A study of brain injury

in

New Zealand sea lion pups

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Abstract

The New Zealand sea lion (*Phocarctos hookeri*) is a threatened species endemic to New Zealand. The majority of breeding in this species occurs on the Auckland Islands in the sub-Antarctic, and recent population estimates indicate that pup production is declining. Trauma is a significant cause of mortality in New Zealand sea lion pups, and much of this is believed to be caused by adult and subadult males, that bite, crush, shake and throw young pups.

In this thesis, a number of techniques are used to determine the role played by traumatic brain injury in the mortality of NZ sea lion pups. The findings of gross necropsy examinations show that pups have numerous lesions indicative of traumatic brain injury, including skull fractures and subdural haemorrhages, and that pups die due to crushing and impact injuries. Although some pups have gross lesions considered in human paediatric medicine to be indicative of shaking injury, detailed histological and microbiological studies of sea lion pups show that most of these are associated with meningitis due to *Klebsiella pneumoniae*. This bacterium is a common cause of pup mortality.

Immunohistochemical techniques are used to demonstrate that axonal injury is common in sea lion pups, but show that shaking is not a common mechanism of this pathological process. Instead, most axonal injury is found to be due to hypoxia-ischaemia, and evidence that raised intracranial pressure has occurred is comparatively common in dead pups. The combined findings of histological and immunohistochemical studies suggest that lesions such as optic sheath haemorrhage, intracranial subdural haemorrhage, spinal sub-meningeal haemorrhage, and optic nerve axonal injury could be caused by pertubations to vascular, intra-ocular, intracranial and subarachnoid pressure rather than being a direct result of trauma as is proposed in shaken baby syndrome.

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Glossary

acceleration	the change in velocity over time. Can be positive or negative (deceleration)
AMPA/KA receptors:	α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid/ kainic acid receptor. A membrane-bound glutamate receptor
ATP:	adenosine triphosphate. An energy-containing nucleotide produced by ATP-synthase
axotomy:	physical separation/tearing of an axon
biomechanics:	the study of mechanical forces as they apply to biological systems
blood-brain barrier:	the anatomical structures responsible for prevention of uncontrolled movement of fluid and solute between the cerebral blood vessels and the brain parenchyma
brain herniation:	movement of brain tissue from one anatomical compartment into another
brain swelling:	enlargement of the brain that occurs due to increased intravascular or extravascular fluid (e.g. cerebral oedema), resulting in flattening of gyri, shallow sulci, and herniation of brain tissue

bridging veins:	the veins that pass from the leptomeningeal surface through the subarachnoid space and dura mater, to empty into the intradural venous sinuses
calvarium:	the domed upper part of the skull comprising the frontal, parietal and occipital bones
cerebral autoregulation:	the maintenance of cerebral blood flow within homeostatic limits in response to changes in central venous pressure, intracranial pressure and metabolic demands
cerebral oedema:	accumulation of excessive amounts of extravascular fluid within brain tissue
compressive strain:	a force that results in tissues or structures being moved closer together
concussion:	transient loss of consciousness following a head injury
contre-coup contusion:	a contusion occurring remote to the site of impact. Historically these were said to occur opposite to the site of impact, but in human beings most occur on the frontal and temporal lobes, irrespective of impact site. The pathogenesis may involve tearing of parenchyma as it moves against bony protuberances or meningeal structures such as the falx cerebri
contusion:	disruption of the brain parenchyma following trauma, leading to haemorrhage and necrosis
coup contusion:	a contusion that occurs at the site of impact

cytoskeleton:	the microtubules, neurofilaments and microfilaments that make up the structural elements of a cell
cytotoxic oedema:	swelling of glial cells that results from damage to the energy-requiring membrane ion pumps, with subsequent influx of ions and fluid
depressed fracture:	the result of a focal impact where the outer table of the skull is depressed below the surface of the unaffected bone, and the inner table of the skull is pushed into the parenchyma
diffuse axonal injury:	both a neuropathological and clinical entity. The clinical syndrome injury involves immediate loss of consciousness followed by prolonged coma in the absence of a mass lesion. The neuropathological entity comprises widespread damage to axons throughout the parasagittal cortex, corpus callosum, internal capsule and long tracts of the brainstem
dynamic loading:	rapid application of a force, usually over a period of between 2 and 25 milliseconds
excitotoxicity:	excessive activation of excitatory glutamate receptors in the brain, resulting ultimately in cell death
fast axonal transport:	rapid (up to 400mm per day) transport of intracellular substances along microtubules
global ischaemia:	inadequate blood supply to the entire brain
hypoxia:	decrease in availability of oxygen to a tissue

impact loading:	the force resulting from direct contact between a tissue and a rigid object
impulse loading:	the force resulting from sudden acceleration or deceleration of tissue
inertia:	acceleration or deceleration forces without impact
intracranial pressure:	pressure within the cranial cavity, dependent upon central venous pressure, cerebral perfusion pressure and soft tissue/fluid volume of the brain and vasculature
intradural haemorrhage:	haemorrhage that originates within the dense fibrous layer of the dura mater
ischaemia:	lack of blood supply to a tissue relative to its needs
lamina cribrosa:	part of the sclera that is penetrated by axons of the optic nerve
mechanical loading:	the application of force(s) to a tissue
mechanoporation:	rapid movement of calcium ions into a neuron following transient membrane depolarisation which occurs as a result of mechanical deformation of the neuronal soma or axon
microtubule:	polymers of tubulin that make up part of the neuronal cytoskeleton and play a role in intra-cellular transport

mitochondrial membrane permeability transition pore:

a protein-lined 'hole' (pore) in the inner membrane of the mitochondria, which can open following traumatic brain injury and allow flux of ions across the membrane

neurocranium: the portion of the skull that encloses the brain, including the calvarium as well as the temporal and basisphenoid bones.

neurofilament: the class of intermediate filament found in neurons

NMDA receptors: *N*-methyl *D*-aspartate receptor. A voltage-dependent membrane-bound glutamate receptor

node of Ranvier: unmyelinated portions of axons found between myelinated internodes

otariids: eared seals (fur seals and sea lions)

pan-necrosis: Death of neurons as well as other cellular elements in an area of brain affected by focal ischaemia

phocids: 'true' seals. These species do not have pinnae

pinnipeds: a suborder of carnivorous marine mammals with limbs specialised as flippers

polygynous: an hierarchical social system whereby mature males defend a territory within which a group of females is sequestered. Females are comparatively free to enter and leave the territory

pond fracture: similar to a depressed fracture, but with no displacement of the inner table of bone

rotational acceleration: acceleration about an axis

selective neuronal necrosis: necrosis of specific populations of neurons that are particularly susceptible to ischaemia. Occurs with global ischaemia

shaken baby syndrome: a syndrome seen in human infants with inflicted brain injury proposed to be due to shaking. The typcial syndrome comprises encephalopathy with subdural and retinal haemorrhages

shear forces: sliding forces involving differential movement between layers of tissue

skull: the bones of the head exclusive of the mandibles but including the neurocranium, zygomatic processes and the facial, maxillary, and palatine bones

spinal sub-meningeal haemorrhage:

haemorrhage between the spinal dura mater and the spinal cord. Can involve haemorrhage between the dura mater and the parietal layer of the arachnoid mater (subdural haemorrhage) or haemorrhage between the parietal layer of the arachnoid mater and the spinal cord parenchyma (subarachnoid haemorrhage)

static loading:	the gradual application of a force over a period of greater than 200 milliseconds
strain:	deformation of tissue resulting from the application of a force
stress:	application of force to a tissue
subdural haemorrhage:	haemorrhage into the subdural compartment, which is made up of loose dural border cells at the inner aspect of the dura mater
tensile strain:	a force that results in tissues or structures being moved further apart
translational acceleration:	acceleration in a linear plane
vasogenic oedema:	loss of intravascular fluid into surrounding parenchyma following damage to cerebral blood vessel walls