



US DEPARTMENT OF DEFENSE

BLAST INJURY RESEARCH PROGRAM COORDINATING OFFICE

Injury to Sensory Systems

Olfactory Deficiency: A Marker of Traumatic Brain Injury (TBI) in US Service Members

This study is funded by the Defense Medical Research and Development Program (DMRDP) managed by the Congressionally Directed Medical Research Program (CDMRP) and conducted by investigators at the Walter Reed National Military Medical Center (WRNMMC). The objective of this study is to determine whether a structured and quantitative assessment of differential olfactory performance—recognized between a blast-injured TBI group and a demographically comparable blast-injured control group—can serve as a reliable antecedent marker for preclinical detection of intracranial neurotrauma. We prospectively and consecutively enrolled 231 polytrauma inpatients, acutely injured from explosions during combat operations in either Afghanistan or Iraq and requiring immediate stateside evacuation and sequential admission to WRNMMC, a tertiary care medical center over a two and a half year period (Figure 1). This study correlates olfactometric scores with both contemporaneous neuroimaging findings as well as the clinical diagnosis of TBI, tabulates population-specific incidence data, and investigates return of olfactory function.¹ The study team found that the olfactometric score predicted abnormal neuroimaging significantly better than chance alone. Normosmia was present in all Service Members with mild TBI (mTBI) (e.g., concussion) and all control subjects (Figure 2). Service Members with radiographic evidence of frontal lobe injuries were three times more likely to have olfactory impairment than Service Members with injuries to other brain regions (relative risk 3.0, 95 percent Confidence Interval (CI) 0.98–9.14). Normalization of scores occurred in all anosmic Service Members available for follow-up testing. The conclusion is that quantitative identification olfactometry has limited sensitivity but high specificity as a marker for detecting acute structural neuropathology from trauma. When considering whether to order advanced neuroimaging, a functional disturbance with central olfactory impairment should be regarded as an important tool to inform the decision process. The clinical trial within the military cohort has produced important clinical and scientific information, which is being used to support a Phase 2 trial in an analogous civilian cohort. The research team is developing a Class II medical device with US Food and Drug Administration (FDA) oversight that will be tested in a civilian trauma cohort through a clinical trial in partnership with the University of California, San Francisco. This test could serve as a field/prehospital screening for TBI in US Troops.

¹ Xydakis, M. S., Mulligan, L. P., Smith, A. B., Olsen, C. H., Lyon, D. M., & Belluscio, L. (2015). Olfactory impairment and traumatic brain injury in blast-injured combat troops: a cohort study. *Neurology*, 84(15), 1559–1567. <https://doi.org/10.1212/WNL.0000000000001475>





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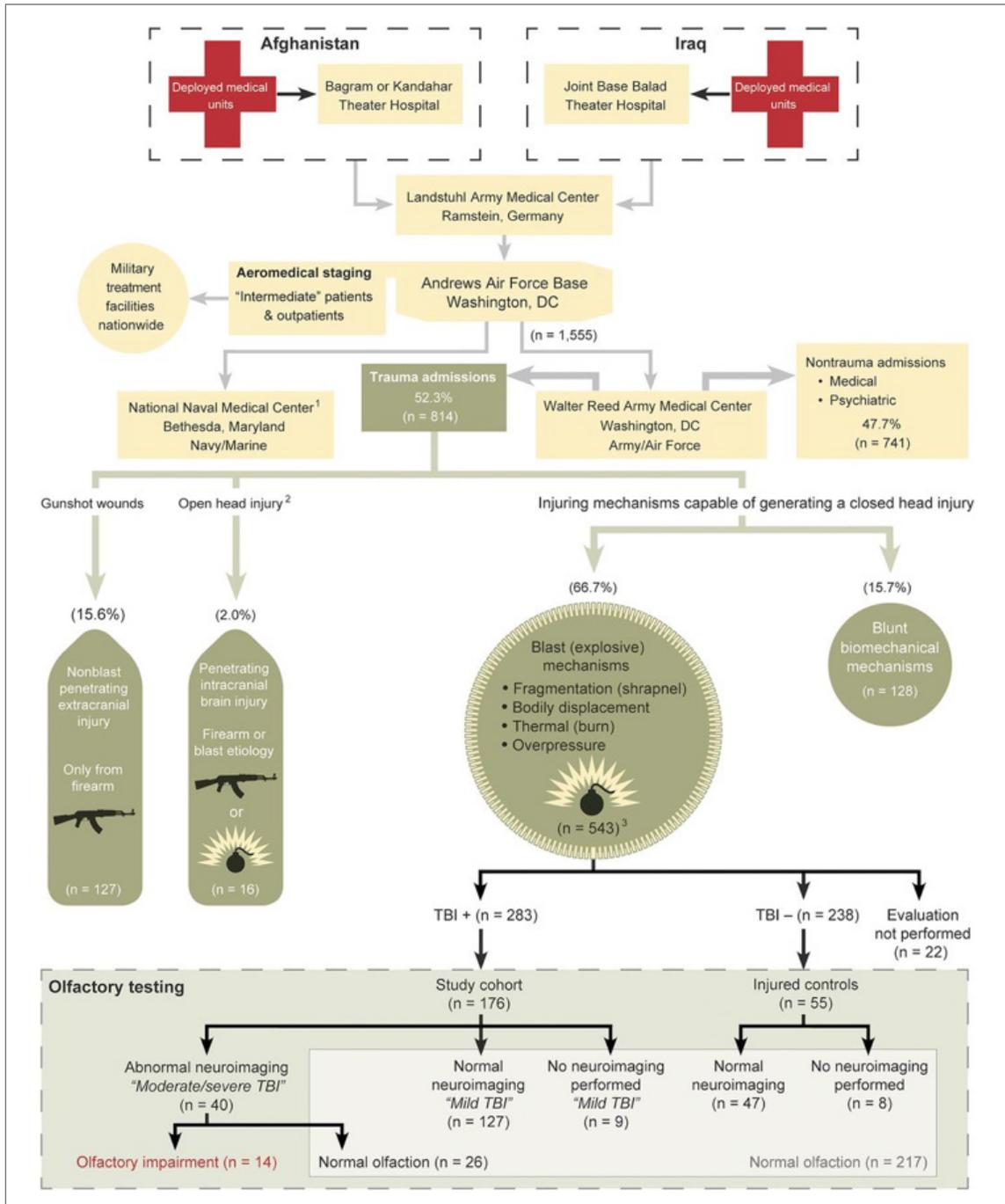


FIGURE 1: Combat Casualty Care Pathway: Interhospital transfer of inpatients from Afghanistan and Iraq to Walter Reed Army Medical Center US Air Force Transportation Regulating Command and Control Evacuation System aircrew mission manifests provided longitudinal tracking of all patient movements from the combat zones to our hospital.





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Location of brain injury	Normal olfactory function (n = 26)	Olfactory impairment (n = 14)	p value
Frontal	11 (42.3%)	11 (78.6%)	0.046
Parietal	11 (42.3%)	5 (35.7%)	0.746
Temporal	5 (19.2%)	6 (42.9%)	0.147
Occipital	2 (7.7%)	2 (14.3%)	0.602
Multifocal	6 (23.1%)	6 (42.9%)	0.281
Frontal OR temporal	13 (50.0%)	12 (85.7%)	0.040
Frontal AND temporal	3 (11.5%)	5 (35.7%)	0.102

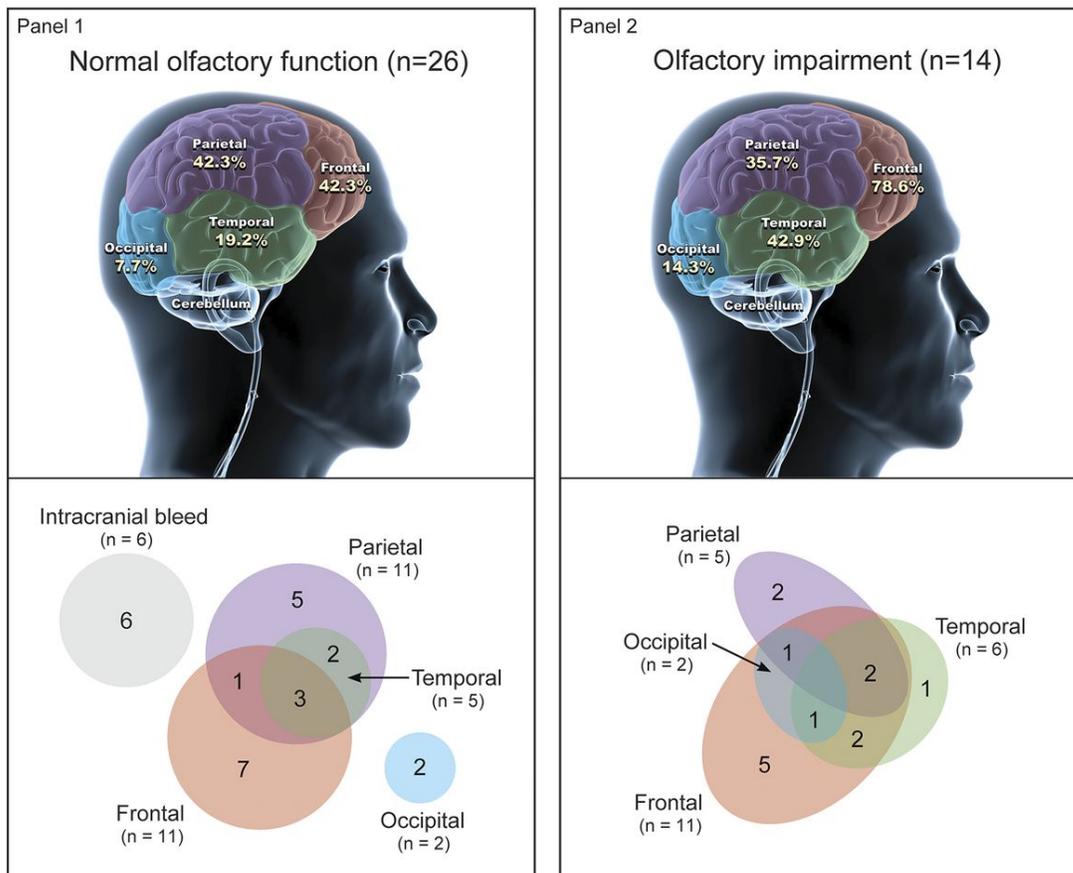


FIGURE 2: Troops with abnormal neuroimaging: Location of injury and its association with olfactory performance and multifocality (n = 40) For specific brain regions, data do not sum to 100% because more than one region could be affected.

