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Childhood cognitive skills trajectories and suicide by mid-adulthood: an investigation of the 1958 British Birth Cohort.

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ABSTRACT

Background: Poor cognitive abilities and low IQ are associated with an increased risk of suicide attempts and suicide mortality. However, knowledge of how this association develops across the life-course is limited. Our study aims to establish whether individuals who died by suicide by mid-adulthood are distinguishable by their child-to-adolescence cognitive trajectories.

Methods: Participants were from the 1958 British Birth Cohort and were assessed for academic performance at ages 7, 11, and 16 and intelligence at 11 years. Suicides occurring by September 2012 were identified from linked national death certificates. We compared mean mathematics and reading abilities and rate of change across 7 to 16 years for individuals who died by suicide versus those still alive, with and without adjustment for potential early-life confounding factors. Analyses were based on 14,505 participants.

Results: Fifty-five participants (48 males) had died by suicide by age 54 years. While males who died by suicide did not differ from participants still alive in reading scores at age 7 (effect size $[g]=-0.04, p=0.759$), their reading scores had a less steep improvement up to age 16 compared to other participants. Adjustments for early-life confounding factors explained these differences. A similar pattern was observed for mathematics scores. There was no difference between individuals who died by suicide versus participants still alive on intelligence at 11 years.

Conclusions: While no differences in tests of academic performance and IQ were observed, individuals who died by suicide had a less steep improvement in reading abilities over time compared to same-age peers.

Key words: Suicide, Cognitive Abilities, Cognition, Academic Performance, Intelligence, Reading, Mathematics, Early-life influences, Longitudinal study, Birth cohort, Cohort Studies.

INTRODUCTION

There is strong and consistent evidence from large prospective studies of an inverse association between measures of cognition in childhood and adolescence (ages 7 to 18), (Sorberg Wallin et al. 2018, Alaraisanen et al. 2006, Osler et al. 2008, Bjorkenstam et al. 2011, Andersson et al. 2008, Gunnell et al. 2011) and/or early adulthood (ages 18 to 20) (Gravseth et al. 2010) and later suicide outcomes (Alaraisanen et al. 2006, Andersson et al. 2008, Batty et al. 2010, Bjorkenstam et al. 2011, Gunnell et al. 2011, Gunnell et al. 2005, Gravseth et al. 2010, Osler et al. 2008, Sorberg Wallin et al. 2018). In a large Norwegian cohort including 610,359 participants, poorer academic performance at 18 years predicted increased risk of suicide mortality up to three decades later (Gravseth et al. 2010). In another cohort following over 26,315 Swedish individuals an association between poor intellectual quotient (IQ) at 13 years and later suicide attempts in adulthood was fully explained by overall poor academic performance at age 16 years (Sorberg Wallin et al. 2018), suggesting that associations of poor IQ with suicide outcomes operate through its effect on educational attainment (Sorberg Wallin et al. 2018). The few studies that reported sex differences suggested that an association of impaired cognition with suicide outcomes is seen in males, but less consistently in females (Gunnell et al. 2011).

However, it remains unclear how cognitive deficits develop across the life-course, as most existing prospective studies have been conducted with measures of cognition at only one point in time. As far as we are aware, only one prior study examined associations between general indicators of cognitive development at different ages (e.g. mother reports of age at first speech, doctor report of overall alertness at age 7 and intelligence test at age 15 years) and later suicide mortality (Neeleman et al. 1998). Delayed speech development and low intelligence were risk factors for accidental death, but not suicide, though the number of suicides was low ($n=11$). To our knowledge, no existing study has documented the development of cognitive abilities in suicidal individuals with prospective repeated measurements of

academic performance and IQ from childhood to adolescence (7, 11, 16 years) while accounting for a broad set of confounding factors. This is a key period in the life-course, as neuroimaging research suggests that intellectual capacity changes during adolescence (Ramsden et al. 2011).

In a previous study based on the 1958 British Birth Cohort, we failed to find evidence of associations between academic performance in reading and mathematics at age 7 and suicide mortality by age 50 years, but statistical power was limited due to the low number of suicides in the cohort (Geoffroy et al. 2014). Here we investigate (a) whether associations between academic performance (reading and mathematics) and/or IQ and suicide mortality emerge with measures recorded later in childhood and adolescence and (b) to determine to what extent such associations (if any) are accounted for by pre-existing early-life potential confounding factors (i.e. child's birth order and weight, mother's age, father social class) known for their associations with both cognition (Mosing et al. 2018) and suicide (Geoffroy et al. 2014, Orri et al. 2019) across the life-course. A better understanding of the development of cognitive impairments in suicidal individuals could provide important information about the etiology of suicide and its prevention.

METHODS

Participants

The 1958 British Birth Cohort is an ongoing longitudinal national birth cohort of 17, 638 individuals born in one week of March 1958 in England, Scotland, and Wales and representing 98% of all births in Britain in that week. Details about the cohort, including study design and response rates can be found elsewhere (Power and Elliott 2006).

Participants were flagged for deaths on the National Health Service Central Register (NHSCR). The end of the mortality follow-up was September 2012 when participants were 54 years old. The NHSCR is not notified of deaths of emigrants; hence cohort members who had emigrated permanently from Britain (up to 2009) were excluded from our analyses. Information on academic performance and IQ was collected in childhood (7 and 11 years) and in adolescence (16 years) via standardized tests. Ethical approval was given (South-East Multicentre Research Ethics Committee ref. 01/01/44), and informed consent was obtained from all participants.

Measures

Suicide mortality

As with our prior publication with the cohort, (Geoffroy et al. 2014) suicides were identified using the International Classification of Diseases, ninth revision (ICD-9) codes E950–59 (suicide) and E980–89 (undetermined intent) or tenth revision (ICD-10) codes X60–84 (suicide) and Y10–34 (undetermined intent). Suicide and death of undetermined intent were combined (Gunnell et al. 2013). We have excluded pending verdicts (ICD-9 code 988.88; ICD-10 code Y33.9).

Cognitive ability from childhood to adolescence

At 7, 11 and 16 years, age-appropriate tests for mathematics and reading were administered by the participant's school teacher. The arithmetic test at age 7 comprised 10 problems with graded levels of difficulty; teachers read the questions to poor readers. At age 11, the mathematics test was constructed by the National Foundation for Educational Research in England and Wales. At 16 years, a mathematics comprehension test was constructed at Manchester University. The Southgate test (Southgate 1962) (range 0–30) was used to detect poor readers at age 7: children selected from several words one that corresponded to a picture, and teachers also read out words that the children identified from a list. Reading tests at ages 11 and 16 years were similar to the Watts Vernon comprehension test. At 11 years, a general ability standardized 80-item test approximating general intelligence (e.g. IQ) with verbal and non-verbal scales was also administered (Douglas 1964). At each age, tests were standardized for month and year of assessment for each sex separately. To ease interpretation, we converted all scores to internally standardized Z scores (mean=0 and SD=1).

Early-life confounding factors

Potential confounding factors were identified from our prior studies with this cohort as risk factors associated with suicide deaths by 49 years ($P \leq 0.10$) in multivariable analyses (Geoffroy et al. 2014, Orri et al. 2019) and cognition (Geoffroy et al. 2016). These include: low birthweight (low: $<2.5\text{kg}$ vs normal: $\geq 2.5\text{kg}$, recorded at birth); child's birth order (reported by mothers when their child was 7 years, including all live and still births and deaths by 7 years; coded 1, 2, 3 or ≥ 4), maternal age at the time of the study member's birth (categorized ≤ 19 , 20-29 and >29 years) and father's social class in 1958 (using the 1951 Registrar General's Classification, categorized as non-manual (I/II/IIINM) and manual (IIIM/IV/V)). We have additionally controlled for fathers' social class at birth as it is strongly associated with cognitive skills (Jefferis et al. 2002).

Statistical analysis

First, using latent growth models we estimated trajectories of reading and mathematics abilities from age 7 to 16 years separately for two vital status groups, i.e., death by suicide versus still alive by September 2012. Models were estimated using maximum likelihood estimator in Mplus version 7.4. A major advantage of growth models is that they rely on the Full Information Maximum Likelihood estimation, which allows each participant with at least one data point to be included in the analysis (Enders and Bandalos 2001). Given that the distribution of reading abilities at age 7 was skewed, we performed sensitivity analyses using a robust (Huber-White) estimator for the standard errors, obtaining virtually identical results. Model fit was good according to the chi-square test of model fit (reading, chi-square 0.532; $p=0.766$; mathematics, chi-square=1.61, $p=0.445$), the Comparative Fit Indices (reading and mathematics, 1.00), and the Root Mean Square Error of Approximation (reading, 0.006 [90%CI 0.00-0.02]; mathematics, 0.00 [90%CI 0.00-0.03]). We used Wald tests to compare reading and mathematics abilities of individuals who died by suicide to those still alive at each time point (i.e., age 7, 11, and 16 years). Similarly, reading/mathematics rate of change (i.e. slopes) were compared using Wald tests to determine whether individuals who died by suicide versus those still alive differed in their rate of change. These differences were expressed as effect size (Hedge's g); values <0.20 are interpreted as "small", 0.21–0.50 "medium", 0.51–0.80 "large", and >0.80 "very large", similarly to Cohen's d . Given known sex differences in suicide mortality in this cohort (Geoffroy et al. 2014) and sex differences in the associations between cognitive and suicide outcomes (Gunnell et al. 2011), cognitive ability trajectories were estimated in the whole sample and separately for males and females (data shown for males only, as there were few suicides in females ($n=7$)), however findings must be interpreted with caution as there was no statistical evidence for sex-differences in the associations (P-values for mathematics =.841 and reading =.812). Second, all models were re-estimated after adjusting for a priori identified potential early-life confounders. We tested for non-linear associations for mathematics and reading skills at any time point, but none

reached significance. In additional analyses, using t-tests we examined associations separately for intelligence and suicide mortality.

Missing data on covariables varied between 1% (father's social class) to 11% (birth order). To minimize further data loss, we imputed missing information on early-life confounders using multiple imputations by chained equations (Azur et al. 2011) and conducted analyses across the 20 imputed data sets (primary analysis). Results based on complete cases were comparable to those based on multiple imputations.

RESULTS

Population

Of 16,470 participants in the birth survey of 1958 and who had not emigrated permanently, we excluded 1524 participants who had died from causes other than suicide by age 54 (most deaths had occurred within the first year of life). A further 441 participants were excluded due to missing information on all mathematics and reading measurements at 7, 11, and 16 years, leaving 14,505 participants for analyses. Of these, 55 participants had died from suicide before age 54 years (48 males and 7 females, including 12 of undetermined intent). The median age of suicide was 41 years (range 18–52 years) for males and 44 years (range 21–49 years) for females.

Reading and mathematics skills trajectories from age 7 to 16 years

Reading and mathematics skills trajectories during childhood for participants who died by suicide compared to those still alive are shown in **Figure 1**. For reading, participants who died by suicide had similar scores to those still alive at age 7 (effect size $[g]=-0.02$; $p = 0.857$) (model 1 in **Table 1**). At subsequent ages, the mean difference between the reading score of participants who died by suicide increased compared to those still alive (at age 11 years, $g=0.09$; $p=0.555$; at age 16 years: $g = 0.18$; $p=0.226$). The effect size for the overall rate of change over time (slope) was moderate ($g=0.21$, $p=0.099$) indicating a less steep improvement in reading abilities for the participants who died by suicide. Restricting the analyses to males yielded similar results. However, the mean slope difference was larger than that observed in the entire sample ($g= 0.30$, $p=0.048$ for males, $g=0.10$, $p=0.830$ for females). For mathematics, a similar pattern was observed (model 1 in **Table 2**). However, the differences between participants who died by suicide and participants still alive were smaller than those observed for reading, including the slope difference (entire sample, $g=0.01$, $p=0.438$; males only, $g=0.07$, $p=0.694$).

Role of early-life factors in explaining reading skills trajectory differences between groups

We tested whether the observed difference in rate of change in reading between participants who died by suicide versus those still alive could be confounded by early-life factors. To do so, models were adjusted for key factors including paternal social class, maternal age at child's birth, birth weight, and birth order. As shown in model 2 in **Table 1**, the estimated mean difference in reading between the slope of individuals who died by suicide versus those still alive reduced in both the entire sample ($g=0.15$, $p=0.336$) and in males only ($g=0.18$ $p=0.483$). The strongest associations with reading slopes were seen for birth order and maternal age. This suggests that the observed differences in the slope were explained by other factors in general, and by birth order and maternal age in particular.

We found no difference in intelligence scores at age 11 years between participants who died by suicide and those still alive (whole sample: suicide, mean= 0.00, SD=0.94; those still alive, mean=-0.10, SD=1.07; $p=0.434$; among males only: suicide, mean=0.01, SD=0.94; those still alive, mean=-0.09, SD=1.12; $p = 0.508$).

DISCUSSION

Our findings suggest that the participants who died by suicide had similar IQ scores and reading and mathematics scores in childhood and adolescence (as assessed with age-appropriate tests at school) than those still alive, but had a less steep improvement in their reading abilities. However, associations between reading ability trajectories and suicide mortality were accounted for by factors measured at birth that are associated with both suicide risk and cognitive skills (low birth weight, birth order, maternal age at childbirth, father's social class) (Geoffroy et al. 2016, Geoffroy et al. 2014).

Alterations (typically deficits) in various cognitive functions have been associated with increased suicide risk in various populations (Keilp et al. 2001, Keilp et al. 2008, Richard-Devantoy et al. 2012, Richard-Devantoy et al. 2014c, Richard-Devantoy et al. 2016, Richard-Devantoy et al. 2014a, Vadini et al. 2018) and in various stages of life (Keilp et al. 2001, Keilp et al. 2008, Richard-Devantoy et al. 2012, Richard-Devantoy et al. 2014c, Richard-Devantoy et al. 2016, Richard-Devantoy et al. 2014a, Vadini et al. 2018). Our results are not consistent with previous studies showing negative associations between childhood cognitive abilities and suicidal risk such as performance (e.g., low grade point average) (Sorberg Wallin et al. 2018, Bjorkenstam et al. 2011, Alaraisanen et al. 2006) or IQ (Andersson et al. 2008, Batty et al. 2010, Gunnell et al. 2013, Sorberg Wallin et al. 2018), but the relatively small number of suicides (n=55) compared with 58-553 in previous studies limits power to detect relatively small effects. Our findings emphasise the importance of the developmental period from childhood to adolescence in understanding suicide (Turecki et al. 2012). To our knowledge, our study is the first to show that differences in reading skills between suicidal and non-suicidal individuals are likely to emerge in the course of childhood and adolescence, rather than being evident in early childhood. Of note a prior study suggested that cognitive function at the age 18 years were more strongly associated to suicide mortality in adulthood than cognitive

function at the age of 12 years, suggesting that the reduction in cognitive abilities per se may be a marker of suicidal risk (Osler et al. 2008).

In the current study, controlling for early-life influences abolished associations between change in reading abilities over time and suicide risk, suggesting that the observed differences could be due to the impact of pre-existing early-life factors. Early-life environment has also been found to be associated with long-lasting cognitive impairments (Skogen et al. 2013, Zhang et al. 2018). For example, low socioeconomic status in the family may result in decreased access to cognitively-stimulating environments for the child, which in turn might influence the development of his/her cognitive abilities (Christensen et al. 2014). Although in our study, father's social class was measured at participants birth, social class is relatively stable over time (Power and Matthews 1997, Hackman et al. 2015), and it is possible that social class later in childhood rather than early-life per se explained the relatively weaker improvement in reading abilities over time. Moreover, young motherhood is associated with psychopathology, lower economic resources and maladaptive parenting practices, which are factors that can affect both suicidal risk and cognitive development of the individual (Pinderhughes et al. 2000). Such hypotheses should be formally tested in well-designed studies aiming to unravel the mechanisms linking early-life factors, development of cognitive skills, and suicidal risk. However, it is worth noting that in several prior studies reporting associations between IQ or school performance and suicide risk, these associations remained, even if attenuated, after controlling for early life variables such as socioeconomic status (Gunnell et al. 2011, Bjorkenstam et al. 2011, Batty et al. 2010, Sorberg et al. 2013).

In our study, the less steep improvement in academic abilities in individuals who died by suicide was of 'moderate' effect size in males and of 'small effect size and non-significant for mathematics. As far as we are aware our study is the first study to compare the development of reading and mathematics abilities in individuals who died by suicide versus those still alive, and further studies are needed to clarify the nature

of associations between development of reading abilities in childhood and adolescence and later suicide mortality. For example, the less steep improvement in reading abilities observed among individuals who died by suicide in comparison to those still alive could be an early marker for poor executive functions which are in turn associated with suicidal risk (Turecki et al. 2012).

This study has a number of strengths including (1) the use of a large population-based sample followed from birth into adulthood (5 decades), (2) the use of validated tests for the assessment of reading and mathematics skills and objective (coroner) information to determine the cause of death, (3) the use of repeated measures of academic abilities allowing us to model the developmental course of reading and mathematics skills from early childhood to adolescence. Despite those strengths, some limitation must be acknowledged. First, the main limitation is the use of reading and mathematics skills measures as a proxy of cognitive performance or abilities. More specific cognitive measures such as tests of executive functions, memory, and decision-making would be more informative as previous studies have shown that deficits in suicidal patients specifically concerned these functions (Richard-Devantoy et al. 2014a, Richard-Devantoy et al. 2014b). For example, a recent meta-analysis including 25 studies revealed that patients with suicide attempt history perform significantly worse in the Iowa Gambling Task (i.e., a measure of decision making), the Stroop Test (i.e., a measure of executive functions), and a categorical verbal fluency test (Richard-Devantoy et al. 2014a). It would be of interest to have such measures incorporated in future longitudinal studies including data points from early life. However, there is a strong correlation between school performance and cognitive skills such as executive function, (Fuhs et al. 2014) and fine grained cognitive evaluation is more suited to small scale cross-sectional studies and are difficult to obtain in large representative population-based samples. Although comparison of our results with published literature is hampered by differences in measures (cognitive tests used in the 1958 British Birth Cohort (i.e. IQ and school performance tests) differ from tests used elsewhere (e.g., The Raven's Standard

Progressive Matrices (Alati et al. 2009), and National Adult Reading Test (NART) (Gunnell et al. 2009)) we expect all tests to be correlated to some extent as recognized by general intelligence (Deary et al. 2010).

A second limitation is that, despite the size of the cohort (n~14,000 participants), suicide is thankfully a relatively rare phenomenon, so we had limited statistical power to detect small effects. Further we were not able to examine the separate associations of cognitive skills with suicide mortality among females because of the small numbers of females who died by suicide in this cohort. Previous studies found that presence of psychosis reverses the association between IQ or school performance and suicide risk, i.e., whereby higher IQ or better school performance predict higher risk of suicide in individuals with psychosis (Alaraisanen et al. 2006, Andersson et al. 2008, Batty et al. 2010). If some of our 55 individuals who died by suicide were affected by psychosis, this might have introduced heterogeneity in our sample and reduced the strength of our associations. However, given that 5% of individuals who died by suicide are affected by psychosis (Hor and Taylor 2010), it is unlikely that our estimates are significantly biased in this manner.

Conclusions

Our findings are consistent with the hypothesis that individuals who died by suicide had a poorer development in terms of their reading abilities in adolescence than those still alive, but no difference in reading abilities was present in the early years of life. Future longitudinal studies are needed to document the development of cognitive abilities of suicidal and control individuals over time. Such a study could help determine if differences in cognitive performance between suicidal and non-suicidal individuals continue to increase over the lifespan.

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Table 1: Estimated means of reading skills from age 7 to 16 years for the entire sample (n=14505) and for males only (N=7368).

Reading										
Model 1						Model 2				
	Alive (n=14450)	Suicide (n=55)	Mean δ	Effect size	p-value	Alive (n=14450)	Suicide (n=55)	Mean δ	Effect size	p- value
<i>Entire sample</i>										
7y	-0.004 (0.008)	0.019 (0.125)	-0.023	-0.02	0.857	-0.003 (0.006)	0.008 (0.088)	-0.011	-0.02	0.156
11y	-0.009 (0.007)	-0.083 (0.126)	0.074	0.09	0.555	-0.012 (0.007)	-0.072 (0.112)	0.060	0.07	0.317
16y	-0.015 (0.009)	-0.211 (0.162)	0.196	0.18	0.226	-0.023 (0.008)	-0.172 (0.146)	0.149	0.15	0.702
Slope	-0.001 (0.001)	-0.026 (0.015)	0.025	0.21	0.099	-0.002 (0.001)	-0.02 (0.007)	0.018	0.15	0.336
	Alive (n=7320)	Suicide (n=48)	Mean δ	Effect size	p-value	Alive (n=7320)	Suicide (n=48)	Mean δ	Effect size	p- value
<i>Males only</i>										
7y	-0.008 (0.011)	0.033 (0.133)	-0.041	-0.04	0.759	-0.007 (0.009)	0.006 (0.008)	-0.013	-0.02	0.296
11y	-0.013 (0.011)	-0.074 (0.14)	0.061	0.06	0.663	-0.018 (0.01)	-0.066 (0.01)	0.048	0.06	0.452
16y	-0.018 (0.012)	-0.207 (0.172)	0.189	0.18	0.274	-0.033 (0.011)	-0.155 (0.012)	0.122	0.13	0.740
Slope	-0.001 (0.001)	-0.027 (0.013)	0.026	0.30	0.048	-0.003 (0.001)	-0.018 (0)	0.015	0.18	0.483

Tables report mean (standard error) for the alive and suicide groups.

Model 1: unadjusted model, not adjusted for sex.

Model 2: adjusted for early-life influences, i.e., sex (entire sample only), low birth weight, birth order, maternal age at child birth, father social class.

Mean δ : mean difference

Table 2: Estimated means of mathematic skills from age 7 to 16 years for the entire sample (n=14505) and for males only (N=7368).

Mathematics										
	Model 1					Model 2				
	Alive (n=14450)	Suicide (n=55)	Mean δ	Effect size	p-value	Alive (n=14450)	Suicide (n=55)	Mean δ	Effect size	p- value
Entire sample										
7y	0 (0.008)	0.033 (0.126)	-0.033	-0.03	0.795	-0.003 (0.009)	0.024 (0.009)	-0.027	-0.03	0.344
11y	-0.014 (0.007)	-0.027 (0.125)	0.013	0.02	0.915	-0.019 (0.009)	-0.061 (0.01)	0.042	0.04	0.145
16y	-0.031 (0.009)	-0.102 (0.159)	0.071	0.07	0.654	-0.04 (0.012)	-0.166 (0.012)	0.126	0.09	0.632
Slope	-0.003 (0.001)	-0.015 (0.015)	0.012	0.10	0.438	-0.004 (0.001)	-0.021 (0.001)	0.017	0.14	0.300
	Alive (n=7320)	Suicide (n=48)	Mean δ	Effect size	p-value	Alive (n=7320)	Suicide (n=48)	Mean δ	Effect size	p- value
Males only										
7y	-0.006 (0.011)	0.045 (0.141)	-0.051	-0.05	0.718	-0.008 (0.009)	0.031 (0.01)	-0.039	-0.05	0.378
11y	-0.018 (0.01)	0.009 (0.139)	-0.027	-0.03	0.844	-0.025 (0.009)	-0.037 (0.01)	0.012	0.02	0.208
16y	0.013 (0.008)	-0.036 (0.17)	0.049	0.07	0.989	-0.048 (0.012)	-0.123 (0.012)	0.075	0.07	0.135
Slope	-0.003 (0.001)	-0.009 (0.015)	0.006	0.07	0.694	-0.004 (0.001)	-0.017 (0.001)	0.013	0.15	0.449

Tables report mean (standard error) for the alive and suicide groups.

Model 1: unadjusted model

Model2: adjusted for early-life influences, i.e., sex (entire sample only), low birth weight, birth order, maternal age at child birth, father social class.

Mean δ : mean difference

