

PLOS Science Wednesday: Hi Reddit, We're Ben Inglis and JB Poline, and we're here to discuss methods for fMRI acquisition and analysis — Ask Us Anything!

PLOSScienceWednesday¹ and r/Science AMAs¹

¹Affiliation not available

April 17, 2023

[REDDIT](#)

PLOS Science Wednesday: Hi Reddit, We're Ben Inglis and JB Poline, and we're here to discuss methods for fMRI acquisition and analysis — Ask Us Anything!

PLOSSCIENCEWEDNESDAY [R/SCIENCE](#)

ABSTRACT

[removed]

[READ REVIEWS](#)

[WRITE A REVIEW](#)

CORRESPONDENCE:

DATE RECEIVED:
October 15, 2015

DOI:
10.15200/winn.144482.24426

ARCHIVED:
October 14, 2015

CITATION:
PLOSscienceWednesday ,
r/Science , PLOS Science
Wednesday: Hi Reddit, We're
Ben Inglis and JB Poline, and
we're here to discuss methods
for fMRI acquisition and
analysis — Ask Us Anything!,
The Winnower
2:e144482.24426 , 2015 , DOI:
[10.15200/winn.144482.24426](https://doi.org/10.15200/winn.144482.24426)

© et al. This article is distributed under the terms of the [Creative Commons Attribution 4.0 International License](#), which permits unrestricted use, distribution, and redistribution in any medium, provided that the original author and source are credited.



JB - Just how bad is reproducibility in the neuroimaging field? Obviously reproducibility is a huge issue in science overall but is it particularly worse for imaging? How standardized are the statistical analyses for things like regional brain volume and activity?

I'm interested because I'm collaborating with some people on a few side projects that are combining fMRI and genetics. And as the geneticist in the project I've only got a vague understanding of the imaging analyses the other people are running.

[ricker2005](#)

JB: Many of us suspect that reproducibility is poor, but we have no quantification of this. Those who believe that reproducibility is not good have good arguments: there is the power issue (Button et al, 2013) : many neuroimaging studies have around 25 subjects, and there is in general a lot of exploration of the data which leads to p-hacking. There are also honest mistakes in the analysis scripts. For large datasets, I would think that the reproducibility is better because of the number of subjects and because analyses are more standardized (less p-hacking). How we can quantify this is to me a key question, but in general, the pressure for publication and a the characteristics of the neuroimaging domain (see Ioannidis 2005 corollaries) makes me think that reproducibility is likely an important issue in our field.

Hi there! I'm also a physicist working in medical imaging, and I'm frequently a critic of your methodologies (i.e.: Ashburner and Friston are my sworn enemies. I also see that Poline should be on my list as well, having signed the original SPM paper :D)

I have lots of complaints against imaging neuroscience, mostly variations about the fact that I think that it's basically data dredging to the extreme and that it lacks biological hypothesis. Probably nothing you haven't heard of, the usual "VBM shouldn't be used with imperfectly registered images", z-scores have no biological meaning (= use units that have meaning!), try to reduce multiple comparisons etc... In particular I specifically don't like the "connectomics" field. How much do we trust that these have a biological meaning and how much can they be just random noise amplified by regularizers?

I know I'm being pretty vague so I'll say... What's your opinion about the most common

criticism of fMRI and SPM (VBM?) studies?

[lucaxx85](#)

BI: I'll let JB comment on the stats and limitations on interpretation, I'll just make one comment on fMRI in its entirety. And I'll paraphrase Winston Churchill: fMRI is the worst form of brain imaging, except for all the others. It is presently the only way we can image entire brains non-invasively and repeatedly. Unless and until a better whole brain imaging method comes along, if we're interested in brains then we have to deal with motion, poor statistics, etc. and try to do better and better work. There is definitely a basis for biological meaning - we know that brain activity takes energy and changes metabolic demand. It may be that we're using an empty beer bottle as a telescope but at the moment it's the only "lens" we have for whole brains. We can use EEG, MEG, fNIRS for some experiments from some parts of the brain, but for other experiments fMRI is the only game in town. If/when someone invents a better method, expect those doing fMRI to flee towards it post haste!

Thanks for doing this Drs. Inglis and Poline. I'm a big fan of practiCal, it has helped me throughout the years as a fellow MR Physicist. We've actually had some contact in the past. Dr. Inglis, when we were trying to sort out the dreaded Siemens vibration artifact (argh!) at UCI and Berkeley. Dr. Poline, I believe we've met briefly in Irvine at IIGC, likely not in a memorable fashion. In any case, I mostly wanted to thank you for public outreach efforts here today. But a couple questions off the top of my head for fun:

Dr. Inglis: My focus is in neonatal MR imaging (body and brain). While there are obvious and expected differences in the newborn versus, say 1 year old brain, I often wonder if imaging findings comparing brain development are amplified simply by the sheer size differences of the brain as it matures in early-life. That is, partial voluming is significantly different in a smaller brain when voxel size is held constant. Can you speak generally on what effects you might expect in resting state connectivity maps with *effectively* different resolutions (same voxel size, different sized brain)?

Dr. Poline: White matter, CSF and whole brain masks are often used as nuisance regressors for physiological signal in resting state fMRI when physio data for other correction techniques are not available. I'd imagine these are highly co-linear regressors. Do you see a role for orthogonalization of these parameters when you are simply trying to residualize the data?

Thanks again!

[jerodras](#)

JB: You should not have to orthogonalize your nuisance regressors. In fact, orthogonalization is very rarely needed (and sometimes mis-used: see Jeanette Mumford's recent Plos paper where this is clarified). When you regress out several nuisance regressors, you are removing all signals that 'correlate' with this set of regressors, and you would be doing the same thing if you were to orthogonalize some regressors with respect to the others. Mathematically, the space spanned by the set of orthogonalized regressors is the same as the space spanned by the original regressors, only your estimated parameters will change, and in case of nuisance signals you generally are not interested in these.

Thanks for doing this Drs. Inglis and Poline. I'm a big fan of practiCal, it has helped me throughout the years as a fellow MR Physicist. We've actually had some contact in the past. Dr. Inglis, when we were trying to sort out the dreaded Siemens vibration artifact (argh!) at UCI and Berkeley. Dr. Poline, I believe we've met briefly in Irvine at IIGC, likely not in a memorable fashion. In any case, I mostly wanted to thank you for public outreach efforts here today. But a couple questions off the top of my head for fun:

Dr. Inglis: My focus is in neonatal MR imaging (body and brain). While there are obvious and expected differences in the newborn versus, say 1 year old brain, I often wonder if imaging findings comparing brain development are amplified simply by the sheer size differences of the brain as it matures in early-life. That is, partial voluming is significantly different in a smaller brain when voxel size is held constant. Can you speak generally on what effects you might expect in resting state connectivity maps with *effectively* different resolutions (same voxel size, different sized brain)?

Dr. Poline: White matter, CSF and whole brain masks are often used as nuisance regressors for physiological signal in resting state fMRI when physio data for other correction techniques are not available. I'd imagine these are highly co-linear regressors. Do you see a role for orthogonalization of these parameters when you are simply trying to residualize the data?

Thanks again!

[jerodras](#)

BI: Thanks for the thanks! It's been really fun having a blog, I encourage all scientists to try it at some point. For me it's been a way to get to hear about interesting problems that I wouldn't otherwise have had access to, so it's definitely a two way street. Re. effective resolutions and partial volume effects, I believe this has been brought up as a major limitation in development studies and even in studies comparing men vs women, where women's brains are on average slightly smaller than men's. Using the same absolute resolution thus imparts some sort of bias. What can be done here? I'm afraid I don't know. You could try smoothing to the same effective resolution based on brain dimensions, perhaps. I couldn't even guess whether this would help or hinder discovery of interesting features. Perhaps one way out of the dilemma would be to try to identify a factor that doesn't depend on effective resolution, a ratio or some other way to factor out the absolute brain size. For fMRI specifically, resting or task-based, in addition to changing effective resolution with development (or brain size), we also can expect non-stationary neurovascular coupling. So again we need ways to factor out concomitant changes in physiology, e.g. hematocrit and other vascular health issues. (This is a big deal in assessing pathology in the brain, too, if one wants to compare to normal brains.) There are ways to approach calibration of vascular dynamics, normalization for hematocrit and so forth, and each step may help address one of the potential confounds, but always there is the chance that what you're measuring has a concomitant change that thwarts you. With regard to connectivity maps at any given stage, the best I can suggest off the top of my head is to try to estimate the effects of resolution. Take your data set at full nominal resolution and compute your outcome measures. Then redo the analysis but after smoothing by some amount. What changes? If you were interested in this general question of effective resolution then you might start with a simple task in adults - say a cued motor response where certain connectivity is predictable - and then do the smoothing assessment. What changes? It won't fix the problem but it could increase your understanding!

Hi! Here's a simple question to get you guys started. Can you explain how an fMRI works to a 5 year old? Can you also explain the difference between fMRI and MRI in this way too?

[legends444](#)

BI: Simple question? Gotta be the hardest you could ask! ;-) Okay, let me try. MRI primarily maps the amount of water in the body. The image brightness goes up as the amount of water in a tissue goes up, modified slightly by the way water interacts with the tissues being investigated. So in the brain we have, essentially, gray matter (cell bodies like neurons), white matter (mostly myelinated axons that connect regions of gray matter), blood and cerebrospinal fluid (CSF). CSF is very close to being pure water. In each of these four substances the MRI will reflect the concentration of water (100% water for CSF, 60-80% for GM, WM & blood) modified by how that water interacts with the other substances present. Water interacts differently with heme molecules in blood than with the cellular machinery of neurons, for example. So we can differentiate all the different constituents based on water

concentration as well as water-large molecule dynamics. Functional MRI is based on the same thing but we add an extra dependence to the signal. Specifically, we add to the image contrast a dependence on the amount of oxygen in the venous blood. In a normal brain the arterial blood - that coming directly from the lungs - is close to fully oxygenated. The oxygen is carried on hemoglobin molecules. Then, when it reaches tissue - in this case the brain - some of the oxygen gets used up as the brain converts fuel (glucose) into useful work. But there is an excess of oxygen delivered to the tissue. If we look at the venous blood - the blood after it's passed through the tissue and is being returned to the lungs for new oxygen - then we find there is something like 60% oxygenation of hemoglobin, and therefore 40% or so has no oxygen attached. We call this 40% fraction the deoxygenated fraction. It turns out that venous and arterial blood differ in their magnetic properties. (They also differ in color, with arteries more red and veins more blue.) The deoxygenated hemoglobin has a much stronger magnetism than oxygenated hemoglobin. So if there is a change in the amount of deoxygenated hemoglobin in the venous blood we can detect that change in our image. We still have the other factors giving an image: the concentration of water and the water interactions with large molecules. But now we've added a new factor: a dependence of the image brightness on the amount of deoxyhemoglobin in the venous blood. If we acquire a series of images over, say, minutes then we find that the water concentration and the water-large molecule dynamics remain essentially constant whereas there are changes in the amount of deoxygenated blood depending on the activity level across the brain. Our functional images are maps of the changes in the deoxygenated blood.

I'll add that this isn't the only way to do functional imaging with MRI but it is the most common way.

Can fMRI be used as a lie detector?

[zombie1939](#)

BI: In someone who is compliant the answer is, perhaps. But it has been shown that simple countermeasures will defeat it in someone who wants to conceal the truth, e.g. <http://www.ncbi.nlm.nih.gov/pubmed/21111834>. There is also the issue of motion sensitivity generally. Someone who doesn't want their brain scanned with fMRI can defeat it simply by not staying still!

There is one other factor that we should always bear in mind when it comes to lie detection, but it's not within my expertise to give you a deeper answer. We must note that the definition of lies and truth is quite a fluid concept. People remember incorrectly, memories of events change over time, etc. It's entirely feasible that someone will believe some memory is "the truth" when it's not accurate. As far as I know, fMRI lie detection has nothing to say about these problems. There's interesting neuroscience and psychology going on! So there are technical as well as principled objections to doing lie detection with fMRI. Like the infamous polygraph, it can be shown to work as an experiment under lab conditions but "in the wild" the results will break down for many reasons.

Hi there,

I'm a graduate student working on quite a few neuroimaging projects. Is there a "best way" to deal with motion during a scan? Seems to be quite a controversial topic and everyone seems to have their own opinions, but a good solid starting point would be great!

[rez00t](#)

BI: Sure! The best way is to avoid it! :-)

And I'm not being facetious. The more you can prevent motion the better. We are putting a lot of work into custom head holders. Bite bars have a checkered history and few subjects will use them for long, but they help. Sadly, if you have motion during your run then you have imparted a threshold on the information you can tease out, and no amount of post processing is going to turn the proverbial sow's ear into the silk purse. Start with silk (if you can)! I am hearing on the wind that optical tracking and feedback into the acquisition can work well to reduce motion contamination even in compliant subjects, but these methods require new hardware and sequences

and tend to be expensive. Whether they will become mainstream or be shown to be no better than better head restraint, only time will tell. For now, then, train your subjects on a mock scanner, make sure they're comfortable (so they don't fidget), have them swallow and adjust for comfort between runs then re-shim, and watch images as they acquire for signs of gross motion.

Grad student in neuroimaging here! Thanks so much for doing this AMA! I have two questions...

- 1. In terms of reproducibility - what do you think is holding the field back the most? I think strong nay-sayers would point fingers at poor statistics, but I think the field is making tremendous strides in statistical rigor with machine learning approaches, etc. Part of me thinks it is the cost of running fMRI studies that slows down progress at this point.**
- 2. Do you think analyzing images directly in k-space would improve the validity of results? Or perhaps would this be impossible to interpret/implement?**

[marsyred](#)

JB: For your first question: Generally speaking, I think this is the fact that we do not have a culture of reproducibility. This would entail making sure that data and code are shared, the analysis can therefore be checked, and one can build upon results that are validated. The cost of acquisition is certainly a factor, but if most of the acquired data were both shared and well documented we could certainly use larger datasets or validate results on other colleagues datasets.

For the second question: if the analysis is made of linear operations and if the reconstruction is also limited to linear operation (eg invers fourrier transform) then we should not gain from working in one space or the other. But as soon as we are using the structure of the brain (say to get a mask of where we have signal in the brain, or for realignment), then having a reconstructed image is necessary.

Grad student in neuroimaging here! Thanks so much for doing this AMA! I have two questions...

- 1. In terms of reproducibility - what do you think is holding the field back the most? I think strong nay-sayers would point fingers at poor statistics, but I think the field is making tremendous strides in statistical rigor with machine learning approaches, etc. Part of me thinks it is the cost of running fMRI studies that slows down progress at this point.**
- 2. Do you think analyzing images directly in k-space would improve the validity of results? Or perhaps would this be impossible to interpret/implement?**

[marsyred](#)

BI: Re. #2, I'm not aware of such methods or how it might be done. Even phase-sensitive imaging is used rarely, almost everyone uses magnitude (positive definite) images.

What are the advantages of fMRI compared to NIRS?

[Press10](#)

BI: Primarily, depth penetration. NIRS is great, a really useful tool with many features that compliment fMRI. But because of the scattering of light as well as absorption (which leads to heating), NIRS doesn't penetrate very deeply into the cortex. Many brain regions simply can't be measured with NIRS.

How did you get into your respective fields? What did your undergraduate and post-graduate years look like?

[schnuckiputz](#)

BI: There's a little of my background in the first question of my PLOS interview:

<http://blogs.plos.org/neuro/2015/01/28/fmri-under-the-microscope-an-interview-with-mri-physicist->

[practical-fmri/](#) But going back a step, I really got into chemistry because my two best high school teachers were chemistry teachers. I always loved physics but my physics teachers were never as engaging, sadly. So it wasn't until halfway through my BSc in chemistry that I began to migrate towards physical chemistry, then into nuclear magnetic resonance (NMR) and finally into MRI. My entry into functional MRI came because of circumstances: Berkeley was looking for someone to run their new Brain Imaging Center in 2000. Until then I'd worked mostly on methods applied to spinal cord injury, work that I'd done as a post doc at U Florida.

Welcome, and thank you for doing this AMA.

First off: I'm not in the imaging field, so please excuse (and correct!) any glaring mistakes.

As I understand it, because of individual variation in neuroanatomy, various smoothing and normalization techniques must be employed in order to compare fMRI data between subjects. One of the methods for doing so seems to be a sort of re-shaping of the subject's brain structure based on the basic structural information captured during the MRI session to conform with some default "idealized brain." This seems like it could be an ok approach for cortical brain regions that are fairly easily identified by [gyri and sulci](#) (the cortical mounds and grooves), but much more challenging to do with subcortical regions. So here's my question: would there be a benefit to employing [diffusion tensor imaging](#) (white matter tract mapping) to help identify individual differences in subcortical organization in order to fine-tune normalization of brain structure between subjects?

Cheers.

[AMPAglut](#)

JB: Actually, the sub-cortical regions are less variable than the cortical anatomy: the early atlases (eg Talairach) were designed for neurosurgery of the sub-cortical regions. But some cortical regions (frontal, parietal, ...) are very variable across subjects and finding good reproducible neuroanatomical landmarks is still challenge. The big neuroscience question remains : how we know or decide that a specific position in one brain for a given subject corresponds to another position in another subject brain. Anatomy (T1) is generally used, but diffusion or functional data can also be used to estimate this matching.

Many hanks for arranging the AMA. I have a practical and a rather general question. What do you recommend to check for the quality of preprocessed data, i.e. which metrics (e.g. SNR, CNR) do you use and which tools? What is your view on real-time fMRI neurofeedback and the aim to take neuroimaging to the therapeutic domaine?

[Arthurekorn](#)

JB: There are a number of metrics proposed for QA, but it really depends on what aspect you want to check. For spatial registration between functional and anatomical data or registration to a common template image I would recommend to visually check the results but also have some quantitative measure of the correspondance, for instance after segmentation and functional brain extraction you could measure the volume of the brain seen in the anatomical scan compared to the functional scan (given the slices acquired). For movement, you could look at the matrix of data in conjunction with values such frame displacements. Your question point to the fact that much more work needs to be done to have a list of standard measures for QA - there are a good number of these measures for raw (reconstructed) data but I have seen less of these for preprocessed, and again, they are no standards.

fMRI techniques identify regions of brain activity by detecting the lowered oxygen level in blood flowing out of different brain regions and infer activity with those with greatest depletion of

oxygen levels --ie a relative measure that is based on statistical differences. This seems to be highly vulnerable to noise and people tweaking the difference levels they decide are statistically significant. Are there any other molecular species that could be imaged instead or the oxygen depletion metabolite? e.g. areas with higher level of neurotransmitters actually detected in the intracellular medium? Also when fMRI first gained currency, the volume of imaged area was on the order of multiple cubic millimeters, which is vastly large compared to the sizes of individual neurons. The time interval over which the fMRI single value was integrated was also fairly long 0.5 seconds. Both of these seem to be very large and very long when talking about specific activation areas and sequencing in the brain. Have these values gotten any smaller and shorter?

[shiningPate](#)

Are there any other molecular species that could be imaged instead or the oxygen depletion metabolite? e.g. areas with higher level of neurotransmitters actually detected in the intracellular medium?

BI: It's possible to do pseudo-quantitative fMRI using cerebral blood flow (CBF) or volume (CBV) contrasts instead of BOLD. But like BOLD they are comparisons between two states and so the choice of the baseline, or control, state remains crucial. Neurotransmitters are so dilute (mM) that imaging is very hard with natural abundance. If you do a literature search for ¹³C-enriched methods, especially those employing offline hyperpolarization before administration, then there is some scope for mapping neurotransmitters. Otherwise, at natural abundance the best that's done at low field is localized spectroscopy. Perhaps these methods will advance as 7 T becomes more common.

Hi, I am curious about what research is being done around the country about concussion research and learning more about them? I know Boston U has the program teamed up with the NFL to laern more about CTE.

[sjc69er](#)

I'm afraid I've only heard of one specific program, administered at UCSF, but the main emphasis is diffusion imaging, perhaps with susceptibility-weighted imaging, as far as I know. Here are two starting links:

<https://www.ucsf.edu/news/2013/10/109851/traumatic-brain-injury-research-advances-188-million-nih-award-administered-ucsf>

<https://www.ucsf.edu/news/2014/10/118596/us-aims-traumatic-brain-injury-clinical-trial-success>

Hello! Thank you so much for doing this AMA. pratiCal has been such a big help to me over the past few years.

I've also struggled with reproducibility issues as well, but more specifically with the large variety of imaging softwares that are being used right now to analyze the same types of data sets. In your opinion, do you think that there should be an eventual shift in the field to consolidate software programs?

[heyitscate](#)

JB: Hi, you are welcome. The question of consolidating imaging software is a really interesting one to me. On one hand, we probably want to see our current software and new software implementing better data analysis methods and keep advancing on that front, and on the other hand you are right that there are few almost standard ways of processing data that could be recommended given our current knowledge. I am confident that these recommendations will however evolve. It seems to me that we should be working much more on better and standard ways to validate data analyses (with simulated or specific datasets). For a simple experiment, the most common software with their recommended

parametrisation are likely to give similar results, but for complex data the number of analysis choices that have to be made is important and sometimes rather arbitrary. One possible solution to avoid p-hacking is to acquire more data and split them, tune the analysis on part of the data and do the inference on the other part. There are also effort for standard reporting with the OHBM (COBIDAS led by T. Nichols) which should be out soon. The other aspect that needs to be developed is the provenance of the data and results. With the Neuroimaging Task Force of the INCF (International neuroinformatics coordinating facility) we are trying to develop this aspect in neuroimaging with NIDM. More generally speaking, if a paper is published, other researchers should be able to reproduce the results from the original data and analysis, which entails sharing data and analysis code, we would be much more efficient and we could check the validity of results if data and code sharing was the norm.

JB: Thanks for all the good questions - sorry it was not possible to answer all !

[PLOSscienceWednesday](#)

BI: Seconded!

Hi there, thanks for doing this AMA. I have read a rather recent approach by Xue et al in which additional DTI data is used in addition to fMRI data to determine functional connectivity more precisely. (<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4335182/>) What is your opinion on this approach?

[lorelon](#)

BI: I know the acquisition methods well but I'm afraid that the modeling is outside my expertise. Hopefully someone else with experience in connectivity will see your question.

How has fMRI affected the medical field and are there any advancements in the technology that could change clinical practices in the future?

[jkwalth17](#)

BI: I'm not up to date on the use of fMRI in the clinic but there have been efforts to use it for pre-surgical planning, e.g. to help understand the margins of salient cortex adjacent to a tumor that needs to be treated or removed. I don't know how much fMRI is used compared to MEG or electrocorticography (ECOG - recording directly off the brain surface with EEG-like electrodes). As to the future, there are some intriguing results concerning connectivity maps and other measures of individuals who have had strokes or traumatic brain injuries and the like. These measures might be useful for understanding current deficits such that treatments can be better tailored. What those treatments might entail will depend on how other areas of medicine evolve, but certainly more focused cognitive therapy, speech therapy and the like would be starting points. But there isn't yet sufficient research data to make specific predictions. There are groups (including two at Berkeley) who are collecting as much fMRI data as they can on patients. It will take a few more years before patterns might emerge is my best guess.

I have heard that using fMRI as a method of polygraphy is 90%+ accurate. Has it truly been shown to be that accurate?

[SavannahWinslow](#)

BI: In a particular, well controlled experiment in which compliant subjects were set the task of deceiving, yes. But see my answer to zombie1939 previously. Countermeasures work very effectively, and movement of any sort will render the data all but useless. Thus, most in the fMRI community don't think it will work as a lie detector, just as the polygraph has demonstrable flaws outside of lab conditions.

