Examining the Association Between Posttraumatic Stress Disorder and Attention-Deficit/Hyperactivity Disorder: A Systematic Review and Meta-Analysis

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ABSTRACT

Objective: To conduct a systematic review and meta-analysis examining the relationship between attention-deficit/hyperactivity disorder (ADHD) and posttraumatic stress disorder (PTSD).

Data Sources: We reviewed literature through PubMed and PsycINFO without a specified date range, utilizing the search (*posttraumatic stress disorder* OR *PTSD*) AND (*ADHD* OR *attention deficit hyperactivity disorder* OR *ADD* OR *attention deficit disorder* OR *hyperkinetic syndrome* OR *minimal brain dysfunction*). References from relevant articles were reviewed.

Study Selection: We identified 402 articles; 28 met criteria. We included original human research in English that operationalized diagnoses of ADHD and PTSD, evaluated the relationship between the disorders, and included controls. We excluded articles that failed to differentiate ADHD or PTSD from nonspecific or subsyndromal deficits or failed to compare their relationship.

Data Extraction: We extracted sample size, age, diagnostic methods, design, referral status, control type, and number of subjects with and without ADHD and PTSD alone and combined. We computed meta-analyses for 22 studies examining ADHD in PTSD and PTSD in ADHD using a random effects model and meta-analytic regression. We assessed for heterogeneity and publication bias and adjusted for intrastudy clustering.

Results: The relative risk (RR) for PTSD in ADHD was 2.9 ($P < .0005$); in samples using healthy controls, the RR was 3.7 ($P = .001$); and in samples using traumatized controls, the RR was 1.6 ($P = .003$). The RR for ADHD in PTSD was 1.7 ($P < .0005$); in samples using traumatized controls, the RR was 2.1 ($P < .0005$). The association was not significant in samples using psychiatric controls.

Conclusions: Results indicate a bidirectional association between ADHD and PTSD, suggesting clinical implications and highlighting the need for neurobiological research that examines the mechanisms underlying this connection.

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Posttraumatic stress disorder (PTSD) is a prevalent and morbid disorder that afflicts 10% of children and adults in the United States.[1,2] While trauma is very common, only a minority of traumatized individuals develop PTSD,[2–5] suggesting that such individuals have predisposing risk factors for PTSD.[6]

One putative risk factor for PTSD is attention-deficit/hyperactivity disorder (ADHD), a prevalent, early onset, persistent, and morbid neurobiological disorder.[7] ADHD is a compelling candidate risk factor for PTSD since it is associated with high levels of risk-taking behavior and impulsivity that could lead to traumatic events.[8,9] Furthermore, deficits in attention and prefrontal cortical function resembling those identified in ADHD have been found in neuroimaging and cognitive studies of PTSD subjects.[6,10] While some studies have suggested an association between ADHD and PTSD,[11,12] uncertainties remain as to the consistency, magnitude, and directionality of this association.

Whether ADHD is a risk factor for PTSD, or vice versa, has important clinical, scientific, and public health implications. Establishing an association between ADHD and PTSD could lead to intervention strategies for patients with ADHD who are exposed to trauma. Awareness of this comorbidity would alert clinicians treating patients with PTSD to screen for ADHD. A better understanding of the association between ADHD and PTSD could provide new insights about the neurobiology of some forms of PTSD associated with ADHD. The nature of this association could also inform the development of policies and screening procedures to identify those at high risk for PTSD.

The main aim of this study was to examine the available evidence linking ADHD to PTSD, attending to the directionality of the association. To this end, we conducted a systematic review of the extant literature on the relationship between ADHD and PTSD and subjected the data to qualitative and quantitative analyses. We hypothesized that the literature would show a robust and bidirectional association between ADHD and PTSD.

METHOD

Data Sources

We performed a systematic literature search of all journal articles accessible through PubMed and PsycINFO without a specified date range, utilizing the search: (*posttraumatic stress disorder* OR *PTSD*) AND (*ADHD* OR *attention deficit hyperactivity disorder* OR *ADD* OR *attention deficit disorder* OR *hyperkinetic syndrome* OR *minimal brain dysfunction*). We excluded reviews and articles not written in English. Our search yielded 391 articles,

Clinical Points

- Clinical and preclinical studies suggest a relationship between attention-deficit/hyperactivity disorder (ADHD) and posttraumatic stress disorder (PTSD) with important clinical, scientific, and public health implications.
- Results show a bidirectional association between PTSD and ADHD not solely explained by trauma.
- Clinicians should screen for PTSD in patients with ADHD, evaluate for ADHD in patients with PTSD, and consider treating both disorders when present.

after duplicates were removed, which were evaluated for inclusion by 3 authors: 2 research assistants and a child psychiatrist (the first author). Disagreements among these authors were resolved by the first and senior authors, both child psychiatrists. References from all articles appropriate for inclusion were reviewed and added if applicable.

Study Selection

We included only original studies that specifically evaluated the relationship between PTSD and ADHD. We implemented the following inclusion criteria: (1) original research, (2) human studies, (3) operationalized diagnoses of ADHD and PTSD using a structured assessment tool, (4) specific analysis of the rate of PTSD or severity of PTSD symptoms in ADHD subjects compared to controls and/or specific analysis of the rate of ADHD or severity of ADHD symptoms in PTSD subjects compared to controls, and (5) comparison control (non-ADHD or non-PTSD) group. Excluded articles were reviews, editorials, letters, and case reports or articles that failed to (1) differentiate ADHD from nonspecific or subsyndromal attentional deficits, (2) differentiate PTSD from subsyndromal symptoms or other sequelae of trauma, (3) evaluate subjects for PTSD or ADHD, and/or (4) compare the relationship between PTSD and ADHD.

Data Extraction and Analysis

Three authors (2 research assistants and the first author, a child psychiatrist) performed the data extraction and 2 sets of checks for errors. Any discrepancies were resolved by discussion with the second author, an experienced psychiatric epidemiologist. We extracted the following variables where available: (1) prevalence of ADHD in PTSD and controls OR prevalence of PTSD in ADHD and controls OR symptom correlation coefficients, (2) number of subjects and controls, (3) mean age (or median age if the mean was not reported or could not be calculated) and age group ("pediatric" if mean or median age < 18 years; "adult" if mean or median age 18+ years), (4) method of PTSD and ADHD assessment, (5) age at onset of PTSD and ADHD, (6) number of subjects with and without ADHD and PTSD alone and combined, and (7) gender of subjects with and without ADHD and PTSD alone and combined. For each study, we defined the control type as *normal* (healthy, without known psychiatric illness), *traumatized* (had experienced a defined traumatic event), and *psychiatric* (selected from a psychiatric treatment setting or having a defined psychiatric illness other than PTSD or ADHD). We also defined referral status as *referred* (from a treatment or other high-risk setting) or *nonreferred* (representative of the community or general population). We also noted study sample as *ADHD* (selected ADHD cases and controls), *PTSD* (selected PTSD cases and controls), or *population* (cohort design). For studies that provided total N and percentages but not numbers of cases, numbers were calculated based on the percentages provided. Only studies that provided sufficient data to make these calculations were included in the meta-analysis.

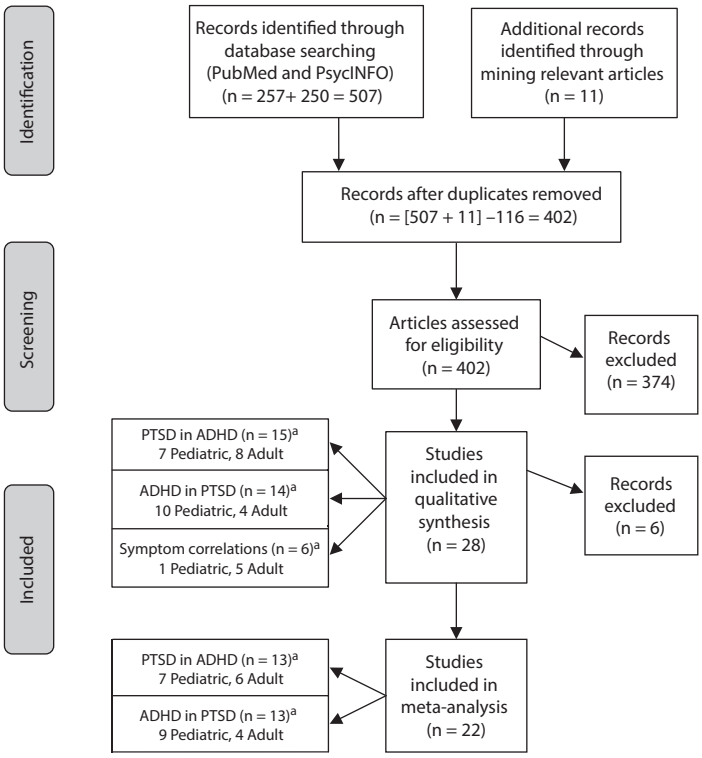
We computed separate meta-analyses for studies examining ADHD in individuals with PTSD and PTSD in individuals with ADHD. Within each set of studies, we conducted separate analyses for studies using different types of control groups (normal, psychiatric, or traumatized). Our meta-analysis used the random effects model of DerSimonian and Laird[13] that computes a pooled relative risk weighted by sample size. We used the I^2 index to assess the heterogeneity of effect sizes.[14] A significant I^2 suggests that the effect sizes analyzed are not estimating the same population effect size. We used the Egger method to assess for publication biases[15] and adjusted standard mean differences (SMDs) for publication bias using the "trim and fill" method of Duval and Tweedie.[16]

We used meta-analytic regression to assess the degree to which the effect sizes varied with the methodological features of each study.[17,18] We estimated a separate model for each feature (control group, sample type, age, and referral status). The meta-analyses and meta-analytic regression were weighted by the reciprocal of the variance of the effect sizes. To address intrastudy clustering, variance estimates for the meta-analytic regression were adjusted using the Huber[19] formula as implemented in STATA (StataCorp).[20] The resulting *P* values are valid even when observations are not statistically independent.

RESULTS

Our search produced 402 unique articles, of which 28 met our search criteria (Figure 1). These were published between 1994 and 2013. Fifteen studies reported rates of PTSD in subjects with ADHD, and 14 reported rates of ADHD in subjects with PTSD (4 studies reported rates in both directions[11,34,37,38]). Six studies examined correlations between severity of ADHD and PTSD symptoms (3 of these reported only symptom correlations without reporting disorder rates[36,39,45]). Thirteen studies used adult subjects, and 15 studied youth (Table 1). Of these studies, 22 could be included in the meta-analysis; 6 lacked sufficient information. All 6 corresponding authors of these papers were contacted, 5 responded, and none could provide supplemental information to allow us to include their findings in the meta-analysis. Three studies reported on rates of the disorders in 2 separate populations, so these populations were entered separately in the analyses.[34,38,40]

Figure 1. PRISMA Flow Diagram



[a]Some studies reported on more than 1 finding (PTSD in ADHD, ADHD in PTSD, and symptom correlations).
Abbreviations: ADHD = attention-deficit/hyperactivity disorder, PTSD = posttraumatic stress disorder.

Risk for PTSD in Individuals With ADHD

Fifteen studies meeting our inclusion and exclusion criteria examined the risk for PTSD in individuals with ADHD. Seven were pediatric and 8 were adult studies. Of the 7 pediatric studies that examined rates of PTSD in children with and without ADHD, 6 showed significantly higher rates of PTSD in children with ADHD. All 7 pediatric studies provided adequate information for inclusion in the meta-analysis. Since 2 of these 7 studies provided 2 separate samples of children for analysis,[34,38] 9 pediatric samples were analyzed. Eight studies examined rates of PTSD in adults with and without ADHD, and all showed a significantly higher rate of PTSD in adults with ADHD relative to controls. However, 2 of these studies did not provide enough information for inclusion in the meta-analysis.[25,27] Thus, in total, 9 pediatric and 6 adult samples (15 samples) were available for the meta-analysis on risk for PTSD in individuals with ADHD (Table 1). These studies combined included a total of 48,760 subjects (1,953 pediatric and 46,807 adult subjects).

Among all 15 samples from the 13 studies included in the meta-analysis, the pooled relative risk for PTSD in ADHD was positive and significant (RR = 2.9, $t_{13} = 5.2$, $P < .0005$). Overall heterogeneity was significant, suggesting that these studies were not estimating a common relative risk ($I^2_{14} = 79\%$, $P < .0005$). As shown in Figure 2A, some of this heterogeneity could be due to variability in the control groups used across studies. In fact, meta-analytic regression revealed a significant effect of control group ($P = .006$) on relative risk. In the 9 samples that used normal controls, we found a statistically significant pooled relative risk for PTSD in ADHD (RR = 3.7, 95% CI, 3.1 to 7.5; $t_8 = 5.5$, $P = .001$). Heterogeneity was low and not significant among these samples, suggesting that they were estimating a common relative risk ($I^2_8 = 0.0\%$, $P = .76$). In the 4 samples that used traumatized controls, we also found a statistically significant pooled relative risk for PTSD in ADHD (RR = 1.6, 95% CI, 1.3 to 2.0; $t_2 = 19.3$, $P = .003$), and heterogeneity was low and not significant among these samples ($I^2_3 = 0.0\%$, $P = .63$). Only in the 2 samples that used psychiatric controls was the pooled relative risk for PTSD in ADHD not statistically significant (RR = 1.7, 95% CI, −1.1 to 4.8; $t_1 = 7.9$, $P = .08$), and heterogeneity was low and not significant ($I^2_1 = 0.0\%$, $P = .82$). We conducted a separate analysis based on referral status and found a statistically significant pooled relative risk for PTSD in ADHD in both referred (RR = 2.0, 95% CI, 0.6 to 4.4; $t_6 = 3.4$, $P = .02$) and nonreferred (RR = 3.5, 95% CI, 2.1 to 6.1; $t_7 = 4.8$, $P = .002$) samples. Meta-regression found no significant effect on relative risk of referral status ($P = .17$), study sample type (case control vs cohort study, $P = .20$), or age group (child vs adult, $P = .20$). However, mean/median age had a significant effect on relative risk ($P = .001$), with studies of older subjects showing greater relative risk. Of note, the largest study with 31,809 subjects could not be included in the mean age meta-analytic regression since no mean or median age could be calculated.[30] Gender could not be included in the meta-regression due to lack of information provided by study authors. In all studies examining risk for PTSD in ADHD, the Egger test for publication bias was not significant ($t = 0.03$, $P = .97$).

Risk for ADHD in Individuals With PTSD

Of the ten studies that compared rates of ADHD in children with and without PTSD, 6 showed a significantly increased rate of ADHD in children with PTSD. One study did not provide enough information to be included in the meta-analysis and found no difference in the rate of ADHD in abused children with PTSD compared to those without PTSD.[41] Two pediatric studies each provided 2 separate samples for the meta-analysis.[34,38] Four studies examined the rates of ADHD in adults with and without PTSD, and 3 of these showed increased rates of ADHD in adults with PTSD. All 4 adult studies could be included in the meta-analysis; 1 study provided 2 separate samples.[40] Thus, in total, 11 pediatric and 5 adult samples (16 samples) were available for inclusion in the meta-analysis on risk for ADHD in individuals with PTSD (Table 1). These studies combined included a total of 4,881 subjects (1,422 pediatric and 3,459 adult subjects).

Table 1. Studies Included in Systematic Review and Meta-Analysis (asterisks indicate inclusion in meta-analysis)

Citation	Subjects	ADHD Assessment Method	PTSD Assessment Method	PTSD in ADHD	ADHD in PTSD	Mean (or Median) Age, y	Control Type	Sample	Trauma History	Age at Onset, y	Gender
*Graham-Bermann et al, 2005[21]	160 Head Start preschool students	Indirect ADHD module of TRP	Indirect PTSD module of TRP; indirect PPSSI	Not reported	↓ADHD in PTSD vs violence exposure and population (12% vs 15.9% and 15.1%)	4.62	Normal	Population	Community violence, child maltreatment, intraparental violence	Not reported	Not reported
*Wozniak et al, 1999[22]	128 ADHD probands: 113 nontrauma, 15 trauma; 109 controls: 101 nontrauma, 8 trauma	ADHD module of K-SADS and SCID	PTSD module of K-SADS and SCID	↑PTSD in ADHD vs controls (2% vs 0%), not significant	Not reported	11.0	Normal	ADHD	Physical/weapon threat, physical/sexual abuse, accident, witness event, combat, medical event	Not reported	100% male
*Hurtig et al, 2007[23]	Northern Finland 1986 birth cohort: 105 ADHD; 172 non-ADHD	Direct/indirect ADHD module of K-SADS (child symptoms)	Direct/indirect PTSD module of SCID (lifetime symptoms)	↑PTSD in ADHD vs controls (4.8% vs 0.6% lifetime)	Not reported	(17)	Normal	ADHD	Long term domestic violence/violent acts in neighborhood	Not reported	ADHD group, 72.4% male; PTSD + ADHD group, 100% female
*Smalley, et al, 2007[24]	Northern Finland 1986 birth cohort subset: 188 ADHD, 166 controls	ADHD module of K-SADS-PL	PTSD module of K-SADS-PL	↑PTSD in ADHD vs non-ADHD controls (9.6% vs 0.6% lifetime)	Not reported	(17)	Normal	ADHD	Not reported	ADHD symptoms required before 7, retrospectively reported	ADHD group, 70% male
Lee et al, 2012[25]	224 Korean army recruits after training	K-AADHDS; K-WURS	IES-R-K	↑PTSD in ADHD vs non-ADHD	Not reported	19.8	Normal	ADHD	Combat deployment after training	ADHD measured before training; PTSD measured after training	100% male
*Ruhl et al, 2009[26]	General Dresden population: 31 ADHD, 2,033 non-ADHD	F-DIPS	F-DIPS	↑PTSD in ADHD vs non-ADHD (16.1% vs 5.1% lifetime)	Not reported	(21.5)	Normal	Population	Not reported	ADHD symptoms required before 7, retrospectively reported	100% female
*Biederman et al, 2013[12]	271 ADHD; 230 controls	Direct/indirect ADHD module of K-SADS and SCID (child/lifetime symptoms)	Direct/indirect PTSD module of SCID (lifetime symptoms)	↑PTSD in ADHD probands vs controls (5.2% vs 1.7%); ADHD and ADHD + PTSD; PTSD did not differ in severity of inattentive or hyperactive-impulsive symptoms	Not reported	21.2	Normal	ADHD	Car accident, witness abuse, sexual abuse/rape, physical abuse	ADHD 3.1; PTSD 13 years later	48.5% male; controls, 49% male; ADHD group, 49% male; ADHD + PTSD group, 36% male
Biederman et al, 2014[27]	Longitudinal family study: 867 ADHD and non-ADHD	Direct/indirect ADHD module of K-SADS and SCID (child/lifetime symptoms)	Direct/indirect PTSD module of SCID (lifetime symptoms)	↑PTSD in ADHD and prenatal maternal smoking exposure (14.5% exposed + ADHD, 4.8% unexposed + ADHD, 6.1% exposed + non-ADHD, 1.9% unexposed + non-ADHD)	Not reported	22.0	Normal	ADHD	Not reported	Not reported	58% male
*Kessler et al, 2006[11]	NCS-R population: 3,199; 154 selected for clinical reappraisal	SCID (whole sample); ACDS (clinical reappraisal extrapolated diagnoses)	WHO CIDI 3.0; SCID	↑PTSD in ADHD vs non-ADHD (11.9% vs 3.3% 12-month prevalence)	↑ADHD in PTSD vs non-PTSD (13.4% vs 3.8%, 12-month prevalence)	(31)	Normal	Population	Not reported	ADHD predated the majority of other psychiatric disorders	ADHD group, 61.6% male

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Table 1 (continued). Studies Included in Systematic Review and Meta-Analysis (asterisks indicate inclusion in meta-analysis)

Citation	Subjects	ADHD Assessment Method	PTSD Assessment Method	PTSD in ADHD	ADHD in PTSD	Mean (or Median) Age, y	Control Type	Sample	Trauma History	Age at Onset, y	Gender
*Antshel et al, 2013[28]	186 ADHD; 123 non-ADHD	Direct/indirect ADHD module of K-SADS (child symptoms)	Direct/indirect PTSD module of SCID (lifetime symptoms)	↑PTSD in ADHD vs control (10% vs 1.6% lifetime; 4.2% vs 0% current); ADHD and ADHD + PTSD; PTSD did not differ in severity of inattentive or hyperactive-impulsive symptoms	Not reported	33.9	Normal	ADHD	Not reported	Within ADHD group, PTSD onset 18.3; ADHD 6.9	49% male; controls, 46% male; ADHD group, 53% male; ADHD + PTSD group, 30% male
*Park et al, 2011[29]	Korean National Epidemiological Survey of Psychiatric Disorders: 69 ADHD, 6,012 controls	K-CIDI 2.1; ASRS 1.1	K-CIDI	↑PTSD in ADHD vs non-ADHD (7.2% vs 1.2% lifetime)	Not reported	(38.5)	Normal	Population	Not reported	Not reported	Not reported
*Bernardi et al, 2012[30]	NESARC population: 807 ADHD, 33,846 controls	ADHD module of AUDADIS-IV (child/ lifetime symptoms)	Anxiety disorders module of AUDADIS-IV (lifetime symptoms)	↑PTSD in ADHD vs non-ADHD (21.99% vs 6.02% lifetime)	Not reported	18+	Normal	Population	Not reported	ADHD onset before 18	ADHD group, 58.69% male; general population, 47.64% male
*Scheeringa et al, 2003[31]	62 trauma: 16 PTSD, 46 non-PTSD; 63 controls	Indirect ADHD module of DISC-IV; indirect CBCL	Indirect PTSD SSIORIYC	Not reported	↑ADHD in PTSD vs non-PTSD with trauma vs controls (38% vs 22% vs 14%); not significant	(3.83)	Trauma	Population	Intensive care trauma center, mental health program, pediatric cancer program	Not reported	Not reported
*Scheeringa and Zeanah, 2008[32]	70 preschoolers who survived Hurricane Katrina	Indirect ADHD module of PAPA	Indirect PTSD module of PAPA	Not reported	↑ADHD in PTSD vs non-PTSD (33% vs 17%)	5.1	Trauma	Population	Trapped, separated, displaced, death of pet/loved one, loss of all toys	Majority ADHD onset pre-Katrina, majority PTSD onset post-Katrina	57.1% male; ADHD group, 59% male vs non-ADHD group, 87% male
*Famularo, et al, 1996[33]	117 abused: 41 PTSD, 76 non-PTSD	Direct ADHD module of DICA	Direct PTSD module of DICA	Not reported	↑ADHD in abused + PTSD vs abused + non-PTSD (37% vs 17%)	8.4	Trauma	Population	Child abuse, trauma (taken from parental custody)	Not reported	41% male; PTSD group, 54% male
*McLeer et al, 1994[34]	26 sexually abused recruited from a child abuse treatment facility	Direct/indirect ADHD module of K-SADS-E	Direct/indirect PTSD module of KSADS-E	↑PTSD in ADHD vs non-ADHD (50% vs 36%)	↑ADHD in PTSD vs non-PTSD (55% vs 40%)	9.0	Trauma	Population	Sexual touching with or without force by anyone 5 years or older	Not reported	31% male
*Glod and Teicher, 1996[35]	19 abused and unmedicated: 13 PTSD, 6 non-PTSD	Direct ADHD module of K-SADS (current/lifetime symptoms)	Direct PTSD module of K-SADS (current/ lifetime symptoms)	Not reported	↑ADHD in abused + PTSD vs abused + non-PTSD (38.46% vs 0%)	9.4	Trauma	Population	Physical or sexual abuse	Age at onset of PTSD in ADHD group was 2.9 years	68% male
Kaplow et al, 2008[36]	156 children (time 1); 56 children (time 2)	CBCL	TSCC	Not reported	+Symptom correlation between inattention and dissociative symptoms (0.53)	10.7	Trauma	PTSD	Child sexual abuse	PTSD predated ADHD; both started in childhood	17% male

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Table 1 (continued). Studies Included in Systematic Review and Meta-Analysis (asterisks indicate inclusion in meta-analysis)

Citation	Subjects	ADHD Assessment Method	PTSD Assessment Method	PTSD in ADHD	ADHD in PTSD	Mean (or Median) Age, y	Control Type	Sample	Trauma History	Age at Onset, y	Gender
*Husain, et al, 2008[37]	791 exposed to Bosnian War	CBCL (1991); APS	PTSD Reaction Index; Impact of Event Scale	↑PTSD in ADHD vs non-ADHD (68.8% vs 39.6% by interviewer; 79% vs 64.4% by self report)	↑ADHD in PTSD vs non-PTSD (8% vs 2.5% by interviewer; 6% vs 3% by self report); self report not significant	10.9	Trauma	Population	Violence during Bosnian War	Not reported	49.2% male
*Daud and Rydelius, 2009[38]	40 refugees with traumatized parents	Indirect ADHD module of K-SADS; direct/indirect DICA-R-C	Direct/ indirect DICA-R-C; PTSS-C	↑PTSD in ADHD (89% vs 67%)	↑ADHD in TP + PTSD (55% vs 22%)	12.1	Trauma	Population	Refugee children told of parents' torture experience	Not reported	50% male; ADHD + PTSD group 60% male
*Daud and Rydelius, 2009[38]	40 refugees with nontraumatized parents	Indirect ADHD module of K-SADS; direct/indirect DICA-R-C	Direct/indirect DICA-R-C; PTSS-C	→PTSD in traumatized parents + ADHD (0% vs 3%)	→ADHD in PTSD (0% vs 8%)	12.5	Trauma	Population	Refugee children	Not reported	50% male
Hanson et al, 2012[39]	260 adult soldiers	WHO; ASRS	PCL-M	+Symptom correlation between ASRS hyperactivity-impulsivity score and PTSD avoidance (0.34) and total score (0.30)	+Symptom correlation between ASRS scores and PTSD avoidance (0.37), hyperarousal (0.25), and total score (0.33)	29.0	Trauma	Population	Combat related traumas	Not reported	236 male (90.8%), 24 female (90.2%)
*Gurvits et al, 2000[40]	12 PTSD + childhood sexual abuse (CSA); 9 non-PTSD + CSA	WURS; neurodevelopmental history	CAPS	Not reported	↑ADHD in PTSD vs non-PTSD; + symptom correlation when veteran and CSA sample combined (0.42)	53.2	Trauma	Population	Childhood sexual abuse	ADHD started in childhood; trauma occurred in childhood	100% female
*Gurvits et al, 2000[40]	23 PTSD veterans; 15 non-PTSD veterans	WURS; Neurodevelopmental history	CAPS	Not reported	↑ADHD in PTSD vs non-PTSD; + symptom correlation when veteran and CSA sample combined (0.42)	47.3	Trauma	Population	Combat during Vietnam War	ADHD started in childhood; trauma occurred in adulthood	100% male
*McLeer et al, 1994[34]	23 nonsexually abused children recruited from outpatient psychiatry	Direct/indirect ADHD module of K-SADS-E	Direct/indirect PTSD module of K-SADS-E	↑PTSD in ADHD vs non-ADHD in (14% vs 6%)	↑ADHD in PTSD vs non-PTSD (50% vs 5%)	10.4	Psychiatric	Population	Not applicable	Not reported	35% male
Dykman et al, 1997[41]	109 abused recruited from treatment facilities: 53 PTSD, 53 non-PTSD	Indirect ADHD module of DICA-P; direct ADHD module of DICA	Indirect PTSD module of DICA-P; direct PTSD module of DICA	Not reported	→ADHD in abused + PTSD vs abused + non-PTSD; rates/numbers not provided	(10)	Psychiatric	Population	Sexually and/or physically abused children	Not reported	39% male

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Table 1 (continued). Studies Included in Systematic Review and Meta-Analysis (asterisks indicate inclusion in meta-analysis)

Citation	Subjects	ADHD Assessment Method	PTSD Assessment Method	PTSD in ADHD	ADHD in PTSD	Mean (or Median) Age, y	Control Type	Sample	Trauma History	Age at Onset, y	Gender
*Ford, et al, 2000[42]	Child psychiatry clinic intakes with ADHD, ODD, ADHD + ODD, and adjustment disorder	CDE; diagnostic checklist of *DSM-IV* ADHD criteria; SNAP-IV	CDE; indirect PCL-C/PR	↑Lifetime PTSD in ADHD vs ADHD + ODD (13% vs 8%); ↓lifetime PTSD in ADHD vs ODD and ADHD + ODD (6% ADHD vs 22% ADHD + ODD vs 24% ODD); ↑PCL-C/PR total score in ADHD, ODD, and ADHD + ODD vs AD; intrusive reexperiencing symptoms most strongly associated with ADHD	Not reported	11.5	Psychiatric	ADHD	Victimization trauma, sexual/physical maltreatment	Not reported	44% male
*Lipschitz et al, 1999[43]	74 inpatients	DICA-R	Direct TEQ-A; CPTS-RI; DICA-R	Not reported	Slight ↑ADHD in PTSD vs non-PTSD (33.3% vs 29.2%); not significant	14.8	Psychiatric	Population	Witness/victim of family/community violence, physical/sexual abuse	Not reported	47.3% male
*Henrichs et al, 2012[44]	Dutch forensic psychiatric outpatients: 116 PTSD, 38 non-PTSD	Direct/indirect ADHD module of SCID (lifetime symptoms)	Direct/indirect PTSD module of SCID (lifetime symptoms)	Not reported	↓ADHD in PTSD vs non-PTSD (12.1% vs 94.7%)	34.2	Psychiatric	Population	Physical/sexual/psychological victimization	Not reported	84.4% male; PTSD group was 79% male, non-PTSD group was 20.7% male
Mitchell et al, 2012[45]	55 non-PTSD smokers,; 68 PTSD smokers; recruited from clinics	Direct CAPS; SCID; CAARS	Direct CAPS; SCID; DTS	Not reported	+Symptom correlation between ADHD and PTSD symptoms (0.55); held true for inattentive symptoms and hyperactivity-impulsive symptoms independently	42.2	Psychiatric	PTSD	Combat, physical/sexual abuse, death, car accident, domestic violence, violence	Not reported	53% male (PTSD group 47% male, non-PTSD group 57% male)
*Adler et al, 2004[8]	25 PTSD veterans with PTSD; 22 non-PTSD veterans with panic disorder	Direct ADHD module of K-SADS (child symptoms); *DSM-IV* criteria (current symptoms)	CAPS	Not reported	↑ADHD in PTSD vs panic controls (36% vs 9% as child, 28% vs 5% as adult)	53.5	Psychiatric	PTSD	Military	ADHD predated PTSD in every case; ADHD started in childhood; trauma occurred as adult	100% male

Symbols: ↓ = lower rate, ↑ = higher rate, → = equal rate, + = positive correlation.

Abbreviations: ACDS = Adult ADHD Clinical Diagnostic Scale; ADHD = attention-deficit/hyperactivity disorder; APS = Attention Problem Scale; ASRS = Adult ADHD Self-Report Scale; AUDADIS-IV = Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV; CAARS = Conners Adult ADHD Rating Scales; CAPS = Clinician Administered PTSD Scale; *CBCL = Child Behavior Checklist;* CDE = Clinical Diagnostic Evaluation; CIDI = Composite International Diagnostic Interview; CPTS-RI = Child Posttraumatic Stress Reaction Index; DICA = Diagnostic Interview for Children and Adolescents, -C = child version, -P = parent version, -R = revised; DISC-IV = Diagnostic Interview Schedule for Children-IV; DTS = Davidson Trauma Scale; F-DIPS = German Diagnostic Interview for Mental Disorders; IES-R-K = Impact of Event Scale-Revised-Korean version; K-AADHDS = Korean Adult ADHD Scale; K-CIDI = Korean version of the Composite International Diagnostic Interview; K-SADS = Kiddie-Schedule for Affective Disorders and Schizophrenia, -E = epidemiological version, -PL = Present and Lifetime version; K-WURS = Korean-Wender Utah Rating Scale; NCS-R = National Comorbidity Survey-Replication; NESARC = National Epidemiologic Survey on Alcohol and Related Conditions; PAPA = Preschool Age Psychiatric Assessment; PCL = PTSD Checklist, -C/PR = child/parent forms, -M = military version; PPSSI = Preschool Posttraumatic Stress Symptoms Inventory; PTSD = posttraumatic stress disorder; PTSS-C = Posttraumatic Stress Symptoms for Children; SCID = Structured Clinical Interview for *DSM-IV* Disorders; SES = socioeconomic status; SNAP-IV = Swanson, Nolan, and Pelham-IV questionnaire; SSIORIYC = Semistructured Interview and Observational Record for Infants and Young Children; SWAN = Strengths and Weaknesses of ADHD Symptoms and Normal Behavior; TEQ-A = Traumatic Events Questionnaire-Adolescent version; TRP = Teachers Report Form; TSCC = Trauma Symptom Checklist for Children; WHO = World Health Organization; WURS = Wender Utah Rating Scale.

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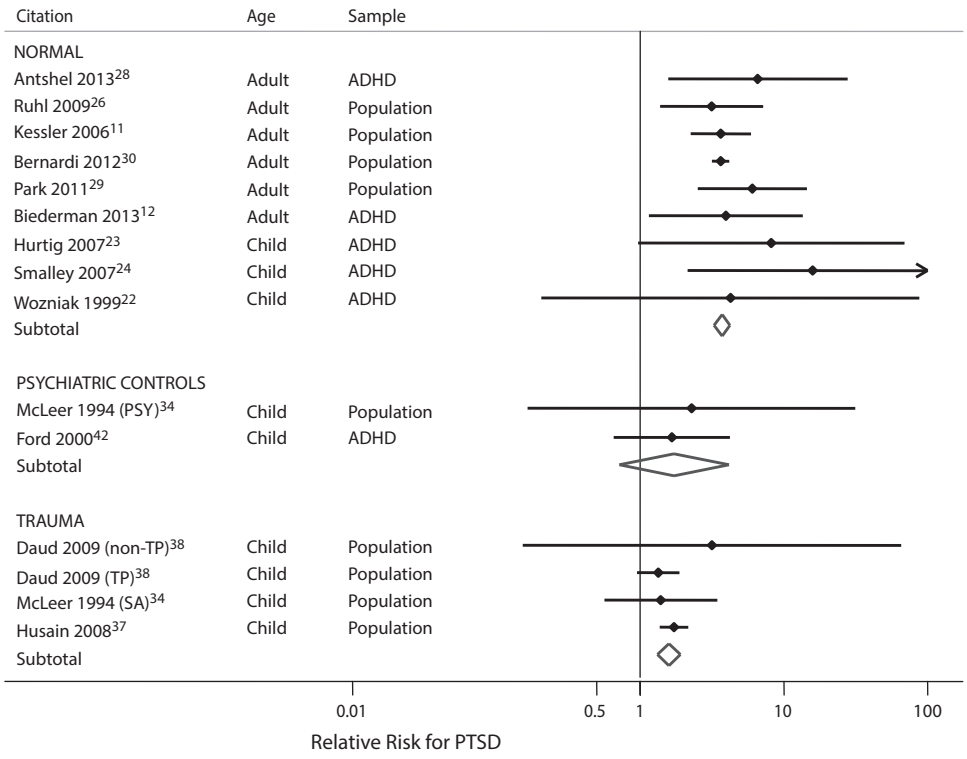
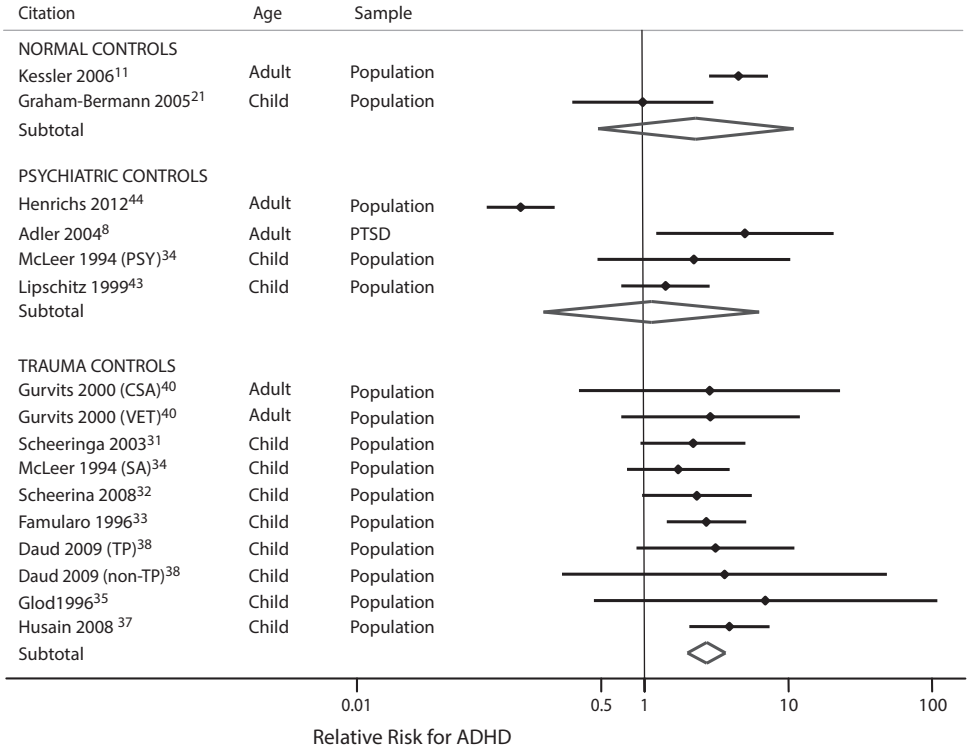
Figure 2. Meta-Analysis of the Relative Risk for PTSD in ADHD (A) and ADHD in PTSD (B)

A. Relative Risk for PTSD in Individuals With ADHD[a]



B. Relative Risk for ADHD in Individuals With PTSD[a]



[a]For each comparison, the dot gives the relative risk and the horizontal line gives the 95% confidence interval. The center of the diamond at the bottom gives the weighted relative risk across all studies, and the width of the diamond gives its 95% confidence interval.

Abbreviations: ADHD = attention-deficit/hyperactivity disorder, CSA = childhood sexual abuse sample, non-TP = sample of refugee children with nontraumatized parents, PSY = psychiatric sample, PTSD = posttraumatic stress disorder, SA = sexually abused sample, TP = sample of refugee children with tortured parents, VET = Veterans sample.

Among all 16 samples from the 13 studies, the pooled relative risk for ADHD in PTSD was positive and significant (RR = 1.7, $t_{13} = 6.6$, $P < .0005$). Overall heterogeneity was high and significant ($I^2_{15} = 87.0\%$, $P < .0005$). Figure 2B shows the forest plot of these results stratified by control group. In the 10 samples with traumatized controls, the pooled relative risk for ADHD in PTSD was statistically significant (RR = 2.1, 95% CI, 1.7 to 2.9; $t_9 = 9.2$, $P < .0005$). Heterogeneity among these samples was low and not significant, suggesting that they were estimating a common relative risk ($I^2_9 = 0.0\%$, $P = .9$). In contrast, the pooled relative risk for ADHD in PTSD was neither statistically significant in the 4 samples that used psychiatric controls (RR = 0.9, 95% CI, −1.0 to 3.9; $t_3 = 1.9$, $P = .16$) nor in the 2 samples that used normal controls (RR = 1.8, 95% CI, −14.9 to 19.7; $t_1 = 1.8$, $P = .32$). Heterogeneity was high and significant in both the psychiatric control samples ($I^2_3 = 93.1\%$, $P < .0005$) and the normal control samples ($I^2_1 = 84.8\%$, $P = .01$). In a separate analysis based on referral status, there was a statistically significant pooled relative risk for ADHD in PTSD in both referred (RR = 1.4, 95% CI, 1.0 to 2.9; $t_{10} = 4.9$, $P = .001$) and nonreferred (RR = 3.1, 95% CI, 2.0 to 4.3; $t_3 = 8.9$, $P = .003$) samples. Meta-regression found no significant effect on relative risk of referral status ($P = .07$), age ($P = .69$), control group ($P = .65$), or mean/median age ($P = .9$). On the other hand, study sample had a significant effect on relative risk ($P < .00005$). Gender could not be included in the meta-regression due to lack of information provided by study authors. In all studies examining ADHD in PTSD, the Egger test for publication bias was not significant ($t = 0.68$, $P = .505$).

Temporality

One pediatric and 5 adult studies reported temporal onset of both disorders, and all 6 reported an earlier ADHD onset compared to PTSD onset.[8,12,25,28,31,40]

Symptom Correlations

One pediatric and 5 adult studies examined correlations between symptoms of PTSD and ADHD, and all showed positive and significant correlations.[11,25,36,39,40,45]

DISCUSSION

Our systematic review and meta-analysis show a robust association between PTSD and ADHD, strongly supporting our study hypothesis. The association was bidirectional in that risk for PTSD was higher in individuals with ADHD compared to those without ADHD and risk for ADHD was higher in individuals with PTSD than those without PTSD. The consistency of the association in referred and nonreferred samples indicates that the findings are not due to referral bias. The results also could not be accounted for by publication bias or unusual results from any one observation.

The highest relative risk was found in studies that examined the risk of PTSD in individuals with ADHD compared to normal controls. In these studies, individuals with ADHD had nearly 4 times the risk of developing PTSD than those without ADHD, strongly supporting the hypothesis that individuals with ADHD are at increased risk for PTSD. While statistical association does not imply causality, the hypothesis that ADHD is an antecedent risk factor for PTSD is supported by the finding that onset of ADHD was consistently earlier than onset of PTSD in all studies examining temporality of the 2 disorders.

Notably, even studies that examined the risk of PTSD in individuals with ADHD using traumatized cohorts found a significantly increased risk of PTSD in those with ADHD. This important finding indicates that the increased risk for PTSD in individuals with ADHD cannot be explained solely by an increased rate of trauma exposure in this population. Additionally, individuals with PTSD had twice the risk of ADHD compared to controls with similar trauma exposure, indicating that the increased rate of ADHD in PTSD is not due solely to trauma exposure, but rather associated with PTSD itself. Taken together, these findings suggest that trauma exposure alone may be necessary but not sufficient to explain the association between ADHD and PTSD. ADHD could reflect another underlying vulnerability factor that increases the risk for developing PTSD after trauma, and traumatized individuals who develop PTSD may have a vulnerability to ADHD symptoms, as well. More work is necessary to examine the potential neurobiological mechanisms underlying this association.

While nearly an equal number of pediatric and adult studies examined the rate of PTSD in ADHD, over twice as many pediatric as adult studies examined the rate of ADHD in PTSD. Due to the small number of overall studies, the analysis of pediatric versus adult samples was not conducted separately in either category. Since mean and median age among studies spanned decades, determining whether the association is stronger at any specific age or developmental stage was not possible. However, when mean or median age was factored into the meta-regression analysis, relative risk of PTSD in ADHD was found to be significantly higher in studies of older subjects. It could be that individuals who continue to struggle with ADHD symptoms as they get older have a particularly high vulnerability to PTSD compared to those whose symptoms improve. More work should help define whether and how age and development affect the association between ADHD and PTSD and explore the possibility that those with persistent ADHD symptoms into adulthood may be particularly vulnerable to PTSD.

The meta-analysis did not reveal a significant association in either direction between ADHD and PTSD in studies using psychiatric controls. This suggests that other psychiatric illnesses could also be associated with increased risk for PTSD or that ADHD increases the risk for developing other psychiatric illnesses besides PTSD. In other words, the association may not be specific to these 2 disorders. However, 1 large study that examined the risk for ADHD in PTSD subjects in a forensic population reported an unusually high rate of ADHD in controls (94%),[44] raising methodological concerns about this particular study. If this

study were to have been excluded, the meta-analysis would have shown a significantly increased risk for ADHD in subjects with PTSD compared to even psychiatric controls ($t_5 = 4.2$, $P = .01$).

Although the reasons for this association between ADHD and PTSD are not entirely clear, several possibilities can be considered. Emerging findings from preclinical, neuroimaging, and genetic research are beginning to provide some interesting clues as to the nature of the vulnerability to PTSD in those with ADHD. Preclinical work in rodents documented that prenatal nicotine exposure leads to both an ADHD-like phenotype[46] as well as to deficits in fear extinction,[47] and fear extinction has been shown to be deficient in PTSD patients.[48,49] Irregularities in dopaminergic neurotransmission and prefrontal cortex dysfunction have been found in preclinical and neuroimaging studies in both ADHD and PTSD.[6,10,50] These findings raise the possibility that abnormalities in specific neural circuits in ADHD may increase the vulnerability for both ADHD and PTSD. Genetic overlap may also explain part of the association between ADHD and PTSD. Both disorders are heritable,[6,51] and genome-wide data has found substantial shared common genetic variation among psychiatric disorders in general.[52] ADHD and PTSD also have common specific genetic risk factors, including polymorphisms in the 3′-untranslated region of the dopamine transporter gene[53,54] and cannabinoid receptor gene.[55] Further research is needed to determine the clinical significance of the genetic and neurobiological underpinnings that are common to ADHD and PTSD. Such research may further delineate vulnerable neural circuits that could guide development of preventive and therapeutic strategies for PTSD.

The literature also shows a consistent positive correlation between symptom severities when PTSD and ADHD coexist. This suggests that when present together, morbidity of the disorders may be linked, possibly due to common neurobiological processes. The association between symptoms also suggests that PTSD symptoms may exacerbate ADHD symptoms and vice versa. In addition, the finding raises the possibility that PTSD may cause an acquired ADHD-like syndrome. This is supported by preclinical work showing that chronic uncontrollable stress impairs working memory and prefrontal cortical function.[50] The same prefrontal cortical regions overlap with those mediating fear extinction in rodents and humans[56,57] and have been shown to be dysfunctional in PTSD patients in the context of fear extinction.[49] Given that PTSD is associated with high levels of functional impairment and disability[58] and that ADHD symptoms could contribute to this dysfunction, further exploration in this area is of great need.

These results should be viewed in light of some limitations. Like all systematic reviews and meta-analyses, we were limited to screening the articles identified with our search criteria. Our analyses of covariates were limited by the information provided by the authors. Methods of included studies were heterogeneous, and our analysis did not account for sample characteristics such as race, ethnicity, socioeconomic status, or sex. Few studies used psychiatric controls, making it difficult to sort out risk conferred by other psychopathological conditions. Additionally, only 2 studies used normal controls to examine the risk for ADHD in individuals with PTSD. While taken together these studies failed to show an association, they had very different designs and findings; more work in this area is needed. Finally, given that ADHD is more prevalent in males and PTSD is more prevalent in females, it would have been interesting to examine how gender affects the association between ADHD and PTSD. Although most studies with 100% female and male samples did find a positive association, we did not have enough information from these articles to include gender in our regression analysis; this is an important area for further exploration.

Despite these limitations, our systematic review and meta-analysis support an association between ADHD and PTSD and indicate that ADHD may be a risk factor for PTSD. These findings have significant clinical, scientific, and public health implications. Clinically, the knowledge that ADHD may be a risk factor for PTSD should encourage clinicians to screen for trauma and PTSD in patients with ADHD. Furthermore, clinicians should be aware that patients with ADHD who are exposed to trauma may be more likely to develop PTSD and should be monitored closely. Clinicians should also be encouraged to screen for ADHD in patients with PTSD, given that ADHD symptoms could contribute to morbidity in this population, and consider treating both disorders when present. Although research on the effect of ADHD medication in patients with PTSD is sparse, preclinical work shows that the α_2 agonist guanfacine may be beneficial for both PTSD and ADHD symptoms in traumatized children.[59] Further research investigating the common neurobiological underpinnings of these disorders may improve our understanding of the link between ADHD and PTSD and guide the use and development of therapeutic strategies. Such research may also define a subtype of PTSD that may respond to unique treatments. From a public health perspective, the increased risk for PTSD in ADHD and for ADHD in PTSD may help guide the development of policy and screening efforts, with the potential to reach broad, at-risk segments of the population.

Drug names: guanfacine (Intuniv, Tenex, and others).

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