

Life-Course Influence of Adolescent Behaviour Problems on Type 2 Diabetes in Midlife: Results from 1958 British Birth Cohort Study

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Purpose: To assess whether there is a long-term relationship between childhood behaviour problems and type 2 diabetes in midlife. The study will also investigate whether any of such relationship is independent of other factors which may be associated with type 2 diabetes.

Design: Cohort study.

Participants: A total of 9377 members of the 1958 British birth cohort participated in the biomedical survey at age 45 years. The cohort has been followed up at regular intervals in childhood (age 7, 11 and 16 years) and adulthood (23, 33, 42 and 45 years).

Predictor Variables: Information regarding childhood behaviour collected during follow-ups at ages 7, 11 and 16 years.

Main Outcome Variables: Type 2 diabetes assessed using HbA1c at age 45 years.

Results: Unadjusted estimates show that teachers reported adolescent behaviour problems at age of 16 are associated with increased risk of type 2 diabetes in midlife. After adjustment for potential confounders and mediators in childhood and adulthood, a relationship was observed between the severity of adolescent behaviour problems and type 2 diabetes risk in midlife (mild behaviour problems: OR 2.17, 95% CI 1.11–4.23; severe behaviour problems: OR 4.40, 95% CI 1.14–16.99). However, no such relationship was observed between behaviour problems at 7 and 11 years and type 2 diabetes in midlife.

Conclusion: There is an association between adolescent behaviour problems and an increased risk of type 2 diabetes in midlife. Further molecular/genetic studies are required to understand the biological basis for this observed association.

Keywords: type 2 diabetes, adolescent behaviour problems, 1958 British birth cohort, National Child Development Study, HbA1c

Introduction

The prevalence of childhood behaviour problems is about 6–11%.¹ Childhood behaviour problems are associated with a range of medical conditions, such as chronic widespread pain,² mental Health problems (depression and anxiety),^{3,4} adult health behaviours (cigarette smoking, alcohol abuse, substance misuse),⁴ injury and mortality in adult life.^{5,6} A previous study from Scotland showed that childhood emotional problems were associated with increased odds of self-reported type 2 diabetes in midlife.⁷ The study assessed childhood behaviour problems among 6- to 12-year olds, and type 2 diabetes was self-reported by participants during a general health survey at 46–51 years. In this study, childhood behaviour was assessed at a single time point in childhood, and diagnosis of type 2 diabetes was based on self-report only. Furthermore, previous studies suggested associations between depression in adulthood and type 2 diabetes, with increased risks of type 2 diabetes by 25% to 60% among individuals with depression.^{8,9} The aim of this study is to assess whether there is a long-term relationship between childhood behaviour problems and type 2 diabetes in midlife using British birth cohort data. The study will also investigate whether any of such relationship is independent of other factors that may be associated with type 2 diabetes, birth weight, gestational age, childhood cognitive ability, family history, smoking, BMI, physical activity and social class.

Subjects and Methods

Participants

The 1958 British birth cohort, also known as the National Child Development Study (NCDS), consists of over 17,000 people born within the first week of March 1958 in Britain. The cohort has been followed up at regular intervals in childhood (age 7, 11 and 16 years) and adulthood (23, 33, 42 and 45 years). During the first 3 follow-ups in childhood, information was obtained from parents, local authority and class teachers. At age 45 years, 9377 members participated in a biomedical survey, accounting for 72.1% of the 13,009 available individuals. Despite attrition due to 45 years of follow-up, the participating sample at 45 years has been shown to be a representative of the surviving cohort.¹⁰ Access to anonymised data from the surveys of the 1958 British birth cohort was granted by the United Kingdom Data Service at the Economic and Social Research Council, University of Essex, UK. Ethical approval for the present study was obtained from the University of Bedfordshire Institute for Health Research Ethics Committee. The data used in the present study can be accessed by researchers through the UK Data Service at the University of Essex.

Childhood Behaviour Problems

Measures of childhood behaviour problems were used as explanatory variables in this study. These measures were obtained during childhood at ages 7, 11 and 16 years from parents and class teachers. Reports from both parents and class teachers rating of the child's behaviour were independently carried out at different age intervals by using different measurement scales. The measurements were mainly focused on behavioural maladjustments, hostility patterns, personality and locus of control. The two scales of child behaviour measurement used were the Bristol Social Adjustment Guide (BSAG) and the Rutter Child Behaviour Questionnaire. The Rutter Child Behaviour Questionnaire was shown to be a valid and reliable tool for assessing behaviour problems in childhood.¹¹ In the present study, teacher-reported childhood behaviour was used because in situations that involve different formal tasks and social demands, teachers are in a better position to assess each child and make comparison with the child's peers. Teachers rated childhood behaviour problems at school using the Rutter behaviour scale B at 16 years¹² (see [Appendix 1](#)). The Bristol Social Adjustment Guide (BSAG) was used by teachers to rate childhood behaviour problems at 7 and 11 years.¹³ In the Rutter behaviour scale B, there were 26 items at 16 years (0–52 scale). Items on this scale were coded as 0 = does not apply/never, 1 = applies somewhat/sometimes or 2 certainly applies/frequently. The score of individual item on the scale was added for each follow-up age to obtain a total behaviour score.² A total of 150 descriptions of behaviour or attitude at school which applies to the child is identified by the BSAG completed by teachers. These were then grouped into core syndromes as follows: unforthcomingness, withdrawal, depression, anxiety for acceptance by adults, hostility towards adults, writing off of adults and adult standards, anxiety for acceptance by children, restlessness, inconsequential behaviour, miscellaneous symptoms and miscellaneous nervous symptoms.¹⁴ To obtain a measure of childhood behaviour for this research, individual scores of each behaviour instrument were added to get a total behaviour score at different childhood ages: Rutter behaviour scale A at 7 and 11 years, 14 items (0–28 scale), and 18 items at age 16 (0–36 scale). Rutter behaviour scale B has 26 items at 16 years (0–52 scale). Each item on both scales (A and B) was recorded to have a uniform coding protocol, 0 = does not apply/never, 1 = applies somewhat/sometimes, or 2 = certainly applies/frequently. The score of the individual items on each scale were added for different follow-up age to obtain a total behaviour score for that age.² A total behaviour score of all items on the BSAG (0–99) was obtained, with a high score indicating social maladjustment. Furthermore, to investigate whether individuals with scores suggesting behaviour problems have higher tendency of having type 2 diabetes, children (at age 7, 11 and 16 years) were grouped into 3 behaviour groups: those with normal behaviour (having a score below the 80th percentile) mild-moderate behaviour problems (having a score between 80th and 95th percentile) and severe behaviour problems (having a score above 95th percentile). This classification of children behaviour was necessary because the original behaviour scores were not comparable across the 3 age points due to different rating scales.

Type 2 Diabetes

At age 45 years, blood samples were collected in a biomedical follow-up survey, blood glucose was measured as glycosylated haemoglobin (HbA1c). HbA1c was assessed by the use of ion-exchange high performance liquid

chromatography HLC-723GHbA1c 2.2; Tosoh Corp, Tokyo Japan.^{15,16} The presence of diabetes was determined by the measurement of glycosylated haemoglobin. Participants were classified as having type 2 diabetes if HbA1c was 6.5% (48 mmol/mol) or above,^{16–18}

Covariates

A range of potential confounders/mediators, such as childhood cognitive ability, social class (at birth and at age 42 years), family history of diabetes, gestational age, birth weight and adult health behaviours (smoking, alcohol consumption and physical activity) were taken into account in the analysis. As a measure of childhood cognition, the Childhood General Ability test¹⁹ was utilised. The test, which had verbal (range = 0–40) and non-verbal (range = 0–40) components was administered to participants (aged 11 years) at school. Social class was classified as professional, managerial/technical, skilled non-manual, skilled manual, semi-skilled and unskilled,²⁰ according to the Registrar General's classification of father's occupation in 1958. Social class at age 42 was based on the most recent occupation at age 42 years or at age 33 years, whichever is available.

Gestational age was calculated as number of weeks from the mothers' last menstrual period to delivery. Birth weight, originally recorded in pounds and ounces,²¹ was converted to kilograms. Family history of diabetes was obtained from parents of study participants. Participant's height was measured using a stadiometer. We computed body mass index (BMI) as weight in kilograms divided by height in meters squared.²² Data on smoking habit were obtained at 42 years, and participants were categorised as current smoker (if smokes 1 or more cigarette per day), former smoker or never smoker. Participant's exercise was obtained at age 42 and was categorised as <2–3 times per month, once a week, 2–3 times per week, or 4–7 times per week. Alcohol consumption was categorised as 0, 1–2, 3–4, 5–6 or >7 units per day.

Analysis

We assessed the association between childhood behaviour problems and type 2 diabetes in adulthood using logistic regression. Odds ratio and 95% confidence interval were used to measure the association. Type 2 diabetes was treated as a binary dependent variable in the regression analysis. Analyses were carried out for teachers' reporting of childhood behaviour problems at age 7, 11 and 16 years. Odds ratios were estimated after adjustment for childhood confounders, such as childhood cognitive ability, social class at birth, birth weight, gestational age and adulthood confounders, such as family history of diabetes, social class at 42 years, alcohol consumed at 42 years, exercise at 42 years and smoking habit. We carried out analyses for individuals with complete data on the variables examined. All analyses were carried out using Stata 13.²³

Results

Table 1 shows the characteristics of study subjects in the cohort. Of the 9408 study subjects, there are 201 individuals with type 2 diabetes. The prevalence of type 2 diabetes was higher in males than females (2.8% vs 1.5%).

Table 2 shows the relationship between childhood behaviour problems and type 2 diabetes at 45. There are increased odds of type 2 diabetes at 45 among individuals with mild behaviour problems at 16 (OR 1.69, 95% CI 1.14–2.51) and among those with severe problems at 16 (OR 2.29, 95% CI 1.14–4.60). These associations become stronger after adjustment for potential childhood and adulthood confounders. Compared to individuals with normal behaviour, those with mild behaviour problems at 16 have more than 2-fold increased odds of type 2 diabetes at 45 (OR 2.17, 95% CI 1.11–4.23) and those with severe behaviour problems have more than 4-fold increased odds of type 2 diabetes (OR 4.40, 95% CI 1.14–16.99), after adjustment for birthweight, gestational age, cognition, diabetes history, smoking status at 42, social class at birth, social class at 42, exercise frequency and daily alcohol consumption. In particular, males with mild-moderate behaviour problems have more than 3-fold increased odds of diabetes compared to those with normal behaviour (OR 3.38, 95% CI 1.33–8.60). Similarly, females with severe behaviour problems have more than 9-fold increased odds of diabetes compared to those with normal behaviour (OR 9.09, 95% CI 1.20–68.96). However, no such relationship was observed between behaviour problems at 7 and 11 years and type 2 diabetes at 45.

Furthermore, we carried out an analysis of parental reporting of childhood behaviour problems. There are no significant findings for childhood behaviour problems at ages 7, 11 or 16 (results not shown).

Table 1 Characteristics of Study Subjects

	Female (n = 4725)		Male (n = 4682)		Total (N = 9408)	
	N	%	n	%	n	%
Diabetes						
Diabetes	72	1.5	129	2.8	201	2.1
No Diabetes	3875	82	3847	82.2	7722	82.1
Missing Values	778	16.5	706	15.1	1485	15.8
Birth Weight						
Low BW	290	6.1	184	3.9	474	5
Not Low BW	4051	85.7	4095	87.5	8146	86.6
Missing Values	384	8.1	403	8.6	788	8.4
Gestational Age						
Preterm	155	3.3	168	3.6	323	3.4
Not Preterm	3880	82.1	3856	82.4	7736	82.2
Missing Values	690	14.6	658	14.1	1349	14.3
Body Mass Index						
Under Weight	39	0.8	12	0.3	51	0.5
Healthy Weight	1943	41.1	1084	23.2	3027	32.2
Over Weight	1492	31.6	2255	48.2	3747	39.8
Obese	1086	23	1160	24.8	2246	23.9
Missing values	165	3.5	171	3.7	337	3.6
Cognition at Age 7						
Below mean	2332	49.4	2168	46.3	4500	47.8
Above mean	1568	33.2	1676	35.8	3244	34.5
Missing values	825	17.5	838	17.9	1664	17.7
Cognition at Age 11						
Below mean	2303	48.7	1997	42.7	4300	45.7
Above mean	1381	29.2	1597	34.1	2978	31.7
Missing values	1041	22	1088	23.2	2130	22.6
Cognition at Age 16						
Below mean	2269	48	2322	49.6	4591	48.8
Above mean	1238	26.2	1122	24	2360	25.1
Missing values	1218	25.8	1238	26.4	2457	26.1
Diabetes History						
No	4242	89.8	4173	89.1	8415	89.4
Yes	110	2.3	90	1.9	200	2.1
Missing values	373	7.9	419	8.9	793	8.4
Social Class at Birth						
Managerial	647	13.7	647	13.8	1294	13.8
Professional	221	4.7	257	5.5	478	5.1
Skilled manual	2262	47.9	2219	47.4	4481	47.6
Skilled non-manual	454	9.6	457	9.8	911	9.7
Other/unknown	174	3.7	176	3.8	350	3.7
Partly skilled	573	12.1	555	11.9	1128	12
Unskilled	381	8.1	353	7.5	734	7.8
Missing values	13	0.3	18	0.4	32	0.3
Social Class at 42						
Managerial	1516	32.1	1767	37.7	3283	34.9
Professional	145	3.1	347	7.4	492	5.2
Skilled manual	332	7	1411	30.1	1743	18.5
Skilled non-manual	1515	32.1	430	9.2	1945	20.7
Other/unknown	241	5.1	184	3.9	425	4.5

(Continued)

Table 1 (Continued).

	Female (n = 4725)		Male (n = 4682)		Total (N = 9408)	
	N	%	n	%	n	%
Partly skilled	767	16.2	393	8.4	1160	12.3
Unskilled	196	4.1	132	2.8	328	3.5
Missing values	13	0.3	18	0.4	32	0.3
Smoking Status at 42						
Current smoker	1126	23.8	1075	23	2201	23.4
Ex/occ-smoker	1321	28	1400	29.9	2721	28.9
Never smoked	2136	45.2	2020	43.1	4156	44.2
Missing value	142	3	187	4	330	3.5
Exercise Frequency						
2–3 times /week	981	20.8	986	21.1	1967	20.9
2–3 times/month	247	5.2	331	7.1	578	6.1
Once a week	780	16.5	911	19.5	1691	18
4–7 times /week	1245	26.3	1089	23.3	2335	24.8
<2–3 times /month	1329	28.1	1178	25.2	2507	26.6
Missing values	143	3	187	4	330	3.5
Daily Alcohol Frequency						
None	168	3.6	712	15.2	880	9.4
1–2	412	8.7	235	5	647	6.9
3–4	2492	52.7	1628	34.8	4120	43.8
5–6	1176	24.9	1231	26.3	2407	25.6
≥7	444	9.4	816	17.4	1260	13.4
Missing values	33	0.7	60	1.3	94	1
Teachers Reported Behaviour at Age 7 (BSAG scale)						
Normal	3675	77.8	3280	70.1	6955	73.9
Mild-Moderate	462	9.8	650	13.9	1112	11.8
Severe	93	2	205	4.4	298	3.2
Missing Values	495	10.5	547	11.7	1043	11.1
Teachers Reported Behaviour at Age 11 (BSAG scale)						
Normal	3545	75	3144	67.2	6689	71.1
Mild-Moderate	461	9.8	706	15.1	1167	12.4
Severe	90	1.9	185	4	275	2.9
Missing Values	629	13.3	647	13.8	1277	13.6
Teachers Reported Behaviour at Age 16 (Rutter B scale)						
Normal	2978	63	2739	58.5	5717	60.8
Mild-Moderate	488	10.3	583	12.5	1071	11.4
Severe	90	1.9	132	2.8	222	2.4
Missing Values	1169	24.7	1228	26.2	2398	25.5

Discussion

In this study, we have shown that childhood behaviour problems at 16 assessed by teachers are associated with an increased risk of type 2 diabetes in midlife. These associations were not explained away by potential childhood and adulthood confounding factors.

However, we should be cautious to draw a causal association. If consistent with other previously published studies of its kind, the observed association could be suggestive of a true causal association. However, to the best of our knowledge, this is the first study to report epidemiological evidence of the effect of childhood behaviour on type 2 diabetes in

Table 2 Risk of Type 2 Diabetes in Midlife (Odds Ratio) According to Teachers' Reporting of Childhood Behaviour

Variables	All		Female		Male	
	Unadjusted OR (CI)	Adjusted OR (CI)	Unadjusted OR (CI)	Adjusted OR (CI)	Unadjusted OR (CI)	Adjusted OR (CI)
Teachers Reported Behaviour at age 7						
Normal (ref)						
Mild-moderate	1.26 (0.83–1.92)	1.13 (0.49–2.62)	1.45 (0.71–3.00)	0.73 (0.18–2.96)	1.08 (0.64–1.80)	1.21 (0.37–3.93)
Severe	2.14* (1.17–3.91)	2.36 (0.74–7.57)	4.25** (1.64–9.82)	1.32 (0.13–13.59)	1.33 (0.61–3.00)	3.71* (0.82 –16.77)
Teachers Reported Behaviour at age 11						
Normal (ref)						
Mild-moderate	1.58* (1.07–2.31)	1.72 (0.85–3.48)	1.10 (0.48–2.36)	0.78 (0.18–3.29)	1.65*(1.0–2.58)	3.04** (1.23–7.47)
Severe	2.26*(1.20–4.25)	1.03 (0.19–5.48)	4.40** (1.69–11.36)	0.94 (0.05 –16.96)	1.41 (0.60–3.29)	0.95(0.09–10.43)
Teachers Reported Behaviour at age 16						
Normal (ref)						
Mild-moderate	1.69**(1.14–2.51)	2.17**(1.11–4.23)	1.73 (0.88–3.39)	1.32(0.41–4.31)	1.59 (0.97–2.5)	3.38** (1.33–8.60)
Severe	2.29*(1.14–4.60)	4.40**(1.14–16.99)	4.59**(1.76–12.01)	9.09** (1.20–68.96)	1.27 (0.45–3.5)	3.04 (0.22–41.88)

Notes: *p < 0.05, **p < 0.001. Adjusted: adjustment for birth weight, gestational age, body mass index, cognition at age 7, cognition at age 11, cognition at age 16, diabetes history, social class at birth, social class at 42, smoking status at 42, exercise frequency, and daily alcohol frequency.

midlife. So at the time of the writing, it is difficult to know whether this result can be repeated in other populations or in different settings. However, this is possible because associations between early life environments and health outcomes in later life have already been reported. For example, studies have demonstrated links between childhood socioeconomic position and adult chronic diseases such as cardiovascular disease²⁴ and type 2 diabetes.^{25,26} Also, exposure to emotional stress during childhood has been found to be associated with the risk of obesity and type 2 diabetes in midlife.^{27,28} It has also been suggested that exposure to psychological stress in childhood may increase the risk of adverse health behaviours like smoking^{29–31} and alcohol abuse.^{32,33} Our finding is consistent with a previous study by Thomas et al which examined the effect of childhood adversities on obesity and glucose control in the 1958 British birth cohort. Their finding suggests that stressful emotional childhood experiences increase the risk of obesity, thereby increasing the risk of type 2 diabetes.²⁷ Similarly, a regional study by von Stumm et al has shown an association between childhood emotional problems among 6–12-year olds and self-reported type 2 diabetes in midlife among women in a Scottish birth cohort.⁷

In this study, the odds of having type 2 diabetes increased with increasing severity of childhood behaviour problems at 16 years. In particular, the pattern was more striking among women. In addition, the observed association with childhood behaviour was not specific to type 2 diabetes in adulthood. Childhood behaviour problems have been found to be associated with other chronic conditions such as chronic widespread pain² and long-term mental health problems in adulthood.^{3,4,34}

The exact mechanism underlying the observed association remains unknown; however, there are possible explanations. It is likely to be a behavioural cause of both childhood behavioural problems and type 2 diabetes. Previous evidence suggests a link between type 2 diabetes on the one hand, and obesity resulting from excess intake of calories and limited physical activity on the other, with potential interplay with other psychosocial factors.^{35–42} In the same vein, behaviour around food intake and activity has been implicated as a cause of the excess type 2 diabetes cases observed among individuals with mental illness and depression.^{43,44} Alternatively, there could be a neuroendocrine or molecular genetic defect underlying this relationship. Childhood behavioural problems could affect the developing brain, especially during the sensitive period. This is supported by genetic studies, both in animals^{45,46} and humans.⁴⁷ Similarly, the role of long-term neuroendocrine dysregulation (hypothalamic–pituitary–adrenal axis (HPA), sympathetic nervous system (SNS) and the sympathoadrenal medullary system (SAMS))^{48–51} are being explored by researchers. Noteworthy, most of the evidence so far is derived from research conducted on rats. Studies have shown that the brain releases counter-regulatory hormones as a response to psychological stress, which counteracts the effect of insulin, hence raising blood glucose level.^{52,53} Furthermore, specific genes and receptors are implicated both in animal and human studies.^{54–58} Childhood behaviour problems may affect the brain via raised levels of glucocorticoids and neuroendocrine dysregulation to confer the risk of obesity, which in turn leads to subsequent type 2 diabetes. A similar suggestion was made for children with emotional disturbances.⁵⁹ Other possible mechanism could be that exposure to psychological stress in early life may lead to alteration in the expression of hypothalamic feeding neuropeptide which may lead to partial increase in food intake and adiposity in adult life, Or remotely, through the mediating effect of 11 β -hydroxysteroid dehydrogenase type I (11 β -HSD1) in metabolic functions.⁶⁰ Further genetic or molecular studies are required.

A major limitation of this study is attrition bias. Attrition bias is possible due to such a long follow-up. Of the 18,558 participants, 9377 individuals participated in the survey at 45 years. However, a recent study showed that the surviving cohort was broadly similar to the original birth population in terms of gender and social class at birth.⁶¹ Another limitation of the study is the use of only the father's occupation to decide social class at birth. A better approach would be to include the mother's occupation, compare the two and then select the one which is higher. The NCDS data lack detailed information about the mother's occupation in 1958. However, father's occupation has been used successfully in the past to denote childhood socioeconomic position in previous studies that used the NCDS data.⁶²

Our study has a number of strengths. First, the study is based on a large population-based data, which is representative of the British population who were born in 1958. Second, an objective measure of type 2 diabetes (glycated haemoglobin, ie HbA1c) was used. Third, data on childhood behaviour problems were collected prospectively at three childhood ages 7, 11, and 16 years, free of recall bias, which is often encountered in a case-control study. Fourth, child's behaviour was rated by both parents and class teachers. In situations that involve different

formal tasks and social demands, teachers are in a better position to assess each child and make comparison with the child's peers.²

Conclusion

In conclusion, for the first time, we demonstrated that there is an association between childhood behaviour problems and an increased risk of type 2 diabetes in midlife.

Highlights

- This study demonstrated that childhood behaviour problems are associated with an increased risk of type 2 diabetes in midlife.
- Further molecular/genetic studies are required to understand the biological basis for this observed association.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare that they have no competing interests.

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