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LETTER TO THE EDITOR

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Comments on Hausmann et al.: Neuronal apoptosis following human brain injury

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To the Editor

We read with interest the article by Hausmann et al. [1] entitled "Neuronal apoptosis following human brain injury". The authors investigated the time-related appearance of apoptotic neuronal cells from 103 individuals who had sustained traumatic closed injuries using in situ nick translation (ISNT). The apoptotic cells could be detected in a cortical contusion with a wound age of 45 min at the earliest and in the majority of the cases with postinfliction intervals up to 2 weeks.

We now have experience with 56 cerebrum samples with macroscopically visible cerebral contusions and the same number of brain samples from injury-free contralateral cerebral hemispheres. For the detection of apoptotic cells we used the APOPDTECT-kit (Chemicon, Hofheim, Germany). This modified TUNEL technique permits the indirect detection of breaks in strands of DNA. Furthermore, the antibody CPP32 (Dako, Hamburg, Germany) was applied against caspase 3, and the antibodies ICE and Mch 3 (Dianova, Hamburg, Germany) against caspases 1 and 7, which activate the repair and regulation of DNA. Hence, these are 4 apoptosis markers that permit immunohistochemical detection. The prospective study was carried out on paraffin-embedded cross-sections after microwave pretreatment.

Results to date indicate a correlation between the age of vital injuries to the cerebrum and the apoptotic status of the neuronal and glial cells. The apoptotic reactions began as perivascular changes in and around the area of the contusion. A central function for the beginning of apoptosis is played by caspase 3 in microglia cells and oligodendrogliacytes. Particularly the microglia cells demonstrated in 90% and the oligodendrocytes in 70.2% of the cases positive staining reactions for caspase 3.

We investigated various injury intervals (<3 h, 3 h–4 days, >4 days). Up to an injury age of 3 h, only an expression of isolated neuronal cells was evident for caspase 3, while the TUNEL reaction was regularly negative. Cerebral injuries with a survival time of between 3 h and 4 days, on the other hand, revealed numerous strongly positively reacting apoptotic neuronal and glial cells in and around the contusion area. The apoptotic reaction of brain injuries older than 4 days was characterized by a decrease in the number of anti-caspase 3 and APOPDETECT-positive neurocytes and gliacytes in the area of the cerebral injury. In the contralateral cortex we also found scattered apoptotic neurocytes and gliacytes in the majority of sections.

In concordance with the literature [2–6] the apoptotic status of neuronal cells as well as glial cells can be used for better estimation of the unknown time since cerebral injury even in the early posttraumatic interval. In the article by Hausmann et al. [1] the apoptotic changes in glial cell reactions were excluded. Although the earliest positive TUNEL reaction was observed similar to the positive ISNT reaction, it is important to know that the positive immunohistochemical reactions against different caspases take place earlier. In contrast to the findings of Hausmann et al. [1] we found a deceleration of apoptotic neuronal and glial cells even after a postinfliction interval of 4 days.

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