Ocular disconjugacy cannot be measured without establishing a solid reference [version 1; peer review: 1 approved, 1 not approved]

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Abstract
This correspondence points out a need for clarification concerning the methodology utilized in the study "Eye tracking detects disconjugate eye movements associated with structural traumatic brain injury and concussion", recently published in Journal of Neurotrauma. The authors of the paper state that binocular eye movements were recorded using a single-camera video-oculography technique and that binocular disconjugate characteristics were analyzed without calibration of eye orientation. It is claimed that a variance-based disconjugacy metric was found to be sensitive to the severity of a concussive brain injury and to the status of recovery after the original injury. However, the reproducibility of the paper’s findings may be challenged simply by the paucity of details in the methodological description. More importantly, from the information supplied or cited in the paper, it is difficult to evaluate the validity of the potentially interesting conclusions of the paper.

Keywords
Mild traumatic brain injury , mTBI screening , vergence

This article is included in the Eye Health gateway.
Correspondence
I wish to point out a need for clarification concerning the methodology utilized in the study “Eye tracking detects disconjugate eye movements associated with structural traumatic brain injury and concussion” by Samadani et al., 2015. The authors state that binocular eye movements were recorded using a single-camera infrared-based video-oculography technique (EyeLink 1000, SR Research, Ontario, Canada) and that binocular disconjugate characteristics were analyzed without calibration of eye orientation. The authors claim that their variance-based disconjugacy metric was sensitive to the severity of a concussive brain injury and to the status of recovery after the original injury.

The EyeLink 1000 system is an excellent eye tracker with a single high resolution camera and an infrared light source affixed to the camera. A typical recording setup consists of a computer monitor with which the visual stimuli are presented to the subject and the camera unit (placed in front of the monitor base) with which the eye movement is recorded monocularly or binocularly. The system has an option of easily outputting image-based, uncalibrated eye coordinates with hundreds of units representing 1° of eye rotation.

The concern I would raise with Samadani et al.’s paper is the unclearness of the relationship between their metric and binocular disconjugacy. Logically, for an identical amount of eye rotation, any asymmetry in the spatial relationship that the camera or the infrared light source has with the two fellow eyes would result in different extents of relocation of the images of the pupils or corneal reflections. Asymmetries exist because there is a physical separation between the two eyes as well as between the camera and the infrared light source. In addition, although the biometric characteristics of eyes are highly symmetrical within individuals, they are not perfectly symmetrical and a 1–2% non-conformity in corneal curvature or axial length is not uncommon, which further confounds the relationship between eye rotation and changes in pixel coordinates. Moreover, each of the two fellow eyes has its own function that maps pixel movement to the eye rotation, and this mapping is not linear. Thus, the arithmetic difference between the uncalibrated coordinates of the two eyes is quite removed from a physical representation of gaze misalignment.

Beyond the factors associated with the raw data, the analytic methods in the paper also do not seem to be constructed with a clear intent. It is puzzling why the disconjugacy metric is represented by the variance of the left-right differences after independently averaging for each eye the uncalibrated coordinates over several cycles for a given stimulus position, as opposed to the straightforward variance of the left-right differences at all sample points. Furthermore, the ranges of outcome values presented in the series of figures run from 0 to at most 0.25, but how the value 0 could have been obtained is not clear. The question arises because in the two eyes’ uncalibrated coordinates there must be a constant bias related to the interocular distance. Lastly, what the high end of the outcome range represents is not clear. Since one unit in EyeLink’s uncalibrated data output is smaller than 0.01° of eye rotation, being able to report differences in 0.25 square units or less seems implausible. If the raw data were numerically centered or scaled, the procedure should have been noted in the text.

The authors discuss some valid points regarding potential pitfalls associated with calibration and phoria. However, these points can be directly addressed by implementing a calibration procedure under monocular viewing. A comparison between the results from thus calibrated and uncalibrated data, and a demonstration of test-retest reliability could have improved the paper.

In summary, the reproducibility of the paper’s findings may be challenged simply by the paucity of details in the methodological description. More importantly, however, from the information supplied or cited in the paper it is difficult to evaluate the validity of the potentially interesting conclusion that deficits in conjugacy of eye movements may quantitate physiologic impact of brain injury.

Competing interests
The author holds stock option in SyncThink, Inc.

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References
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Overall, this Correspondence does not offer a significant criticism of the paper of Samadani et al. (2015). The author does not specify what kinds of asymmetries exist due to the camera/source geometry. Usually the subject is centered in the Eyelink viewing aperture, so the view of the eyes would be symmetric. The attempt to argue that a 1-2% asymmetry between the eyes would significantly degrade the assessment capability does not seem plausible.

The criticism of methodological unclarity may be justified in itself, but it has no bearing on the outcome of the paper since all patients would be equally subject to the same degree by the effects of asymmetry and lack of calibration. As stated, none of the criticisms suggest a systematic bias between the different patient categories. The significant differences among categories cannot therefore be attributed to any of the factors raised by the author, and controlling these factors should only improve the significance of the Samadani et al. results. The author’s challenge to the findings of the paper is thus easily refuted.

Moreover, despite the fact that this Correspondence is entirely concerned with calibration, it neglects to mention the fact that a core motivation for the Samadani et al. paper is the issue of a misleading spatial calibration metric. They are making the point that restrictions of eye movement may restrict the array of calibration positions, providing a false assessment that the subsequent test movements are normal. Their goal is thus to use the uncalibrated differences between the two eyes (which they term “temporal calibration”) as a probe for deficits that would be masked by the spatial calibration procedure. It is this strategy that the author should have addressed directly.

On a stylistic note, I do not favor using the English possessive “s” on the Latin phrase “et al(ia)” and recommend the form above, as in “the Samadani et al. paper”.

**Competing Interests:** No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of
expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Author Response 10 Apr 2015

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I thank Dr. Tyler for his comments and the opportunity to think through what I had written again. One revision I can make in the second paragraph of the original text is to add “a side of” to “an infrared light source affixed to the camera” so that the phrase reads “an infrared light source affixed to a side of the camera.” This revision would make it clearer that the camera may be centered in front of the subject but the infrared light source cannot be centered simultaneously, the consequence of which is an asymmetric view of the corneal reflections. I can also specify that EyeLink 1000 uses a dark pupil-corneal reflection principle for tracking eye movements.

Another clarification I can offer is to point out that the physical separation of the two eyes is individually variable [1,2]. This variability contributes to variations in the extent of asymmetry in the camera view of the landmark features of the eyes. With this consideration, Dr. Tyler's assertion, that all subjects would be equally subject to the same degree by the effects of asymmetry, may be only partially correct. A systematic bias may indeed be created when the demographic composition of the subject groups are different. For example, having a larger male-to-female ratio in one group could increase the extent of binocular asymmetry in uncalibrated data since men tend to have a larger interpupillary distance [1,2]. Incidentally, Samadani et al. note a tendency toward the positive head CT group having more males than the non-injured control, with the positive head CT group of 13 patients being 35.9% female and the control group of 64 subjects being 47.9% female. (Curiously, the percentage of female subjects times the group size does not yield a whole number in any of the four subject groups in the Samadani et al. paper.)

The assessment capability claimed by Samadani et al. appears to be variability of binocular alignment on the order of 0.01° magnitude. This value seems too small in light of the two sources of asymmetries discussed above in uncalibrated gaze-associated binocular measures, and also in light of 1-2% asymmetry between the two eyes.

Regarding the problems that Samadani et al. point out in terms of spatial calibration, my intent is not to dispute the existence of alternatives to eye movement assessments based on spatial calibration. Rather, my emphasis is that disconjugacy itself is spatial in nature, and thus its quantification requires a solid spatial reference frame. This intent may be made clearer by including the term “spatial” in the title so that it reads “Ocular disconjugacy cannot be measured without establishing a solid spatial reference.”

Finally, in my future writing I will keep in mind your recommendation regarding mixing the English possessive on the Latin phrase “et al.”

References:

**Competing Interests:** No competing interests were disclosed.

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The author makes a justified appeal for clarification of methodological issues concerning the study “Eye tracking detects disconjugate eye movements associated with structural traumatic brain injury and concussion” by Samadani *et al.*, 2015. The arguments raised by J. Maruta are very valid. Apart from clarification there is also a need for validation before this technique can be introduced in e.g. emergency rooms to quantify the severity of a concussive brain injury and the degree of recovery.

**Competing Interests:** No competing interests were disclosed.

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