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Title: Association of neighbourhood and individual-level socioeconomic disadvantage in childhood and adulthood with cognitive function in mid-adulthood: Cardiovascular Risk in Young Finns Study

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Key words: socioeconomic disadvantage, cognitive function, life course, neighbourhood, cohort study, longitudinal study

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Abstract

Socioeconomic disadvantage at individual level is associated with poor cognitive outcomes but the link of neighbourhood disadvantage with cognitive function is unclear. We used data from Young Finns Study, a population-based cohort, to examine the associations of neighbourhood and individual-level disadvantage in childhood (age 3-21 years) and adulthood (age 22 up to the time of cognitive assessment) with cognitive function in mid-adulthood (age 35-49 years). Neighbourhood disadvantage was ascertained based on register data, including geo-coded address history. Compared to individuals who experienced neither individual-level nor neighbourhood disadvantage in childhood, those who experienced both had, on average, 0.236 standard deviations (SDs) lower overall cognitive function scores (95% confidence interval, CI: -0.355 to -0.116) and those who experienced individual-level but not neighbourhood disadvantage had 0.196 SDs lower scores (95% CI: -0.323 to -0.070). The estimates were slightly larger for adult individual-level and neighbourhood disadvantage. The findings were similar across the cognitive domains and robust to adjustment for a polygenic risk score for cognitive ability. We found no clear evidence of sleep difficulties, depressive symptoms or cardiovascular health mediating the associations. Our findings suggest that socioeconomic disadvantage at individual- but not neighbourhood-level, from childhood to adulthood, may impact on cognitive function in mid-adulthood.

Keywords socioeconomic disadvantage, cognitive function, life course, neighbourhood, cohort study, longitudinal study

Key messages

We examined the extent to which neighbourhood socioeconomic disadvantage in childhood or adulthood, alone or together with individual-level disadvantage, is associated with cognitive function in mid-adulthood.

Individual- and neighbourhood-level socioeconomic disadvantage were ascertained in childhood (age 3-21 years) and adulthood (age 22 up to 49 years). Overall and domain-specific cognitive function were ascertained in mid-adulthood (age 35 to 49 years).

Individuals who experienced neighbourhood and individual-level socioeconomic disadvantage or individual-disadvantage only in childhood or adulthood had lower cognitive function scores in mid-adulthood than those who experienced neither type of disadvantage. Neighbourhood disadvantage alone, during either time period, was not associated with mid-life cognitive function.

Our findings suggest that socioeconomic disadvantage at individual- but not neighbourhood-level, from childhood to adulthood, may impact on cognitive function in mid-adulthood.

Introduction

Cognitive function and ability refer to a person's mental capability for reasoning, problem solving, planning, abstract thinking, comprehension of complex ideas and learning from experience.[1] Cognitive function plays a key role in a person's everyday functioning and quality of life across the life span, impacting on performance in education, work, social relationships and independent living. Individual differences in cognitive function are partly inherited but cognitive function may also be influenced by socioeconomic and environmental factors.[2-5] Cross-sectional studies indicate that compared to people living in affluent neighbourhoods, those living in disadvantaged neighbourhoods tend to perform poorly in tests of cognitive function. [6 7] In terms of associations over time, findings from a longitudinal study in the USA suggest that adolescents who had lived in socioeconomically deprived neighbourhoods during childhood had, on average, poorer overall cognitive function than adolescents who had lived in affluent neighbourhoods, independently of their parents' education or household income.[8] Observations from birth cohort study in Scotland indicate that individuals who lived in deprived neighbourhood in mid- to late adulthood had poorer general cognitive function at age 70 years and an exacerbated decline in this function from age 70 to 82 years, when compared to those not living in deprived neighbourhoods. [9] Overall, the existing evidence is limited by many studies relying on single-time point measures of socioeconomic disadvantage and utilising relatively one-dimensional, general measures of cognitive function.[10 11] Consequently, the association of long-term exposure to neighbourhood and individual-level disadvantage with the overall and domain-specific cognitive function is incompletely understood. In a similar vein, it is unclear whether the effect of disadvantage on cognitive outcomes is cumulative [12 13] or whether there are sensitive periods during the life course when exposure to socioeconomic disadvantage is particularly detrimental to cognitive function. [14 15] Neighbourhood and individual-level socioeconomic characteristics are associated not only with diverse health and functional outcomes but also with one another, and these associations may be bidirectional.[16 17] Evidence suggests that poor quality sleep, depression and cardiovascular risk factors (e.g. smoking, overweight and obesity, physical inactivity and hypertension) are associated with socioeconomic disadvantage [18-20] as well as poor cognitive function among adults, but the direction of these associations is not clear [21-26]. We hypothesised that these factors could mediate the association of neighbourhood and individual-level socioeconomic disadvantage with cognitive function.

To disentangle the contextual and individual-level effects, we investigated the associations of neighbourhood and individual-level socioeconomic disadvantage across the early part of the life course with cognitive function in mid-adulthood, using data from a population-based, prospective cohort study, with measures of neighbourhood and individual-level disadvantage across four decades, from childhood to mid-adulthood. [27] We also examined the extent to which the associations of neighbourhood and individual-level disadvantage with cognitive function were mediated by potentially modifiable factors which previous research suggests are associated with cognitive function, i.e. sleep difficulties, depressive symptoms and markers of cardiovascular health.

Methods

Study design and participants

We used data from the Cardiovascular Risk in Young Finns Study, a population-based, prospective cohort study in Finland. The study design, sampling and data collection have been described in detail previously and are provided in the online supplement. [27] Briefly, 3,596 children and adolescents (1,832 girls, 51%) aged 3 to 18 years were enrolled in the study at baseline in 1980. Participants were followed-up with questionnaires and clinical examinations at regular intervals up to 2011, and their study records were linked to nationwide healthcare registers and Statistics Finland population data for the ascertainment of health and healthcare outcomes and address history. Participants were eligible for our analyses if they remained alive and had not refused the use of their study data and participated in the 2011 data collection wave (n=2,063). The study was approved by local ethics committees and all participants provided written informed consent to participate (appendix, p. 3).

Baseline variables

Neighbourhood disadvantage was operationalised as a composite score based on information on education, income and unemployment [28], which are key measures of the socioeconomic composition of residential areas, households and individuals.[29 30] Neighbourhood socioeconomic disadvantage was ascertained from the participants' geocoded residential address history, which was linked to a nationwide geographical grid database containing Statistics Finland data on education, income and employment status of the residents (appendix, p. 4). We calculated a disadvantage score for each neighbourhood (250m x 250m grids) with ≥10 residents. The disadvantage score was based the proportion of adult residents (age ≥18 years) who had primary education only, the proportion of adult residents who were unemployed and the median annual income of the households in each grid. We calculated a z-score for each of the three components as well as an overall socioeconomic disadvantage score (mean of the component scores) for each neighbourhood. [31] Exposure to neighbourhood socioeconomic disadvantage was calculated by summing up the overall disadvantage score of all the neighbourhoods where the participant lived during childhood (age 3 to 21 years) and adulthood (age 22 up to the time of cognitive assessment, age 35 to 49 years), with each score multiplied by the number of years the participant lived in each neighbourhood.[32 33] Neighbourhood disadvantage scores were divided into least disadvantaged (≤ -0.5 SD), intermediate-low (-0.5 to ≤0 SD), intermediate-high (>0 to <0.5 SD) and the most disadvantaged (≥0.5 SD). As a binary exposure, neighbourhoods were defined as disadvantaged (>0 SD) or not disadvantaged (≤0 SD).

Individual-level socioeconomic disadvantage during childhood was ascertained from questionnaire data on the participants' parents' education, income and employment when the participant was 3 to 21 years old; individual-level disadvantage during adulthood was ascertained from the participant's own education, income and employment from age 22 years up to the time of cognitive assessment (at age 35-49 years; appendix, p. 5). Each participant's exposure to childhood individual-level socioeconomic disadvantage was calculated as the mean of the disadvantage z-scores at age 3 to 21 years, and their adult individual-level socioeconomic disadvantage as the mean of the disadvantage z-scores from age 22 years up to the time of cognitive assessment, age 35 to 49 years. Individual-level disadvantage scores during both time periods were divided into least disadvantaged (≤-0.5 SD), intermediate-low disadvantage (-0.5 to ≤0 SD), intermediate-high disadvantage (>0 to <0.5 SD) and most disadvantaged (≥0.5 SD). Binary disadvantage indicators were generated by was splitting childhood and adult disadvantage scores into disadvantaged (>0 SD) and not disadvantaged (≤0 SD).

An indicator for the separate and joint exposures to neighbourhood and individual-level disadvantage was operationalised by combining the indicators of neighbourhood and individual-level disadvantage in childhood and adulthood: no exposure to neighbourhood or individual-level disadvantage (reference category: neighbourhood disadvantage score ≤0 SD and individual-level disadvantage score ≤0 SD); exposure to neighbourhood but not individual-level disadvantage (neighbourhood disadvantage score >0 SD and individual-level disadvantage score ≤0 SD); exposure to individual-level but not neighbourhood disadvantage (neighbourhood disadvantage score ≤0 SD and individual-level disadvantage score >0 SD); and exposure to neighbourhood and individual-level disadvantage (neighbourhood disadvantage score >0 SD and individual-level disadvantage score >0 SD).

Potential confounders were age, sex and a polygenic risk score for cognitive function. Age and sex were ascertained from baseline questionnaires and health examination. The polygenic risk score was determined based on data from genotyped blood samples collected in 2001, 2007 and 2011 (appendix, p. 6-7). Potential mediators were sleep difficulties, depressive symptoms and Ideal Cardiovascular Health score, which were ascertained during the same data collection wave as the cognitive assessment but represent characteristics and behaviours over a period of time leading up to the time of cognitive assessment. Sleep difficulties (difficulties falling asleep or staying asleep ≥2 nights/week), depressive symptoms (Beck Depression Inventory Score ≥10), smoking, physical activity and diet were ascertained from self-report questionnaires. Ideal Cardiovascular Health score was operationalised using the American Heart Association Ideal Cardiovascular Health metrics: non-smoker (never smoked or has quit); body mass index<25 kg/m^2; physically active: ≥75 min/week of vigorous physical activity or ≥150 min/week of moderate -to-vigorous physical activity; healthy diet: 4 or 5 healthy dietary components as defined below; total cholesterol <5.172 mmol/litre and no cholesterol lowering medication; blood pressure <120/80 mm Hg and no antihypertensive medication; and fasting glucose <5.55 mmol/l and no medication for diabetes (appendix, p. 7-8). Each ideal cardiovascular health metric was given one point and the overall ideal cardiovascular health score for each participant was calculated as the sum of the scores, which ranged from 0 (all metrics unhealthy) to 7 (all metrics healthy) [34].

Outcome ascertainment

Cognitive function in mid-adulthood was measured in 2011 (when participants were 34 to 49 years old) using Cambridge Neuropsychological Test Automated Battery (CANTAB; Cambridge Cognition, Cambridge, United Kingdom). A detailed description of the tests and the validation of the cognitive data have been published previously.[35] Briefly, the test battery comprises four tests, each assessing a separate cognitive domain: paired-associates learning (PAL) test measuring visual and episodic memory and visuospatial associative learning (hereafter learning and memory); reaction time (RTI) test measuring reaction and movement speed and attention (hereafter reaction time); rapid visual information (RVP) test measuring visual information processing, recognition, and sustained attention (hereafter information processing); and spatial working memory (SWM) test measuring short-term and spatial working memory and problem solving (hereafter working memory) (appendix, p. 6). We used all available data for each test and consequently, the number of participants included in the analyses of specific cognitive domains varied (figure 1; appendix, p. 6).

Statistical analyses

We used linear regression to model the associations of neighbourhood and individual-level socioeconomic disadvantage in childhood and adulthood with cognitive function in mid-adulthood, adjusting the estimates for age and sex, with additional analyses including adjustment for the polygenic risk score for cognitive function. To examine the extent to which our findings were influenced by the inclusion of individuals younger than 40 years, we undertook sensitivity analyses restricting the study population to those aged ≥40 at the time of cognitive assessment. We also conducted counterfactual mediation analyses to examine the potentially mediating effects of sleep difficulties, depressive symptoms and cardiovascular health score at the time of cognitive assessment on the association between socioeconomic disadvantage and cognitive function.[36] (appendix, p. 6-8) Linear and logistic regression models were used to investigate the exposure-mediator and mediator-outcome associations. Analyses were conducted using SAS 9.4 (SAS Institute, Cary, North Carolina, USA) and Stata SE 18 (Stata Corporation, College Station, Texas, USA).

Results

Our main analyses and mediation analyses were based on data from 1,706 men and women with complete data on age, sex, neighbourhood and individual-level socioeconomic disadvantage in childhood and adulthood, mid-adult cognitive function in at least one domain and at least one potential mediators (appendix, p. 8). The analyses with additional adjustment for genetic risk were based on data from 1,492 individuals who also had data on the polygenic risk score for cognitive function (figure 1). The 1,706 participants included in our analyses represented 42.0%% of the male and 52.8% of the female baseline participants. Their mean age at baseline (10.5 years, SD 5.0) was similar to that of the excluded participants (10.4 years, SD 5.0, p=0.3). Participants in our analyses were less likely to have lived in disadvantaged neighbourhoods as children (age 3-21 years; n=860, 50.3%) than those excluded from the analyses (n=1 133, 60.1%; p<0.0001).

The participants in our analytical sample were, on average, 41.5 years old (standard deviation: 5.0 years) at the time of cognitive assessment and 56.6% were women (table 1). Over a third lived in middle to low disadvantage neighbourhoods during childhood (33.4%) and adulthood (39.2%), and the majority experienced middle to high individual-level disadvantage during these times (32.2% and 40.0%, respectively) (table 1).

Associations of neighbourhood and individual-level socioeconomic disadvantage in childhood and adulthood with the overall cognitive function in mid-adulthood are shown in table 2. On average, cognitive function did not differ across the categories of neighbourhood disadvantage during childhood. Participants who as adults lived in neighbourhoods with disadvantage scores higher than the national median had lower overall cognitive function than those living in less disadvantaged neighbourhoods. There was a consistent dose-response association between childhood as well as adult individual-level disadvantage and poorer cognitive function in mid-adulthood.

Associations of neighbourhood and individual-level disadvantage in childhood and adulthood with domain-specific cognitive function mid-adulthood are shown in table 3. Cognitive function in learning and memory, reaction time and working memory did not markedly differ by childhood or adult neighbourhood disadvantage but individuals who had lived in disadvantaged neighbourhoods as children or as adults had poorer scores in information processing. Individual-level disadvantage in childhood and adulthood was associated with a lower average score in learning and memory, reaction time and information processing; adult individual-level disadvantage was also associated with a worse function in the working memory domain.

Associations of separate and joint exposure to neighbourhood and individual-level disadvantage in childhood and adulthood with cognitive function in mid-adulthood are shown in figure 2. The estimates indicate that on average, individuals who experienced individual-level disadvantage during childhood or adulthood had reduced overall cognitive function as adults, regardless of their exposure to neighbourhood disadvantage. The findings were similar for all cognitive domains, with the largest average differences observed for learning and memory, and information processing. The estimates were similar in models with additional adjustment for the polygenic risk score for cognitive ability, suggesting that genetic risk did not have a strong influence on these (Table S1). This is likely because in our dataset, the polygenic risk score was a poor predictor of cognitive function, with the R^2 statistics indicating that it explained <3.5% of variance in the overall cognitive function and <0.001% of variance in the domain-specific cognitive function. Findings from the sensitivity analyses restricted to participants aged ≥40 years were similar to our main findings, suggesting that the inclusion of adults younger than 40 years did not have a marked influence on our observations (Table S2).

The decomposition of the association of childhood and adult disadvantage with the overall cognitive function is shown in Table S3. We found no clear evidence of sleep difficulties, depressive symptoms or cardiovascular health mediating the association of individual-level or neighbourhood socioeconomic disadvantage in childhood or adulthood with cognitive function in mid-adulthood. Socioeconomic disadvantage was not strongly associated with sleep difficulties or depressive symptoms in mid-adulthood, but increased deprivation was associated with poorer cardiovascular health (Table S4). However, these potential mediators were not associated with the cognitive outcomes (Table S5).

Discussion

Summary of findings

Our observations suggest that relative socioeconomic disadvantage during childhood and adulthood is associated with relatively poorer cognitive function in mid-adulthood. The associations were the most marked for two domains of cognition: learning and memory and information processing, and appeared to be driven by individual-level, rather than neighbourhood disadvantage. Our findings are in line with those of many previous studies, which have reported independent and joint associations of individual and neighbourhood socioeconomic disadvantage with worse cognitive function in various age groups. [6 10 11 17 23] In some studies, cognitive function was particularly poor among disadvantaged adults living in disadvantaged neighbourhoods, whereas in others, disadvantaged adults and older people living in affluent neighbourhoods had poorer cognitive function pointing to a potential role of the disparity of the individual and neighbourhood circumstances in shaping cognitive function [6 10 11] Our analysis of a socioeconomic disadvantage regime across a significant part of the life course and cognitive function in multiple domains takes this research further, pointing to adult individual-level disadvantage as a risk factor to poor cognitive function, with learning and memory and information processing as the key areas of cognition affected. Our previous findings suggest that socioeconomic disadvantage during sensitive developmental periods is s associated with the risk of adverse health outcomes, e.g. obesity and depressive symptoms, [37-39] but the findings from this study point to a role of cumulating disadvantage as a potential determinant of adult cognitive function.

Potential mechanisms

The mechanisms for an association of socioeconomic disadvantage with cognitive function are not fully understood. One hypothesis is that neighbourhood and individual socioeconomic disadvantage might influence people's cognitive function via mechanistic pathways related to stress and adverse health behaviours. [4 40-42] However, we found no clear evidence for mediating effects of sleep difficulties, depressive symptoms or a cardiovascular health score in the association of socioeconomic disadvantage and cognitive function. Emerging evidence points to developmental mechanisms involving links between exposure to area deprivation and brain structure and function: findings from a longitudinal study in the US suggest that exposure to neighbourhood deprivation during childhood predicted not only performance in a test of neurocognitive ability but also prefrontal cortex morphology in adolescence, independently of parents' education and household income.[8] Stress is one potential mechanism linking individual-level socioeconomic disadvantage in adulthood to poor cognitive outcomes. For example, unemployment and low income are important sources of psychosocial stress, and in general, socioeconomically disadvantaged individuals and families have fewer buffering resources to help counterbalance the effects of stress.[43] There is also evidence to suggest that stress can impair learning and memory.[44] Data on long-term stress exposure across the life course were unavailable in our dataset, and we were thus unable to explore this potential mechanism further. It is also possible that the association of socioeconomic disadvantage with cognitive function is bidirectional: for example, cognitive function is a powerful predictor of educational achievement, which can influence an individual's income and employment opportunities.

Strengths and limitations

A key strength of our analyses is that we used longitudinal, prospectively collected data, including repeated measures of neighbourhood and individual-level socioeconomic disadvantage across four decades extending from the participants' childhood up to mid-adulthood. This was made possible by a unique resource of individual address history linked to geocoded nationwide data on indicators of socioeconomic disadvantage (education, income and employment). We examined the separate and joint associations of neighbourhood and individual-level disadvantage with cognitive outcomes by operationalising disadvantage as a combined exposure. This approach allowed us to circumvent issues with the directions of the associations in investigating disadvantage consisting of exposures which have strong and potentially mutually confounding associations with cognitive outcomes. Cognitive function in mid-adulthood was measured using a comprehensive test battery, enabling us to examine the overall cognitive function as well as function in specific cognitive domains.

We excluded individuals with incomplete data on childhood or adult socioeconomic disadvantage (n=327, 15.9%) and those with no data on cognitive function (n=30, n=1.5%). These data were likely missing at random. Data on neighbourhood disadvantage were not available prior to 1980 (precluding us from ascertaining childhood neighbourhood disadvantage for participants who were 18 years old at the study baseline). We did not have sufficiently rich covariate data to impute the socioeconomic characteristics that constituted indicators of neighbourhood and individual-level disadvantage, and consequently excluded participants with these data missing, which limits the generalisability of our findings to time periods preceding the study baseline. Data on cognitive function were incomplete due to technical issues or some participants' refusal to complete one or more tests. Given the size of our dataset, we were unable to investigate a finer categorisation of disadvantage across the life course (ie. combinations of neighbourhood and individual-level disadvantage e.g. by calendar year). As the operationalisation of disadvantage was based on three characteristics (income, education and employment), other, potentially important aspects of disadvantage (e.g. household size or residential over-crowding) were not considered. Also, the participants in the Young Finns Study were children 40-50 years ago and the socioeconomic circumstances from that era are not directly comparable to those of today. However, as the measures of disadvantage were standardised to the average values of the time, we are confident that the estimates of the relative associations remain interpretable across the follow-up period. It is a limitation of our investigation that the potential mediators were measured at the same time as cognitive function. These factors were ascertained from self-report questions on symptoms or health behaviours during the month or weeks leading up to the cognitive assessment (sleep, depressive symptoms, diet, physical activity and smoking) or clinical or anthropometric characteristics (hypertension, elevated glucose or cholesterol and body mass index) that develop over time. Consequently, the mediating effects we examined reflect relatively short-term effects and cannot be interpreted as the effects of health behaviours or characteristics across several years preceding cognitive assessment. The study was conducted in one country, in an ethnically homogeneous population of White individuals, and the sample attrition between the study baseline and the time of cognitive assessment was 47%, which limit the generalisability of our findings to other populations.

Our study shares the methodological challenge of all studies of socioeconomic disadvantage exposures, namely the possibility that the observed association of indicators of disadvantage with cognitive function derives from factors that are common causes of disadvantage and cognitive function, rather that disadvantage itself. Also, the association of socioeconomic disadvantage with cognitive function may be bidirectional. As data on cognitive function were only available in mid-adulthood, we were unable to explore these issues further utilising repeated measures. Adjustment for a polygenic risk score (as a marker of a participant's basal cognitive function) did not markedly alter our findings but as genetic factors account only for a small proportion of variance in cognitive function, [45] this adjustment has only partially helped to account for the individual-level variation in cognitive function. . Also, the proportion of time people spend in their residential neighbourhoods and the amount of interaction they have with their surrounding area is likely to vary, which may have diluted the observed associations of neighbourhood disadvantage with cognitive outcomes. With no data available on the participants' level of engagement with their neighbourhood, we were unable to examine this further.

Conclusion

Our findings suggest that socioeconomic disadvantage in childhood and adulthood is associated with poorer cognitive function in mid-adulthood, with the association being the most marked for two domains of cognition: learning and memory and information processing, and driven by individual-level, rather than neighbourhood disadvantage.

Ethics approval

The Young Finns study was approved by the local ethical committees (1st Ethical Committee of the Hospital District of Southwest Finland, Regional Ethics Committee of the Expert Responsibility area of Tampere University Hospital, Helsinki University Hospital Ethical Committee of Medicine, The Research Ethics Committee of the Northern Savo Hospital District and Ethics Committee of the Northern Ostrobothnia Hospital District) of the participating sites (ETMK:88/180/2010). All participants or their parents as proxies provided informed consent to take part in the study.

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Table 1. Participant characteristics

Demographic characteristics	
Female, n (%)	966 (56.6)
Age at study baseline, mean (SD)	10.5 (5.0)
Range: 3-18	
Age at cognitive assessment, mean (SD)	41.5 (5.0)
Range: 34-49	
Neighbourhood socioeconomic disadvantage	N (%)
In childhood (age 3 to 21 years)	
least disadvantaged (≤-0.5 SD)	405 (23.7)
middle-low (>-0.5 to ≤0 SD)	570 (33.4)
middle-high (>0 to ≤0.5 SD)	392 (23.0)
most disadvantaged (>0.5 SD)	339 (19.9)
In adulthood (age 22 up to 49 years)	
least disadvantaged (≤-0.5 SD)	430 (25.2)
middle-low (>-0.5 to ≤0 SD)	669 (39.2)
middle-high (>0 to ≤0.5 SD)	442 (25.9)
most disadvantaged (>0.5 SD)	165 (9.7)
Individual-level socioeconomic disadvantage	N (%)
In childhood (age 3-21 years)	
least disadvantaged (≤-0.5 SD)	360 (21.1)
middle-low (>-0.5 to ≤0 SD)	487 (28.6)
middle-high (>0 to ≤0.5 SD)	550 (32.2)
most disadvantaged (>0.5 SD)	309 (18.1)
In adulthood (age 22 up to 49 years)	
least disadvantaged (≤-0.5 SD)	302 (17.7)
middle-low (>-0.5 to ≤0 SD)	503 (29.5)
middle-high (>0 to ≤0.5 SD)	682 (40.0)
most disadvantaged (>0.5 SD)	219 (12.8)
Cognitive function scores (mean, SD)	
Overall	0.038 (0.979)
Memory and learning	0.033 (0.983)
Reaction time	-0.009 (0.981)
Information processing	0.039 (0.986)
Working memory	0.015 (1.008)
Potential mediators	N (%)
Sleep difficulties ≥2 times/week	549 (32.2)
Beck Depression Inventory score ≥10	340 (20.9)
Ideal Cardiovascular Health score	
0	11 (1.0)
1	73 (6.3)
2	188 (16.3)
3	269 (23.3)
4	257 (22.3)
5	213 (18.4)
6	132 (11.4)
7	12 (1.0)

Table 2. Associations of neighbourhood and individual-level socioeconomic disadvantage in childhood and adulthood with overall cognitive function in mid-adulthood

Socioeconomic disadvantage	N (%)	Mean (SD)	Unadjusted difference in means (95% CI)	Adjusted[2] difference in means (95% CI)
Neighbourhood[1]				
Childhood (age 3 to 21 years)				
least disadvantaged (≤-0.5 SD)	366 (24.0)	0.084 (0.963)	ref. cat.	ref. cat.
middle-low (>-0.5 to ≤0 SD)	509 (33.4)	0.087 (0.966)	0.003 (-0.128 to 0.135)	0.019 (-0.106 to 0.144)
middle-high (>0 to ≤0.5 SD)	347 (22.8)	-0.187 (0.975)	-0.102 (-0.246 to 0.041)	-0.059 (-0.196 to 0.078)
most disadvantaged (>0.5 SD)	302 (19.8)	-0.042 (1.022)	-0.126 (-0.275 to 0.023)	-0.068 (-0.211 to 0.074)
Adulthood (age 22 to 49 years)				
least disadvantaged (≤-0.5 SD)	401 (26.3)	0.097 (0.915)	ref. cat.	ref. cat.
middle-low (>-0.5 to ≤0 SD)	600 (39.4)	0.064 (0.969)	-0.033 (-0.156 to 0.091)	-0.079 (-0.196 to 0.039)
middle-high (>0 to ≤0.5 SD)	383 (25.1)	-0.001 (0.962)	-0.098 (-0.235 to 0.039)	-0.144 (-0.274 to -0.014)
most disadvantaged (>0.5 SD)	140 (9.2)	-0.153 (1.208)	-0.250 (-0.438 to -0.062)	-0.298 (-0.478 to -0.120)
Individual-level				
Childhood (age 3 to 21 years)				
least disadvantaged (≤-0.5 SD)	324 (21.3)	0.282 (0.839)	ref. cat.	ref. cat.
middle-low (>-0.5 to ≤0 SD)	444 (29.1)	0.107 (0.962)	-0.175 (-0.314 to -0.036)	-0.171 (-0.303 to -0.039)
middle-high (>0 to ≤0.5 SD)	487 (32.0)	-0.071 (0.989)	-0.353 (-0.489 to -0.217)	-0.295 (-0.425 to -0.165)
most disadvantaged (>0.5 SD)	269 817.7)	-0.181 (1.070)	-0.463 (-0.619 to -0.306)	-0.358 (-0.509 to -0.208)
Adulthood (age 22 to 49 years)				
least disadvantaged (≤-0.5 SD)	277 (18.2)	0.373 (0.843)	ref. cat.	ref. cat.
middle-low (>-0.5 to ≤0 SD)	447 (29.3)	0.209 (0.865)	-0.164 8-0.306 to -0.022)	-0.158 (-0.294 to -0.021)
middle-high (>0 to ≤0.5 SD)	604 (39.6)	-0.108 (0.965)	-0.482 (-0.917 to -0.347)	-0.435 (-0.565 to -0.305)
most disadvantaged (>0.5 SD)	196 (12.9)	-0.388 (1.190)	-0.761 (-0.935 to -0.588)	-0.663 (-0.831 to -0.495)

[1] SDs for socioeconomic disadvantage are calculated in relation to the overall, national mean disadvantage.

[2] Adjusted for age and sex (n=1 524).

Table 3. Associations of neighbourhood and individual-level disadvantage in childhood and adulthood with domain-specific cognitive function in mid-adulthood

Socioeconomic disadvantage	Adjusted[1] difference in mean (95% CI) in cognitive test scores							
	N (%)	Learning and memory (n=1,568)	N (%)	Reaction time (n=1,546)	N (%)	Information processing (n=1,662)	N (%)	Working memory (n=1,695)
Neighbourhood								
Childhood								
least disadvantaged (≤-0.5 SD)	380 (24.2)	ref. cat.	375 (24.3)	ref. cat.	391 (23.5)	ref. cat.	403 (23.8)	ref. cat.
middle-low (>-0.5 to ≤0 SD)	522 (33.3)	0.067 (-0.060 to 0.192)	517 (33.4)	-0.093 (-0.221 to 0.035)	556 833.5)	-0.086 (-0.212 to 0.041)	567 (33.5)	0.044 (-0.080 to 0.168)
middle-high (>0 to ≤0.5 SD)	358 (22.8)	0.019 (-0.119 to 0.157)	352 822.8)	-0.093 (-0.232 to 0.047)	381 (22.9)	-0.122 (-0.260 to 0.016)	388 (22.9)	-0.069 (-0.204 to 0.066)
most disadvantaged (>0.5 SD)	308 (19.6)	-0.022 (-0.165 to 0.122)	302 (19.5)	-0.101 (-0.247 to 0.044)	334 (20.1)	-0.153 (-0.296 to -0.009)	337 (19.9)	-0.064 (-0.205 to 0.076)
Adulthood								
least disadvantaged (≤-0.5 SD)	409 (26.1)	ref. cat.	406 (26.3)	ref. cat.	422 (25.4)	ref. cat.	429 (25.39	ref. cat.
middle-low (>-0.5 to ≤0 SD)	617 (39.4)	-0.047 (-0.167 to 0.072)	608 (39.3)	-0.057 (-0.179 to 0.065)	651 (39.2)	-0.119 (-0.238 to 0.001)	662 (39.1)	-0.089 (-0.207 to 0.029)
middle-high (>0 to ≤0.5 SD)	399 (25.5)	-0.058 (-0.189 to 0.073)	391 (25.3)	-0.068 (-0.202 to 0.065)	427 825.7)	-0.223 (-0.354 to -0.092)	439 (25.9)	-0.115 (-0.244 to 0.014)
most disadvantaged (>0.5 SD)	143 (9.1)	-0.188 (-0.370 to -0.007)	141 (9.1)	-0.120 (-0.305 to 0.064)	162 (9.8)	-0.433 (-0.609 to -0.257)	165 (9.7)	-0.085 (-0.259 to 0.090)
Individual-level								
Childhood								
least disadvantaged (≤-0.5 SD)	339 (21.6)	ref. cat.	333 (21.5)	ref. cat.	345 (20.8)	ref. cat.	357 (21.1)	ref. cat.
middle-low (>-0.5 to ≤0 SD)	453 (28.9)	-0.118 (-0.252 to 0.015)	448 (29.0)	-0.087 (-0.223 to 0.049)	478 (28.8)	-0.298 (-0.431 to -0.165)	486 (28.7)	-0.102 (-0.234 to 0.031)
middle-high (>0 to ≤0.5 SD)	502 (32.0)	-0.213 (-0.344 to -0.082)	494 (32.0)	-0.164 (-0.298 to -0.031)	356 (32.3)	-0.433 (-0.564 to -0.303)	545 (32.2)	-0.079 (-0.209 to 0.051)
most disadvantaged (>0.5 SD)	274 (17.5)	-0.258 (-0.410 to -0.106)	271 (17.5)	-0.228 (-0.383 to -0.073)	303 (18.2)	-0.559 (-0.709 to -0.409)	307 (18.1)	-0.046 (-0.195 to 0.103)
Adulthood								
least disadvantaged (≤-0.5 SD)	292 (18.6)	ref. cat.	287 (18.6)	ref. cat.	287 (17.3)	ref. cat.	298 817.6)	ref. cat.
middle-low (>-0.5 to ≤0 SD)	456 (29.1)	-0.090 (-0.229 to 0.048)	452 (29.2)	-0.062 (-0.204 to 0.008)	494 (29.7)	-0.247 (-0.385 to -0.109)	502 (29.6)	-0.099 (-0.127 to 0.040)
middle-high (>0 to ≤0.5 SD)	620 (39.5)	-0.296 (-0.428 to -0.164)	610 (39.5)	-0.138 (-0.274 to -0.002)	667 (40.1)	-0.554 (-0.686 to -0.422)	677 (39.9)	-0.170 (-0.303 to -0.037)
most disadvantaged (>0.5 SD)	200 (12.8)	-0.474 (-0.646 to -0.303)	197 (12.7)	-0.188 (-0.364 to -0.012)	214 (12.9)	-0.816 (-0.986 to -0.647)	218 (12.9)	-0.229 (-0.400 to -0.058)

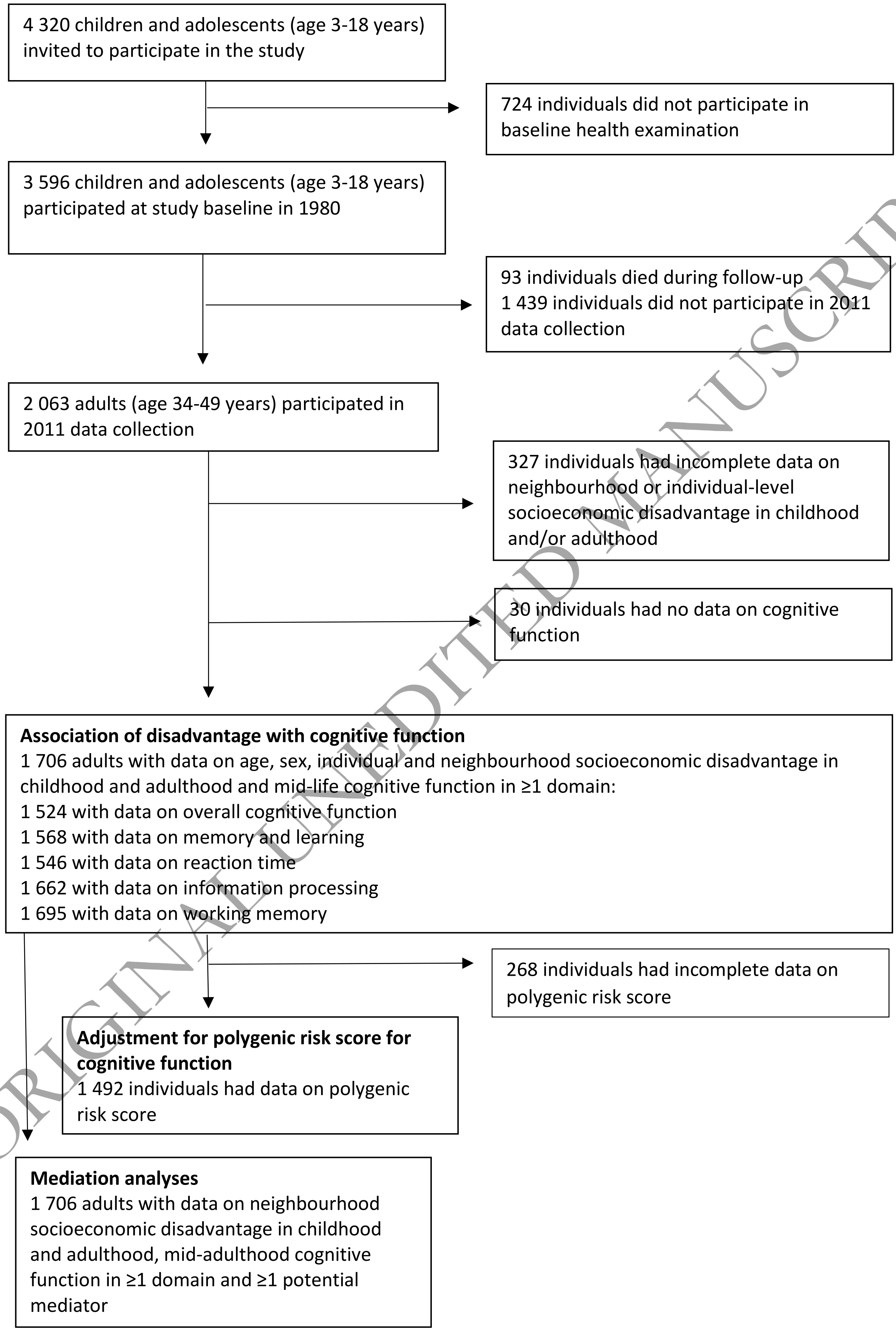
[1] Adjusted for age and sex

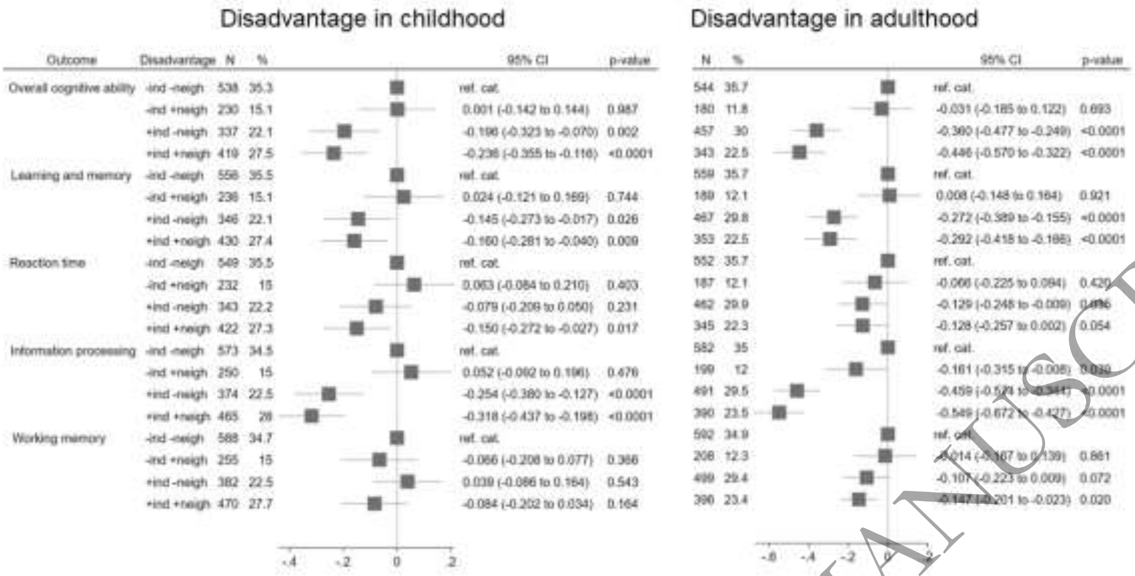
Figure legends

Figure 1. Participant flow chart

Figure 2. Associations of combinations of neighbourhood and individual-level socioeconomic disadvantage in childhood and adulthood with overall and domain-specific cognitive function in mid-adulthood

Note to figure 2: Disadvantage defined as disadvantage score >0 SD vs. ≤0 SD and indicated in the table as disadvantage (+) and no disadvantage (-) at individual level (ind) and neighbourhood level (neigh).


4 320 children and adolescents (age 3-18 years) invited to participate in the study
724 individuals did not participate in baseline health examination
3 596 children and adolescents (age 3-18 years) participated at study baseline in 1980
93 individuals died during follow-up
1 439 individuals did not participate in 2011 data collection
2 063 adults (age 34-49 years) participated in 2011 data collection
327 individuals had incomplete data on neighbourhood or individual-level socioeconomic disadvantage in childhood and/or adulthood
30 individuals had no data on cognitive function
Association of disadvantage with cognitive function
1 706 adults with data on age, sex, individual and neighbourhood socioeconomic disadvantage in childhood and adulthood and mid-life cognitive function in ≥1 domain:
1 524 with data on overall cognitive function
1 568 with data on memory and learning
1 546 with data on reaction time
1 662 with data on information processing
1 695 with data on working memory
268 individuals had incomplete data on polygenic risk score
Adjustment for polygenic risk score for cognitive function
1 492 individuals had data on polygenic risk score
Mediation analyses
1 706 adults with data on neighbourhood socioeconomic disadvantage in childhood and adulthood, mid-adulthood cognitive function in ≥1 domain and ≥1 potential mediator


Disadvantage in childhood
Disadvantage in adulthood
Outcome
Disadvantage
N
%
95% CI
p-value
Overall cognitive ability
-ind -neigh 538 35.3 ref. cat.
-ind +neigh 230 15.1 0.001 (-0.142 to 0.144) 0.987
+ind -neigh 337 22.1 -0.196 (-0.323 to -0.070) 0.002
+ind +neigh 419 27.5 -0.236 (-0.355 to -0.116) <0.0001
Learning and memory
-ind -neigh 556 35.5 ref. cat.
-ind +neigh 236 15.1 0.024 (-0.121 to 0.169) 0.744
+ind -neigh 346 22.1 -0.145 (-0.273 to -0.017) 0.026
+ind +neigh 430 27.4 -0.160 (-0.281 to -0.040) 0.009
Reaction time
-ind -neigh 549 35.5 ref. cat.
-ind +neigh 232 15 0.063 (-0.084 to 0.210) 0.403
+ind -neigh 343 22.2 -0.079 (-0.209 to 0.050) 0.231
+ind +neigh 422 27.3 -0.150 (-0.272 to -0.027) 0.017
Information processing
-ind -neigh 573 34.5 ref. cat.
-ind +neigh 250 15 0.052 (-0.092 to 0.196) 0.476
+ind -neigh 374 22.5 -0.254 (-0.380 to -0.127) <0.0001
+ind +neigh 465 28 -0.318 (-0.437 to -0.198) <0.0001
Working memory
-ind -neigh 588 34.7 ref. cat.
-ind +neigh 255 15 -0.066 (-0.208 to 0.077) 0.366
+ind -neigh 382 22.5 0.039 (-0.086 to 0.164) 0.543
+ind +neigh 470 27.7 -0.084 (-0.202 to 0.034) 0.164
-.4 -.2 0 .2
544 35.7 ref. cat.
180 11.8 -0.031 (-0.185 to 0.122) 0.693
457 30 -0.360 (-0.477 to -0.249) <0.0001
343 22.5 -0.446 (-0.570 to -0.322) <0.0001
559 35.7 ref. cat.
189 12.1 0.008 (-0.148 to 0.164) 0.921
467 29.8 -0.272 (-0.389 to -0.155) <0.0001
353 22.5 -0.292 (-0.418 to -0.166) <0.0001
552 35.7 ref. cat.
187 12.1 -0.066 (-0.225 to 0.094) 0.420
462 29.9 -0.129 (-0.248 to -0.009)
345 22.3 -0.128 (-0.257 to 0.002) 0.054
582 35 ref. cat.
199 12 -0.161
491 29.5 -0.459
390 23.5 -0.549
592 34.9
208 12.3 0.861
499 29.4 0.072
396 23.4 0.020
-.6 -.4 -.2 0