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# Grapheme-color Synesthesia and PTSD: Preliminary Results from the Veterans Health Study

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## Abstract

**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 multi-hospital system in Pennsylvania. All veterans had served at least one warzone deployment. PTSD and grapheme-color synesthesia were assessed using a validated research instruments.

**Results—**The mean age of veterans was 59 and 96% were men. The prevalence of current PTSD was 7% (95% C.I. = 5.1–8.8) and current partial PTSD was 11% (95% C.I. = 9.3–14.0). The prevalence of current depression was 6% (95% C.I. = 4.7–8.3). Altogether, 6% (95% C.I. = 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 = 0.004) and current partial PTSD (OR = 2.4, p = 0.013), but not current depression (OR = 1.1, p = 0.91). Multivariate logistic regression results, adjusting for age, gender, marital status, level of education, current psychotropic medication use, and concussion history, confirmed these results.

**Conclusion—**Grapheme-color synesthesia appears 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.

### Keywords

Posttraumatic stress disorder; Depression; Synesthesia; Veterans; Risk factors; Trauma exposure

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## 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). While synesthesia can occur in response to drugs, sensory deprivation, or brain injury, most research has focused on heritable variants, comprising less than 3–4% 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 byproduct 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 such medical conditions as irritable bowel syndrome and migraine headache (4, 5).

Previously, we reported that post-traumatic 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).

Since brain activity during synesthetic color experiences appears 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 effect of military service. All veterans in this study were outpatients in the Geisinger Health System (GHS), a large multi-hospital system located in central and northeastern Pennsylvania. Geisinger provides inpatient, outpatient, and community-based services for about 500,000 residents residing within more than 40 counties in the state. About 30,000 of Geiesinger'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 under 74 years of age. 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 posttraumatic stress disorder (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 have been identified that may explain this risk, including, biologic pathways involving the hypothalamic-pituitary-adrenal (HPA), locus

coeruleus/noradrenergic, and the limbic systems, 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* (DSM-IV) criteria and adopted from the National Women's Study PTSD Scale (17–19). To meet 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 criteria for the 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% reported that a natural disaster and 41% reported that 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-base trauma studies involving more than 20,000 persons (16–24). This scale has been clinically validated against the SCID 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% CI = 7.6–12.0), with the mean age of PTSD onset equal to 28 years old (SD=13.6). The median age of onset among the veterans was 22 years old.

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. While 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 were also collected related to the presence of current depression. The latter assessment was also based on use of a clinically validated instrument and based on the DSM-IV diagnostic criteria that had been used in previous community research (17, 18, 28–30). We hypothesized that current depression would not be associated synesthesia, given that mood disorders likely encompass different neurocircuitry 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, gender, race, employment status, education level, 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 (CES), 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, gender, 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, Texas). 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, while 21% served in the Air Force, 55% Army, 11% Navy, and 12% served in the Marine Corps (Table 1, footnote). Additionally, as shown in Table 1, the mean age of veterans was 59 years of age (SD = 11), 96% were men, and 93% were classified as White race. Also, 80% were married, 45% were currently employed, and 57% had and 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 healthcare services, while 21% were classified as having high combat exposure based on the CES 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. In terms of PTSD status, the prevalence of current PTSD among veterans was 7% (95% C.I. = 5.1–8.8) and the prevalence of current partial PTSD was 11% (95% C.I. = 9.3–14.0). The prevalence of current depression was was 6% (95% C.I. = 4.7–8.3). Finally, the prevalence of grapheme-color synesthesia among these veterans, based on the survey assessment, was 6% (95% C.I. = 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 ratio (OR) for current PTSD and current partial PTSD and synesthesia, respectively, are both statistically significant, with an OR = 3.4 (p = 0.004) for current PTSD and an OR = 2.4 (p = 0.013) for current partial PTSD. As hypothesized, synesthesia was not associated with current depression (OR = 1.1, p = 0.91). Multivariate logistic regression results, adjusting for age, gender, 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 = 3.2, p = 0.015 and the adjusted results for current partial PTSD resulted in an OR = 2.2, p = 0.048. The adjusted results for current depression remained non-significant (OR = 0.9, p = 0.82).

## Discussion

Based on 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 were 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 have been reported for those with mixed handedness, lower intelligence, attention deficits, and with 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), as well as enhanced sensory processing (35, 36), these findings are based on studies performed on participants under well-controlled laboratory conditions. However, a synesthete under severe stress, sleep deprivation, and poly-stimulus overload, as 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 that our interview data were based on self- report and could include recall bias and that 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 over-estimated the prevalence of this condition. Typically, synesthesia is reported to be less than 4% in the populations studied (2). As was shown, our estimate appeared to be somewhat higher than this figure (6.4%, 95% C.I. = 4.8–8.5%). Also, the current study only included US veterans who had been deployed and most were white men. These factors may have biased our results and could limit study generalization. Furthermore, the total number of PTSD cases in our study was also limited. As suggested, while 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, gender. education, and marital status), current psychotropic medication use, and concussion history to control for possible bias and variable forms of synesthesia. Nevertheless, since 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 ~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 healthcare 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 these finding might be generalized to non-veteran 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 finding, 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 finding among trauma-exposed nonveterans in the future. It is worth noting that lifetime PTSD also appears to be likely associated with synesthesia among veterans, with an odds ratio approaching statistical significance (OR = 2.1, p = 0.077). It is noteworthy that the mean age of PTSD onset among veterans was 28 years old (SD=13.6) and the median age of onset was 22. As shown in Table 1, the mean age of veterans in the current study was 59 years old, so most of these veterans that probably had PTSD for some time. Finally, we suspect that the PTSD-synesthesia association found is probably not specific to combat trauma, 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 prevention and treatment of PTSD. Further research is advised.

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## Abbreviations

| | |
|---|---|
| **CES** | Combat Experience Scale |
| **DSM-IV** | Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition |
| **GHS** | Geisinger Health System |
| **PTSD** | Posttraumatic Stress Disorder |
| **SCID** | Structured Clinical Interview for DSM Disorders |
| **VA** | Veterans Affairs |

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## Table 1

Profile of Veterans With Deployment History in Geisinger's Veteran Cohort Study (N=700)*

| Study Variable | (N)† | % or Mean | 95% CI |
|---|---|---|---|
| Age (mean) | (700) | 58.9 | 58.1–59.7 |
| Male gender | (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 healthcare 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 meds | (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 |

*Study veterans included Vietnam veterans (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%).

†The N represents the number of participants with the demographic or health characteristic shown.

## Table 2

Association of synesthesia with PTSD and depression: Unadjusted & adjusted results (N=700)

| Outcomes assessed* | OR | OR 95% CI | P-value |
|---|---|---|---|
| PTSD - Past year | 3.4 | 1.5–7.8 | 0.004 |
| Partial PTSD - Past year | 2.4 | 1.2–4.7 | 0.013 |
| Major depression - Past year | 1.1 | 0.3–3.6 | 0.91 |

| Outcomes assessed** | Adj. OR | Adj. OR 95% CI | Adj. P-value |
|---|---|---|---|
| PTSD - Past year | 3.2 | 1.3–8.1 | 0.015 |
| Partial PTSD - Past year | 2.2 | 1.0–5.0 | 0.048 |
| Major depression - Past year | 0.9 | 0.2–3.1 | 0.82 |

* Unadjusted bivariate logistic regression results.

** Adjusted for age, gender, marital status, education, current psychotropic medication use, and history of concussion in multivariable logistic regressions.