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Childhood Abuse and Cognitive Function in a Large Cohort of Middle-Aged Women

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Abstract

Cognitive function at middle age is of particular public health interest, as it strongly predicts later dementia. Children who have experienced abuse subsequently have worse cognitive function than those who have not. However, it remains unclear whether the association of abuse with cognitive function persists into middle age. In 2014–2016, 14,151 women ages 49–69 years who had previously responded to a childhood abuse questionnaire completed a cognitive battery. In models adjusted for childhood socioeconomic status and head trauma, combined physical, emotional, and sexual abuse was associated with lower scores on both Learning/Working Memory (severe abuse, lower scores similar to that observed in women 4.8 years older in our data) and Psychomotor Speed/Attention (severe abuse, lower scores similar to that observed in women to 2.9 years older in our data). Adjustment for adulthood socioeconomic status and health factors (e.g., smoking, hypertension) slightly attenuated associations. In exploratory analyses further adjusted for psychological distress, associations were attenuated. Women exposed versus unexposed to childhood abuse had poorer cognitive function at mid-life. Associations were particularly strong for learning and working memory and were not accounted for by adulthood health factors. Childhood abuse should be investigated as a potential risk factor for cognitive decline and dementia in old age.

Cognitive function at middle age and older is of particular public health interest, as it is a strong predictor of subsequent dementia (Crooks, Lubben, Petitti, Little, & Chiu, 2008; Elias et al., 2000; Kawas et al., 2003; Linn et al., 1995; Tierney, Yao, Kiss, & McDowell, 2005), as well as a risk factor for decline in physical functioning (Elovainio et al., 2009) and death (Sabia et al., 2010). Lower cognitive function in later life is also associated with poorer health in a wide variety of domains (Hartanto, Yong, & Toh, 2019; Shah et al., 2013; Wu, Plassman, Crout, & Liang, 2008), possibly because it is associated with poorer medication management (Stilley, Bender, Dunbar-Jacob, Sereika, & Ryan, 2010), medication non-adherence (Chodosh et al., 2004; Stilley et al., 2010), lower healthcare literacy (Lee & Son, 2018), and poorer health-related coping (Kim & Kang, 2016).

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Conflicts of Interest

None.

Childhood abuse is a common early life stressor that has been linked to reduced cognitive function. US national surveys report high lifetime occurrence of childhood physical abuse (18.1%), emotional abuse (23.9%), and sexual abuse (26.6% for females, 5.1% for males) (David Finkelhor, Shattuck, Turner, & Hamby, 2014; David Finkelhor, Turner, Shattuck, & Hamby, 2015).

Evidence from human and animal studies indicates that dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis resulting from abuse (e.g., elevated glucocorticoids) affects brain development (Ehlert, 2013). Child maltreatment reduces hippocampus volume, increases amygdala volume, and causes alterations to the corpus callosum and neocortex (Martin H Teicher, Samson, Anderson, & Ohashi, 2016). These brain regions play central roles in memory, attention, emotional regulation, language, calculation, spatial reasoning, and sensory perception (Huang et al., 2015). Numerous studies of children and adolescents have found that prior experience of childhood abuse is associated with deficits in working memory, verbal episodic memory, intelligence, processing speed, and executive function (Kavanaugh, Dupont-Frechette, Jerskey, & Holler, 2017; Masson, Bussieres, East-Richard, R-Mercier, & Cellard, 2015; R.-Mercier, Masson, Bussières, & Cellard, 2018; Su, D'Arcy, Yuan, & Meng, 2019), with few contradictory studies (Dunn et al., 2016). However, it is largely unknown whether lower cognitive function associated with childhood abuse persists into middle age (35 to 65 years) or later (>65 years).

In addition to the possibility that lower cognitive function that developed in childhood may persist into adulthood, differences in cognitive function by childhood abuse exposure may also emerge in adulthood, due to adulthood exposure to cognitive risk factors. Childhood abuse leads to emotional dysregulation, poor self-esteem, ineffective coping, diminished social competence, poor self-efficacy, and impulsivity, as well as physiological dysregulation in hormonal stress response, the serotonin and oxytocin systems, and immune function (Michael D. De Bellis & Zisk, 2014; Hallowell et al., 2019; McCrory, Ogle, Gerin, & Viding, 2019; Sachs-Ericsson, Medley, Kendall-Tackett, & Taylor, 2011). Partly as a result, childhood abuse is associated with adulthood risk factors for poor cognitive function, including lower socioeconomic status (Zielinski, 2009), smoking (Debette et al., 2011; Jun et al., 2008), high body mass index (BMI)(Anstey, Cherbuin, Budge, & Young, 2011), low physical activity (Felitti et al., 1998), diabetes (Gregg et al., 2000; J. W. Rich-Edwards et al., 2010), high blood pressure (Riley, Wright, Jun, Hibert, & Rich-Edwards, 2010), heart disease (Lang et al., 2008; Janet W. Rich-Edwards et al., 2012) and stroke (Janet W. Rich-Edwards et al., 2012). Thus, it possible that lower adulthood socioeconomic status or worse adulthood health and health behaviors in persons exposed to childhood abuse could lead to cognitive decline in middle and old age, regardless whether childhood cognitive function was altered.

Studies of adults have generally found lower cognitive function in persons exposed to childhood neglect, but have not found differences in cognitive function among those exposed to physical or sexual abuse, although studies have been limited by inadequate assessments of abuse, low prevalence of reported abuse (likely reflecting inadequate assessment), or lack of measurement of abuse severity (Danese et al., 2017; Geoffroy, Pinto Pereira, Li, & Power, 2016; Nikulina & Widom, 2013). Only three studies have examined cognitive function in

older middle age (50 to 65 years) or old age (>65 years) in association with childhood abuse. The largest study, the Irish Longitudinal Study on Ageing (n=6,912), measured multiple aspects of cognitive function (e.g., visual memory, executive function) in association with retrospectively reported childhood sexual abuse and found *better* global cognitive function and immediate word recall in participants who reported childhood sexual abuse versus those who did not, and no differences in other cognitive measures (Feeney, Kamiya, Robertson, & Kenny, 2013). However, possible reporting bias was suggested by the unexpected association of abuse with higher childhood and adulthood socioeconomic status, which may be due to greater willingness to acknowledge abuse among persons with higher socioeconomic status in this sample, particular as participants were not asked about specific acts, but rather were asked to characterize their experiences as "abuse" (e.g., "were you ever sexually abused by either of your parents?"). A second study, using a random sample of Canadians (n=1,282), reported a prevalence of only 2% of either sexual abuse or severe physical abuse ($n_{exposed}$=26) and found no differences in cognitive function by abuse history (Ritchie et al., 2009; Ritchie et al., 2011). Finally, a study of Aboriginal and Torres Strait Islander Australians ages 60–92 years (n=296), found an association of abuse exposure, assessed by a composite abuse measure, with higher risk of dementia and Alzheimer's disease (Radford et al., 2017).

In the present study, we addressed limitations in the existing literature, including few studies of older persons, inadequate measures of abuse, and lack of assessment of potentially mediating health-related factors. We used data from a large cohort of women at ages 49–69 years, with validated, multi-item measures of childhood abuse that capture a range of abuse severity. We examined the association of childhood physical, emotional, and sexual abuse with several domains of cognitive function, including simple psychomotor reaction time, attention, working memory, executive function, and learning. These domains are commonly affected in aging and in Alzheimer's Disease, the most common form of dementia, thus are of particular relevance to our aging cohort.

We further investigated whether a possible association of childhood abuse with cognitive function was partly accounted for by adulthood socioeconomic status or adulthood cognition-related health factors, including smoking, body mass index (BMI), physical activity, and physician-diagnosed history of diabetes, high blood pressure, myocardial infarction, and stroke. Childhood abuse may also be associated with lower cognitive function in middle and old age due to risk factors that co-occur with or precede abuse (Danese et al., 2017), including low parental educational attainment, low childhood socioeconomic status, and childhood head trauma. We therefore conducted analyses adjusted for these factors, as well as sensitivity analyses restricted to participants with high childhood socioeconomic status.

In addition, psychological distress, including depression and posttraumatic stress disorder (PTSD), has been associated with lower cognitive function (Diniz, Butters, Albert, Dew, & Reynolds, 2013; Sumner et al., 2017), and is more prevalent in persons exposed to childhood abuse (Lindert et al., 2014). However, the relation between psychological distress and cognitive function in adulthood is complex, as risk of distress is greater in persons with lower cognitive function or cognitive decline (David, Zammit, Lewis, Dalman, & Allebeck,

2008; Gilbertson et al., 2006; Kremen et al., 2007). In addition, depression, PTSD, and reduced cognitive function could be common consequences of child-abuse-related brain alterations (Saleh et al., 2017). Finally, there is evidence that depression is an early indicator, or prodromal feature, of cognitive decline leading to dementia (Bennett & Thomas, 2014; Brommelhoff et al., 2009). We therefore conducted exploratory analyses examining the association of childhood abuse with cognitive function further adjusted for adulthood depression and PTSD symptoms, and separately among women who did not have probable depression or PTSD symptoms.

We hypothesized that childhood abuse would be associated with worse cognitive function, and that women exposed to the most severe abuse, especially women who experienced high levels of physical, emotional, and sexual abuse, would have the poorest cognitive function.

METHODS

Participants.

The Nurses' Health Study II enrolled 116,429 female U.S. nurses in 1989 and has followed them with biennial health questionnaires (Bao et al., 2016). In 2001, a supplemental violence questionnaire queried experiences of childhood abuse. From 2014 to 2016, 40,082 women who had returned the violence questionnaire and a follow-up questionnaire, and with known email addresses, were invited to complete an online cognitive battery. 14,151 women completed this assessment (35% response rate). Exposure to childhood abuse was similar in cognitive battery responders and non-responders: 22.9% of both responders and non-responders experienced severe physical/emotional abuse, and 9.2% of non-responders versus 9.8% of responders experienced moderately frequent or frequent sexual abuse. Prior comparisons of responders and non-responders to the cognitive battery have found them extremely similar in age, childhood and adulthood socioeconomic indictors, and health behaviors, including smoking, BMI, and physical activity (Sumner et al., 2017). The study protocol was approved by the institutional review board of the Brigham and Women's Hospital. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Measures

Cognitive function.—Cognitive function was measured in 2014–2016 using a self-administered online battery, the Cogstate Brief Battery (Fredrickson et al., 2010). The Cogstate Brief Battery is sensitive to cognitive impairment associated with aging and neurodegenerative conditions. Scores differentiate healthy persons from those with mild cognitive impairment and Alzheimer's Disease (Y. Y. Lim et al., 2012; P. Maruff et al., 2009), and predict Alzheimer's Disease pathology in non-cognitively impaired persons (Darby et al., 2011). The Cogstate Brief Battery includes four tasks designed to assess simple psychomotor reaction time, attention, working memory, learning, and executive function. Each Cogstate task involves a response to a playing card initially displayed face down on a green background. The Detection task, which captures reaction time and measures psychomotor function, requires the respondent to press the "Yes" key as soon

as the card is turned face up. The Identification task, a choice reaction time task which measures visual attention, executive function, and vigilance, requires a “Yes” response if the card is red and a “No” response if the card is black. The One Card Learning task, which measures visual learning and memory, requires the respondent to press “Yes” if the card has appeared in the test previously and “No” if it has not. The One-back task, which measures working memory, attention, and executive function, requires the respondent to press “Yes” if the card is the same as the previous card. Following published guidelines (Hammers et al., 2012), we $\log_{10}$ transformed mean response times for correct trials for the Detection, Identification, and One Back tasks, and arcsine transformed the square root of the proportion of correct responses for the One Card Learning task. We then standardized scores on individual tasks and summed the resulting z-scores to create two composite scores.

Research suggests that composites formed from scores on Cogstate tasks may be more sensitive measures of cognitive function than individual task scores (Yen Ying Lim et al., 2013; Paul Maruff et al., 2013); this approach is consistent with neuropsychological models that highlight the benefit of using composite scores in clinical research (Crane et al., 2008; Nuechterlein et al., 2008). Following this prior work, the One Card Learning and One Back scores were summed to create a Learning/Working Memory composite, and the Detection and Identification scores were summed to create a Psychomotor Speed/Attention composite. The Cogstate has good test-retest reliability (coefficient of variation range=0.01–0.09 for the 4 tasks)(Fredrickson et al., 2010), construct validity, and criterion validity (Hammers et al., 2012). The composite scores also have good test-retest reliability across 4 months (Learning/Working Memory, intra-class correlation [ICC]=0.95; Psychomotor Speed/Attention, ICC=0.90)(Paul Maruff et al., 2013). The composite scores are sensitive indicators of early cognitive deficits (P. Maruff et al., 2009) and discriminate persons with mild cognitive impairment and Alzheimer’s Disorder from healthy controls with moderate-to-large differences (Paul Maruff et al., 2013).

Childhood abuse.—Childhood physical/emotional abuse up to age 11 was assessed in 2001 with 5 questions from the Physical/Emotional Abuse Subscale of the Childhood Trauma Questionnaire (Bernstein et al., 1994). Frequency of experiencing cruel punishments, being yelled and screamed at, insulted, punished with a belt or other hard object, and being hit so hard it left bruises or marks were queried. Responses were summed according to scoring recommendations for the measure, and the resulting continuous variable was divided approximately into quartiles to investigate a possible dose-response relation of severity of abuse with cognitive function (Murray A. Straus, 1990). Childhood sexual abuse was ascertained with four questions from the Sexual Maltreatment Scale of the Conflict Tactics Scales (M. A. Straus, Hamby, Finkelhor, Moore, & Runyan, 1998), querying unwanted or forced sexual touching up to age 11 years and at ages 11–17 years. Each question has response options: 0: never, 1: once, and 2: more than once. Points were summed across responses. Women were considered to have no sexual abuse if they responded “never” to each question. One or two points was coded as “infrequent abuse”, 3–4 points as “moderately frequent abuse”, and ≥5 points was considered “frequent” sexual abuse. As children exposed to both physical/emotional and sexual abuse may have worse health outcomes than children exposed to a single type (D. Finkelhor, Ormrod, &

Turner, 2007), following prior work (Roberts, Lyall, Rich-Edwards, Ascherio, & Weisskopf, 2013), we summed the two measures to create a combined physical, emotional, and sexual abuse measure. Because few women were exposed to the most severe levels of abuse, we combined the top two categories to create a measure that ranged from 0: no abuse to 5: severe combined abuse.

Demographic and health factors.—Childhood socioeconomic status indicators were assessed in 2005 and included parents' education, occupation, and home ownership. Parents' education in participant's infancy was coded separately for mother and father as: <9 years of school, 1–3 years high school, 4 years high school, 1–3 years college, 4 or more years college. Parents' occupation during participant's infancy was coded separately for mother and father as: unskilled laborer or service, blue collar (sales, service, skilled worker, machine operator, or military), farming, professional or manager, or don't know/missing (3.2%). Parents' home ownership in participant's infancy was coded as yes or no. Childhood head trauma was assessed in 2001 with the question, "Have you ever suffered from head trauma with loss of consciousness?" Age of occurrence was queried. We considered any loss of consciousness before age 20 as exposure to childhood head trauma.

For adulthood demographic and health factors, we included measurements closest to the time of the cognitive assessment. Adulthood socioeconomic status was measured with three variables. Participants reported their current perceived social standing in both the community and in the U.S. in 2001 (Giatti, Camelo Ldo, Rodrigues, & Barreto, 2012). Level of education completed by spouse/partner was queried in 1999 and coded as: <high school, high school, 2-year college, 4-year college, graduate school, not applicable, or missing (2.9%). Marital status was queried in 2013. Self-identified race/ethnicity was coded as White, Black/African-American, Asian, or other races. BMI was calculated in kg/m^2 from self-reported height in 1989 and weight in 2013. Self-reported weight has good validity in this cohort (Rimm et al., 1990). Smoking in 2013 was coded as never, former, or current. Physical activity in 2013 was calculated from self-reported time spent per week in 10 different activities (e.g, jogging, lap swimming) and was coded as <3, 3−<9, 9−<18, 18−<27, or ≥27 metabolic equivalent hours per week (METS/week). History of physician-diagnosed type 2 diabetes, high blood pressure, myocardial infarction, and stroke was queried biennially, 1989–2013. Participants were considered to have a history of these disorders if they had ever endorsed them. Depressive symptoms were assessed in 2013 with the Center for Epidemiologic Studies Depression Scale (CESD-10) and dichotomized, with ≥10 symptoms indicating probable depression (Andresen, Malmgren, Carter, & Patrick, 1994). Current PTSD symptoms were assessed in 2008 with Breslau's Short Screening Scale for DSM-IV PTSD (Breslau, Peterson, Kessler, & Schultz, 1999).

Analyses—We examined the association of demographic and health factors with combined childhood physical, emotional, and sexual abuse. Next, to ascertain the association of childhood abuse with cognitive function, we fit a generalized estimating equation with a normal distribution and an identity link with each of the Learning/Working Memory and Psychomotor Speed/Attention composites as dependent variables, with: 1) childhood physical/emotional abuse; 2) childhood sexual abuse; and 3) combined physical, emotional,

and sexual abuse as independent ordinal variables in separate models. The reference groups were, respectively, women who had experienced: 1) the lowest quartile of physical/emotional abuse; 2) no sexual abuse; and 3) the lowest quartile of physical/emotional abuse and no sexual abuse. To test whether more abuse was associated with worse cognitive function across the range of abuse, we calculated tests of trend by fitting models with abuse as a continuous variable. The base model adjusted for age at cognitive assessment and race/ethnicity. A second model further adjusted for potential childhood confounders, including socioeconomic indicators, e.g., parents' education, parents' occupation, and parents' home ownership, and childhood head trauma. To separately examine the extent to which adulthood socioeconomic status and health factors might account for a possible association between childhood abuse and cognitive function, we fit two additional models, further adjusted for: 1) indicators of adulthood socioeconomic status, including husband's education, the perceived social standing scales, and marital status; and 2) adulthood socioeconomic status and BMI, smoking, and exercise, and history of high blood pressure, diabetes, and myocardial infarction. Finally, we fit a model with adulthood socioeconomic status, health factors, and depressive symptoms and PTSD symptoms, and separately estimated the association of child abuse with cognitive function in the subsample of women without probable depression or PTSD symptoms.

High childhood socioeconomic status is associated with cognitively-protective environmental factors, such as high-quality schools (Quinn, 2015), low exposure to environmental pollutants (Hajat et al., 2013), and cognitively enriched home environment (Sarsour et al., 2011). High socioeconomic status may also be protective against childhood adversities such as abuse. We therefore conducted additional analyses examining associations of child abuse with cognitive function restricted to women with high childhood socioeconomic status (defined as having a parent with a 4-year college degree, or a parent employed as a manager or professional).

As cognitive decline related to aging is a well-understood phenomenon, following other studies of environmental exposures (Power et al., 2011; Weuve et al., 2009), we also report associations of child abuse with cognitive function in terms of years of age. We estimated cognitive differences associated with one additional year of age by fitting separate models for Learning/Working Memory and Psychomotor Speed/Attention with age as the independent variable, adjusted for race. Next we divided the beta estimate associated with child abuse by the beta estimate associated with one year of age, separately for the two cognitive composites. Models were fit using PROC GENMOD in SAS 9.4.

RESULTS

The sample was mostly white (97.7%), with a mean age of 61.2 years (range=49 to 69 years). Women who experienced higher levels of childhood physical/emotional abuse were more likely to experience frequent sexual abuse. Among women who reported severe physical/emotional abuse, 14.4% reported frequent sexual abuse, compared to 1.4% of women who reported no physical/emotional abuse. Women exposed to childhood abuse were more likely to have indicators of lower socioeconomic status in both childhood and adulthood (Table 1). For example, only 13.2% of women with no combined physical,

emotional, or sexual abuse had mothers with less than high school education, while 26.9% of women with severe abuse had mothers with less than high school education. Each indicator of adulthood socioeconomic status was lower in women exposed to severe abuse versus women unexposed to abuse (e.g., 29.6% of women with no abuse had husbands with <4 years of college education, versus 33.7% of women exposed to severe abuse). In addition, women who experienced childhood abuse were far more likely to report childhood head trauma (no abuse, 5.4% versus severe abuse, 13.7%).

Women with versus without histories of childhood abuse had higher prevalence of cognition-related health risk factors in adulthood. For example, 36.3% of women severely abused had BMI≥30 kg/m^2, indicating obesity, versus 22.8% of women with no abuse history (Table 1). Women with severe abuse versus those with no abuse had higher prevalence of smoking (4.5% versus 2.6%), low physical activity (11.9% versus 9.4%), and history of physician-diagnosed high blood pressure (45.3% versus 35.4%), diabetes (2.3% versus 1.0%), and myocardial infarction (9.6% versus 6.0%).

In models adjusted for age and race, moderate and severe physical/emotional abuse was associated with lower scores on the Learning/Working Memory composite (p-trend<0.0001, Table 2, Model 1a). Further adjustment for childhood socioeconomic status and childhood head trauma slightly attenuated the association, although they remained strong (age and race adjusted, β-$estimate_{severe\ abuse}$= −0.10, 95% CI=−0.14, −0.05; further adjusted, β-$estimate_{severe\ abuse}$= −0.09, 95% CI=−0.13, −0.05, p-trend<0.0001, Table 2, Model 2a). Each additional year of age was associated with lower Learning/Working Memory scores (β-estimate= −0.03) and lower Psychomotor Speed/Attention scores (β-estimate= −0.04). In models adjusted for childhood socioeconomic status, severe physical/emotional abuse (the top quartile) was associated with a lower Learning/Working Memory score similar to those observed in women 3.3 years older. Moderate abuse (the third quartile) was associated with a lower score similar to those observed in women 1.6 years older. Childhood physical/emotional abuse was also associated with lower Psychomotor Speed/Attention scores, but this difference did not reach statistical significance (age and race adjusted, β-estimate= −0.03, 95% CI=−0.08, 0.03, p-trend=0.08, Table 2, Model 1b). Further adjustment for adulthood socioeconomic status and health factors very slightly attenuated associations of child physical/emotional abuse with Learning/Working Memory, but did not change associations with Psychomotor Speed/Attention (Table 2, Models 3 & 4).

Similarly, childhood moderately frequent and frequent sexual abuse was associated with lower scores on Learning/Working Memory (p-trend=0.006) equivalent to 1.4 and 2.8 additional years of age, respectively, in models adjusted for age, race, and childhood socioeconomic status (Table 3, Model 2a). Further adjustment for childhood socioeconomic status did not notably alter associations, compared with the model adjusted only for age and race (age and race adjusted, β-estimate= −0.11, 95% CI=−0.17, −0.04; further adjusted, β-estimate= −0.10, 95% CI=−0.17, −0.04, Table 3, Model 1a). Sexual abuse was associated with lower Psychomotor Speed/Attention scores at borderline statistical significance (p-trend=0.05, Table 3, Model 1b). Further adjustment for: 1) childhood socioeconomic status and head trauma, 2) adulthood socioeconomic status, and 3) adulthood cognition-related health factors slightly attenuated associations in women exposed to infrequent or moderately

frequent abuse, but no attenuation was observed in women exposed to frequent sexual abuse (Table 3, Models 2, 3 & 4).

Combined childhood emotional, physical, and sexual abuse was associated with lower cognitive function on both composites in an approximately monotonic fashion, in models adjusted for age, race, and childhood socioeconomic status (p-trend<0.001 for both, Figure 1; Supplemental Table 1, Model 2). For comparison, the Figure 1 shows the association of one additional year of age with each composite. Severe combined abuse was associated with an effect equivalent to that observed in women 4.8 years older on the Learning/Working Memory composite (-estimate=−0.13, 95% CI=−0.19, −0.07) and 2.9 years older on the Psychomotor Speed/Attention composite (-estimate=−0.11, 95% CI=−0.18, −0.04). Adjustment for adulthood socioeconomic status and adulthood health very slightly attenuated associations of combined abuse with both the Learning/Working Memory and the Psychomotor Speed/Attention construct (Supplemental Table 1, Models 3 & 4).

In exploratory analyses further adjusted for adulthood depressive and PTSD symptoms, the association of physical/emotional abuse with Learning/Working Memory was attenuated yet remained statistically significant (severe abuse, -estimate=−0.05, 95% CI=−0.10, −0.02, p<0.05; p-trend=0.01). The association of childhood sexual abuse with Learning/Working Memory was attenuated and no longer statistically significant. In analyses of combined physical, emotional, and sexual abuse, associations were attenuated but remained substantial (Learning/Working Memory: severe abuse, -estimate=−0.08, 95% CI=−0.13, −0.02, p-trend=0.004; Psychomotor Speed/Attention: severe abuse, -estimate-0.07, 95% CI=−0.14, 0.01, p-trend=0.01). In the subsample of women with no probable depression or PTSD symptoms (n=8,331), child abuse was strongly associated with lower cognitive function (severe combined abuse, Learning/Working memory -estimate=−0.09, 95% CI=−0.19, 0.00, p-trend=0.008; Psychomotor Speed/Attention -estimate=−0.13, 95% CI=−0.25, −0.01, p-trend=0.003, Supplemental Table 2).

In the sub-sample of women with high childhood socioeconomic status (defined as having a parent with a 4-year college degree, or a parent employed as a manager or professional, n=5,498), associations of childhood abuse with cognitive function were similar to associations in the whole sample (severe combined abuse: Learning/Working Memory -estimate=−0.14, 95% CI= −0.23, −0.04, p-trend<0.0001; Psychomotor Speed/Attention -estimate=−0.10, 95% CI= −0.22, 0.02, p-trend=0.02).

DISCUSSION

We found that women exposed to childhood physical, emotional, and sexual abuse had poorer cognitive function in mid-life than women without abuse exposure, with particularly strong associations with learning and working memory. We observed an approximately monotonic relationship, where women exposed to more severe abuse had lower cognitive function than women exposed to less severe abuse. Potential childhood confounders, including socioeconomic indicators and head trauma, accounted for very little of the association of abuse with cognitive function. Abuse also remained associated with lower cognitive function in the subset of women with college-educated or professional parents,

suggesting that lower childhood socioeconomic status among women exposed to abuse was not driving the associations we found.

We examined a broad range of cognition-related health factors as possible mediators of the association between childhood abuse and cognitive function at middle age and found that these factors accounted for only a small part of the associations. In exploratory models further adjusted for adulthood psychological distress, associations of child abuse with cognitive function were greatly attenuated, although in the subsample of women with no significant distress, the association of abuse with cognitive function remained strong. We cannot determine from our study the extent to which: 1) child abuse causes distress that then leads to decreased cognitive function; or 2) distress and cognitive function are associated because they are common outcomes of child abuse; or 3) risk of distress is increased due to lower cognitive function in women who have experienced abuse. Nonetheless, findings in the subsample of women with no indicators of psychological distress suggest that other mechanisms aside from distress are also involved in the association.

Prior studies have similarly found poorer working memory in younger adults with child abuse histories. A meta-analysis of 17 studies (n=1,416 persons with psychiatric disorders, mean age=8 to 40 years) found the largest differences associated with childhood abuse were in working memory (g=−0.56), and the smallest in processing speed (g=−0.21), mirroring our results (R.-Mercier et al., 2018). While there is much overlap in brain regions that subserve different cognitive functions, some regions play larger roles in specific types of cognitive functions. For example, learning tasks are heavily dependent on temporal regions of the brain, while working memory and executive function (e.g., planning and coordination of actions) are more dependent on frontal cortical regions and the deeper brain structures that are linked to those, and the hippocampus contributes to both. Effects of exposures that adversely affect the brain can sometimes affect brain regions broadly, leading to more global effects on cognition. Studies examining brains of children exposed and unexposed to abuse suggest that child abuse affects many regions of the brain, including ones particularly relevant for working memory, like the prefrontal and cingulate cortices and the hippocampus, but also other regions like the temporal, parietal, and occipital lobes, amygdala, and cerebellum (De Brito et al., 2013; Hanson et al., 2013; Hanson et al., 2012; Hanson et al., 2010; Hart & Rubia, 2012; Martin H. Teicher, Anderson, & Polcari, 2012). In addition, it is not known whether brain differences related to abuse found in children persist into adulthood, as few studies have examined persons at middle age or older.

It is also possible that childhood abuse is an indicator of early life or genetic factors that lead to lower cognitive function. A study examining cognitive function at 38 years found that adjustment for maternal IQ (measured at child age 3 years) greatly attenuated the association of childhood abuse with cognitive function (Danese et al., 2017). These findings are also consistent with intergenerational transmission of childhood abuse, whereby both the mother and the child experience abuse and subsequent cognitive decrements.

Thus, childhood abuse and cognitive function in middle age may be associated through multiple pathways. First, the extreme psychological stress of childhood abuse may cause alterations to the developing brain that reduce cognitive function across the lifecourse (M.

D. De Bellis, 2001; De Brito et al., 2013; Hanson et al., 2013; Hanson et al., 2012). Second, higher prevalence of adulthood psychological distress in persons exposed to childhood abuse may lead to lower cognitive function. Third, exposure to childhood abuse and genetic risk for lower cognitive function may become correlated across generations, as parents with lower cognitive function may be more likely to be perpetrators of childhood abuse (Crandall, Deater-Deckard, & Riley, 2015; Deater-Deckard, Wang, Chen, & Bell, 2012; Johnston, Mash, Miller, & Ninowski, 2012; Mokrova, O'Brien, Calkins, & Keane, 2010) or children with poor cognitive function may be at elevated risk for abuse (Dubowitz et al., 2011; Jones et al., 2012; Spencer et al., 2005; Sullivan & Knutson, 2000).

Our study has several limitations. Our sample was comprised of female nurses who were predominantly white. Compared with the US population, our sample was better educated (US Census Bureau, 2017), less likely to smoke (Hasin & Grant, 2015), and less likely to be obese (Hales, Carroll, Fryar, & Ogden, 2020). Therefore, our results may not be generalizable. The response rate to the cognitive assessment was modest, although no substantive differences emerged in comparisons of responders and non-responders. Some potential adulthood mediators were collected several year prior to the cognitive assessments. Thus, we may have underestimated the extent to which adulthood factors, including socioeconomic status, health factors, depression, and PTSD, mediated the association of childhood abuse with cognitive function. Childhood abuse was queried retrospectively at ages 36–56 years; therefore, faulty recall may have lead to misclassification of abuse. However, we assessed cognitive function and childhood abuse 10 years apart, which would make priming unlikely. Thus, misclassification of abuse may be unrelated to later cognitive function; non-differential misclassification would typically bias associations toward the null hypothesis. Our study also has significant strengths. We used validated measures of child abuse in a large sample of middle-aged women. The childhood abuse measures captured sexual as well as physical and emotional abuse, and the spectrum of abuse from mild to severe. We accounted for multiple childhood and adulthood socioeconomic and health factors as potential confounders and mediators, and the cohort was large enough to enable us to examine associations in the stratum of women with high childhood SES.

We found the strongest associations between childhood abuse and the Learning/Working Memory composite. Lower scores on memory tests (Kawas et al., 2003; Tierney et al., 2005) and memory decline (Chen et al., 2001) have been particularly predictive of subsequent Alzheimer's Disease diagnosis, compared with other cognitive measures, in prospective studies. In addition, the Cogstate working memory tasks best distinguished healthy controls from subjects with mild cognitive impairment and dementia in a validation study (Hammers et al., 2012). Together, these prior findings and the results of the present study suggest that childhood abuse should be investigated as a potential risk indicator for cognitive decline, mild cognitive impairment, and dementia in old age. Additionally, the causal structures underlying the association of childhood abuse with cognitive function, particularly regarding the role of psychological distress, must be better understood, to facilitate intervention and prevention.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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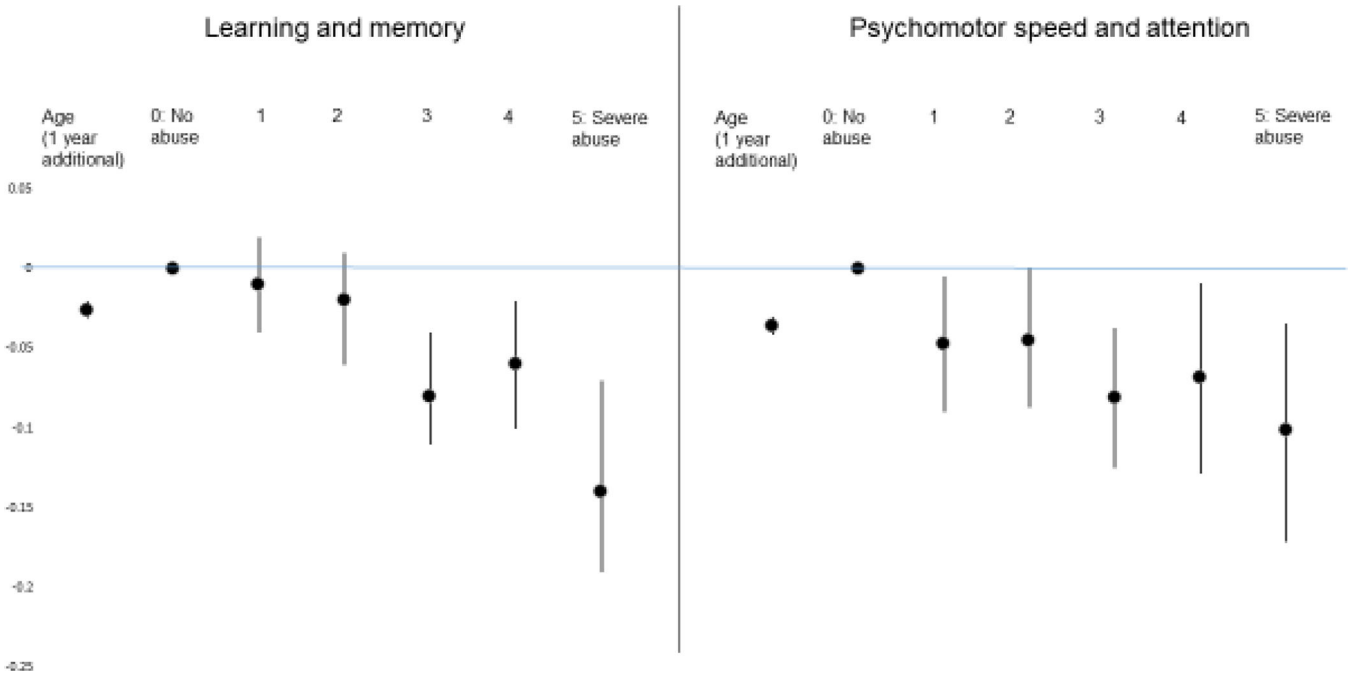

Figure: Association of combined physical, emotional, and sexual abuse with cognitive function in middle age (n=13,975), adjusted for age, race, and childhood factors, Nurses' Health Study II, 2014–2016.

Associations of cognitive function with age were estimated in models adjusted for race.

Table 1:

Demographic and health factors by combined physical, emotional, and sexual childhood abuse, Nurses' Health Study II, n=13,984

		0: no abuse	1	2	3	4	5: severe abuse
		n=3668	n=3102	n=2723	n=2630	n=1122	n=739
Age at cognitive assessment (years)	Mean (SD)	61.2 (4.7)	61.2 (4.7)	61.1 (4.6)	61.1 (4.5)	61.3 (4.4)	61.3 (4.3)
Race							
White	% (n)	98.5 (3614)	98.2 (3047)	97.8 (2664)	97.3 (2558)	97.3 (1092)	94.3 (697)
Black	% (n)	0.2 (7)	0.4 (13)	0.7 (18)	0.7 (19)	0.5 (6)	2.2 (16)
Asian	% (n)	0.8 (31)	1.1 (35)	0.9 (24)	1.2 (32)	1.3 (15)	1.8 (13)
Parental education							
Mother, <high school	% (n)	13.2 (483)	16.2 (501)	18.4 (502)	19.5 (513)	23.3 (261)	26.9 (199)
Father, <high school	% (n)	19.7 (722)	23.8 (737)	25.6 (697)	27.3 (717)	29.2 (328)	34.5 (255)
Parents owned home	% (n)	53.8 (1972)	50.7 (1573)	50.7 (1380)	48.2 (1268)	47.0 (527)	48.0 (355)
Parental occupation, unskilled laborer	% (n)	9.2 (336)	9.7 (302)	10.5 (286)	11.4 (301)	14.3 (160)	15.0 (111)
Childhood head trauma	% (n)	5.4 (197)	6.8 (212)	7.3 (198)	7.4 (195)	10.4 (117)	13.7 (101)
Perceived social standing in the US, 2001†	% (n)	3.7 (1.2)	3.8 (1.3)	3.8 (1.2)	3.9 (1.3)	3.9 (1.3)	4.1 (1.4)
Perceived social standing in the community, 2001†	% (n)	3.9 (1.5)	3.9 (1.5)	4.0 (1.5)	4.1 (1.6)	4.1 (1.6)	4.3 (1.7)
Husband's education, <4 years college, 1999	% (n)	29.6 (1087)	31.5 (977)	31.7 (862)	30.3 (797)	30.8 (346)	33.7 (249)
Currently married, 2013	% (n)	80.4 (2949)	79.0 (2452)	78.2 (2129)	75.1 (1976)	71.3 (800)	69.6 (514)
Body mass index, 2013	% (n)						
<25 kg/m^2	% (n)	46.0 (1688)	45.4 (1408)	43.4 (1181)	41.2 (1084)	37.3 (419)	34.1 (252)
25 to <30 kg/m^2	% (n)	29.8 (1093)	28.3 (878)	29.2 (796)	29.5 (777)	29.9 (336)	28.1 (208)
≥30 kg/m^2	% (n)	22.8 (837)	25.3 (786)	26.3 (715)	28.0 (736)	30.9 (347)	36.3 (268)
Smoking, 2013	% (n)						
Never	% (n)	71.0 (2603)	68.4 (2121)	66.3 (1804)	60.9 (1601)	59.1 (663)	56.0 (414)
Former	% (n)	26.3 (966)	28.4 (880)	30.8 (838)	35.1 (924)	36.6 (411)	39.4 (291)
Current	% (n)	2.6 (95)	3.2 (98)	2.9 (79)	3.9 (102)	4.3 (48)	4.5 (33)
Exercise, <3 metabolic equivalent hours, 2013 (METS)/ week	% (n)	9.4 (345)	9.7 (302)	10.1 (275)	10.2 (269)	11.9 (134)	11.9 (88)
History of high blood pressure, 2013†	% (n)	35.4 (1300)	37.0 (1149)	36.7 (999)	39.7 (1044)	41.2 (462)	45.3 (335)
History of diabetes mellitus, 2013†	% (n)	1.0 (36)	1.3 (40)	1.0 (28)	1.2 (32)	2.0 (23)	2.3 (17)

		0: no abuse	1	2	3	4	5: severe abuse
		n=3668	n=3102	n=2723	n=2630	n=1122	n=739
History of myocardial infarction, 2013†	% (n)	6.0 (221)	6.7 (208)	6.7 (182)	6.5 (172)	9.7 (109)	9.6 (71)
History of stroke, 2013†	% (n)	1.0 (37)	1.0 (31)	1.3 (36)	1.5 (40)	1.5 (17)	1.8 (13)

†Perceived social standing indicates subjective social standing in the US and the community. Smaller values indicate higher social standing. Women were considered to have a history of high blood pressure, diabetes mellitus, myocardial infarction, or stroke prior to the cognitive testing if they reported these conditions on any of the biennial questionnaires, 1989–2013.

Table 2.

Association of childhood physical/emotional abuse with cognitive function in middle age (n=13,992), Nurses' Health Study II, 2014–2016[†]

	Physical/emotional abuse				
Learning/working memory					
	No abuse	Mild	Moderate	Severe	Test of trend
	n=6554	n=2887	n=3329	n=1222	
	Beta coefficients				
Model 1a: Age and race	0.0 [Ref]	0.01 (−0.02, 0.04)	−0.05 (−0.08, −0.02)**	−0.10 (−0.14, −0.05)***	p<0.0001
Model 2a: + childhood factors[†]	0.0 [Ref]	0.01 (−0.02, 0.04)	−0.04 (−0.07, −0.01)**	−0.09 (−0.13, −0.05)***	p<0.0001
Model 3a: + adulthood socioeconomic indicators	0.0 [Ref]	0.01 (−0.02, 0.04)	−0.04 (−0.07, −0.01)**	−0.09 (−0.13, −0.05)***	p<0.0001
Model 4a: + health factors	0.0 [Ref]	0.01 (−0.02, 0.04)	−0.04 (−0.07, −0.01)**	−0.09 (−0.13, −0.04)***	p<0.0001
Model 5a: + psychological distress	0.0 [Ref]	0.01 (−0.02, 0.05)	−0.03 (−0.06, 0.00)	−0.05 (−0.10 –0.01)*	p=0.01
Psychomotor speed/attention					
	No abuse	Mild	Moderate	Severe	Test of trend
	n=6546	n=2882	n=3327	n=1217	
	Beta coefficients				
Model 1b: Age and race	0.0 [Ref]	−0.03 (−0.06, 0.01)	−0.03 (−0.07, 0.01)	−0.03 (−0.08, 0.03)	p=0.08
Model 2b: + childhood factors[†]	0.0 [Ref]	−0.02 (−0.06, 0.02)	−0.04 (−0.07, 0.00)	−0.03 (−0.08, 0.03)	p=0.07
Model 3b: + adulthood socioeconomic indicators	0.0 [Ref]	−0.03 (−0.06, 0.01)	−0.03 (−0.07, 0.00)	−0.03 (−0.08, 0.03)	p=0.10
Model 4b: + health factors	0.0 [Ref]	−0.03 (−0.07, 0.01)	−0.03 (−0.07, 0.00)	−0.03 (−0.08, 0.03)	p=0.07
Model 5b: + psychological distress	0.0 [Ref]	−0.02 (−0.06, 0.02)	−0.02 (−0.06, 0.01)	0.00 (−0.06, 0.06)	p=0.41

** p<0.01,

*** p<0.001.

†Childhood factors include mother's occupation, father's occupation, mother's education, father's education, parents' home ownership in participant's infancy and any head trauma with loss of consciousness before age 20 years. Adulthood socioeconomic indicators include husband's education, marital status, and subjective social standing in the community and in the U.S. Health factors include smoking, BMI, physical activity, and history of physician-diagnosed hypertension, myocardial infarction, diabetes, and stroke.

Table 3.

Association of childhood sexual abuse with cognitive function in middle age (n=13,982), Nurses' Health Study II, 2014–2016[†]

	Sexual abuse				
Learning/working memory					
	No abuse	Infrequent	Moderately frequent	Frequent	Test of trend
	n=9200	n=3406	n=918	n=458	
Model 1a: Age and race	0.0 [Ref]	0.00 (−0.03, 0.03)	−0.06 (−0.11, −0.01)*	−0.11 (−0.17, −0.04) **	p=0.001
Model 2a: + childhood factors	0.0 [Ref]	0.01 (−0.02, 0.03)	−0.05 (−0.10, −0.00)*	−0.10 (−0.17, −0.04) **	p=0.006
Model 3a: + adulthood socioeconomic indicators	0.0 [Ref]	0.01 (−0.02, 0.03)	−0.05 (−0.10, −0.00)*	−0.10 (−0.17, −0.03) **	p=0.008
Model 4a: + health factors	0.0 [Ref]	0.01 (−0.02, 0.04)	−0.05 (−0.09, −0.00)	−0.09 (−0.16, −0.03) **	p=0.01
Model 5a: + psychological distress	0.0 [Ref]	0.02 (−0.01, 0.04)	−0.03 (−0.07, 0.02)	−0.05 (−0.11, 0.02)	p=0.36
Psychomotor speed/attention					
	No abuse	Infrequent	Moderately frequent	Frequent	Test of trend
	n=9186	n=3403	n=917	n=456	
Model 1b: Age and race	0.0 [Ref]	−0.03 (−0.06, 0.01)	−0.04 (−0.10, 0.03)	−0.05 (−0.14, 0.03)	p=0.05
Model 2b: + childhood factors[†]	0.0 [Ref]	−0.02 (−0.06, 0.01)	−0.03 (−0.09, 0.03)	−0.05 (−0.14, 0.03)	p=0.06
Model 3b: + adulthood socioeconomic indicators	0.0 [Ref]	−0.02 (−0.06, 0.01)	−0.03 (−0.09, 0.03)	−0.05 (−0.14, 0.03)	p=0.07
Model 4b: + health factors	0.0 [Ref]	−0.02 (−0.06, 0.01)	−0.03 (−0.09, 0.03)	−0.05 (−0.13, 0.04)	p=0.09
Model 5b: + psychological distress	0.0 [Ref]	−0.01 (−0.05, 0.02)	−0.02 (−0.08, 0.04)	−0.01 (−0.10, 0.07)	p=0.46

** p<0.01,

*** p<0.001.

[†]Childhood factors include mother's occupation, father's occupation, mother's education, father's education, parents' home ownership in participant's infancy, and head trauma with loss of consciousness before age 20 years. Adulthood socioeconomic indicators include husband's education, and subjective social standing in the community and in the U.S. Health factors include smoking, BMI, physical activity, and history of physician-diagnosed hypertension, myocardial infarction, diabetes, and stroke. Models 4a and 5a do not include hypertension, since it is an effect modifier.