### Title

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# Brain amygdala volume increases in veterans and active-duty military personnel with combat-related Post-traumatic Stress Disorder and mild Traumatic Brain Injury

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## Abstract

**Objective:** To identify amygdalar volumetric differences associated with PTSD in individuals with co-morbid mTBI compared to those with mTBI only. Also to examine the effects of intracranial volume (ICV) on amygdala volumetric measures.

**Setting:** Marine Corps Base and VA Healthcare System

**Participants:** A cohort of veterans and active-duty military personnel with combat-related mTBI (n= 89).

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The authors declare no conflicts of interest.

**Design:** 29 participants were identified with co-morbid PTSD and mTBI. The remaining 60 formed the mTBI-only control group. Structural images of brains were obtained with a 1.5T MRI scanner using a T1-weighted 3D-IR-FSPGR pulse sequence. Automatic segmentation was performed in Freesurfer.

**Main Measures:** Amygdala volumes with/without normalizations to ICV.

**Results:** Co-morbid mTBI and PTSD group had significantly larger amygdala volumes, when normalized to ICV, compared to mTBI-only group. The right and left amygdala volumes after normalization to ICV were 0.122 ± 0.012% and 0.118 ± 0.011% respectively in the co-morbid group, compared to 0.115 ± 0.012% and 0.112 ± 0.009% in the mTBI-only group (corrected p-value <0.05).

**Conclusions:** The ICV normalization analysis performed here may resolve previous literature discrepancies. This is an intriguing structural finding, given the role of the amygdala in the challenging neuro-emotive symptoms witnessed in casualties of combat-related mTBI and PTSD.

### Keywords

Amygdala; Brain Concussion; Brain Injuries; Traumatic; Neuroanatomy; Magnetic Resonance Imaging; Stress Disorders; Post-Traumatic

## Introduction:

Combat-related post-traumatic stress disorder (PTSD) and mild traumatic brain injury (mTBI) are leading healthcare concerns in veterans and military personnel, and often co-occur in the same individual, based on evidence from cross-sectional[1–7] and prospective studies[8–10] However, the neural mechanisms of PTSD, mTBI, and particularly the co-morbidity of PTSD and mTBI have not been fully understood. In recent conflicts, the use of improvised explosive devices (IED) has increased the prevalence of mTBI in today's service members.[1] Injury rates, resulting in loss of consciousness or altered mental status, have been reported at around 15% by Operation Enduring Freedom and Operation Iraqi Freedom (OEF/OIF) service members. Among Marine and Navy personnel who served in OIF, TBI was found in the majority who were wounded in action by IED.[11]

The co-occurrence of PTSD in OEF/OIF service members with mTBI has been reported at rates of 33% - 66% in various studies.[12] This PTSD comorbidity in service members with mTBI negatively affects psychosocial outcomes, neuropsychological performance and functional capacity.[13–15] Moreover, the conditions share some similar symptoms, including depression, sleep disturbances, and cognitive and neuropsychiatric impairments, the mechanisms of which are not yet fully understood.[9,15]

There is great interest in improving combat-related PTSD detection and assessment, and identifying the biological risk factors and explanatory mechanisms involved in its development. Part of this effort includes the use of neuroanatomical magnetic resonance imaging (MRI). MRI's millimeter resolution and grey/white matter contrast, along with advancements in automated segmentation programs such as Freesurfer, have made identification and comparison of brain structural volumes quite accessible and comparable to

manual segmentation, which is currently considered the gold standard.[16] Neuroanatomic MRI investigations of PTSD have focused on brain regions thought to be involved in fear memory and extinction, including the amygdala, anterior cingulate cortex (ACC) and hippocampus.[17]

Several volumetric studies have employed methodologies to control for confounding non-pathological and inter-personal variables such as age, gender, and head size. One such method is to normalize the regional brain volumes by the individual's intracranial volume (ICV) in order to remove or reduce the confound due to different head sizes.[18] The ICV is the volume within the cranium and includes the brain, cerebrospinal fluid, and meninges.[19] This method takes into account the non-pathological differences in individuals, unrelated to the neurological disorders. The normalization to ICV also accounts for the voxel size variation.[20]

Unfortunately, the number of neuroimaging studies of combat-related co-morbid mTBI and PTSD are sparse [9,21,22]. In the case of amygdala volume and PTSD, several volumetric imaging analyses have presented seemingly contradictory findings.[23–26] A 2006 meta-analysis reviewed 11 studies involving various PTSD etiologies, such as combat, intimate partner violence, and childhood maltreatment, among others.[26] This meta-analysis showed that PTSD groups had significantly smaller left amygdala volumes compared to both trauma-exposed and healthy groups, but the meta-analysis is limited to a small number of studies and diverse articles including pediatric populations. A more recent meta-analysis of 44 articles by O'Doherty et al., (2015) concludes that PTSD is associated with volume reductions in the bilateral amygdala, hippocampus and ACC of PTSD subjects compared to healthy controls.[25] In this 2015 meta-analysis, there was variability of the amygdala volume response. A medium effect size reduction was found in bilateral amygdala volume when compared with findings in healthy controls. But no difference in volume was found between PTSD subjects and trauma-exposed controls. The meta-analysis is limited by comparing studies with heterogeneous study designs, imaging techniques, and variable statistical analysis involving left versus right versus bilateral combined data. One study in the meta-analysis was written by Morey et al., who found decreased amygdala volumes in individuals with PTSD compared to health controls.[23] This was not seen when the PTSD individuals were compared to other trauma-exposed controls. Another study in the meta-analysis provides a contrasting result. Kuo et al. found that combat-exposed veterans with PTSD had increased amygdala volumes when compared to their counterparts without PTSD.[24] A factor differentiating the Morey et al. and Kuo et al. studies is the influence of intracranial volume ICV. Kuo et al., but not Morey et al., normalized amygdala volume to total ICV in the effort to control for head size issues.

Previously, studies considered mTBI as a confounding factor, and it was assumed that mTBI may even be a protective factor against PTSD.[27] A case control study of OEF/OIF veterans showed that the amygdala volume was decreased in the co-morbid group compared to the controls and that the decrease in volume was associated with increased impulsivity.[28] However, the study had a small sample size, with a total of only 37 participants, and the control group consisted of healthy individuals without combat exposure.

Two theories may explain the above findings, but do not explain the discrepancy of the results. One theory proposes that fear conditioning produces increased arborization and dendritic hypertrophy in the amygdala, and this leads to larger amygdala volumes.[29] The other theory states that a smaller amygdala may predispose trauma victims to PTSD via increased fear conditioning and stress reactivity.[30] Both theories may be at play simultaneously, complicating the association of amygdala volumes with PTSD.

In summary, the above studies show that mTBI may substantially influence PTSD, but there have been few structural neuroimaging studies in PTSD that have carefully controlled the mTBI factor, especially not in active-duty service members or Veterans with combat-related experiences. It has been reliably shown that mTBI substantially increases the likelihood of PTSD development.[8–10] However, previous studies of PTSD and brain volumes have excluded subjects with mTBI, due to potential confounding. For example, blast-related mTBI has been associated with brain architecture alterations, such as decreased cortical thickness and decreased thalamus and amygdala volume compared to healthy controls.[31] Recently, research has advanced the understanding of the neural mechanisms and structural connectivity in mTBI and PTSD subjects. Lopez et al. analyzed 39 veterans through diffusion tensor imaging and found that compared to the mTBI group, the mTBI and PTSD group had a significantly larger right entorhinal cortex and decreased white matter integrity in the right cingulum bundle.[32] A pre-clinical study showed rats exposed to percussion injury and fear conditioning exercises had general enhancement of fear expression to both conditioned or novel stimuli.[33] The brain histopathology was examined and showed no evidence of abnormalities. However, the protein analysis revealed increased uptake of excitatory NMDA (N-methyl-D-aspartate) receptors in the basolateral amygdala complex.

We chose to study combat-related co-morbid PTSD and mTBI due to their frequent co-occurrence, and used a combat-related control mTBI group to limit possible confounding effects of mTBI. The objective of this study was to identify volumetric differences in amygdala associated with partial or full PTSD in active-duty military members or veterans with co-morbid PTSD/mTBI as compared to individuals with mTBI only. A related goal of the present study was to examine the effect of ICV normalization on the amygdala volumetric measures. In addition to amygdala, the volumetric measures of caudate, hippocampus, and ACC were also examined, owing to findings of anatomic imaging or functional imaging differences in these regions from prior studies (see references cited in [17]).

## Material and Methods:

The study protocol was approved by institutional review boards of the VA San Diego Healthcare System and Naval Health Research Center at San Diego. All participants gave written informed consent prior to study procedures. The informed consent followed the ethical guidelines of the Declarations of Helsinki (sixth revision, 2008).

### Research Subjects

Table 1 lists the demographic information of the study participants. This retrospective study involves a cohort of veterans and active-duty military personnel with combat-related mTBI.

All participants (n=89) were either active-duty military service members or outpatient OEF/OIF veterans recruited from a Marine Corps Base or a VA Healthcare System under separate VA Merit and DoD grants listed in the Acknowledgement. Participants were then divided into two groups after screening for PTSD: mTBI only (n= 60, age 29.1 ± 5.4, all males) and co-morbid mTBI and PTSD (n= 29, age 31.5 ± 6.4, 28 males). The post-injury period information is also listed in Table 1. All participants were seen in the chronic phase, except 1 participant in each group who were seen during the second month after injury. Because this was a study with retrospective data analysis, participants were not selected for the presence of PTSD, and the ratio of mTBI-only versus co-morbid mTBI and PTSD reflects the characteristics of the sample.

### Inclusion/exclusion criteria

All participants had combat-related mTBI that was diagnosed and classified based on standard VA/DOD diagnostic criteria with inclusion requiring: 1) Loss of consciousness less than 30 min or transient confusion, disorientation or impaired consciousness immediately after trauma, 2) Post-traumatic amnesia (PTA) less than 24 hours; and 3) Initial Glasgow Coma Scale between 13 and 15.[34] Mechanisms of injury were varied and included blast exposure, direct trauma, and motor vehicle accidents.

Exclusion criteria for this study were: 1) Any other neurological, developmental or psychiatric disorder (e.g. brain tumor, stroke, epilepsy, Alzheimer's, schizophrenia, bipolar, learning disability, abnormal lesions in structural MRI; 2) Substance/alcohol abuse within the last 6 months as defined by DSM-IV; 3) History of metabolic or other disorder known to affect the central nervous system. The inclusion/exclusion criteria were verified by self-report during a mental health examination (see below) and medical records.

### PTSD Assessment

PTSD was diagnosed prior to recruitment in the study. The PTSD diagnosis was made by a licensed psychiatrist and verified by medical records. As this is a study with retrospective analysis, data on PTSD symptoms and severity were derived from questionnaires included in study batteries, either the Clinical Administered PTSD Scale (CAPS) or the PTSD Checklist (PCL) according to the Diagnostic and Statistical Manual of Mental Disorders IV-TR for participants that were given those evaluations.[35,36] The reason for using different PTSD diagnostic criterion (i.e., CAPS versus PCL) was because the participants from different studies (see Acknowledgement) were pooled together for this analysis. In a subset of participants, the CAPS was not available. Thus, in these participants, the PCL was used instead. For those who did not have CAPS or PCL we relied on the previous confirmed diagnosis by a licensed psychiatrist. The percentages were 54% and 10% for the PTSD participants diagnosed with CAPS and PCL, respectively. The remaining 36% of participants who lacked a CAPS or PCL were diagnosed with combat-related PTSD by a treating, licensed psychiatrist based on a comprehensive clinical interview. Study participants with a co-occurring diagnosis of combat-related PTSD were analyzed together to maintain statistical power and to examine broad group differences in PTSD neurocircuitry. All other participants, who had no PTSD diagnosis, became the mTBI-only group. After screening, a

total of 29 participants were in the co-morbid mTBI and PTSD group, while there were 60 in the mTBI-only group.

Participants who completed the CAPS met the criteria for PTSD if they reported at least one re-experiencing symptom, three avoidance symptoms, and two hyperarousal symptoms.[37] Symptoms must have occurred at least once within the past month (frequency ≥ 1) and have caused a moderate amount of distress (intensity ≥ 2). Participants who completed the PCL questionnaire and had a minimum total score of 50 met the criteria for PTSD.[1,36,38,39]

### Imaging Techniques

Structural images of the subjects' brains were obtained with a General Electric 1.5T Excite MRI scanner using a T1-weighted 3D-IR-FSPGR pulse sequence and a resolution of 0.94 × 0.94 × 1.2 $mm^3$. These structural images were originally collected as part of magnetoencephalography (MEG) functional imaging studies for superimposing the functional data. Other conventional MRI sequences typical for identifying structural lesions were also performed: 1) GRE T2*-weighted; 2) Axial FLAIR; and 3) Axial T2-weighted ASSET. The imaging protocol for the MRI was 1 hour including setup and arrangement in the scanner. These MRIs were carefully reviewed by a board-certified neuro-radiologist to determine if the participant had visible lesions on MRI. No subjects in the present study showed lesions visible in MRI.

Automatic segmentation was performed in Freesurfer (version 3.0.3 http://surfer.nmr.mgh.harvard.edu) using the library tool recon-all. Briefly, the T1 weighted images were stripped of non-brain tissue, transformed into Talairach space and segmented into regions of subcortical white matter, deep gray matter (including amygdala), and ICV volumetric structures. One confounding factor that may affect the regional volumes is the head size which can be characterized by the ICV. In the present study, to examine the effect of ICV (or head size) on the volumetric measures, amygdala volumes were also divided by total ICV to correct for subject variation in head size and create normalized amygdala volumes. (Figure 1).

### Statistical Analysis

Statistical analysis was done with Matlab software (The MathWorks, Inc., version 8.2). Group differences in age, education and regional brain volumes were compared using the Student's t-test (two-tailed) with a p-value of $< 0.05$ considered significant. Levene's test for homogeneity of variances between groups was used to determine whether similar variances were assumed in the Student's t-tests. Pearson's correlation coefficients were calculated within groups and in all subjects together for significant correlations between regional brain volumes and age or education. Because of the number of volume comparisons, the statistical false discovery rate (FDR) was controlled using a Benjamani and Hochberg/Yekutieli function and the reported scores are corrected for multiple comparisions.[40]

## Results:

Participant demographic information is reported in table 1. All participants were right-handed and either active-duty military service members or military veterans. All participants

were male except for one in the co-morbid PTSD/mTBI group. There were no significant differences between combat-related mTBI-only and co-morbid mTBI/PTSD groups based on age, gender, or years of education.

Automated segmentation of regional brain volumes revealed an increased left and right amygdala volume in the co-morbid mTBI/PTSD group compared to the mTBI-only when normalized to ICV (see Figure 2 and Table 2). In the mTBI-only group, the right amygdala volume, normalized to ICV, was 0.115 ± 0.012 % of the ICV and the left amygdala was 0.112 ± 0.009 % (mean ± SD). The co-morbid mTBI/PTSD group had a mean amygdala volume of 0.122 ± 0.012 % in the right and 0.118 ± 0.011 % in the left after normalizing to ICV.

The co-morbid mTBI/PTSD group was associated with 6% larger amygdala volumes (both left and right) when normalized to ICV as compared to mTBI-only participants. The group differences were statistically significant for both the right ($t = 2.73$, $df = 87$, FDR corrected $p < 0.05$) and left amygdala ($t = 2.61$, $df = 87$, FDR corrected p-value $< 0.05$). Non-normalized amygdala volumes showed no significant difference between groups.

Compared to the mTBI-only group, the overall ICV was significantly smaller in the comorbid mTBI/PTSD group with a mean difference of 0.032% ($t = 2.25$, FDR corrected p-value $< 0.05$). There was a significant correlation between ICV and age with a correlation coefficient of $r = -0.28$ ($df = 87$, p-value = 0.027) when all subjects from both groups (mTBI-only and co-morbid mTBI/PTSD) were pooled together. However, when comparing the mTBI-only group to the comorbid mTBI/PTSD group, there was no significant difference in age between the groups. There were no significant group differences in the correlation of ICV versus age (i.e., the ICV did not decrease faster or slower with age in the comorbid mTBI/PTSD group than the mTBI-only group) when analyzing the two groups separately.

The cerebral cortex volume was also measured and normalized to ICV. The results showed that all of the participants had decreased cortex volume with age. Correlation coefficients for age and the right and left cerebral cortex volumes were $r = -0.53$ and $r = -0.51$ respectively ($df = 87$, p-value $<0.001$). After ICV normalization, the left and right cerebral cortex showed correlation coefficients of $r = -0.42$ and $r = -0.46$ respectively with age ($df = 87$, p-value $<0.001$).

In addition to amygdala values, we also examined other brain regions including caudate, hippocampus, and ACC, but did not find significant group differences in these regions, whether normalized by ICV or not (see ICV normalized values in Table 2). No statistical group differences were found for the volumes of cerebral cortex or other brain regions. Also, we reran the analysis without the female participant in the co-morbid mTBI/PTSD group, and all levels of statistical significances stayed the same.

## Discussion:

This study has shown that combat-exposed individuals with co-morbid mTBI and PTSD have significantly larger normalized amygdala volumes compared to those with mTBI only.

Overall, amygdala volumes in the co-morbid mTBI and PTSD group were 6% larger when normalized to ICV calculated through automated segmentation of brain volumes. It is also noted that the right amygdala was larger than the left in our sample. Combat-related PTSD and mTBI have been studied with neuroanatomical imaging to identify the effects of stress and trauma on gross pathology and to find possible risk factors or explanatory mechanisms for the symptom development related to PTSD and mTBI. There were some unique features in the present study of co-morbid mTBI/PTSD in veterans and active-duty military personnel: 1) we used a combat-deployed mTBI-only comparison group, and 2) we measured both voxel and surface-based morphometry.

Our main finding of larger amygdala volume, when normalized to ICV, in the comorbid PTSD and mTBI group compared to the mTBI-only group is consistent with the finding by Kuo and colleagues.[24] However, our finding is in conflict with the study by Morey and colleagues that showed decreased amygdala volumes associated with PTSD.[23] It is interesting that normalization to ICV was used in both our study and the one by Kuo and colleagues, but not in the study by Morey and colleagues. ICV normalization is a common practice that limits the confounding by subject's body habitus. This may explain the discrepancy in findings.

Our findings are also consistent with a large number of previous studies in animal models (see reviews by Cacciaglia and colleagues)[41] that showed a persistent amygdala hypertropy was associated with prolonged multiple traumatic stresses,[42–44] single stress,[45] or corticosterone administration leading to corticosterone-mediated amygdala growth.[46] The molecular mechanisms through which stress enlarges amygdala volume are not yet fully understood.[41] Previous studies suggested that a prominent role by a glucocorticoid-driven expression of brain-derived neurotrophic factor,[47] along with other neurochemical modulators such as endocannabinoids[48] that act under epigenetic control.[49]

The present study, which provides data normalized to overall brain volume, is also supportive of the neuroplasticity theory: Fear conditioning produces larger amygdalae through arborization and dendritic hypertrophy.[30] However, the present study does not claim causality. The association seen here could alternatively mean that individuals with pre-morbidly larger amygdala volumes are predisposed to PTSD. In either of these two scenarios, the imaging technique described in this study could be useful. In the first case, imaging could track psychological exposure histories and monitor amygdala volume or track the effects of treatment interventions. In the alternative scenario, imaging could be used to screen individuals at risk for PTSD symptoms. Further research is required to investigate and validate these differing hypotheses.

It has been established that the amygdala plays a central role in control of fear and aversion of unpleasant stimuli whether it is trauma-related or generic stimuli.[50,51] In functional PTSD neuroimaging studies monitoring altered neural activity, fMRI and PET scans show that the most hyperactive regions are the anterior cingulate cortex and bilateral amygdala in PTSD subjects exposed to such stimuli.[52] Biological changes are also evident in the hormonal and neuroregulatory factors. The hyperactivity of the sympathetic system in PTSD results in increased release of norepinephrine which is thought to potentiate memory consolidation.

[53,54] TBI may increase the risk for developing and maintaining PTSD symptoms as it affects the neural circuits that regulate fear conditioning.[21]

In the present study, we found a significant negative correlation between ICV and age when all subjects from both groups (mTBI-only and comorbid mTBI/PTSD) were pooled together. When comparing the mTBI-only group to the comorbid mTBI/PTSD group, there was no significant difference in age between the groups. There also were no significant group differences in the correlation of ICV with age (i.e., the ICV did not decrease faster with age in the comorbid mTBI/PTSD group than the mTBI-only group) when analyzing the two groups separately. This means that the smaller ICV in the comorbid mTBI/PTSD group over the mTBI-only group is unlikely to be age-related. In a recent study with healthy controls in the same age range, a negative correlation between age and ICV was also found.[55] Yet, it is generally found that the effect of age on ICV tends to be small over the years,[56,57] so it is likely that our findings are related to our narrow age range and that with more participants, this correlation might not hold.

There are several future implications for PTSD and co-morbid TBI research. New and existing imaging tools are being constantly updated and enhanced. Saygin et al. labeled ex-vivo MRI data for the nine amygdala nuclei and developed an atlas that is publicly available through Freesurfer software.[58] Further understanding of the amygdala's role in mTBI/PTSD can be evaluated through functional examinations using magnetoencephalography MRI (MEG-MRI) to study the electrical network activity of the brain.[59,60] Imaging technologies can be used in conjunction with other developing innovations such as biomarkers and genetic studies to further our understanding of mTBI and co-morbid PTSD as a help in diagnosis, monitoring, and treatment.[61]

The current study was conducted in a combat-related mTBI population. Our findings suggest that the enlargement of amygdala volume may be a characteristic of combat-related PTSD. It remains to be seen how applicable this is to a civilian population or to sports related concussions. mTBI, whether from military or athletic trauma, can have devastating consequences and both etiologies are associated with post-concussion syndrome, PTSD, and chronic traumatic encephalopathy.[62,63] These syndromes are characterized by a range of shared mood (e.g. anxiety, fearfulness, apathy, hopelessness, irritability, flatness of affect, insomnia), cognitive (e.g. problems with concentration, impaired memory) and behavioral (e.g. aggression, rage, disinhibited behavior, impulsivity, social isolation) features.[64] The pathological and clinical features overlap, and suggest that post-concussion syndrome, PTSD, and chronic traumatic encephalopathy do share biological underpinnings[65] as such, a collective biological marker across these mechanisms of mTBI could result in a unified approach to interventions.

We attempted to limit confounders by normalizing volumes to ICV in our analysis, a method not performed in some previous studies. However, there are several other limitations to this study. The study primarily focuses on male participants who were involved in combat, and while we speculate that the finding may hold for female participants, those studies need to be done. With the increasing number of women serving in combat roles, future research could systematically explore the effects of female comorbid mTBI/PTSD. Secondly, we did

not have a group of normal subjects without PTSD or mTBI who had *matching combat experience* for comparison, we plan to address this limitation in future studies. Lastly, in a subset of participants, structured diagnostic measurement (i.e. CAPS and PCL) was not available. A portion (36%) of the participants were diagnosed with PTSD by a licensed psychiatrist using a comprehensive clinical interview. This poses a limitation in evaluating and quantitating current ongoing PTSD symptoms, but was likely sufficient for group assignment into mTBI/PTSD and TBI only groups. In future studies we plan to collect CAPS scores on all participants to have quantitative data to perform a correlational analysis between CAPS total and sub-scale scores and amygdala volume. Future studies will also be needed to examine amygdala volume in relationships with lifetime trauma, duration of PTSD, level of combat exposure, duration of combat exposure, depression symptoms, anxiety symptoms, and medication. Due to the retrospective nature of the study, these variables were not consistently collected across all participants.

## Conclusions:

The results show that the amygdalae in the combat-related co-morbid mTBI/PTSD group are significantly larger compared to combat-related mTBI-only subjects. The method of normalizing to intracranial volume may explain previous discrepancies of amygdala comparisons in the literature. This is an intriguing structural finding, given the role of the amygdala in the challenging neuro-emotive symptoms witnessed in casualties of mTBI and PTSD. Further investigation is needed to determine whether amygdala size could be used to screen individuals at risk for PTSD, or whether it could be used to monitor efficacy of interventions.

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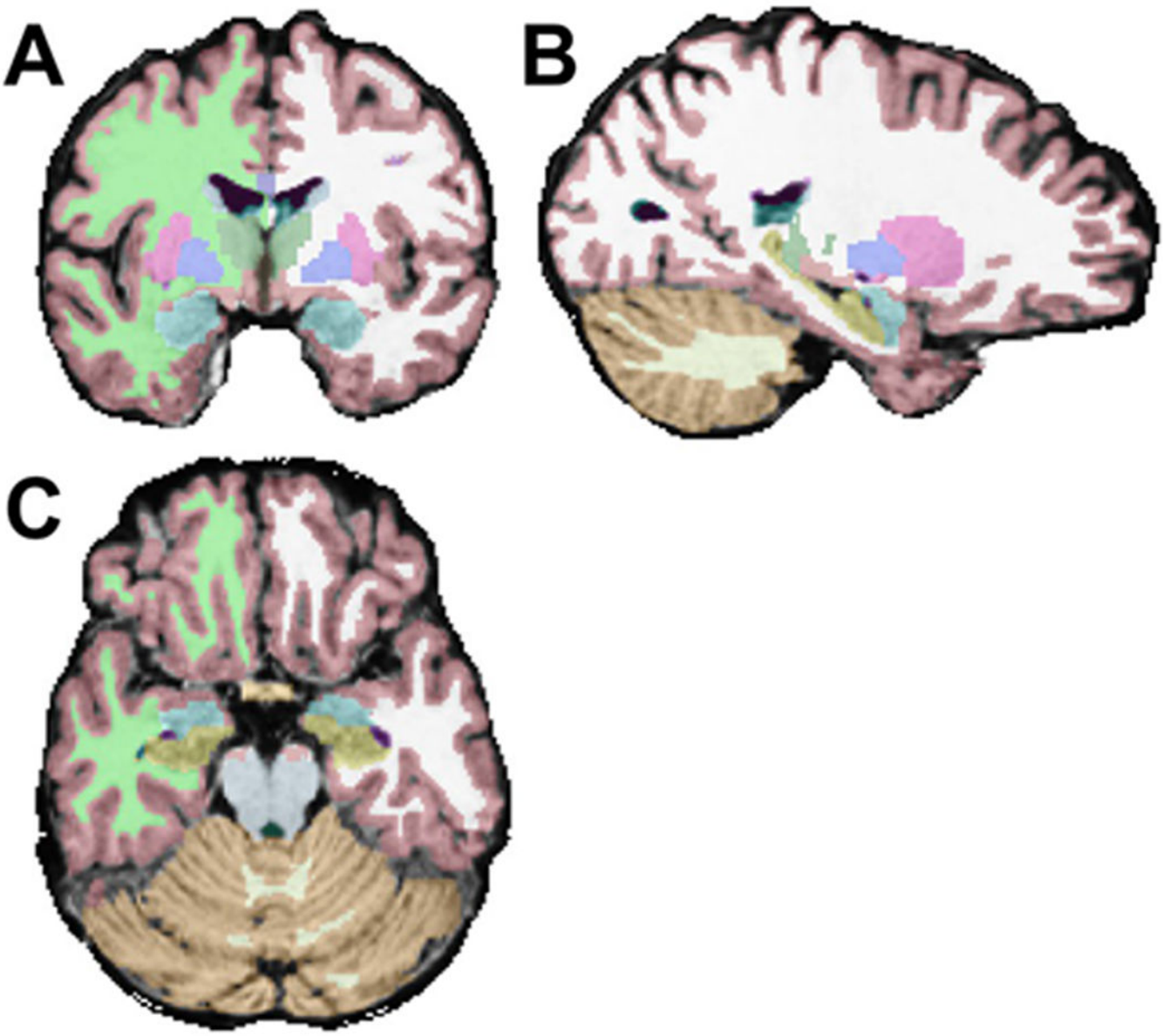


**Figure 1.**

A) Coronal B) sagittal and C) axial sections showing automated segmentation of subcortical structures using Freesurfer software. The amygdala is shown in light teal .

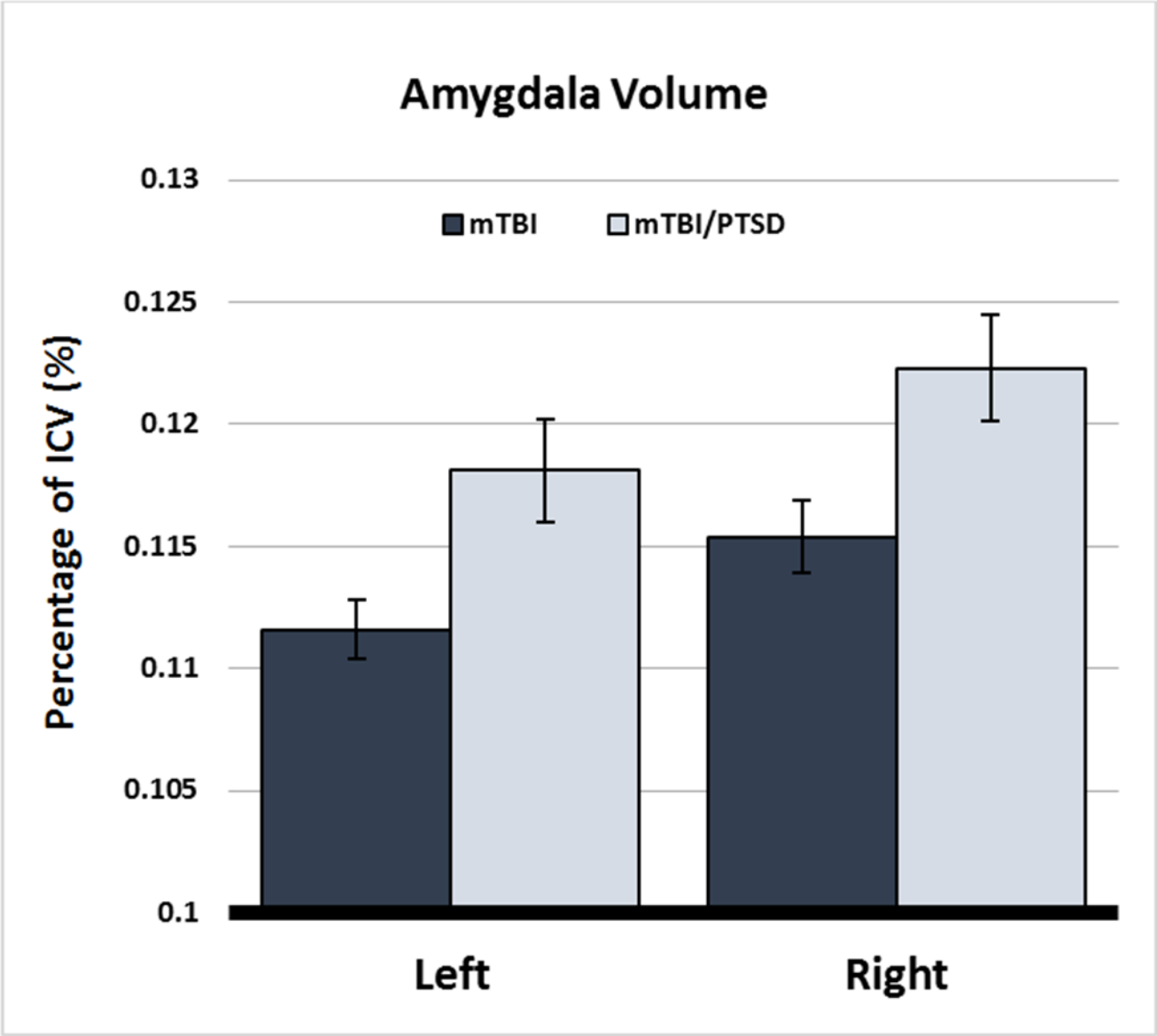


**Figure 2.**

Co-morbid mTBI/PTSD group had significantly larger amygdala volumes when normalized to ICV. The statistical false discovery rate (FDR) corrected p-value is < 0.05 in the co-morbid mTBI/PTSD compared to mTBI-only group.

**Table 1.**

Subject demographics of the clinical groups. The mTBI-only and co-morbid mTBI/PTSD groups show no significant difference in any demographic characteristic or handedness.

| Characteristic | mTBI (n=60) | Co-morbid mTBI/PTSD (n=29) |
|---|---|---|
| Age (SEM) | 29.1 (0.7) | 32 (1) |
| Years Education (SEM) | 12.9 (0.2) | 13.2 (0.3) |
| Race (% White) | 73.3% | 75.9% |
| Gender (% Male) | 100% | 96.6% |
| Handedness (% Right) | 100% | 100% |
| Post-injury period (Days) | 2425.8 ± 2705.9 | 1937.2 ± 1785.2 |

**Table 2.**

ICV-normalized volume for different brain regions in the mTBI-only and co-morbid mTBI/PTSD groups.

| Brain Regions | ICV normalized volume (%) in mTBI (n=60) | ICV normalized volume (%) in Co-morbid mTBI/PTSD (n=29) | t-value | p-value |
|---|---|---|---|---|
| L Caudate | 0.231 ± 0.027 | 0.238 ± 0.027 | −1.12 | 0.26 |
| L Hippocampus | 0.271 ± 0.022 | 0.279 ± 0.028 | −1.48 | 0.14 |
| L Amygdala | 0.112 ± 0.009 | 0.118 ± 0.011 | −2.73 | 0.01** |
| L ACC | 0.152 ± 0.021 | 0.144 ± 0.019 | 1.82 | 0.07 |
| R Caudate | 0.231 ± 0.027 | 0.242 ± 0.030 | −1.64 | 0.11 |
| R Hippocampus | 0.286 ± 0.022 | 0.296 ± 0.026 | −1.79 | 0.08 |
| R Amygdala | 0.115 ± 0.012 | 0.122 ± 0.012 | −2.61 | 0.01** |
| R ACC | 0.146 ± 0.021 | 0.143 ± 0.023 | 0.50 | 0.62 |

** indicates significant statistical differences.