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Comparing fMRI activation during smooth pursuit eye movements among contact sport athletes, non-contact sport athletes, and non-athletes

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A B S T R A C T

Objectives: Though sub-concussive impacts are common during contact sports, there is little consensus whether repeat blows affect brain function. Using a "lifetime exposure" rather than acute exposure approach, we examined oculomotor performance and brain activation among collegiate football players and two control groups. Our analysis examined whether there are group differences in eye movement behavioral performance and in brain activation during smooth pursuit.

Methods: Data from 21 off-season Division I football "starters" were compared with a) 19 collegiate cross-country runners, and b) 11 non-athlete college students who were SES matched to the football player group (total $N = 51$). Visual smooth pursuit was performed while undergoing fMRI imaging via a 3 Tesla scanner. Smooth pursuit eye movements to three stimulus difficulty levels were measured with regard to RMS error, gain, and lag.

Results: No meaningful differences were found for any of the standard analyses used to assess smooth pursuit eye movements. For fMRI, greater activation was seen in the oculomotor region of the cerebellar vermis and areas of the FEF for football players as compared to either control group, who did not differ on any measure.

Conclusion: Greater cerebellar activity among football players while performing an oculomotor task could indicate that they are working harder to compensate for some subtle, long-term subconcussive deficits. Alternatively, top athletes in a sport requiring high visual motor skill could have more of their cerebellum and FEF devoted to oculomotor task performance regardless of subconcussive history. Overall, these results provide little firm support for an effect of accumulated subconcussion exposure on brain function.

1. Introduction

The public and research emphasis on concussions can sometimes obscure the fact that athletes in a variety of sports experience hundreds of sub-concussive impacts each year (McAllister et al., 2012a). Estimates for sub-concussive impact exposure in football players at the high school and collegiate level range from 244 to 1444 per season (Broglio et al., 2010; Crisco et al., 2010; Greenwald et al., 2008). In contrast, the per season concussion risk is 7.25% for high school and 5.52% for collegiate football athletes (Dompier et al., 2015). Beginning with the documentation of "punch-drunk" dementia in the 1920's (Carroll, 1936; Martland, 1928; Parker, 1934) and the coining of the term Dementia Pugilistica in the 1930's (Millspaugh, 1937), scientists and clinicians have been concerned about the cumulative dose effects of impacts to the skull, including those that do not produce acute concussion but nevertheless result in clinical signs and symptoms. The animal model literature began documenting the cumulative effects of repeated "sub-concussive" impacts to the skull in the 1940's (Tedeschi, 1944). Research on this topic burgeoned further with heightened public awareness of the issue and with the development of key research tools such as cognitive testing, brain imaging and wearable accelerometers. Despite the availability of these tools, however, there remains a striking lack of agreement within the literature as to whether repeat sub-concussive blows has a measurable effect on the brain and in what areas.

Studies on cognition examine a variety of neurocognitive functions, including: verbal learning, verbal recognition, spatial recognition, visual working memory, visual-motor speed, impulse inhibition, visual attention, and concentration. Using athletes from a variety of sports but primarily soccer, some studies find an effect on cognition (Downs and Abwender, 2002; Ellemberg et al., 2007; Killam et al., 2005; Matser et al., 1999, 2001, 1998; McAllister et al., 2012a; Miyashita et al., 2017; Straume-Naesheim et al., 2009; Talavage et al., 2014; Tsushima et al., 2016; Tysvaer and Løchen, 1991; Witol and Webbe, 2003; Zhang et al., 2013), while others find no effect (Abreau et al., 1990; Guskiewicz et al., 2002; Janda et al., 2002; Kaminski et al., 2008; Kemp et al., 2016;

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Miller et al., 2007; Putukian et al., 2000; Rutherford et al., 2009; Salinas et al., 2009; Stephens et al., 2010; Straume-Naesheim, 2005; Vann Jones et al., 2014). The subconcussive effect of hits on balance is also inconclusive with some reporting a positive effect (Haran et al., 2013; Miyashita et al., 2017), and others reporting no effect (Broglio et al., 2004; Gysland et al., 2012; Mangus et al., 2004; Schmitt et al., 2004). A meta-analysis of 30 studies on the subconcussive effects on cognition of soccer players concluded that there are too many shortcomings of the current research to draw conclusions. Common shortcomings include small sample sizes, inappropriate selection of control groups, low quality assessment of head impact frequency, and inappropriate control for type 1 errors (Tarnutzer et al., 2016). Examining the potential effects on cognition of subconcussive hits is important from a symptom and quality of life standpoint, but from a scientific standpoint, it is also challenging. Learning and memory skills are easily affected by a large number of relatively difficult to control factors, such as motivation, sleep, age, drug use, blood sugar levels, hydration, etc. Combining neurocognitive testing with neuroimaging may be more promising (Tarnutzer et al., 2016).

Though imaging is not a viable method for diagnosing concussion, the sheer number of subconcussive hits to the skull during contact sports could conceivably result in visible damage to brain matter. Both EEG (Tysvaer and Storli, 1989), and CT (Sortland and Tysvaer, 1989) have been utilized in this effort. More recently, numerous MRI studies have been conducted on subconcussion, including using diffusion imaging and the diffusion tensor model (DTI), which looks for damage in the white matter (Bahrami et al., 2016; Bazarian et al., 2014; Chappell et al., 2008, 2006; Davenport et al., 2016, 2014; Helmer et al., 2014; Koerte et al., 2017, 2012; Lipton et al., 2013; Mayinger et al., 2017; McAllister et al., 2014; Shin et al., 2014). A smaller number of studies have addressed anatomical defects (grey matter changes) (Adams et al., 2007; Davenport et al., 2014; Koerte et al., 2016). Once again, however, these studies do not yield a clear consensus (for review see (Bailes et al., 2013; Belanger et al., 2016; Koerte et al., 2015; Maher et al., 2014)).

To more accurately identify athletes who experience the largest and/or greatest number of subconcussive blows during a season, a small number of researchers have begun using head-mounted accelerometers. So far, the use of this technique has resulted in positive findings. Both McAllister et al. (2014) and Bazarian et al. (2014) reported significant correlations between total accelerometer-based hit exposure and white matter measures of the brain using the DTI model of diffusion imaging. One study used helmet accelerometers and neurocognitive measures among football and hockey players and found a weak effect (McAllister et al., 2012b). Talavage et al. (2014) found a significant correlation with functional MRI (fMRI) activation while athletes performed the short-term memory n-back task. The use of accelerometers in research is limited by cost (of equipment, installation and maintenance), hassle (some players find them cumbersome), and concerns over accuracy. When tested against biomechanical sensors in a laboratory setting, the accuracy of helmet-based accelerometers must be interpreted cautiously (O'Connor et al., 2017; Siegmund et al., 2016).

The study by Talavage and colleagues highlights yet another promising but thus far minimally explored approach: the use of fMRI in combination with behaviorally relevant neurocognitive testing. Research involving resting-state fMRI conducted while subjects relax in an MRI scanner has not shown consistent results (Abbas et al., 2015; Johnson et al., 2014; Slobounov et al., 2017), but the study by Talavage et al. evaluated memory, a neurocognitive function known to be affected by head trauma generally and concussion specifically. Another known sequelae of concussion is sensory motor deficits (Howell et al., 2017; Kontos et al., 2017). Sensory motor testing holds promise for the detection of subconcussive damage in part because it is multimodal. To the best of our knowledge, there is one study series examining fMRI activation during a oculomotor sensorimotor task (Johnson et al., 2015a, 2015b). We chose to examine eye movement behavior due to the solid body of literature showing ocular motor performance to be one of the most robust indicators of concussion (Balaban et al., 2016; Brahm et al., 2009; Capó-Aponte et al., 2012a, 2012b; Cifu et al., 2015; DeHaan et al., 2007; Drew et al., 2007; Heitger et al., 2009, 2007a, 2007b, 2006, 2004; Hoffer et al., 2017; Kraus et al., 2007; Liston et al., 2017; Maruta et al., 2017; Master et al., 2016; Mucha et al., 2014; Pearce et al., 2015; Samadani et al., 2015; Storey et al., 2017; Thiagarajan et al., 2011). Oculomotor control has been strongly linked to neural integrity (John Leigh and Zee, 2015; Pierrot-Deseilligny et al., 2004) and tasks that assess oculomotor function are linked to a number of cognitive functions including attention, visuospatial processing, working memory, processing speed and predictive behavior (Barnes, 2008; Hutton, 2008; John Leigh and Zee, 2015; Pierrot-Deseilligny et al., 2004; Schütz et al., 2011). In addition, unlike other sensory motor behaviors (e.g., balance and gait), eye movements lend themselves well to fMRI neuroimaging.

The aim of this study is to measure differences in the oculomotor control network in athletes playing in concussion-prone sports as compared to two control groups (non-concussion-prone sport, cross country runners, and socioeconomically matched, SES, non-athletes college students). To do so we used a smooth pursuit task, which has been demonstrated to show reduced performance in concussion patients. The smooth pursuit task in particular has been thoroughly studied in both primates and humans and is known to engage many regions of the brain, both cortical and subcortical (Fukushima et al., 2013). FMRI studies have revealed a network of brain regions linked to the task, including the frontal eye fields (FEF) and supplementary eye fields (SEF) in the frontal lobe, the intraparietal cortex, the occipital cortex, and the cerebellum (Lencer and Trillenberg, 2008; Petit and Haxby, 1999). Smooth pursuit has the additional advantages of being an almost autonomic process and being shown in concussion and post-concussion studies to be impaired in concussed patients (Cifu et al., 2015; Heitger et al., 2009, 2006; Hoffer et al., 2017).

We compared athletes from an NCAA Football Bowl Subdivision team to both athlete and non-athlete control groups. A pattern in the research design of much of the existing literature is the use of either a single athlete control group from non-contact sports or a single control group drawn from the general student body. Using a non-athlete control group only does not take into account any effects on the brain of years of athletic training and competition. Another pattern within the literature is the lack of matching of either athlete or non-athlete control groups on socioeconomic (SES) status, despite the fact that SES status is known to be related to cognitive abilities (Ursache et al., 2015) and health (Meyer et al., 2014). Depending on the study setting, the socioeconomic backgrounds of even athlete control group participants may be significantly different from that of the concussion prone sport athletes. We therefore included both a non-contact sport control group (drawn from the cross country team) and a non-athlete group matched to the football players on age, gender and SES.

If repetitive sub-concussive impacts have a deleterious effect on neural processing, collegiate football players should show performance decrements on the smooth pursuit task and differences in brain activation when compared to both control groups. At the present time there is insufficient literature to attempt to predict which regions of the network implicated in oculomotor processing (i.e., cerebellum, parietal cortex, or frontal regions) might be affected, but greater activation within the smooth pursuit network, along with possible recruitment of additional regions to handle the increased processing load, would be suggestive of an effect of subconcussion.

2. Methods

2.1. Participants

A total of 51 male subjects participated in the study. Of these 21 were 4th and 5th year undergraduates (many were red-shirts) who were