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Igor V. Zaitsev

CUNY Borough of Manhattan Community College

Ling Chen

CUNY Borough of Manhattan Community College

Susie Boydston-White

CUNY Borough of Manhattan Community College

Manita Pavel

CUNY Borough of Manhattan Community College

Svetlana N. Shugaeva

Irkutsk State Medical Academy of Postgraduate Education

See next page for additional authors

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Authors

Igor V. Zaitsev, Ling Chen, Susie Boydston-White, Manita Pavel, Svetlana N. Shugaeva, Alla G. Petrova, and Oksana V. Williams



CORRESPONDENCE

The prion dilemma confounding science educators [v1; ref status: indexed, <http://f1000r.es/ku>]

Igor V Zaitsev¹, Ling Chen¹, Susie Boydston-White¹, Manita Pavel¹, Svetlana N Shugaeva², Alla G Petrova³, Oksana V Williams⁴

¹Borough of Manhattan Community College, The City University of New York, New York, 10007-1097, USA

²Irkutsk State Medical Academy of Postgraduate Education, Irkutsk, 664003, Russian Federation

³Irkutsk Medical University, Irkutsk, 664003, Russian Federation

⁴American International School of Bucharest, Bucharest, 077190, Romania

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Abstract

In this paper, the issue of the prion hypothesis, a simmering controversy within the scientific community, is addressed. We inquire into the appropriateness of the use of certain augmentations and rhetoric approaches used during scientific debates, as well as the aptness of unequivocal statements in textbooks that indicate “abnormal prions” as a primary cause of Transmissible Spongiform Encephalopathies.

Article Status Summary

Referee Responses

Referees	1	2	3
v1 published 09 Jan 2013	 report	 report	 report

- 1** **Jose Valpuesta**, Centro Nacional de Biotecnología, Campus Universidad Autónoma de Madrid Spain
- 2** **Kai Zinn**, California Institute of Technology USA
- 3** **Hidehiro Mizusawa**, Tokyo Medical and Dental University Japan

Latest Comments

Vitaly Citovsky, Department of Biochemistry and Cell Biology, State University of New York at Stony Brook, USA
 09 Jan 2013 (V1)

Associated Short Research Article

Karapetyan YE » Long double stranded RNA is present in scrapie infected cells and tissues, *F1000Research* 2012, 1:52 (doi: 10.12688/f1000research.1-52.v1)

Corresponding author: Igor V Zaitsev (izaitsev@bmcc.cuny.edu)

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Correspondence

According to some in the field, one should refrain from discussions concerning controversial issues in science if one is not actively conducting experimental research¹. We must dissent, most particularly when the prions controversy is under consideration. One does not have to conduct scientific experiments to recognize not only the flaws of the prion protein (PrP) hypothesis², but the inappropriate vocabulary used during discussions of the issue. As science educators, we are still confounded when trying to present the cause of Transmissible Spongiform Encephalopathy (TSE) to our students.

To start with, for the past twenty years, the majority of biology text books unequivocally identified PrP^{Sc} as the causative agent of TSE, and some texts even refer to the “prion hypothesis” as the “prion theory”, please see [Table 1](#). Yet, when introducing the scientific method in high schools and college classes, we establish that in order for a hypothesis to become a scientific theory, it has to be supported many times over through experimentation³ providing a substantial and conclusive body of evidence⁴. Upon reviewing experimental work on PrP, one notes that initial studies are rarely, if ever,

repeated by other scientists. Instead, they move on without giving reconsideration to the assumption upon which they base their work⁵.

When describing the scientific method, it is important that we emphasize the difference between faith and fact. Nevertheless, during discussions of the PrP hypothesis in meetings, conferences and private discussions of scientists, “I think” is too often replaced by “I believe”. Perhaps, this inclination began when the Karolinka neurologist Lars Edison told *The Times* newspaper, upon the announcement of the Prusiner’s Noble Prize: “There are still people who don’t believe that a protein can cause these diseases, but we believe it”⁶. There should be no place in science for such a subjective declaration. Even recent publications emphasize that the scientific community has been split into PrP “believers” and “nonbelievers”. Laura Manuelidis, one of the main scientists who rejects the PrP hypothesis, has been portrayed as a “prion heretic”⁷. Upon entering the combination of “prions” and “belief” in a Google search, we generated an astonishing 918,000 hits. Another recent tendency in modern science is marginalizing scientists as the “minority” versus the “majority”, as is seen in the PrP controversy⁷, a partition more suitable for political rather than scientific discussions.

Table 1. The indisputable textbook statements concerning infectious agent of Transmissible Spongiform Encephalopathies.

Authors	Name of the textbook	Publishing company	Year of the publication	Statements
McKee T., McKee J.R.	Biochemistry: The molecular Basis of Life	McCraw Hill	2003	“Prion disease are caused when the conformation of PrP ^C is converted to PrP ^{Sc} ”.
Gladwin M., Trattler W.	Clinical Microbiology Made Ridiculously Simple	MedMaster	2004	“The prion-only hypothesis is the most widely accepted theory today”.
Freeman S.	Biological Science	Pearson Benjamin Cummins	2008	“Over the past several decades, evidence has accumulated that certain proteins can act as infectious, disease causing agents”.
Russell P.J., Wolfe S.L., Hertz P.E., Starr C., McMillan B.	Biology: the Dynamic Science	Thomson Brooks/Cole	2008	“Prions ... are the only known infectious agents that do not include a nucleic acid molecule”. “Prions have been identified as the causal agents of certain diseases that degenerate the nervous system in mammals”.
Campbell M.K., Farrell S.O.	Biochemistry	Thomson Brooks/Cole	2009	“It has been established that the causative agent of mad-cow disease, as well as the related diseases scrapie in sheep, chronic wasting (CWD) in deer and elk, and human spongiform encephalopathy in humans is a small (28-kDa) protein called a prion”.
Tymoczko J.L., Berg J.M., Lubert S.	Biochemistry: A Short Course	W.H. Freeman & Company	2010	“Certain infectious neurological diseases were found to be transmitted by agents that were similar in size to viruses but consisted only of protein”.
Talaro K.P.	Foundations in Microbiology	McGraw Hill	2009	“Prions are incredibly hardy “pathogens”. They are known to cause diseases called transmissible spongiform encephalopathies”.
Cowan M.K., Bunn J.	Microbiology Fundamentals: A Clinical Approach	McGraw Hill	2013	“The transmissible agent in CDJ is a prion”.
Tortora G.J., Funke B.R., Case C.L.	Microbiology: An Introduction	Pearson	2013	“Several fatal diseases affecting the human central nervous system are caused by prions”.

In covering the PrP hypothesis in classrooms, are we also to employ a vocabulary in which the scientific community is divided into “believers” and “nonbelievers” or “majority” and “minority” as if we were referring to a religious conviction or a political debate rather than a scientific dilemma?

Author contributions

IVZ was involved in reviewing the literature and writing the letter. LC, SB-W, MP, SNS, AGP and OVW equally contributed to

the emerged discussion and conceptualization of the paper and all approved the final version of the manuscript.

Competing interests

No competing interests were disclosed.

Grant information

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5. Zaitsev IV: **Could Prion Protein Assumptions Engender Misleading Sensational Conclusions?** 2010. [Reference Source](#)
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Current Referee Status:

Referee Responses for Version 1



Hidehiro Mizusawa

Department of Neurology and Neurological Science, Tokyo Medical and Dental University, Tokyo, Japan

Approved: 09 September 2013

Referee Report: 09 September 2013

I agree with the authors on how important open discussion is in science. However, the prion hypothesis has been well and openly discussed for many years. Due to the hypothesis, many achievements have been obtained. Abnormal prion proteins resulting from prion protein gene mutations clearly cause genetic prion diseases.

Minor point: "Abnormal prions" should be "prions", because prions all are abnormal.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Competing Interests: No competing interests were disclosed.



Kai Zinn

Division of Biology, California Institute of Technology, Pasadena, CA, USA

Approved with reservations: 25 January 2013

Referee Report: 25 January 2013

The scientific community has been split in the past into those who believed the prion hypothesis and those who did not. During the 1980s and part of the 1990s, most work on the prion hypothesis was from [Stanley Prusiner's](#) group, and those who questioned the prion hypothesis were doing so largely by finding potential errors in the work of one laboratory. However, now we have hundreds of papers on mammalian PrP, including, most importantly, the demonstration that transmissible disease can be caused by a pure recombinant prion protein ([Wang et al, \(2010\)](#)), that are not from Prusiner and whose results are consistent with the prion hypothesis. In addition, work by many groups on yeast prions demonstrated the validity of the generalized prion hypothesis (inheritance mediated by conformational changes in proteins) in a more experimentally tractable system in which controls that were not possible for mammalian PrP could easily be done. So, at this point, I see no problems with the statements made in the textbooks that are listed in the Table. The prion hypothesis is as well-established, at least for mammalian PrP, as the chemiosmotic (Mitchell) hypothesis for ATP synthesis by mitochondria, which was controversial at the time it was proposed in the early 60s, but which is now the only mechanism described in textbooks. It is no longer necessary to even mention the alternative ideas from the 60s, such as chemical coupling.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Competing Interests: No competing interests were disclosed.



Jose Valpuesta

Centro Nacional de Biotecnología, Campus Universidad Autónoma de Madrid, Madrid, Spain

Approved: 17 January 2013

Referee Report: 17 January 2013

I agree with what I think is the main message of the authors, that the scientific debate should be open and should rest in facts and not in beliefs. The first point is very important and the same 'prion hypothesis' is a good example of this, as it was under attack for a long time until substantial evidence was produced in its favour. I agree with the authors in that in science one should refrain from using statements ('I believe ...') more adequate for religious or political debates, but when dealing with educational matters, simple statements need be used to convey a certain message or information. Time will tell whether these messages are correct, and the text books and scientific journals are full of information that later has been proven to be wrong, but which has been useful to stir the scientific debate.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Competing Interests: No competing interests were disclosed.

Article Comments

Comments for Version 1

Vitaly Citovsky, Department of Biochemistry and Cell Biology, State University of New York at Stony Brook, USA

Posted: 09 Jan 2013

I am not a prion researcher, but this Correspondence is not really on prions but on dogmas and professional politics in science. Overall, I agree with the authors that teaching and, importantly, discussing/reviewing science (e.g., in review articles or when reviewing papers or grant proposals) should be based on facts and not on "beliefs" or political correctness. This seemingly obvious notion, however, is not trivial as it is not always followed by scientists as well as by laypeople.

Vitaly Citovsky

Department of Biochemistry and Cell Biology
State University of New York

Stony Brook, NY 11794-5215

Tel.: 631.632.9534

Fax: 631.632.8575

E-mail: vitaly.citovsky@stonybrook.edu

Competing Interests: no competing interests
