Clin-IQ Project

Clinical Question: In patients with concussions, is the probability of permanent neurological damage predicted better by total number of concussions than by severity and duration of individual concussions?

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Answer: No

Level of Evidence for the Answer: B

Search Terms: Concussion, Severity, Cumulative effects

Date Search was Conducted: August 2012

Inclusion and Exclusion Criteria:

Inclusion Criteria: All studies comparing individuals or animal cell lines with single traumatic brain injuries vs. multiple traumatic brain injuries.

Exclusion Criteria: Studies with participants that included a history of alcohol abuse, substance abuse, psychiatric illness, seizure disorder, brain tumor, those currently taking medications, or participants with a previous traumatic brain injury unrelated to contact sports.

Summary of the Issues:

As contact sports continue to grow in popularity in the United States, it is estimated that between 50,000 and 300,000 athletes sustain concussive head injuries during the course of a single sports season.[1] Concern for the physical and mental health of these young athletes has prompted extensive research to determine short- and long-term cognitive effects of traumatic brain injuries (TBIs). Initially, research efforts were focused on long-term and cumulative effects of athletes that sustain multiple TBIs by evaluating cognitive function and incidence of dementia

later in life.[2] It has been relatively easy for researchers to prove that contact-sports athletes with a history of concussions are more likely to sustain further concussions, to suffer from more severe postconcussion symptoms, and to recover more slowly from future concussions.[3] However, objective clinical data comparing the long-term effects of a single severe TBI with multiple mild TBIs is relatively lacking.

In 2007, researchers learned for the first time that sports concussions result in chronic subclinical motor system dysfunctions that are linked to intracortical inhibitory system abnormalities.[4] When transcranial magnetic stimuli are delivered over the motor cortex while the subject imposes voluntary muscle contraction, there is a pause in ongoing EMG activities directly after the motor-evoked potential. This pause is called the cortical silent period (CSP) and is related to activation of intracortical inhibitory interneurons that are mediated by GABA-G receptors. Further, repeat TBIs exacerbate the intracortical inhibitory system abnormalities and the duration of the abnormality is positively correlated with the severity of the TBI sustained by the contact-sport athlete.[4] These results have far-reaching implications when it comes to evaluating contact-sports athletes after what appear to be mild concussions and utilizing this clinical data to determine if and when they are ready to return to play.

Summary of the Evidence:

We reviewed two scientific studies that compared the effects of single and multiple traumatic brain injuries on short- and long-term cellular structure and function. Both studies took into consideration the severity of insult and time between events.

In 2007, De Beaumont et al. hypothesized that athletes with a history of recurrent concussions would show greater subclinical motor system abnormalities than those with a history of only one concussion.[4] Forty-five participants were chosen from the University of Montreal football team and separated into three groups.

Table 1: Group Category by Number of Concussions

	# of athletes	# of concussions	Last concussion
Group 1	15	2-5	>9 mos ago
Group 2	15	1	>9 mos ago
Group 3	15	0	n/a

The three groups, see Table 1, were matched according to age and level of education. Baseline neuropsychological assessments were performed and transcranial magnetic stimulation (TMS) recordings were obtained with particular attention paid to the CSP. Results indicated that the duration of CSP was prolonged in athletes that experienced multiple concussions when compared to normal control participants. Further linear regression indicated that the main factor related to motor cortex dysfunction was concussion severity, see Figure 1.[4]

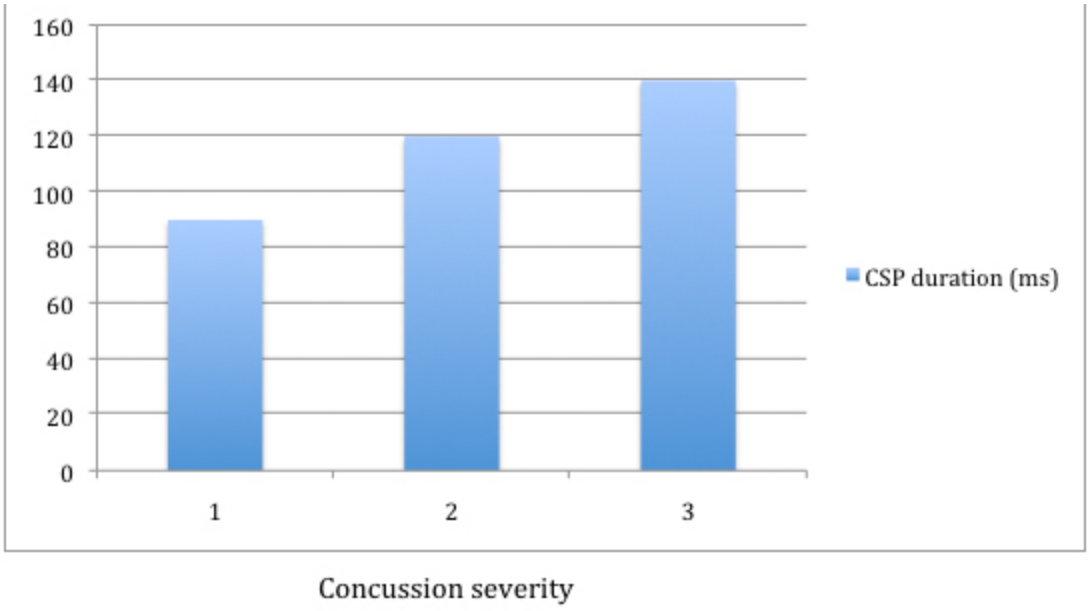

Figure 1: Pearson correlations between cortical silent-period (CSP) duration and concussion severity (Grades 1 to 3) in concussed athletes.

With a $P < 0.019$, findings indicate that the severity of concussion (rated per the American Academy of Neurology practice parameter) was a better predictor of abnormal CSP lengthening in multiple-concussion athletes than the total number of concussions sustained.[4]

In 2002, Slemmer et al. attempted to create an *in vitro* model demonstrating the effects of mechanical insult on specific cells of the brain. The researchers used hippocampal cell cultures from mouse embryos and injured them with an established model for TBI utilizing compressed nitrogen. Results of the study indicated that a pro-apoptotic protein was released from the mitochondrial membrane and resulted in cell death after stretch injury *in vitro*.[5] This information agrees with previous data established by studies utilizing *in vivo* models of TBI.[6,7] The cellular changes after stretch injury were significantly correlated with the degree of stretch. Data analysis showed that higher levels of stretch were associated with greater immediate and long-term cellular changes, see Figure 2.[5]

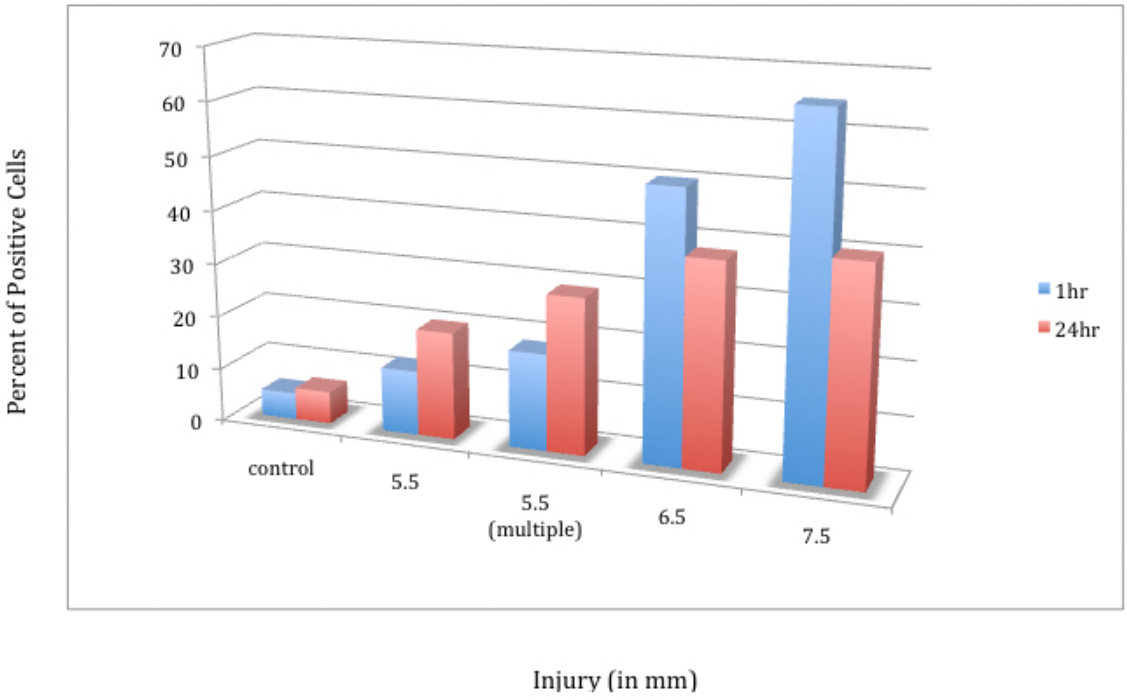

Figure 2: Effect of stretch injury on hippocampal cultures.

Propidium iodide (PrI) uptake is positively correlated to the degree of stretch. Data shown are at 1 hour and 24 hours post-injury. With a $P < 0.01$, uptake of PrI increases with mild (5.5 mm),

mild double (5.5 mm), moderate (6.5 mm) and severe (7.5 mm) levels of stretch are statistically significant when compared with control. At 24 hours, PrI levels remained elevated at all levels of injury compared with control.[5]

Conclusion:

In patients with concussions, severity of the traumatic brain injury appears to be more predictive of long-term cognitive deficit than total number of concussions. Consideration of these implications is important when reviewing the health of athletes that play contact sports and determining their ability to return to the game. This is especially true for children and young patients that may experience long-term cognitive dysfunction after only a single traumatic brain injury. It is hoped that the manufacturers of protective sports equipment will continue to review the evidence and employ the findings in pursuit of helmets that minimize the severity of concussions and other traumatic brain injury.

Reference List:

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of Sports Concussion on Motor Cortex Inhibition. Neurosurgery 2007; 61(2):329-337.

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