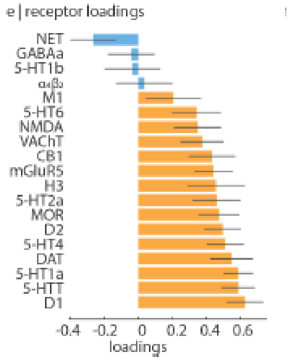
MNI (volume) and FreeSurfer Average (Surface)

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

www.jcbfm.com

Review Article

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

Robert B Innis[1], Vincent J Cunningham[2], Jacques Delforge[3], Masahiro Fujita[1], Albert Gjedde[4], Roger N Gunn[5], James Holden[6], Sylvain Houle[7], Sung-Cheng Huang[8], Masanori Ichise[9], Hidehiro Iida[10], Hiroshi Ito[11], Yuichi Kimura[12], Robert A Koeppe[13], Gitte M Knudsen[14], Juhani Knuuti[15], Adriaan A Lammertsma[16], Marc Laruelle[2], Jean Logan[17], Ralph Paul Maguire[18], Mark A Mintun[19], Evan D Morris[20], Ramin Parsey[9], Julie C Price[21], Mark Slifstein[9], Vesna Sossi[22], Tetsuya Suhara[11], John R Votaw[23], Dean F Wong[24] and Richard E Carson[25]

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

JCBFM

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

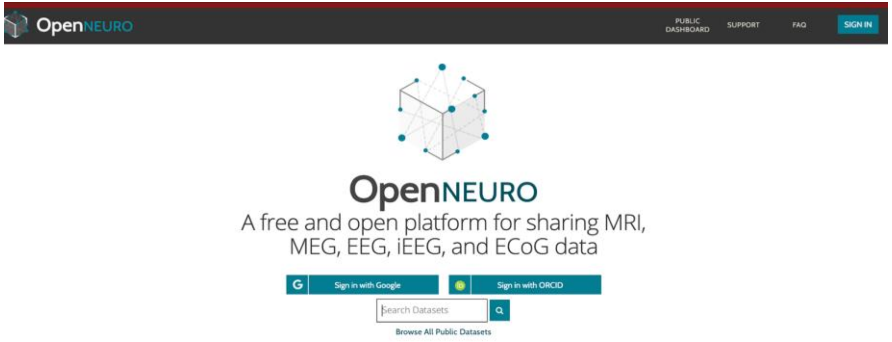
DOI: 10.1177/0271678X20905433
journals.sagepub.com/home/jcbfm
SAGE

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

Gitte M Knudsen[1], Melanie Ganz[1], Stefan Appelhoff[2], Ronald Boellaard[3], Guy Bormans[4], Richard E Carson[5], Ciprian Catana[6], Doris Doudet[7], Antony D Gee[8], Douglas N Greve[6], Roger N Gunn[9], Christer Halldin[10], Peter Herscovitch[11], Henry Huang[5], Sune H Keller[12], Adriaan A Lammertsma[3], Rupert Lanzenberger[13], Jeih-San Liow[14], Talakad G Lohith[15], Mark Lubberink[16], Chul H Lyoo[17], J John Mann[18], Granville J Matheson[10], Thomas E Nichols[19], Martin Nørgaard[1], Todd Ogden[20], Ramin Parsey[21], Victor W Pike[14], Julie Price[6], Gaia Rizzo[9], Pedro Rosa-Neto[22,23], Martin Schain[20], Peter JH Scott[24], Graham Searle[9], Mark Slifstein[21], Tetsuya Suhara[25], Peter S Talbot[26], Adam Thomas[27], Mattia Veronese[28], Dean F Wong[29], Maqsood Yaqub[3], Francesca Zanderigo[30], Sami Zoghbi[14] and Robert B Innis[14]

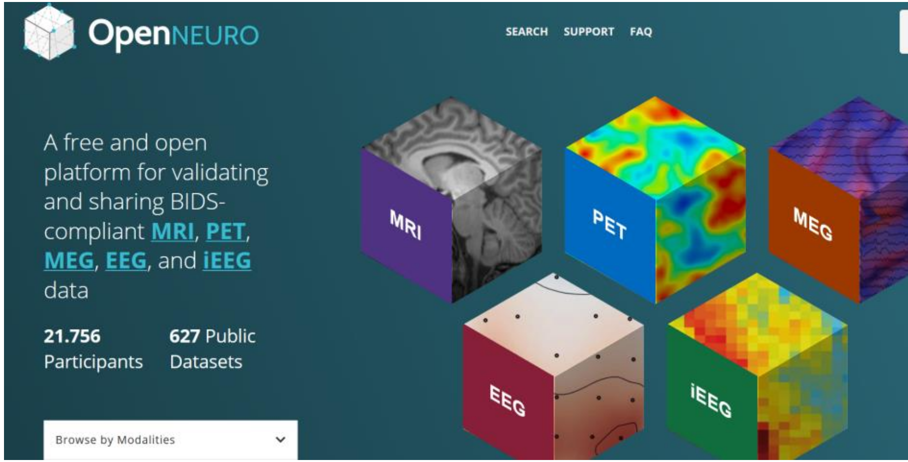
From OpenNeuro ...

- 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

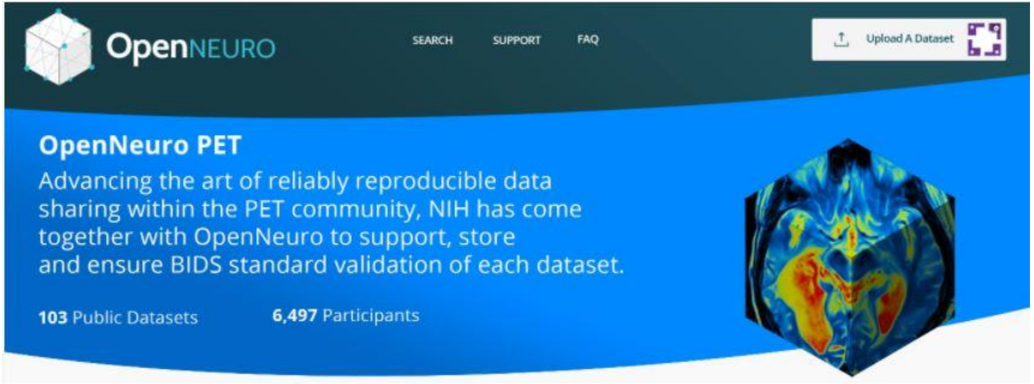


- Educate and seek feedback from the PET user community

- Establish average images of receptor density, connecting to the larger fMRI community

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

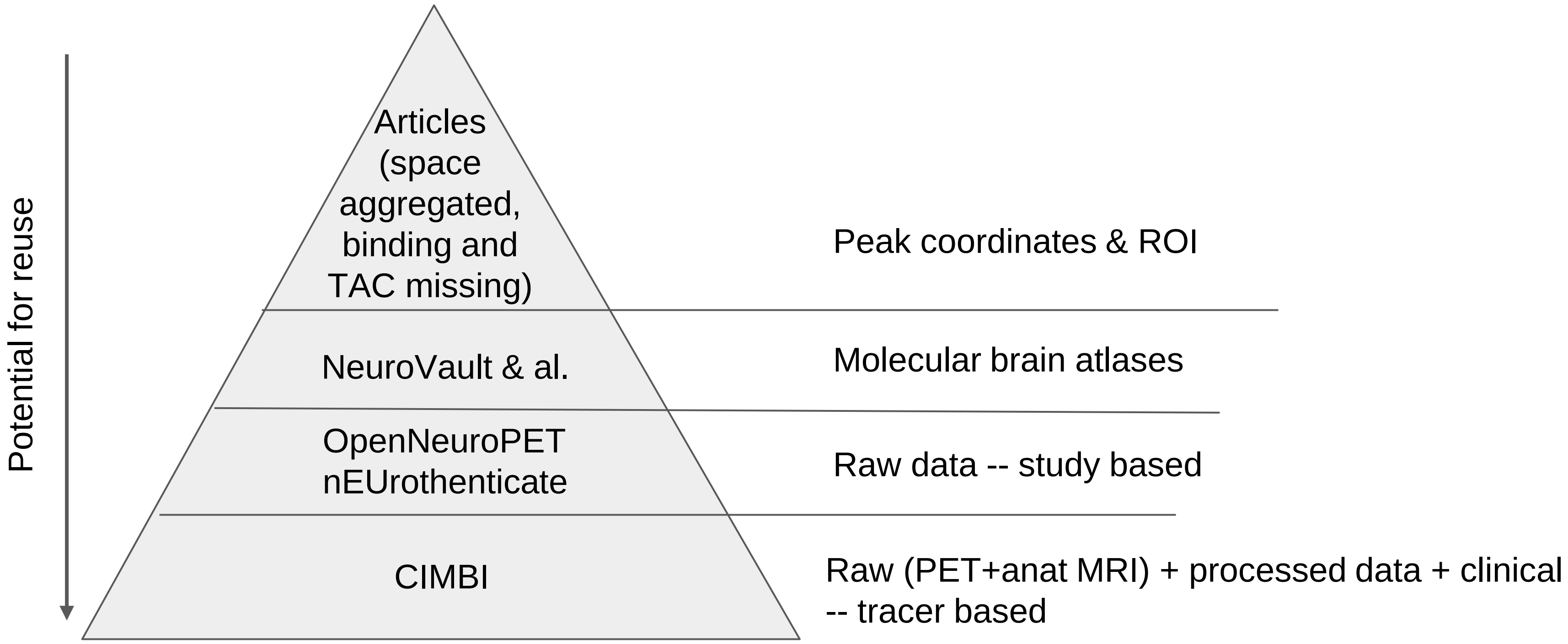
Funding: Novo Nordisk Foundation (Research Infrastructure program)

Duration: Jan 2021 – Dec 2025

Collaborator: NIMH; MGH

Consultant: Russell Poldrack (Stanford)

Data scales in neuroimaging (OpenNeuro PET version)



Adapted from Poldrack & Gorgolewski (2014) https://www.nature.com/articles/nn.3818

Raw Data harmonization

Opinion

JCBFM

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

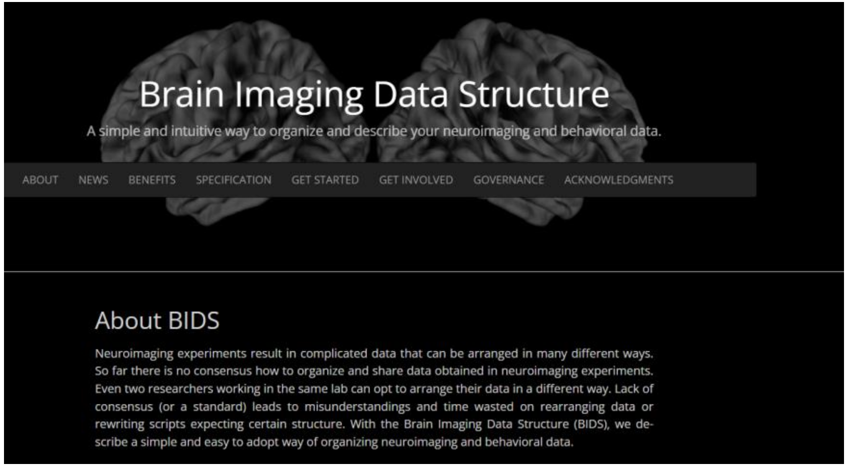
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/0271678X20905433
journals.sagepub.com/home/jcbfm
SAGE

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

Gitte M Knudsen[1], Melanie Ganz[1], Stefan Appelhoff[2], Ronald Boellaard[3], Guy Bormans[4], Richard E Carson[5], Ciprian Catana[6], Doris Doudet[7], Antony D Gee[8], Douglas N Greve[6], Roger N Gunn[9], Christer Halldin[10], Peter Herscovitch[11], Henry Huang[5], Sune H Keller[12], Adriaan A Lammertsma[3], Rupert Lanzenberger[13], Jeih-San Liow[14], Talakad G Lohith[15], Mark Lubberink[16], Chul H Lyoo[17], J John Mann[18], Granville J Matheson[10], Thomas E Nichols[19], Martin Nørgaard[1], Todd Ogden[20], Ramin Parsey[21], Victor W Pike[14], Julie Price[6], Gaia Rizzo[9], Pedro Rosa-Neto[22,23], Martin Schain[20], Peter JH Scott[24], Graham Searle[9], Mark Slifstein[21], Tetsuya Suhara[25], Peter S Talbot[26], Adam Thomas[27], Mattia Veronese[28], Dean F Wong[29], Maqsood Yaqub[3], Francesca Zanderigo[30], Sami Zoghbi[14] and Robert B Innis[14]

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

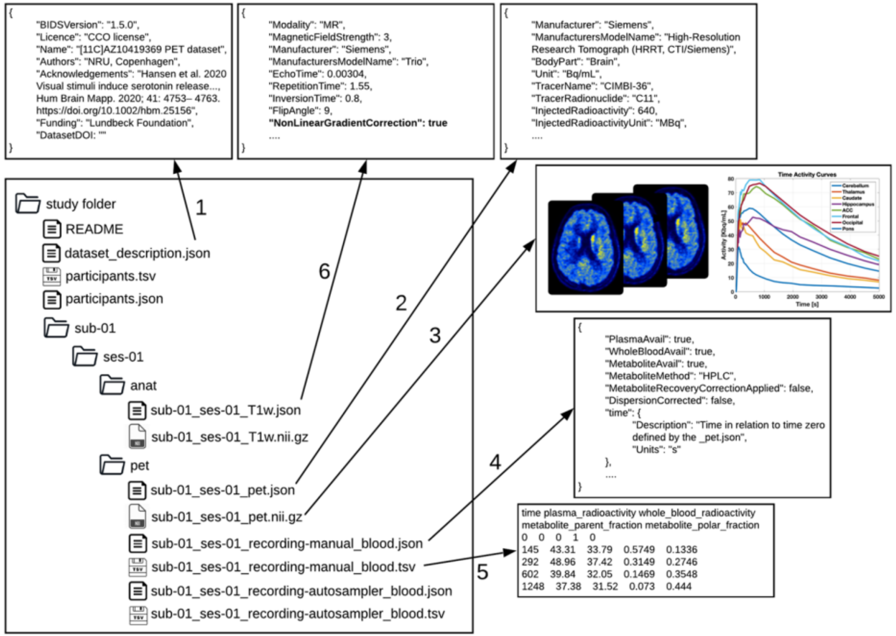
PET-BIDS, an extension to the brain imaging data structure for positron emission tomography

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 Betthauser, 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

Image courtesy of Melanie Ganz 10/08/2022

Data Processing harmonization

Original Article

JCBFM

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

Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/0271678X211015101
journals.sagepub.com/home/jcbfm
SAGE

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

Mattia Veronese[1,]*, Gaia Rizzo[2,]*, Martin Belzunce[3], Julia Schubert[1], Graham Searle[2], Alex Whittington[2], Ayla Mansur[2,4], Joel Dunn[3,5], Andrew Reader[3] and Roger N Gunn[2,4]; and the Grand Challenge Participants[#]

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 [^{11}C]DASB PET Study

Martin Nørgaard[1,2], Melanie Ganz[1,3], Claus Svarer[1], Vibe G. Frokjaer[1], Douglas N. Greve[5], Stephen C. Strother[4], 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 [^{11}C]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)

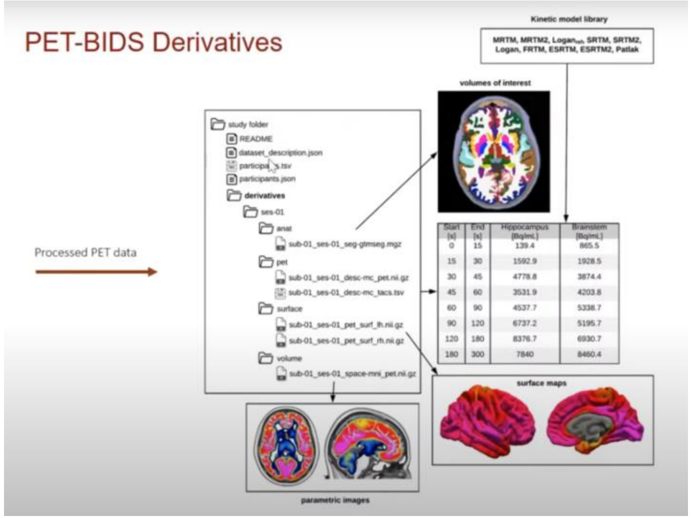
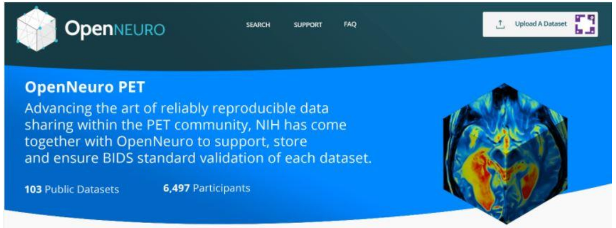
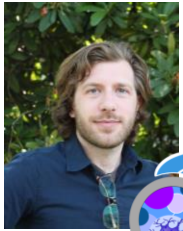


Image courtesy of Martin Nørgaard 15/12/2021

Thank you!








novo nordisk fonden


NIH National Institute of Mental Health





Athinoula A. Martinos Center For Biomedical Imaging

Stanford University

HST Harvard–MIT Health Sciences & Technology

MGH MASSACHUSETTS GENERAL HOSPITAL

REGION H Rigshospitalet