

# Grapheme-Color Synesthesia and Posttraumatic Stress Disorder: Preliminary Results From the Veterans Health Study

STUART N. HOFFMAN, DO, XIAOPENG ZHANG, MD, PhD, PORAT M. ERLICH, PhD, MPH, AND JOSEPH A. BOSCARINO, PhD, MPH

**Objective:** Posttraumatic stress disorder (PTSD) is associated with altered neuropsychological function, possibly including complex visual information processing. Grapheme-color synesthesia refers to the phenomenon that a particular letter or number elicits the visual perception of a specific color. The study objective was to assess if grapheme-color synesthesia was associated with PTSD among US veterans. **Method:** We surveyed 700 veterans who were outpatients in a multihospital system in Pennsylvania. All veterans had served at least one warzone deployment. PTSD and grapheme-color synesthesia were assessed using validated research instruments. **Results:** The mean age of veterans was 59 years, and 96% were men. The prevalence of current PTSD was 7% (95% confidence interval [CI] = 5.1–8.8), and current partial PTSD was 11% (95% CI = 9.3–14.0). The prevalence of current depression was 6% (95% CI = 4.7–8.3). Altogether, 6% (95% CI = 4.8–8.5) of veterans screened positive for grapheme-color synesthesia. Bivariate analyses suggested that grapheme-color synesthesia was associated with current PTSD (odds ratio [OR] = 3.4,  $p = .004$ ) and current partial PTSD (OR = 2.4,  $p = .013$ ), but not current depression (OR = 1.1,  $p = .91$ ). Multivariate logistic regression results, adjusting for age, sex, marital status, level of education, current psychotropic medication use, and concussion history, confirmed these results. **Conclusions:** Grapheme-color synesthesia seems to be associated with PTSD among veterans who had been deployed. This finding may have implications for PTSD diagnostic screening and treatment. Research is recommended to confirm this finding and to determine if synesthesia is a risk indicator for PTSD among nonveterans. **Key words:** posttraumatic stress disorder, depression, synesthesia, veterans, risk factors, trauma exposure.

PTSD = posttraumatic stress disorder; VA = Veterans Affairs; CI = confidence interval; OR = odds ratio.

## INTRODUCTION

Synesthesia is a perceptual phenomenon in which stimuli presented through one sense modality evoke sensations in an unrelated sense modality (1). The condition occurs from increased communication between sensory regions and is typically involuntary and stable over time (1). Although synesthesia can occur in response to drugs, sensory deprivation, or brain injury, most research has focused on heritable variants, comprising less than 3% to 4% of the general population (2). Research on synesthesia suggests that the phenomenon is heterogeneous and polygenetic, yet it remains unclear whether synesthesia provided a selective advantage or is merely a by-product of some other useful selected trait (1). The most common form of synesthesia is the grapheme-color type, whereby individuals see specific colors associated with a particular letter or number (3). Recently, synesthesia has been associated with medical conditions such as irritable bowel syndrome and migraine headache (4,5).

Previously, we reported that posttraumatic stress disorder (PTSD) was associated with mixed handedness (6–8). The reason for the association of PTSD with handedness is because it is thought that the right brain hemisphere is significant in

threat identification and in the regulation of emotional response. Persons with reduced cerebral lateralization for language, as indexed by mixed handedness, are thought to be more sensitive to perceived threat and prone to experience emotions more intensely because their cerebral organization tends to give greater primacy to right hemisphere contributions in cognitive processes (8).

Because brain activity during synesthetic color experiences seems to arise from within the ventral temporal lobe, including the color-selective cortical area V4, it has been speculated that grapheme-color synesthesia results from disinhibited feedback or abnormal cross-wiring between brain regions involved in extracting visual form and color (9). Given this possible abnormality and that other neurologic signs and subtle neurologic compromises have been previously associated with PTSD (8,10), we hypothesized that grapheme-color type synesthesia would be a predictor of PTSD, similar to the trait of mixed handedness.

## METHODS

The study population for the current research includes a random sample of community-based US military veterans who were recruited as part of a study of the health effects of military service. All veterans in this study were outpatients in the Geisinger Health System, a large multihospital system located in central and northeastern Pennsylvania. Geisinger provides inpatient, outpatient, and community-based services for approximately 500,000 residents residing within more than 40 counties in the state. Approximately 30,000 of Geisinger's patients report serving in the US armed forces. For the current study, 700 of these veterans were randomly recruited for diagnostic interviews. With patient consent, trained and supervised interviewers administered structured diagnostic mental health interviews by telephone from December 2011 through January 2012. All veterans recruited for this survey had at least one deployment in a warzone during their military service and were younger than 74 years. The study cooperation rate in the survey was estimated to be approximately 65% (11).

It is well known that most adults have experienced traumatic events, yet few of them go on to develop PTSD (6,12). The reasons for this are unclear at this time. Available twin and family studies suggest that PTSD is moderately heritable, with approximately 30% of variance of this disorder accounted for by genetic factors (13). To date, several genetic components for PTSD that may explain this risk have been identified, including, biologic pathways involving the hypothalamic-pituitary-adrenal, locus coeruleus/noradrenergic, and the limbic systems,

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From the Departments of Neurology (S.N.H.) and Anesthesiology (X.Z.), Center for Health Research (P.M.E., J.A.B.), Geisinger Clinic, Danville, PA; Departments of Medicine (P.M.E.) and Psychiatry (J.A.B.), Temple University School of Medicine, Philadelphia, PA.

Address correspondence and reprint requests to Joseph A. Boscarino, PhD, MPH, Center for Health Research, Geisinger Clinic, 100 N Academy Ave, Danville, PA 17822-4400. E-mail: jaboscarino@geisinger.edu

Support for this study was provided, in part, by the Geisinger Auxiliary Fund, the Kline & Ditty Health Fund, and the National Institute of Mental Health (Grant No. R21-MH-086317; to Dr. Boscarino).

Received for publication April 18 2012; revision received August 22, 2012.

DOI: 10.1097/PSY.0b013e3182731007

## SYNESTHESIA AND PTSD

among others (14–16). However, additional research needs to be done to better understand the key risk factors associated with PTSD.

To assess PTSD in the current study, we used a validated questionnaire based on the *Diagnostic and Statistical Manual of Mental Disorder, Fourth Edition* criteria and adopted from the National Women's Study PTSD Scale (17–19). To meet the criteria for PTSD in the current study, veterans had to meet the full diagnostic criteria for PTSD, known as the "A through F" criteria (17). To meet the criteria for current PTSD, they had to meet the A-F criteria in the past 12 months. The A-F criteria include exposure to a traumatic event (criterion A); experiencing intense fear, helplessness, or horror during the event (criterion A2); re-experiencing the event (criterion B); avoidance of stimuli associated with the event (criterion C); experiencing increased arousal related to the event (criterion D); experiencing symptoms for more than a month (criterion E); and experiencing psychological impairment or distress related to these symptoms (criterion F). Altogether, 81% of veterans reported that one of the significant lifetime stressors they experienced was warzone or combat exposure. By comparison, 52% and 41% reported that a natural disaster and a serious accident were significant lifetime stressors, respectively. The National Women's Study PTSD scale was developed in the early 1990s and subsequently adopted and used in numerous community-based trauma studies involving more than 20,000 persons (16–24). This scale has been clinically validated against the *Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders* interview in diagnostic field trials and reported to be a valid measure of PTSD (25). We note that the prevalence of lifetime PTSD in the current study was 9.6% (95% confidence interval [CI] = 7.6–12.0), with the mean (M) (standard deviation [SD]) age of PTSD onset equal to 28 (13.6) years. The median age of onset among the veterans was 22 years.

Our study also included a measure of partial or subclinical PTSD (26). For this classification, the veteran had to meet criterion A and also have at least one or more symptoms within each of the B, C, and D criteria, respectively, with the latter three symptoms being experienced concurrently. Although those with partial PTSD tend not to be as impaired as those with the full PTSD syndrome, they, nevertheless, tend to be impaired and display symptoms of this disorder (26). In the current study, synesthesia was assessed by a survey question used in previous research (27). This question was related to seeing colors associated with a letter or a number, the most common form of synesthesia (e.g., "...when you look at a certain letter or number, do you see a certain color?"). Responses to this question were collected on a 4-point Likert scale, from "strongly disagree" to "strongly agree" (27). In addition to PTSD and synesthesia assessments, the survey collected data related to the veteran's military history, medical history, and demographic factors. Data related to the presence of current depression were also collected. The latter assessment was also based on use of a clinically validated instrument and based on the *Diagnostic and Statistical Manual of Mental Disorder, Fourth Edition* diagnostic criteria that had been used in previous community research (17,18,28–30). We hypothesized that current depression would not be associated with synesthesia, given that mood disorders likely encompass different neuro-circuitry than PTSD and other fear-circuitry disorders (16).

Statistical analyses included descriptive statistics describing the study population and statistical analyses related to testing the association between PTSD and synesthesia. For descriptive purposes, we describe the age, sex, race, employment status, education level, Veterans Affairs (VA) service use, combat exposure level, concussion history, mental health use, and mental health status of the study population (Table 1). Combat exposure in the study was assessed using the Combat Experience Scale, a commonly used measure of combat exposure used in military health studies (31). Concussion history was based on a measure of reported concussions experienced during military service (e.g., ever dazed, confused, saw stars, or knocked out) that has been used in previous research (32). The mental health service measures were assessed using standard mental health measures also used in previous research (17).

For multivariate analyses testing the study hypothesis, we used multivariate logistic regression, whereby synesthesia was used to predict PTSD and depression, respectively, while controlling for age, sex, marital status, level of education, current psychotropic medication use, and history of concussion. These covariates were used in the multivariate analysis to control for potential bias and confounding. All analyses were conducted using Stata, version 12.1 software (College Station, TX). This study was approved by the institutional review board of the Geisinger Clinic.

## RESULTS

Examination of the veterans recruited for the study indicated that 72% were Vietnam, 10% were Gulf War, 14% were Afghanistan/Iraq, and 5% were other warzone veterans, whereas 21% served in the Air Force, 55% in the Army, 11% in the Navy, and 12% in the Marine Corps (Table 1, footnote). In addition, as shown in Table 1, the M (SD) age of veterans was 59 (11) years, 96% were men, and 93% were classified as white. Also, 80% were married, 45% were currently employed, and 57% had an educational level that included some college education or higher. Also noteworthy is that only 51% of these community-based veterans reported having ever used the VA for health care services, whereas 21% were classified as having high combat exposure based on the Combat Experience Scale measure. Altogether, 26% of veterans reported a concussive injury during military service, 50% reported having sought mental health services in the past, and 21% reported that they were currently taking psychotropic medications for mental health problems. For PTSD status, the prevalence of current PTSD among veterans was 7% (95% CI = 5.1–8.8), and the prevalence of current partial PTSD was 11% (95% CI = 9.3–14.0). The prevalence of current depression was 6% (95% CI = 4.7–8.3). Finally, the prevalence of grapheme-color synesthesia among these veterans, based on the survey assessment, was 6% (95% CI = 4.8–8.5) (Table 1).

Table 2 (top) presents the unadjusted bivariate results assessing the association between mental health status and synesthesia. As can be seen, the odds ratios (OR) for current PTSD and current partial PTSD and synesthesia, respectively,

**TABLE 1. Profile of Veterans With Deployment History in Geisinger's Veteran Cohort Study (N = 700)<sup>a</sup>**

Study Variable	n <sup>b</sup>	% or Mean	95% CI
Age (mean), y	700	58.9	58.1–59.7
Male sex	671	95.9	94.1–97.1
White race	653	93.3	91.2–94.9
Married	557	79.6	76.4–82.4
Employed	313	44.7	41.1–48.4
Some college or higher	399	57.0	53.3–60.6
Ever used VA health care services	354	50.6	46.9–54.3
High combat exposure	148	21.1	18.3–24.3
History of concussion in service	181	25.9	22.7–29.2
Ever used mental health services (any)	351	50.1	46.4–53.9
Currently on psychotropic medicines	144	20.6	17.7–23.7
PTSD, past year	47	6.7	5.1–8.8
Partial PTSD, past year	80	11.4	9.3–14.0
Major depression, past year	44	6.2	4.7–8.3
Synesthesia	45	6.4	4.8–8.5

CI = confidence interval; VA = Veterans Affairs; PTSD = posttraumatic stress disorder.

<sup>a</sup> Study veterans included Vietnam (72%), Gulf War (10%), Afghanistan/Iraq (14%), and other warzone veterans (5%). Service branches included were Air Force (21%), Army (55%), Navy (11%), and Marine Corps (12%).

<sup>b</sup> The n represents the number of participants with the demographic or health characteristic shown.

**TABLE 2. Association of Synesthesia with PTSD and Depression: Unadjusted and Adjusted Results (N = 700)**

Outcomes assessed <sup>a</sup>	OR	OR 95% CI	<i>p</i>
PTSD, past year	3.4	1.5–7.8	.004
Partial PTSD, past year	2.4	1.2–4.7	.013
Major depression, past year	1.1	0.3–3.6	.91

  

Outcomes assessed <sup>b</sup>	Adjusted OR	Adjusted OR 95% CI	Adjusted <i>p</i>
PTSD, past year	3.2	1.3–8.1	.015
Partial PTSD, past year	2.2	1.0–5.0	.048
Major depression, past year	0.9	0.2–3.1	.82

PTSD = posttraumatic stress disorder; OR = odds ratio; CI = confidence interval.

<sup>a</sup> Unadjusted bivariate logistic regression results.

<sup>b</sup> Adjusted for age, sex, marital status, education, current psychotropic medication use, and history of concussion in multivariable logistic regressions.

are both statistically significant, with an OR of 3.4 ( $p = .004$ ) for current PTSD and an OR of 2.4 ( $p = .013$ ) for current partial PTSD. As hypothesized, synesthesia was not associated with current depression (OR = 1.1,  $p = .91$ ). Multivariate logistic regression results, adjusting for age, sex, marital status, education level, current psychotropic medication use, and concussion history, confirmed these bivariate results (Table 2, bottom). As can be seen, the final adjusted logistic regression results for current PTSD resulted in an OR of 3.2 ( $p = .015$ ), and the adjusted results for current partial PTSD resulted in an OR of 2.2 ( $p = .048$ ). The adjusted results for current depression remained nonsignificant (OR = 0.9,  $p = .82$ ).

## DISCUSSION

On the basis of past research (8,10), we hypothesized that veterans with the most common form of synesthesia, the grapheme-color type, would have a higher prevalence of current PTSD but not current depression. These hypotheses were confirmed. As shown, the association between current PTSD and synesthesia was statistically significant for both full and partial PTSD. Current depression was not associated with synesthesia. To our knowledge, this is the first study to report this association for PTSD and synesthesia. The possible reasons for this correlation include the fact that veterans with synesthesia may be subtly compromised neurologically and/or may be more vulnerable psychologically, such as for those who have been reported with mixed handedness, lower intelligence, attention deficits, and other neurologic symptoms or problems (6,8,10).

We speculate that although synesthesia is often associated with cognitive and perceptual benefits such as heightened memory for synesthetic experiences (33,34) and enhanced sensory processing (35,36), these findings are based on studies performed on participants under well-controlled laboratory conditions. However, synesthetes under severe stress, sleep deprivation, and polystimulus overload, as what might occur under combat conditions, could find their synesthesia to be a hindrance that could predispose them to PTSD symptoms.

Study limitations for this research include the following: our interview data were based on self-report and could include recall bias, and our sample size was limited. In addition, synesthesia was based on a single survey question, although this question was used in past research (27). This may have overestimated the prevalence of this condition. Typically, synesthesia is reported to be less than 4% in the populations studied (2). As was shown, our estimate seemed to be somewhat higher than this figure (6.4%; 95% CI = 4.8%–8.5%). Also, the current study only included US veterans who had been deployed and who were mostly white men. These factors may have biased our results and could limit study generalization. Furthermore, the total number of participants with PTSD in our study was also limited. As suggested, although synesthesia can occur temporarily in response to drugs, sensory deprivation, or brain injury, most synesthesia is thought to be a characteristic trait (1). In the current study, we adjusted for demographics (including age, sex, education, and marital status), current psychotropic medication use, and concussion history to control for possible bias and variable forms of synesthesia. Nevertheless, because our study design was cross sectional, we cannot rule out that PTSD and/or trauma exposure could have caused synesthesia. Thus, further replication is required. It is noted that the prevalence of current PTSD in this community-based sample of veterans was approximately 7%, which is the typical rate reported in national studies of community-based veterans (8). Also, the prevalence of lifetime PTSD in our study sample was 9.6% (95% CI = 7.6–12.0), similar to the rate often reported for community-based veterans (37). In addition, 51% of veterans surveyed reported ever having used VA health care services, which is typical of community-based studies of veterans (38). Given the latter finding and the fact that we controlled for demographic factors, we think that these findings might be generalized to nonveteran populations, but further research is needed to confirm this conjecture.

Despite these limitations, we report that grapheme-color synesthesia is associated with PTSD in a sample of community-based veterans. Further research is recommended to confirm these findings, to explore whether other forms of synesthesia are predictive of PTSD, and to investigate the neurobiology of synesthesia. Additional replication is important because, as suggested, veterans recruited for this survey had at least one deployment in a warzone during their military service. In addition, 21% of these veterans were classified as having high combat exposure and 81% reported that warzone exposure was a significant lifetime stressor. It is anticipated that these exposures would be negligible among nonveterans, so it will be important to confirm these findings among trauma-exposed nonveterans in the future. It is worth noting that lifetime PTSD also seems to be likely associated with synesthesia among veterans, with an OR approaching statistical significance (OR = 2.1,  $p = .077$ ). It is noteworthy that the M (SD) age of PTSD onset among veterans was 28 (13.6) years, and the median age of onset was 22 years. As shown in Table 1, the mean age of veterans in the current study was 59 years, so most of these veterans probably had PTSD for some time. Finally, we suspect that the PTSD-synesthesia association found is probably not specific to combat trauma,

## SYNESTHESIA AND PTSD

per se, but also likely associated with noncombat trauma, just as has been reported for handedness (6,7). Recognition that synesthesia is associated with PTSD may open new approaches for the prevention and treatment of PTSD. Further research is advised.

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