

## Open and reproducible neuroimaging: from study inception to publication

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# **Open and reproducible neuroimaging:** from study inception to publication

Guiomar Niso<sup>1,2,\*</sup>, Rotem Botvinik-Nezer<sup>3,\*</sup>, Stefan Appelhoff<sup>4</sup>, Alejandro De La Vega<sup>5</sup>, Oscar Esteban<sup>6, 7</sup>, Joset A. Etzel<sup>8</sup>, Karolina Finc<sup>9</sup>, Melanie Ganz<sup>10,11</sup>, Rémi Gau<sup>12</sup>, Yaroslav O. Halchenko<sup>3</sup>, Peer Herholz<sup>13</sup>, Agah Karakuzu<sup>14,15</sup>, David B. Keator<sup>16</sup>, Christopher J. Markiewicz<sup>7</sup>, Camille Maumet<sup>17</sup>, Cyril R. Pernet<sup>10</sup>, Franco Pestilli<sup>1,18</sup>, Nazek Queder<sup>16,19</sup>, Tina Schmitt<sup>20</sup>, Weronika Sójka<sup>21</sup>, Adina S. Wagner<sup>22</sup>, Kirstie J. Whitaker<sup>23</sup>, Jochem W. Rieger<sup>24</sup>

<sup>\*</sup>These authors contributed equally; <sup>1</sup>Psychological & Brain Sciences, Indiana University, Bloomington, IN, USA; <sup>2</sup>Universidad Politecnica de Madrid, Madrid and CIBER-BBN, Spain; <sup>3</sup>Department of Psychological and Brain Sciences, Dartmouth College, Hanover, NH, USA; <sup>4</sup>Center for Adaptive Rationality, Max Planck Institute for Human Development, Berlin, Germany; <sup>5</sup>Department of Psychology, University of Texas at Austin, Austin, TX, USA; <sup>6</sup>Dept. of Radiology, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland; <sup>7</sup>Department of Psychology, Stanford University, Stanford, CA, USA, <sup>8</sup>Department of Psychological and Brain Sciences, Washington University in St. Louis, St. Louis, MO, USA; 9Centre for Modern Interdisciplinary Technologies, Nicolaus Copernicus University, Toruń, Poland; <sup>10</sup>Neurobiology Research Unit, Rigshospitalet, Copenhagen, Denmark; <sup>11</sup>Department of Computer Science, University of Copenhagen, Copenhagen, Denmark; <sup>12</sup>Institute of Psychology, Université catholique de Louvain, Louvain la Neuve, Belgium; <sup>13</sup>Montreal Neurological Institute-Hospital, McGill University, Montréal, Quebec, Canada; <sup>14</sup>Biomedical Engineering Institute, Polytechnique Montréal, Montréal, Quebec, Canada; <sup>15</sup>Montréal Heart Institute, Montréal, Quebec, Canada; <sup>16</sup>Department of Psychiatry and Human Behavior, University of California, Irvine, CA, USA; <sup>17</sup>Inria, Univ Rennes, CNRS, Inserm -IRISA UMR 6074, Empenn ERL U 1228, Rennes, France; <sup>18</sup>Department of Psychology, The University of Texas at Austin, Austin, TX, USA; <sup>16</sup>Department of Neurobiology and Behavior, University of California, Irvine, CA, USA; <sup>20</sup>Neuroimaging Unit, Carl-von-Ossietzky Universität, Oldenburg, Germany; <sup>21</sup>Faculty of Philosophy and Social Sciences, Nicolaus Copernicus University, Toruń, Poland; <sup>22</sup>Institute for Neuroscience and Medicine, Research Centre Juelich, Germany; <sup>23</sup>The Alan Turing Institute, British Library, London, UK; <sup>24</sup>Department of Psychology, Carl-von-Ossietzky Universität, Oldenburg, Germany

#### ABSTRACT

Empirical observations of how labs conduct research indicate that the adoption rate of open practices for transparent, reproducible, and collaborative science remains in its infancy. This is at odds with the overwhelming evidence for the necessity of these practices and their benefits for individual researchers, scientific progress, and society in general. To date, information required for implementing open science practices throughout the different steps of a research project is scattered among many different sources. Even experienced researchers in the topic find it hard to navigate the ecosystem of tools and to make sustainable choices. Here, we provide an integrated overview of community-developed resources that can support collaborative, open, and reproducible neuroimaging throughout the entire research cycle from inception to publication and across different neuroimaging modalities. We review tools and practices supporting study inception and planning, data acquisition, research data management, data processing and analysis, and research dissemination. We believe it will prove helpful for researchers and institutions to make a successful and sustainable move towards open and reproducible science and to eventually take an active role in its future development.

Keywords: Open Science, Reproducibility, MRI, PET, MEG, EEG

#### Highlights:

- There is a rising interest in openness and reproducibility in neuroimaging
- Despite its clear benefits, adoption is slow and information is scattered
- We provide an integrated review of open resources covering the full research lifecycle
- Consortium of 20+ experts across neuroimaging modalities (MRI, PET, MEG, EEG)
- List of ca. 250 resources supporting openness and reproducibility in neuroimaging

# Open and reproducible neuroimaging:

from study inception to publication

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## **1. Introduction**

Science is an incremental progress towards creating and organizing knowledge through theories and testable predictions. Reproducibility is a core part of science: being able to repeat or recreate scientific results is essential for the complex process of knowledge accumulation. Due to its relevance, different terms have been introduced (e.g., "reproducibility", "replicability", and "reliability") to describe specific aspects of the process, depending, for example, on whether the same or different data or analysis methods are being used to reproduce the results (Goodman, Fanelli, and Ioannidis 2016; Plesser 2018; Poldrack, Whitaker, and Kennedy 2020; The Turing Way Community et al. 2019). Here, we will use "reproducibility" as an umbrella term comprising them together to refer to the ability of recreating scientific results (Poldrack, Whitaker, and Kennedy 2020). Open science tools and practices have been developed to advance reproducibility, as well as accessibility and transparency at all stages of the research cycle and across all levels of society. Together, they remove barriers to sharing and facilitate collaboration, with the goal of improving reproducibility and, ultimately, accelerating scientific discoveries.

Empirical observations of how labs conduct research indicate that the adoption rate of open practices and tools for reproducible and collaborative science, unfortunately, remains in its infancy. Even when members of a specific scientific community have taken a central role in open science advocacy and tool development, like in the neuroimaging community, the impact on the rest of the very same community is limited. A recent survey (Paret et al. 2021) including researchers who are senior and likely to hold a positive attitude towards open science, indicated that 42% have never pre-registered a neuroimaging study and 34% have never shared their raw neuroimaging data. Many of those who indicated that they pre-registered or shared their data at least once likely did not do so in all their studies, and thus, the actual rate of pre-registration and data sharing in neuroimaging is likely much lower. This limited adoption is at odds with the overwhelming evidence that a lack of open practices and tools can hinder reproducibility with costs for scientific progress and for society. Indeed, reproducibility issues have been undermining the foundation of scientific research in several fields, such as psychology (Open Science Collaboration 2015; Klein et al. 2018), social sciences (Camerer et al. 2016, 2018), neuroimaging (Munafò et al. 2017; Botvinik-Nezer et al. 2020; Li et al. 2021), preclinical cancer biology research (Errington, Mathur, et al. 2021; Errington, Denis, et al. 2021), and more (Hutson 2018; Nissen et al.

2016; Serra-Garcia and Gneezy 2021). As a response, there has been a rise in the development of tools and approaches to facilitate reproducibility and open science, in the spirit of Findability, Accessibility, Interoperability, and Reusability principles (FAIR) (Wilkinson et al. 2016; Gorgolewski and Poldrack 2016; Nosek et al. 2018; Nosek, Spies, and Motyl 2012; Nosek and Lakens 2014; Poldrack et al. 2017; Poldrack, Huckins, and Varoquaux 2020; Poldrack et al. 2019; Clayson, Keil, and Larson 2022). Beyond mitigating transparency and reproducibility issues, these practices provide important benefits for individual researchers by increasing exposure, reputation, chances of publication, number of citations, media attention, potential collaborations, and position and funding opportunities (Allen and Mehler 2019; McKiernan et al. 2016; Nosek et al. 2022; Markowetz 2015; Hunt 2019). Hence, one could have expected a higher uptake for such beneficial practices and tools.

Recently, there is a parallel top-down change of policies to further support the adoption of open science practices and tools. For example, funding agencies are now enforcing the implementation of certain open data practices for publicly funded research (de San Román 2021; e.g., the NIH in the U.S. and the ERC in Europe; de Jonge, Cruz, and Holst 2021), and some require a plan for research data storage and sharing, openly accessible publication formats and dissemination plans beyond the classical journal publication. Additionally, they provide funding for the development of necessary software, hardware, and collaborative infrastructure) to support the transition to open and reproducible neuroscience (e.g., the NIH BRAIN Initiative, NIH ReproNim project (Kennedy et al. 2019), NSF CRCNS, EU Human Brain Project, German NFDI). These efforts by funding agencies are complemented by stakeholder institutions like the OHBM, the International Neuroinformatics Coordinating Facility (INCF), the Chinese Open Science Network (COSN), and the OSF, who provide platforms for the development of standards and best practices of open and FAIR neuroscience research, assemble training material, guality control, and promote open science practices. Moreover, journals have started changing their policies with regard to open access options and data sharing. Together, these institutional measures aim at fostering the benefits of open science practices, and the adoption of open and reproducible science standards will be increasingly required for labs and individual researchers.

Nevertheless, multiple barriers of entry to open science practices are driving the modest rate of adoption in the general research community. Among them are lack of knowledge or training and lack of skills or resources. A survey by Borghi and Van Gulick (2018) found that 65% of researchers reported openness and reproducibility as motivation for implementing research data management in MRI, but between 40-50% pointed to the lack of best practices/tools and knowledge/training as main obstacles for embracing these practices. Likewise, a more recent survey indicated that similar percentages of researchers in neuroimaging have never learned how to pre-register or share their data online and that they know too little about pre-registration platforms and suitable data repositories (Paret et al. 2021). These later challenges could be alleviated by a simplified overview of the open resources available. However, information required for implementing open science practices over the full research cycle is currently scattered among many different sources. Even experienced researchers in the topic often find it hard to navigate the ecosystem of community-developed tools and to make sustainable choices.

This manuscript provides an integrated overview of community-developed resources critical to support open and reproducible neuroimaging throughout the entire research cycle and across different neuroimaging modalities (particularly MRI, MEG, EEG, and PET). We believe this overview is urgently needed to accelerate the wider adoption of open science tools and practices by the general research community. The goal is to foster scientific reproducibility and improve scientific quality by allowing scientists to select the best instruments offered by open science at every step of their research workflow. We provide justification on why each of them implements good practices and information on how to access and how to integrate them in the research workflow. We also encourage the readers to join the development teams and leadership of those tools, becoming an active part of the open neuroimaging community.

The manuscript is organized following the different steps of the researchcycle: study inception and planning, data acquisition, research data management, data processing and analysis, and research dissemination. To further guide the readers, the manuscript is accompanied by a detailed table containing links and pointers to the resources featured in the text of each section (see Table S1). We believe this thorough review will prove helpful for

researchers and institutions to make a successful and sustainable move to take an active role in open and reproducible science.

## 2. Study inception, planning, and ethics

Each individual decision from the beginning of the study will contribute to facilitate or hamper reproducibility. In the current section, we will describe practices and tools for preparation, piloting, pre-registration, obtaining participants' consent and ongoing quality control and assessment.

STUDY INCEPTION AND PLANNING				
Study Preparation	Pre-Registration	Ethics and Sharing plan	Monitoring Quality	
Ensure quality of data and experiment Standard Operating Procedures Piloting	Thorough research plan: study design, hypotheses and analysis Best practices Pre-registration and Registered Reports	Meet ethical and regulatory requirements Informed consent Internationally oriented data governance	Ensure quality of acquired data <ul> <li>Quality control checkpoints</li> <li>Quality assurance</li> <li>Positive Control analyses</li> </ul>	
protocolexchange	OSF PREREGISTRATION ASPREDICTED ClinicalTrials.gov	Open Brain Consent	MRIQC           KINAT         VisualQX	

#### Figure 1. Study inception and planning

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#### 2.1. Study Preparation and Piloting

Research projects usually begin with descriptions of general, theoretical questions in documents such as grants or thesis proposals. Such foundations are essential but necessarily broad. When the project moves from proposal to implementation, these descriptions are translated into concrete protocols and stimuli, a process that can be streamlined by the incorporation of open procedures and comprehensive piloting. The promise is that the more preparation and piloting is conducted prior to data collection, the more likely it is that the project will be successful: that analyses of its data can contribute to answering its motivating ideas and questions (Strand 2021).

Standard Operating Procedures (SOPs) can take different forms, and are powerful tools for planning, conducting, recording, and sharing projects. Ideally, SOPs describe the entire data collection procedure (e.g., recruitment, performing the experiment, data storage, preprocessing, quality control analyses), in sufficient detail for a reader to conduct the

experiment themselves with minimal supervision. SOPs may begin as an outline with vague descriptions, and then become more detailed over time. For example, if a session is lost due to a button box signal failure, an image of its correct settings could be added to the SOPs. At the end of the project, its SOPs should be released along with its publications and datasets, to provide a source of answers for the detailed procedural information that may be needed for experiment replication or dataset reuse, but are not included in typical publications.

Many resources can assist with experiment planning and SOP creation. Documents and experiences from similar studies conducted locally are valuable, but should not be the only source of information during planning, since, for example, a procedure may be considered standard in one institution but not in another. Public SOPs can serve as examples, as can protocols published on specialized sites (e.g., Protocol Exchange, protocols.io, Nature Protocols; see Table S1). Best practices guides are now available for many imaging modalities (MRI: Nichols et al. 2017; MEG/EEG: Pernet, Garrido, et al. 2020; fNIRS: Yücel et al. 2021; PET: Knudsen et al. 2020). Open resources for stimulus presentations and behavioral data acquisition are also recommended to increase reproducibility (see section 3.5).

Piloting should be considered an integral part of the planning process. By "piloting" we mean the acquisition and evaluation of data prior to the collection of the actual experimental data; verifying the feasibility of the whole research workflow. A piloting stage before starting data collection is important, not only for ensuring that the protocol will go smoothly when the first participant arrives, but also that the SOPs are complete and, critically, that the planned analyses can be carried out with the actual experimental data recorded. For example, pilot tests may be set up to confirm that the task produces the expected behavioral patterns (e.g., faster reaction time in condition A than B), that the log files are complete, and that image acquisition can be synchronized with stimulus presentation. Piloting should also include testing the data storage and retrieval strategies, which may include storing consent documents (section 2.3), questionnaire responses, imaging data, and quality control reports. SOPs also prescribe how data will be organized, preferably according to a schema (e.g., the Brain Imaging Data Structure, section 4.1). Data

organization largely determines the efficient implementation of analysis pipelines and improved reproducibility, reusability, and shareability of the data and results.

Analyses of the pilot data are very important and can take several forms. One is to test for the effects of interest: establishing that the desired analyses can be performed and that the data quality and effect sizes are sufficient to produce valid and reproducible results (section 2.2. and 2.4; for power estimation tools see Table S1). A second type of pilot analysis is to establish tests for effects not of direct interest, but suitable for controls. As discussed further in section 2.4, positive control analyses involve strong, well-understood effects that must be present in a valid dataset. It is worth mentioning that well structured and documented openly available datasets (see section 4) could also serve for analysis piloting though they would lack the test for potential site specific technical issues. Simulations could also be used to ensure that the planned analysis is doable and valid.

#### 2.2. Pre-registration

Pre-registration is the specification of the research plan in advance, prior to data collection or at least prior to data analysis (Nosek and Stephen Lindsay 2018). Pre-registration usually includes the study design, the hypotheses and the analysis plan. It is submitted to a registry, resulting in a frozen time-stamped version of the research plan. Its main aim is to distinguish between hypothesis-testing (confirmatory) research and hypothesis-generating (exploratory) research. While both are necessary for scientific progress, they require different tests and the conclusions that can be inferred based on them are different (Nosek et al. 2018).

Registered reports is a relatively novel publishing format that can be seen as advanced pre-registration. This format is becoming very common, with a growing number of hundreds of participating journals (Hardwicke and Ioannidis 2018; Chambers 2019). In a registered report, a detailed pre-registration is submitted to a specific journal, including introduction, planned methods and potentially preliminary data. Then, it goes through peer review prior to data collection (or prior to data analysis in certain cases, for example for studies that rely on large-scale publicly shared data). If the proposed plan is approved following peer review, it receives an "in-principle acceptance", indicating that if the researchers follow their accepted plan, and their conclusions fit their findings, their paper will be published. An in-principle

accepted registered report is sometimes required to be additionally pre-registered. Recently, a platform for peer review of registered reports preprints was launched, named "Peer Community in registered reports" (see Table S1).

There are many benefits to pre-registration, from the field to the individual level. Transparency with regard to the research plan, and whether an analysis is confirmatory or exploratory, increases the credibility of scientific findings. It helps to mitigate some of the effects of human biases on the scientific process, and reduces analytical flexibility, p-hacking (Simmons, Nelson, and Simonsohn 2011) and hypothesizing after the results are known (Nosek et al. 2019; Munafò et al. 2017; Nature 2015; Kerr 1998). There is initial evidence that the quality of pre-registered research is judged higher than in conventional publications (Soderberg et al. 2021). Nonetheless, it should be noted that pre-registration is not sufficient to fully protect against questionable practices (Paul, Govaart, and Schettino 2021; Devezer et al. 2021; Rubin 2020). Registered reports also mitigate publication bias by accepting papers based on hypothesis and methods, independently of the findings, and indeed it has been shown that pre-registration and registered reports lead to more published null findings (Allen and Mehler 2019; Kaplan and Irvin 2015; Scheel 2020) and report lower effect sizes (Schäfer and Schwarz 2019). For the individual researcher, registered reports with a two-stage review are an excellent example in which authors benefit from feedback on their methods before even starting data collection. They can help improve the research plan and spot mistakes in time, and provide assurance that the study will be published (Wagenmakers and Dutilh 2016; Kidwell et al. 2016).

While pre-registration is not the common practice yet, it is becoming more common over time (Nosek and Stephen Lindsay 2018) and requirements by journals and funding agencies are already changing. There are many available templates and forms for pre-registration, organized by discipline or study types, for example for fMRI and EEG (see Table S1), and published guidelines for pre-registration in EEG are also available (Paul, Govaart, and Schettino 2021). There are different approaches with respect to what should be pre-registered. For instance, some believe it should be an exhaustive description of the study, including the background and justification for the research plan, while others believe it should be short and concise, including only the necessary details to reduce the likelihood

of p-hacking and allowing reviewers to review it properly during the peer review process (Simmons, Nelson, and Simonsohn 2021).

Once researchers develop an idea and design a study, they can write and pre-register their research plan (Nosek and Stephen Lindsay 2018; Paul, Govaart, and Schettino 2021). Pre-registration could be performed following the piloting stage (section 2.1), but studies can be pre-registered irrespective of whether they include a piloting stage or not. There are many online registries where researchers can pre-register their study. The three most frequently used platforms are: (1) The Open Science Framework (OSF), a platform that can also be used to share additional information about the study/project (such as data and code), with multiple templates and forms for different types of pre-registration, in addition to extensive resources about pre-registration and other open science practices; (2) Aspredicted.org, a simplified form for pre-registration (Simmons, Nelson, and Simonsohn 2021); and (3) Clinicaltrials.gov, which is used for registration of clinical trials in the U.S. (see Table S1).

Once the pre-registration is submitted, it can remain private or become public immediately, depending on the platform and the researcher's preferences. Then, the researcher collects the data and executes the research plan. When writing the manuscript to report the study, the researcher is advised to include a link to the pre-registration, clearly and transparently describe and justify any deviation from the pre-registered plan and also report all registered analyses. Additional analyses to deepen some results or look into unexpected effects are encouraged, and are part of the normal scientific investigation. The added benefit of pre-registration is that such analyses do not need to reach pre-specified levels of significance because they are reported as exploratory.

#### 2.3. Ethical review and data sharing plan

The optimism of the scientific community about improving science by making all research assets open and transparent has to take into account privacy, ethics and the associated legal and regulatory needs for each institution and country. Whereas on the one hand sharing data (most often collected with public funds) is critical to advance science, on the other hand, sharing data can in some situations become infeasible to safeguard privacy. Data governance concerns the regulatory and ethical aspects of data management and sharing of data files, metadata and data-processing software (see sections 6.1-3). When data sharing crosses national borders, data governance is called International Data Governance (IDG). IDG depends on ethical, cultural and international laws.

Data sharing is necessary for both reproducibility and the exploration and formulation of new hypotheses. Therefore, it is important to ensure, prior to data collection, that the collected data could be later shared. Consent forms for neuroimaging studies should contain, or be accompanied with, a specific section to allow data sharing. Such data sharing forms should include information about where and in what form the data will be shared, as well as who will have access and how restrictive this access will be. Data sharing forms should also make explicit how these factors determine to what extent a later withdrawal or editing of the data on the repository is possible. Additional requirements might be in place depending on the location where the research is being conducted. Given the international nature of the majority of neuroscience projects, IDG has become a priority (Eiss 2020). Further work will be needed to implement an IDG approach that can facilitate research while protecting privacy and ethics. Specific recommendations on how to implement IDG have been proposed by (Eke et al. 2022).

Open and reproducible neuroimaging thus starts by (1) planning which data would be collected; (2) planning how these data would later be shared; (3) having ethical and legal clearance to share data; but also (4) the infrastructural means for this sharing (for more information about data sharing and available platforms, see section 6; for data governance see section 4). The practice of collecting informed consent from human research participants has developed from the Nuremberg Code which led to the Declaration of Helsinki. The latter comprises a set of ethical principles which are now common practice and required by many funding institutions and journals, but which are not legally binding. The informed consent should include a statement about the research goals, inform about the experimental procedures, its expected duration, potential risks, who can participants that participation is voluntary, and that the consent can be withdrawn at any time during the experiment without a disadvantage for the participant. If limited intervals for consent withdrawal exist, they should be clearly stated. Furthermore, it should also include a statement that the participant understood the information provided and agreed to

participate. Clinical research may require adherence to additional, country specific regulations.

Since 2014, founded under ReproNim project umbrella, the Open Brain Consent project (see Table S1) provides examples and templates translated to multiple languages to help researchers prepare consent forms, including the recent development of an EU GDPR-compliant template (The Open Brain Consent working group 2021). When planning the recruitment procedures, it is important to aim for equity, diversity and inclusivity (Henrich, Heine, and Norenzayan 2010; Forbes, Aneja, and Guest 2021), avoiding obtaining results that may not generalize to larger populations and improving the quality of research (e.g., Baggio et al. 2013).

#### 2.4. Looking at the data early and often: monitoring quality

Inevitably, unexpected events and errors will occur during every experiment and in every part of the research workflow. These can take many forms, including dozing participants, hardware malfunction, data transfer errors, and mislabeled results files. The impact of such surprises can range from the trivial and easily corrected to the catastrophic, rendering the collected data unusable or conclusions drawn from it invalid. Identifying issues and errors as early as possible is important to enable adding corrective measures to the protocol, but also because some issues are much easier to detect when the data are in a less-processed form. For example, a number of typical artifacts in anatomical MRI are known to be easier to identify in the background of the image and regions of no-interest (Mortamet et al. 2009), therefore, they can easily remain undetected if the first quality control check is set up after, e.g., brain extraction, which masks out non brain tissue. As data progresses through the workflow, issues are likely to cascade and amplify, perhaps masking or mediating experimental effects, thereby damaging the reliability of the results. Therefore, it is fundamental to pre-establish within the SOPs (section 2.1) the mechanisms set in place to ensure the reliability of the study. There are several mechanisms available that help to ensure that all required data are being recorded with sufficient quality and in a way that makes them analyzable.

**Quality control checkpoints.** Establishing quality control (QC) checkpoints (Strother 2006) is necessary for every project: which data are usable for analyses, and which are not? At these key points in the preprocessing or analysis workflow the data's quality is checked,

and if insufficient, it does not move on to the next stage. Critically, the exclusion criteria of each checkpoint must be defined in advance (preferably stated in the SOPs and the pre-registration document, see sections 2.1 and 2.2) to preempt unintentional cherry-picking (i.e., excluding data points to reinforce the results). Some criteria are widely accepted and applicable, for example, that all neuroimaging data should be screened to eliminate clear artifacts, such as data corrupted by incidental electromagnetic interference or participants movements. A similarly well-established checkpoint of the workflow is visualizing and inspecting the outputs of surface reconstruction methods in MRI, checking time activity curves in high binding regions for PET or power spectral content in MEG and EEG; these fundamental QC checkpoints and their implementation are heavily dependent on the immediately previous processing step. Such QC may be conducted manually by experts using software aids, like visual summary reports or visualization software such as MRIQC (Esteban et al. 2017). More objective, automatic exclusion criteria, are currently an open and active line of work in neuroimaging. Some QC checkpoints, such as for acceptable task performance or participant movement, are often defined for individual tasks, experiments and hypotheses.

**Quality assurance (QA).** Tracking QC decisions will also enable identifying structured failures and artifacts that require not just dropping affected datasets, but rather taking corrective actions to preempt propagation to additional datasets. When a mishap occurs, the experimenters should investigate its cause, and if possible, change the SOPs (section 2.1) and related materials to reduce the chance of it happening again. For example, if many participants report confusion about task instructions, the training procedure and experimenter script could be altered. Automated checks and reports can be very effective, such as real-time monitoring of participant motion during data collection (Heunis et al. 2020), or validating that image parameters are as expected before storage (e.g., with XNAT (Marcus et al. 2007) or ReproNim tools (Kennedy et al. 2019)).

**Positive control analyses.** A final aspect of ensuring high-standards of the research workflow is the incorporation of positive control analyses: analyses included not because they are of interest for the scientific questions, but because they provide evidence that the dataset is of sufficient quality to conduct the analyses of interest, and that the analysis is valid. Ideally, positive control analyses focus on strong, well-established effects that must

be present if the dataset is valid. For example, with task fMRI designs, button pressing, which should be associated with contralateral motor activation, is often a convenient target for positive control analysis. In MEG and EEG, participants can be asked to blink their eyes, open their mouths, or clench their jaws, and the recordings checked for the associated artifacts. Positive control analyses should also be carried out during piloting, when changes to the protocol are still possible (see section 2.1). For example, if button presses are not clearly detectable during piloting, the acquisition sequence may not have sufficient SNR for the planned analyses and so need modification.

## 3. Data acquisition

Data acquisition is largely carried out with vendored systems. Manufacturers typically keep their software and hardware closed or semi-open at most. As a result, researchers often receive highly processed (e.g., reconstructed) data as 'raw' data from the devices. The lack of transparency in the acquisition details and downstream proprietary processing prevents end-to-end reproducible neuroimaging workflows. Reproducibility is endangered, for instance, by heterogeneity in data formats, definition of critical experimental parameters, and technological differences that are translated into the data as spurious, non-biological differences between acquisition devices.

A central issue is the proprietary nature of acquisition protocols. Many imaging device manufacturers require developers to use building blocks from vendor-exclusive toolboxes. This closes the door on open-source development and hampers multi-center consensus for modern imaging methods, especially in research. These shortcomings of mostly closed solutions have triggered a growing interest in open-source acquisition hardware and software (Winter et al. 2016), Here, we provide a brief review of these developments and accompanying solutions aimed at fostering open and collaborative acquisition method development across imaging modalities.



#### Figure 2. Data acquisition

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#### 3.1. Brain data acquisition

A common approach advocated by MRI researchers is establishing consensus protocols to standardize data acquisition. One of the flagship applications of this strategy is the Human Connectome Project (HCP) protocol, which achieved this within the confines of a single vendor (Smith et al. 2013). The HCP acquisition sequences and reconstruction software are compiled for different MRI scanner versions of a single vendor, openly distributed and maintained for fMRI applications (Uğurbil et al. 2013). However, it is generally difficult to achieve good inter vendor agreement using off the shelf software even for widely used protocols, such as apparent diffusion coefficient and longitudinal relaxation time (Sasaki et al. 2008; Lee et al. 2019). In addition, not all software options are available from all vendors (for example, compressed sensing (Lustig et al. 2008) and frequency-domain based parallel imaging methods (Breuer et al. 2005; Griswold et al. 2002)). Moreover, even seemingly simple image enhancement protocols, such as image inhomogeneity corrections, are often scarcely documented and validated but can affect inferences drawn from an experiment (Schmitt and Rieger 2021; e.g., Jellús and Kannengiesser 2014). Users typically have access to key parameters of pulse sequences, which are at the center of data acquisition. The exact pulse sequence descriptions are vendor-specific and may even change between software upgrades of a single vendor. This makes it difficult to evaluate multi-center validity of new acquisition methods or to acquire longitudinal data with confidence.

Fortunately, in the last decade, several vendor-neutral data acquisition pulse sequences and reconstruction frameworks have been developed to mitigate this problem: Pulseq (Layton et al. 2017), PyPulseq (Ravi, Geethanath, and Vaughan 2019), GammaStar (Cordes et al. 2020), TOPPE (Nielsen and Noll 2018), ODIN (Jochimsen and von Mengershausen 2004), and SequenceTree (Magland et al. 2016) (see Table S1). Although these tools vary in vendor compatibility and the flexibility of their acquisition runtime, they enable vendor-neutral deployment of pulse sequences with transparent access to all the details needed. Nevertheless, vendor-neutral raw data (k-space) collection is half the battle.

To complete the puzzle of MR image acquisition, interoperable and open-source reconstruction frameworks are essential. Thanks to ISMRM-RD (Inati et al. 2017), a k-space data standard, community-developed reconstruction tools can have a unified way to run advanced reconstruction algorithms against undersampled raw data (Maier et al. 2021). Some of these tools include Gadgetron (Hansen and Sørensen 2013), BART (Uecker et al. 2015), MRIReco.JI (Knopp and Grosser 2021) (see Table S1 for further tools and details). By streamlining these acquisition and reconstruction tools using data standards at multiple levels (Karakuzu, Appelhoff, et al. 2021; Inati et al. 2017) on a data-driven and container-mediated workflow engine (Di Tommaso et al. 2017), end-to-end reproducible MRI workflows can be developed. A recent study has shown that this approach can significantly reduce inter-vendor variability of quantitative MRI measurements (Karakuzu, Biswas, et al. 2021; Karakuzu et al. 2020). Given the growing open-source MRI acquisition ecosystem, a variety of end-to-end workflows are possible. Therefore, community-driven validation frameworks have a key importance for interoperable solutions (Tong et al. 2021). Facilitated by these standards, effective and open communication methods development sets the future direction for reproducible MRI research (Stikov, Trzasko, and Bernstein 2019).

In PET, the variety between different scanners is even larger than in MRI. An overview over different scanner types based on their usage for a specific radiotracer targeting the serotonin transporter, namely [<sup>11</sup>C]DASB, is given in (Nørgaard, Ganz, et al. 2019). Different PET scanners export images in slightly different data formats with little overlap in the Digital Imaging and Communications in Medicine (DICOM) PET specific tags. As with MRI, reconstruction is vendor/machine specific but open source solutions to image reconstruction are being developed, for instance the OMEGA toolbox (Wettenhovi, Vauhkonen, and Kolehmainen 2021). Data acquisition for PET is further complicated by the

use of different PET tracers, injection methods, scan duration and scan framing or injected radioactivity dose.

In MEG and EEG, the problem of standardized data acquisition starts even earlier: unlike the common DICOM data format used across vendors in MRI or PET, MEG and EEG manufacturers do not use a common data format, and format specifications are rarely made public. More importantly, equipment implementation significantly differs between vendors. MEG systems contain various sensor types (e.g., magnetometers, gradiometers) with different spatial configurations, which pick up different features of magnetic fields and varying signal-to-noise ratios from different depths and brain extensions (Taulu et al. 2014). Furthermore, some of them require daily adjustments of sensor tuning, not typically reported anywhere. Vendors supply hardware (e.g., reference sensors, internal/external active shielding) and software noise suppression techniques (e.g., higher-order gradients, signal space separation), which may affect the signal differently, for example depending on the choice of free parameters. Some of these techniques can introduce new artifacts that require additional proprietary software compensation tools (e.g., active shielding requires signal space separation). In some installations, these tools are even necessary to enhance the signal-to-noise ratio to a level where MEG measurements are possible at all. Similarly, EEG equipment differs among the multitude of manufacturers, in terms of amplifiers and electrodes (e.g., active versus passive; number and spacing on the scalp; preparation method: dry, with gel, with saline solution; single electrodes or "nets", etc.). Moreover, there have been some efforts on developing open versions of some proprietary tools, for example, the Maxwell filtering for signal space separation by the MNE-python team (Gramfort et al. 2014). Additionally, initiatives, such as the OpenBCI, offer open EEG hardware and tools for biosensing and brain computer interfacing through continuous community driven development. As we have mentioned, very little is known on how the variability of data acquisition parameters affect downstream comparability of results. The EEGManyLabs project (Pavlov et al. 2021) will provide a comprehensive dataset in this regard, as many labs with different equipment try to replicate the same studies.

Given the large variations across different vendors for all neuroimaging modalities, which often cannot be overcome, it is crucial to report all data acquisition parameters in a comprehensive and standardized manner to make potential differences in data acquisition across studies and sites transparent (for a discussion of reporting guidelines see section 6.4).

#### 3.2. Stimulus presentation and behavior

Several actively maintained programs for stimulus presentation and response logging are available. Open source software includes PsychoPy (Peirce et al. 2019) in Python and Psychtoolbox (Brainard 1997; Pelli 1997; Kleiner, Brainard, and Pelli 2007) in MATLAB. Both have many users, making it possible to get assistance and perhaps find an already-implemented task protocol (e.g., on Pavlovia for Psychopy). Modality specific resources also exist, for instance the ERP CORE (Compendium of Open Resources and Experiments; Kappenman et al. 2021) openly provides optimized paradigms for several widely used ERP components, along with scripts, data processing pipelines, and sample data.

Using open stimuli and presentation software generally increases the likelihood a dataset will be useful to others, and its results reproducible. Although desirable, it is not always possible to use fully open stimuli, particularly in the case of commercial movies, audio plays, and image databases. This should also be considered when planning studies. Stimuli, presentation scripts, behavioral tests and related material should be shared whenever possible (see DuPre, Hanke, and Poline 2019 for a list of datasets sharing naturalistic stimuli and section 6). To facilitate stimuli feature analysis and exact reproducibility of the experimental paradigms, such projects as ReproNim's ReproStim (Connolly and Halchenko 2022) could automate recording and archival of the delivered to audio-video stimulation. When specific stimuli or material can not be released, they should be described as unambiguously as possible and, if possible, providing the source, such as identification number (e.g., a GTIN), and scripts to (re)produce used stimuli from the commercial media.

#### 4. Research Data Management

Good research data management (RDM), i.e. how data are organized, maintained, annotated, tracked, stored, and accessed throughout a research project, forms the basic foundations of result reproducibility, data reusability, and research efficiency (Wilkinson et

al. 2016; Gorgolewski and Poldrack 2016; Nosek et al. 2018; Nosek, Spies, and Motyl 2012; Nosek and Lakens 2014; Poldrack et al. 2017; Poldrack, Huckins, and Varoquaux 2020; Poldrack et al. 2019; Borghi and Van Gulick 2021a; Poline et al. 2022). Consequently, it is widely required by funders (e.g., NIH and NSF in the U.S., ERC in Europe), increasingly expected by scientific peers, and holds considerable benefits for individual researchers. While specific RDM requirements vary across subdisciplines, this section highlights RDM standards and tools applicable across neuroimaging, ranging from data organization to annotation and publication.



#### Figure 3. Research data management

Sources: Icons from the Noun Project: Structure by Adam Baihaqi from NounProject.com; Metadata by M. Oki Orlando; Data Management by ProSymbols; Logos: used with permission by the copyright holders.

#### 4.1. Data organization and standards

Neuroimaging experiments result in complicated data that can be arranged in many different ways. Historically, data were organized differently between institutions and even within a lab. This lack of consensus (or a standard) could lead to misunderstandings and suboptimal usage of various resources: human (e.g., time wasted on rearranging data or rewriting scripts expecting certain structure), infrastructure (e.g., data storage space, duplicates), and financial (e.g., disorganized data has limited longevity and value after first publication). Finally, and most importantly, it produces poor reproducibility of results, even within the lab where data were collected. Therefore, the need for a data standard in the neuroimaging community became essential.

The Brain Imaging Data Structure (BIDS) is a community-led standard for organizing, describing, and sharing neuroimaging data [RRID:SCR\_016124]. BIDS is an evolving standard, which supports multiple neuroimaging modalities including MRI (Gorgolewski et al. 2016), MEG (Niso et al. 2018), EEG (Pernet et al. 2019), intracranial EEG (Holdgraf et al. 2019), PET (Nørgaard, Ganz, et al. 2019), Microscopy (Bourget et al. 2022), and imaging genetics (C. A. Moreau et al. 2020). Many more extensions are under active development, for example, fNIRS, motion capture, and animal neurophysiology. The BIDS specification documents how to organize the data, generally based on simple file formats (such as NIfTI for tomographic data (Cox et al. 2004), and JSON for metadata) and folder structures. This specification can be extended through community-driven processes to incorporate new neuroimaging modalities or sets of data types.

Multiple applications and tools have been released to make it easy for researchers to incorporate BIDS into their current workflows, maximizing reproducibility, enabling effective data sharing, and supporting good data management practices. For example, BIDS converters make it easier to convert data into BIDS format (e.g., MNE-BIDS (Appelhoff, Sanderson, et al. 2019) for MEG and EEG, dcm2bids, ReproNim's HeuDiConv (Halchenko, Goncalves, et al. 2021) and ReproIn (Visconti di Oleggio Castello et al. 2020) for MRI and PET2BIDS for PET; see many more on Table S1). The BIDS validator can help researchers make sure their dataset is BIDS-valid following conversion.

Once data are in BIDS, users need tools that ease interaction with the data. Two commonly used software packages are PyBIDS (Yarkoni et al. 2019), and BIDS-Matlab (Gau et al. 2022) (ref). These tools facilitate useful dataset queries—such as how many participants are part of a dataset or what tasks were performed— as well as programmatically retrieving specific files—such as all functional runs for a specific subject. Finally, BIDS apps are containerized analysis pipelines that use full BIDS datasets as their input and produce derivative data (Gorgolewski et al. 2017). Examples of BIDS apps include MRIQC (Esteban et al. 2017), for MRI quality control, fMRIPrep (Esteban et al. 2019) for fMRI preprocessing, and PyMVPA (Hanke et al. 2009) for statistical learning analyses of large datasets (see more at Table S1).

BIDS is a community-led standard and thus, open and inclusive. The BIDS specification is the result of the ongoing collaboration, shared knowledge, discussion, and consensus through the email discussion list, shared Google docs, and GitHub. Questions are also answered on the Neurostars forum and the Brainhack Mattermost channel. BIDS has a well-specified governance structure where everybody is welcome to participate, and the BIDS Starter Kit is a growing resource intended to simplify the learning process for newcomers.

#### 4.2. Metadata and Data annotation

Metadata and data annotation induce consistency and facilitate data replication and reuse. It improves the clarity of the dataset, the ability for collaborators to understand the conditions in which the data were collected, and the ability to effectively share and reuse them. Commonly, metadata files are data dictionaries that map key terms from an agreed-upon vocabulary to data values that contain detailed and standardized information about the key terms. For example, a key called "SampleFrequency" might map to a numerical value, or a key "TaskDescription" might map to a free-form text that describes the task used in a specific experiment. The BIDS standard has proposed a consistent metadata structure in its specification along with a set of specification terms and tags.

Data annotation is also crucial for most data analyses in neuroimaging. For example, when analyzing task-based data, an experiment's reproducibility is largely determined by the extent to which events are clearly documented. Beyond reproducing previous findings, exhaustively annotated events can allow researchers to re-use the data for means that were originally not thought of at data collection time (Bigdely-Shamlo et al. 2020). However, even if each study is fully annotated, without a standard to consistently describe facets of events, all annotations will remain cumbersome and error-prone to work with, and achieving a state of machine readability will require effortful labor.

To address this problem, the Hierarchical Event Descriptor (HED) standard has been continuously developed over the past years (Robbins, Truong, Jones, et al. 2021; Robbins, Truong, Appelhoff, et al. 2021). Drawing on a set of hierarchical vocabulary structures (the HED base schema) and application rules, the HED standard allows for both human- and machine readability, validation, and search of annotations across studies. HED is

furthermore fully integrated with the BIDS standard (see section 4.1), and can be extended by researcher supplied schemas.

Additionally, the Neuroimaging Data Model (Maumet et al. 2016; NIDM; Keator et al. 2013) effort aims to build a core structure for neuroscience datasets to improve searching across publicly-available datasets. The initiative also provides tools to create and use NIDM documents from BIDS datasets (Appelhoff, Bates, et al. 2019). To effectively describe neuroscience data, well-developed community-driven vocabularies are needed. NIDM is built using semantic web techniques and builds off the PROV (provenance) vocabulary (L. Moreau et al. 2015). Moreover, the NIDM-Terms effort has begun to collect and extend sets of community-developed controlled vocabularies and techniques for associating concepts with selected study variables of publicly-available neuroimaging datasets (i.e., OpenNeuro, ABIDE, ADHD200, and CoRR). This keeps a registry of the domain-relevant vocabularies and concepts used to annotate datasets, further facilitating concept reuse, and improved inter-dataset search. The NIDM team has developed a JavaScript web application, as well as Python-based command line annotation tools, that allow researchers to annotate their BIDS structured datasets and single tabular files (e.g., csv and tsv spreadsheets), and export both BIDS sidecar file JSON-formatted data dictionaries, NIDM JSON-LD data dictionaries, and NIDM semantic web documents. Currently, the NIDM-Terms annotation tools allow researchers to associate their study variables with concepts available in the Cognitive Atlas (Poldrack et al. 2011), the InterLex information resource, and those in the canonical NIDM terminology/ontology as well as encourage them to add descriptive information to improve the clarity of their variables. Such an effort harmonizes and improves the consistency of neuroimaging data and thus makes querying across neuroimaging datasets more efficient.

#### 4.3. Data management and tracking

Raw data and derivatives (outputs from processed data) form the basis for scientific analyses and insights. Being able to efficiently store, retrieve, and update data, derivatives, and metadata across a variety of available storage options is crucial to enable further research (Borghi and Van Gulick 2021b). As files change and evolve over the course of a project, there is a need to identify which data have been used in the generation of a result, and, in case the data were subject to change or updates, which exact version of the data

has been used. The ability to manage data and metadata and track the data-analysis process provides a basis for rigor and reproducibility.

DataLad (Halchenko, Meyer, et al. 2021) is an open-source, community-developed, general purpose tool for managing and version controlling digital files in a decentralized manner. It tracks data of any type or size in a scalable. Git-repository-based overlay structure, called the dataset (practically, a structure of folders and files). DataLad allows tracking data and metadata files stored on local devices as well as remote or cloud infrastructure. DataLad can retrieve public data from major providers such as OpenNeuro, the Canadian Open Neuroscience Platform, the International Neuroimaging Data-sharing Initiative, the Healthy Brain Network Serial Scanning Initiative, Data sharing for Collaborative Research in Computational Neuroscience, the Human Connectome Project's open access dataset (Van Essen et al. 2013), and many more. Beyond public data, with appropriate permissions or authentication, it can retrieve data from web-based storage providers including major cloud storage services, and local and remote paths (Halchenko, Meyer, et al. 2021; Hanke et al. 2021). DataLad implements this decentralized data management functionality in order to ensure streamlined access to tracked data regardless of hosting service, and to expose datasets for easy access on repository hosting structure. It separates management of file content from lean metadata management by tracking pointers to the services that host managed files (i.e., local infrastructure, remote hosting services, or multiple storage solutions at once). Using these pointers, it enables streamlined on-demand file retrieval in uniquely identified versions from the registered source. Importantly, data retrieval works via streamlined commands regardless of where the data are hosted. Information about DataLad can be found in the DataLad Handbook (Wagner et al. 2021, see Table S1). Entire computing environments could be efficiently managed in DataLad using datalad-container extension (K. Meyer et al. 2021) developed in collaboration between DataLad and ReproNim projects.

Brainlife.io is another open science project that allows data management. Brainlife.io is a free and open community-oriented, non-commercial cloud platform that provides web services to support reproducible data management and analysis. Brainlife.io tracks data provenance automatically for the users. As data are analyzed using the Graphical User Interfaces (GUI) and the platform's data processing applications, provenance metadata

information is automatically generated and stored associated with the data derivatives. The users do not have to manually save data versions, the platform does that automatically and it allows visualizing data provenance graphs.

DataLad and Brainlife.io are synergistic but not overlapping projects that address different user bases and needs. Indeed, DataLad and Brainlife.io interact nicely with one another and all published datasets retrieved by DataLad are readily accessible at brainlife.io/datasets.

## 5. Data processing and analysis

Researchers typically execute a set of signal pre-processing steps prior to advanced data analysis, to, for instance, identify and remove noise, align data spatially and temporally, segment spatio-temporal regions of interest, identify patterns and latent signal structures (e.g., clustering), integrate the information from several modalities, introduce prior knowledge about the device or the physiology of the specimen, etc. The combination of the operations that take the unprocessed data as the input, prepare the data for analysis, and finally, perform advanced analysis, comprise a full *analysis pipeline* or *workflow*. In implementing such analysis workflows, software has emerged as a critical research instrument greatly relevant to ensure the reproducibility of studies.

DATA PROCESSING AND ANALYSIS					
Software	Standardizing workflows	Statistical modelling	Multiverse analysis		
Many open tools available <ul> <li>High analytical variability</li> <li>Openly share code</li> <li>Version Control for tracking and collaboration</li> </ul>	Enhance reproducibility <ul> <li>Analysis agnostic preprocess</li> <li>Standardized data structure</li> <li>Portable using containers (Docker, Singularity)</li> </ul>	Reproducible advanced analysis <ul> <li>Analysis pipelines with automatic (machine readable) documentation</li> <li>Standardized data structure</li> </ul>	Explore effects of variations in analysis pipeline on study results Vary critical analysis parameters Re-run analysis with different tools		
Image: Second	MRICE MREProp NiPreps BIDS S <sup>-</sup> A docker	FitLins	FUZZY Explorable Multiverse Analyses		

Figure 4. Data processing and analysis

Sources: Icons from the Noun Project: Software by Adrien Coquet; Workflow by D. Sahua; Statistics by Creative Stall; Chaos Sigil by Avana Vana; Logos: used with permission by the copyright holders.

## 5.1. Software as a research instrument

Digitization has stimulated a massive increase in the net amounts of daily acquired data, placing software as a central instrument of the neuroimaging research workflow. As a result,

many toolboxes containing utilities ranging from early steps of preprocessing to statistical analysis and visualization of results have emerged, and some have largely shaped the software development in the field, e.g., AFNI (Cox 1996; Cox and Hyde 1997), FSL (Jenkinson et al. 2012; only free for academic use), SPM (Penny et al. 2011; Litvak et al. 2011; Flandin and Friston 2008), FreeSurfer (Dale, Fischl, and Sereno 1999; Dale and Sereno 1993), Brainstorm (Tadel et al. 2011, 2019), EEGLAB (Delorme and Makeig 2004; Delorme et al. 2021), MNE-Python (Gramfort et al. 2013, 2014), FieldTrip (Oostenveld et al. 2011) (see Table S1). More recently, some software packages have been developed to cover additional aspects of the neuroimaging workflow. For instance, nibabel (Brett et al. 2020) to read and write images in many formats, the Advanced Normalization Tools (ANTs) for image registration and segmentation, or Nilearn (Abraham et al. 2014) for statistical analysis and visualization. Workflow engines conveniently connect between the building blocks and determine how the steps are executed in the computational environment. Solutions range from general-purpose scripting (e.g., Bash or Python) to neuroimaging-specific libraries (e.g., NiPype; Gorgolewski et al. 2011). Researchers have all these tools (and others) at their disposal to "mix-and-match" in their workflow. Therefore, ensuring the proper development and operation of the software engine is critical to ensure the reproducibility of results (Tustison et al. 2013).

Relatedly, the variety of software implementations is an additional motive of concern. As remarked by Carp (2012a, [b] 2012) based on the analysis of thousands of fMRI pipelines, analytical flexibility in combination with incomplete reporting precludes the reproducibility of the results. A recent comprehensive investigation, the Neuroimaging Analysis Replication and Prediction Study (NARPS; Botvinik-Nezer et al. 2020) found that when 70 different teams were asked to analyze the same fMRI data to test the same hypotheses, each team chose a distinct pipeline and results were highly variable. Other studies suggest similar problems in EEG (Šoškić et al. 2021; Clayson et al. 2021), PET (Nørgaard et al. 2020) and diffusion MRI (Schilling et al. 2021).

There are two crucial aspects of the high analytical variability and its effect on results in neuroimaging. First, when high analytical variability (that potentially affects results) is combined with partial reporting or with incentives to find significant effects, it can alarmingly undermine the reliability and reproducibility of results. Second, even in the apparently ideal

scenario in which the researcher performs a single pre-registered valid analysis and reports it fully and transparently, it is still likely that the results are not robust to arbitrary analytical choices. Therefore, new tools are needed to allow researchers to perform a "multiverse analysis" (section 5.4), where multiple data workflows are used on the same dataset and all the results are reported and their agreement or convergence discussed. Community-led efforts to develop high-quality "gold standard" data workflows may also reduce researchers' degrees of freedom as well as accelerate data analysis, although different pipelines are optimal for different research questions and data.

Nevertheless, neuroimaging researchers frequently encounter gaps that readily available toolboxes do not cover. These gaps, amongst a number of other reasons (e.g., deploying a data workflow on a high-performance computer), pushes researchers into creating their own software implementations. However, most neuroimaging researchers are not formally trained in related fields of computer science, data science, or software engineering. This mismatch often results in undocumented, hard to maintain, and disorganized code; largely as a consequence of unawareness of software development practices. It also increases the likelihood of undetected errors that may remain even after running tests on the code.

The first and foremost strategy available to maximize the transparency of research methods is openly sharing the code with the minimal restrictions possible (see section 6.2; Barnes 2010; Gorgolewski and Poldrack 2016). Complementarily, version control systems, such as Git (Blischak, Davenport, and Wilson 2016, see Table S1), are the most basic and effective tool to track how software is developed, and to collaboratively produce code. Beyond open-sourcing the code, software tools implement further transparency strategies by thoroughly documenting their tools and by supporting implementations with scientific publications (Barnes 2010; Gorgolewski and Poldrack 2016).

#### 5.2. Standardizing preprocessing and workflows

Although the diversity in methodological alternatives has been key to extracting scientific insights from neuroimaging data, appropriately combining heterogeneous tools into complete workflows requires substantial expertise. Traditionally, researchers used default workflows distributed along with individual software packages, or alternatively, individual laboratories have developed in-house analysis workflows that resulted in highly specialized

pipelines. Such pipelines are often not thoroughly validated and difficult to reuse due to lack of documentation or accessibility to outside labs. In response, several community-led efforts have spearheaded the development of robust, standardized workflows.

An early effort towards workflow standardization was the Configurable Pipeline for the Analysis of Connectomes (C-PAC; Craddock et al. 2013), which is a "nose-to-tail" preprocessing and analysis pipeline for resting state fMRI. C-PAC offers a comprehensive configuration file, editable directly with a text editor or through C-PAC's graphical user-interface, prescribing all the tools and parameters to be executed, and thereby making strides towards keeping methodological decisions closely traced. Similarly, large-scale acquisition initiatives released workflows tailored for their official imaging protocols (e.g., the HCP Pipelines (Glasser et al. 2013) and the UK Biobank (Alfaro-Almagro et al. 2016)). Conversely, fMRIPrep (Esteban et al. 2019) proposed the alternative approach of restricting the pipeline goals to the preprocessing step, while accepting the maximum diversity possible of the input data (i.e., not tailored to a particular experimental design or analysis-agnosticity). This approach has recently been proposed for additional modalities (e.g., dMRI, ASL, PET) and population/species of interest (e.g., fMRIPrep-rodents, fMRIPrep-infants) under common framework called NiPreps (Neurolmaging а PREProcessing toolS). NiPreps is a community-led endeavor with the goal of ensuring the generalization of the building blocks of preprocessing across modalities (e.g., the alignment of fMRI and dMRI with the same participant / animal's anatomical image) and specimens (e.g., using the same brain extraction from anatomical data using the same algorithm and implementation on both human adults and rodents). Similar standardization efforts are starting to be adopted for EEG (Desjardins et al. 2021) and MEG (e.g., MNE-BIDS pipeline; Jas et al. 2018). Further examples of standardized workflows are found in Table S1.

An additional and relevant premise of standardized workflows is transparency — tools must be transparent not only in their implementation, but also in their reporting. For example, fMRIPrep produces visual reports with the double goal of assessing the quality of results, and also providing the researcher with a resource to comprehensively understand every step of the workflow. In addition, the report includes a text description which comprehensively describes each major step in the pipeline, including the exact software version and principle citation. This text, referred to as the "citation boilerplate", is released under a public domain license, and therefore can be included verbatim in researcher's manuscripts, facilitating accurate reporting and proper referencing of academic software. A final relevant aspect towards transparency is the comprehensive documentation of pipelines.

In most cases, standardized workflows preprocess datasets in a fully automated manner, taking a BIDS dataset as input and outputting data that is ready for subsequent analysis with little manual intervention. Importantly, such workflows are typically designed to be as robust as possible to diverse input data (e.g., with varying parameters or sampling distant populations), a challenge that is facilitated by data standardization (i.e., BIDS). Additionally, workflows must be portable, enabling users to execute them in a wide variety of environments. A key technology in this endeavor is containers-such as Docker and Apptainer/Singularity—which facilitate packaging specific versions of heterogeneous dependencies while ensuring cross-platform compatibility (e.g., high-performance computing clusters, desktop, or cloud services). The BIDS apps framework (section 4.1) leverages containers by standardizing input parameters to make it trivially easy to execute a wide variety of standardized workflows on BIDS datasets. An example of a higher-level combination of workflows is found in Esteban et al. (2020), which describes an MRI research protocol using MRIQC and fMRIPrep. Finally, recent efforts to standardize the outputs of workflows (BIDS Derivatives), further enhances the interoperability of workflows, by ensuring their outputs are compatible with subsequent analysis.

#### 5.3. Statistical modeling and advanced analysis

Analysis of neuroimaging data is particularly heterogeneous and prone to excessive analytical flexibility and underspecified reporting. Whereas preprocessing is ideally performed once per dataset, there is often a large number of types of analyses that may be used with the preprocessed data. In MRI and fNIRS, for example, analyses range from multi-stage general linear models (GLMs), multivariable decoding analyses, to anatomical and functional connectivity, and more. In PET, analyses consist of region-wise averaging, although voxel-wise approaches are gaining popularity, followed by kinetic modeling and subsequent statistical analyses, which can be GLM or more advanced, such as latent variable models. In MEG and EEG, the broad variety includes analyses such as evoked response potentials, power spectral density, source reconstructions, time-frequency, connectivity, advanced statistics and more. Each type of analysis also has a wide variety of subtypes, parameters, and statistical models that can be specified, and the form of that specification varies across the dozens of analysis packages that implement each type of analysis.

Data analysis reporting is made more transparent when sharing code that relies on open-source software. A prime example is SPM (Flandin and Friston 2008), which has been open source since its inception in 1991. Additional widely used open-source tools for data analysis are FSL and AFNI for MRI, and some examples of reproducible pipelines for MEG and EEG developed based on each of the following software: EEGLAB (Pernet, Martinez-Cancino, et al. 2020) Fieldtrip (Andersen 2018b; M. Meyer et al. 2021; Popov, Oostenveld, and Schoffelen 2018), Brainstorm (Niso et al. 2019; Tadel et al. 2019), SPM (Henson et al. 2019) and MNE-Python (Andersen 2018a; van Vliet et al. 2018; Jas et al. 2018) (see Niso et al. (2022) for a detailed review on main EEG and MEG open toolboxes and reproducible pipelines). Reproducibility is also improved when relying on modular and well-documented software such as Nilearn, which offers versatile methods to perform advanced analyses of fMRI data, from GLM to connectomic and machine learning (Abraham et al., 2014). Ideally, a single analysis script is made creating a report, from signal extraction, data analysis, and reproducing all figures.

An additional challenge for the reproducibility of analysis workflows is the representation of statistical models across distinct implementations of analysis software. For example, GLM approaches to analyze fMRI time series are prevalent and supported by all of the major statistical packages (e.g., AFNI, SPM, FSL, Nilearn). However, specifying equivalent models across packages is non-trivial and requires time consuming package specific model specification (Pernet 2014), which obfuscates details of the statistical model, exacerbates variability across pipelines, and makes it difficult to perform multiverse analyses (see section 5.4). The BIDS Stats Model (BIDS-SM, see Table S1) specification has been proposed as a implementation-independent representation of fMRI GLM models; BIDS-SM describes the inputs, steps, and specification details of GLM-type analyses, and encodes them in a machine readable JSON format. The PyBIDS library provides tooling to facilitate reading BIDS-SM, and FitLins (Markiewicz, De La Vega, et al. 2021) is a reference workflow that fits BIDS-SM using AFNI or Nilearn. The transformative potential of BIDS-SM is

showcased by Neuroscout (de la Vega et al. 2022), a turnkey platform for fast and flexible neuroimaging analysis. Neuroscout provides a user-friendly web application for creating BIDS-SM on a curated set of public neuroimaging datasets, and leverages FitLins to fit statistical models in a fully reproducible and portable workflow. By standardizing the entire process of statistical modeling, users can formally specify a hypothesis and produce statistical results in a matter of minutes, while simultaneously ensuring a fully reproducible and transparent analysis that can be readily disseminated to the scientific community.

#### 5.4. Multiverse analysis

The variety of data workflows reflects the enormous interest and the need for novel software instruments, but it also poses an important risk to reproducibility. The multitude of possible combinations of methods and parameters in each of the analysis steps creates an extremely large number of combinations to select from. This problem is often referred to as "researcher degrees of freedom" or "the garden of forking paths" (Gelman and Loken 2013). Importantly, analytical choices affect results. This has been shown for preprocessing of fMRI data already back in 2004 (Strother et al. 2004). More work in this direction followed in 2012 (Churchill, Oder, et al. 2012; Churchill, Yourganov, et al. 2012). While this work focused mainly on the aspect of tailoring preprocessing to e.g. maximize predictive models, recent efforts in fMRI (task fMRI: (Botvinik-Nezer et al. 2020; Carp 2012a); preprocessing of resting-state fMRI: (Li et al. 2021)) and PET (specifically for preprocessing: Nørgaard et al. 2020) focused more on the variability of outcomes in general when analysis pipelines were varied. In addition, recent studies showed high variability in diffusion-based tractography dissection (Schilling et al. 2021) and event-related potentials in EEG preprocessing (Šoškić et al. 2021; Clayson et al. 2021). Another large-scale attempt to estimate the analytical variability for EEG, EEGManyPipelines (see Table S1), is currently ongoing.

The converging findings of these studies across modalities suggest that it is important to test the robustness of reported results to specific analytical choices. One proposed solution to tackle the analytical variability, where many different analytical approaches are compared, is multiverse analysis (Hall et al. 2022). There are two broad types of multiverse tools. In a "numerical instabilities" approach, different setups and numerical errors or uncertainties in computational tools are evaluated, analyses are rerun several times, and variability, robustness, and "mean answer" are estimated (Gregory Kiar et al. 2020). One tool of this type that is being developed is "Fuzzy" (Greg Kiar et al. 2021). Alternatively, in a

"classic multiverse analysis", multiple pipelines are used with the same data and the results are compared across pipelines. Such an analysis could be conducted by a single or by multiple researchers (Aczel et al. 2021). Although multiverse analysis was suggested before in other fields (Steegen et al. 2016; Simonsohn, Simmons, and Nelson 2015; Patel, Burford, and Ioannidis 2015), there are not yet mature "classic multiverse analysis" tools for high-dimensional data like in neuroimaging. Explorable Multiverse Analyses is an R-tool that allows the readers to explore different statistical approaches in a paper (Dragicevic et al. 2019). Other tools, such as the Python-based Boba (Liu et al. 2021), aim to facilitate multiverse analyses by allowing users to specify the shared and the varying parts of the code only once and by providing useful visualizations of the pipelines and results. However, these tools currently fit simpler analyses and datasets compared to the ones common in neuroimaging.

In neuroimaging, recent progress has been made in creating infrastructure for multiverse analysis in fMRI, based on the C-PAC tool (see section 5.2; Li et al. 2021). Ongoing efforts to formalize machine-readable standards for statistical models (BIDS-SM) and pipelines to estimate them (e.g., FitLins; Markiewicz, De La Vega, et al. 2021), and their integration with datasets using platforms such as brainlife.io (Avesani et al., 2019), could facilitate the development of multiverse tools. In order to make sense of a multiverse analysis, one needs methods to test for convergence across results of diverse analysis pipelines with the same data. Such a method for fMRI image-based meta-analysis was recently used in NARPS (Botvinik-Nezer et al. 2020) as well as in subsequent projects (Bowring, Nichols, and Maumet 2021). Another simple statistical approach to a multiverse analysis was presented with PET data (Nørgaard, Ozenne, et al. 2019), although it lacks statistical power, due to the use of a very conservative statistic. A different approach is to use active learning to approximate the whole multiverse space (Dafflon et al. 2020). Moreover, Boos et al. (2021) provided an online application to explore the effects of the choice of parameters on the results (data-driven auditory encoding, see Table S1). Progress is still needed until such tools are mature enough to allow scalable multiverse analysis in neuroimaging.

## 6. Research dissemination

Through the whole research cycle a range of outputs far beyond publications are produced, and each of them can have different levels of reproducibility and openness. For shared resources to be useful, they need to follow the FAIR principles (Wilkinson et al. 2016), to ensure they are: *Findable* (e.g., using persistent identifiers, such as Digital Object Identifiers (DOI) or Research Resource Identifiers (RRIDs), and described with rich metadata indexed in a searchable resource), *Accessible* (e.g., shared in public repositories, under open access or controlled access depending on regulations, so they can be retrievable by their identifier using standardized communication protocols), *Interoperable* (e.g., richly described, with detailed provenance and an appropriate license). Indeed, without a license, materials (data, code, etc.) become unusable by the community due to the lack of permission and conditions for reuse, copy, modification, or distribution. Therefore, consenting through a license is essential for any material to be publicly shared.

A useful general purpose resource, beyond neuroimaging, to find practical guidelines on reproducible research, project design, communication, collaboration, and ethics is *The Turing Way* (TTW, The Turing Way Community et al. 2019, see Table S1). TTW is an open collaborative community-driven project, aiming to make data science accessible and comprehensible to ensure more reproducible and reusable projects.



#### Figure 5. Dissemination

Sources: Icons from the Noun Project: Data Sharing by Design Circle; Share Code by Danil Polshin; Data by Nirbhay; Publication by Adrien Coquet; Broadcast by Amy Chiang; Logos: used with permission by the copyright holders.

#### 6.1. Data sharing

Making data available to the community is important for reproducibility, allows more scientific knowledge to be obtained from the same number of participants (animal or

human), and also enables scientists to learn and teach others to reuse data, develop new analysis techniques, advance scientific hypotheses, and combine data in mega- or meta-analyses (Poldrack and Gorgolewski 2014; Laird 2021; Madan 2021). Moreover, the willingness to share has been shown to be positively related to the quality of the study (Wicherts, Bakker, and Molenaar 2011). Because of the many advantages data sharing brings to the scientific community (Milham et al. 2018), more and more journals and funding agencies are requiring scientists to make their data public (curated and archived with a public record, but controlled access) or open (public data with uncontrolled access) upon the completion of the study (see section 7).

For data to be interoperable and reusable, it should be organized following an accepted standard, such as BIDS (section 4.1) and with at least a minimal set of metadata. Free data-sharing platforms are available for publicly sharing neuroimaging data, such as OpenNeuro (Markiewicz, Gorgolewski, et al. 2021), brainlife (Avesani et al. 2019), GIN (G-Node Infrastructure), Distributed Archives for Neurophysiology Data Integration (DANDI), International Neuroimaging Data-Sharing Initiative (INDI), NeuroImaging Tools & Resources Collaborator (NITRC), etc. (see Table S1). Data could also be shared on institutional and funder archives such as the National Institute of Mental Health Data Archive (NDA); on dedicated repositories, such as the the Cambridge Centre for Ageing and Neuroscience, Cam-CAN (Shafto et al. 2014; Taylor et al. 2017) or The Open MEG Archive, OMEGA (Niso et al. 2016); or on generic archives that are not neuroscience or neuroimaging specific, such as figshare, GitHub, the Open Science Framework, and Zenodo. If allowed by the law and participants' consent (see section 2.3), data sharing can be made open, or at least public.

Once curated and archived, data can further benefit the individual researcher, for example by adding them to the scientific literature in the form of data descriptors. Such an article type is not intended to communicate findings or interpretations but rather to provide detailed information about how the dataset was collected, what it includes and how it could be used, along with the shared data. In addition, an "open science badge" for data sharing is available in an increasing number of scientific journals (Kidwell et al. 2016) and some prizes are also available as a recognition for such efforts (e.g., OHBM's Data Sharing prize).

#### 6.2. Methodological transparency

Documenting performed analysis steps is key for reproducing studies' results. For studies containing a small number of procedures, the methods section of an article could detail them in full length. This is, however, often not the case in current neuroimaging studies, where authors may need to summarize content in order to fit into the designated space, probably omitting relevant details. Therefore, the programming code itself becomes the most accurate source of the exact analysis steps performed on the data, and is anyway needed for reproducibility. Thus, it needs to be organized and clear (see recommendations suggested by Sandve et al. 2013; van Vliet 2020; Wilson et al. 2017), otherwise, results may not be reproducible, or even correct (Casadevall and Fang 2014; Pavlov et al. 2021). It should be noted that sharing an imperfect code is still much better than not sharing at all (Barnes 2010; Gorgolewski and Poldrack 2016).

While GUIs are a great and interactive way to learn to analyze data, one has to pay special attention to properly report the steps followed, as clicks are more difficult to be reported and reproduced than code (Pernet and Poline 2015). Some toolboxes using GUIs keep track of data 'history' and 'provenance' (e.g., Brainlife, Brainstorm, EEGLAB, FSL's Feat tool) facilitating this task. Efforts are being put to improve these features.

To ensure long-term preservation of the shared code, we suggest using version control systems such as Git, and social coding platforms such as GitHub in combination with an archival database for assigning permanent DOI to code served for research, for instance, Zenodo (Troupin et al. 2018), brainlife.io/apps (Avesani et al. 2019) or Software Heritage (Di Cosmo 2018). These platforms help keep a snapshot of the version of the code used for the paper published, allowing exact reproduction in case of later code updates.

#### 6.3. Derived data sharing

Sharing data derivatives is perhaps the most critical yet most challenging aspect of data sharing in support of reproducible science. The BIDS standard provides a general description of derivative data (i.e. common derivatives) and is actively working towards extending advanced specific derivatives for the different neuroimaging modalities. Yet as of today, standards for the description of advanced derivatives (such as activation or connectivity maps, or diffusion measures) are not available or mature for wide use. As a result, to date, the community lacks clear guidance and tools on how derived data should

be organized to maximize its reuse and to encompass its provenance, and where such data could be shared.

Solutions for sharing derivatives comprise a mixture of in-house and semi-standardized data-tracking and representation methods. Examples of data-derivative sharing are the high-profile, centralized projects, such as the Human Connectome Projects (Van Essen et al. 2012), Ebrains of the Human Brain Project (Amunts et al. 2019, 2016), the UK-Biobank (Alfaro-Almagro et al. 2016), the NKI-Rockland sample (Nooner et al. 2012), and the Adolescent Brain Cognitive Development (ABCD; Feldstein Ewing and Luciana 2018) to name a few (see Table S1). These projects have developed project-specific solutions and in doing so also have provided a first-level implementation of what could be considered a data derivative standard. Yet, these projects are far from being open or community-developed as they must be centrally governed and mandated by the directives of the research plan.

As a result of the paucity of community-oriented standards, archives and software methods, sharing highly-processed neuroimaging data is still the frontier of reproducible science. One community-open archive for highly processed neuroimaging data derivatives is NeuroVault (Gorgolewski et al. 2015). The archive accepts brain statistical maps derived from fMRI with the goal of being reused for meta-analytic studies. Data upload is open to researchers world-wide and the archive can accept brain maps submitted using most major formats but preferably using the NeuroImaging Data Model (NIDM; see section 4.2). Another interesting example for automated and standardized composition and sharing of derived data is TemplateFlow (Ciric et al. 2021), which provides an open and distributed framework for establishment, access, management, and vetting of reference anatomies and atlases.

Another general neuroimaging platform, which allows lowering the barrier to sharing highly processed data derivatives, is Brainlife. Brainlife provides methods for publishing derivatives integrated with the data-processing applications used for generating results from the data via easy-to-use web interfaces for data-upload, processing, and publishing. Different licenses can be selected when publishing a record, allowing reuse of data and derivatives to other researchers (see sources that support the selection of an appropriate license listed in Table S1).

Sharing lighter-weight data products such tables and figures is easier using generic repositories under, for example, CC-BY license. This allows authors to retain rights on the figures they created, and others to re-use their figures freely, either in other publications or for educational purposes. Additional material, such as slide presentations, or supporting content, should be shared using accessible formats (e.g., image files, pdf, PowerPoint slides, Markdown, jupyter notebooks, etc) via online repositories (e.g., GitHub or Bitbucket), or shareable links (e.g., Google Drive, Dropbox) or institutional platforms, with appropriate licenses to indicate how the work could be reused. Whenever possible, using platforms that ensure long-term preservation is recommended (e.g., Zenodo, FigShare, OSF).

#### 6.4. Publication of scientific results

Scientific papers are currently the most important means for disseminating research results. However, they should also be written with reproducibility in mind. Guidelines to improve reproducibility can support the writing. The OHBM Committee on Best Practices in Data Analysis and Sharing (COBIDAS), has been promoting best practices, including open science. Recommendations from the committees for MRI (Nichols et al. 2017) and MEG and EEG (Pernet, Garrido, et al. 2020) provide guidance on what to report. Other recent community efforts also led to guidelines for PET (Knudsen et al. 2020) and EEG reporting (e.g., Agreed Reporting Template for EEG Methodology - International Standard (ARTEM-IS) (Styles et al. 2021)). One tool that could help authors follow these guidelines while writing their report are their web-based apps (see Table S1). For the data description and preprocessing aspects, some tools (pyBIDS, bids-matlab) or pipelines (fMRIPrep) can also generate reports automatically, and/or method templates are provided (see section 5.2). Exact description of methods is mandatory for reproducibility alongside detailed quantitative reporting of results, and reporting of all results is necessary for replicability.

In recent years, it has become very common in neuroimaging to publish papers as preprints, on servers such as bioRxiv, medRxiv, PsyArXiv or OSF (see Table S1), prior to peer review in scientific journals. Preprints are publicly available, expedite the process of releasing new findings, and also, importantly, allow authors to get feedback on their paper from a broader audience prior to final publication (Moshontz et al. 2021). There are also initiatives for open community reviews of preprints, such as PREreview. Other initiatives have emerged to adapt to this paradigm shift, such as the recently launched Open Europe

Research platform for publication and open peer review, which also includes the different outputs obtained throughout the research cycle (e.g., study protocol, data, methods and brief reports through the process) for research stemming from Horizon 2020 and Horizon Europe funding. In addition, novel publication formats have been developed, like NeuroLibre, a preprint server to publish hybrid research objects including text, code, data, and runtime environment (DuPre et al. 2022). More traditional publishers have successfully partnered with companies such as CodeOcean (Cheifet 2021) to provide similar services.

Crucially, papers should be accessible to others, preferably to everyone. Many scientific publications are hidden behind paywalls, practically denying access from many people who could have gained from them. This is now slowly changing (Piwowar et al. 2018), with both researchers and funding agencies pushing towards open access, meaning that papers are fully open to all. Although the adoption of the concept of open access by major publishers is in itself a positive development, the way it was adopted could be considered arguable. For example, several journals considerably increased article processing charges (Khoo 2019; Budzinski et al. 2020) and some publishers implement massive tracking technology with the argument to protect their rights and offer the data or derivatives of them for sale, as a recent report published by the German Research Foundation criticizes (DFG 2021). This raises many questions, related, for example, to the influence publishers and their algorithms will have in the future on strategic decisions of science institutions and freedom of science.

#### 6.5. Beyond publication

The research lifecycle continues beyond paper publication. Disseminating scientific results to the broader scientific community and to the society in general is of utmost importance, to translate the newly acquired knowledge and give back to society. Oral and poster presentations at conferences contribute to the dissemination of results (including preliminary or intermediate results) within the scientific community, and also provide opportunities for feedback prior to publication. Workshops and other educational events contribute to expand the knowledge further and induce new communities. Popular and social media (e.g., press releases, interviews, podcasts, blog posts, twitter, facebook, linkedin, youtube, etc.) may outreach an even wider and more heterogeneous audience. Different types of audiences may have different degrees of expertise and scientific knowledge, hence, for an effective communication, each of the outreach events should

adapt accordingly (e.g., avoiding jargon and over interpretation, identifying your audience, promoting accessibility in content and language (Amano et al. 2021), and considering disabilities). See the TTW Guide for Communication for recommendations (Table S1). Slides presentations, and further outreach content should be shared FAIRly for higher impact (see section 6.3).

Hackathons - such as the Brainhacks in the neuroimaging community (Gau et al. 2021) - typically offer times for "unconferences" in which attendees can propose a short talk to present some work-in-progress, an open question, or any other topic they wish to discuss with other participants. This deviates from more typical conferences in which only well-polished, finalized results can be presented. Other initiatives, such as Neuromatch Academy, Neurohackademy, OHBM Open Science Room, and Brainhack school MLT facilitate open science and provide opportunities for researchers to learn and get hands-on experience with open science practices, and also to engage with other researchers in the community. Those hackathons and the related online communities are also well-known as kick-starters for the development of community tools and standards in which researchers and engineers from different labs join forces. As those tools and standards get shaped, typically in multi-lab collaborations, researchers get the chance to exchange their views and practices. Overall, open science practices, slowly but surely, help shape a research culture that is driven by open collaborative communities rather than single groups of researchers.

#### 6.6. Towards inclusive, diverse and community driven research

Taken to the next level, the described developments and introduced tools provide an opportunity for a paradigm shift: rather than carrying out a study from inception to results and only then disseminating the findings to the community, researchers now get multiple opportunities to share their ideas and results as they are being developed. Scientific research can now become more transparent, inclusive and collaborative throughout the research cycle.

In collaborative projects, having a well defined Code of Conduct is critical to ensure a welcoming and inclusive space for everyone regardless of background or identity. Initiatives such as TTW or the OHBM Conference have detailed Code of Conducts that can be of inspiration to adapt and use in new collaborative projects.

Community efforts should aim for equity, diversity and inclusivity. Unfortunately, as a reflection of our societies and cultures, the lack of these values is also prevalent in research and academia, contributing to gender bias, marginalization, and underrepresentation of racial, ethnic, and cultural minorities (Leslie et al. 2015; Dworkin et al. 2020; Hofstra et al. 2020). These inequalities are produced at all stages, even at the time of recruiting participant samples for experiments (Henrich, Heine, and Norenzayan 2010; Laird 2021; Forbes, Aneja, and Guest 2021) (see examples in section 2). Importantly, observing equity, diversity, and inclusivity in the recruitment of study participants can also improve the quality of research results (e.g., Baggio et al. 2013). Over the past years, the awareness and number of initiatives to mitigate bias and inequity at individual and institutional levels are growing (Llorens et al. 2021; Levitis et al. 2021; Malkinson et al. 2021; Schreiweis et al. 2019). These aim to produce better research powered by a broader range of perspectives and ideas and to reduce the negative impact on the careers, work-life balance, and mental health of underrepresented groups. By providing open resources and promoting welcoming and inclusive spaces, we are also contributing to empower minoritized communities to conduct high quality research and to take an active role in the development and leadership of neuroimaging, which will accelerate discoveries, and ultimately, advance science.

## 7. Conclusions

Recent years have marked the rise of "open science", producing numerous tools and practices that enhance the reproducibility, transparency, inclusivity and diversity of research in general and in neuroimaging specifically. These tools and practices yield profits at multiple levels ranging from the individual researcher to the society. At the societal level, they can increase transparency and credibility of research, foster the public understanding of scientific findings, and promote participation. Higher credibility of research results in the public can support decision-makers in basing their decisions on scientific knowledge. For the scientific community, such practices increase the quality and validity of scientific products. They also increase the cost-effectiveness of invested resources (money, time, personnel, etc.), by, for example, enabling reuse of collected data and developed methods and tools. For individual researchers, the application of open science practices can improve their chances for funding and recognition in the community by meeting related requirements from funding institutions, agencies, and scientific journals. Furthermore, the use of open

science tools and practices can ease the use of novel analysis techniques and open the researcher new opportunities for collaborations and contributions.

The abundance of tools and practices for open and reproducible neuroimaging is both promising and challenging. This review was written to assist neuroimaging researchers to make informed and sustainable choices with regard to their implementation in their own research, by understanding the purpose of each tool, how they interact together, how to use them and where to look for further information. We believe it will prove helpful for researchers and institutions to make a successful and sustainable move towards open and reproducible science, contributing to improving scientific research and, ultimately, accelerating scientific discoveries.

## 8. Author Contributions

Author contributions are reported following the CRediT Contributor Roles:

Conceptualization: G.N., R.B.-N., S.A., A.D.L.V., O.E., J.A.E., Y.O.H., P.H., A.K., C.M., C.R.P., F.P., N.Q., A.S.W., and J.W.R. Project administration: G.N., R.B.-N., and J.W.R. Supervision: G.N., R.B.-N., and J.W.R. Writing - original draft: G.N., R.B.-N., S.A., A.D.L.V., O.E., J.A.E., K.F., M.G., Y.O.H., P.H., A.K., D.B.K., C.M., C.R.P., F.P., N.Q., T.S., A.S.W., and J.W.R. Writing - review & editing: G.N., R.B.-N., S.A., A.D.L.V., O.E., J.A.E., K.F., M.G., C.M., C.J.M., C.R.P., F.P., N.Q., T.S., A.S.W., and J.W.R. Writing - review & editing: G.N., R.B.-N., S.A., A.D.L.V., O.E., J.A.E., K.F., M.G., C.M., C.J.M., C.R.P., F.P., N.Q., T.S., A.S.W., and J.W.R.

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#### 8.2. Conflict of Interest

The authors declare no conflict of interest related to this work.

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