Persistent Cognitive Impairment in a Multiply Concussed Female Athlete: Is it Chronic Traumatic Encephalopathy? A Case Study

Robert Eme
Kari Gilbertson
Susan Oehler
Illinois School of Professional Psychology, Argosy University, Schaumburg

Abstract

Recent reviews of current issues in pediatric sports concussion have concluded that there appears to be a growing population of multiply concussed young athletes who may experience as-yet-undiagnosed cognitive impairments later in life. In addition, repetitive mild head trauma has been linked to chronic traumatic encephalopathy (CTE). Chronic traumatic encephalopathy is a progressive neurodegenerative disease thought to be caused, at least in part, by multiple concussive or subconcussive head impacts associated with sports as well as other head trauma. Early appearing symptoms included apathy and impairments in attention, memory and executive functioning. Despite the fact that female athletes sustain more concussions than male athletes in similar sports, the study of chronic traumatic encephalopathy in females is virtually non-existent. This article reports a case study of a multiply concussed former female athlete (ice hockey) in her twenties who has presented with the early symptoms of CTE for 10 years. Although a definite diagnosis can only be made by a post-mortem neuropathological examination, the fact that these symptoms cannot be plausibly explained in any way other than resulting from repetitive concussive head impacts strongly suggests CTE and underscores the need for the study of CTE in females.

Recent reviews (Borchers, 2011; Shatz & Moser, 2011) of sports concussion literature have concluded that there appears to be a growing population of multiply concussed young athletes who may experience as-yet-undiagnosed cognitive impairments later in life . In addition, repetitive mild head trauma has been linked to chronic traumatic encephalopathy (CTE) (McCrory, 2011; McKee et al., 2009, McKee et al., 2012). CTE is a progressive neurodegenerative disease thought to be caused, at least in part, by multiple concussive or subconcussive head impacts associated with sports as well as other activities such as physical abuse, head banging, and military combat (Baugh et al., 2012; Gavett, Stern, & McKee, 2011; McKee et al., 2009; McKee et al., 2012). Early appearing symptoms included apathy and impairments in attention, memory and executive functioning (Baugh et al., 2012; McKee et al., 2012). Later in the course of the disease the cognitive symptoms worsen**,** and mood and behavioral changes such as irritabil-

ity and poor impulse control occur. The advanced stage of CTE as seen in cases 65 years or older is characterized by dementia (Baugh et al., 2012).

Although repetitive brain trauma seems to be a *necessary* condition for CTE to occur, it is not a *sufficient* condition as there are numerous individuals with a history of repeated brain trauma who do not have CTE (Baugh et al., 2012). Consequently, it appears that other risk factors must be involved in initiating CTE such as the age at which the brain starts to be exposed to the trauma, genetic vulnerability, and perhaps sex of the individual (i.e., female) (Baugh et al., 2012). Furthermore, although the onset of CTE is typically in midlife (Gavett, Stern, & McKee, 2011), it can occur much earlier as evidenced by the autopsy results of an 18 year-old who sustained multiple concussions playing high school football (Miller, 2007). Currently, although attempts are underway to diagnose CTE while an individual is alive using sophisticated Positron emission tomography brain scans (e.g., Small et al., 2013), a definite diagnosis can only be made by a post-mortem neuropathological examination which finds a unique pattern of tangles of tau proteins that contribute to the neurodegeneration of CTE (Baugh et al., 2012; Gavett, Stern, & McKee, 2011; McKee et al., 2012). Under normal conditions in the human nervous system, tau proteins are primarily associated with helping to maintain the integrity of microtubules in axons. However, brain trauma causes some tau to become dissociated from the microtubules. The dissociated tau may become hyperphosphorylated (i.e., the addition of an excessive number of phosphate groups) and misfolded. This causes a neurotoxicity which begins locally and spreads slowly over the decades to involve widespread regions in the neurocortex (McKee et al., 2012).

Although there is a paucity of research on sex differences in the sports concussion literature (Harvey, Freeman, Broshek, & Barth, 2011), the studies that have been conducted have found that female athletes (high school and college) sustain more concussions than male athletes in similar sports (Blume & Hawash, 2012; Covassin & Elbin, 2011; Covassin et al., 2012; Daneshvar et al., 2011; Harvey et al., 2011). For example, in a review of the frequency and rates of concussions in the NCAA from 1988 through 2004, Daneshavar, Nowinski, McKee, and Cantu (2011) reported that the most frequent injury rate per 1000 athletic exposures for all sports was .91 for women's ice hockey. This rate was almost twice as large as the second most frequent rate — .54 for men's spring football. Female athletes also present with more concussion symptoms acutely (as well as one year later), and take a longer period to recover from concussions than male athletes (Covassin & Elbin, 2011; Covassin, Elbin, Harris, Parker, & Kontos, 2012; Harvey et al., 2011). Numerous explanations have been proposed to account for these findings including the possibility that females may simply be more willing to admit to symptoms than males (Covassin & Elbin, 2011; Covassin et al., 2012). However, this explanation is rendered less plausible as a complete explanation by the most recent study of concussed athletes which found that females were more impaired not only on self-reported symptoms of concussion but also on objective measures of memory and postural stability (Covassin et al.,

2012). Hence, it may be that females are biologically more vulnerable than males to sustaining concussions. One reason for this may be that females have a decreased head-neck segment mass compared with male athletes, which could result in greater angular acceleration to the head after a concussive impact (Covassin & Elbin, 2011**).**

If there is a greater female vulnerability to concussion, it might be expected that this would result in a greater female vulnerability to the development of CTE. However, the study of CTE in multiply concussed female athletes is virtually non-existent. For example, in the largest study to date of CTE (McKee et al., 2012), of the 85 brains from former athletes (*N*=64), military veterans (86% of whom were also athletes) and civilians with a history of repetitive mild brain trauma that were evaluated for CTE, only one was that of a female (competitive skier). Evidence of CTE was found in 68 of the male subjects but not in the single female subject. Hence, there is a neglect in the investigation of CTE in female athletes with a history of multiple concussions. The case history information in this article will support the need to rectify this neglect.

Case Study

Subject

The subject of the case report is a 29-year-old female student (who will be referred to by the pseudonym "Jane"**)** currently enrolled in a doctoral program in clinical psychology whose doctoral dissertation is on CTE. The dissertation is based in part upon her history of concussions sustained from participation in ice hockey. The first author of this paper is her dissertation chair.

Method

Two methods were used to gather information. The first was self-report of history of concussions and symptoms following the concussions. Concussions were defined as her recall of head impacts that resulted in at least three of the 22 symptoms listed in the *Sports Concussion Assessment Tool 2* (McCrory et al., 2009). This tool is the consensus choice of the 3rd annual international conference on concussion in sport of a standardized method for evaluating injured athletes for concussion. The conference defined concussion as "a complex pathophysiological process affecting the brain, induced by traumatic biochemical forces" and "results in a graded set of clinical symptoms" (McCrory et al., 2009, p 186). This instrument asks the athlete "How do you feel now?" with regard to 22 clinical symptoms (e.g., dizziness, blurred vision, difficulty remembering, etc.). A concussion is "suspected" if one or more of the 22 symptoms is reported. In this case study, a conservative approach of requiring at least 3 symptoms was adopted for a head impact to be judged a concussion.

Secondly, information was reviewed from five neuropsychological evaluations she underwent from ages 16 to 29 and two Magnetic Resonance Imaging (MRI) tests at ages 21 and 27 The first neuropsychological evaluation at age 16

was as a result of a referral from an education consultant for untimed testing for the SAT due to her having difficulty with completing tests on time. No significant cognitive impairments were found in any domain including, attention, nor were there any self- or maternal-reported impairments in attention, as assessed by the *Brown Attention-Deficit Disorder Scales*. The evaluation concluded that the difficulty in test completion was attributed to test anxiety caused by perfectionist tendencies. The four subsequent evaluations, beginning at age 22 with the most recent evaluation at age 29, were all a result of referrals for assessment of the chronic cognitive impairments she had been experiencing after her 6th concussion at age 20. In addition to these tests, Jane was also evaluated at age 29 on a new self-report instrument to assess deficits in executive functioning (EF): the *Deficits in Executive Functioning Scale* (BDEFS) (Barkley, 2011). The BDEFS has been normed on a nationally representative sample and is based upon self or other report of functioning on five major dimensions of EF in daily life: self-management to time, self-organization and problem solving, self discipline (inhibition), self-motivation, and self-regulation of emotion (Barkley, 2011). Support for the validity of the BDEFS comes from studies that have found it to be more predictive of impaired functioning in major life activities and occupational functioning among adults with ADHD than EF tests (Barkley & Fischer, 2011; Barkley & Murphy, 2010, 2011). This instrument was chosen to add to the traditional battery of neuropsychological assessments she had previously received because these traditional tests of executive functioning (EF) have been shown to have low or no ecological validity when judged against ratings of EF in daily life (Barkley, 2011; Bigler, 2008). This results in unacceptably high rates of "false negatives" (i.e., the individual really has an impairment in EF but the tests falsely report no impairment, Barkley, Murphy, & Fischer, 2008). A striking example of this disjunction between the results of neuropsychological testing and patient self-report as provided by Bigler (2004), involved the case of a 47-year-old-college educated male who suffered from a persistent postconcussive syndrome (PPCS) for 7 months following a mild traumatic brain injury (TBI) prior to an expected death unrelated to the TBI. The PCCS resulted in significant "real-world" difficulty in his functioning as an appraiser (problems not evident prior to the TBI) based upon self-report and verified by his spouse and co-workers. Furthermore, an autopsy found clear evidence of brain injury. Yet the results of the antemortem comprehensive clinical neuropsychological testing were generally within normal limits. As Bigler (2008, p.12) concluded, "Obviously cognitive skills, in particular, working memory and executive function, can place much higher demands on neural integrity in the real world than what can be assessed by current neuropsychological technique in the laboratory."

Self- Report Results

Jane sustained a total of 10 concussions from ages 13 through 29 from participation in ice hockey. After her 6th concussion at age 20, she began experiencing symptoms of significant cognitive impairment (which will subsequently be discussed) that have persisted for 9 years to age 29. These symptoms are iden-

tical to those reported by Baugh and colleagues (2012) and McKee and colleagues (2012) as occurring in early stage CTE. In high school, prior to the onset of these symptoms, Jane reported struggling with an eating disorder, depression, anxiety, and fainting caused by the eating disorder. Since high school, she has been symptom free with the exception fainting spells which are of unknown origin.

Mood Symptom: Apathy

> Jane reported:
> In the past year the hardest part to deal with has been my lack of energy and motivation. One would think that it'd be easier just to sit down and finish an assignment and study, but I just can't. I used to always have a lot of energy and be doing something. But now I seriously could sit in a chair and stare at the wall for hours.

Cognitive Symptoms

- **Impaired Attention.** She reports becoming easily distracted, has trouble remaining focused, and her "mind wandering from one thing to another." As a result, her college classes became "confusing." She also reported slowed speed of information processing which commonly accompanies impaired attention in TBI (Lezak, Howieson, Bigler, & Tranel, 2012; McAllister, 2008).
- **Impaired Memory.** She reports the need to carry a pen around everywhere she goes so that she can immediately write things down, otherwise she will forget. She also reports word-finding difficulties.
- **Impaired Executive Functioning.** She scored in the clinically impaired range[1] on four of the five EF dimensions on the BDEFS: *Self-management of Time, Self Organization/Problem Solving, Self Restraint, and Self Motivation* but not on *Self Regulation of Emotion*. The failure to score in the clinically impaired range on the latter dimension may be because impairments on this dimension tend to become prominent in the later stages of CTE (McKee et al., 2012).

This cascade of symptoms became so impairing that Jane was dismissed from a requisite clinical training experience in her doctoral program because she was not able to complete her reports in a timely fashion.

Results of Neuropsychological Evaluations

Because the results of the most recent neuropsychological evaluation at age 29 are essentially similar to the 4 preceding evaluations, only the salient details of this evaluation will be reported. The evaluation focused on assessing atten-

[1] Clinical impairment is defined as scoring 1.5 standard deviations 93rd percentile) above of the mean of the female (aged 18-34) norm group (Barkley, 2010).

tion, executive function, and memory. Because of Jane's familiarity with neuropsychological measures, as a result of her 4 prior evaluations, the neuropsychologist administered tests with which she had no experience. The tests were: *Rey Auditory Learning Test, Form A; Brief Visuospatial Memory Test-Revised, Form 2; Delis-Kaplan Executive Functioning System (select subtests); Ruff 2&7 Selective Attention Test; Gordon Diagnostic System.* Overall, the neuropsychologist concluded that she exhibited good attentional function on a variety of measures but difficulty with impulsivity on a measure of sustained concentration and vigilance. Executive functions, verbal memory, and visual memory were all intact. Thus, the results of 4 neuropsychological evaluations since the onset of her self-report of chronic cognitive impairments have all generally been within normal limits.

The MRI findings were all negative with the exception of a finding of multiple calcifications in the temporal/parietal regions, which was interpreted by the neurologist as being caused by the multiple concussions. Although this finding is not indicative of CTE because a definite diagnosis can only be made by a post-mortem neuropathological examination (Baugh et al., 2012; Gavett, Stern, & McKee, 2011; McKee et al., 2012), the MRI findings validate the interpretation of the cognitive impairments as due to early onset CTE as opposed to other medical or psychological conditions.

Discussion

At age 20, after her 6th concussion, Jane began experiencing chronic, worsening symptoms of mood and cognitive dysfunction. Prior to age 20, she was symptom free in this regard, as reported by a neuropsychological evaluation at age 16. Furthermore, her prior history of psychological problems (e.g., eating disorder and depression), which ceased after high school, cannot explain this onset at age 20 and the chronic course of the mood and cognitive impairments. Thus, although a definite diagnosis of CTE can only be made by an autopsy, which finds the unique pattern of tangles of tau protein (Baugh et al., 2012), it is clear that Jane presents with the typical early appearing symptoms and impairments of CTE for which no other explanation is currently plausible. The failure of neuropsychological testing to detect these impairments is best interpreted as reflecting the previously discussed low ecological validity of these tests. In addition, her case lacks the common ambiguities that can make the attribution of these symptoms to a history of repetitive mild brain trauma difficult. For example, there is no history of significant substance abuse, and the challenges of differential diagnosis from Alzheimer's or frontotemporal dementia that occur when onset of CTE is in midlife (Gavett, Stern, & McKee, 2011) are clearly not relevant. Lastly, the possibility that the impairments are best understood as a *persistent* postconcussive syndrome, as defined by Bigler (2008) as symptoms that persist beyond three months, rather than CTE is inadequate. Namely, the 9-year duration of the symptoms, which so far exceeds 3 months, is indicative of a condition different

from what Bigler (2008) originally conceptualized as a persistent postconcussive syndrome.

The principal limitation of this case study, as is true of all cases studies,[2] is that it is an uncontrolled study (in contrast to group research designs with random assignment) and information is limited to one person (Kazdin, 2011). However, as Kazdin (2011) has pointed out, case studies can be quite useful and have played a strong role in elaborating the relation between brain and behavior. Because the central goal of scientific research is to draw causal inferences by "minimizing, ruling out, or making implausible alternative explanations that would obscure the interpretations of the findings" (Kazdin, 2011, p. viii), it is possible for this goal to be achieved in many cases involving brain damage. This is because in such instances, as in the classic case of Phineas Gage whose tragic traumatic brain injury which occurred more than 160 years ago (1848) still has relevance today (Damasio,1994), the abruptness and scope of injury and subsequent cognitive impairments makes the causal agent clear, such that other explanations are implausible (Kazdin, 2011). In the present case study, the same logic applies, in the sense that explanations other than multiple concussions are implausible.

In conclusion, this case study clearly illustrates that there can be early onset of serious impairments due to multiple sports-related concussions. As such, this case study provides support for the concern that there appears to be a growing population of young athletes, perhaps especially female, who may experience as-yet-undiagnosed cognitive impairments later in life. Furthermore, because these early onset serious impairments are representative of the early symptoms of CTE, and other explanations for the impairments seem unlikely, the most plausible interpretation is CTE. If so, it underlines the urgency of including multiply concussed female athletes (which heretofore has been an almost totally neglected population), in studies which are attempting to identify ante mortem the neurological signature of CTE.

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[2] See Kazdin (2011) for an exhaustive discussion of the strengths and limitations of case studies.

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