

ANSWERING REVIEWERS

April 26, 2016



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 25579-Revised manuscript.doc).

Title: Clinical consequences of centipede bite: Is it neurotoxic?

Author: Ioannis N. Mavridis, Maria Meliou, Efstratios-Stylianos Pyrgelis

Name of Journal: *World Journal of Neurology*

ESPS Manuscript NO: 25579

The manuscript has been improved according to the suggestions of reviewers:

Reviewer 1

I have no specific suggestions. English Language must be revised.

We would like to thank the Reviewer for finding our editorial article very good and acceptable after minor revision. We revised English language appropriately.

Reviewer 2

The editorial by Dr. Mavridis and colleagues provides a nice review of literature on centipede bites and clinical consequences. Through a thorough review of relevant reports, the authors made a convincing case that centipede bites are generally not lethal. The manuscript is well written and structured, with interesting illustrations.

We would like to thank the Reviewer for finding our review nice, thorough and well written and also for finding our illustrations interesting.

Our understanding of centipede venoms is still at its infancy; however, two recent reviews (Yang et al. *Mol. Cell. Proteomics*, 2012, 11:640-650; Undheim and King, *Toxicon*, 2011; 57: 512-524) and related reports cited there and published thereafter provide updated summaries of current scientific investigations. These reviews should be cited, perhaps together with some of the original studies.

We cited the suggested articles. Thank you.

Three recent breakthroughs highlight how individual centipede venom components interact with distinct targets of the nervous system (Yang et al., *PNAS*, 2013, 110: 17534-17539; Chen et al., *J. Peptide Sci.* 2014, 20:159-164; Yang et al., *Nature Communications*, 2015, 6:8297). As these mechanistic studies are directly relevant to the topic of this review, they should be cited and discussed.

We cited and discussed the suggested articles. Thank you.

Venomous animals use venoms for both hunting and self-defense. Most of the active venom components have neuronal targets. Lethal venom intoxication causes paralysis and other disabling consequences, exhibiting a role in hunting. Pain-producing venom components, on the other hand, appear to present a warning signal for defensive purposes. While the lethal venom components are clearly “toxins”, the pain-inducing ones could also be disabling (at least temporally). Therefore, it is suggested that the review either presents a more inclusive view or clearly defines what neurotoxic refers to in the context of this review.

We did so. Thank you.

Minor comments:

1. Abstract, line 7 from bottom: “local and generalized SYMPTOMS,...”;

We corrected our text. Thank you.

2. Page 3, Morphology section, second paragraph: *Scolopendra* are most dangerous; it is perhaps due to the venomous bites, not just the size.

We modified our text. Thank you.

3. Page 3, near bottom: “poisonous” apparently is misused here. “Poisonous” and “venomous” are distinct.

We corrected our text. Thank you.

4. Page 3, near bottom: Aren’t birds, rodents, and other animals also predators?

We modified our text. Thank you.

Finally, we would like to thank the Reviewer for finding our editorial article very good and acceptable after minor revision.

Thank you again for publishing our manuscript in the *World Journal of Neurology*.

Sincerely yours,

A handwritten signature in dark ink, appearing to read 'Ioannis N. MAVRIDIS', with a long horizontal flourish extending to the right.

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