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Parametric Comparisons of Intracranial Mechanical Responses from Three Validated Finite Element Models of the Human Head

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Abstract

A number of human head finite element (FE) models have been developed from different research groups over the years to study the mechanisms of traumatic brain injury. These models can vary substantially in model features and parameters, making it important to evaluate whether simulation results from one model are readily comparable with another, and whether response-based injury thresholds established from a specific model can be generalized when a different model is employed. The purpose of this study is to parametrically compare regional brain mechanical responses from three validated head FE models to test the hypothesis that regional brain responses are dependent on the specific head model employed as well as the region of interest (ROI). The Dartmouth Scaled and Normalized Model (DSNM), the Simulated Injury Monitor (SIMon), and the Wayne State University Head Injury Model (WSUHIM) were selected for comparisons. For

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CONFLICT OF INTEREST

Richard M. Greenwald, Jonathan G. Beckwith, and Simbex have a financial interest in the instruments [HIT System, Sideline Response System (Riddell, Inc.)] that were used to collect data used in this study. The remaining authors have no financial interests associated with this study.

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model input, 144 unique kinematic conditions were created to represent the range of head impacts sustained by male collegiate hockey players during play. These impacts encompass the 50th, 95th, and 99th percentile peak linear and rotational accelerations at 16 impact locations around the head. Five mechanical variables (strain, strain rate, strain × strain rate, stress, and pressure) in seven ROIs reported from the FE models were compared using Generalized Estimating Equation statistical models. Highly significant differences existed among FE models for nearly all output variables and ROIs. The WSUHIM produced substantially higher peak values for almost all output variables regardless of the ROI compared to the DSNM and SIMon models ($p < 0.05$). DSNM also produced significantly different stress and pressure compared with SIMon for all ROIs ($p < 0.05$), but such differences were not consistent across ROIs for other variables. Regardless of FE model, most output variables were highly correlated with linear and rotational peak accelerations. The significant disparities in regional brain responses across head models regardless of the output variables strongly suggest that model-predicted brain responses from one study should not be extended to other studies in which a different model is utilized. Consequently, response-based injury tolerance thresholds from a specific model should not be generalized to other studies either in which a different model is used. However, the similar relationships between regional responses and the linear/rotational peak accelerations suggest that each FE model can be used independently to assess regional brain responses to impact simulations in order to perform statistical correlations with medical images and/or well-selected experiments with documented injury findings.

Keywords

Traumatic brain injury; Sports-related concussion; Injury threshold; Finite element model; Head impact exposure

INTRODUCTION

Traumatic brain injury (TBI), including mild TBI (mTBI), is a major public health problem in the United States. Understanding the biomechanical mechanisms of mTBI, including sports-related concussion, is critical for establishing injury tolerance criterion as well as for developing protective devices to prevent injury. Kinematics-based injury metrics such as linear and rotational peak accelerations, as well as their variants (the Gadd severity index (GSI),[11] head injury criterion, HIC,[35] a generalized acceleration model for brain injury threshold (GAMBIT),[28] head impact power (HIP),[29] and Head Impact Technology severity profile (HITsp) [13]), have historically been proposed to estimate the risk of brain injury. However, these metrics do not account for differences in brain material properties across regions or individuals, and are therefore, insufficient to describe different types and severity of brain injury or tolerance limits for all populations.[20] Studies of neuronal and cellular responses to mechanoactivated deformation demonstrate that mechanical forces in the brain during mTBI are capable of triggering both acute and chronic changes in function.[26] Injury thresholds for axonal stretching have also been established in terms of the magnitudes of axonal strain and/or strain rate.[26] These *in vivo* animal and *in vitro* studies indicate the mechanical conditions under which functional deficits appear or cell death results in important brain regions, and inform our understanding of how mTBI occurs at the microstructural level.

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To bridge the gap between kinematic and micro-structural level brain injury studies and to understand how mechanical energy from an external impact is transferred into stress/strain in the brain, computational finite element (FE) models of the head are playing an increasingly important role in estimating regional brain mechanical responses to external impact[6,7,12,16,22,24,25,33,41,42] (see Yang *et al*.[39] for a recent review). This is because, once validated, they provide information on the complex characteristics of brain responses that are otherwise difficult, if not impossible, to measure in live humans under injury-causing impacts. In addition, these models can account for regional differences in material properties and anisotropy, potentially allowing region-specific injury tolerance limits to be established.[30] Although physical, animal and, cadaver models[14,15,27,34] allow testing under controlled conditions and provide important biomechanical data related to head impact, they are unable to provide tissue-level mechanical responses due to the inability to recreate physiological conditions.

Over the past several decades, a number of computational FE models of the human head have been established from different research groups to study the mechanisms of mTBI.[23] More recently, there is a growing interest in utilizing head FE models to understand the biomechanical basis of sports-related concussion[20,25,33,36] because direct measurement of on-field head impact exposure in athletes and other at-risk populations is now available with the use of instrumented helmets [Head Impact Telemetry (HIT) System[2,3,8,13]; Simbex, Lebanon NH]. However, these FE models can vary significantly in model complexity (e.g., from relatively few brain regions[25,33] to more refined anatomical details[22,42]), tissue material properties especially for the brain (hyperelastic[22,25] vs. viscoelastic,[33,42] and whether or not anisotropy is incorporated in tissue properties[7]), head dimensio,[9,23] individual anatomical variations, and in interface conditions between the brain and skull. Consequently, efforts from different research groups to establish injury criteria based on model-estimated regional brain mechanical responses from analyses of real-world injury events such as reconstructed NFL football impacts,[22,24,36,42] pedestrian and motorcycle[24] accidents, and instrumented helmets from collegiate football players[33] have not yielded consensus on an injury tolerance threshold.[30] Interestingly, most of the models have been validated (or, perhaps more appropriately, compared) against similar sets of data derived from a relatively few cadaveric head impact experiments (intracranial pressure,[27,34] relative brain-skull displacement data under direct[14] or helmeted impacts[15]) that involve head impact conditions that typically represent moderate to severe head injuries. More recent experiments on *live* humans using MRI have been performed to provide additional brain biomechanical data. However, these tests have been limited to quasi-static[18] or low-rate impact conditions[32] well below injury levels. Due to the limited experimental data available for model validation and the apparent lack of a universally adopted standard in quantifying model-data comparison, it is possible that multiple “validated” head FE models may produce discordant regional brain responses such as head impact experienced in contact sports.

Because brain injury tolerance thresholds derived from computational simulations are based on model-estimated regional brain responses,[30] it is critical to evaluate whether simulation results from one model are readily translatable into another, and whether response-based injury thresholds established from a specific model can be generalized when a different

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model is employed. We hypothesized that regional brain responses estimated from head FE models under identical biomechanical impact are dependent on the specific head model employed as well as the region of interest (ROI). We conducted a parametric comparison of regional brain responses estimated from three validated head FE models when subjected to identical kinematic inputs representative of actual on-field head impact exposure in contact sports.

MATERIALS AND METHODS

Three models with varying geometrical complexity and material properties of the brain were selected for parametric comparisons in this study. A set of head kinematic data were generated that are representative of the range of head impact exposure (i.e., linear and rotational accelerations and impact locations) sustained by ice-hockey athletes in the field. Model output comparisons including five mechanical variables that have been proposed as potential injury predictors in the literature were conducted in seven specific ROIs. A schematic illustration of the overall dataflow and analysis strategy is shown in Fig. 1.

Characteristics for Three Validated Head FE Models

The three validated models assessed in this study (Fig. 2) are the Dartmouth Scaled and Normalized Model (DSNM[25]), the Simulated Injury Monitor (SIMon[33]) model, and the Wayne State University Head Injury Model (WSUHIM[41]). All these models have been used in brain injury studies, while WSUHIM has also been used in other head injury studies due to its additional head structures included. These models represent a spectrum of model features and parameters, mesh resolutions, and different types of material properties characterizing the brain.

DSNM is based on a standard high-resolution MRI atlas brain[17] and was scaled in this study to represent a 50th percentile adult male. This model features relatively few brain anatomical regions and includes the cerebrum, cerebellum, brainstem, corpus callosum, skull, cerebrospinal fluid (CSF), ventricles, and falx cerebri. A hyperelastic material model[22] is used to characterize the brain mechanical behavior under impact. DSNM has been validated against the most recent cadaveric head impact tests using relative brain-skull displacement data[15] as previously reported.[25]

The SIMon was developed by NHTSA that includes major brain regions such as the cerebrum, cerebellum, falx, tentorium, CSF, pia arachnoid complex, ventricles, brainstem, and bridging veins. Material properties of the different regions are reported in Takhounts *et al*.[33] and the model was validated using cadaveric intracranial pressure[27,34] and relative brain-skull displacement data.[14] As with DSNM, the mesh was created using TrueGrid®.

The most recent WSUHIM[41] was developed using Hypermesh for meshing after a long history of revisions and improvements. The entire head model is made up of over 330,000 elements and uses 15 different material properties for various tissues of the head. It features fine anatomical details including the scalp, the skull (with an outer table, diploë, and inner table), dura, falx cerebri, tentorium, pia, sagittal sinus, transverse sinus, CSF, hemispheres of the cerebrum (with differentiation of white and gray matter), cerebellum, brainstem, lateral

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ventricles, third ventricles, and bridging veins. In addition, facial components (e.g., bones, nasal cartilage, temporal mandibular joint, ligaments, soft tissue, and skin) are also included for facial injury simulations. In this study, the facial components and the scalp were simplified to rigid bodies in order to reduce runtime, as they were not needed for modeling brain responses. Throughout its evolution, WSUHIM has been validated against a series of cadaveric intracranial pressure data[27,34] and relative brain-skull displacement data.[14] This model has been used to study mechanisms of concussion in NFL football players,[36] Indy racecar drivers,[40] real-world automotive crashes,[10] and more recently, for a full spectrum of diffuse brain injuries.[41]

Additional comparisons of model characteristics are provided in the Appendix Tables A1–A5. DSNM uses Abaqus (Version 6.12; Dassault Systemes Simulia Corp., Providence, RI) for impact simulations, whereas LS-DYNA (Livermore Software Technology Corp.) is the solver adopted in SIMon and WSUHIM.

Simulated Head Kinematic Input Based on On-Field Data

Characteristics of model kinematic input was based on head impacts from varsity ice hockey players from Dartmouth College enrolled between 2007 and 2010 as part of an ongoing study of the biomechanical basis of concussion and the effects of repetitive head impacts in collegiate contact sport athletes (approved by the Institutional Review Board and all participants gave written informed consent). Specifically, template resultant acceleration time series for both linear and rotational acceleration (40 ms duration at 1 kHz) were created from 22,402 on-ice head impacts sustained by male collegiate hockey players who wore helmets instrumented with the HIT System during practices and games.[3] Principal component analysis was performed on the resultant head accelerations recorded from all of the impacts to develop characteristic waveforms (Fig. 2). The first principal components were used as the template waveforms and captured 52% of the variance. These time series were then scaled to represent the 50th (17 g, 1534 rad/s^2), 95th (49 g, 4499 rad/s^2), and 99th percentile (96 g, 7812 rad/s^2) peak linear and rotational accelerations of all recorded head impacts, providing nine combinations of linear and rotational head accelerations.

The resulting linear and rotational accelerations were reduced to *x*, *y*, and *z* components across sixteen locations on the head. Using an elliptical coordinate system based on the head dimensions of the 50th percentile male Hybrid III (HIII) anthropomorphic test device (Fig. 3a), five azimuth (θ of 0°, 45°, 90°, 135°, and 180°; angle relative to the *X*-axis; Fig. 3a) and three elevation (α of −45°, 0°, and 45°; angle relative to the *Y*-axis; Fig. 3a) angles were selected to create 15 unique impact locations on the right side of the head. Impacts to the left side of the head were omitted due to head left/right symmetry in geometry. An additional impact location to the apex of the head (α of 90°) was also evaluated. Each impact was assumed to occur perpendicular to the head surface and vector contributions were calculated based on the impact location relative to the head center of gravity (CG). For example, an impact occurring to the direct right side (θ of 90°) midway between the CG and crown of the head (α of 45°) would result in equal contributions of linear *y* and linear *z* (Fig. 3b). Components of rotational acceleration were calculated by taking the cross product of the linear acceleration components with a moment arm relative to the point of rotation (Fig. 3b).

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A point of rotation in the *Z*-axis was assumed to be 3.45 cm below the head CG. This point of rotation was derived experimentally from on-field head impacts in football and has been shown to be consistent with kinematics of the HIII during laboratory impact reconstructions.[1,31] Combining each of the nine acceleration magnitude conditions with the 16 impact locations resulted in a matrix of 144 unique impact conditions for parametric comparisons of the FE models.

Regional Brain Mechanical Variables

For each model, the seven ROIs included for analyses (common in all models) were the left/right cerebrum, left/right cerebellum, left/right brainstem, and whole-brain, as individually defined by their respective developers. The five brain mechanical variables used for comparisons were the maximum principal strain (ε), maximum principal strain rate $(\dot{\varepsilon})$, their product $(\varepsilon \times \dot{\varepsilon})$, von Mises stress (δ), and pressure (*P*). For each model, values of ε, $\dot{\varepsilon}$; δ, and *P* for each element were directly retrieved from the simulation database at each temporal point (at a resolution of 1 ms), whereas values of $\varepsilon \times \dot{\varepsilon}$ for each element were obtained by multiplying the corresponding ε and $\dot{\varepsilon}$ at the same temporal point.

For both DSNM and SIMon, regional average values (weighted by element volumes) for each variable and ROI were first calculated for all temporal points, and the maximum value over the impact duration was obtained to represent the regional peak magnitude for the corresponding variable. In contrast, WSUHIM did not provide mechanical variable average values for a specific anatomical region. Instead, the maximum peak value of each response variable throughout the entire loading period was taken from the average value of the top five element responses at each time point (at a resolution of 1 ms). The maximum value from all sub-regions was used to represent the peak response magnitude for the whole brain.

Data Analysis

To determine the differences among the three FE models, a multivariable Generalized Estimating Equation (GEE) statistical model was utilized that combined linear/rotational acceleration peak values and FE model as independent variables while clustering impact location (i.e., combinations of azimuth and elevation). To assess correlations between each output variable (i.e., ε, $\dot{\varepsilon}$, $\varepsilon \times \dot{\varepsilon}$, δ, and *P*) and head impact kinematics, each FE model and ROI was analyzed separately with two GEE statistical models using either linear or rotational acceleration as an independent variable again with clustering on impact location. No adjustment for multiple comparisons was applied in these analyses. The statistical software R (version 2.14.0) was used and a p value less than 0.05 was considered statistically significant.

RESULTS

Multivariable analyses show highly significant differences among FE models for nearly all output variables and ROIs. The pairwise comparisons indicate that model differences were the greatest between WSUHIM and the other two models as WSUHIM produced substantially higher peak values for all output variables regardless of the ROI ($p < 0.05$; with the exception of δ in the cerebellum region when comparing with DSNM; Table 1).

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Although DSNM also produced significantly different ε and *P* compared with SIMon for all ROIs ($p < 0.05$), such a relationship was not consistent across ROIs for the remaining variables (Table 1), and the pairwise differences were much smaller in magnitude than those when comparing with the WSUHIM counterparts (Fig. 4). As an illustration, Fig. 4 compares the five output variables in the right cerebrum ipsilateral to impact location among the three models as a function of combined linear and rotational peak accelerations while clustering on impact location, showing much larger response ranges for WSUHIM relative to both DSNM and SIMon.

To further demonstrate disparities in model responses, fringe plots of e were generated for each model at the temporal point when their whole-brain responses reached their respective peak values for a representative impact simulation (Fig. 5). Both DSNM and SIMon produced similar magnitudes of ε, while the response level from WSUIBM was approximately twice as high (as indicated by the fringe plot scales), consistent with previous statistical comparisons. In addition, significant differences in the spatial distributions are also apparent. These significant differences are likely a result of their different choices of brain material properties used.

The univariate analyses exploring each FE model separately show that most output variables were highly correlated with both linear and rotational peak accelerations for all models (Table 2). Specifically, brain regional pressure, *P*, significantly increased with the increase in peak linear accelerations for all ROIs, regardless of the model ($p < 0.05$). For the remainder of variables (i.e., ε, $\dot{\varepsilon}$, $\varepsilon \times \dot{\varepsilon}$, and δ), however, such correlations were not uniformly significant across the ROIs (Table 2). In contrast, all regional outputs significantly increased with the increase in rotational peak accelerations, regardless of the model or variable ($p < 0.05$; with the exception of $\dot{\varepsilon}$ in the brainstem ($p = 0.2$) and whole-brain ($p = 0.08$) for WSUHIM. This finding is also similar to that in Weaver *et al.*,[37] where the Cumulative Strain Damage Measure (CSDM) and its variants were used for analyses *via* SIMon.

DISCUSSION AND CONCLUSION

Human head FE models are important tools increasingly employed to investigate the mechanisms of mTBI, as evidenced by numerous head models developed by different institutions/researchers in the last several decades.[38,39] These models, however, differ greatly in model features and parameters such as mesh geometry and the choice of the material properties. Because head FE models are utilized to estimate regional tissue mechanical responses and to derive injury tolerance criteria based on real-world injury scenarios,[10,22,24,33,40–42] it is important to evaluate the feasibility of comparing model-dependent regional brain responses across different head FE models and to assess the applicability of injury tolerance thresholds across different studies. In this work, we simulated head impacts derived from collegiate ice-hockey athletes during play in three validated head FE models. The resulting model-estimated brain responses were then quantitatively compared in terms of five response variables that have been proposed as potential injury predictors of concussion[20] in seven ROIs.

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Results from our study clearly demonstrate signifi-cant disparities in brain responses across the models for nearly all output variables following simulated head impacts ($p < 0.05$) in both magnitude and spatial distribution, even though all the models have been previously validated against similar cadaveric head impact data. Pairwise comparisons indicate the greatest differences in model responses are between WSUHIM and DSNM/SIMon. As shown in Table 1 and Fig. 5, nearly all output variables in the right cerebrum from WSUHIM were much larger than their DSNM or SIMon counterparts. Such substantial differences in brain responses cannot be solely attributed to different data reporting strategies (i.e., localized maximum by WSUHIM vs. the regional averaging in DSNM and SIMon adopted in this study). Differences in model characteristics (e.g., most likely, the brain material properties in this case) were also responsible for these large variations as demonstrated by the disparities in magnitude as well as distribution in the fringe plots (Fig. 5). For example, areas of high e in the mid-sagittal plane were comparable in both DSNM and WSUIBM but were significantly larger than the SIMon counterpart (likely due to its much thicker CSF layer between the brain and the falx that acted as cushion as indicated in the top views). In addition, both SIMon and WSUHIM predicted lower e in the brainstem region, which was opposite in DSNM (likely because a closed head was adopted in DSNM, whereas an open foramen magnum with an elastic membrane was used in both SIMon and WSUHIM; Fig. 5). Although DSNM and SIMon produced responses of similar order of magnitude, they were, nevertheless, statistically different in nearly all ROIs as well (Table 1). These findings strongly suggest that model-predicted brain responses from one study should not be compared with or extended to other studies in which a different head FE model is utilized. Consequently, response-based injury tolerance thresholds from a specific model also should not be generalized to other studies when a different model is used, even if all the models have been validated.

There are two important reasons that lead to significant variations in these validated models and highlight the challenges currently facing model-based biomechanical brain injury researches. First, only limited experimental data are available for partial but incomplete model validation, which is further exacerbated by the lack of a standard universally adopted for successful model-data validation (often qualitative or visual evaluation in practice). Most of the cadaveric head impact experiments are limited to measurements at isolated locations (e.g., coup/contrecoup sites,[27] or at neutral density target embedding locations[14,15]). It is possible that two models with discordant characteristics may generate comparable mechanical responses at these discrete locations but result in statistically different estimates for specific anatomical regions[38,39] or in locations where no measurement data is available from cadaveric experiments (e.g., brainstem). In addition, data from cadaveric experiments are not entirely suitable for head model validation because of degradation in brain tissue properties and loss of perfusion and vascular pressure.[38] Therefore, it remains an open question whether an FE model validated against these cadaveric experiments is sufficiently representative of brain biomechanics in *live* humans. Although full-field brain responses (as opposed to responses at discrete locations) in live humans under quasi-static[18] or mild-rate impact and inertial loading conditions[32] are becoming available using MRI, the loading conditions in these studies are limited to magnitudes far below injurious levels (2–3 g and ~100–200 rad/s^2 with ~300 ms duration), and it warrants further investigation how best to

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extrapolate these data for head FE model validations under typically much higher impact severities that could potentially cause injury (~50–200 g and ~5–20 k rad/s^2 with ~10–40 ms duration) (Fig. 6).

Second, typical head FE models usually undergo multiple revisions throughout their respective evolutions (e.g., in order to improve model sophistication in anatomical details and/or to update brain material properties to reflect the latest experimental data), whereas model validations may not all have been performed on the most recent version. Based on our results, it is unlikely that model validations from a previous version can be readily translated to a different version, even if they were developed within the same research group. Further, it is also worthy of note that researchers may revise model characteristics to reflect the most recent experimental data available (especially the material properties of the brain) after it has been previously validated (for example, from a Mooney–Rivlin[23] to an Odgen[22] type of hyperelastic material for the brain). Additionally, mesh resolution, structural details, boundary conditions between the brain and skull, and even different numerical solvers could all contribute to the differences found in model comparisons, which cannot be neglected when interpreting model estimated results.

These findings underscore the lack of consistency in FE model-based impact simulations across research groups as well as within each group, and highlight the challenges in generalizing model-estimated results from one study to others. Regional brain responses, and hence, the resulting response-based injury thresholds, are clearly model-dependent and are not directly translatable across diffrent FE models. It is important to further note that although our results demonstrate significant variations in model-estimated brain responses, they do not indicate which model is “better” or produces “closer” match with actual brain responses in live humans, because there is no ground-truth data to compare against. Going forward, therefore, it is important to recognize this model-dependency in simulated brain responses and exercise caution when comparing results from different mTBI studies. To facilitate the exchange of model estimation results in the future, it may be important to establish a set of criteria for model qualities such as mesh element qualities, numerical stability, mesh convergence, hourglass energy, *etc*. It may also be informative to perform additional sensitivity analyses for a validated head FE model relative to model components and associated properties as well as to experimental data (e.g., peak linear and rotational accelerations) in order to establish a “confidence interval” in model-estimated brain responses. In addition, quantitative model validations should be reported[19] to assess model estimation performance when compared with experiments, instead of qualitative, and often visual, comparisons. Further improvements in model validation may also be possible by quantitatively correlating estimated mechanical responses with medical images and/or well-selected experiments with documented injury findings that identify specific regions of injury for direct verification of simulation results.[30] In the case of sports-related concussion, for example, changes in diffusion tensor imaging (DTI) parameters from concussed athletes have the potential to serve as a promising imaging biomarker for brain injury and be used as verifications of model-derived brain responses.[25] However, a subject-specific instead of a 50th percentile generic model may be preferred or necessary in these situations as it offers a

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more direct link between brain mechanical responses and the corresponding imaging signature.

Despite these challenges for comparing simulation results from different FE models, similar trends of brain responses with respect to peak kinematic measures of linear and rotational accelerations are observed for all three models in this study, and findings are in agreement with previous findings in the literature. For example, univariate analyses indicated that pressure is most sensitive to peak linear accelerations[22,42] whereas peak maximum principal strain is most sensitive to rotational acceleration magnitudes.[33,36] Although the magnitudes and spatial distributions of mechanical variables vary, general trends on the regions of higher-level responses are consistent. These observations suggest that each FE model can be used independently in practice to inform regional brain responses for specific head impact simulations.

Several limitations in this study are notable. Our statistical analysis in the differences in model responses was limited to the peak values of each output variable, while their differences in temporal evolutions during the simulated impact were not considered. Another limitation was that the kinematic conditions used for FE simulations were developed from head impacts sustained by male collegiate ice-hockey players only. While the majority of published head impact data is derived from football players, ice-hockey impacts were selected because the processing algorithm paired with HIT System instrumented hockey helmets provides a direct solution for 6-DOF linear and rotational acceleration time series data,[3] allowing the development of characteristic resultant time series. The top percentile peak linear and rotational accelerations experienced by male hockey players are similar to those experienced by football players,[3] inclusive of those experienced by female hockey players, and are above the median values reported for diagnosed concussion.[2] While these general on-field parameters provide a wide range of conditions for FE model comparison, the simulated kinematic events should not be considered exhaustive of all potential impact conditions that occur in either the breadth of sports or that may result in moderate to severe head injuries (e.g., contusion, hematoma, or skull fracture). Further, although brain responses at different impact locations were simulated, their significance on disparities in model simulation results was not analyzed due to the small sample sizes. Because head impacts in helmeted sports typically result in accelerations of limited duration range (8.99 ± 3.01 ms[5]) and varying the additional temporal characteristics would have exponentially increased the number of kinematic events required for parametric evaluation, we chose to limit our analyses to a single linear and rotational resultant time series. While exclusion of impact location and duration from our statistical analysis does not affect the general findings in this study, a comprehensive evaluation of model sensitivities to these impact parameters is recommended in the future. In addition, because head impact direction significantly affects brain responses,[21] additional study is needed to understand its implications to brain injury given the asymmetric distribution of impact locations on the head for contact-sports athletes accumulated from a typical play season.[4] Finally, we have only included three models for quantitative comparisons in this study; however, we anticipate that the general conclusions regarding model differences and the resulting disparities in responses will apply for other models as well.

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To conclude, brain responses from three "validated" head FE models were compared under identical head impacts in the context of helmeted collegiate ice-hockey athletes. We found significant disparities in brain responses in nearly all ROIs across the models regardless of the output variable, although general trends in the brain responses relative to the level of head impact kinematics are similar. These findings strongly suggest that model-predicted intracranial responses, and hence, response-based injury tolerance thresholds, from one study based on a specific head FE model cannot and should not be extended or generalized to other studies in which a different model is utilized. However, the trend between regional brain responses and linear and rotational peak accelerations were similar across the models, suggesting that each model can be used independently to simulate head impacts. Although our analysis was in the context of sports-related head impacts, we expect that these conclusions will apply equally for other (more severe) forms of head kinematic response. Going forward, additional model validation/verification using medical images and/or well selected experiments with documented injury findings for positive, region-specific identification of brain injury is recommended whenever possible (e.g., using DTI in the case of mTBI). In addition, more research is needed to accurately characterize material properties of the brain *in vivo*, as these properties will be critical for effective and successful deployment of head FE models for investigations of the mechanisms of mTBI in the future.

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APPENDICES

The following tables report comparisons of the meshes and runtimes (Table A1) and the material properties for the various components of the brain (Tables A2–A4) for the three models.

TABLE A1

Comparisons of model meshes, brain-skull BCs, and runtimes for the three head FE models (all solid elements are hexahedral).

	No. of Nodes	No. of Elem.	Typical elm. size (mm)	Mesh generator	Simulation software	Type of brain-skull BCs	Typical runtime for one head impact
DSNM	102,400	97,800	2-5	TrueGrid + MATLAB	Abaqus	Frictional	2.5 h
SIMon	42,500	40,700	1-4	TrueGrid	LS-DYNA	Common nodes	40 min
WSUHIM	391,000	333,000	2-3	Hypermesh	LS-DYNA	Frictional	9.0 h

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TABLE A2

Comparisons of volumes of major model components for the three head FE models (units in cc).

	Cerebrum	Cerebellum	Brainstem	Ventricle	CSF
DSNM	1190	120	20	18	72
SIMon	932	98	16	11	364*
WSUHIM	1160	122	38	26	161

* "CSF" for SIMon includes CSF and pia arachnoid complex (Fig. 2; 12).

TABLE A3

Hyperelastic and viscoelastic material model (identical to the "average model" used in Kleiven[22]) for the whole-brain in DSNM showing the Ogden constants (μ_i, and α_i) and Prony series constants (g_i and τ_i) in Abaqus convention.

μ_1 (Pa)		α_1		α_1 (Pa)		α_2
271.7		**10.1**		**776.6**		**–12.9**
	***i* = 1**	***i* = 2**	***i* = 3**	***i* = 4**	***i* = 5**	***i* = 6**
g_i	7.69e–1	1.86e–1	1.48e–2	1.90e–2	2.56e–3	7.04e–3
τ_i (s)	1.0e–6	1.0e–5	1.0e–4	1.0e–3	1.0e–2	1.0e–1

Material properties for other parts are in McAllister *et al*.[25]

TABLE A4

Viscoelastic material properties for the brain used in SIMon.

Component	Density (kg/mm^3)	Bulk modulus (MPa)	Short term shear modulus (kPa)	Long term shear modulus (kPa)	Decay constant (ms^{-1})
Whole-brain	1.04e–06	558.47	1.66	0.928	16.95

Material properties for other parts are in Takhounts *et al*.[33]

TABLE A5

Viscoelastic material properties for the brain components for WSUHIM.

Component	Density (kg/mm^3)	Bulk modulus (MPa)	Short term shear modulus (kPa)	Long term shear modulus (kPa)	Decay constant (ms^{-1})
Gray matter	1.02e–06	2.00	12.00	2.00	0.10
White matter	1.06e–06	2.00	10.00	1.00	0.10
Brainstem/corpus callosum	1.06e–06	2.00	7.00	0.70	0.10
Cerebellum	1.06e–06	2.00	10.00	2.00	0.10
Ventricles/CSF	1.06e–06	2.19	0.10	0.01	0.1

Material properties for other parts are in Zhang and Gennarelli.[41]

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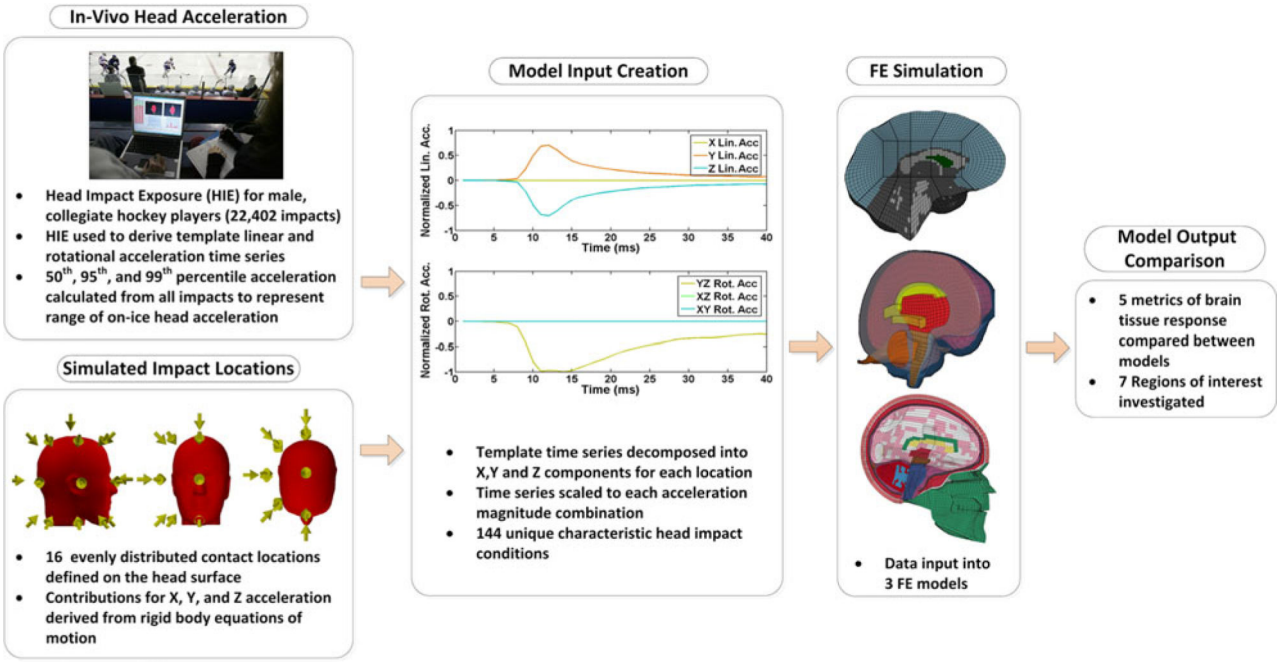

FIGURE 1.

Schematic illustration of the data flow and analysis strategy in this study: 144 representative kinematic events were derived from a set of head impacts recorded from male collegiate ice hockey players (n = 22,402) to drive three validated head FE models. The resulting regional brain responses were then compared between models across seven regions of interest.

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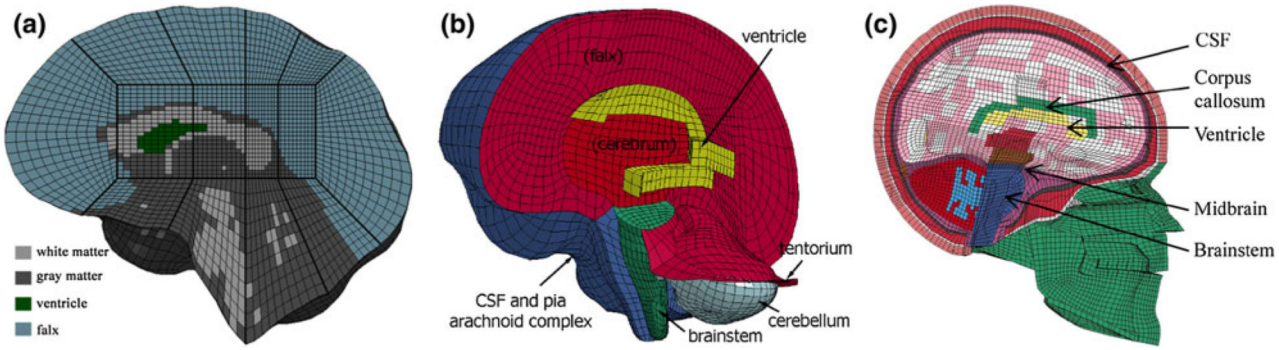

FIGURE 2.

Comparison of the three "validated" FE models of the human head assessed in this study (a: DSNM; b: SIMon, c: WSUHIM). These models represent a spectrum of model features and parameters, mesh resolutions, and different types of material properties. Volumes of major brain components are compared in Table A2.

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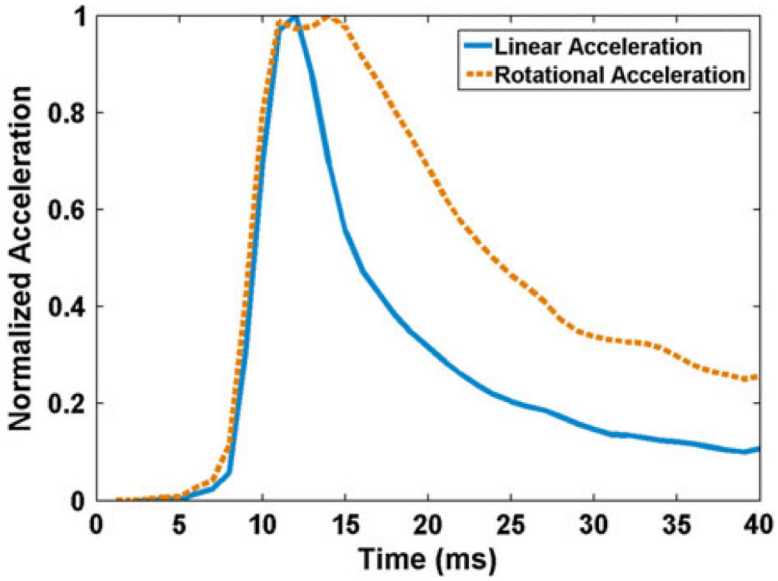

FIGURE 3.

Characteristic time series for linear and rotational accelerations that were subsequently scaled to represent 50th, 95th, and 99th percentile magnitudes.

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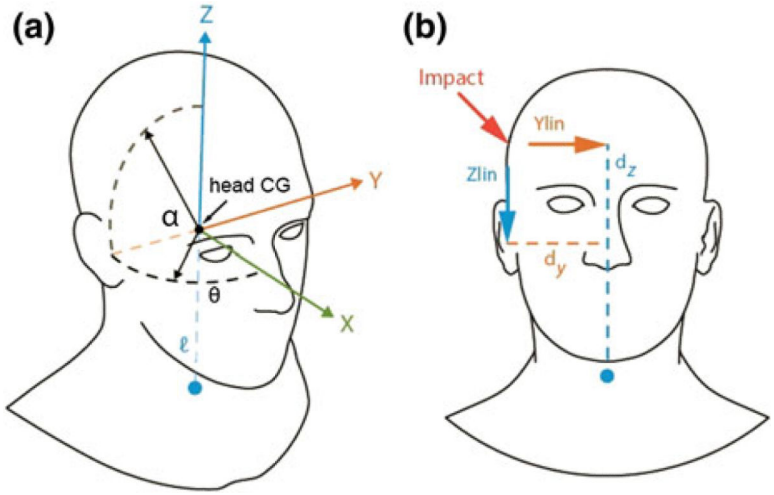

FIGURE 4.

(a) Sixteen impact locations were defined using combinations of azimuth, θ, and elevation, α (see text for details). A pivotal point of rotation about the neck was estimated to occur 3.45 cm below the head CG (i.e., *l* in the figure[31]). The rotational acceleration components were calculated by crossing the linear components by the distance relative to the pivotal point. (b) An impact location that represents θ of 90 and α of 45° is shown.

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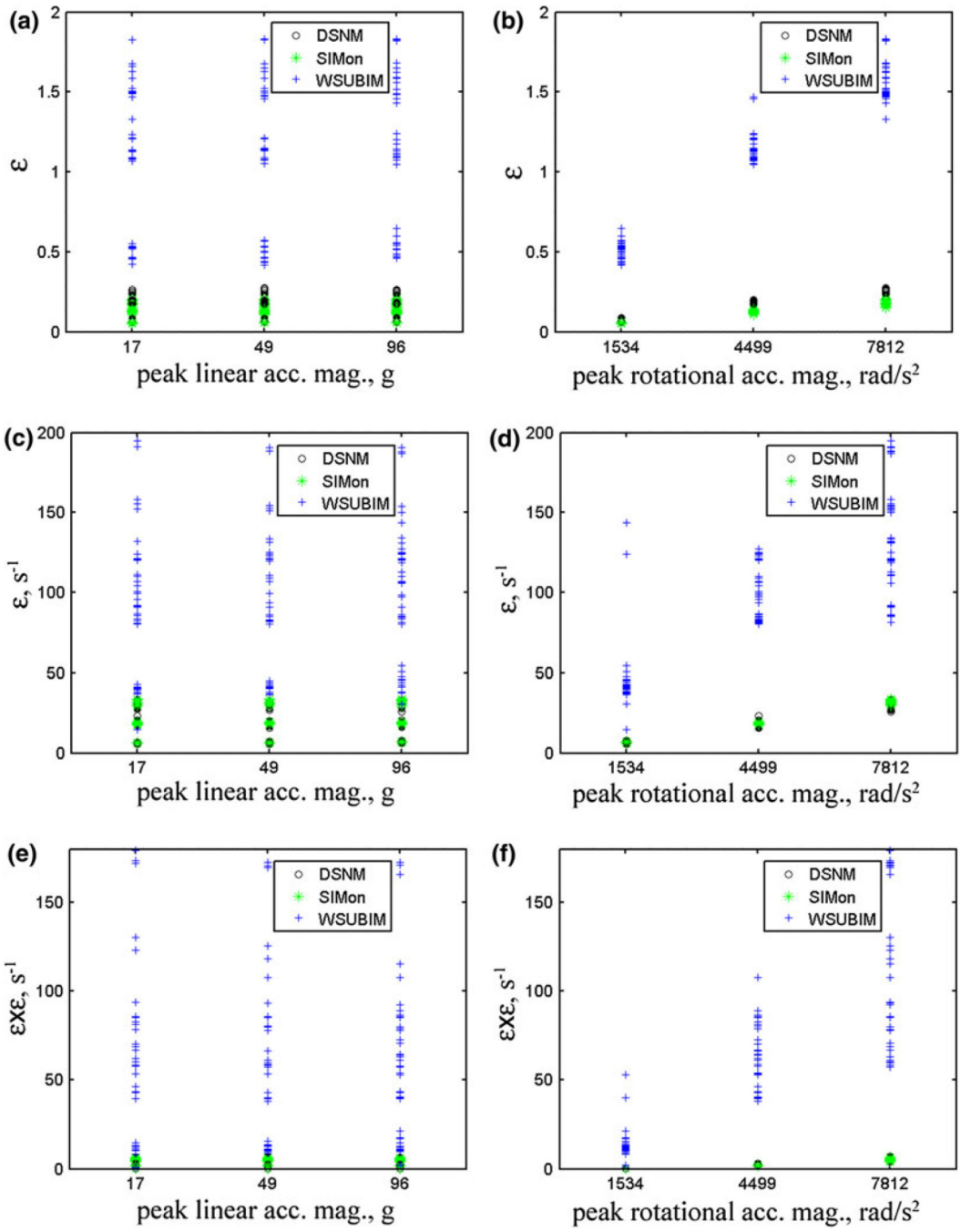

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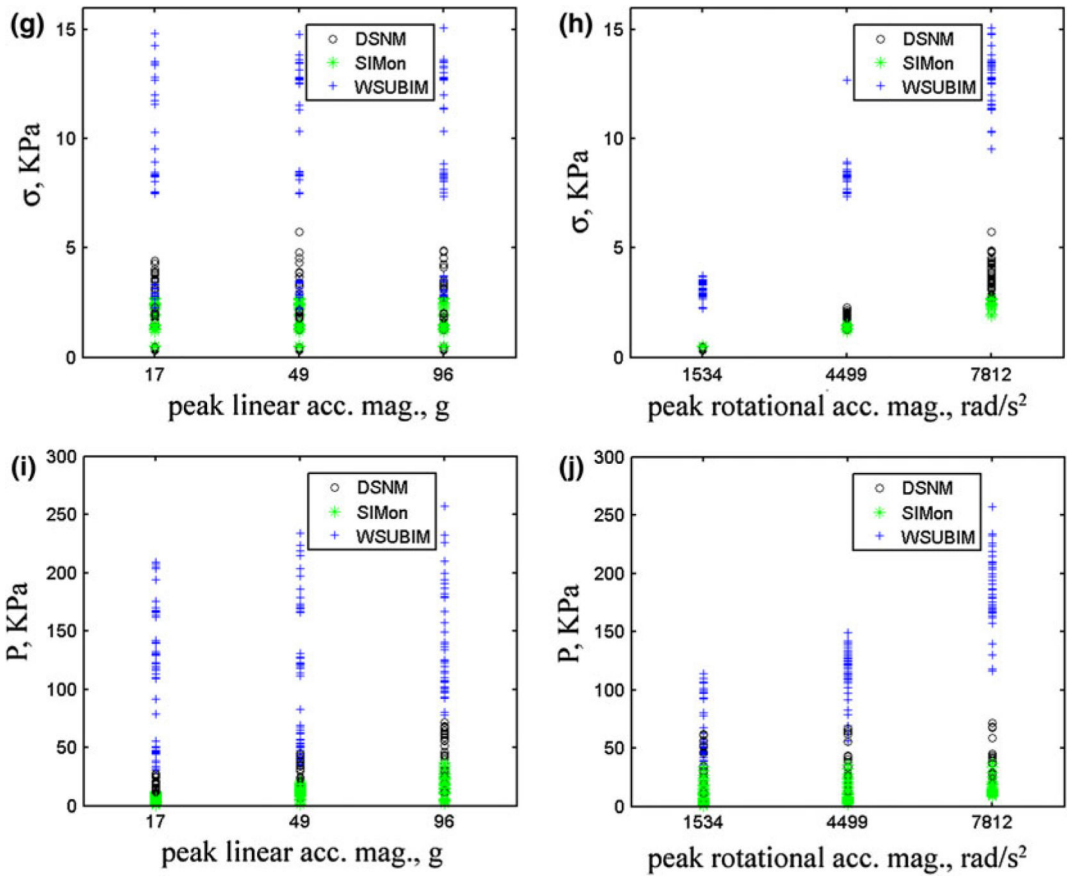

FIGURE 5.

Comparisons of brain mechanical variables from the three FE models as a function of linear and rotational peak accelerations for the right cerebrum: (a, b) ε; (c, d) $\dot{\varepsilon}$, **(e, f)** $\varepsilon \times \dot{\varepsilon}$, **(g, h) δ, and (i, j)** ***P***.

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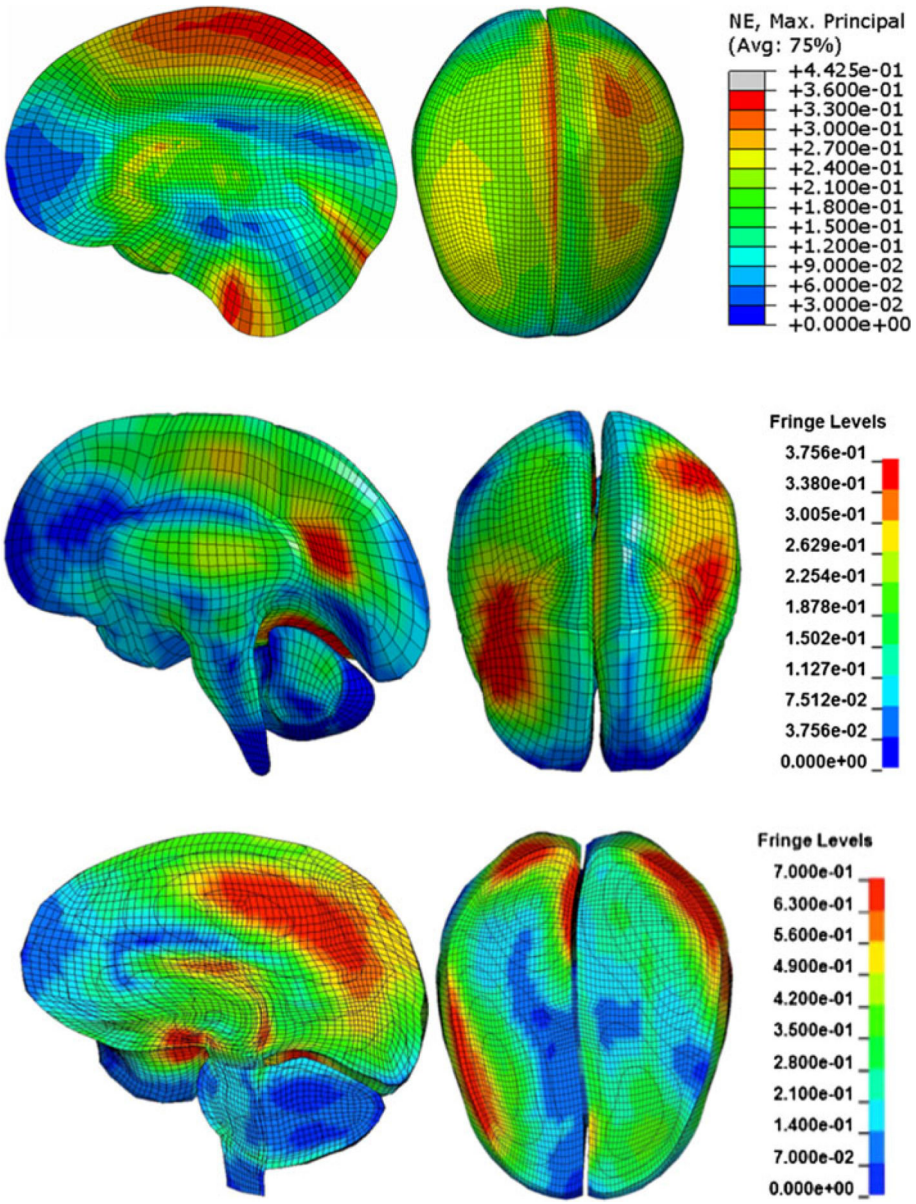

FIGURE 6.

Distributions of ε in the mid-sagittal plane and top views for the three models when the whole-brain response reached their respective peak values. All models were subjected to identical head kinematics (the linear and rotational peak accelerations, and the azimuth and elevation of 49 g, 4499 rad/s^2, 135°, and 45°, respectively, representing a 95th percentile linear and rotational peak acceleration impact to the upper right frontal region of the brain).

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TABLE 1

Summary of the significance of differences between FE models from pairwise comparisons (p values ≥ 0.05 in bold).

Variable/model	SIMon vs. DSNM	WSUBIM vs. DSNM	WSUBIM vs. SIMon
ε			
Whole brain	<2e–16	<2e–16	< 2e–16
Left cerebrum	5.53e–10	<2e–16	< 2e–16
Right cerebrum	1.51e–13	<2e–16	< 2e–16
Left cerebellum	<2e–16	<2e–16	< 2e–16
Right cerebellum	<2e–16	<2e–16	< 2e–16
Left brain stem	0.000186	<2e–16	< 2e–16
Right brain stem	0.00109	<2e–16	< 2e–16
$\dot{\varepsilon}$			
Whole brain	< 2e–16	<2e–16	< 2e–16
Left cerebrum	**0.775**	<2e–16	< 2e–16
Right cerebrum	0.00331	<2e–16	< 2e–16
Left cerebellum	2.84e–11	<2e–16	< 2e–16
Right cerebellum	8.38e–10	<2e–16	< 2e–16
Left brain stem	**0.422**	<2e–16	< 2e–16
Right brain stem	**0.198**	<2e–16	< 2e–16
$\varepsilon \times \dot{\varepsilon}$			
Whole brain	<2e–16	<2e–16	< 2e–16
Left cerebrum	**0.317**	<2e–16	< 2e–16
Right cerebrum	**0.303**	<2e–16	< 2e–16
Left cerebellum	< 2e–16	<2e–16	< 2e–16
Right cerebellum	3.33e–16	<2e–16	< 2e–16
Left brain stem	**0.218**	<2e–16	< 2e–16
Right brain stem	**0.493**	<2e–16	< 2e–16
σ			
Whole brain	**0.808**	<2e–16	< 2e–16
Left cerebrum	1.52e–05	<2e–16	< 2e–16
Right cerebrum	4.08e–06	<2e–16	< 2e–16
Left cerebellum	1.5e–12	**0.283**	0.00137
Right cerebellum	1.29e–08	**0.516**	< 2e–16
Left brain stem	7.5e–05	0.000583	4.12e–08
Right brain stem	2.22e–05	0.00101	1.36e–07
P			
Whole brain	<2e–16	<2e–16	< 2e–16
Left cerebrum	<2e–16	<2e–16	< 2e–16
Right cerebrum	7.02e–05	<2e–16	< 2e–16
Left cerebellum	0.000711	3.61e–08	1.69e–07

Variable/model	SIMon vs. DSNM	WSUBIM vs. DSNM	WSUBIM vs. SIMon
Right cerebellum	0.00282	7.22e–10	8.07e–09
Left brain stem	4.87e–08	<2e–16	< 2e–16
Right brain stem	1.31e–07	<2e–16	< 2e–16

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TABLE 2

Summary of the significance of peak linear accelerations on the five mechanical output variables (p values ≥0.05 in bold).

	DSNM	SIMon	WSUBIM
ε			
Whole brain	**0.053**	0.0073	**0.22**
Left cerebrum	0.0088	0.016	**0.74**
Right cerebrum	**0.22**	0.0045	**0.45**
Left cerebellum	0.00041	**0.094**	0.022
Right cerebellum	5.7e–05	**0.083**	0.00011
Left brain stem	0.02	**0.39**	2.9e–12
Right brain stem	0.0029	**0.05**	9.2e–06
$\dot{\varepsilon}$			
Whole brain	0.032	< 2e–16	7.6e–07
Left cerebrum	7.7e–05	0.025	**0.29**
Right cerebrum	**0.14**	2e–09	**0.054**
Left cerebellum	**0.061**	6.3e–07	7.7e–05
Right cerebellum	0.00061	4.4e–10	7.8e–06
Left brain stem	**0.55**	< 2e–16	2.9e–07
Right brain stem	**0.062**	7.8e–16	3e–07
$\varepsilon \times \dot{\varepsilon}$			
Whole brain	**0.092**	1.2e–11	0.00021
Left cerebrum	**0.41**	0.0021	**0.54**
Right cerebrum	**0.18**	0.0022	**0.4**
Left cerebellum	**0.11**	8.7e–07	0.0014
Right cerebellum	0.0021	4e–04	0.0023
Left brain stem	**0.29**	**0.064**	0.00013
Right brain stem	0.0028	0.022	9.9e–05
σ			
Whole brain	0.034	**0.12**	0.0012
Left cerebrum	**0.11**	**0.25**	**0.85**
Right cerebrum	0.0036	**0.39**	**0.23**
Left cerebellum	0.0038	**0.16**	**0.16**
Right cerebellum	3.9e–05	**0.067**	0.0042
Left brain stem	0.017	0.0087	**0.87**
Right brain stem	6.5e–08	**0.16**	1.8e–06
P			
Whole brain	<2e–16	1.7e–09	2.7e–09
Left cerebrum	<2e–16	4.1e–09	3e–04
Right cerebrum	2.3e–12	3.8e–09	1.5e–11
Left cerebellum	3.6e–06	5.9e–13	5.4e–05

	DSNM	SIMon	WSUBIM
Right cerebellum	3.4e–10	1.2e–11	3.5e–08
Left brain stem	2.4e–06	5.2e–08	7.7e–07
Right brain stem	1.4e–06	6.1e–09	4.5e–08

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