Simulated Kick Injury to the Mandible in Horses: Study of Fracture Configurations and Physical Parameters of the Impact

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Abstract

Objective The goal of this study was to generate mandibular fractures in three regions of the diastema using a metal impactor to simulate a kick from a horse and to determine the mean deceleration in the initial phase of the impact event, the maximum contact force, the impact energy necessary to create a fracture and the duration of the impact.

Study Design Thirty heads of horses aged between 5 and 20 years and euthanatized for various reasons were used. The heads were attached to a steel bar at the occiput at an axial angle of 45 degrees so that the body of the mandible was positioned horizontally and directly under the trajectory of the impactor. A 2 kg solid impactor was dropped with velocities of 6 to 14 m/s to simulate a kick from a horse. The impact was recorded using a high-speed video camera with a frame rate of 30,000 frames per second. Radiographs of the heads were obtained before and after the simulated kick.

Results Mandibular fractures with configurations similar to those seen in clinical practice were generated at all three locations. The mean deceleration increased with impact velocity and with more cranially located impact positions. Absorbed energy increased with increasing impact velocity when no fracture was generated.

Conclusion The susceptibility to experimental fracture of the diastema increased from rostral to caudal locations, which is most probably caused by decreasing mandibular bone strength and an increase in the curvature at the lateroventral aspect of the mandible in that region. Physical parameters depended on fracture occurrence and type.

Keywords
- horses
- mandibular fracture
- experimental study
- impact injury
- kick injury

Introduction

Fractures of the head, particularly those of the mandible, are common in horses.[1,2] A review of fractures in horses caused by a kick from another horse revealed that 12% of all fractures involved the head.[3] Most skull fractures are caused by a kick from another horse or result from a collision with an object or, rarely, from entrapment.[4,5] To create a horse-friendly environment and to satisfy behavioural needs, horses are

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commonly kept in groups in paddocks, open barns or on pasture. However, horses kept in groups often fight for social dominance and incur physical injuries. A recent study from Switzerland showed that head fractures doubled in frequency from 1992/2002 to 2003/2013.[6]

The mandible consists of two hemimandibles fused rostrally at the intermandibular suture. The hemimandibles consist of vertical (ramus), horizontal (body) and rostral (pars incisiva) parts. The ramus is connected to the skull via the temporomandibular joint. The body contains the alveoli for the molar and premolar teeth and the diastema, which is devoid of teeth. The pars incisiva contains the alveoli for the incisor teeth. Although mandibular fractures can occur in any region, fractures rostral to the first premolar are common and usually the result of a kick from another horse.[6]

Surgeons are often confronted with these types of fractures, most of which are oblique fractures that run from rostrodorsal to caudoventral across the diastema.[2] However, unlike many other bones in the horse, a concise fracture classification does not exist. Likewise, forces and impact energy and other physical parameters of the impact involved in mandibular fractures have not been measured. The force of a kick from a horse has been estimated experimentally,[7] and several studies have investigated the effects of simulated kicks on long bones[7–11] and the orbit.[12] Analogous studies for the mandible are lacking.

The goal of this experimental study was to create mandibular fractures under controlled conditions with a configuration similar to that of naturally occurring fractures and to determine various physical parameters of the impact, such as the mean deceleration (a) in the initial impact phase, the maximum contact force (F_{peak}), the impact energy necessary to create a fracture (E_{fracture}) and the duration of the impact (t_{impact}). The study had two main objectives: First, to produce mandibular fractures with a configuration similar to naturally occurring fractures using controlled conditions and a specific experimental design; and second, to investigate whether the mandibular fracture configuration varies with the impact position in the region between the mental foramen and the second premolar tooth. To explain the differences in fracture probability and configuration, physical parameters that characterize the impact process were measured.

Materials and Methods

Selection and Preparation of the Heads

The heads of 30 warmblood horses ranging in age from 5 to 20 years and euthanazized for various reasons were used. An initial computed tomography scan ensured that the skulls were free of lesions and other abnormalities. Processing and storage of the heads until the time of the experiments have been described in previous studies.[8,10–12] Prior to the experiments, lateral and oblique radiographic views of the mandibles were obtained. In contrast to the studies on long bones, the soft tissue envelope was left on the heads to mimic natural conditions.

Table 1 Number of skulls tested at the three impact positions at different impactor velocities (test matrix)

	6 m/s	8 m/s	10 m/s	12 m/s	14 m/s
P1		2	3	3	3
P2	3	3	3		
P3	3	4	3		

The three impact positions (P1, P2 and P3) are defined in Figure 3.

Allocation of Horse Heads to Impact Positions and Velocities

The 30 horse heads were divided into 10 groups of two to four heads each, and each group was randomly allocated to an impact position and impactor velocity (►**Table 1**).

Impact Facility and Fixation of the Heads

The dropping facility and the cylindrical impactor head were reused from previous studies with long bones.[8,10–12] The impact energy (E_{impact}) was controlled by varying the impactor's drop height, and thus the impactor's velocity. The drop heights were chosen such that the impactor reached a velocity of 6, 8, 10, 12, or 14 m/s immediately before hitting the mandible. The corresponding levels of kinetic energy were 36, 64, 100, 144 and 196 Joules (nominal values). The head was rigidly attached to a steel bar at the occiput and positioned at an axial angle of 45 degrees so that the body of the mandible was in a horizontal position directly under the trajectory of the impactor (►**Figs. 1** and **2**).

Experimental Design

Assuming that most kick injuries affect the diastema, we chose three positions on the mandible between the second premolar and the mental foramen. The first, position 1, was at the level of the mental foramen, the second, position 2, was midway between the mental foramen and the most rostral part of the crown of tooth 406 and the third, position 3, was at the level of the most rostral part of the crown of tooth 406

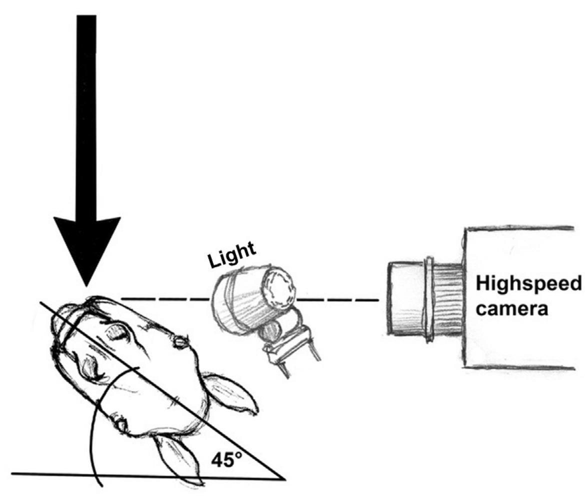

Fig. 1 Position of the head relative to the position of the high-speed video camera and the trajectory of the impactor. The head is at an axial angle of 45 degrees with the mandible in a horizontal position.

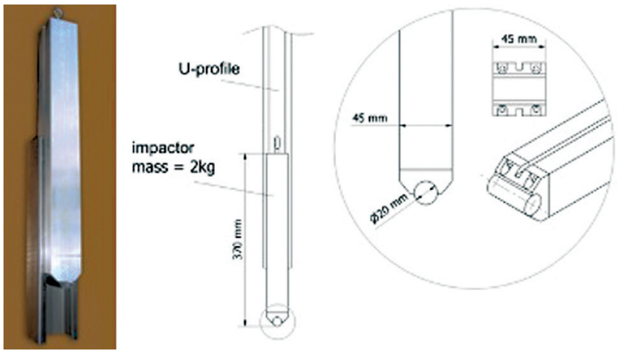

Fig. 2 Impactor (left) and schematic representation of the impactor and impactor head (right).

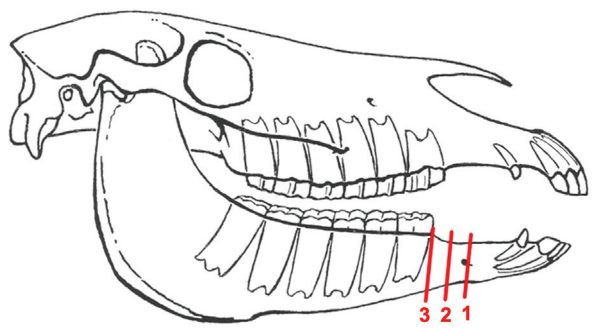

Fig. 3 Illustration of the three impact positions on the mandible. The right mandible was used in this study.

(►**Fig. 3**). The three positions were marked at the ventral edge of the mandible with a staple, which served to position the head properly under the trajectory of the impactor and to facilitate orientation when viewing the radiographs.

While the impact positions were chosen according to clinical relevance, the range of adequate impact velocity had to be first investigated. To allow for optimal experimental conditions, an impactor velocity with a fracture probability of about 80% should be chosen.[10] For long bones, a velocity of 8 m/s fulfilled this requirement.[11] To define the adequate impact velocity for the present study, nine heads (three heads for each position) were used in a pilot study. Impact velocity was gradually increased from 6 to 14 m/s with 2 m/s increments and the presence of a fracture was determined. Based on the results of those experiments, the starting velocity used in the main study was set at 8 m/s for position 1 and 6 m/s for positions 2 and 3. The final test matrix consisted of three different impact positions and five different levels of impactor velocity (►**Table 1**).

Fracture Classification

Lateral and oblique radiographic views of all right mandibles were obtained after the impact experiments to assess the occurrence and type of fracture (►**Fig. 4A–D**). Simple fractures were classified as type *1a*, which were oblique fractures with the fracture line running from rostrodorsal to caudoventral, or type *1b*, which were transverse fractures with the fracture line running ventrally. Multiple fractures with multiple fragments were classified as type *2a*, which were comminuted fractures with an oblique main fracture, or type *2b*, which were comminuted fractures with a transverse main fracture.

Determination of Physical Parameters

The impact was recorded using a high-speed video camera (MotionXtra HG-100K, Redlake, DEL Imaging Systems, Woodsville, NH 03785) with a frame rate of 30,000 frames per second, and the video-tracking software Tracker was used for quantitative analysis of the recordings. The recordings made in the first few milliseconds after contact of the impactor with the mandible were of interest; during this very brief phase, the free-falling impactor undergoes rapid deceleration and its kinetic energy is partly transferred to the mandible.

The movement of the impactor was quantitatively described as the time course of the impactor speed and the time course of the contact force (►**Fig. 5**). Based on the studies on long bones,[11] the following physical parameters were determined from the time courses mentioned above:

- kinetic energy of the impactor immediately before it hits the mandible (E_{impact})
- average deceleration in the first phase of the impact (a)
- maximum contact force (F_{peak})
- duration of the impact (t_{impact})
- energy absorbed by the head (E_{absorbed})

These parameters could be derived using the first approximately 90 frames of the high-speed video camera, which

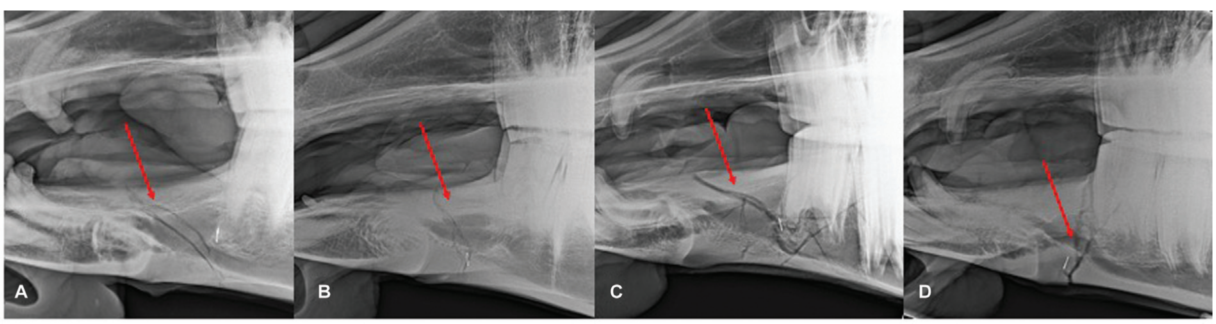

Fig. 4 Typical fractures observed in this study: (**A**) type 1a: simple oblique fracture (8m/s, Pos. 3), (**B**) type 1b: simple transverse fracture (8 m/s, Pos. 2), (**C**) type 2a: comminuted fracture with oblique component (10 m/s, Pos. 3), (**D**) type 2b: comminuted fracture with transverse component (10 m/s, Pos. 2).

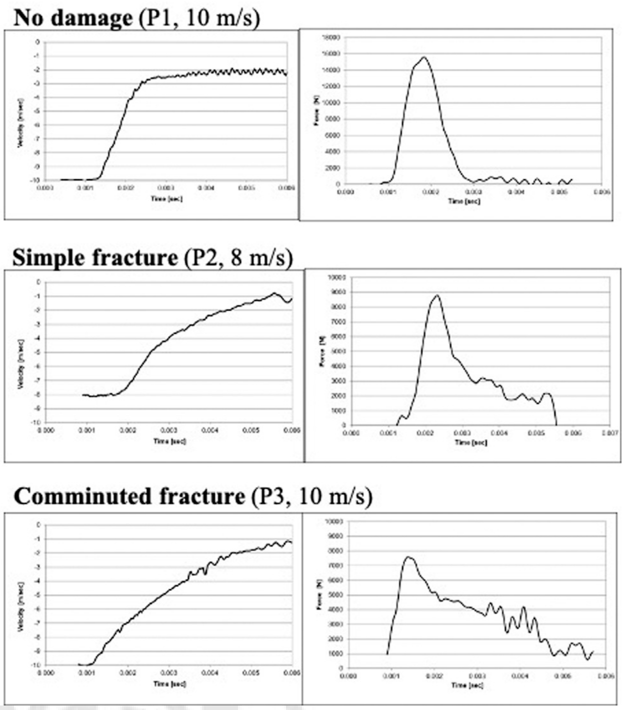

Fig. 5 Characteristic examples of the time course of velocity (v) and the contact force (F) based on analysis of the high-speed videos using video tracking and numerical derivation. Note that for the mean deceleration a (which is the slope of the time course of the velocity), the curve is steepest where no fracture is produced. For simple and comminuted fractures, the curve becomes progressively flatter, which means a is lower.

corresponded to about 3 milliseconds. The physical parameters characterizing the impact, which were the deceleration (negative acceleration) of the impactor, changes in kinetic energy of the impactor and the contact force between impactor and mandible, were determined using observations of the movements of the impactor tracked on the high-speed video recordings. The tracker software determined the vertical position of the impactor over time with a resolution of 3.33×10^{-5} seconds. With the velocities chosen (14 m/s or less), the resolution for localization of the impactor was better than 0.5mm. Deceleration and decrease in kinetic energy of the impactor were analysed based on changes in the position of the impactor over time (distance) derived from the tracking software. The current impactor velocity, $v = \Delta s/\Delta t$, was calculated from changes in the position of a reference point on the impactor in two consecutive frames, and the acceleration/deceleration of the impactor, $a = \Delta v/\Delta t$, was calculated from the difference in velocity calculated for consecutive frames. The impactor velocity immediately before contact with the mandible and thus the kinetic energy of the impactor (E_{impact}) was calculated using the formula: $E = 0.5 \times m \times v_s^2$, where m is the mass and v_s is the velocity of the impactor immediately before the impact. The contact force between the impactor and the mandible was calculated based on Newton's law: $F_{peak}(t) = m \times a_{max}(t)$, where m is the mass and $a(t)$ is the deceleration of the impactor as a function of time. The amount of energy transferred from the impactor to the mandible was calculated using this formula:

Table 2 Number of cases with fracture at the three impact positions at different impactor velocities

	6 m/s	8 m/s	10 m/s	12 m/s	14 m/s
P1		0	0	0	2
P2	0	1	3		
P3	0	4	3		

$E_{absorbed} = 0.5 \times m \times (v_s^2 - v_r^2)$, where v_s is the velocity of the impactor immediately before and v_r the velocity immediately after the impact.

Duration of the impact (t_{impact}) was defined as the time between the impactor hitting the mandible and the appearance of the maximum contact force.

Results

Incidence and Type of Fracture

The fracture occurrence and type of fracture varied with impact position and velocity (►**Table 2**). At position 1, only the maximum impactor velocity (14 m/s) resulted in fractures and in only two of three impact events. Both followed a transverse path; one mandible had a simple fracture and one a comminuted fracture. At position 2, all fractures had a transverse path. At 8m/s, one of three impact events resulted in a simple fracture. At 10 m/s, comminuted fractures occurred in all impact events. At position 3, comminuted fractures occurred in the majority of impact events (5 with an oblique and 1 with a transverse fracture path). At 8 m/s, only a simple fracture occurred in one mandible. Thus, an impactor velocity of 14 m/s was required to cause a fracture at position 1 compared with 8 m/s at positions 2 and 3. All fractures at positions 1 and 2 followed a transverse path, whereas most fractures (85.7%) at position 3 had an oblique path.

Physical Parameters Characterizing the Impact

Mean deceleration (a), maximum contact force (F_{Peak}), impact duration (t_{impact}) and absorbed energy ($E_{absorbed}$) are shown in ►**Table 3**.

Mean Deceleration (a)

The mean deceleration increased with impact velocity, except for the impacts at position 3, where it decreased when the impact velocity was 10 m/s compared with 8m/s. In mandibles that did not sustain a fracture, the mean deceleration increased with increasing impactor velocity at positions 1 and 2. The mean deceleration a was lower when a fracture occurred, which was particularly true for comminuted fractures as shown for position 3 in ►**Fig. 5**.

Maximum Contact Force (F_{peak}) and Impact Duration (t_{impact})

The maximum contact force increased with impactor velocity but only at positions 1 and 2; at position 3, it decreased. The maximum contact force did not depend on the impact

Table 3 Average of mean deceleration (a), absorbed Energy ($E_{absorbed}$), impact energy in brackets, percentage of energy absorbed with respect to impact energy, maximum contact force (F_{peak}) and time to reach peak force (t_{impact}) as well as fracture probability in % (% *Fx*) of all 3 positions at 6m/s, 8m/s, 10m/s, 12 m/s and 14 m/s

	6 m/s					8 m/s					10 m/s				
	Ø a	Ø E	Ø F_{peak}	t_{impact}	Fx	Ø a	Ø E	Ø F_{peak}	t_{impact}	Fx	Ø a	Ø E	Ø F_{peak}	t_{impact}	Fx
Pos 1						5758 m/s^2	43J (65.8J) 65.3%	12.1 kN	0.93 ms	0	7052 m/s^2	64J/ 104.2J 61.4%	17.7 kN	0.94 ms	0
Pos 2	4503 m/s^2	22.1J (33.6J) 65.8%	10.8 kN	0.82 ms	0%	5312 m/s^2	46.1J (66.6J) 69.2%	12.9 kN	0.98 ms	33.3%	5548 m/s^2	45.4J (106.4J) 42.7%	15.4 kN	1.11 ms	100%
Pos 3	3672m/s^2	27.7J (35.8J) 77.4%	11.3 kN	1.11 ms	0%	4462 m/s^2	31.7J (71.8J) 44.2%	11.2 kN	0.79 ms	100%	2901 m/s^2	20.4J (101.8J) 20.0%	9.7 kN	0.84 ms	100%

	12 m/s					14 m/s				
	Ø a	Ø E	Ø F_{peak}	t_{impact}	Fx	Ø a	Ø E	Ø F_{peak}	t_{impact}	Fx
Pos 1	7640 m/s^2	79.3J (148.9J) 53.3%	18.8 kN	0.76 ms	0%	9089 m/s^2	77.1J (206.1J) 37.4%	32.7 kN	0.69 ms	66.7%

position. It was relatively constant at all positions for impactor velocities of 6 m/s and 8 m/s. However, it decreased from position 1 to 3 when an impactor velocity of 10m/s was used.

The impact duration (t_{impact}) varied randomly from 0.76 to 1.11 time, ms except for an impactor velocity of 14 m/s, where the peak force was reached after 0.69 ms.

Absorbed Energy ($E_{absorbed}$)

The energy transferred from the impactor and absorbed by the mandible ($E_{absorbed}$) was a function of impactor velocity, impact position and generation of a fracture. The average energy absorbed increased with impact velocity in mandibles that did not incur a fracture. The energy absorbed decreased from position 1 to position 3 in mandibles that sustained a fracture. The amount of energy absorbed by the mandible was smaller when a fracture occurred compared with a mandible that remained intact. The absorbed energy was > 50% of the impact energy in intact mandibles and < 50% in fractured mandibles. When a comminuted fracture occurred, the amount of absorbed energy decreased further; for instance, only 20% of the impact energy was absorbed at position 3 with an impactor velocity of 10 m/s and generation of a comminuted fracture (►**Table 3**).

Energy Needed for a Fracture of the Mandible ($E_{fracture}$)

The absorbed energy needed to create a fracture in the mandible was highly dependent on the position of the impact. For a fracture to occur at position 1, 77.1 Joules were needed, whereas at position 3, only 20.4 Joules were required. The energy needed to create a fracture at position 2 was 45.4 Joules.

Discussion

This study has shown that under controlled experimental conditions, it is possible to produce mandibular fractures that resemble those created by a kick from another horse.[2,13] The configurations of the experimentally produced fractures were similar to those encountered in clinical practice and therefore the first objective of the study was achieved. Analogous findings have been found for long bones and the orbit of horses.[8–12] In addition to the energy of the impact (which is equal to the velocity squared and therefore increased with increasing impactor velocity), the likelihood of a mandibular fracture depended on the position of the impact. An impact energy of 64 Joules, which is the kinetic energy of our experimental impactor travelling at a velocity of 8 m/s, resulted in a fracture near tooth 406 (position 3) in all four trials, but no fractures occurred at the mental foramen (position 1) in two trials. An impactor velocity of 14 m/s was required to create a fracture at the latter position. Considering that 8 m/s is the velocity of an average kick from a horse,[10,11] a kick to the mandible at the level of the mental foramen is therefore less likely to result in a fracture compared with a kick that impacts the mandible close to the second premolar (position 3). The high fracture resistance of the mandible at the level of the mental foramen

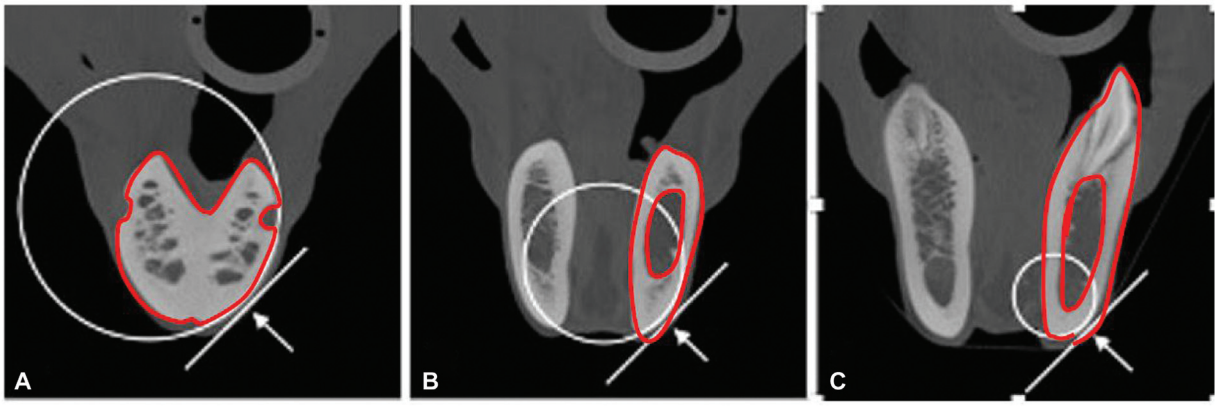

Fig. 6 Transverse computed tomographic images of a mandible of a 15-year-old Warmblood horse. **A**, impact position 1; **B**, impact position 2; **C**, impact position 3. The red lines mark the bone contours, showing the cross-sectional area at each impact position. The white circles represent the curvature of the bone at the 3 impact positions: Impact position 3 had the largest curvature followed by positions 2 and 1. The larger the curvature, the higher the local pressure during the impact (represented by the arrow) (Hertzian pressure).

(position 1) compared with more caudal positions is most likely attributable to anatomical features. The mandibles are fused at the level of the mental foramen, which means that the cross-sectional area of the bone involved in the impact event is much larger compared with more caudal regions (►**Fig. 6A**, red lines).

Thus, a substantial amount of energy was needed to fracture the mandible in the region of the mental foramen (position 1). Comparison of an impact midway between the mental foramen and the rostral end of the second premolar (position 2) and an impact at the rostral end of the second premolar (position 3) revealed that the mandible becomes progressively narrower (►**Fig. 6B and C**) and weaker more caudally and therefore a lower fracture resistance would be expected close to the second premolar (position 3). Other indications of lower fracture resistance at the rostral end of the second premolar (position 3) were less rapid achievement of peak force (1.11 vs. 0.82 ms) and lower mean deceleration (3,672 vs. 4,503 m/s^2) provided that the bone did not fracture. Both findings are related to lower bone stiffness attributable to a smaller cross-sectional area at position 3 compared with position 2 (►**Fig. 6C** vs. B, red lines).

The differences in resistance of various parts of the mandible to fracture may also be attributable to inertia of the head. A horse kick is a highly dynamic impact event, in which inertia forces are relevant. According to Newton's second law, the resultant contact force is dependent on the amount and distribution of the inertial mass of the bodies involved. For a body that is hit eccentrically, the body reacts with a rotational movement. Thus, when the rostral aspect of the mandible is kicked by a horse, the head moves passively away from the direction of the impact, because the mass resisting the impact of the kick is smaller. Most of the kinetic energy of the kick is transferred into moving the rostral region of the head, leaving less energy for injury to the mandible. As a consequence, more energy is required to generate a fracture in more rostrally located impact positions. This was observed with impacts at positions 1 and 2 compared with position 3. In our experiments, the impactor had a centrically located inertial mass of 2 kg and the head was much heavier, and its mass was not centrically located with respect to the impact position. It is important to point out that for such high-velocity impact loads, fixation of the head does not influence the impact process because it is too far away from the impact location. The attachment was a force-fit, which allowed the head to rotate once the reaction force at the occiput exceeded a threshold. However, when the impactor hit the mandible, the head, which was stationary, was a heavy target with a high inertia mass. The impact event is independent of boundary conditions at the point of fixation because the fracture happens before the fixation can have an effect.

Based on the discussion above, we concluded that kicks to more caudal regions of the head do not result in as much movement of the head and the majority of kinetic energy is transferred to the bone causing injury. In contrast, considerably more kinetic energy is required for a kick to generate a fracture of the rostral aspect of the mandible.

The association between impact position and resultant fracture configuration was interesting. Impact position 2 incurred mostly transverse fractures, whereas most fractures at position 3 had an oblique fracture path. We were unable to explain this empirical finding but perhaps it is related to a difference in the amount of bending involved in addition to the shear.

Another interesting observation was that impacts at position 3 resulted in more comminuted fractures than at position 2. This may be related to the build-up of local pressure during the impact: The local pressure at the contact area between two bodies is called Hertzian pressure. In addition to other factors, it is dependent on the anatomy at this location including the curvature of the surfaces of the bodies at the impact site.

The Hertzian pressure increases with an increase in the curvature of a body. Impact locations with a large curvature have a higher local pressure during the impact. In ►**Fig. 6**, the curvature of impact positions 1 to 3 is illustrated as a white circle. The largest curvature is at impact position 3. Thus, position 3 underwent a higher local pressure upon impact than positions 1 and 2, which may explain the higher incidence of comminuted fractures at position 3. Taken together, these findings lead to the conclusion that fracture configuration varied with the impact position on the mandible. Therefore, the second objective of the study was achieved.

The comparisons of the physical parameters associated with generation of a fracture, for example, mean deceleration (a), maximum contact force (F_{peak}), absorbed energy ($E_{absorbed}$) and the energy needed to fracture the mandible ($E_{fracture}$) showed the following:

The mean deceleration (a) changed with impact position and velocity. Based on all measurements except one (position 3 at 10 m/s), the mean deceleration increased with impact velocity and with more cranially located impact positions. The mean deceleration was lowest at position 3 and highest at position 1.

At position 1, no fractures were sustained with impactor velocities less than 14 m/s. Peak contact forces (F_{peak}) (18.8 kN) at position 1 on the mandible using an impactor velocity of 12 m/s were similar to those in long bones using an impactor velocity of 8 m/s. However, a peak force of 18.8kN (12 m/s) did not generate a fracture, which serves to emphasize the resistance of this part of the mandible. Using an impactor velocity of 8 m/s, the mean peak contact force (F_{peak}) was 13 kN at position 2 and 11.2 kN at position 3, which were both lower than the mean peak contact force (18.8 kN at 8m/s) on long bones with similar fractures but higher than the force involved in generation of orbital fractures (5.6 kN at 7 m/s).[7,10] The experimental studies involving long bones and the orbit only investigated bones without damage, whereas the current study included data on both intact and fractured bones because the numbers of heads per position and the range of velocity were small. Thus, only part of our results can be used for comparative purposes.

To create a mandibular fracture, the impact energy had to be greater than or equal to at least 66.6 Joules; the impact to the area between the mental foramen and the second premolar with an impactor velocity of 8 m/s illustrated this. Experimentally generated fractures of long bones in horses determined the following association between impact energy (E_i) and bone damage: $E_i < 40$ J = no bone damage; 40 J $> E_i > 90$ J = fracture or fissure possible; $E_i > 90$ J = frequent bone fracture.[11] Considering those results, it appears that the fracture resistance at positions 2 and 3 on the mandible is similar to that of long bones, at least under experimental conditions, in which fractures occur at impact energies of 66.6 J and greater. In contrast, a minimum impact energy of 206.1 J was required to generate a fracture at position 1. Comparison of the two studies must be tempered with the knowledge that the skin and soft tissues had been removed in the long bone study but were left intact on the skulls to more closely simulate natural events.[10] Many studies have shown that soft tissues provide a certain degree of protection against kick injuries.[14,15]

Absorbed energy ($E_{absorbed}$) increased with increasing impact velocity when no fracture was generated. When a fracture occurred, the absorbed energy did not increase further. This can be illustrated by comparing the impact at the mental foramen (position 1) using an impactor velocity of 14 versus 12m/s; the absorbed energy was similar at 79.3 and 77.1 Joules respectively. Another example is the comparison of the impact on the mandible midway between the mental foramen and the second premolar (position 2) using an impactor velocity of 10 versus 8m/s; the absorbed energy was similar at 45.4 and 46.1 Joules respectively.

The energy absorbed by the mandible when a fracture occurred ($E_{fracture}$) was strongly dependent on the position of the impact. A fracture at the mental foramen (position 1) absorbed 77.1 Joules, which was markedly more than at more caudal positions (position 2 and 3), where a fracture absorbed only 45.4 and 20.4 Joules respectively.

Limitations of the study included the small number of heads per group and possible small variations in the location and marking of the three impact positions. However, we were able to show that a simulated kick can generate fractures with configurations consistent with naturally occurring fractures of the mandible. In addition, the impact energy needed to generate a fracture and the fracture configuration differed at each position on the mandible. Position 1 was the strongest followed by positions 2 and 3. These differences in fracture susceptibility can be explained by differences in mean deceleration, peak contact force and absorbed energy.

Author's Contribution

L. G., S. M., A. F., G. P., B. W., S. M., and M. J. were involved in conception of study, study design, acquisition of data, data analysis and interpretation, drafting or revising of manuscript, approval of submitted manuscript, and publicly accountable for relevant content.

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Conflict of Interest

None declared.

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