The Effect of Traumatic Brain Injury on Callus Formation and on the Biomechanical Characteristics of Long Bone Fractures: an Experimental Study in Mice.

Serafeim Tsitsilonis, MD, MSc, PhD1, Ricarda Locher, MD2, Tim Lünemann, MD2, Anja Garbe3, Florian Wichlas, MD2, Georg Duda, Prof. PhD1, Norbert P. Haas, Prof. MD2, Klaus-Dieter Schaser, Prof. MD2.

1Charité - University Medicine Berlin, Berlin, Germany, 2Charité - University Medicine Berlin, Center for Musculoskeletal Surgery, Berlin, Germany, 3Charité - University Medicine Berlin, Julis Wolff Insitute, Berlin, Germany.

Disclosures: S. Tsitsilonis: None. R. Locher: None. T. Lünemann: None. A. Garbe: None. F. Wichlas: None. G. Duda: None. N.P. Haas: None. K. Schaser: None.

Introduction: It is empirically believed that trauma patients that have sustained a traumatic brain injury (TBI) and a concomitant fracture of the long bones have an accelerated fracture healing with increased callus formation (1-3). Up to now there has been no detailed quantitative evidence of this hypothesis, as the existing clinical and experimental studies have mainly based their results on the evaluation of x-rays and on clinical symptoms (4-6). The aim of the present study was to radiologically examine fracture healing with the use of micro-CT and to biomechanically compare callus formation in mice sustaining a combination-injury of TBI and femoral fracture to mice sustaining only a femoral fracture.

Methods: For the needs of the present study 60 C57/BL6 female mice (Charles Rivers Lab.), aged 10-12 weeks were randomly divided into two groups. The first group (Polytrauma Group (PTG) / n=30) received a combination injury of TBI with the use of the Control Cortical Impaction Injury Model (CCII) and of a femoral fracture (0.7mm osteotomy) stabilized with a mini external fixator (RiSystem AG, Switzerland); the second group (Fracture Group (FXG) / n=30) received only a femoral fracture stabilized with the external fixator. Callus formation was examined in vivo on a weekly basis with the use of a micro-CT (callus volume in mm3 / callus density in cm3) (Scanco vivaCT 40, Scanco Medical AG, Switzerland). Twenty animals per group were sacrificed after micro-CT examination at three weeks after trauma; the remaining ten animals per group were euthanized at four weeks after trauma; the femoral bones of the animals were biomechanically tested ex vivo (torsional strength in Nmm / torsional rigidity) (Bose GmbH ElectroForce Systems Group, Germany). The groups were compared with the use of the Mann-Whitney-U-Test. Statistical significance was set at p<0.05.

Results: A statistically significant difference in callus volume formation between the two groups was observed at two weeks after trauma in favor of the PTG (p=0.02). This difference remained statistically significant at three and four weeks after trauma (p=0.039 and p<0.001 respectively). No differences in callus density were observed between the two groups at any time point. The torsional strength of the femoral bones of PTG showed higher torsional strength at 4 weeks after trauma compared to the FXG (p=0.029). No statistically significant differences in torsional rigidity were observed; however, a trend in favor of the PTG was observed at four weeks after trauma (p=0.057).

Discussion: The present study shows that traumatic brain injury results in an increased callus formation at the presence of a concomitantly fractured long bone fracture. The formed callus was of equal quality; no differences in callus density were observed compared to normal fracture healing. This increased callus formation of non-inferior quality resulted also to biomechanically superior fracture healing, as showed by the increased torsional strength of the PTG towards the FXG. The combination of TBI and concomitant long bone fracture results in an accelerated and increased callus formation that offers biomechanical advantages compared to fracture healing after monotrauma. The present detailed quantitative evidence confirms the hypothesis that TBI results in increased callus formation. The comprehension of the biological mechanisms responsible for the above observation would be of great importance in stimulation of fracture healing.

Significance: The present study presents detailed quantitative radiological and biomechanical evidence on the effect of TBI on fracture healing of long bones and proves that TBI results in increased callus formation of equal quality to that of normal fracture healing of long bones.

Acknowledgments: The authors would like to thank Dr. Katharina Schmidt-Bleek for her support during the conduction of the experimental animal procedures.

4. Giannoudis, P.V., et al., Accelerated bone healing and excessive callus formation in patients with femoral fracture and head

ORS 2014 Annual Meeting
Poster No: 1520