WriteClick: Editor's Choice

Editors' Note: Dr. Martinez-Ramirez et al. comment on study limitations that might have led to the authors' conclusions in "Microbleeds do not affect rate of cognitive decline in Alzheimer disease." Dr. Vanacore, in reference to "Neurodegenerative causes of death among retired National Football League players," raises the 12-fold higher risk of death from ALS in professional Italian soccer players, specifically midfielders, and calls for further cohort studies in other professional athletes.

Megan Alcauskas, MD, and Robert C. Griggs, MD

MICROBLEEDS DO NOT AFFECT RATE OF COGNITIVE DECLINE IN ALZHEIMER DISEASE

Sergi Martinez-Ramirez, Steven M. Greenberg, Anand Viswanathan, Boston: van der Vlies et al.[1] found no effect of cerebral microbleeds (MBs) on the rate of cognitive decline in patients with Alzheimer disease (AD). The same cohort previously demonstrated an association between MBs and mortality.[2] Therefore, the current findings suggest that this increase in mortality was not a simple reflection of cognitive decline as measured here. However, MBs have been shown to independently affect several cognitive domains in subjects without dementia[3,4] and in patients with cerebral small-vessel disease.[5]

Several limitations may have precluded demonstration of such effects in patients with AD: a small number of patients with lobar MBs, the use of a relatively crude measure of cognitive decline, or the overwhelming effect of AD pathology on cognition compared with any presumed MB-related effects.

The mechanisms by which MBs may affect cognition are still unclear. Do MBs exert their effects through direct tissue disruption or are they merely markers of accompanying cerebrovascular pathologies such as cerebral amyloid angiopathy? If MBs have direct effects on cognitive function, it is possible that specific anatomical location of MBs would have a role.[4,5] Further larger studies in elderly patients with cognitive impairment may help answer some of these questions.

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NEURODEGENERATIVE CAUSES OF DEATH AMONG RETIRED NATIONAL FOOTBALL LEAGUE PLAYERS

Nicola Vanacore, Rome: Lehman et al.[1] reported an increased risk of death from amyotrophic lateral sclerosis (ALS) and AD among retired National Football League players, especially among players in speed positions. A 40-fold higher prevalence rate for ALS was reported in football players who played after 1960.[2] There was no risk of ALS in high school students who played football from 1946 to 1956, when headgear was less protective than today.[3] I am surprised that Lehman et al. discussed only the causal hypothesis of recurrent traumatic brain injuries or concussions whereas other possible etiologic factors were not mentioned (i.e., intense physical activity, use of drugs, exposure to neurotoxins).[1] In Italy, a 12-fold higher risk of death from ALS in professional soccer players was observed but not from AD or Parkinson disease.[4] In 6 of 8 subjects, age at death was younger than 59 years.[4] The risk of ALS was also significantly increased for midfielders but not for other positions.[5] Lehman et al. found a different pattern of risk of death for ALS and AD vs Parkinson disease[1] so this may indicate a different origin for these diseases. It might be important to know the mean age at death of players deceased from ALS and AD in this study.[1] Further cohort studies in professional players of different sports should be conducted with particular attention to the position of players because this could supply important etiologic cues.

Author Response: Everett J. Lehman, Misty J. Hein, Sherry L. Baron, Christine M. Gersic, Cincinnati: We thank Dr. Vanacore for commenting on our article.[1] We are aware of the important research that Vanacore and others conducted during

the mid-2000s that found increased risk of ALS among professional Italian soccer players.[4] We noted that there were position-specific and duration-specific elevations reported in one study.[5] Further follow-up of the soccer cohort will be important because of the young age of the players in the cohort.[6] The same is true for our football cohort. We acknowledged that what we found among long-term professional players may not be applicable to high school, college, or shorter-term professional players. However, we do not believe that there is enough current evidence to relate type of helmet to either concussion or neurodegeneration. That is fertile area for future study. We did not report mean age of death for the players because we adjusted for race, age, and calendar year in our analysis. We also noted in our discussion of study limitations that we did not have information on other possible etiologic factors, including genetic factors.

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CORRECTION

Cerebellar ataxia with *SYNE1* mutation accompanying motor neuron disease

In the Clinical/Scientific Note "Cerebellar ataxia with *SYNE1* mutation accompanying motor neuron disease" by Y. Izumi et al. (*Neurology*® 2013;80:600–601), there are errors in the Results and figure e-2. Mutation c.22456_22457insG, p.R7486fs7488X (patient 1) should read c.224455dupG, p.I7486Dfs7488X. Mutation c.13600_13601insA, p.Y4534fs4539X (patient 3) should read c.13599dupA, p.Y4534Ifs4539X. The original figure e-2 was replaced with a corrected version on March 25, 2013. The authors regret the errors.

Author disclosures are available upon request (journal@neurology.org).

Neurodegenerative causes of death among retired National Football League players

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