Pre-trauma verbal ability at five years of age and the risk of post-traumatic stress disorder in adult males and females

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Abstract:

Previous studies have shown that high cognitive ability, measured in childhood and prior to the experience of traumatic events, is protective of PTSD development. Our aim was to test if the association between pre-trauma verbal ability ascertained at 5 years with DSM-IV lifetime post-traumatic stress disorder (PTSD) at 21 years was subject to effect modification by gender, trauma type or prior behaviour problems. Using a prospective birth cohort of young Australians, we found that both trauma type and behaviour problems did not change the association between cognitive ability and PTSD. During multivariate analysis, testing for the interactive effect of gender revealed that verbal ability was linearly and inversely associated with PTSD in females only, with those in the lowest verbal ability quintile having strongly increased odds of PTSD (OR = 3.89: 95% CI; 1.50, 10.10) compared with those in the highest quintile. A graph of the interaction revealed lower verbal ability placed females, but not males, at an increased risk of PTSD . Our results indicate that that lower verbal ability in early childhood is a vulnerability factor for PTSD in females but not in males, and suggest that lower verbal ability may constitute a gender-specific risk factor responsible for part of the increased risk of PTSD found in females compared with males.

Key words: Post-traumatic stress disorders, cognitive functioning, gender

Background:

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Epidemiological research has found an inverse relationship between cognitive ability with morbidity and mortality. Individuals with a lower cognitive ability have an increased risk of a number of conditions in later life including schizophrenia (Zammit et al., 2004), depression, hypertension, lung disease (Der, Batty, & Deary, 2009), increased depression persistence and comorbidity (Koenen, et al., 2009). However, the mechanisms by which cognitive ability may lead to a decline in individual health outcomes over time remains unclear and intercorrelated with a number of environmental and developmental factors. For this reason, even studies which have conducted extensive cognitive testing prior to the onset of poor health (pre-morbid testing) and controlled for important related affects including socio-economic position (SEP), familial circumstances and indicators of fetal and child development are unable to completely rule out possible residual confounding due to these factors (Batty, Deary, & Gottfredson, 2007; Batty et al., 2009; Der, et al., 2009).

Despite this, different health outcomes are arguably more or less directly linked to pre-morbid measures of cognitive ability. In this regard, findings from a number of prospective and well-controlled studies of military populations, which suggest a causal link between pre-trauma cognitive ability and Post-Traumatic Stress Disorder (PTSD), appear relatively robust to confounding owing in part to the clearly defined principle determinant of the disorder (combat exposure). This evidence suggests that various measures of pre-combat cognitive ability predict PTSD risk in returned soldiers (Kremen, et al., 2007; Macklin, et al., 1998){Gilbertson, 2006 #231}{Marx, 2009 #227}.

Regarding the mechanism by which lower cognitive ability may result in a greater risk of PTSD, these papers offer multiple explanations owing partly to the variety of neurocognitive performance measures used to predict PTSD. Three studies suggest that higher cognitive ability (Kremen, et al., 2007; Macklin, et al., 1998) and a high capacity to effectively and flexibly manipulate verbal information (Gilbertson, et al., 2006) reduce the negative impact of trauma on the individual by increasing their ability to process and build meaning from their trauma. Another paper suggests that high visual-spatial memory affords the individual an increased capacity in the initial acquisition of the visual aspects of the traumatic episode, which aides in rehearsal and later habituation to the trauma (Marx, et al., 2009).

While military studies have the advantage of being well controlled and often use sophisticated testing, participants are typically recruited at the age of enlistment. Although this does not affect the ability of these studies to demonstrate an association between cognitive ability and PTSD, environmental factors and circumstances during childhood and adolescence are unavailable or collected retrospectively. This may result in misspecification during analysis and decreased ability to interpret temporal relationships between cognitive ability and PTSD.

To date, there have been only three prospective, population-based studies that have been able to investigate these life course factors. One study from Storr and colleagues has found no association between early scholastic ability and PTSD (Storr, Ialongo, Anthony, & Breslau, 2007). The other two studies have found inverse associations between cognitive ability with PTSD risk in late adolescence (Breslau, Lucia, & Alvarado, 2006) and early adulthood (Koenen, Moffitt, Poulton, Martin, & Caspi, 2007). There were some methodological

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weaknesses in the studies where associations were found. The first study assessed PTSD when the participants were 17 years of age and yet to pass through the peak period of trauma exposure, affecting generalisability to young adults and also resulting in the identification of very few PTSD cases (Breslau, et al., 2006). The second study did not account for trauma type (Koenen, et al., 2007). Trauma type is likely to play a confounding role in the relationship between child cognitive ability with PTSD risk, as measures of cognitive and scholastic ability have been found to predict the type of traumas a young person will subsequently experience (Breslau, et al., 2006; Storr, et al., 2007), and specific types of trauma are highly predictive of PTSD outcomes (Breslau, Chilcoat, Kessler, Peterson, & Lucia, 1999; Brewin, Andrews, & Valentine, 2000; Frans, Rimmo, Aberg, & Fredrikson, 2005). Additionally, individuals in this study were classed as trauma exposed only if they had experienced an acute reaction to the trauma (criterion A2). This resulted in those who were potentially the most resilient individuals (those who experienced trauma but reported no immediate reaction) being classified as unexposed to trauma (Koenen, et al., 2007). A final limitation relevant to both studies was the use of sample sizes too small to permit testing for gender differences. Emerging evidence is showing that gender interacts differently in the relationship between cognition and a range of mental health outcomes. One recent study {Glaser, 2011 #306} found that the relationship between cognitive ability and depression in men and women changes over time, especially around puberty, and differs for males and females. The other study {Hatch, 2007 #305} found that lower cognitive ability was associated with higher internalizing symptoms in women only. Although neither study assessed PTSD as an outcome, these findings show the need to assess whether the relationship between cognitive ability and PTSD is present only in females, as found previously by these studies in relation to other mental health outcomes.

In this study, we use data from a large prospective birth cohort study to test the hypothesis that verbal ability at 5 years of age according to the Peabody Picture Vocabulary Test-Revised (PPVT-R) is inversely associated with the risk of DSM-IV lifetime PTSD at 21 years of age. We will take into account a range of developmental and environmental characteristics and expand the existing evidence, by testing for the role of gender, trauma type and behaviour problems in the association between verbal ability and PTSD.

Materials and methods:

Sample and Data

Participants were from the Mater University Study of Pregnancy (MUSP), a prospective birth cohort based in Brisbane, Australia. Between 1981 and 1984 a total of 7,223 pregnant mothers were recruited from the Mater Misericordiae Hospital. The first wave of data collection occurred before the birth of the child, after which subsequent data collections were carried out on both mother and child at birth and 6 months, 5, 14 and 21 years after birth. Further information regarding the MUSP has been detailed previously (Keeping et al., 1989; Najman et al., 2005). At 21 years of age, 2,547 (35%) of the offspring completed the Composite International Diagnostic Interview (CIDI-Auto) (49% male and 51% female). Of these, 1,010 (125 PTSD cases) participants reported trauma exposure and had complete data for multivariable analysis. Informed consent was gained from all participants, all data was

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coded for confidentiality and ethics was approved for the cohort was approved by the institution and funding body.

Measurement of Verbal Ability

The Peabody Picture Vocabulary Test-Revised (PPVT-R) was administered to children at the five year follow-up. The test requires the examinee to indicate which one of four pictures best describes a word which the examiner expresses verbally, with the resulting score used as a measure of the subject's verbal intelligence (Jongsma, 1982). The PPVT-R has been validated against other standardised intelligence tests used on children (Childers, Durham, & Wilson, 1994; Dunn, 1981; Johnson, Howie, Owen, Baldwin, & Luttman, 1993).

Measurement of PTSD

At the 21 year follow-up, participants were screened for DSM-IV lifetime Post-Traumatic Stress Disorder (PTSD) (First, 2004) using the Composite International Diagnostic Interview (CIDI-Auto) Version 2.1 (World Health Organisation, 1997). The CIDI-Auto was administered by trained interviewers and has been found to have good validity and reliability (Peters, Clark, & Carroll, 1998). Individuals who experienced one or more of the eleven possible traumatic events were asked further questions regarding the presence of 17 PTSD symptoms from three distinct categories including re-experiencing, hyperarousal and avoidance, in addition to questions assessing the level of functional impairment caused by the symptoms. Importantly, participants needed to have reported an acute reaction to trauma (criteria A2) to be diagnosed with PTSD, but not to be classed as trauma exposed. For

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participants who experienced multiple traumas, PTSD was assessed with regard to the most 'stressful or upsetting' event. No participants designated combat exposure or being victim of torture or terrorism as their most stressful or upsetting event. We created a four category trauma exposure variable consisting of (1) interpersonal victimisation (rape, molestations, physical assault, threatened with a weapon or kidnapped), (2) interpersonal victimisation and at least one more traumatic exposure (3) non-interpersonal victimisation (accident, witness to death/injury, natural disaster, other) and (4) non-interpersonal victimisation and at least one more traumatic exposure.

Measurement of Confounding Factors

Birth weight, maternal age at birth and parity were selected *a priori* to be included in all models due to earlier findings from this cohort reporting an inverse association between birth weight and a number of mental health and behaviour problems (Alati et al., 2007; Alati et al., 2009; Betts, Williams, Najman, & Alati, 2011) and because of its central role in the proposed mechanism (Gale, Hatch, Batty, & Deary, 2009). We constructed birth weight z-scores which were internally adjusted for gender and gestational age as a crude measure of fetal development. Birth weight and gestational age (in weeks) were taken from obstetric records at the time of birth, along with maternal age at birth and parity.

We selected other covariables based on the previous prospective and military studies (Breslau, et al., 2006; Gale, et al., 2008; Gilbertson, et al., 2006; Koenen, et al., 2007; Kremen, et al., 2007; Macklin, et al., 1998; Marx, et al., 2009; Storr, et al., 2007; Thompson

& Gottesman, 2008). Internalising and externalising behaviour problems were assessed in the offspring at 5 years using a shortened version of the child behaviour checklist (CBCL) (Achenbach, 1991a) completed by mothers, fully described elsewhere (Bor et al., 1997). At 14 years internalising and externalising behaviour was assessed using the Youth Self Report (YSR) (Achenbach, 1991b) completed by the children, and shown previously to have good validity and reliability in the MUSP cohort (Alati et al., 2008). We were only interested in behaviour problems which developed before exposure to trauma and thereby did not originate as part of a PTSD sequelae. Individuals exposed to trauma before 5 were excluded from analyses, individuals exposed to trauma between 5 and 14 were designated as having a behaviour problem according to the CBCL (measured at 5 years), individuals exposed to trauma after 14 were designated as having a behaviour problem according to the YSR (measured at 14 years). As done in previous studies, at both 5 and 14 years the highest scoring 10% of the sample were categorised as having either an internalising or externalising behaviour problem (Alati, et al., 2008; Bor, et al., 1997). Family income and maternal education were measured at baseline. At the time of birth, maternal anxiety and depression symptoms were ascertained using the Delusions-States-Symptoms Inventory (DSSI) (A. Bedford, & Folds, GA, 1977). The DSSI has been found to correlate well with the Edinburgh Postnatal Depression Scale (EPDS) and the Hospital Anxiety/Depression Scale (A. Bedford, & Deary, I, 1999). As in previous studies, symptoms of anxiety and depression were defined as having four or more symptoms (Alati, et al., 2009). At five years maternal use of alcohol and tobacco were used as indicators of maternal life style.

Statistical Analysis

We began by testing if PPVT-R as a continuous variable predicted (1) exposure to trauma among the full sample (*n* = 2,547) using univariate logistic regression, and (2) the type of trauma among those exposed to trauma (*n* = 1,010) using univariate multinomial regression. We used univariable logistic regression to test the associations between DSM-IV lifetime PTSD with the PPVT-R quintiles and the confounders. We used a backwards elimination method in which all the covariables found to be significantly associated with PTSD from the univariable analysis were entered into a single model. Variables were subsequently removed from the model one-by-one, removing those with the weakest association first. The final model included all variables with significant coefficients at the $p < 0.05$ level as well as all *a priori* confounders, included in all models. The PPVT-R scores were entered into the final model firstly as quintiles using the highest performing quintile as the reference category, and then separately as a continuous variable in which the odds of PTSD was calculated per one quintile increase in the PPVT-R score.

We tested a number of interactions including gender, prior behaviour problems and trauma type in separate, fully adjusted models in which the PPVT-R was entered as a continuous variable. As we found a significant interaction by gender, we then presented gender estimates separately. We used multivariate logistic regression to compare the odds of individuals being included in the study to those lost to follow-up by the variables included in the final model, and replicated the final analysis using inverse probability weighting to adjust for loss to follow-up (see supplementary sections).

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Results:

When we assessed whether PPVT-R predicted firstly trauma exposure, and then trauma type, all results were non-significant (available upon request). In unadjusted analyses, there was evidence of a linear relationship between the PPVT-R quintiles and PTSD, with a significant difference observed in the odds ratio between the highest and lowest quintiles (table 1). Females were at a significantly increased risk of being diagnosed with PTSD and birth weight was inversely associated with PTSD risk. Those reporting the experience of interpersonal

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victimisation and had experienced more than one trauma were at a greatly increased risk of PTSD compared with those who reported only a single experience of non-interpersonal victimisation. While prior internalising behaviour and maternal tobacco use at 5 years were significantly associated with the odds of PTSD diagnosis in univariate analyses (table 2), in multivariate analyses they produced non-significant coefficients (p >0.1) and were excluded.

The relationship between PPVT-R and PTSD remained after adjustment for gender, trauma type and birth weight adjusted for gestational age, maternal age at birth and parity. We found evidence of a gender interaction in the association between PPVT-R and PTSD. The interaction term showed that females were at a differentially increased risk of PTSD due to decreasing PPVT-R compared with males, in both univariate (p = 0.028) and fully adjusted analyses (p = 0.049). After adjustment, females in the lowest cognitive functioning quintile had strongly increased odds of PTSD (OR = 3.89: 95% CI; 1.50, 10.10) compared with those in the highest functioning quintile (table 3). There was no evidence of an association in males. Graphing the linear regressions of the predicted values for males and females separately (figure 1) revealed that females were at increased risk of PTSD compared with males due to lower cognitive functioning.

We found no evidence that trauma type or prior behaviour internalising or externalising problems modified the relationship between PPVT-R and PTSD. Multivariate attrition analysis showed that those in the lower quintiles of cognitive functioning were differentially lost to follow-up at the 21 year follow-up compared with those in the higher quintiles (table 4). The results of the inverse probability weighting analysis showed increased odds of

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developing PTSD in females with the lowest performing quintile compared with females in the highest quintile [OR 4.26; 95% CI 1.88, 9.65] (supplementary table 1). All point estimates were similar to those presented in the final model of our complete case analysis.

Discussion:

This study aimed to determine if higher levels of verbal ability in early childhood, measured by the PPVT-R prior to trauma exposure, protected trauma-exposed individuals against the risk of developing PTSD in later life. We found gender differences such that a linear and inverse relationship between childhood verbal ability and PTSD affected females only. These results suggest that lower verbal ability at five years of age increases the risk of young adult females to develop PTSD after experiencing traumatic situations. Our results confirm the

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findings of two previous studies, which both identified an inverse association between child cognitive ability and PTSD (Koenen, et al., 2007), but also add to this new evidence, as our large sample size allowed capacity to test for several interactions. This is the first time that a population study, with enough power to test for a gender interaction has found a gender difference in the association between cognitive abilities and PTSD. One previous study which tested for this interaction, perhaps did not have the sample size capacity to detect a difference (Breslau, et al., 2006). The relationship we found was independent of a range of socio-economic and lifestyle measures and indicators of fetal and child development which were collected prospectively. These included indicators of prior psychopathology which unlike an earlier study did not affect the association between cognitive ability and PTSD (Breslau, et al., 2006). Further, the inclusion of birth weight adjusted for gestational age slightly weakened the association, but did not confound it, suggesting that cognitive ability in childhood and later PTSD may not be linked via impaired neural development during fetal growth (Gale, et al., 2009).

The mechanism by which lower cognitive ability may result in a greater risk to PTSD is still largely unknown and explanations vary depending on the measure of neurocognitive performance measured. Military studies, which employ sophisticated measures of neurocognitive performance unsuitable for use in young children, coupled with the use of combat as a clearly defined determinant of PTSD, provide some of the strongest available evidence concerning the mechanism behind the association. Some of these studies suggest that higher cognitive ability may allow the individual to better translate their trauma into a narrative, and in this way make meaning of the experience, allowing the individual to overcome the trauma (Gilbertson, et al., 2006; Kremen, et al., 2007; Macklin, et al., 1998). While we might expect an increased verbal ability to assist an individual in making meaning of their trauma, our finding that cognitive ability predicts PTSD in females only is difficult to interpret, as these military studies have demonstrated strong associations exist in males (Gilbertson, et al., 2006; Kremen, et al., 2007; Macklin, et al., 1998).

In addition to the above inconsistency, civilian studies have found that cognitive ability plays a role in the development of many types of psychopathology (Gale, et al., 2008; Glaser, et al., 2011; Hatch, et al., 2007; Koenen, et al., 2009). Therefore, we must consider that the association we found may be part of a broader relationship by which cognitive ability plays a dynamic role in the development of many psychopathologies across the lifespan. Viewed from this perspective, lower cognitive ability may constitute a general vulnerability to mental illness, with specific aspects of cognitive ability having impacts upon specific types of mental illness, perhaps also dependent upon gender and the period of development in which measurements are taken. In further support of this notion, two papers based on two large birth cohort studies found significant gender differences between higher cognitive ability in childhood and decreased mental health symptoms at multiple ages in adolescence and adulthood (Glaser, et al., 2011; Hatch, et al., 2007). One of these studies found the relationship changed depending on the age and gender of the participants (Glaser, et al., 2011). Cognitive ability was positively associated with depression at ages 13 and 14, but this relationship changed in females by age 17 but not in males (Glaser, et al., 2011). The other study of adults in their fifties found higher cognitive ability was protective of depression and anxiety in females only (Hatch, et al., 2007). Our study is the first to suggest that similar

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processes may apply to pre-trauma cognitive functioning and the development of PTSD after experiencing a traumatic event. Importantly however, both of these studies interpret their findings as higher cognitive functioning having a protective effect on female mental health symptoms, while males are not benefited by higher cognitive functioning. Our graph on the other hand reveals that males and females have a similar risk of PTSD at higher levels of verbal ability, but that as verbal ability declines the risk of PTSD for females increases linearly, while that of males remains stable. Our study had a number of strengths, the most notable of which was an increased capacity to perform tests of gender interaction. We were also able to account for trauma type with increased specificity compared with previous studies (Breslau, et al., 2006; Koenen, et al., 2007; Storr, et al., 2007) by controlling for multiple trauma exposure, which has been shown to increase the risk of PTSD (Copeland, Keeler, Angold, & Costello, 2007). Another important strength was the age at which we attained measures. Both the PPVT-R and behaviour problems were measured at 5 years. For all but a few who were removed from our analyses, this was prior to the age at which trauma was reported to have occurred. Trauma experience and PTSD symptoms were taken at 21 years, meaning this sample had passed through the point of late adolescents, found to be the peak period of trauma exposure in young people (Breslau, et al., 2006).

As discussed earlier, of direct relevance to any purported mechanism is the measure of cognitive ability. A limitation of our analysis may be the PPVT-R, which despite being validated against other standard intelligence tests for children and considered a strong indicator of verbal intelligence (Childers, et al., 1994; Dunn, 1981; Johnson, et al., 1993; Jongsma, 1982), provides a less comprehensive measure of childhood intelligence than can be obtained by alternative tests such as the Wechsler Intelligence Scale for Children-Revised (WISC-R) (Wechsler, 1974). However our findings were very similar to previous findings using the WISC-R (Breslau, et al., 2006), which points to the robustness of the PPVT-R as a measure of IQ at least for the purpose of this study. A second and related limitation is that we were only able to use a single and general aspect of neurocognitive performance, verbal ability. Military studies have shown the importance of using more specific measures of neurocognitive performance, including non-verbal measures such as visual-spatial memory, when testing for an association with PTSD (Gilbertson, et al., 2006; Marx, et al., 2009). Therefore, although our results are supported by military studies which found a relationship between a general construct of cognitive ability (Kremen, et al., 2007; Macklin, et al., 1998) and verbal memory (Gilbertson, et al., 2006) with PTSD, future studies with the capacity to test a wider range of neurocognitive performance measures are needed to show what specific aspects of both verbal and non-verbal abilities are related to the symptoms of trauma. A third limitation, common to many longitudinal birth cohort studies is our considerable loss to follow-up. Results from our attrition analysis found that attrition was biased towards children of lower cognitive ability, this is likely to have led us to underestimate the true effect size. Thus, had these individuals been included in the study it is very unlikely that the magnitude or the significance of the association would have reduced. The inverse probability weighting analysis revealed very similar results when comparing the lowest and highest functioning quintiles and importantly the gender interaction test was significant. We are aware of the limitations in the use of inverse probability weights in adequately dealing with loss to follow-up. However, given that this analysis produced similar results and given also that we disproportionately lost individuals of lower cognitive ability, it is likely that the relationship would have been found at a similar or greater strength had we collected PTSD data at the 21 year follow-up on all individuals with a PPVT-R score.

Our findings suggest that lower early childhood verbal ability may reduce the capacity of females to cope with trauma. If our results are replicated in future studies, we will have identified a gender-specific risk factor which may explain part of the increased risk of PTSD found to occur in females. In conclusion, more studies with the capacity to test for gender specific responses to psychopathology, and which employ different measures of neurocognitive performance collected at different stages of development, are needed to further explore what appears to be a dynamic relationship between cognitive ability and psychopathology.

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References:

Achenbach, T. M. (1991a). *Manual for the Child Behavior Checklist 4/18 and 1991 Profile*. Burlington, VT: University of Vermont Department of Psychiatry.

Achenbach, T. M. (1991b). *Manual for the Youth Self Report and 1991 Profile*. Burlington, VT: University of Vermont Department of Psychiatry.

Alati, R., Kinner, S. A., Hayatbakhsh, M. R., Mamun, A. A., Najman, J. M., & Williams, G. M. (2008). Pathways to ecstasy use in young adults: anxiety, depression or behavioural deviance? *Drug Alcohol Depend, 92*(1-3), 108-115. doi: S0376-8716(07)00278-5 [pii]

10.1016/j.drugalcdep.2007.07.007

Alati, R., Lawlor, D. A., Mamun, A. A., Williams, G. M., Najman, J. M., O'Callaghan, M. (2007). Is there a fetal origin of depression? Evidence from the Mater University Study of Pregnancy and its outcomes. *Am J Epidemiol, 165*(5), 575-582. doi: kwk036 [pii]

Alati, R., Najman, J. M., O'Callaghan, M., Bor, W., Williams, G. M., & Clavarino, A. (2009). Fetal growth and behaviour problems in early adolescence: findings from the Mater University Study of Pregnancy. *Int J Epidemiol, 38*(5), 1390-1400. doi: dyp252 [pii]

10.1093/ije/dyp252

Batty, G. D., Deary, I. J., & Gottfredson, L. S. (2007). Premorbid (early life) IQ and later mortality risk: systematic review. *Ann Epidemiol, 17*(4), 278-288. doi: S1047-2797(06)00196-7 [pii]

10.1016/j.annepidem.2006.07.010

Batty, G. D., Wennerstad, K. M., Smith, G. D., Gunnell, D., Deary, I. J., Tynelius, P. (2009). IQ in early adulthood and mortality by middle age: cohort study of 1 million Swedish men. *Epidemiology, 20*(1), 100-109. doi: 10.1097/EDE.0b013e31818ba076

00001648-200901000-00018 [pii]

Bedford, A., & Deary, I. (1999). The Delusions-Symptoms-States Inventory (DSSI): constructions, applications and analysis. *Personality and Individual Differences, 26*(3), 397-424.

Bedford, A., & Folds, GA. (1977). Validation of the Delusion-Symptom- States Inventory. *British Journal of Medical Psychology, 50*(2), 163-171.

Betts, K. S., Williams, G. M., Najman, J. M., & Alati, R. (2011). The association between birth weight and anxiety disorders in young adults. *J Anxiety Disord, 25*(8), 1060-1067. doi: S0887-6185(11)00121-6 [pii]

10.1016/j.janxdis.2011.07.002

Bor, W., Najman, J. M., Andersen, M. J., O'Callaghan, M., Williams, G. M., & Behrens, B. C. (1997). The relationship between low family income and psychological disturbance in young children: an Australian longitudinal study. *Aust N Z J Psychiatry, 31*(5), 664-675.

Breslau, N., Chilcoat, H. D., Kessler, R. C., Peterson, E. L., & Lucia, V. C. (1999). Vulnerability to assaultive violence: further specification of the sex difference in post-traumatic stress disorder. *Psychol Med, 29*(4), 813-821.

Breslau, N., Lucia, V. C., & Alvarado, G. F. (2006). Intelligence and other predisposing factors in exposure to trauma and posttraumatic stress disorder: a follow-up study at age 17 years. *Arch Gen Psychiatry, 63*(11), 1238-1245. doi: 63/11/1238 [pii]

10.1001/archpsyc.63.11.1238

Brewin, C. R., Andrews, B., & Valentine, J. D. (2000). Meta-analysis of risk factors for posttraumatic stress disorder in trauma-exposed adults. *J Consult Clin Psychol, 68*(5), 748-766.

Childers, J. S., Durham, T. W., & Wilson, S. (1994). Relation of performance on the Kaufman Brief Intelligence Test with the Peabody Picture Vocabulary Test--Revised among preschool children. *Percept Mot Skills, 79*(3 Pt 1), 1195-1199.

Copeland, W. E., Keeler, G., Angold, A., & Costello, E. J. (2007). Traumatic events and posttraumatic stress in childhood. *Arch Gen Psychiatry, 64*(5), 577-584. doi: 64/5/577 [pii]

10.1001/archpsyc.64.5.577

Der, G., Batty, G. D., & Deary, I. J. (2009). The association between IQ in adolescence and a range of health outcomes at 40 in the 1979 US National Longitudinal Study of Youth. *Intelligence, 37*(6), 573-580. doi: 10.1016/j.intell.2008.12.002

Dunn, L. (1981). *Peabody Picture Vocabulary Test-Revised: Circle Lines*. MN: American Guidance Service.

First, M., & Tasman, A. (2004). *DSM-IV-TR Mental Disorders: Diagnosis, Etiology and Treatment*. West Sussex: Wiley.

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Frans, O., Rimmo, P. A., Aberg, L., & Fredrikson, M. (2005). Trauma exposure and post-traumatic stress disorder in the general population. *Acta Psychiatr Scand, 111*(4), 291-299. doi: ACP463 [pii]
10.1111/j.1600-0447.2004.00463.x
Gale, C. R., Deary, I. J., Boyle, S. H., Barefoot, J., Mortensen, L. H., & Batty, G. D. (2008). Cognitive ability in early adulthood and risk of 5 specific psychiatric disorders in middle age: the Vietnam experience study. *Arch Gen Psychiatry, 65*(12), 1410-1418. doi: 65/12/1410 [pii]
10.1001/archpsyc.65.12.1410
Gale, C. R., Hatch, S. L., Batty, G. D., & Deary, I. J. (2009). Intelligence in childhood and risk of psychological distress in adulthood: The 1958 National Child Development Survey and the 1970 British Cohort Study. *Intelligence, 37*(6), 592-599. doi: 10.1016/j.intell.2008.09.002
Gilbertson, M. W., Paulus, L. A., Williston, S. K., Gurvits, T. V., Lasko, N. B., Pitman, R. K. (2006). Neurocognitive function in monozygotic twins discordant for combat exposure: relationship to posttraumatic stress disorder. *J Abnorm Psychol, 115*(3), 484-495. doi: 2006-09167-010 [pii]
10.1037/0021-843X.115.3.484
Glaser, B., Gunnell, D., Timpson, N. J., Joinson, C., Zammit, S., Smith, G. D. (2011). Age- and puberty-dependent association between IQ score in early childhood and depressive symptoms in adolescence. *Psychol Med, 41*(2), 333-343. doi: S0033291710000814 [pii]
10.1017/S0033291710000814
Hatch, S. L., Jones, P. B., Kuh, D., Hardy, R., Wadsworth, M. E., & Richards, M. (2007). Childhood cognitive ability and adult mental health in the British 1946 birth cohort. *Soc Sci Med, 64*(11), 2285-2296. doi: S0277-9536(07)00076-7 [pii]
10.1016/j.socscimed.2007.02.027
Johnson, D. L., Howie, V. M., Owen, M., Baldwin, C. D., & Luttman, D. (1993). Assessment of three-year-olds with the Stanford-Binet Fourth Edition. *Psychol Rep, 73*(1), 51-57.
Jongsma, E. A. (1982). Peabody Picture-Vocabulary Test - Revised (Ppvt-R) - Dunn,Lm, Dunn,Lm. *Journal of Reading, 25*(4), 360-364.
Keeping, J. D., Najman, J. M., Morrison, J., Western, J. S., Andersen, M. J., & Williams, G. M. (1989). A prospective longitudinal study of social, psychological and obstetric factors in pregnancy: response rates and demographic characteristics of the 8556 respondents. *Br J Obstet Gynaecol, 96*(3), 289-297.
Koenen, K. C., Moffitt, T. E., Poulton, R., Martin, J., & Caspi, A. (2007). Early childhood factors associated with the development of post-traumatic stress disorder: results from a longitudinal birth cohort. *Psychol Med, 37*(2), 181-192. doi: S0033291706009019 [pii]
10.1017/S0033291706009019
Koenen, K. C., Moffitt, T. E., Roberts, A. L., Martin, L. T., Kubzansky, L., Harrington, H. (2009). Childhood IQ and adult mental disorders: a test of the cognitive reserve hypothesis. *Am J Psychiatry, 166*(1), 50-57. doi: appi.ajp.2008.08030343 [pii]
10.1176/appi.ajp.2008.08030343
Kremen, W. S., Koenen, K. C., Boake, C., Purcell, S., Eisen, S. A., Franz, C. E. (2007). Pretrauma cognitive ability and risk for posttraumatic stress disorder: a twin study. *Arch Gen Psychiatry, 64*(3), 361-368. doi: 64/3/361 [pii]
10.1001/archpsyc.64.3.361
Macklin, M. L., Metzger, L. J., Litz, B. T., McNally, R. J., Lasko, N. B., Orr, S. P. (1998). Lower precombat intelligence is a risk factor for posttraumatic stress disorder. *J Consult Clin Psychol, 66*(2), 323-326.
Marx, B. P., Doron-Lamarca, S., Proctor, S. P., & Vasterling, J. J. (2009). The influence of pre-deployment neurocognitive functioning on post-deployment PTSD symptom outcomes

among Iraq-deployed Army soldiers. *J Int Neuropsychol Soc, 15*(6), 840-852. doi: S1355617709990488 [pii]
10.1017/S1355617709990488
Najman, J. M., Bor, W., O'Callaghan, M., Williams, G. M., Aird, R., & Shuttlewood, G. (2005). Cohort Profile: The Mater-University of Queensland Study of Pregnancy (MUSP). *Int J Epidemiol, 34*(5), 992-997. doi: dyi119 [pii]
10.1093/ije/dyi119
Olff, M., Langeland, W., Draijer, N., & Gersons, B. P. (2007). Gender differences in posttraumatic stress disorder. *Psychol Bull, 133*(2), 183-204. doi: 2007-02367-001 [pii]
10.1037/0033-2909.133.2.183
Peters, L., Clark, D., & Carroll, F. (1998). Are computerized interviews equivalent to human interviewers? CIDI-Auto versus CIDI in anxiety and depressive disorders. *Psychol Med, 28*(4), 893-901.
Storr, C. L., Ialongo, N. S., Anthony, J. C., & Breslau, N. (2007). Childhood antecedents of exposure to traumatic events and posttraumatic stress disorder. *Am J Psychiatry, 164*(1), 119-125. doi: 164/1/119 [pii]
10.1176/appi.ajp.164.1.119
Thompson, W. W., & Gottesman, II. (2008). Challenging the conclusion that lower preinduction cognitive ability increases risk for combat-related post-traumatic stress disorder in 2,375 combat-exposed, Vietnam War veterans. *Mil Med, 173*(6), 576-582.
Wechsler, D. (1974). *Wechsler Intelligence Scale for Children-Revised Manual*. New York: Psychological Corp.
World Health Organisation. (1997). *Composite International Diagnostic Interview, version 2.4*. Geneva: WHO.
Zammit, S., Allebeck, P., David, A. S., Dalman, C., Hemmingsson, T., Lundberg, I. (2004). A longitudinal study of premorbid IQ Score and risk of developing schizophrenia, bipolar disorder, severe depression, and other nonaffective psychoses. *Arch Gen Psychiatry, 61*(4), 354-360. doi: 10.1001/archpsyc.61.4.354
61/4/354 [pii]

Table 1: Univariable associations between lifetime DSM-IV PTSD with PPVT-R quintiles and *a priori* selected confounders [expressed in OR with 95% Confidence Intervals (CI)]

Predictor	Prevalence % (*n*)	Odds Ratio (95% CI)	p value
Peabody quintiles	**(*n* = 1,010)**		
Quintile 1	17.6% (n=178)	2.02 (1.08, 3.79)	0.028
Quintile 2	21.8% (n=220)	1.64 (0.88, 3.06)	0.116
Quintile 3	18.6% (n=188)	1.59 (0.83, 3.02)	0.162
Quintile 4	20.9% (n=211)	1.52 (0.81, 2.87)	0.194
Quintile 5	21.1% (n=213)	1.00	
Gender	**(*n* = 1,318)**		
Female	46.5% (n=613)	3.67 (2.54, 5.30)	<0.001
Male	53.5% (n=705)	1.00	
Trauma type	**(*n* = 1,318)**		
int. victim multiple	25.3% (n=333)	13.38 (7.02, 25.49)	<0.001
int. victim	9.9% (n=131)	2.69 (1.11, 6.49)	0.028
non-int. victim multiple	36.8% (n=485)	3.17 (1.61, 6.230	0.001
non-int. victim	28.0% (n=369)	1.00	
Birth weight z-score	(n = 1,318)	0.82 (0.68, 0.97)	0.023
Maternal age at birth	**(*n* = 1,318)**		
13-19	15.0% (n=198)	1.87 (0.79, 4.43)	0.157
20-34	79.7% (n=1,050)	1.16 (0.52, 2.59)	0.715
35+	5.3% (n=70)	1.00	
Previous births	**(*n* = 1,318)**		
Three or more	10.6% (n=140)	1.03 (0.58, 1.82)	0.922
one or two	49.0% (n=646)	1.07 (0.75, 1.52)	0.716
None	40.4% (n=532)	1.00	

Table 2: Univariable associations between lifetime DSM-IV PTSD with confounding factors [expressed in OR with 95% Confidence Intervals (CI)]

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Predictor	Prevalence % (*n*)	Odds Ratio (95% CI)	p value
Internalising behaviour	**(*n* = 1,267)**		
Yes	16.4% (n=208)	1.55 (1.02, 2.35)	0.041
No	83.6% (n=1,059)	1.00	
Externalising behaviour	**(*n* = 1,267)**		
Yes	15.9% (n=202)	1.20 (0.77, 1.88)	0.417
No	84.1% (n=1,065)	1.00	
Maternal anxiety	**(*n* = 1,315)**		
Yes	9.7% (n=128)	1.58 (0.96, 2.58)	0.070
No	90.7% (n=1,187)	1.00	
Maternal depression	**(*n* = 1,315)**		
Yes	3.2% (n=42)	0.97 (0.38, 2.52)	0.958
No	96.8% (n=1,273)	1.00	
Maternal alcohol (/day)	**(*n* = 1,165)**		
None	19.5% (n=227)	1.00	
>0 to 0.5	63.4% (n=738)	1.28 (0.80, 2.08)	0.307
>0.5 to 1.00	10.4% (n=121)	1.11 (0.55, 2.23)	0.776
>1.00	6.8% (n=79)	1.09 (0.48, 2.45)	0.840
Maternal tobacco (/day)	**(*n* = 1,163)**		
None	60.3% (n=701)	1.00	
Smoker	20.6% (n=240)	1.81 (1.18, 2.76)	0.006
Heavy smoker	19.1% (n=222)	1.80 (1.17, 2.79)	0.008
Maternal education	**(*n* = 1,309)**		
High school incompleted	17.7% (n=232)	1.29 (0.74, 2.26)	0.375
Completed high school	64.4% (n=843)	1.17 (0.74, 1.87)	0.491
Completed tertiary study	17.9% (n=234)	1.00	
Family income	**(*n* = 1,241)**		
Low	32.5% (n=403)	1.33 (0.75, 2.37)	0.329
Middle	55.5% (n=689)	0.98 (0.56, 1.71)	0.935
High	12.0% (n=149)	1.00	

Table 3: Multivariate associations between PPVT-R quintiles and lifetime DSM-IV PTSD at age 21 years separately by gender [expressed in OR with 95% Confidence Intervals (CI)] (complete case analysis *n* = 1,010)

PPVT-R	**Unadjusted**		**Fully adjusted***	
	Females	Males	Females	Males
Quintile 1	4.20 (1.83, 9.64)	0.78 (0.26, 2.320	3.89 (1.50, 10.10)	0.77 (0.25, 2.40)
Quintile 2	2.23 (0.99, 4.98)	0.90 (0.32, 2.570	2.22 (0.90, 5.45)	0.81 (0.27, 2.40)
Quintile 3	2.06 (0.89, 4.78)	1.03 (0.36, 2.93)	2.43 (0.95, 6.20)	0.94 (0.32, 2.78)
Quintile 4	1.99 (0.87, 4.54)	0.93 (0.32, 2.64)	2.53 (1.01, 6.36)	0.97 (0.33, 2.85)
Quintile 5	1.00	1.00	1.00	1.00
Linear term	0.75 (0.63, 0.90)	1.05 (0.83, 1.34)	0.79 (0.65, 0.97)	1.07 (0.83, 1.37)
P-value	0.002	0.677	0.022	0.592
P for linear PPVT-R by gender interaction	0.028		0.049	

* Adjusted for trauma type, birth weight z-score, maternal age and parity

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Table 4: Multivariate attrition analysis comparing those included in the analysis versus those lost since the 5 year follow-up and showing the odds of *not* being included in the study by variables included in the multivariate model [expressed in OR with 95% Confidence Intervals (CI)] (complete case analysis *n* = 3,999)

Effect	OR (95% CI)	P-value	P for LRT
PPVT-R Quintiles	*reference: quintile 5*		
Quintile 1	1.74 (1.43, 2.12)	<0.001	
Quintile 2	1.26 (1.04, 1.53)	0.021	
Quintile 3	1.47 (1.19, 1.80)	<0.001	
Quintile 4	1.04 (0.86, 1.27)	0.676	<0.001
Offspring gender	reference: male		
Female	0.79 (0.70, 0.90)	<0.001	<0.001
Birth weight z-score	reference: male		
1 SD increase	0.97 (0.91, 1.04)	0.382	0.382
Mother's age at birth	reference: male		
1 year increase	0.89 (0.77, 1.04)	0.144	0.144

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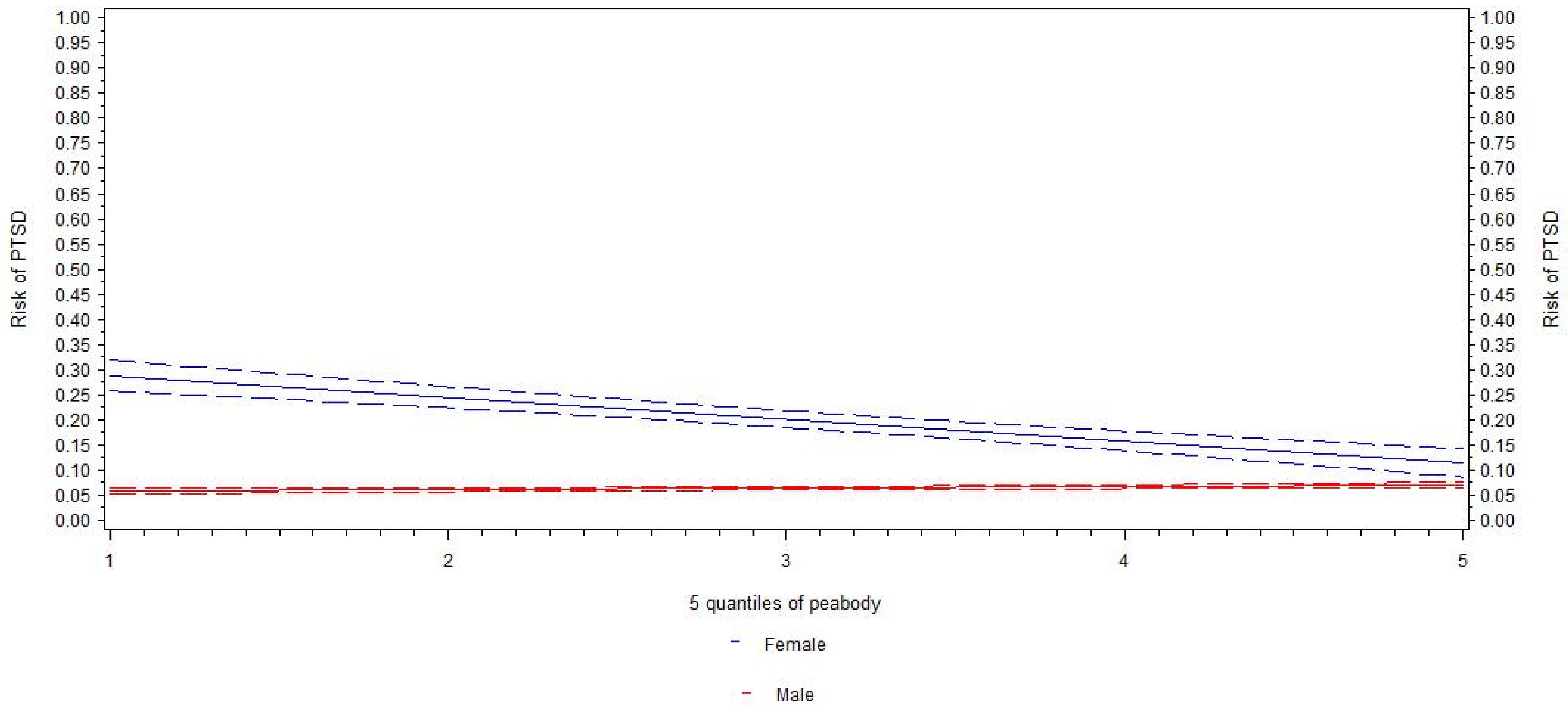

Figure 1: Multivariate associations between PPVT-R quintiles [highest functioning group (5), to lowest functioning group (1)] at 5 years and lifetime DSM-IV PTSD at age 21 years separately by gender. The predicted values were calculated on 551 males and 459 females (complete case analysis *n* = 1,010) and are adjusted for all variables in the final model. Both linear regression lines include 95% confidence intervals (dashed lines).

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