Journal of the mechanical behavior of biomedical materials 68 (2017) 88–102

Contents lists available at ScienceDirect

Journal of the Mechanical Behavior of Biomedical Materials

journal homepage: www.elsevier.com/locate/jmbbm

Influence of high deformation rate, brain region, transverse compression, and specimen size on rat brain shear stress morphology and magnitude

Henry W. Haslach Jr.*, Jenna M. Gipple, Lauren N. Leahy

Department of Mechanical Engineering, University of Maryland, College Park, MD 20742, USA

ARTICLE INFO

Keywords:
Rat brain mechanical response
High-rate translational shear deformation
Combined translational shear and compression
Specimen size effect
Solid-fluid interaction

ABSTRACT

An external mechanical insult to the brain, such as a blast, may create internal stress and deformation waves, which have shear and longitudinal components that can induce combined shear and compression of the brain tissue. To isolate the consequences of such interactions for the shear stress and to investigate the role of the extracellular fluid in the mechanical response, translational shear stretch at 10/s, 60/s, and 100/s translational shear rates under either 0% or 33% fixed transverse compression is applied without preconditioning to rat brain specimens. The specimens from the cerebrum, the cerebellum grey matter, and the brainstem white matter are nearly the full length of their respective regions.

The translational shear stress response to translational shear deformation is characterized by the effect that each of four factors, high deformation rate, brain region, transverse compression, and specimen size, have on the shear stress magnitude averaged over ten specimens for each combination of factors. Increasing the deformation rate increases the magnitude of the shear stress at a given translational shear stretch, and as tested by ANOVAs so does applying transverse fixed compression of 33% of the thickness. The stress magnitude differs by the region that is the specimen source: cerebrum, cerebellum or brainstem. The magnitude of the shear stress response at a given deformation rate and stretch depends on the specimen length, called a specimen size effect. Surprisingly, under no compression a shorter length specimen requires more shear stress, but under 33% compression a shorter length specimen requires less shear stress, to meet a required shear deformation rate. The shear specimen size effect calls into question the applicability of the classical shear stress definition to hydrated soft biological tissue.

1. Introduction

A blast wave incident on the head can induce mild traumatic brain injury by generating a deformation wave in the brain. In military personnel, exposure to a blast wave insult apparently causes a different type of physical neuropathology than the chronic traumatic encephalopathy from repeated impact insults seen in contact sport athletes (Shively et al., 2016). A common animal model for the blast wave effect is a rat subjected to a high-pressure compressed air blast from a shock tube. However, shock tube or blast tests are too uncontrolled to produce insight about reconfiguration of the tissue in different brain regions. Further, one cannot directly measure the applied internal deformation during the insult to the brain of the animal exposed to the blast from the shock tube, and therefore computational models play an important role to characterize the response of brain tissue to blast exposure. The usefulness of such numerical models depends strongly on knowledge of the shear stress response to applied deformations of the tissue. A finite element method (FEM) model of the event in the rat brain requires stress-stretch data that leads to a constitutive model for each of the heterogeneous cerebrum, the highly vascularized grey matter of the cerebellum, and the white matter of the brainstem, the three major regions of the rat brain.

Brain tissue is composed of solid matter as well as extracellular fluid (ECF) that surrounds brain cells and lies in the extracellular space comprising about 20% of the brain parenchymal volume. The ECF is the medium for diffusion-based functions such as nutrient transport to, and waste removal from, the cells and non-synaptic cell-cell communication (e.g. Verkman, 2013). The ECF is a candidate for the medium through which deformations from external insults are transmitted to deeper brain regions.

External mechanical insults to the brain induce high strain rate shear as well as simultaneous compressive deformation waves in the brain tissue (Cernak and Noble-Haeusslein, 2010) because the deformation wave is a combination of translational shear and compression waves (Taber et al., 2006). Translational shear tests without compression have applied small strain sinusoidal loading (Arbogast et al., 1997;

* Corresponding author.
E-mail address: haslach@umd.edu (H.W. Haslach).

http://dx.doi.org/10.1016/j.jmbbm.2017.01.036
Received 29 September 2016; Received in revised form 3 January 2017; Accepted 23 January 2017
Available online 26 January 2017

Nicolle et al., 2004) and large deformation, constant rate deformations followed by stress relaxation (Darvish and Crandall, 2001; Prange and Margulies, 2002; Ning et al., 2006). Torsional shear tests may not relate to the shear caused by a wave inside the brain because the shear wave component induces translational shear in vivo rather than rotational shear.

The application of fixed compression in the thickness direction during shear is a first approximation to the interaction of the shear and compression components of a deformation wave in the brain to begin to understand the influence of compression on the high deformation rate translational shear response. Compression may modify the paths in which the ECF flows under shear. Our hypothesis is that the ECF influences the combined shear and compression response as reflected in the shear stress supported.

Our goal is to determine the influence of high-rate translational shear deformation, the regional source of the specimen, the presence of transverse unconfined compression, and the size of the specimen on the morphology of the translational shear stress curve and on the magnitude of the shear stress. The morphology of the translational shear stress curves provides indicators of minor internal reconfiguration that is not proof of tissue damage. We also report instances of visible large-scale severe damage in the small cerebrum specimens sheared to large deformations at the higher rates that may eventually in future studies give insight into the mechanical contributors to brain injury.

In particular, we produce high-rate large deformation translational shear stress data that represent the average response within each of the three rat brain regions individually for translational shear deformation up to 1000 mm/s. This investigation of the shear stress response to high shear deformation constant rates uses the same apparatus and the same protocol, but with fast deformation rates, previously used to study the slow deformation rate shear response (Haslach et al., 2015a). Since the rat brain is small enough to fit in a 2.5×2×2 cm volume, one can approximate the mechanical response of the full rat brain with specimens that are nearly the length of the cerebrum or the full lateral dimension of the cerebellum grey matter, or the width of the brainstem respectively, in contrast to specimens chosen from within a particular brain region of a larger mammal such as a pig, sheep or cow. Large relative to the rat brain size, heterogeneous, rather than localized, rat brain specimens allow room for extracellular fluid (ECF) redistribution and include the interactions of substructures in each regions of the brain. But if one centers a smaller sample on a smaller region, one must examine whether smaller specimens generate the same shear stress response as the larger specimens. The specimen size is investigated because no standard specimen size criterion exists for mechanical studies of brain tissue.

The published high-rate shear stress data from porcine and human cerebrum tissue from the cerebrum (Rashid et al., 2013; Donnelly and Medige, 1997) differ drastically in magnitude. In an investigation of whether the specimen geometric size influences the stress response of soft biological tissue, Carew et al. (2003) found a specimen size effect in their tensile tests of porcine aortic valve tissue. Because it is unknown whether a specimen size effect occurs in all hydrated biological soft tissue, different size specimens from the rat brain are sheared at the same rate. Such a size effect, if it exists, would make mathematical modeling a more complex problem than anticipated. We investigate whether the geometric size of the sample influences the magnitude of the shear stress response under no compression and whether any size effect found is modified by the presence of transverse compression.

2. Methods and materials

The whole rat brains harvested from freshly euthanized Sprague Dawley rats (6–9 mo) are approximately 2 cm long and 1.2 cm wide. These brains are stored in Mg^{+}/Ca^{2+}-free phosphate buffered saline solution (PBS) at room temperature until testing within two hours of harvest in order to minimize tissue degradation. PBS has an osmolality and ion concentration similar to that of the body to keep cells in an isotonic state. Refrigeration is avoided since the internal specimen temperature would not be known once removed from refrigeration.

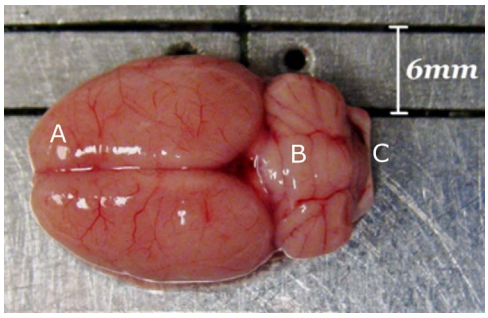

Fig. 1. The rat brain after extraction with the brain regions indicated. A is the cerebrum; B is the cerebellum; C is the brainstem beneath the cerebellum. The anterior is the left end.

2.1. Specimen preparation

After excising the brain from the rat, an incision parallel to the coronal plane separates the cerebellum from the cerebrum and an incision along the center line of the cerebrum separates the cerebral hemispheres. To produce specimens from each rat brain cerebrum that are nearly the length of the cerebrum, a scalpel guided by grooves properly spaced in a metal fixture slices four sagittal planar slabs of thickness 3 mm, two from each hemisphere (Fig. 1). The specially made cutting fixture has three precision-machined guide grooves, which are cut 4, 5, and 6 mm apart and have a width that accepts #10 and #11 scalpel blades. The sagittal slab closest to the joint between the hemispheres is called an *inner* cerebrum specimen and the other is called *outer*. Each slab contains an unknown proportion of white and grey matter, but the inner specimen contains white matter from the corpus callosum. The specimens are trimmed at the anterior and posterior ends as well as the top and bottom to create a 10 by 6 mm surface and a thickness of 3 mm. The shear in the 10 mm anterior to posterior direction and normal compression in some tests are applied on the 10×6 mm cerebrum specimen surface. One 10×6 mm surface specimen each is cut from the grey matter portion of the cerebellum (Fig. 1) that is naturally about 4.5 mm thick. After the cerebellum is separated from the cerebrum by a cut in a coronal plane and the white matter brainstem is separated by a cut in the horizontal plane, the cerebellum is trimmed by cuts in the inferior horizontal (transverse) plane and on the lateral ends in the sagittal plane. The 10 mm dimension in the horizontal plane lies in the lateral direction and is the shear direction. Some sets of grey specimens are not trimmed to 3 mm thickness, while other sets are trimmed to 3 mm thickness by removing matter from the inferior horizontal surface. The white specimens cut from the brainstem portion under the cerebellum are 6×6×3 mm because the brainstem is about 6 mm wide (Fig. 1). The shear direction is along the longitudinal direction of the brainstem, parallel to the presumed dominant axonal direction.

To obtain smaller length specimens for the size effect study, symmetric trimming the ends of the specimen to shorten the dimension in the shear direction ensures that all specimens are centered in the same brain location. The 6 mm width and the thickness are not modified.

2.2. Apparatus

A shear fixture (Fig. 2) to accommodate such specimens was designed and built to apply translational shear from 25 mm long flat grips to flat rectangular plate specimens excised from the rat brain. The