Re-Executability Assessment of the Recent Autism Literature

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Introduction: There is concern about the stats of reproducibility in science in general and neuroimaging neuroscience in particular (Gorgolewski and Poldrack 2016; Button et al. 2013). A particularly germain concern was expressed by Insel and colleagues in lamenting: “a profusion of statistically significant, but minimally differentiating, biological findings; ‘approximate replications’ of these findings in a way that neither confirms nor refutes them” (Kapur, Phillips, and Insel 2012). The replication of a specific finding (or reproducibility of a specific analysis), as reflected in a publication, has many details and nuances to it (Kennedy et al. 2019). Often, we are searching for the ‘generalizability’ of a finding: does the finding hold true when using ‘similar’ data and a ‘similar’ analysis.

In this poster, we: 1) develop a specification for what constitutes an assessment of the re-executability for a given publication, in each of the domains of: data, software, execution environment, statistics and results; 2) codify this assessment in survey form; and 3) apply the survey to a subset of the autism neuroimaging literature published recently (~2018). From the results of this survey, we can begin to generalize the state of the re-executability of the recent autism neuroimaging literature, in order to identify trends and opportunities for the enhancement of the re-executability status in support of greater overall generalizability (and hence reproducibility) of the literature.

Methods

Survey Development: In order to assess the prospects of re-execution of a given paper, we assess 1) the availability of the starting data, 2) the precision of the analysis description (both data processing and statistical assessment), and 3) the availability of the detailed complete results (in order to verify accuracy of re-execution). Regarding the ‘availability of the starting data’, we assess if the publication indicates how someone (other than the authors themselves) could appropriately access the data. The ‘precision of the analysis description’ ultimately asks if a reader who is reasonably skilled in the necessary domains, could precisely carry out the prescribed analysis steps. Specifically, are the software versions, operating system and complete parameters somehow made available to the reader? The ‘detailed complete results’ assesses if the publication indicates how to obtain the complete results, in order to both verify that the re-execution generates the same result and to overcome the limitations of selected summary only being presented, which impedes a more complete meta analysis of the literature.

***Literature Identification*:** On January 23, 2019, the following pubmed query was executed:

((“autistic disorder”[MeSH Terms] OR (“autistic”[All Fields] AND “disorder”[All Fields]) OR “autistic disorder”[All Fields] OR “autism”[All Fields]) AND (“magnetic resonance imaging”[MeSH Terms] OR (“magnetic”[All Fields] AND “resonance”[All Fields] AND “imaging”[All Fields]) OR “magnetic resonance imaging”[All Fields] OR “mri”[All Fields])) AND (“2014/01/25”[PDat] : “2019/01/23”[PDat] AND “humans”[MeSH Terms])

This is the expansion of the general query for ‘autism AND MRI, qualified to select publications between 1/25/2014 - 1/23/2019 and where the MeSH term includes ‘human’. This query generated 811 resultant publications at the time of the query.

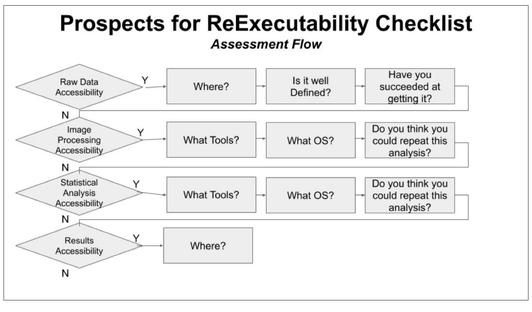

Figure 1: Overview of the survey design.

Results

Survey Application: A high-level summary of the survey results are represented in Figure 2.

Discussion

The recent past literature of autism neuroimaging presents a somewhat consistent picture with respect to the prospects of re-executability with regard to the characteristics we examined in this report.

Publication Availability: Thirty-six of the 50 (72%) publications appear to have ‘free full text’ available, according to the PubMed search. Of these, 33 are indexed in PubMed Central. Overall, all are freely available through either PubMed Central or publisher websites.

Enter the publication PubMed ID (PMID)	Does the publication provide information about how to access the raw imaging data?	Are the software tools/packages specified?	Is the operating system used for tool execution specified?	Do you think a reasonably skilled image analyst could re-execute this analysis?	Are the statistical tools/packages specified?	Do you think a reasonably skilled statistical analyst could re-execute this statistical analysis?	Are the complete results (derived images, summary data, etc.) available?
28887198	No	No	No	No	Yes	No	No
28917059	Yes	Yes	No	Approximately	No	No	No
28923933	No	Yes	No	Yes	No	No	Partially
28938219	No	Yes	No	Yes	Yes	I'm not sure	No
28940401	No	Yes	No	I'm not sure	Yes	I'm not sure	No
28940697	No	No	No	No	Yes	I'm not sure	No
28940848	Yes	Yes	No	I'm not sure	Yes	Approximately	No
28941767	No	Yes	No	I'm not sure	Yes	Approximately	No
28942672	No	Yes	No	Approximately	Yes	Approximately	No
29045575	No	Yes	No	Approximately	Yes	Yes	No
29064008	No	No	No	No	No	No	No
29079524	No	Yes	No	Approximately	No	No	No
29088456	No	Yes	No	Approximately	Yes	Approximately	No
29129723	No	Yes	No	Approximately	Yes	Approximately	No
29141188	No	Yes	No	Approximately	No	No	No
29152901	No	No	No	No	No	No	No
29169826	No	Yes	No	Yes	Yes	Yes	No
29177509	No	Yes	No	Approximately	No	No	No
29206318	No	Yes	No	I'm not sure	Yes	Approximately	No
29223496	No	Yes	No	I'm not sure	Yes	Approximately	No
29224969	Yes	Yes	No	Approximately	No	No	No
29247748	No	Yes	No	Yes	No	No	No
29249338	Yes	Yes	No	I'm not sure	No	No	No
29257126	Yes	Yes	No	Yes	No	No	No
29265723	No	Yes	No	I'm not sure	No	No	No
29272297	Yes	No	No	No	No	No	No
29274502	No	Yes	No	I'm not sure	No	No	No
29275843	No	Yes	No	Approximately	Yes	Approximately	No
29278772	Yes	No	No	No	No	No	No
29309854	No	Yes	No	I'm not sure	No	No	No
29423135	Yes	Yes	No	Yes	Yes	Yes	Yes
29449909	No	Yes	No	Approximately	Yes	I'm not sure	No
29484149	No	Yes	No	I'm not sure	Yes	I'm not sure	No
29541439	Yes	Yes	No	Approximately	No	No	Partially
29578027	No	Yes	No	Approximately	Yes	Approximately	No
29584599	No	Yes	No	Approximately	No	No	No
29664902	Yes	Yes	No	Approximately	Yes	Approximately	No
29718384	No	Yes	No	Approximately	Yes	Approximately	No
29795565	Yes	Yes	No	Approximately	No	No	No
29946509	No	Yes	No	Approximately	Yes	Approximately	No
29995885	Yes	Yes	Yes	No	Yes	Approximately	No
30013915	Yes	Yes	No	Approximately	Yes	I'm not sure	No
30091324	No	Yes	No	Approximately	Yes	Yes	No
30128280	No	Yes	No	No	No	No	No
30148064	No	Yes	No	I'm not sure	Yes	I'm not sure	No
30218016	No	Yes	No	I'm not sure	No	No	Yes
30232359	No	Yes	No	No	No	No	Yes
30235257	Yes	Yes	No	Yes	No	No	Yes
30237783	Yes	Yes	No	No	Yes	Yes	Partially
30302187	Yes	Yes	No	Approximately	Yes	Approximately	No
Totals: Yes	16	44	1	7	27	5	4
No	34	6	49	10	23	24	43
Approximately/ Partially/I'm not sure				33		21	3

Data Availability: Sixteen of the 50 (32%) publications make reference to the availability of the data used in the publication. However, publications that indicate availability are reusing data from the large repositories, whereas the publications that do not indicate data availability are principally locally conducted studies. Thus, this indicates that a large fraction of the data being used in publications are not available to the community.

Image Analysis: Virtually all of the publications surveyed indicate the imaging analysis software used (44 of 50 (88%)). Most publications indicate the use of multiple tools. However, specific tool versions are indicated only about half of the time. While this may seem a minor point, software version can make a difference in results (Glatard et al. 2015; Ghosh et al. 2017). Thirty-five different publicly released tools (plus a number of in-house packages) are used in this collection of 50 papers. The specific operating system use is rarely reported (1 out 50 (2%)). Overall, our raters felt that in 80% of the publications that a skilled image analyst could (or might be able to) repeat the analysis.

Statistical Analysis: In a little more than half of the publications (54%), the statistical software is indicated, again with variable indication of version and no reporting of the operating system upon which the software was running. In summary, our raters felt that in 29 of the 50 papers (58%), a skilled statistical analyst could (or might) be able to repeat the analysis.

Results Availability: Availability of the detailed results is fairly rare. All or partial results are available in 7 of the 50 publications (14%). Lack of results availability causes a number of problems. One, it is harder to confirm replication (or the degree to which replication was or was not achieved) without the complete set of reported observations, not just the summary tables or figures. Resorting to visual interpretations of ‘similarity’ of published figures remains fraught with issues that can hamper true understanding of new results compared to prior results.

Conclusions: We feel that the survey results presented here reflect a state of neuroimaging publication practices that leaves ample room for improvement. While reuse of existing data is good, the majority of new data being collected for use in publications is not made publically available. While the listing of software used is good, important details for reproducibility, such as version, detailed parameters, operating system, etc. are not fully disclosed. Similarly, statistical assessment details are variably reported, making re-execution problematic and approximate. Finally, as very little of the complete results of a publication are disclosed, assessment of the similarity of future replication attempts is severely hampered. Given the overall state of uncertainty about how reproducible (and representative) specific neuroimaging findings are, it seems prudent to begin to tighten up the variables that we as authors do have in order to better support the effective accumulation of knowledge about conditions we study.

Authors, reviewers and editors should insist on the complete declaration of: data source and availability status, all software and versions used for data analysis and statistical assessment, the operating system (and version) for data and statistical analysis, and the disposition of the analytic results. Such a ‘checklist’ would be a valuable asset for the community and will be the subject of future efforts.

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References:

Button, Katherine S., John P. A. Ioannidis, Claire Mokrysz, Brian A. Nosek, Jonathan Flint, Emma S. J. Robinson, and Marcus R. Munafò. 2013. “Power Failure: Why Small Sample Size Undermines the Reliability of Neuroscience.” Nature Reviews. Neuroscience 14 (5): 365–76.

Gorgolewski, Krzysztof J., and Russell A. Poldrack. 2016. “A Practical Guide for Improving Transparency and Reproducibility in Neuroimaging Research.” PLoS Biology 14 (7): e1002506.

Kapur, S., A. G. Phillips, and T. R. Insel. 2012. “Why Has It Taken so Long for Biological Psychiatry to Develop Clinical Tests and What to Do about It?” Molecular Psychiatry 17 (12): 1174–79.

Kennedy, David N., Sanu A. Abraham, Julianna F. Bates, Albert Crowley, Satrajit S. Ghosh, Tom H. Gillespie, Mathias Goncalves, et al. 2019. “Everything Matters: The ReproNim Perspective on Reproducible Neuroimaging.” Frontiers in Neuroinformatics 13. https://doi.org/10.3389/fninf.2019.00001.

Articles Included in the Survey

First Author	Reference	PMID
Mann C	Mol Autism. 2018 Oct 1;9:49. doi: 10.1186/s13229-018-0232-6. eCollection 2018.	30302187
Gray JC	PLoS One. 2018 Sep 20;13(9):e0204011. doi: 10.1371/journal.pone.0204011. eCollection 2018.	30235257
Gertsvolf N	Sci Rep. 2018 Sep 19;8(1):14057. doi: 10.1038/s41598-018-32288-3.	30232359
Chin R	Sci Rep. 2018 Sep 14;8(1):13858. doi: 10.1038/s41598-018-32290-9.	30218016
Vavla M	Front Neurol. 2018 Sep 6;9:747. doi: 10.3389/fneur.2018.00747. eCollection 2018.	30237783
Kim N	Yonsei Med J. 2018 Sep;59(7):897-903. doi: 10.3349/ymj.2018.59.7.897.	30091324
Na S	Neuroimage Clin. 2018 Aug 10;20:485-497. doi: 10.1016/j.nicl.2018.08.015. eCollection 2018.	30148064
Duret P	Neuroimage Clin. 2018 Aug 4;20:415-423. doi: 10.1016/j.nicl.2018.04.036. eCollection 2018.	30128280
Murakami Y	Neurosci Res. 2018 Aug;133:28-37. doi: 10.1016/j.neures.2017.11.003. Epub 2017 Nov 12.	29141188
Zhao G	PLoS One. 2018 Jul 11;13(7):e0196964. doi: 10.1371/journal.pone.0196964. eCollection 2018.	29995885
Adamson K	Neuroimage. 2018 Jul 1;174:393-406. doi: 10.1016/j.neuroimage.2018.02.064. Epub 2018 Mar 22.	29578027
Li SJ	Radiology. 2018 Jul;288(1):209-217. doi: 10.1148/radiol.2018170059. Epub 2018 Mar 27.	29584599
Karahano ğlu FI	Neuroimage Clin. 2018 Jun 7;19:840-847. doi: 10.1016/j.nicl.2018.06.002. eCollection 2018.	29946509
Guzman GEC	PLoS One. 2018 May 24;13(5):e0195906. doi: 10.1371/journal.pone.0195906. eCollection 2018.	29795565
Feczko E	Neuroimage. 2018 May 15;172:674-688. doi: 10.1016/j.neuroimage.2017.12.044. Epub 2017 Dec 21.	29274502
Zhang F	Neuroimage. 2018 May 15;172:826-837. doi: 10.1016/j.neuroimage.2017.10.029. Epub 2017 Oct 25.	29079524
Tsoi L	Soc Cogn Affect Neurosci. 2018 May 1;13(5):460-470. doi: 10.1093/scan/nsy029.	29718384
Sen B	PLoS One. 2018 Apr 17;13(4):e0194856. doi: 10.1371/journal.pone.0194856. eCollection 2018.	29664902
Yan W	Neuroimage Clin. 2018 Apr 13;19:320-330. doi: 10.1016/j.nicl.2018.04.013. eCollection 2018.	30013915
Wadsworth HM	Behav Brain Res. 2018 Apr 2;341:1-8. doi: 10.1016/j.bbr.2017.12.012. Epub 2017 Dec 13.	29247748
Ktena SI	Neuroimage. 2018 Apr 1;169:431-442. doi: 10.1016/j.neuroimage.2017.12.052. Epub 2017 Dec 24.	29278772
Floris DL	Mol Autism. 2018 Mar 6;9:17. doi: 10.1186/s13229-018-0192-x. eCollection 2018.	29541439
Ni HC	Prog Neuropsychopharmacol Biol Psychiatry. 2018 Mar 2;82:233-241. doi: 10.1016/j.pnpbp.2017.11.008. Epub 2017 Nov 9.	29129723
Hu Y	Brain Cogn. 2018 Mar;121:11-16. doi: 10.1016/j.bandc.2018.01.001. Epub 2018 Jan 6.	29309854
Gibbard CR	Hum Brain Mapp. 2018 Mar;39(3):1270-1282. doi: 10.1002/hbm.23915. Epub 2017 Dec 19.	29265723
White T	Hum Brain Mapp. 2018 Mar;39(3):1218-1231. doi: 10.1002/hbm.23911. Epub 2017 Dec 5.	29206318
Stivaros S	Mol Autism. 2018 Feb 22;9:12. doi: 10.1186/s13229-018-0190-z. eCollection 2018.	29484149
Boets B	Mol Autism. 2018 Feb 8;9:10. doi: 10.1186/s13229-018-0188-6. eCollection 2018.	29449909
Hegarty JP 2nd	Prog Neuropsychopharmacol Biol Psychiatry. 2018 Feb 2;81:153-160. doi: 10.1016/j.pnpbp.2017.09.016. Epub 2017 Sep 21.	28941767
Bernas A	Comput Methods Programs Biomed. 2018 Feb; 154:143-151. doi: 10.1016/j.cmpb.2017.11.017. Epub 2017 Nov 16.	29249338
Ciaramidaro A	Eur Neuropsychopharmacol. 2018 Feb;28(2):264-275. doi: 10.1016/j.euroneuro.2017.12.005. Epub 2017 Dec 21.	29275843
Kohls G	Mol Autism. 2018 Jan 30;9:9. doi: 10.1186/s13229-018-0195-7. eCollection 2018.	29423135
Marusak HA	Behav Brain Res. 2018 Jan 15;336:211-218. doi: 10.1016/j.bbr.2017.09.010. Epub 2017 Sep 5.	28887198
Balci TB	Am J Med Genet B Neuropsychiatr Genet. 2018 Jan;177(1):101-109. doi: 10.1002/ajmg.b.32610. Epub 2017 Nov 20.	29152901
White T	Eur J Epidemiol. 2018 Jan;33(1):99-125. doi: 10.1007/s10654-017-0319-y. Epub 2017 Oct 24.	29064008
Wei L	Eur Neuropsychopharmacol. 2018 Jan;28(1):48-62. doi: 10.1016/j.euroneuro.2017.11.018. Epub 2017 Dec 7.	29224969
Naaijen J	Eur Neuropsychopharmacol. 2018 Jan;28(1):118-129. doi: 10.1016/j.euroneuro.2017.11.010. Epub 2017 Nov 21.	29169826
Abbott AE	Soc Cogn Affect Neurosci. 2018 Jan 1;13(1):32-42. doi: 10.1093/scan/nsx129.	29177509
Dona O	PLoS One. 2017 Dec 22;12(12):e0190081. doi: 10.1371/journal.pone.0190081. eCollection 2017.	29272297
Alexander LM	Sci Data. 2017 Dec 19;4:170181. doi: 10.1038/sdata.2017.181.	29257126
Braden BB	Autism Res. 2017 Dec;10(12):1945-1959. doi: 10.1002/aur.1842. Epub 2017 Sep 21.	28940848
Carlisi CO	Cereb Cortex. 2017 Dec 1;27(12):5804-5816. doi: 10.1093/cercor/bhx265.	29045575
Chien YL	Hum Brain Mapp. 2017 Dec;38(12):6053-6067. doi: 10.1002/hbm.23810. Epub 2017 Sep 20.	28940697
Bottelier MA	Psychiatry Res Neuroimaging. 2017 Nov 30;269:36-42. doi: 10.1016/j.pscychresns.2017.09.009. Epub 2017 Sep 12.	28938219
Hotier S	Acta Psychiatr Scand. 2017 Nov;136(5):517-525. doi: 10.1111/acps.12814. Epub 2017 Sep 22.	28940401
Joshi G	Brain Connect. 2017 Nov;7(9):558-573. doi: 10.1089/brain.2016.0483.	28942672
Stanfield AC	Schizophr Bull. 2017 Oct 21;43(6):1220-1228. doi: 10.1093/schbul/sbx083.	29088456
Bruno JL	Proc Natl Acad Sci U S A. 2017 Oct 3;114(40): 10767-10772. doi: 10.1073/pnas.1620994114. Epub 2017 Sep 18.	28923933
Ramot M	Elife. 2017 Sep 16;6. pii: e28974. doi: 10.7554/eLife.28974.	28917059