Reviewer's report

Title: The Posttraumatic Stress Disorder Project in Brazil: Neuropsychological, Structural and Molecular Neuroimaging Studies in Victims of Urban Violence

Version: 1 Date: 4 March 2009

Reviewer: Thomas Elbert

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I have carefully read all three ms. Together, they describe a huge and laudable effort to advance our understanding of violence-related mental illness with an emphasis on PTSD. In essence, the planned methodology is sound, whether it is actually realistic and feasible is currently an unresolved question. Each of the papers describes the methods sufficiently detailed that replication will be possible.

In the epidemiological survey, non-professionals are trained to apply structured clinical interviews. While I think that it may be possible to achieve valid results for a diagnosis of PTSD when non-experts are adequately trained to apply the CIDI, the actual outcome achieved by the interviewers would have to be validated. This could, in principal, be realized using the expert interviews (based on the CAPS), as indicated by the second ms (the research strategy would have to be adequately adjusted). More difficult to apply are the instruments that determine peri-traumatic responding. These will require partial imaginative exposure to the traumatic events - a task that requires a profound understanding of the psychophysiology of trauma and considerable clinical experience with techniques to overcome avoidance and to prevent dissociation at the same time. In addition, a clinically experienced expert would have to assure habituation of fear-responses in order not to potentially harm traumatized respondents.

The number of measurements in the neuroimaging and neuropsychological studies is extraordinarily high and I doubt that severely traumatized patients are able to complete the whole battery of tests. Moreover, the patients' ability to concentrate as well as their anxiety level may comprise a potential confound that is not controlled for.

While the combination of measures is unique and some of the variables, like the peri-traumatic responding, have not been tested before, it seems that the designs of the intended investigations go quantitatively but not qualitatively beyond previously presented research designs. Therefore, I believe, an active researcher would gain little from studying these protocols. I think that data should be added.

MS 3331631292169694 describes a RCT to further assess the efficacy of topiramate an anticonvulsant drug. This trial is registered and I cannot see much additional information provided the present ms. I may add, that the drug,
probably via its GABAergic modulation can reduce intrusions but will not cure the underlying illness, i.e., it has the potential to be (ab)used in this context like alcohol or benzodiazepines.

"Also we would like to know if MS: 1693870893248808 should contain a power calculation or if the authors’ reasons for not giving such a sample size calculation are correct."

Over the last decade, evidence has accumulate that there may be two subtypes of trauma response, one characterized by intrusive memories and hyperarousal and the other predominately dissociative, representing distinct pathways to chronic stress-related psychopathology. Results reviewed e.g., by Lanius et al. (2006) suggest that comparable patterns may also be seen in the neuroimaging lab. Hence, assumptions that would have to be used for power calculations for the neuroimaging studies are largely unknown.