Author's response to reviews

Title: Body mass index in relation to truncal asymmetry of healthy adolescents, a pathogenetic concept. Summary of an electronic focus group debate of the IBSE

Authors:

Theodoros B Grivas (tgri@otenet.gr)
Geoffrey Burwell (gburwell@tiscali.co.uk)
Peter H Dangerfield (spine92@liv.ac.uk)

Version: 2 Date: 18 April 2013

Author's response to reviews: see over
The Editor-in-Chief
Scoliosis
Biomed Central

MS ID : 5321093198627699

26 March 2013

Dear Sir

Re: Body mass index in relation to truncal asymmetry of healthy adolescents, a pathogenetic concept. Summary of an electronic focus group debate of the IBSE
Theodoros B Grivas, Geoffrey Burwell and Peter H Dangerfield

We write to respond to the Comments of the two Reviewers of our paper.

Reviewer 1

Thank you for your comments.

Comment 1. I'm not able to decide on this specific paper and prefer to leave the decision to the Chief-Editor or to the Associate Editor that the Chief-Editor has chosen.
Response: In view of the polarised views the two Reviewers we are happy for this suggestion to be enacted. One option is to seek another Reviewer (please see below).

Comment 2. The publication of this paper depends on a political choice by the Editors. In fact, unfortunately, even if a work has been done, my doubt is that the results are not useful to the readership of the Journal.
Response. The paper is directed at those readers of scoliosis who have an interest in the problem of solving the aetiopathogeneis of idiopathic scoliosis – not for all the readers of Scoliosis.

Comment 3. In my view, in fact, the paper does not offer any new insight about the theory proposed by Dr. Grivas et al originally. In the focus only some minor comments by other participants have been done, but these comments in my view do not add concepts to the original paper. I'm sorry to
say that the only effect of this paper is to re-state the concept of the original work, and report on a discussion that has been attempted but in reality did not drive to new insights.

**Response.** The paper provides a summary of a discussion by interested IBSE members. In doing so, the need for further research on TA and AIS aetiopathogeneis is implicit. The discussion is novel for this field in relation to:

- ribcage asymmetries
- widespread corporeal skeletal asymmetries
- Scoliometer readings
- BMI and later menarche
- central nervous system
- girls susceptibility to leptin where a new concept is outlined in the response to Comment 11 (last paragraph).
- this research at the borderland between the genesis of TA (physiogenesis) and AIS (pathogenesis) is novel and here regarded as in common with AIS.

**Comment 4.** Level of interest: Reject as not of sufficient priority to merit publishing in this journal

**Response.** Given a sound review, priority is not in publication but in the view of this Reviewer. By not publishing papers such as this, opportunity for open discussion and development of concepts relating to aetiology is lost.

**Reviewer 2**

Thank you for your comments.

**Comment 1:** Scoliosis should absolutely publish the paper, considering a few minor revisions.

**Response.** Thank you.

**Comment 2.** Title: there is a discrepancy between the first part of the title considering "healthy adolescents" and the second part concerning "pathogenetic concept" - of what? The second part of the title could take into account idiopathic scoliosis ("consequence on pathogenetic concept of idiopathic scoliosis").

**Response.** We have altered the title to:
Body mass index in relation to truncal asymmetry of healthy adolescents, a physiopathogenetic concept in common with idiopathic scoliosis. Summary of an electronic focus group debate of the IBSE.

To accommodate this change of title, a phrase has been added to –

a) Abstract. Last sentence but two, after, “This EFG discusses the findings and interpretations of the paper by Grivas and colleagues” insert “as research at the borderland between the genesis of TA (physiogenesis) and AIS (pathogenesis).

b) Abstract Last sentence but one, after, “It is suggested that TAs “insert “here regarded as in common with AIS”

c) Background, last paragraph where “interpretation” has been changed to, “physiopathogenetic concept in common with idiopathic scoliosis”

Comment 3. Affiliation: I'm not sure whether the triple affiliation of the third author is to be listed under one unique number (3) or three consecutive numbers (3,4,5).
Response. This really rests with the editors. If they wish to use more than one number, there is not problem at all.

Comment 4. It is not clear why the term "truncal asymmetry, TA" has been enlarged into "truncal bilateral asymmetry, TA". What additional information the word "bilateral" contributes?
Response. The word “bilateral” is used to mean “right-left” to distinguish it from “sagittal” asymmetry “Bilateral” has been removed from the text.

Comment 5. The term of "truncal asymmetry, TA" does it cover the upper limbs asymmetries, the lower limbs asymmetries and the head asymmetries (in general - body asymmetries), mentioned in the paper?
Response. The term “truncal asymmetry” does not include these other skeletal asymmetries. These are mentioned to, provide perspective.

Comment 6. Polemic against Huang et al comprises contra-productive argumentation.
Response. When Huang et al (1988) commented on the effectiveness and value of scoliometer in school scoliosis screening (that needed further evaluation), there was no documentation for the age range of the screened children in their study. When published years later the correlation of surface and radiographical deformity was not statistically significant. Hence, our statement “As we discuss below in this age range …. therefore the author’s findings were expected and predicted” is reality, not a polemic, and meant to
imply that we accord with their 1988 opinion.

Comment 7. The usefulness of scoliometer for scoliosis screening should concern younger not older children.  
Response. Yes, it is correct. This statement is based on the findings of our referred study revealing that the scoliometer reading corresponds statistically significant with central axis asymmetry -spine- in older children, a relationship which is not statistically significant in younger children.

Comment 8. It is not clear why the authors agree with a comment: "if surgeons only used radiographs in forward bending position, many would be less keen for surgery". Do the authors mean spine radiography or rib cage radiography? Spine radiography was never reported to be made in forward bending position (frontal view, vertical beam) so it is not possible to have idea on how the spine presents on such X-ray. Rib cage radiography (axial view, horizontal beam) in scoliotic patients is very impressive in demonstrating rib hump and a frequent pro-surgery argument.  
Response. In the response to Comment 3 we have deleted the following phrase: “; and that if scoliosis surgeons only used radiographs in the forward bending position, i.e. rib horizon, many would be less keen for surgery. “

Comment 9. An article whose findings are important to those with closely related research interests.  
Response. We agree.

Reviewer 3

Thank you for your comments.

Comment 1. The authors describe that severe TAs are caused by a genetically-determined selectively increased sensitivity of the hypothalamus to circulating leptin and hypothalamic functional asymmetry is expressed via the sympathetic nervous system bilaterally to produce left-right asymmetry in ribs and/or vertebrae. Please clarify whether these concepts are based on the evidence or only speculations.  
Response. The concepts are speculative. This is stated INTRODUCTION.” As with a recent speculative hypothesis for the pathogenesis of AIS in girls, Grivas et al suggested that the severe TAs involve a genetically-determined
selectively increased sensitivity (up-regulation) of the hypothalamus to circulating leptin with asymmetry as an adverse response to stress (hormesis)."

**BACKGROUND.** “In interpreting their findings, Grivas et al [9] speculatively applied to TAs the autonomic component of the double neuro-osseous pathogenetic theory for girls with AIS [6].”

**Comment 2.** Why hypersensitivity to leptin matters in girls with low leptin level?  
**Response.** In the BACKGROUND it is stated: “They suggested that severe TAs involve a genetically-determined selectively increased hypothalamic sensitivity to leptin.” This is a requirement of the hypothesis.

**Comment 3.** How may the hypothalamus affect the sympathetic nervous system asymmetrically?  
**Response.** In the STATEMENT by Dr Grivas, it is stated: “As with a recent hypothesis for the pathogenesis of AIS in girls [6], it is suggested that severe TAs are caused by a genetically-determined selectively increased sensitivity (up-regulation, i.e. increased sensitivity) of the hypothalamus to circulating leptin with asymmetry as an adverse response to stress (hormesis)(LHS concept).” This concept was approved in a personal communication to GB, by an authority in the field of hormesis, Dr EJ Calabrese. A recent reference to the field of hormesis in medicine where somatic asymmetry is not mentioned, is:  

**Contrasting opinions of the two Reviewers**

The polarised views of the two Reviewers in our opinion reflects their differing levels of interest in research into the borderland between the genesis of TA (physiogenesis) and AIS (pathogenesis). It is a new field which we term “physiopathogenesis” now used in the new suggested title of this paper.

The paper is not aimed at all Scoliosis readers, but at those interested in etiology and particularly surgeons and scientists with a serious interest in solving the problem of causation of TA and AIS. If one researcher takes up this baton, it will have been worth publishing.

The options seem to be:  
1) Reject the paper
2) Accept the paper
3) Seek another Reviewer
4) Seek other Reviewers

In connection with 3) and 4), in our opinion the verdict would depend again on the interest level of the chosen Reviewer(s) in this new field of the physiopathogenesis of TA and AIS.

If Scoliosis accepts this opinion then we recommend the decision about publication be made after deliberation by the Editorial Board of Scoliosis.

Should the Board decide to publish the paper, a note might be added to our responses to explain its decision.

Sincerely

PH Dangerfield
Corresponding author

(RG Burwell)

E-mail addresses of authors
TB Grivas <tgri69@otenet.gr>
R G Burwell <gburwell@tiscali.co.uk>
PH Dangerfield <spine92@liverpool.ac.uk>