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Joshua Ricker
Wright State University Lake Campus, rjoshua@bgsu.edu

Kylee Smith
Bowling Green State University, kyleesmtih@utexas.edu

Alexandra Schmidt
Bowling Green State University, ars0056@mix.wvu.edu

Andrea Cripps
Bowling Green State University, acripps@bgsu.edu

Palguna Thalla
The University of Toledo, palguna.thalla@utoledo.edu

See next page for additional authors

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Concussion-related Alterations in Neural Activity During Emotion Recognition: Case Studies of Short-term and Residual Effects

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Concussion-Related Alterations in Neural Activity During Emotion Recognition: Case Studies of Short-Term and Residual Effects

Joshua Ricker, PhD*; Kylee Smith€; Alexandra Schmidt€; Andrea Cripps, PhD, ATC€; Palguna Thalia#; Howard C. Cromwell, PhD€; Xin Wang, MD, PhD#
*Wright State University Lake Campus; € Bowling Green State University; #The University of Toledo

Purpose: Concussions have recently become an area of concern among the general public, but a clear understanding of their total consequence is still being developed. Symptoms of concussions are wide-ranging, encapsulating a plethora of cognitive and emotional abilities that could be affected. Concussions transiently disrupt neural activation as well as behavioral responses across multiple categories. Skills pertaining to various aspects of emotions are often affected yet have rarely been studied after concussions. **Methods:** We present two case studies of collegiate athletes with a history of multiple concussions. This paper highlights the case of a collegiate athlete who had obtained two previous concussions with the most recent being sustained sixteen days prior to neuroimaging. A second athlete with two lifetime concussions was tested one year after the most recent injury. The current study utilized a novel emotional recognition task to assess the behavioral and neural effects of this injury. **Results:** A group of five controls responded with high accuracy rates and quick response times to the task. They showed activation in regions of the frontal lobe as well as facial recognition areas of the occipital lobe. The 16-day case subject was impaired in recognizing emotions relative to controls and showed little to no overlap in brain activity for regions involved in emotional face processing. The athlete with a longer post-concussion period also showed residual effects of neural activity alteration when compared to controls with few overlapping active regions. Specific brain regions were activated in this group but not in controls including the sensorimotor cortex, supramarginal gyrus, and lateral occipital cortex. **Conclusion:** By taking a more individual approach in examination of neural activity post-concussion, we may be able to gain a better understanding of this heterogeneous injury. ***Keywords:*** *affective states, case study, emotion recognition, functional magnetic resonance imaging, neuroplasticity, traumatic brain injury*

INTRODUCTION

Sport-related concussions have become a topic of great concern over the last decade with the United States seeing approximately 300,000 concussions occurring per year at the lowest estimates.[1] A better understanding of this injury has led to an increase in the estimate to 1.6 – 3.8 million.[2] This substantial increase has been related to detection of underreporting,[3] progress on developing a clear definition of concussion,[4] and increased usage of objective measures that can be used to diagnose whether or not a person has sustained a concussion.[5]

One aspect complicating the ability to diagnose concussions or track recovery is the absence of any structural damage associated with the injury. Functional disruptions are the only objectively measurable effects observed in the brain that result from concussions.[6] With these injuries being functional as opposed to structural in nature, a great deal of research has been dedicated to using functional brain imaging techniques such as positron emission tomography (PET) or functional magnetic resonance imaging (fMRI) to gain a better understanding of the underlying neurological changes that occur as a result of sustaining a concussion.[7,8] Currently, research has shown contrasting results of altered patterns of neural activation resulting from concussions.[9,10] Some studies have revealed that there is a task-specific decrease in neural activation after one has been sustained,[9] while others have shown task-related hyperactivation.[10,11] Multiple

factors could be responsible for the lack of clarity existing in the current literature.

The amount of time that has elapsed between time of injury until testing could be playing a role in the conflicting results often found in the literature.[12] Many of the symptoms of concussions tend to subside within the first few weeks following the injury.[13] A problem arises when much of the research focuses on those who sustained their injury months before being tested in an experiment.[14] The range of recovery time between subjects within the same study can reach months.[9] This would mean that conclusions are being drawn after equating those who may be in the acute phase of concussion to those who have had nearly a year to recover. It then becomes much more difficult to determine areas of potential neural recruitment in response to injury, as subjects between groups may perform similarly on tasks and report comparable symptoms while exhibiting different activation of brain regions.[15] The vast range of findings in the current fMRI literature demonstrates a clear need for further investigation into the effects concussions have on neural activity in both the acute and prolonged recovery period. [16,17]

Concussions affect a wide range of behavioral skills. Emotional regulation is one realm that has been very much neglected yet is likely to be impacted by the injury. Various aspects of emotional processing are affected when one is concussed, and these changes can be seen years after the injury has occurred.[18] The Emotional Face Assessment Task (EFAT) is a novel task that can be used to measure the ability to recognize emotions.[19] This task requires subjects to match the emotion being displayed by two test stimuli to that of a target stimulus. When applied to brain imaging studies, this condition is compared to a motor control condition where subjects are instructed to match the orientation of test shapes to a target shape. This comparison allows for any brain activation that may occur from motor activity during response selection or visual perception to be controlled for. This procedure has been shown to be a reliable measure of emotion recognition through multiple studies assessing its reliability and validity.[20] Within and between-subjects studies across multiple sites have shown robust and reliable activation in regions involved in emotion recognition.[20] Similar emotion recognition tasks have been shown to consistently elicit activation in these regions across multiple populations.[21,22] In regards to the current study, the EFAT has also been shown to illustrate differences in event-related activation when comparing healthy populations to those where emotion recognition has been shown to be disrupted.[23]

The amygdala is the brain region most commonly associated with the processing of stimuli depicting negative affect such as fear or anger.[24] Limited research using this specific task has shown activation in the amygdala[19] while regions of the frontal lobe are also active during various emotional tasks.[25] The profile of activation to stimuli of positive affect such as a face depicting happiness is less clear. Research has shown instances of increased amygdala activation to happy faces[26] with decreased amygdala activation in others.[27] The recognition of happiness may involve a complex interplay between the amygdala and nuclei of the basal ganglia, as it is possible that this group of nuclei is assigning rewarding value to viewing a positive stimulus.[28] Deactivation in comparison to resting state has also been shown in a group of nuclei referred to as the default mode network (DMN).[29] Structures in this network show a relative decrease in activation from resting state when engaged in emotional processing.[30] How concussions may impact activation or deactivation in these systems during the emotion recognition process is yet to be determined.

Concussions have a wide range of effects[31], which makes them a very difficult injury to treat on a general basis. This injury lacks an objective measure that can be used to

diagnose whether or not a person has sustained a concussion leaving clinical testing and self-reporting as the current "gold standard".[32] An examination of emotional impairments and neural biomarkers of emotional processing could be a part of the move in implementing more complete, objective measures or features in clinical work and sports medicine. Current work data mining for neurological signs and symptoms has used many, diverse features to identify factors and develop novel approaches to improve prediction and diagnosis of concussions.[33] Potentially more work that reveals novel features (e.g., emotional impairments) to incorporate into these types of analyses will enable even greater accuracy when diagnosing and treating the heterogeneous impairment of concussion.

The aims of the current pilot study were to clarify how sustaining a concussion may affect neural activation involved in emotion processing and performance a novel emotion recognition test. In general, the impact of concussions on emotional processing has been very much neglected. An impairment in emotional processing following concussions can lead to mood disorders and problems with social functioning.[18] These impairments could interact with other psychological or behavioral symptoms leading to slower, more debilitative recovery post-concussion. We provide a case study of a collegiate athlete who had sustained a concussion sixteen days prior to being tested on the EFAT in an fMRI scanner, henceforth referred to as the short-term effects case (STE). A second athlete was tested who had received a concussion one year prior to testing, and was used as a comparison for residual effects. This subject will be referred to as the residual effects case (RE). Performance and activation were compared to a group of five healthy control athletes who had reported having no history of concussion. Decrements in performance on the EFAT or neural activation alterations for either concussion cases were interpreted as being a short-term result of the injury. Given the results presented in the literature,[34,9] we expected to find no significant differences in task performance between the cases and the control group; however, we did expect to find short-term effects in the neural response to the EFAT with the STE individual showing few areas of overlap with the controls. By further investigating and comparing cases such as these, we can obtain a better understanding for the effects of concussions and how to treat them.

METHODS

All participants were right-handed males 18 to 23 years of age, and were members of the university hockey or football teams. The control group consisted of five right-handed males. Participants were only excluded if there were any instances of self-reported history of drug use, mental illness, or if they had a pacemaker as this would not be safe in the scanner. All participants provided informed consent before taking part in the study. All procedures were approved by the University of Toledo Medical Center IRB according to protocol 201703 and the Bowling Green State University IRB according to protocol 929059-11.

Cases

STE was a twenty-three-year-old collegiate hockey player who had sustained a concussion sixteen days prior to testing, which was confirmed by a team doctor. STE had sustained one prior concussion at the age of twelve, which was reported to be confirmed by a family doctor. RE was a nineteen-year-old collegiate hockey player with a past medical history of two concussions. The most recent concussion occurred one year prior to testing and had been diagnosed by a team doctor. The first concussion was self-reported and was sustained at the age of twelve. Both athletes reported having no history of mental illness or substance use (see Table 1).

	RE	STE
Age at time of study	19 years	23 years
Age at time of first concussion	12 years	12 years
Age at time of second concussion	18 years	23 years
Time elapsed between most recent concussion and testing	1 year	16 days
Sport of participation	Hockey	Hockey
PCS Score	2	6

Table 1. Profile of Concussed Individuals

Instrumentation and Procedure

Concussion history of each participant was assessed using the Ohio State University Traumatic Brain Injury Identification Form (OSU-TBI-ID). Participants completed emotion processing tasks by viewing a computer screen while in the scanner by looking through an MRI specialized set of goggles (NordicNeuroLab). Responses were recorded on a five-button fiberoptic response system (Psychology Software Tools, Inc). The response system was always placed under the right hand of the participant. All computerized tests were programmed using E Prime 2.0 software (PST, Inc., Pittsburgh, PA).

A modified version of the Rivermead Post-Concussion Symptom questionnaire (Appendix 1). was used to obtain a Post Concussion Symptom (PCS) score for all participants. This questionnaire assesses symptoms occurring over the last month that may pertain to the participant's injury. The questionnaire consisted of twenty-two questions that range from zero, indicating the athlete did not consider the symptom a problem, to ten, indicating the athlete believed the symptom to be a major problem. Results can fall into one of three categories of scores : 0 – 6 (no post-concussion symptoms), 6 – 21 (low symptoms), and 22 – 84 (moderate / high symptoms).[35]

Emotional Face Assessment Task

The EFAT is a novel task that is used to assess one's ability to recognize emotional expressions being displayed by various faces. The reliability of this task has been shown to be robust through previous research.[20] Concussions have been shown to have a range of effects on numerous emotional processes; however, to the best of our knowledge, the effects on emotional recognition are yet to be studied.[18] The EFAT consisted of presenting participants with a target face located centrally above two probe faces against a black background changing at a rate of every three seconds (Figure 1). Participants were instructed to choose which probe face depicted the same emotion as the target face by pressing with their index finger for the face located on the left or with their middle finger for the face located on the right. Emotions were presented in blocks of six at a time and the faces displayed anger, fear, or happiness. These emotions were chosen as there is some existing literature that can provide a basis for comparison.[19] A sensorimotor control condition was presented between each block and consisted of matching the orientation of white ovals that were positioned similarly as the faces and required the same response. Participants performed two runs of 96 trials.

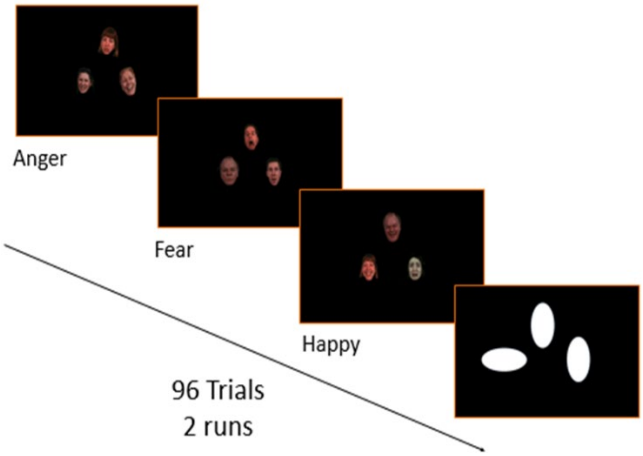


Figure 1. Visual Schematic of the EFAT

fMRI Imaging

fMRI images were obtained in a 3.0 tesla General Electric Signa HDx MRI scanner. A 3D Volume Inversion Recovery Fast Spoiled Gradient Recall Echo protocol was used to receive high resolution structural MRI images. A $T2^*$ -weighted, Echo Planar Imaging pulse sequence with a repetition time of 2000 milliseconds was used to obtain functional images. Data was processed in FSL (version 5.2.0, FMRIB, Oxford, UK). Whole brain family-

wise error rate correction set a voxel threshold of $z > 2.3$ ($p < .01$) and a cluster significance threshold of $p < .05$. Contrasts of parameter estimates were taken by including a 4 millimeter sphere from the voxel of peak activation in each cluster. Contrasts for the EFAT

included total activation to each emotion relative to their baseline activity. Only activation during correct responses was analyzed. We also performed a baseline-emotion contrast to examine a relative decrease in activation to each portion of the task. All images presented are of radiology scans, therefore, right and left are reversed.

Behavioral Data

All behavioral data is compared to five healthy control subjects. We report accuracy as the percent of correct responses across all trials. Only correct responses were included in the calculation of reaction times (RT), which was calculated as the amount of time between the presentation of the slide containing faces until the response button was pressed. Since no statistical test can detect significant differences between a case and group, 95% confidence intervals were calculated for the control group to determine if scores of each case fell within this range. Behavioral data were analyzed using IBM SPSS Statistics 24 (Armonk, NY).

RESULTS

PCS Score

RE and STE scored a 6 and 2 on the PCS, respectively, which falls into the range category of no symptoms. Given these results, no further action was taken in assessment of the scores.

Behavioral Performance

A one-way ANOVA revealed that there were significant differences in labeling accuracy of emotions among the control participants ($F(2,8) = 7.27$, $p = .016$) (Figure 2). Pairwise comparisons found that controls labeled anger ($M = 77.50\%$, $SEM = 4.44$) less accurately than both fear ($M = 97.50\%$, $SEM = 1.53$) ($t(4) = -.436$, $p = .012$) and happiness ($M = 86.67\%$, $SEM = 6.64$) ($t(4) = -2.93$, $p = .043$). STE and RE both exhibited similar behavior by performing less accurately on the anger trials. The performance of STE (64.58%) and RE (64.58%) fell just below the confidence interval range of controls for anger trials (65.17% - 89.83%). The same was true for STE (85.42%) and RE (87.50%) for fear trials (93.25 – 101.75). Both STE (95.83%) and RE (91.67%) fell within the 95% confidence intervals for the control group (68.23% - 105.10%) for happiness trials. These results suggest that both cases were unable to perform as well as the control group on trials depicting emotions related to negative affect such as fear and anger, yet they performed similarly during happiness trials.

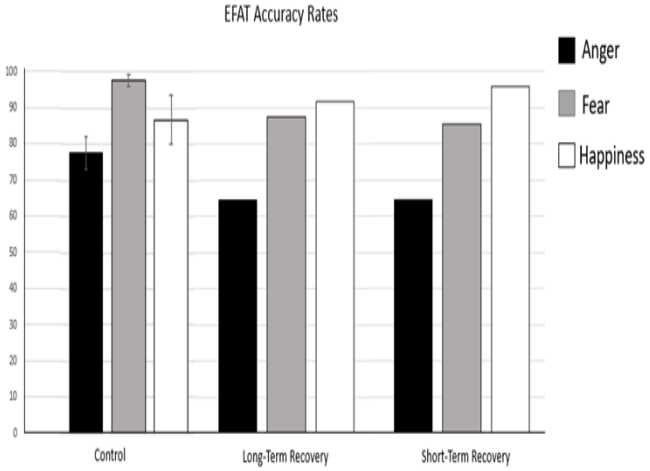


Figure 2. EFAT Behavioral Results

Neural activation during the EFAT

Anger

Specific details of regions of activation are given in Appendices 1 through 3. During performance of anger trials, controls demonstrated greater activation compared to baseline in the right occipital fusiform gyrus (OFG), the inferior frontal gyrus pars opercularis bilaterally (IFG), and the right medial prefrontal cortex (mPFC) (Appendix 3). Controls also showed a relative decrease in activation from baseline in the right intracalcarine cortex for anger trials. STE failed to show any significant activation during the anger trials, while exhibiting a

decrease in the left IFG, right thalamus, left middle frontal gyrus (MFG), right lingual gyrus, and the right OFG (Appendix 3). RE showed activation in the right OFG, the right sensorimotor cortex, and the right lateral occipital cortex (LOC). RE only showed a relative decrease in the right subcallosal cortex to anger (Appendix 4). Anger trial activation can be seen in Figure 3.

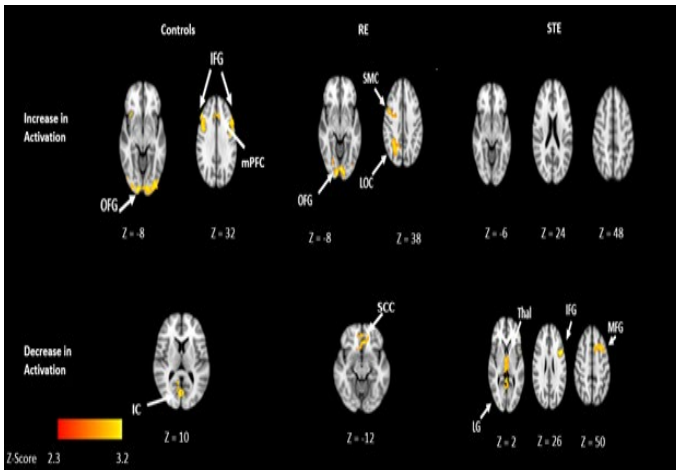


Figure 3. Imaging Results for Anger Trials

Fear

fMRI f analysis of fear trials revealed activation bilaterally in the OFG, the right paracingulate, and the left IFG for control subjects. A relative decrease was seen in the right intracalcarine cortex (Appendix 2). As with anger, STE showed no increase in activation during fear trials, but there was a relative decrease in activation in the right intracalcarine cortex, and the left superior frontal gyrus (Appendix 3). RE had significant activation in the right lateral occipital cortex, the right sensorimotor cortex, the right supramarginal gyrus, and the left frontal pole, and a relative decrease in activation in the left orbitofrontal cortex (OFC) during fear trials (Appendix 4). Activation associated with fear trials is shown in Figure 4.

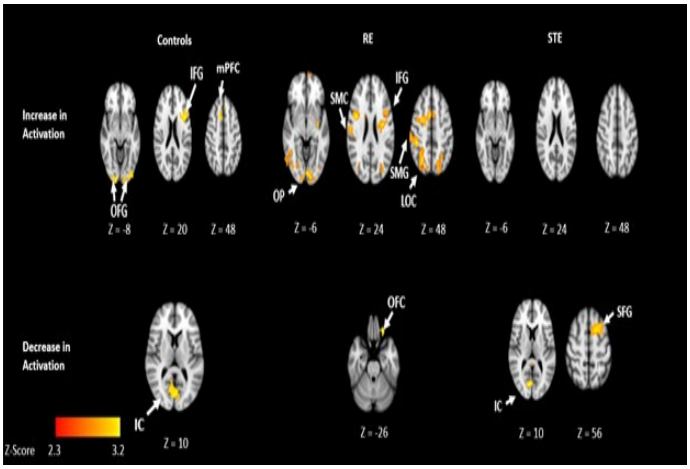
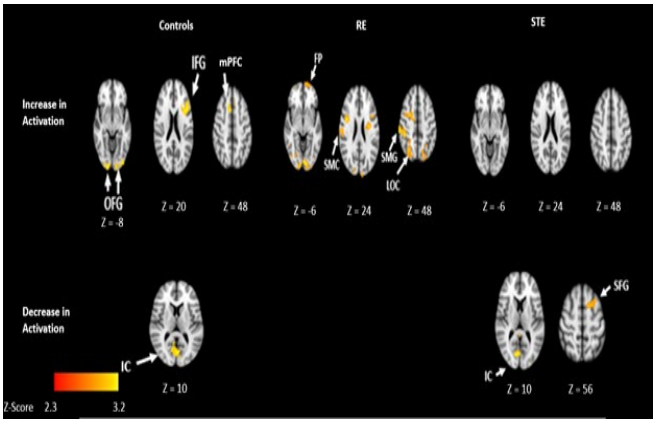


Figure 4. Imaging Results for Fear Trials

Happiness

Controls showed a similar profile of activation to happy trials as was shown in fear trials, with activation in the occipital fusiform gyrus bilaterally, the right mPFC, and the left IFG. The control group once again only showed a relative decrease in activation in the right intracalcarine cortex (Appendix 2). Again, STE showed no increase in activation to the trials requiring assessment of happiness. STE showed the same decrease as in fear trials, with a decrease in activation in the right intracalcarine cortex and the left superior frontal gyrus (Appendix 3). RE showed an increase in activation in the right occipital pole, the right lateral occipital cortex, the right sensorimotor cortex, the left frontal pole, and the supramarginal gyrus bilaterally. A relative decrease in activation was displayed in the left OFC (Appendix 4). Activation related to happiness trials is shown in Figure 5.



DISCUSSION

Concussions can lead to an altered neural profile based on how much time an athlete has had to recover at the time of testing.[9] Sustaining a concussion sixteen days prior to testing resulted in our STE case demonstrating a neural activation profile that differed from that of the control subjects who had never sustained a concussion, while also leading to an underperformance in the negative emotion recognition. The sixteen-day recovery period resulted in short-term effects that were qualitatively different than the residual effects exhibited by the RE who was tested one year after the most recent injury. Number of concussions probably did not play a primary role in the differences found for STE and RE as both athletes had sustained two concussions in their lifetime. We argue that a better understanding of these activation profiles could, on an individual level, lead to the development effective treatments for those suffering from the effects of concussion in the near future.

Neural Effects

We used the EFAT to determine how the brain may be affected by concussions during emotion expression recognition (Table 2). Each region that showed an increase in activation in the fMRI has previously been implicated in either emotional tasks or face recognition tasks. The IFG and mPFC are often active during the processing and evaluation of emotional stimuli that requires the generation of an outward emotional response, while the activation shown by the OFG can be explained by the region's role in processing facial stimuli.[36,37] The simultaneous activation of these regions may signify their essential role in the EFAT as the main task is to identify and assess facial displays of emotion. The additional activation of the right sensorimotor cortex and the right LOC for the RE during anger and the frontal pole and supramarginal gyrus for fear and happy trials falls in line with what has previously been shown with compensatory mechanisms engaging in the brain to allow for better task performance.[9] Similar compensation may not have been possible for the STE given the sixteen-day timeframe since being injured.

The STE showed a drastic difference from the controls with no areas of significant activation found after analysis. In contrast, the STE had many areas that showed a relative decrease in activation during the EFAT which was dissimilar to controls. A decrease in activation was seen in the right OFG, right thalamus, left MFG, left IFG, and right lingual gyrus during the anger trials. The intracalcarine cortex and superior frontal gyrus showed this decrease in the fear and happiness trials. These patterns of deactivation are consistent with those that are often found during emotion processing in the default mode network (DMN: see below).[38,39] The STE was able to perform as well as controls on certain elements of the task while showing this extreme difference in neural activity. We believe the short recovery period of sixteen days provides a window of time where the cognitive recovery has preceded the neural recovery.[9] Providing a longer recovery period, possibly on the timescale of months,[9] for the STE would potentially lead to results more similar to that of the RE, and normalization to that of the controls with extended time.

We also analyzed a relative decrease in activation from baseline corresponding to each emotion. Control subjects only had a relative decrease in the right intracalcarine cortex, which is a part of the DMN.[40] Brain regions of the DMN show a decrease in neural activity in response certain tasks.[29] While a complete understanding of the DMN is still underway, some have suggested that it may play a role in emotional processing,[41] which fits in line with the performance of the controls in our study.

	Happy		**Anger**		**Fear**	
Activation	Increased	Decreased	Increased	Decreased	Increased	Decreased
RE	R. Occipital Pole R. LOC R. SMC L. Frontal Pole R. SG L. CWM L. SG	L. Frontal Orbital Cortex	R. OFG R. LOC R. SMC L. CWM	R. Subcallosal Cortex	R. SMC R. LOC L. IFG R. SMG L. Frontal Pole	L. Frontal Orbital Cortex
STE	N/A	R. Intracalcarine Cortex L. SFG	N/A	L. IFG R. Thalamus L. MFG R. Lingual Gyrus R. OFG	N/A	R. Intracalcarine Cortex L. SFG
Controls	R. OFG L. OFG L. IFG R. Paracingulate Gyrus	R. Intracalcarine Cortex	R. OFC L. IFG Pars Opercularis R. IFG Pars Opercularis	R. Intracalcarine Cortex	R. OFG L. OFG L. IFG R. Paracingulate Gyrus	R. Intracalcarine Cortex

Table 2. Comparisons of Increased and Decreased Activation

Abbreviations for regions listed in Table 2: OC = Occipital Cortex, SMC = Sensorimotor Cortex, SG = Supramarginal Gyrus, OFG = Occipital Fusiform Gyrus, IFG = Inferior Frontal Gyrus, CWM = Cerebral White Matter, MFG = Middle Frontal Gyrus, SFG = Superior Frontal Gyrus, OFC = Orbitofrontal Cortex

The RE showed an additional relative decrease in activity in the subcallosal cortex during anger trials, which meshes with other DMN findings.[42] There was also a decrease in the OFC which is a curious result as it has been year passing since the athlete's most recent concussion.

Behavioral Effects

There is currently an astounding lack of research investigating the effects of concussions on emotional processing. Due to this, we wanted to determine if a history of concussion would affect one's ability to accurately recognize emotions being depicted by others. Disturbances in emotional recognition only occurred with in trials where the target faces were displaying the negative emotions of anger or fear with STE falling outside of the range of the controls. STE performed at similar levels as controls in trials where the target face depicted happiness. RE displayed a similar performance on the EFAT. This falls in line with results such as those reported by Léveillé and colleagues[18] where asymptomatic males who had been concussed over a year prior to testing exhibited difficulty in recognizing negative emotions.

known to be active during tasks of emotional processing and decision-making.[43] While there were clear discrepancies in activation, some overlap remained. This again is most likely due to almost a

Our findings support the fact that the degree of impairment can vary between the behavioral and neural findings. Other work has also found severe neural alterations without similar behavioral deficits.[11] As time progresses and athletes have the opportunity to recover, activity can return to a similar level of activity found in healthy control subjects.[9] It is believed that this is a way for the brain to employ compensatory mechanisms in order

to alleviate performance decrements that could potentially be caused by concussions. Further research is needed to determine any pattern that may be associated with how these regions are recruited.

Multiple concussions can lead to deficits in emotion recognition years after the last concussion was experienced.[18] Our results are consistent with previous findings that behavioral performance of those with a history of multiple concussions matches that of healthy control subjects while neurophysiological differences exist.[44] The disruption of neural activity may be reflective of the short-term emotional dysregulation often experienced by athletes after sustaining a concussion.[45]

Future Directions

The current study can be built upon for multiple areas of future research. The case studies provide examples of how we can use precision medicine for future treatment of this injury, and N-of-1 trials such as these are the basis for this growing field of research.[46,47] The precision medicine approach involves collecting information, such as medical or injury status, from a specific individual to help create a more detailed method of treating an injury.[48] This information is analyzed and applied with hopes of reducing side effects and the application of ineffective treatments.[49] The precision medicine approach seems to have the potential to be more beneficial in studying diseases or injuries where symptomology is inconsistent between those who share a diagnosis.[46] With concussions being heterogenous in nature, using individual behavioral and neural profiles could make for a more successful outcome for the individual, as well as providing more information for how these individual differences may arise from such injuries.

While the EFAT was not intended to be used to diagnose concussions, we used it to measure differences that could occur based on one's history of concussion. We believe it may be beneficial to include a different approach when examining concussions, one similar to precision medicine approaches. Precision medicine aims to provide a more specific picture of individual diseases or injuries that share an overlapping diagnosis yet contain a range of symptoms or severity.[48] Developing a method of measuring responses to this task and being able to correlate it to a general neural profile could be an important step in developing a more thorough version of precision medicine treatment methods. Several research teams have begun exploring this individualized approach for diagnosing/treating concussions.[50,51] These newer models utilize both intrinsic and extrinsic factors to develop individualized assessment and management and make physical rehabilitation more effective.[52] Our findings support the broadening of the factors involved in these network analyses to include emotional processing of information. Most approaches also include the timing of the injury and duration of symptoms. Our results suggest that acutely there may be a shared, general symptomology which includes altered abilities to use emotion information, and that alterations could persist but become more individualized as chronic residual effects that can last several months to years post-concussion. More research is clearly needed in order to better understand how concussions lead to these diverse forms of acute and chronic differences in neural functioning and to develop more effective methods to predict, diagnose and treat concussions.

Limitations and Conclusion

This was a pilot study with a small control group used for a comparison. Further research is needed using a larger sample of controls as well as more short-term concussed subjects for replication. Future studies using a population of female athletes would add crucial information in determining neural profiles as well. The sex of the athlete may influence the ability to accurately determine emotional expression,[18] with

females showing better emotion recognition after concussion. Female athletes have also shown a decrease in reaction time and report more symptoms associated with concussion.[53]

Clinical diagnosis of concussions has proven to be difficult due to the wide range of symptoms associated with the injury. Symptoms can fall under the categories of cognitive, physical, and neurobehavioral.[54] Most cognitive symptoms, such as attention and memory deficits, have been shown to be alleviated after approximately two weeks of recovery;[13] however, psychological symptoms may linger.[34] Previous work has shown that the severity of symptoms can be linked to abnormal activation patterns of task-related activity in the brain.[9] No athletes in the current study reported significant scores on a Post-Concussion Symptom Questionnaire. While this questionnaire aided in determining symptoms the athletes may have had at the time, it did rely on self-reporting of symptoms from athletes that were currently in mid-season. This leaves the accuracy of the reports as a fair topic of concern. Also, while using imaging provides a more objective measurement, the RE and STE were only imaged post-injury. It would be helpful to include baseline scores for a stronger comparison.

Disclosure of Interest

The authors report no conflict of interest.

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Appendix 1. Post-Concussion Symptom Questionnaire

Participant ID _____

Post-concussion Symptoms in the past month

The following questions ask about any problems you may have had with other symptoms in the past month. Please select the response that best describes how much of a problem you have had in the past month with the following symptoms, where zero means no problem and 10 means a major problem.

	NO PROBLEM										**MAJOR PROBLEM**
1. Headaches	0	1	2	3	4	5	6	7	8	9	10
2. Dizziness	0	1	2	3	4	5	6	7	8	9	10
3. Nausea	0	1	2	3	4	5	6	7	8	9	10
4. Noise Sensitivity	0	1	2	3	4	5	6	7	8	9	10
5. Light Sensitivity	0	1	2	3	4	5	6	7	8	9	10
6. Concentration Difficulty	0	1	2	3	4	5	6	7	8	9	10
7. Fatigue	0	1	2	3	4	5	6	7	8	9	10
8. Taking longer to think	0	1	2	3	4	5	6	7	8	9	10
9. Blurred Vision	0	1	2	3	4	5	6	7	8	9	10
10. Double Vision	0	1	2	3	4	5	6	7	8	9	10
11. Restlessness	0	1	2	3	4	5	6	7	8	9	10
12. Upset Stomach	0	1	2	3	4	5	6	7	8	9	10
13. Persistent Fatigue	0	1	2	3	4	5	6	7	8	9	10
14. Sensitive or tender skin	0	1	2	3	4	5	6	7	8	9	10
15. Ringing in ears	0	1	2	3	4	5	6	7	8	9	10
16. Itchy eyes or skin	0	1	2	3	4	5	6	7	8	9	10
17. Racing heart	0	1	2	3	4	5	6	7	8	9	10
18. Insomnia or difficulty sleeping	0	1	2	3	4	5	6	7	8	9	10
19. Hands trembling or Shaking	0	1	2	3	4	5	6	7	8	9	10
20. Feeling faint	0	1	2	3	4	5	6	7	8	9	10
21. Abdominal pain	0	1	2	3	4	5	6	7	8	9	10
22. Constipation and/or diarrhea	0	1	2	3	4	5	6	7	8	9	10

Appendix 2. Details of Activation for Controls During the EFAT

		location	Number of voxels	P- value	Peak Voxel X	Peak Voxel Y	Peak Voxel Z
Anger	Increased Activation	R. Orbitofrontal Gyrus	4,970	$9.75e^{-15}$	40	-58	-28
		L. Inferior Frontal Gyrus Pars Opercularis	1,532	$4.77e^{-06}$	-46	14	24
		R. mPFC	1,227	$4.81e^{-05}$	10	20	48
		R. Inferior Frontal Gyrus Pars Opercularis	1,064	.000179	44	24	20
	Decreased Activation	R. Intracalcarine Cortex	627	.00891	6	-76	8
Fear	Increased Activation	L. Occipital Fusiform Gyrus	1,863	$1.94e^{-08}$	-38	-68	-24
		R. Occipital Fusiform Gyrus	1,766	$5.96e^{-08}$	40	-58	-28
		R. mPFC	581	.00377	8	12	48
		L. Inferior Frontal Gyrus	432	.0239	-44	14	22
	Decreased Activation	R. Intracalcarine Cortex	975	$5.26e^{-05}$	6	-76	8
Happy	Increased Activation	R. Occipital Fusiform Gyrus	1,382	$6.56e^{-06}$	30	-82	26
		L. Occipital Fusiform Gyrus	1,348	8.64e-06	-38	-68	-24
		L. Inferior Frontal Gyrus	806	.000975	-44	14	22
		R. MPFCGyrus	458	.036	8	12	48
	Decreased Activation	R. Intracalcarine Cortex	772	.00135	6	-76	6

Appendix 3. Details of Activation for the RE During the EFAT

		location	Number of voxels	P- value	Peak Voxel X	Peak Voxel Y	Peak Voxel Z
Anger	Increased Activation	R. Occipital Fusiform Gyrus	3,127	$9.71e^{-11}$	12	-88	-14
		R. Sensorimotor Cortex	1,505	$4.41e^{-06}$	42	4	28
		R. Lateral Occipital Cortex	1,084	.000125	26	-66	66
		L. Cerebral White Matter	984	.000295	-26	-4	18
	Decreased Activation	R. Subcallosal Cortex	920	.000518	2	28	-8
Fear	Increased Activation	R. Lateral Occipital Cortex	9,004	$2.00e^{-24}$	26	-66	66
		R. Sensorimotor Cortex	2,446	2,446	46	4	30
		L. Inferior Frontal Gyrus	1,380	1,380	-48	10	-22
		R. Supramarginal Gyrus	1,163	1,163	44	-38	50
		L. Frontal Pole	509	509	-12	64	-22
	Decreased Activation	L. Frontal Orbital Cortex	632	.00499	-22	34	-26
Happy	Increased Activation	R. Occipital Pole	4,752	9.38e-15	14	-90	-14
		R. Lateral Occipital Cortex	1,658	$1.19e^{-06}$	26	-66	66
		R. Sensorimotor Cortex	1,396	$8.88e^{-06}$	42	4	28
		L. Frontal Pole	1,137	$7.21e^{-05}$	-20	62	-12
		R. Supramarginal Gyrus	1,050	.000151	60	-30	48
		L. Supramarginal Gyrus	606	.00955	-34	-44	38
	Decreased Activation	L. Frontal Orbital Cortex	480	.0363	-24	34	-26

Appendix 4. Details of Activation for the STE During the EFAT

		Location	Number of voxels	P- value	Peak Voxel X	Peak Voxel Y	Peak Voxel Z
Anger	Increased Activation	N/A					
	Decreased Activation	L. Inferior Frontal Gyrus	458	.00341	-46	12	26
		R. Thalamus	448	.004	2	-8	0
		L. Middle Frontal Gyrus	413	.00704	-28	12	52
		R. Lingual Gyrus	399	.00887	6	-60	-2
		R. Occipital Fusiform Gyrus	306	.0437	38	-76	-38
Fear	Increased Activation	N/A					
	Decreased Activation	R. Intracalcarine Cortex	795	.00267	12	-78	6
		L. Superior Frontal Gyrus	777	.00313	-20	8	56
Happy	Increased Activation	N/A					
	Decreased Activation	R. Intracalcarine Cortex	700	.000322	12	-78	6
		L. Superior Frontal Gyrus	396	.0201	-20	14	50