

INFLUENCE OF ANGULAR ACCELERATION DURATION ON FUNCTIONAL OUTCOMES FOLLOWING MILD DIFFUSE BRAIN INJURY

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ABSTRACT

Diffuse brain injury (DBI) manifests as a spectrum of injuries and severity has been associated with several kinematic based metrics. However, influence of angular acceleration duration is often overlooked. This study provides a focused analysis of angular acceleration duration as a nonexclusive indicator of DBI severity. Functional deficits in rats, measured as time to reappearance of corneal and righting reflexes, were assessed following rotationally induced mild DBI. Subjects were exposed to mean angular acceleration durations of 2.0 ± 0.2 msec (mean \pm standard deviation), and 3.0 ± 0.1 msec in short and long duration groups respectively. All other rotational kinematics were held constant. Functional deficits increased significantly ($p < 0.05$) as a function of angular acceleration duration. Angular velocity was not sensitive to these functional deficits. Understanding the influence of duration independent of other influencing factors may highlight its role in the DBI mechanism and help identify appropriate DBI metrics.

Keywords: angular acceleration, angular acceleration duration, concussion, diffuse brain injury, mild traumatic brain injury

TOLERANCE CRITERIA correlate kinetic and kinematic measures to injury levels. The most effective criteria are sensitive to specific, clinically defined injury gradations and include all biomechanical factors influencing injury outcome. Traditional injury levels associated with diffuse brain injury (DBI) include concussion and diffuse axonal injury (DAI), although more specific injury levels were associated with the Abbreviated Injury Scale (Gennarelli *et al.* 2003; Gennarelli and Wodzin 2002; Mucciardi *et al.* 1977). DBI determinants previously associated with injury severity include brain mass (Douglass *et al.* 1968; Ommaya *et al.* 1967), plane of rotation (Gennarelli *et al.* 1987; Ono *et al.* 1980; Shatsky *et al.* 1974), angular acceleration magnitude (Abel *et al.* 1978; Higgins and Schmall 1967; Ommaya and Gennarelli 1974; Unterharnscheidt and Higgins 1969), and angular velocity (Hirsch *et al.* 1968; Meaney *et al.* 1993; Smith *et al.* 2000). Some experimental studies have identified angular acceleration magnitude as the sole determinant of DBI severity, with increasing magnitudes associated with more severe injuries (Gennarelli *et al.* 2003; Ommaya and Hirsch 1971). Other studies developed concussive injury tolerance levels highlighting a relationship between angular acceleration magnitude and angular velocity, with lower tolerance at higher angular velocities (Hirsch *et al.* 1968; Margulies and Thibault 1992; Thibault and Gennarelli 1990). Components of angular velocity computation include angular acceleration magnitude and duration. Therefore, those studies indirectly identified a role of angular acceleration duration in DBI injury susceptibility. However, due to its dependence on both magnitude and duration of angular acceleration, angular velocity may not be the best indicator of injury tolerance. To date, no study has experimentally outlined the independent role of angular acceleration duration in DBI.

The confounding effects of insult magnitude and duration on traumatic brain injury severity for linear head acceleration was highlighted during the development of the Head Injury Criteria (HIC) (Gurdjian 1966; Lissner and Rinder 1960). Six experimentally obtained data points were used to describe decreased injury tolerance with decreased linear acceleration magnitude and increased duration. Derivations of HIC include temporal limits during which angular acceleration magnitude is integrated (Chou and Nyquist 1974; Kamarajan *et al.* 1999; Newman *et al.* 2000; Takhounts and

Eppinger 2003). A similar relationship may exist for DBI, wherein decreased angular acceleration magnitude requires increased angular acceleration duration to induce equivalent DBI severity. However, HIC is not directly applicable to DBI as it considers only linear head accelerations and DBI most commonly results from head angular accelerations. Literature supports this assertion as DBI results from head angular acceleration and focal-type injuries result from linear acceleration (Gennarelli *et al.* 1972; Gennarelli *et al.* 1987; Higgins and Schmall 1967; Hodgson *et al.* 1983; Ommaya and Hirsch 1971; Ono *et al.* 1980; Stalnaker *et al.* 1973; Unterharnscheidt 1971). Epidemiological studies highlight the need for tolerance criteria specific to rotational head injury as DBI occurrence continues throughout sports related activities, motor vehicle collisions, falls, and assaults (Delaney and Frankovich 2005; Echemendia *et al.* 2001; Imajo and Kazee 1992).

Although the independent effect of angular acceleration duration on DBI tolerance was not experimentally investigated, studies have cited a confounding role in addition to angular acceleration magnitude (Hayashi 1970; Ommaya *et al.* 1967). This role is highlighted by experimental studies listed in Table 1, resulting in varying levels of DBI severity through sagittal plane head acceleration. Because those studies implemented different species, angular acceleration magnitude and duration were scaled to the human for cross-comparison.

Table 1. Experimental DBI studies scaled to the human (mean \pm standard deviation).

Collection	Author	Ang. Accel. Magnitude (krad/s ²)	Ang. Accel. Duration (msec)	Loading Plane	Injury Severity
1	Ono <i>et al.</i> (1980)	13 \pm 8	11 \pm 4	Sagittal	Concussion
	Unterharnscheidt and Higgins (1969)	14 \pm 5	11 \pm 3	Sagittal	Concussion
	Thibault and Gennarelli (1990)	18 \pm 6	18 \pm 8	Sagittal	Concussion
	Gennarelli and Thibault (1982)	20 \pm 7	15 \pm 6	Sagittal	Concussion
2	Gennarelli <i>et al.</i> (1987)	19 \pm 5	20 \pm 2	Sagittal	Diffuse Axonal Injury
	Gennarelli and Thibault (1982)	20 \pm 2	18 \pm 2	Sagittal	Diffuse Axonal Injury
3	Gennarelli and Thibault (1982)	32 \pm 9	14 \pm 4	Sagittal	Acute Subdural Hematoma

The importance of angular acceleration duration is clearly demonstrated by Gennarelli & Thibault (1982), wherein substantially increased durations from 15 \pm 6 msec to 18 \pm 2 msec with insignificant changes in angular acceleration magnitude led to increased DBI severity from concussion to DAI. This finding is supported through comparison of data from Thibault & Gennarelli (1990) and Gennarelli *et al.* (1987). Retrospective analysis of those data demonstrated that substantially increased durations from 18 \pm 8 msec to 20 \pm 2 msec with slightly increased angular acceleration magnitudes also resulted in increased DBI severity from concussion to DAI. Additionally, studies highlighted in Table 1 may indicate a lower threshold for both magnitude and duration of angular acceleration. Studies in Collection 1 demonstrated increased angular acceleration magnitude greater than 50% and increased duration of 38%, while the resulting injury level remains unchanged. Therefore, to fully characterize the influence of angular acceleration duration on DBI severity, experimental studies should be conducted to independently assess the contribution of this important variable to injury severity and outcomes.

This study was designed to experimentally investigate effects of angular acceleration duration on DBI severity using an in vivo model originally presented at the 2006 IRCOBI meeting. Angular acceleration magnitude was held constant and duration was varied to two independent levels. Due to the absence of more severe pathology, injury severity was assessed using functional deficits. The present hypothesis, based upon experimental results in Table 1, was that duration can independently affect DBI severity and that increasing duration will lead to more severe functional deficits.

METHODS

EXPERIMENTAL MODEL: Mild DBI was induced in rats using a modified version of our experimental model presented at the 2006 IRCOBI Conference (Fijalkowski *et al.* 2006). The previous version of the model used a spring-based launching system to propel an impactor down a guide tube. For increased accuracy, the launching system was replaced by an extended drop tube without springs, relying exclusively on gravity to accelerate the impactor.

The impactor was propelled down a guide tube to contact a laterally extended moment arm on the helmet fixture. Initial height and mass of the impactor was used to control angular acceleration magnitude. An elastomer interface between the impactor and moment arm was used to modulate angular acceleration duration. Following impact, a pin joint constrained helmet motion to pure coronal plane rotation, without translation. An approximately rigid head/helmet interface facilitated strict transfer of rotational helmet motion to head rotation. Maximum helmet rotation was limited to 90 degrees by a foam stopping interface that minimized deceleration magnitude.

Preliminary testing was conducted using a rat surrogate to determine experimental model parameters (drop height, impactor mass, and elastomer thickness) required for 435 krad/s² angular acceleration magnitude and 2.0 or 3.0 msec durations. All other rotational kinematics were held constant. This methodology enabled functional outcome differences in experimental rats to be attributed solely to changes in angular acceleration duration. Insults were designated as either short-(2 msec) or long-(3 msec) durations. Along with three control animals, four and six rats were subjected to short- and long-duration insults, respectively (Table 2).

Table 2. Test matrix including experimental model parameters.

Parameter	Control	Short duration	Long duration
Number of animals	3	4	6
Target Angular Acceleration Duration (msec)	...	2.0	3.0
Target Angular Acceleration Magnitude (krad/s ²)	...	435	435
Impactor Mass (g)	...	450	500
Drop Height (m)	...	6.1	6.1
Elastomer Thickness (cm)	...	1.0	1.5

EXPERIMENTAL SETUP: Two high resolution (0.875 mm/pixel) video cameras were used to track displacement of reflective targets attached to the helmet fixture. The primary camera was oriented perpendicular to the coronal plane and used to track targets attached at the center of helmet rotation and on the lateral extent of the moment arm at 18,000 frames per second. The secondary camera was oriented perpendicular to the sagittal plane and used to quantify out-of-plane helmet displacement, and closing velocity of the impactor at 3,000 frames per second.

Two targets were attached to the helmet system in sagittal and coronal planes (Fig. 1). Videographic images were used to measure temporal target displacements using motion analysis software (Image Express, Cheshire, CT). In the coronal plane, displacement of the moment arm target

relative to the anterior fixture target was used to compute helmet rotation. Linear displacement of the sagittal plane anterior fixture target relative to the front mount target was used to determine out-of-plane helmet motion.

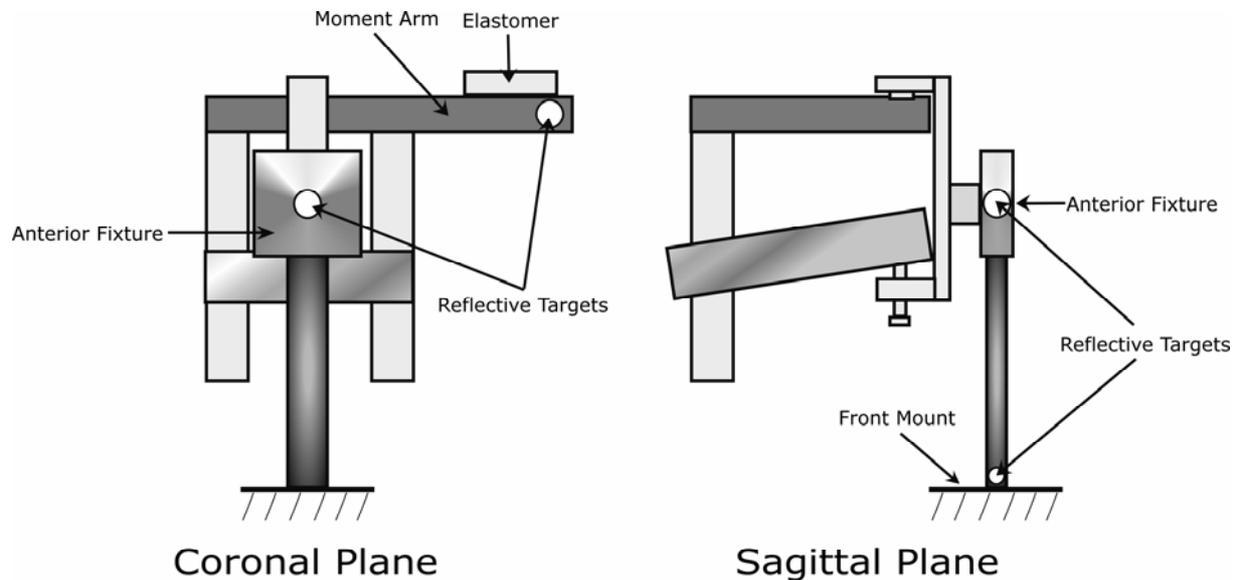


Fig. 1 – Reflective target locations.

FUNCTIONAL OUTCOME ASSESSMENT: All experimental protocols involving animals were approved by the Institutional Animal Care and Use Committee at the Medical College of Wisconsin. Ten adult female Sprague-Dawley rats weighing 304 ± 9 grams (mean \pm standard deviation) were administered general anesthesia using a mixture of ketamine (75 mg/kg) and medetomidine (0.5 mg/kg) and subjected to rotational loading. A reversal agent (1 mg/kg atipamizole) was administered following insult to alleviate effects of anesthesia. Three additional female Sprague-Dawley rats weighing 311 ± 11 grams served as control animals and were subjected to an identical protocol without insult.

Following reversal agent delivery, two standard reflexes were evaluated as measures of functional recovery. The corneal reflex was continuously assessed by observing eye blink. The righting reflex was assessed by laying the animal supine on the observation table. The righting reflex was apparent when the animal was able to roll over into the prone position three consecutive times. Time to reappearance of both reflexes was measured as the time from reversal agent administration. Reflex reappearance was evaluated by a blinded observer. Time from reversal agent administration to return of corneal reflex was unconscious time, a methodology commonly used in animal investigations (Abel *et al.* 1978; Adelson *et al.* 1996; Denny-Brown and Russell 1941; Dixon *et al.* 1987; Smith *et al.* 2000). Time from reversal agent administration to righting reflex return was considered reflex recovery.

DETERMINATION OF FILTER CUTOFF FREQUENCY: Coronal plane rotational displacement data were separated according to short- and long-duration angular acceleration groups. Group-dependent acceleration and deceleration pulses were influenced by unique characteristics of the elastomer contacting surface during helmet acceleration and foam stopping interface during helmet deceleration. Therefore, acceleration and deceleration were assessed as separate events. To determine appropriate low-pass filter cutoff frequencies for short- and long-duration acceleration and deceleration groups, temporal rotational displacement traces from each test were aligned to create mean rotation versus time traces. During analysis of acceleration data, rotation traces were aligned according to 5% of the maximum rotation for each test. During analysis of deceleration data, rotation traces were aligned according to 95% of the maximum rotation for each test. Mean traces were created by averaging rotation data on a time-point by time-point basis. This was done to eliminate random noise from the signal. Mean rotation traces for acceleration and deceleration in short- and

long-duration groups were low-pass filtered with variable cutoff frequencies between 100 and 4,000 Hz. Filtered traces were differentiated twice to compute temporal angular acceleration/deceleration. Angular acceleration magnitude was plotted versus lowpass filter cutoff frequency. These plots were independently analyzed for acceleration and deceleration to determine appropriate cutoff frequencies for short- and long-duration insults, defined as the cutoff frequency wherein acceleration/deceleration magnitude leveled off and was not attenuated by the filtering process (Fig. 3).

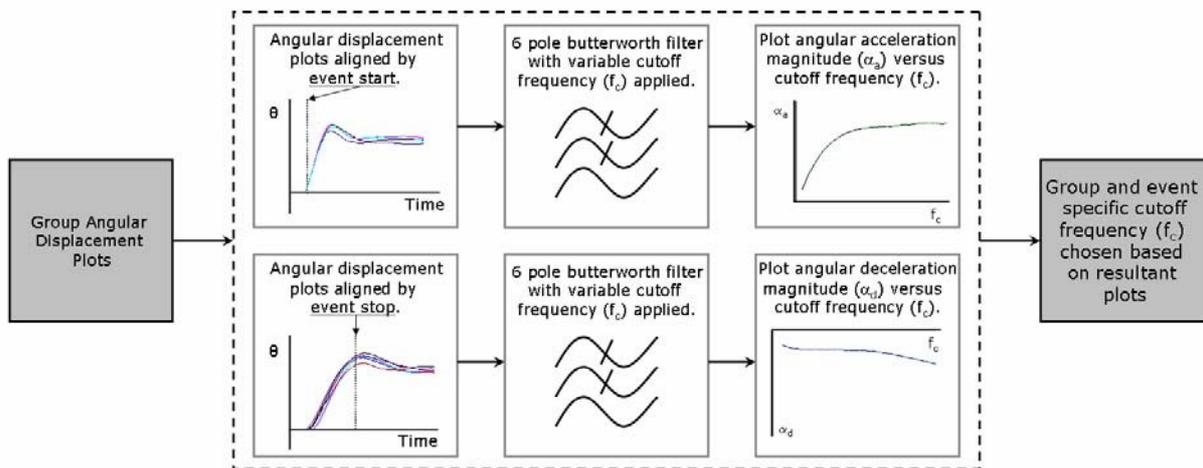


Fig. 2 – Signal processing block diagram.

ROTATIONAL KINEMATICS: The following rotational parameters were obtained: peak angular velocity, angular acceleration and deceleration magnitude, duration of angular acceleration and deceleration, and time of free rotation. Peak angular velocity, angular acceleration, and angular deceleration were obtained from derived traces. Angular acceleration and deceleration durations were determined as the time between zero crossings for the respective acceleration versus time traces. Time of free rotation (i.e. zero acceleration) was the time that angular velocity remained within 5% of the peak magnitude.

STATISTICAL EVALUATIONS: Experimental specimens were divided into short- and long-duration angular acceleration groups to evaluate effects of angular acceleration duration on functional outcomes. T-tests determined statistically significant differences ($p < 0.05$) in kinematic parameters between experimental groups. A single-factor Analysis of Variance (ANOVA) determined statistically significant differences ($p < 0.05$) in time to reappearance of corneal and righting reflexes between experimental groups. A Dunnett's Multiple Comparison test compared control and experimental groups in terms of reflex return times, by computing a two sided confidence interval based on differences in mean values between experimental and control groups. Significant differences ($p < 0.05$) were obtained when confidence intervals did not contain zero. Tukey's Multiple Comparison test was used to determine statistically significant differences ($p < 0.05$) between experimental groups. Confidence intervals for all pairwise differences between level means were computed. Significant differences ($p < 0.05$) were obtained when confidence intervals did not contain zero.

RESULTS

Impactor closing velocity was 9.5 ± 1.0 and 9.8 ± 1.0 m/s for short- and long-duration groups. Maximum coronal plane angular displacement of the helmet was 93 ± 4 and 92 ± 3 degrees for short- and long-duration groups. Impactor closing velocities and maximum coronal plane helmet rotations were not significantly different ($p < 0.05$) between short- and long-duration groups. Sagittal plane rotation of the anterior fixture was less than one degree in all tests.

Due to differing mechanical interfaces, acceleration and deceleration traces required different lowpass filter cutoff frequencies. Angular acceleration magnitudes derived from mean helmet rotational data lowpass filtered with cutoff frequencies between 1,000 and 1,400 Hz differed by less than 4% (Fig. 3).

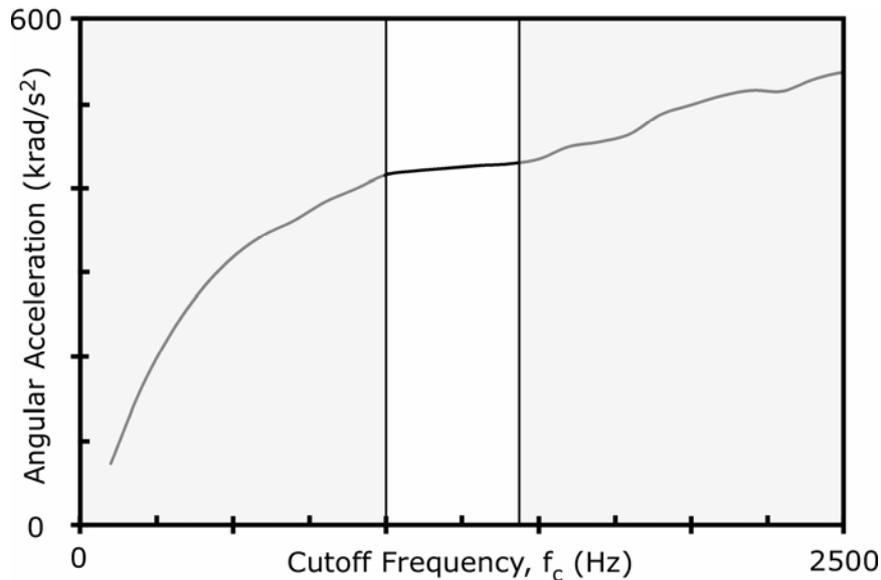


Fig. 3 – Representative trace of angular acceleration magnitude versus filter cutoff frequency.

Therefore, angular displacement versus time traces from each test were lowpass filtered at 1,200 Hz and differentiated to resolve angular velocity and angular acceleration. Angular deceleration magnitudes derived from mean helmet rotational data lowpass filtered with cutoff frequencies between 500 and 900 Hz differed by less than 5% (Fig. 4). Therefore, angular displacement versus time traces from each test were lowpass filtered at 700 Hz and differentiated to resolve angular deceleration.

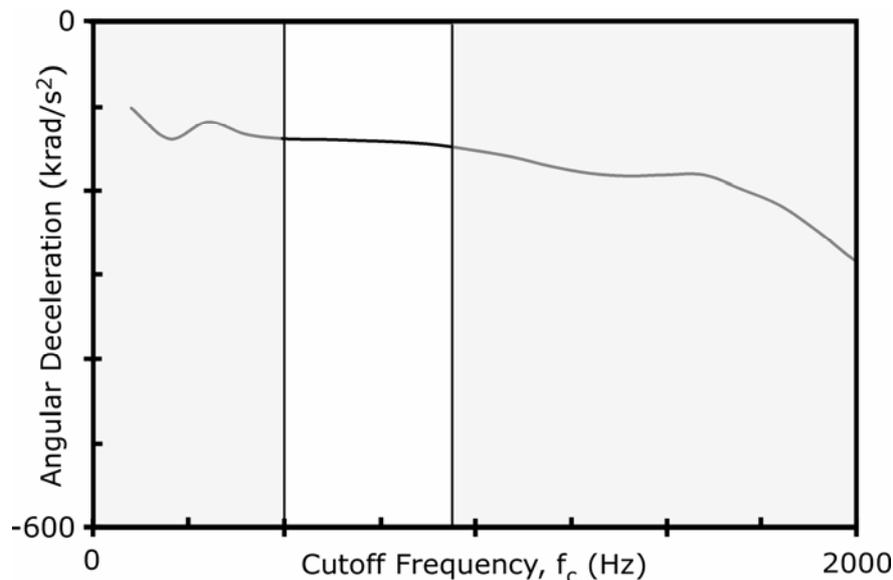


Fig. 4 – Representative trace of angular deceleration magnitude versus filter cutoff frequency.

Angular acceleration duration was the only kinematic parameter that was significantly different between experimental groups. Short-duration group angular acceleration duration was 2.0 ± 0.2 msec (Fig. 5) while long-duration group angular acceleration duration was 3.0 ± 0.1 msec (Fig. 6). Values for angular acceleration and deceleration magnitude and duration, and free rotation time are presented on the figure. Mean angular velocity was 389 ± 11 rad/s and 416 ± 8 rad/s for the short- and long-duration groups. T-tests demonstrated statistical equivalence between short- and long- duration groups in all other kinematic parameters including angular velocities, angular acceleration magnitudes, free rotation times, angular deceleration magnitudes, and angular deceleration durations (Table 3). To minimize the effect of angular deceleration, peak deceleration magnitude was limited to less than 38% of peak acceleration magnitude. Previous literature demonstrated that the present rotational kinematics were sufficient to induce mild DBI in rats (Fijalkowski *et al.* 2006).

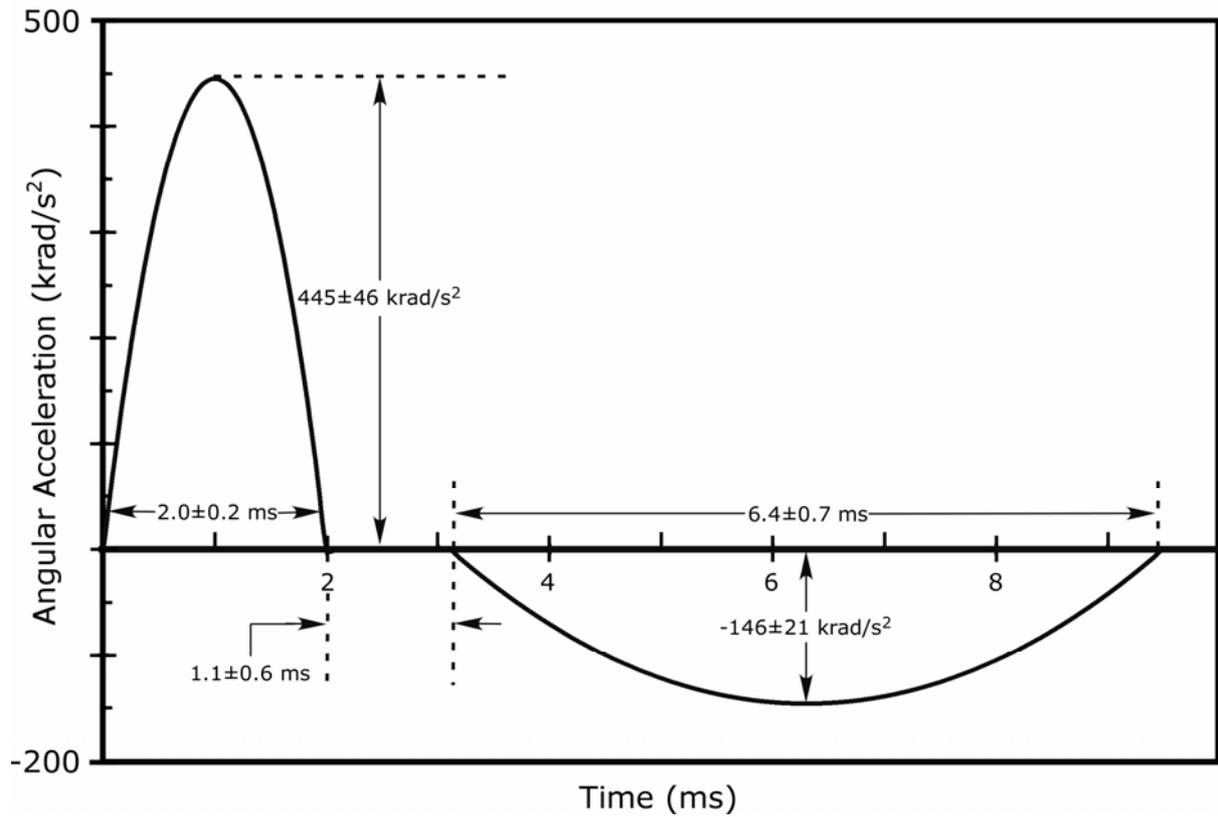


Fig. 5 – Representative angular acceleration traces from short duration insults.

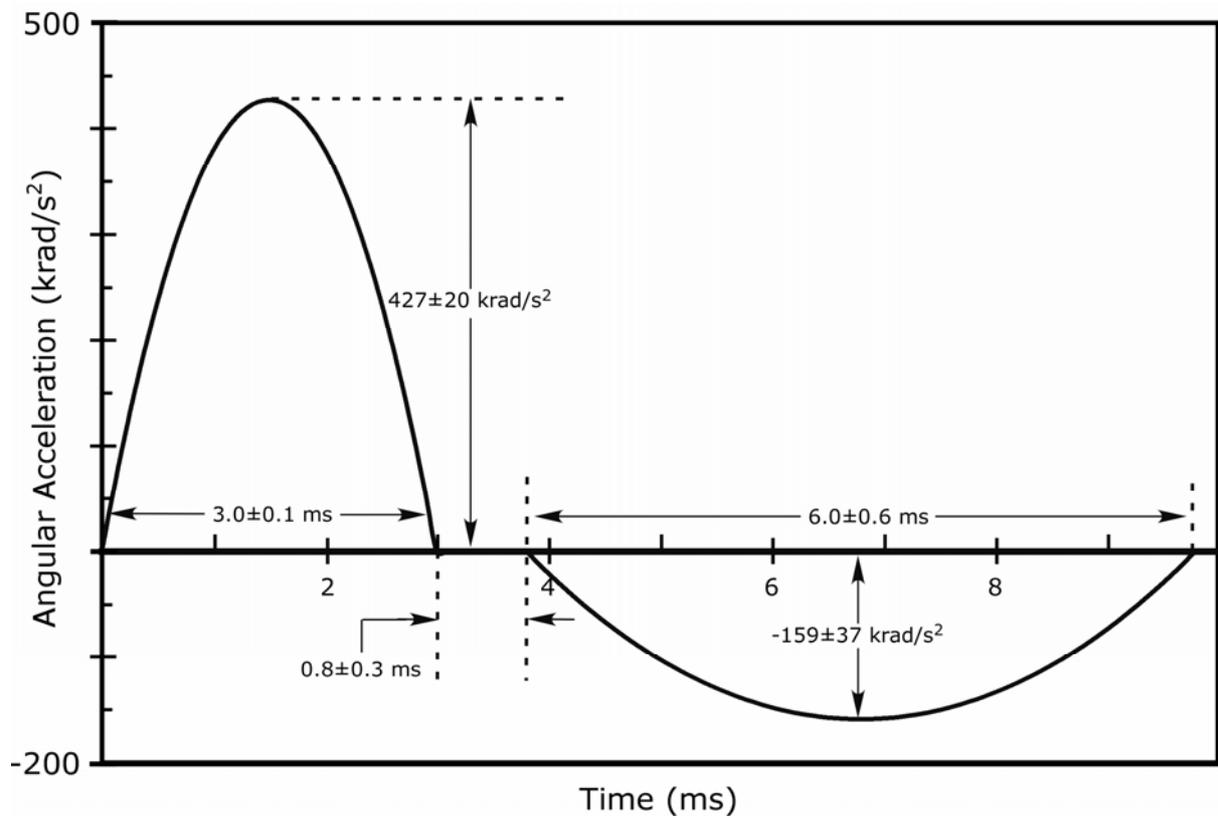


Fig. 6 – Representative angular acceleration traces from long duration insults.

Table 3. Statistical comparison of group rotational kinematics.

Parameter of Comparison	T-Value	P-Value
Peak Angular Velocity	1.96	0.11
Angular Acceleration Magnitude	-0.71	0.527
Angular Acceleration Duration	10.48	<0.001
Free Rotation	-1.03	0.381
Angular Deceleration Magnitude	-0.66	0.530
Angular Deceleration Duration	-0.96	0.382

Corneal reflex return time was 109 ± 2 sec following reversal agent administration in control animals, and 274 ± 25 sec and 630 ± 157 sec in short- and long-duration groups, respectively. Single-factor ANOVA analysis indicated corneal reflex return time was significantly different between control, short-duration, and long-duration groups ($p < 0.05$). Dunnett's confidence interval indicated corneal reflex return time was not significantly different between control and short-duration groups and was significantly different between control and long-duration groups. Tukey's confidence interval indicated a significant difference in corneal reflex return time between short- and long-duration groups.

Righting reflex return time was 225 ± 7 s following reversal agent administration in control animals, and 442 ± 64 s and 819 ± 134 s in short- and long-duration groups, respectively. Single-factor ANOVA analysis indicated righting reflex return time was significantly different between control, short-duration, and long-duration groups ($p < 0.05$). Dunnett's confidence interval indicated righting reflex return time was significantly different between control animals and short- and long-duration insult groups. Tukey's confidence interval indicated a significant difference in righting reflex return time between short- and long-duration groups.

Table 4. Reflex return time statistical comparison.

Reflex	ANOVA		Dunnett's Confidence Interval		Tukey's Confidence Interval
	F-statistic	P-value	C vs. SD	C vs. LD	SD vs. LD
Corneal	25.24	<0.001	-51.4, 384.9	320.4, 724.3	-554.5, -156.7
Righting	38.90	<0.001	23.0, 417.6	415.2, 780.5	-557.4, -197.6

C = control group, SD = short duration group, and LD = long duration group.

DISCUSSION

The present study investigated the effects of angular acceleration duration on functional outcomes following mild DBI in the rat. As such, it was critical that angular acceleration magnitude be sufficient to induce mild DBI while being statistically equivalent between both experimental groups. Previous literature demonstrated angular acceleration magnitudes were sufficient to induce mild DBI in the rat for all animals in both experimental groups (Fijalkowski *et al.* 2006). Furthermore, individual T-tests demonstrated statistical equivalence in all kinematic parameters except angular acceleration duration. Therefore, differences in functional outcomes could be attributed solely to changes in angular acceleration duration. This was the first study to isolate duration by subjecting rats to coronal plane head rotations of equal magnitude with either 2.0 or 3.0 msec durations.

Functional outcomes demonstrated possibly different injury levels between short- and long-duration groups. Time to reappearance of corneal reflex was previously used as a measure of unconscious time (Abel *et al.* 1978; Adelson *et al.* 1996; Denny-Brown and Russell 1941; Dixon *et al.*

1987; Smith *et al.* 2000) and longer unconscious times may be indicative of more severe injuries (Fijalkowski *et al.* 2007; Morehead *et al.* 1994; Teasdale and Jennett 1974). Present results demonstrated that unconscious times in short- and long-duration groups were longer than in control animals, although only significantly longer for long-duration insults. Additionally, time to reappearance of righting reflex, another measure of recovery, was significantly longer than control animals in both experimental groups. These findings indicate the presence of DBI in all experimental rats due to coronal plane head rotation. However, the finding of significantly longer unconscious time for long-duration insults indicates a higher level of injury. This finding highlights a possible role of angular acceleration duration in the presence and severity of DBI.

Previous investigations have identified angular velocity as a determinant in DBI (Hirsch *et al.* 1968; Margulies and Thibault 1992; Thibault and Gennarelli 1990). Components of angular velocity include angular acceleration magnitude and duration. Therefore, brain injury tolerance criteria incorporating angular velocity indirectly include duration. However, present results demonstrated an independent role of angular acceleration duration in injury outcomes following rotationally induced DBI, as all other rotational parameters were not significantly different between groups. This important finding indicates the possibility of a complex relationship between angular acceleration magnitude and duration in the biomechanical sequelae resulting in diffuse brain injury. Although continued investigation is required, future development of injury tolerance criteria should account for this relationship in terms of the lower threshold as well as graded injury levels associated with DBI.

Rotational kinematics from the present study were scaled to the human using an accepted brain-mass scaling procedure (Margulies and Gennarelli 1985; Ommaya *et al.* 1967). Angular acceleration magnitude and duration levels would be 7.6 krad/s² and 15 msec for short-duration insults, and 7.3 krad/s² and 23 msec for long-duration insults. A comparison to previous mild DBI literature cited in Table 1 demonstrates lower angular acceleration magnitudes and longer durations in the present study. This finding also highlights the relationship between angular acceleration magnitude and duration in that similar injury levels were attained from insults with 50% decreased magnitudes and longer durations. This demonstrates a potential inverse relationship, wherein increased angular acceleration magnitudes require decreased durations for equivalent levels of DBI severity.

Rotational kinematics measured in this study were subject to increased noise due to the differentiation process. As a result, signal to noise ratio decreased dramatically, leading to unreliable measures for angular acceleration magnitude. Lowpass filtering specifications were not previously defined for the present system. To solve this problem, insult was separated and independently assessed according to acceleration and deceleration events, due to differing mechanical properties of the insult (acceleration) and stopping (deceleration) mechanisms. Event-dependent mean rotation versus time traces were derived to eliminate random noise, a methodology commonly used in electrocardiogram analysis (Challis and Kitney 1990). Mean angular acceleration and deceleration magnitudes were computed over a range of filter cutoff frequencies. Signal amplitude consistency was demonstrated over specific and different bandwidths for acceleration and deceleration (Figs. 3 and 4). Filter cutoff frequencies were chosen at the midpoint of those bandwidths. Test-specific angular velocity, acceleration, and deceleration were derived using those cutoff frequencies. Therefore, measured rotational kinematics were computed with minimal interference from differentiation noise.

All rotational kinematics beside angular acceleration duration were statistically equivalent between experimental groups. Angular deceleration magnitude was 65% reduced and duration 70% increased compared to angular acceleration. Previous experimental literature suggested a deceleration pulse with these levels was non-injurious (Ellingson *et al.* 2005; Fijalkowski *et al.* 2006; Fijalkowski *et al.* 2007). Therefore, functional deficits can be attributed to the acceleration event. As angular acceleration duration was the only significantly different kinematic parameter and deceleration considered non-injurious, this study effectively investigated the independent influence of angular acceleration duration on DBI severity.

The present study demonstrated angular acceleration duration was an influencing factor in DBI severity. However, this nonexclusive indicator has important limitations. For example, as angular acceleration duration decreased, literature suggested injury type variation from diffuse to focal pathologies (Gennarelli and Thibault 1982). Furthermore, it is well accepted that substantial increases in angular acceleration duration may serve as a protective mechanism. This is evidenced by the incorporation of impact-absorbing foam in contemporary automotive and sporting helmets. Thus, independent maximum and minimum thresholds for angular acceleration magnitude and duration must be identified due to the important implications in threshold criteria.

CONCLUSIONS

Present results identified a nonexclusive and independent role of angular acceleration duration in DBI severity. Specifically, as angular acceleration duration increased, acute functional deficits including time to reappearance of corneal and righting reflexes also increased. Results suggest a possible inverse relationship exists between angular acceleration magnitude and duration wherein increasing angular acceleration magnitude requires decreased angular acceleration duration to induce equivalent DBI levels. However, the effect of angular acceleration duration was only investigated at a mild DBI severity level. Further investigation is required to fully describe the complex relationship between angular acceleration magnitude and duration.

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