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Item Type	Response or Comment
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Citation	Proc Natl Acad Sci U S A. 2015 Jan 27;112(4):E350. doi: 10.1073/pnas.1422473112. Epub 2015 Jan 13. Link to article on publisher's website
DOI	10.1073/pnas.1422473112
Publisher	National Academy of Sciences
Rights	Publisher PDF posted as allowed by the publisher's author rights policy at http://www.pnas.org/site/aboutpnas/authorfaq.xhtml .
Download date	2026-03-15 11:27:55
Link to Item	https://hdl.handle.net/20.500.14038/43730

Reply to Scahill: Behavioral outcome measures in autism

We thank Lawrence Scahill for his comments (1) on our use of outcome measures in our clinical trial of sulforaphane in autism spectrum disorder (ASD) (2). Scahill identifies some differences in our use of these scales from how they have been used in some other trials, but we believe that our interpretations of the trial results are accurate. We chose the Social Responsiveness Scale (SRS) because we were especially interested in assessing sociability in autism, which is a cardinal feature of ASD and is frequently reported to improve during fever. To our knowledge, this is the first clinical trial in ASD in which the SRS was a primary outcome measure and has also shown positive results. The Aberrant Behavior Checklist (ABC) and Clinical Global Impression Improvement (CGI-I) are more conventional measures in ASD clinical trials.

The baseline ABC and its subscale scores are reported in table S1 of the original article (2). We agree that the differences between sulforaphane and placebo ABC subscale scores are modest. We reported the total ABC (and SRS) scores because the study was powered on them. A statistical analysis on the ABC subscale scores did reveal that,

although modest, the differences in change from baseline were significant in the ABC irritability and lethargy subscales (figure 3 from ref. 2).

We used a version of CGI-I [The Ohio Autism Clinical Impressions Scale (OACIS)] that has been specifically adapted for use in autism spectrum disorders by The Ohio State University Research Unit on Pediatric Psychopharmacology, which, in addition to considering the overall severity or improvement of autism symptoms, also considers nine different subdomains of ASD symptoms. Thus, we believe use of the OACIS provided us a more precise assessment of severity (and improvement) of our study participants. The general level of autism was improved in only three domains of autistic behavior.

The discontinuation phase was indeed placebo controlled, and the trial remained double blind until all subjects had completed the study. The sample size in this phase was reduced due to lower rates of follow-up for the final study visit.

We respectfully point out that the three expert reviewers (identified in the paper) and

the accepting editor for PNAS found no problems with our method of assessment of behavior in ASD.

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1 Scahill L (2015) Uncommon use of common measures in sulforaphane trial. *Proc Natl Acad Sci USA* 112:E349.

2 Singh K, et al. (2014) Sulforaphane treatment of autism spectrum disorder (ASD). *Proc Natl Acad Sci USA* 111(43): 15550–15555.

Author contributions: P.T. and A.W.Z. designed research; A.W.Z. performed research; P.T. contributed new reagents/analytic tools; P.T. and A.W.Z. analyzed data; P.T. and A.W.Z. wrote the paper; and P.T. supplied sulforaphane-rich broccoli sprout extract.

The authors declare no conflict of interest.

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