Consistent Association Between Mixed Lateral Preference and PTSD: Confirmation Among a National Study of 2490 US Army Vietnam Veterans

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Objective: To evaluate the research-based association between mixed lateral preference for handedness and risk for posttraumatic stress disorder (PTSD) in a large-scale sample of US Army Vietnam veterans exposed to war zone stressors. **Method:** We used a national sample of 2490 male US Army veterans, who completed the Edinburgh Handedness Inventory (EHI), a measure ranging from -100 (pure left-handedness) to +100 (pure right-handedness). We developed several classifications representing levels of mixed laterality: a) an EHI -70 to +70 (EHI 70, moderate mixed); b) an EHI -50 to +50 (EHI 50, consistent mixed); and c) an EHI 0, plus reports of using either hand on $\geq 50\%$ of the tasks assessed (EHI 0+, extreme mixed). We controlled for intelligence, race, Army entry age, and Army volunteer status, and we assessed the impact of combat exposure. **Results:** Although all three handedness measures were associated with current PTSD in bivariate analyses, only Edinburgh 0+ was associated with PTSD in the multivariate model (odds ratio (OR) = 2.1; p = .021). However, when we classified handedness by high combat exposure, all three measures were associated with PTSD, with ORs = 2.5, 2.8, and 4.7 for EHI 70, EHI 50, and EHI 0+, respectively (all p < .001). Veterans with mixed laterality and high combat exposure also had significantly increased PTSD symptoms (all p < .001). **Conclusion:** Our study confirmed findings reported among mostly smaller clinical samples and suggested that mixed lateral preference was associated with PTSD, especially among those individuals exposed to more severe psychological trauma. **Key words:** mixed lateral preference, handedness, cerebral organization, posttraumatic stress disorder, combat exposure, vulner-ability.

EHI = Edinburgh Handedness Inventory; **PTSD** = posttraumatic stress disorder; **DIS** = Diagnostic Interview Schedule; **NSS** = neurological soft signs; **RTI** = Research Triangle Institute

INTRODUCTION

t has been hypothesized that individuals with a lesser degree of cerebral lateralization have a greater likelihood of developing posttraumatic stress disorder (PTSD) (1,2). This hypothesis suggests that the right brain hemisphere is significant in threat identification and in the regulation of emotion response. Persons with reduced cerebral lateralization for language, as indexed by mixed handedness (3), are thought to be more sensitive to perceived threat and prone to experience emotions more intensely because their cerebral organization is thought to give greater primacy to right hemisphere contributions in cognitive processes (1). Investigating this hypothesis, researchers have reported that mixed lateral preference among right-handed male Israeli combat veterans was associated with increased susceptibility to combat-related PTSD (4). Furthermore, researchers have reported that disaster-exposed adolescents with mixed lateral preference had more trauma symptoms than did adolescents with consistent lateral preference (5). In addition, among a sample of US combat veterans, it has also been reported that right-handed participants with mixed lateral preference were more likely to have PTSD than right-handed participants with consistent lateral preference (1).

Recent reports demonstrated that subtle neurological compromise represented vulnerability for combat-related PTSD (6). For example, in a case-control study of 49 identical twin Vietnam veterans, investigators reported that combat veterans

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(NSS) scores than did combat veterans without PTSD (6). NSS scores are based on simple, nonspecific neurological tests, such as figure drawings, mirror movements, walking tiptoe, a road map test, a tongue twister, and standing on one foot. Previous investigators have reported NSS in patients with PTSD, but the cause and effect were unclear. To resolve this, a case-control study was designed for twin Vietnam veterans and their combat-unexposed identical (monozygotic) co-twin (6). Combat veterans with PTSD had significantly higher NSS scores than combat veterans without PTSD. The unexposed co-twins of the former also had significantly higher NSS scores than the unexposed co-twins of the latter. These results could not be explained by self-selection, age, number of traumatic lifetime events, alcoholism, or the presence of affective or anxiety disorders. These findings supported the conclusion that NSS in individuals with PTSD was not acquired along with the trauma or PTSD but represented an antecedent vulnerability for PTSD. We suspected that mixed handedness represented a similar NSS vulnerability for PTSD.

with PTSD had significantly higher neurological soft sign

In this study, we attempted to replicate the findings related to mixed laterality and PTSD. Previous studies, all retrospective, that have linked PTSD to mixed laterality have often involved small, mostly clinical convenience samples recruited from diverse populations. One study included 80 male combat-related PTSD patients from the Israel Defense Forces (IDF) recruited from a larger PTSD study in the early 1990s and 100 healthy age-matched control veterans also recruited from the IDF (4). Another study included 203 students recruited from a single high school in Hawaii after Hurricane Iniki in 1992 (5). Another study included 118 US combat veterans from all conflicts, who were recruited locally through newspaper advertisements, Veterans Administration clinics, community organizations, and other sources (1). Another study recruited 59 traumatized children from local service agencies and clinics and 40 matched controls from an existing clinical database (2). Finally, another study included 68 mothers recruited from childcare centers located near the World

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Trade Center site after the terrorist attacks on September 11, 2001 (7). Interestingly, all of these mixed handedness studies suggested a positive link between handedness and PTSD. However, given the fact that these prior studies involved mostly convenience samples, had no preexposure measures, and included limited statistical controls, such as matching on only one study variable, selection biases could have significantly affected the results reported.

In the current study, we assessed the link between PTSD and mixed handedness among a national random sample of 2490 community-based Vietnam veterans exposed to war zone stressors during the Vietnam War. Based on previous research (1), we also sought to investigate if the degree of trauma exposure—namely, combat exposure—interacted with mixed lateralization, thereby increasing the risk for PTSD. In our national study, we controlled for preexposure intelligence, preexposure volunteer status, preexposure service entry age, and race—factors not usually controlled in previous studies.

METHODS

Our study population consisted of a random, representative sample of enlisted men who served in the US Army during the Vietnam War. These men were identified by a computer search of all service records at the National Personnel Records Center (St. Louis, MO), which contains the files of all the personnel who served in the US Army during the Vietnam War. From these records, 18,581 randomly selected veterans met the following study inclusion criteria: a) being male; b) entering the military between 1965 and 1971; c) serving one enlistment; and d) having a service rank no higher than E5. Participants were classified as Vietnam theater veterans if they served in Vietnam or as Vietnam era veterans if they served elsewhere. Starting in January 1985, attempts were made to complete telephone interviews. From these efforts, 87% (n = 7924) of theater veterans and 84% (n = 7364) of the era veterans were interviewed by telephone (overall completion rate = 86%). Among these, a random sample was selected for personal interviews. Altogether, 75% (n = 2490) of the theater veterans and 63% (n = 1972) of era veterans participated in this study phase. For the current study, we only reported the results for the 2490 combat-exposed Vietnam theater veterans. Although the study response rate was lower than desired, a detailed nonresponse analysis found no significant differences between participants and nonparticipants (8). Further details regarding this study have been published (8,9). The Centers for Disease Control's Human Subject Review Committee approved the study protocols for this study (8,9). Personal interviews and physical examinations were administered at Lovelace Medical Foundation, Albuquerque, New Mexico, between June 1985 and September 1986.

Our measure of PTSD was based on a telephone survey administered by Research Triangle Institute (RTI) before the personal interviews and examinations (9). For this scale, veterans were asked to report 15 PTSD symptoms that occurred in the past 6 months. Consistent with the *Diagnostic and Statistical Manual of Mental Disorders, Third Edition* (10), a veteran was classified as having current PTSD if he reported at least one criterion B symptom (reexperiencing), at least one criterion C symptom (avoidance), and at least two criterion D symptoms (hyperarousal). Comparison of the RTI-PTSD scale results with Version III of the Diagnostic Interview Schedule (DIS) administered during the personal interviews (11,12) indicated that RTI-PTSD was consistent with the presence of PTSD (13). We did not use the current DIS-PTSD measure administered during the personal interview because this scale was based on the past 30 days and resulted in a prevalence rate significantly lower than reported in other national population studies of Vietnam veterans (13,14).

Our study also included the following measures: Army entry age, race, Army volunteer status, Vietnam volunteer status, intelligence, and combat exposure level (8). Army entry age was taken from the military record and used as a continuous variable. Race was based on the veteran's reported race (White 82%; Black 11%; Hispanic 5%; other 2%) and used as a two-category indicator variable (White versus non-White). Army volunteer status was classified as "volunteer" versus "draftee" and based on the military record. Vietnam volunteer status was based on whether the veteran reported volunteering for Vietnam service. Intelligence was taken from the military record and was based on the General Technical Score from the Army Classification Battery administered at induction—a scale considered to be a valid measure of general intelligence (8). This measure was used as a continuous variable. Combat exposure was based on the combat exposure index and used as a categorical scale, with the top tertile defined as the high exposure category. This measure, described elsewhere (9), was shown to be a valid and reliable measure of combat exposure in Vietnam (15). Army entry age, Army volunteer status, Vietnam volunteer status, and intelligence were all preexposure measures in our study.

To assess handedness, we used the Edinburgh Handedness Inventory (EHI) (16). The EHI ascertains handedness by asking respondents to report which hand they normally used for 10 common tasks, such as writing, throwing a ball, or using scissors. Based on these responses, respondents were scored as $(100 \times (\text{Right} - \text{Left})/(\text{Right} + \text{Left}))$, which resulted in a score ranging from -100 to +100, where -100 indicated pure left-handedness and +100 indicated pure right-handedness. A score of 0 indicated pure mix handedness (16). In accordance with EHI scoring conventions (17), we classified respondents who scored -70 to +70 as moderate mixed-handed respondents (EHI 70). In addition, we developed two additional mixed classifications. Next, we classified respondents who scored -50 to +50 as consistent mixed-handed respondents (EHI 50). Finally, we classified those who scored 0 on the EHI or reported that they normally used either hand on the majority of assessed tasks as extreme mixed-handed respondents (EHI 0+).

For our analyses, we described the prevalence of mixed handedness and PTSD and the prevalence of handedness by PTSD and high combat exposure status. We also presented results classified by our study control variables. Next, we presented handedness results using multivariate logistic regressions to predict PTSD and at the same time controlled for our demographic and predisposition variables. In addition, we used analysis of covariance (ANCOVA) to model PTSD symptoms by mixed handedness and combat exposure, controlling for the demographic and predisposition variables. For our ANCOVA, we also tested for a mixed handedness \times combat exposure interaction effect. For this assessment, we recoded combat level into four equal-sized exposure categories (representing a quartile distribution) to minimize sparse cell sizes. Statistical analyses were performed using SPSS version 14 (Chicago, IL). All *p* values presented were based on two-tail tests.

RESULTS

The first part of Table 1 shows the prevalence of mixed handedness in our study population based on the three definitions discussed. The broadest definition (Edinburgh -70 to +70) resulted in 15.3% of men meeting the criterion for mixed laterality. Using a more restrictive criterion (Edinburgh -50 to +50) reduced this to 7%. Finally, the most restricted criterion for mixed laterality, including only men who scored a 0 on the EHI or who reported that they normally used either hand on the majority of tasks assessed, resulted in 2.5% of men meeting this standard. Further stratifying these classifications by high combat exposure-defined as the top exposure tertile for combat-reduced the prevalence of mixed handedness to 6.3%, 2.8%, and 1.1%, for EHI 70, EHI 50, and EHI 0+ concurrent with high combat exposure, respectively. The second panel down shows mixed laterality by PTSD and demonstrates that these are all positively associated, especially in terms of mean PTSD symptom levels (p < .01). Noteworthy is that 22.6% of those in the EHI 0+ category had PTSD

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TABLE 1. Mixed Laterality, Posttraumatic Stress Disorder (PTSD), and High Combat Exposure by Study Research Variables (n = 2490)

Study Variables	Total Sample, % (<i>n</i>)	Total Edinburgh 70 (Moderate), % (n)	Total Edinburgh 50 (Consistent), % (n)	Total Edinburgh 0+ (Extreme), % (<i>n</i>)	
Prevalence of mixed laterality and mixed					
laterality, plus high combat exposure					
% Mixed laterality	—	15.3 (381)	7.0 (174)	2.5 (62)	
% Mixed laterality with high combat	—	6.3 (157)	2.8 (69)	1.1 (27)	
PTSD by mixed laterality	% (<i>n</i>)	% (<i>n</i>)	% (n)	% (<i>n</i>)	
Mean PTSD symptom (SD)	11.7 (8.6)	13.2 (8.6) ^d	13.4 (9.3) ^c	$16.2(10.3)^d$	
% PTSD	10.2 (255)	12.6 (48) ^a	14.9 (26) ^b	22.6 (14) ^c	
Combat exposure by mixed laterality	% (n)	% (<i>n</i>)	% (<i>n</i>)	% (<i>n</i>)	
% Higher combat	35.6 (887)	41.2 (157) ^b	39.7 (69)	43.5 (27)	
Study control variables by mixed laterality	% (n)	% (<i>n</i>)	% (<i>n</i>)	% (<i>n</i>)	
% Entry age ≤18 years	15.0 (374)	17.6 (67)	17.8 (31)	25.8 (16) ^b	
% Non-White race	17.5 (436)	18.4 (70)	20.7 (36)	24.2 (15)	
% Lower intelligence (quartile)	27.3 (681)	26.0 (99)	31.0 (54)	38.7 (24) ^b	
% Army volunteer	38.3 (953)	40.7 (155)	42.0 (73)	50.0 (31) ^a	
% Vietnam volunteer	22.1 (551)	25.7 (98) ^a	25.3 (44)	30.6 (19)	

 $^{^{}a} p < .10.$

 $[\]bar{p} < .001.$

TABLE 2.	Multivariate Models Predicting PTSD Cases and Mean PTSD Symptom Levels by Mixed Laterality Type and Mixed Laterality
	Type × Combat Exposure

Handedness Measures	Mixed Laterality ^a		Mixed Laterality With High Combat Exposure ^a		Mean Symptoms for Mixed Laterality Cases ^a		Mean Symptoms for Laterality With High Combat Exposure ^a		Interaction for Mixed \times Combat ^b				
	OR	95% Cl	р	OR	95% Cl	р	Mean	95% CI	р	Mean	95% CI	р	p
Mixed–Edinburgh 70 (Moderate)	1.3	0.9–1.8	.146	2.5	1.6–3.7	<.001	13.1	12.2–13.9	<.001	15.3	14.0–16.6	<.001	.031
Mixed–Edinburgh 50 (Consistent)	1.5	0.9–2.3	.100	2.8	1.6–5.0	<.001	13.0	11.8–14.2	.028	15.5	13.6–17.4	<.001	.045
Mixed–Edinburgh 0+ (Extreme)	2.1	1.1–4.0	.021	4.7	2.1–10.6	<.001	15.2	13.2–17.2	.001	18.2	15.1–21.3	<.001	.356

^a All models controlled for Army entry age, race, intelligence, Army volunteer status, and Vietnam volunteer status. For PTSD case prediction, logistic regression was used; for mean PTSD symptom prediction, analysis of covariance was used.

^b Results for interaction effects for mixed laterality × combat exposure (classified as low, moderate, high, and very high combat) based on analyses of covariance, which was adjusted for the above control variables. For moderate laterality = F(3,2481) = 2.96; p = .031. For consistent laterality = F(3,2481) = 2.69; p = .045. For extreme laterality = F(3,2481) = 1.10; p = .356.

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

(p < .01). This association was less consistent across laterality classifications by combat exposure alone, as well as for the study control variables (Table 1).

Table 2 presents the multivariate results. By itself, only Edinburgh 0+ was significantly associated with PTSD in our multivariate model, with an odds ratio (OR) of 2.1 (p = .021). However, when we classified mixed laterality by high combat exposure, all the mixed laterality measures were significant in these models, with ORs = 2.5, 2.8, and 4.7, respectively, for Edinburgh 70, 50, and Edinburgh 0+ (all p < .001). Similar results are shown for PTSD symptom levels by mixed laterality. Veterans with mixed laterality and high combat exposure, however, had significantly higher PTSD symptom levels

(all p < .001), especially those in the Edinburgh 0+ category (mean = 18.2 versus 11.6 for those not classified EHI 0+). Because this finding suggested an interaction, we tested for this in our ANCOVA models (Table 2). These effects were significant, except Edinburgh 0+ by combat. To evaluate if the lack of significance was due to the sparse distribution of EHI 0+ by the combat exposure cases (n = 27), we also assessed for interaction using combat exposure as a continuous variable. When this assessment was done, the interaction approached statistical significance (p = .087), suggesting that the lack of significance was likely due to sparse cell sizes for those individuals in the higher combat and the EHI 0+ categories.

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 $b^{b} p < .05.$

 $p^{c} p < .01.$

DISCUSSION

Our study confirmed previously reported results based on smaller convenience samples. Among a national representative sample of community-based US Army veterans, mixed handedness was associated with PTSD, especially among those with higher combat exposure. Our assumption was that "handedness" occurred before combat exposure and, therefore, represented a vulnerability for PTSD. It is possible, however, that the onset of psychopathology related to PTSD might have affected cerebral lateralization (18) and, therefore, possibly handedness (17). Only a longitudinal study or one including additional biometric information among cases and matched controls could answer this question more definitively (6). As noted elsewhere (13), another limitation in our study was that our PTSD measure was based on an early version of this diagnostic nomenclature and might not reflect current measurement technology. Furthermore, our study included only male veterans exposed to combat stressors and it might not be possible to generalize to other demographic groups or traumatic exposures. Finally, recent studies suggested that cerebral lateralization is more complex than had been previously recognized (19); hence, mixed handedness might only be a limited index for mixed cerebral lateralization. Nevertheless, our findings were consistent with previous reported studies among diverse populations, including those involving adults and children, as well as persons exposed to both combat and noncombat traumas (1,2,4,5,7). The fact that our national study was consistent with results from smaller local studies, we think, supports the validity of our findings. In addition, the fact that our findings were consistent with those from noncombat exposed populations helps rule out, although does not eliminate, the possibility that nonright-handed persons might be prone to PTSD in the Army because military equipment was primarily designed for right-handed persons. Furthermore, our study included several key preexposure measuressuch as preexposure intelligence and volunteer status—that were missing from other previous studies, thereby strengthening our reported results.

Recent research has suggested that there are genetic liabilities for PTSD as well as exposure to psychological trauma (6,20,21). In addition, there is evidence that the effects of psychological stressors are mediated by gene \times environment interactions (22). Nevertheless, the causal pathways involved in these associations are unclear at this time and likely involve broader biologic mechanisms related to neurobiologic dysfunction (6). For example, it has been reported that auditory probe-evoked potential attenuation as an index of hemispheric activity among subjects with a history of childhood trauma showed a significant left dominant asymmetry during neural memory, which markedly shifted to the right during unpleasant memory, compared with control subjects without childhood trauma (23). Similar findings were reported elsewhere (24). However, it is still unclear if these findings represent a cause or an effect or if these results are specific to PTSD (23). Perhaps the most compelling evidence to date is the twin study

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mentioned earlier that was related to the assessment of NSS and PTSD. This study suggested that subtle neurological dysfunction in PTSD was not acquired along with the trauma or PTSD but represented an antecedent familial vulnerability for developing PTSD on exposure to psychological trauma that could not be explained by the presence of other comorbid mental health disorders or other factors (6). This association had been reported in other studies as well (25). The latter finding, we think, hints at the polygenetic basis that underlies the risk for PTSD (and other mental health disorders) that is worthy of future investigation (26).

Given this current body of research, even though the underlying mechanisms seem unclear at this time, it might be beneficial to screen individuals entering high-risk occupations for handedness or NSS, or at least follow-up such persons after traumatic exposure to ensure adequate access to treatment interventions (27). Thus, handedness, along with other risk factor information (28), might be useful for screening persons before or after exposure to psychological trauma, or both. These findings might be useful in mitigating some of the sequelae now associated with traumatic stressor exposures, particularly those related to exposure to armed conflict (13,29). This information might have implications for warfighters and others returning from current theaters of war (30).

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