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Reaction Time in Adolescence, Cumulative Allostatic Load, and Symptoms of Anxiety and Depression in Adulthood: The West of Scotland Twenty-07 Study

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ABSTRACT

Objective: To examine the relation between reaction time in adolescence and subsequent symptoms of anxiety and depression and investigate the mediating role of sociodemographic measures, health behaviors, and allostatic load.

Methods: Participants were 705 members of the West of Scotland Twenty-07 Study. Choice reaction time was measured at age 16. At age 36 years, anxiety and depression were assessed with the 12-item General Health Questionnaire (GHQ) and the Hospital Anxiety and Depression Scale (HADS), and measurements were made of blood pressure, pulse rate, waist-to-hip ratio, and total and high-density lipoprotein cholesterol, C-reactive protein, albumin, and glycosolated hemoglobin from which allostatic load was calculated.

Results: In unadjusted models, longer choice reaction time at age 16 years was positively associated with symptoms of anxiety and depression at age 36 years: for a standard deviation increment in choice reaction time, regression coefficients (95% confidence intervals) for logged GHQ score, and square-root–transformed HADS anxiety and depression scores were 0.048 (0.016–0.080), 0.064 (0.009–0.118), and 0.097 (0.032–0.163) respectively. Adjustment for sex, parental social class, GHQ score at age 16 years, health behaviors at age 36 years and allostatic load had little attenuating effect on the association between reaction time and GHQ score, but weakened those between reaction time and the HADS subscales. Part of the effect of reaction time on depression was mediated through allostatic load; this mediating role was of borderline significance after adjustment.

Conclusions: Adolescents with slower processing speed may be at increased risk for anxiety and depression. Cumulative allostatic load may partially mediate the relation between processing speed and depression.

Key words: reaction time, anxiety, depression, allostatic load.

INTRODUCTION

There is evidence from several cross-sectional studies of adults that depression is often accompanied by less efficient cognitive function, as indicated by slower speed of information processing. People diagnosed as having major depression and those who report symptoms of depression have been shown to perform less well on a range of measures of processing speed, such as the Processing Speed Index of the Wechsler Adult Intelligence Scale-III (1), the

GHQ = General Health Questionnaire, **HADS** = Hospital Anxiety and Depression Scale, **HbA1c** = glycosolated hemoglobin, **HDL** = high-density lipoprotein, **SD** = standard deviation

Trailmaking Test (2), the Stroop Color-Word Test (3), inspection time (4), and reaction time (5). Slowed processing speed has also been found in depressed children (6). Whether the presence of anxiety is accompanied by slower processing speed has been much less studied, but the few investigations of people with various types of anxiety disorder—all based on small samples—have found no evidence of this (7,8).

It is unclear from these studies whether the slower processing speed observed in people with depression was an effect of the disorder or whether it preceded the onset of illness and was in fact a risk factor for it. Findings that people who have recovered from an episode of depression tend to have slower processing speed than healthy controls suggests the deficit might be trait dependent rather than state dependent (2,9), but evidence from longitudinal studies is needed to establish whether slower processing speed is a risk factor for onset of depression. To our knowledge, there have been no such studies to date. There is, however, a body of longitudinal evidence that lower scores on tests of intelligence or general cognitive ability in youth are a risk factor for later diagnosis with depression or anxiety and for reporting symptoms of these disorders (10–15).

Scores on tests of intelligence are moderately highly correlated with reaction time and scores on other measures of processing speed, such that people with higher intelligence tend to process information faster (16–19). It is therefore plausible that scores on a measure of processing speed in youth may be predictive of depression and anxiety later in life.

The concept of allostatic load may provide a potential biological mechanism for understanding any links between processing speed in youth and later mental health. Allostasis refers to the long-term functional changes that take place in physiological systems to maintain stability in the face of stressors (20). Such adaptations, which may affect the operating range of biological systems, are protective in the short-term but can come at a cost in terms of increased risk of morbidity or death (21). This cost, termed *allostatic load* by McEwen and Stellar (22), may result in maladaptive stress responding (23).

Slower processing speed and its links to lower intelligence may lead to increased stress and difficulties responding to adversity earlier in life—increasing the burden of allostatic load. This can lead to a vicious circle in that prolonged elevated allostatic load can adversely affect neurological processes, particularly in the prefrontal cortex and hippocampus (23,24). These brain regions are important for cognitive functioning, including processing speed, and neurobiological impairments in these regions have also been implicated in mental disorders. Evidence in 17-year-olds has shown that increased allostatic load is associated with cognitive deficits in the form of poorer working memory (25). Conversely, higher ability may increase the likelihood of entry into a healthy and stimulating environment that, in turn, offsets increases in allostatic load. This also increases the likelihood of

making healthy life-style choices, which again reduce allostatic load. Animal models suggest that the psychological sequelae of high allostatic load may include depression and anxiety (26), but evidence for this in humans is still relatively limited (27). It is possible that any link in humans between processing speed and subsequent symptoms of depression and anxiety might be mediated through allostatic load.

We used data from the population-based West of Scotland Twenty-07 Study to investigate the prospective relationship between processing speed, as measured by reaction time, at around age 16 years and symptoms of depression and anxiety 20 years later, and to explore the potential mediating role of cumulative allostatic load.

METHODS

Participants

The Twenty-07 Study was established in the West of Scotland in 1986 to investigate longitudinally the processes producing or maintaining inequalities in health (28,29). It consists of three age cohorts, born around 1932, 1952, and 1972, members of which were randomly selected from the Central Clydeside Conurbation. Comparison of these cohorts with an equivalent sample from the United Kingdom's 1991 Census Samples of Anonymised Records revealed no significant differences in terms of sex, social class, car ownership, or household tenure (30). Baseline interviews (Wave 1) were carried out in 1987/1988, and the most recent wave of data collection (Wave 5) took place in 2007/2008. In the current study, we use data collected at Wave 1 and Wave 5 on the 1972-born cohort. We restricted our study to this youngest cohort as levels of anxiety and depression at Wave 1 when the cohort was aged approximately 16 years were low; therefore, there was less likelihood that any association we found between reaction time at that age and subsequent symptoms of anxiety or depression would be due to reverse causation. The age of this cohort also made it unlikely that somatic illness at Wave 1 would have affected both reaction time and propensity to anxiety or depression.

Ethical approval for Wave 1 was granted in 1986 by the ethics subcommittee of the West of Scotland Area Medical Committees and the GP Sub-Committee of Greater Glasgow Health Board. Wave 5 was approved by Tayside Committee on Medical Research Ethics A. Written consent to participate was obtained from parents at Wave 1 (when participants were aged 16 years) and from the participants at Wave 5.

Measures

Reaction Time

Four-choice reaction time was measured at Wave 1 with a portable device designed for the UK Health and Lifestyle Survey (31), as has been described previously (16). The participant rested the second and third fingers of the left and right hands on keys marked 1, 2, 3, and 4, respectively. When a number (between 1 and 4) appeared on the liquid crystal display screen, the participant attempted to press the correct key as quickly as possible. There were eight practice trials and 40 test trials, and an interstimulus interval that varied between 1 and 3 seconds. The mean and standard deviation (SD) of correct and incorrect trials were calculated separately. The current analyses are based on the mean of the correct trials.

Symptoms of Anxiety and Depression

Symptoms of anxiety and depression were assessed at Wave 5 using the 12-item General Health Questionnaire (GHQ) (32) and the Hospital Anxiety and Depression Scale (HADS) (33). The latter has two subscales each of

seven items. Both these self-completion questionnaires measure the common mental health problems of anxiety and depression. The GHQ items include four response options (0–3), giving a total score that ranges from 0 to 36. Higher scores indicate more severe distress.(34) The HADS items include four response options (0–3), giving a total score for each subscale ranging from 0 to 21, with higher scores indicating more severe symptoms (35).

Allostatic Load

We used data from Wave 5 on nine biomarkers representing different contributing factors to allostatic load, namely, C-reactive protein, glycosolated hemoglobin, albumin, total and high-density lipoprotein (HDL) cholesterol, systolic and diastolic blood pressure, pulse rate, and waist-to-hip ratio. Nonfasting venous blood samples were collected and assayed for C-reactive protein (using latex-enhanced turbidimetry), glycosylated hemoglobin (HBA1c; using Menarini method), albumin (using cholesterol oxidase), and total and HDL cholesterol (using the accelerator selective detergent method) at the Glasgow Royal Infirmary. The coefficient of variation for each of the assays was as follows: C-reactive protein, ≤6%; glycosolated hemoglobin, ≤1%; albumin, ≤3.8%; and total cholesterol, ≤3%. Systolic and diastolic blood pressure and pulse rate were measured using an Omron HEM-705CP automated oscillometric device. Waist and hip circumferences were measured by a trained nurse using a standard protocol, and their ratio subsequently calculated. Participants provided information about current medication. For the small number of participants who were currently using antihypertensive medication (of our analytical sample, $n = 12$), diabetes medication ($n = 5$), statins ($n = 11$), diuretics ($n = 2$), or β-blockers ($n = 5$), values of systolic and diastolic blood pressure, total and HDL cholesterol, and C-reactive protein were adjusted to take account of the effect of the medication as follows. Systolic and diastolic blood pressures were increased by 10 and 5 mm Hg, respectively, in those on antihypertensive medication; total cholesterol was increased by 1.8 mM in those on statins and reduced by 4% in those on diuretics (36,37); HDL cholesterol was increased by 10% in those on β-blockers (37); HbA1c was increased by 1% in those on medication for diabetes (38); and C-reactive protein by increased by 0.02 mg/dl in those on statins (39). Participants who reported having an operation or accident within the last month were excluded from analyses.

There remains much debate about the best way to operationalize allostatic load (27). Here, we calculated SD scores (zero mean, unit SD) for each component of allostatic load (systolic and diastolic blood pressures, pulse rate, total and HDL cholesterol, albumin, HbA1c, C-reactive protein, and waist-to-hip ratio) for men and women separately, and the sum of these SD scores was taken as a measure of allostatic load. Table S1 (Supplemental Digital Content 1, http://links.lww.com/PSYMED/A211) shows mean (SD) or median (interquartile range) values of allostatic load and each of its components and the correlations between these variables in the sample on which our analysis is based.

Other Covariates

Symptoms of anxiety and depression at Wave 1 were assessed using the 12-item GHQ. Parental occupational social class was based on the father's current or previous job or, if no father was present, the mother's current or previous job at Wave 1, classified in six categories (professional, managerial/technical, skilled nonmanual, skilled manual, partly skilled, unskilled) (40). We regarded GHQ score at Wave 1 and parental social class as potential confounding factors. Educational attainment by Wave 5 was based on years of full-time education. Participants also provided information at Wave 5 on their smoking status (never, ex-smoker, current smoker), their current alcohol consumption (units of alcohol per week), and their physical activity (number of brisk walks undertaken in an average week). We regarded educational attainment and health behaviors as potential mediating factors. Health-related behaviors such as smoking, alcohol intake, and physical activity are likely to contribute to allostatic load by altering its biomarkers.

Statistical Methods

We used Pearson correlation coefficients to examine the relation between choice reaction time at age 16 years, the measures of mental health at age 36 years, and the covariates. To allow us to adjust for the covariates, we then used linear regression to examine the relation between choice reaction time and the mental health outcomes. The distribution of scores for all three mental health outcomes was positively skewed. To convert scores to a nearer-normal distribution, we used a logarithmic transformation for the GHQ-12 scores and a square-root transformation for the HADS anxiety and depression scores. We used these transformed scores as the dependent variables in the linear regression analyses. Because some studies show a nonlinear relation between alcohol intake and anxiety and depression, we created a categorical variable for the regression analyses, defining participants as abstainers (no alcohol), or drinkers within or above sex-specific recommended weekly limits (≤21 versus 22+ units for men, ≤14 versus 15+ units for women) (41). We used the Sobel-Goodman mediation tests in STATA version 12 to examine the extent to which mediating variables carried the influence of choice reaction time at age 16 years to mental health outcomes at age 36 years.

There were 1515 participants at Wave 1, of whom 942 (62%) took part in Wave 5. Nonrespondents at Wave 5 had a slightly longer mean choice reaction time (575 versus 563) at Wave 1 than respondents ($p = .020$), but there was no difference between these groups in Wave 1 GHQ-12 score ($p = .35$). The analyses that follow are based on 705 participants with complete data on choice reaction time, mental health outcomes, and the covariates.

RESULTS

At the time of the Wave 5 follow-up, the study participants (54% female) were aged 36.6 (SD = 0.42) years. Table 1 shows the correlations among choice reaction time at age 16 years, scores on the GHQ, HADS anxiety and HADS depression scales at follow-up, allostatic load at follow-up, and the covariates. Longer choice reaction time—in other words, slower processing speed—at age 16 years was associated with greater parental socioeconomic disadvantage ($r = 0.162$), poorer mental health as indicated by higher scores on the GHQ and HADS anxiety and depression scales at age 36 years ($r = 0.146, 0.104,$ and 0.118), higher allostatic load at age 36 ($r = 0.128$), fewer years of full-time education ($r = −0.234$), and greater likelihood of ever having smoked ($r = 0.187$). Greater allostatic load was associated with greater parental socioeconomic disadvantage, fewer years of full-time education, higher scores on the GHQ and HADS depression scales, and poorer health behavior in terms of smoking, alcohol consumption, and exercise. Allostatic load was also positively correlated with scores on the HADS anxiety subscale, but this association was not statistically significant. Table S2 (Supplemental Digital Content 2, http://links.lww.com/PSYMED/A212) shows correlations of allostatic load and its components with choice reaction time at age 16 years, GHQ score at age 16 years, GHQ score at age 36 years, and HADS anxiety and depression scores at age 36 years. The size of the correlations between each of the allostatic load components and reaction time, GHQ, or HADS scores varied.)

The associations between choice reaction time at 16 years and logged GHQ score, and square-root-transformed HADS

TABLE 1. Pearson Correlations Among Choice Reaction Time at Age 16 Years, GHQ and HADS Scores at Age 36 Years, and the Covariates

Variable	Correlation Coefficients											M (SD) or Median (IQR)
	Choice Reaction Time at 16 y	GHQ at 36 y	HADS Anxiety at 36 y	HADS Depression at 36 y	Parental Social Class at 16 y[a]	GHQ at 16 y	Allostatic Load at 36 y	Smoking Status at 36 y[a]	Alcohol Units Per Week at 36 y	Exercise, Days Per Week at 36 y	Years of Full-Time Education by 36 y	
Choice reaction time at 16 y	—											
GHQ at 36 y	0.146***	—										
HADS anxiety at 36 y	0.104***	0.612***	—									
HADS depression at 36 y	0.118***	0.634***	0.634***	—								
Parental social class at 16 y[a]	0.162***	0.004	−0.029	0.104***	—							
GHQ at 16 y	0.039	0.129***	0.151***	0.089***	−0.061	—						
Allostatic load at 36 y	0.126***	0.098***	0.041	0.167***	0.173***	−0.033	—					
Smoking status at 36 y[a]	0.187***	0.130***	0.120***	0.141***	0.101***	0.001	0.150***	—				
Alcohol units per wk at 36 y	0.015	0.063	0.025	0.037	0.014	−0.036	0.179***	0.145***	—			
Exercise, days per wk at 36 y	−0.018	−0.044	−0.074*	−0.141***	−0.088***	−0.016	−0.075*	0.054	−0.013	—		
Years of full-time education by 36 y	−0.234***	−0.056	−0.029	−0.121***	−0.385***	0.056	−0.194***	−0.179***	−0.038	0.112***	—	
M (SD) or median (IQR)[b]	10.6 (4.88)	10 (7–12)	7 (4–9)	2 (1–5)	4 (2–4)	8 (6–11)	0.031 (4.20)	1 (1–3)	6 (0–15)	3 (2–5)	13 (11–17)	—

GHQ = General Health Questionnaire; HADS = Hospital Anxiety and Depression Scale; M = mean; SD = standard deviation; IQR = interquartile range.

[a] Parental social class and smoking status should be interpreted here as if they were continuous variables. Higher values of each variable indicate greater socioeconomic disadvantage or greater exposure to smoking respectively.

[b] Median (IQR) was used instead of M (SD) for ordinal variables or continuous variables that were not normally distributed.

* $p < .05$, *** $p < .001$.

TABLE 2. The Association Between Choice Reaction Time at Age 16 Years With GHQ Scores at Age 36 Years (Unadjusted and Adjusted Models)

Models	Regression Coefficient (95% Confidence Interval)	p	Adjusted R^2
Model 1			
Choice reaction time, per SD[a]	0.048 (0.016 to 0.080)	.003	0.011
Model 2			
Choice reaction time, per SD[a]	0.044 (0.011 to 0.076)	.008	0.026
Female sex	0.038 (−0.026 to 0.102)	.25	
Logged GHQ score at age 16 y	0.093 (0.011 to 0.174)	.027	
Parental social class[b]			
Professional	Reference		
Managerial/Technical	−0.037 (−0.158 to 0.083)	.54	
Skilled nonmanual	−0.082 (−0.217 to 0.053)	.23	
Skilled manual	−0.107 (−0.226 to 0.012)	.079	
Semiskilled	−0.029 (−0.167 to 0.109)	.68	
Unskilled	−0.205 (−0.372 to −0.038)	.016	
Years of full-time education	−0.012 (−0.024 to −0.001)	.033	
Model 3			
Choice reaction time, per SD[a]	0.037 (0.005 to 0.069)	.026	0.057
Female sex	0.034 (−0.032 to 0.099)	.32	
Logged GHQ score at age 16 y	0.103 (0.020 to 0.185)	.015	
Parental social class[b]			
Professional	Reference		
Managerial/Technical	−0.043 (−0.164 to 0.077)	.48	
Skilled nonmanual	−0.086 (−0.221 to 0.048)	.20	
Skilled manual	−0.127 (−0.246 to −0.078)	.037	
Semiskilled	−0.051 (−0.189 to 0.088)	.47	
Unskilled	−0.223 (−0.391 to −0.056)	.009	
Years of full-time education	−0.009 (−0.020 to 0.002)	.13	
Smoking status			
Never smoker	Reference		
Ex-smoker	−0.006 (−0.085 to 0.074)	.89	
Current smoker	0.080 (0.001 to 0.159)	.046	
Alcohol units per week			
None	0.071 (−0.005 to 0.147)	.068	
≤14 (women)/≤21 (men)	Reference		
≥15 (women)/≥22 (men	0.034 (−0.050 to 0.117)	.43	
Exercise (brisk walking), d/wk	−0.016 (−0.030 to −0.003)	.019	
Model 4			
Choice reaction time, per SD[a]	0.035 (0.002 to 0.068)	.035	0.041
Female sex	0.055 (−0.010 to 0.127)	.092	
Logged GHQ score at age 16 y	0.101 (0.018 to 0.183)	.016	
Parental social class[b]			
Professional	Reference		
Managerial/Technical	−0.046 (−0.166 to 0.074)	.46	
Skilled nonmanual	−0.091 (−0.226 to 0.043)	.18	

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TABLE 2. *(Continued)*

Models	Regression Coefficient (95% Confidence Interval)	*p*	Adjusted R^2
Skilled manual	−0.128 (−0.247 to −0.009)	.035	
Semiskilled	−0.056 (−0.195 to 0.083)	.43	
Unskilled	−0.237 (−0.406 to −0.069)	.006	
Years of full-time education	−0.009 (−0.020 to 0.002)	.14	
Smoking status			
Never smoker	Reference		
Ex-smoker	−0.01 (−0.089 to 0.070)	.81	
Current smoker	0.079 (0.001 to 0.158)	.048	
Alcohol units per week			
None	0.093 (0.011 to 0.174)	.026	
≤14 (women)/≤21 (men)	Reference		
≥15 (women)/≥22 (men	−0.049 (−0.171 to 0.073)	.43	
Exercise (brisk walking), d/wk	−0.015 (−0.028 to −0.112)	.032	
Allostatic load	0.003 (−0.005 to 0.011)	.40	

SD = standard deviation; GHQ = General Health Questionnaire.

[a] Data presented are unstandardized regression coefficients indicating the association between 1-SD increment in choice reaction time and the logged GHQ score.

[b] The numbers in each category of parental social class are as follows: professional, 71; managerial/technical, 157; skilled nonmanual, 96; skilled manual, 242; Semiskilled, 96; and unskilled, 43.

anxiety score and HADS depression score at 36 years did not differ significantly by sex. In the case of logged GHQ score, the coefficient for the interaction term was −0.028 (*p* = .38). In the case of square-root–transformed HADS anxiety or HAD depression scores, the coefficients for the interaction terms were −0.022 (*p* = .70) and −0.099 (*p* = .14), respectively. Hence, in each case, the strength of the association between reaction time and the mental health measure was slightly stronger in women than in men, but none of these differences were statistically significant. In the linear regression analyses, we therefore pooled data for men and women.

Table 2 shows the results of linear regression analyses of the relation between choice reaction time at age 16 years, expressed as SD scores, and logged GHQ scores at age 36 years. In the unadjusted Model 1, 1-SD longer choice reaction time was associated with a 5% (95% confidence interval [CI] = 2%∓8%) higher GHQ score. This model explained 1% of the variance in GHQ score. Adjustment for sex, GHQ score at age 16 years, parental socioeconomic status, years of full-time education (Model 2), then in addition for health behaviors at age 36 years (Model 3), and then allostatic load at age 36 years (Model 4) had negligible effects on this association. Adding the covariates did little to increase the predictive power of the initial model: the model containing all the covariates explained the most variance in GHQ score at 4.1%. The results of Sobel-Goodman

mediation tests confirmed that education, allostatic load, and the health behaviors had no significant mediating effects.

Table 3 shows the results of linear regression analyses of the relation between choice reaction time at age 16 years, expressed as SD scores, and HADS anxiety scores at age 36 years. In the unadjusted Model 1, 1-SD longer choice reaction time at age 16 years was associated with an increase in the square-root–transformed HADS anxiety score at age 36 years of 0.06 (95% CI = 0.01−0.12). This model explained 0.6% of the variance in the HADS anxiety score. Adjustment for sex, GHQ score at age 16 years, parental social class, and years of full-time education (Model 2) had little attenuating effect on this association. Further adjustment for health behaviors (Model 3) weakened the association, and it became of borderline significance. Additional adjustment for allostatic load (Model 4) had only slight attenuating effects. Model 3 explained the largest proportion of the variance, at 5.9%. Results of Sobel-Goodman mediation tests showed that of the health behaviors, only current smoking status had a significant mediating effect (*p* = .038). Of the total effect of reaction time at age 16 years on HADS anxiety score at age 36 years, 17% was mediated through smoking status.

Table 4 shows the results of linear regression analyses of the relation between choice reaction time at age 16 years, expressed as SD scores, and HADS depression scores

TABLE 3. The Association Between Choice Reaction Time at Age 16 Years With the Hospital Anxiety and Depression Scale Anxiety Subscale Score At Age 36 Years (Unadjusted and Adjusted Models)

Models	Regression Coefficient (95% Confidence Interval)	p	Adjusted R^2
Model 1			
Choice reaction time, per SD[a]	0.064 (0.009 to 0.118)	.023	0.006
Model 2			
Choice reaction time, per SD[a]	0.062 (0.005 to 0.118)	.031	0.037
Female sex	0.162 (0.051 to 0.273)	.004	
Logged GHQ score at age 16 y	0.165 (0.022 to 0.307)	.023	
Parental social class[b]			
Professional	Reference		
Managerial/Technical	0.067 (−0.141 to 0.275)	.53	
Skilled nonmanual	0.080 (−0.153 to 0.314)	.50	
Skilled manual	0.010 (−0.196 to 0.217)	.92	
Semiskilled	−0.043 (−0.282 to 0.197)	.73	
Unskilled	−0.205 (−0.495 to 0.086)	.17	
Years of full-time education	−0.006 (−0.026 to 0.013)	.54	
Model 3			
Choice reaction time, per SD[a]	0.048 (−0.008 to 0.104)	.095	0.059
Female sex	0.147 (0.034 to 0.261)	.011	
Logged GHQ score at age 16 y	0.176 (0.033 to 0.319)	.016	
Parental social class[b]			
Professional	Reference		
Managerial/Technical	0.062 (−0.146 to 0.271)	.56	
Skilled nonmanual	0.082 (−0.151 to 0.315)	.49	
Skilled manual	−0.013 (−0.209 to 0.194)	.90	
Semiskilled	−0.070 (−0.309 to 0.170)	.57	
Unskilled	−0.228 (−0.518 to 0.062)	.12	
Years of full-time education	0.001 (−0.019 to 0.020)	.97	
Smoking status			
Never smoker	Reference		
Ex-smoker	0.056 (−0.082 to 0.194)	.43	
Current smoker	0.189 (0.052 to 0.325)	.019	
Alcohol units per week			
None	0.158 (0.026 to 0.289)	.019	
≤14 (women)/≤21 (men)	Reference		
≥15 (women)/≥22 (men	0.009 (−0.135 to 0.154)	.90	
Exercise (brisk walking), d/wk	−0.020 (−0.044 to 0.003)	.091	
Model 4			
Choice reaction time, per SD[a]	0.046 (−0.010 to 0.103)	.11	0.040
Female sex	0.157 (0.041 to 0.273)	.008	
Logged GHQ score at age 16 y	0.176 (0.032 to 0.319)	.016	
Parental social class[b]			
Professional	Reference		
Managerial/Technical	0.057 (−0.152 to 0.266)	.59	
Skilled nonmanual	0.081 (−0.152 to 0.314)	.50	

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TABLE 3. *(Continued)*

Models	Regression Coefficient (95% Confidence Interval)	p	Adjusted R^2
Skilled manual	−0.018 (−0.224 to 0.189)	.86	
Semiskilled	−0.079 (−0.319 to 0.162)	.52	
Unskilled	−0.239 (−0.531 to 0.052)	.11	
Years of full-time education	0.001 (−0.018 to 0.021)	.89	
Allostatic load	0.006 (−0.007 to 0.020)	.37	
Smoking status			
Never	Reference		
Ex-smoker	0.056 (−0.083 to 0.193)	.43	
Current smoker	0.185 (0.048 to 0.322)	.008	
Alcohol units per week			
None	0.153 (0.021 to 0.285)	.023	
≤14 (women)/≤21 (men)	Reference		
≥15 (women)/≥22 (men	0.002 (−0.142 to 0.147)	.97	
Exercise (brisk walking), d/wk	−0.020 (−0.043 to 0.004)	.10	

SD = standard deviation; GHQ = General Health Questionnaire.

[a] Data presented are unstandardized regression coefficients indicating the association between 1-SD increment in choice reaction time and the square-root–transformed HADS anxiety score.

[b] The numbers in each category of parental social class are as follows: professional, 71; managerial/technical, 157; skilled nonmanual, 96; skilled manual, 242; semiskilled, 96; and unskilled, 43.

at age 36 years. In the unadjusted Model 1, 1-SD longer choice reaction time was associated with an increase in the square root–transformed HADS depression score of 0.10 (95% CI = 0.03−0.16). This amounts to 1.1% of the variance. After adjustment for sex, GHQ score at age 16 years, parental socioeconomic status, and years of full-time education (Model 2), this association became of borderline statistical significance. It was further attenuated and no longer significant after additional adjustment for health behaviors (Model 3) and allostatic load (Model 4). Model 3 explained 9.9% of the variance in HADS depression score. Results of Sobel-Goodman mediating tests showed that before adjusting for any of the covariates, allostatic load and years of full-time education each had a significant mediating effect on this association: 17% was mediated through allostatic load (*p* = .010) and 26% through years of full-time education (*p* = .005). After adjustment for the other covariates, the percentage mediated by allostatic load fell slightly to 16% (*p* = .074) and that mediated through education fell to 20% (*p* = .059), and in neither case were these statistically significant at conventional levels.

In total, 18% of the participants who had data on reaction time at age 16 years and mental health at age 36 years had missing data on one or more of the covariates, primarily allostatic load, so they were excluded from our analytical sample. To investigate whether this exclusion

might have biased the associations, we reran the initial models that were adjusted for sex only in the 861 people with data on reaction time and mental health. Associations were almost identical to those found in the 705 people in our analytical sample.

DISCUSSION

In this 20-year longitudinal study of 705 adolescents, boys and girls who had longer choice reaction time at age 16 years had more symptoms of anxiety and depression at age 36 years, as measured by their scores on the GHQ and the HADS anxiety and depression subscales. All these effect sizes were small. The strength of the association between reaction time and score on the GHQ persisted and was only slightly changed, after adjustment for the potential confounding or mediating variables, sex, GHQ score at age 16 years, parental social class, educational attainment, allostatic load, and health behaviors that contribute to allostatic load. The associations between reaction time and scores on the HADS anxiety and depression subscales were attenuated after these adjustments and no longer statistically significant. Formal tests of mediation showed that part of the effect of reaction time on HADS anxiety score was significantly mediated through smoking status at age 36 years. Part of the effect of reaction time on HADS depression score was mediated through cumulative allostatic load and educational attainment, but formal tests of these

TABLE 4. The Association Between Choice Reaction Time at Age 16 Years With the Hospital Anxiety and Depression Scale Depression Subscale Score at Age 36 Years (Unadjusted and Adjusted Models)

Models	Regression Coefficient (95% Confidence Interval)	p	Adjusted R^2
Model 1			
Choice reaction time, per SD[a]	0.097 (0.032 to 0.163)	.004	0.011
Model 2			
Choice reaction time, per SD[a]	0.064 (−0.003 to 0.130)	.062	0.043
Female sex	0.011 (−0.122 to 0.143)	.88	
Logged GHQ score at age 16 y	0.213 (0.043 to 0.383)	.014	
Parental social class[b]			
Professional	Reference		
Managerial/Technical	0.173 (−0.076 to 0.422)	.17	
Skilled nonmanual	0.140 (−0.138 to 0.419)	.32	
Skilled manual	0.219 (−0.027 to 0.465)	.081	
Semiskilled	0.293 (0.008 to 0.579)	.044	
Unskilled	0.082 (−0.264 to 0.429)	.64	
Years of full-time education	−0.031 (−0.054 to −0.007)	.010	
Model 3			
Choice reaction time, per SD[a]	0.053 (−0.013 to 0.119)	.11	0.099
Female sex	−0.042 (−0.175 to 0.091)	.54	
Logged GHQ score at age 16 y	0.240 (0.072 to 0.407)	.005	
Parental social class[b]			
Professional	Reference		
Managerial/Technical	0.170 (−0.075 to 0.414)	.17	
Skilled nonmanual	0.111 (−0.162 to 0.384)	.43	
Skilled manual	0.153 (−0.89 to 0.395)	.22	
Semiskilled	0.225 (−0.056 to 0.505)	.12	
Unskilled	0.028 (−0.312 to 0.368)	.87	
Years of full-time education	−0.020 (−0.043 to 0.003)	.083	
Smoking status			
Never smoker	Reference		
Ex-smoker	−0.123 (−0.284 to 0.039)	.14	
Current smoker	0.143 (−0.017 to 0.303)	.080	
Alcohol units per week			
None	0.277 (0.123 to 0.432)	<.001	
≤14 (women)/≤21 (men)	Reference		
≥15 (women)/≥22 (men	−0.0198 (−0.189 to 0.149)	.82	
Exercise (brisk walking), d/wk	−0.064 (−0.091 to −0.036)	<.001	
Model 4			
Choice reaction time, per SD[a]	0.046 (−0.020 to 0.111)	.17	0.091
Female sex	−0.001 (−0.135 to 0.134)	.99	
Logged GHQ score age 16 y	0.239 (0.072 to 0.405)	.005	
Parental social class[b]			
Professional	Reference		
Managerial/Technical	0.150 (−0.093 to 0.393)	.22	
Skilled nonmanual	0.107 (−0.164 to 0.378)	.44	

TABLE 4. *(Continued)*

Models	Regression Coefficient (95% Confidence Interval)	*p*	Adjusted R^2
Skilled manual	0.133 (−0.108 to 0.373)	.28	
Semiskilled	0.188 (−0.092 to 0.468)	.19	
Unskilled	−0.018 (−0.092 to 0.467)	.92	
Years of full-time education	−0.017 (−0.040 to 0.006)	.16	
Allostatic load score	0.025 (0.009 to 0.041)	.002	
Smoking status			
Nonsmoker	Reference		
Ex-smoker	−0.131 (−0.292 to 0.030)	.11	
Current smoker	0.149 (0.010 to 0.309)	.070	
Alcohol units per week			
None	0.259 (0.106 to 0.413)	.001	
≤14 (women)/≤21 (men)	Reference		
≥15 (women)/≥22 (men	−0.045 (−0.214 to 0.124)	.60	
Exercise (brisk walking), d/wk	−0.061 (−0.088 to −0.034)	<.001	

SD = standard deviation; GHQ = General Health Questionnaire.

[a] Data presented are unstandardized regression coefficients indicating the association between 1-SD increment in choice reaction time and the square-root–transformed HADS depression score.

[b] The numbers in each category of parental social class are as follows: professional, 71; managerial/technical, 157; skilled nonmanual, 96; skilled manual, 242; semiskilled, 96; and unskilled, 43.

mediating effects did not reach conventional levels of significance after adjustment.

So far as we are aware, there have been no previous longitudinal studies of the relation between reaction time and subsequent symptoms of anxiety and depression. Cross-sectional studies, mostly based on clinical samples, have found that people with more severe depressive symptoms tend to have slower reaction times and other cognitive deficits (9,42,43). These findings have generally been interpreted as indicating that the presence of depression can cause psychomotor slowing and have an adverse effect on task performance. However, that a few studies have found persisting cognitive deficits in people who have recovered from depression suggests that they may not be simply epiphenomena of depression, but may reflect enduring cognitive traits (9). The few small studies that have examined the cross-sectional relation between reaction time and anxiety disorders have found no association (7). In the present larger study, we found small but significant associations between longer reaction time in adolescence and higher scores on the GHQ and on the HADS anxiety and depression subscales 20 years later. These associations was only slightly changed by adjustment for the confounding factors, parental social class, and GHQ score at age 16 years, but were attenuated to varying degrees by adjustment for mediating factors. In the present study, there was little variance in mood among our sample: most of the participants had low scores on the GHQ and HADS. Further longitudinal

studies are needed—preferably in samples with greater variation in levels of psychological distress—to confirm our observations that longer reaction time might be a risk factor for symptoms of anxiety and depression.

We found only partial support for the hypothesis that cumulative allostatic load might mediate links between reaction time in adolescence and later symptoms of anxiety and depression. Allostatic load at age 36 years was not associated with scores on the HADS anxiety subscale or on the GHQ scale, but it was significantly positively correlated with HADS depression score. Of the total effect of reaction time in adolescence on depression scores at age 36 years, 17% was mediated through allostatic load before adjustment for covariates, although this mediating effect did not reach statistical significance after adjustment. It is possible that the potential explanatory effect of allostatic load might have been more pronounced if there had been greater variance in depression scores among our participants. A few studies have reported cross-sectional (44,45) and longitudinal associations (46) between cumulative allostatic load and severity of depressive symptoms in people 60 years and older. Our findings suggest that this link may be present at a much younger age.

In our study, people who smoked at age 36 years had higher levels of anxiety and depression. This might, at least in part, reflect the use of cigarettes as a method of relieving or coping with psychological symptoms. However, there is

a growing body of evidence that smoking in childhood or adolescence leads to increased levels of anxiety and heightened risk of developing anxiety disorders later in life (47,48). Various biological pathways may potentially underlie this link, including neurotransmitter systems, inflammation, oxidative and nitrosative stress, mitochondrial dysfunction, neurotrophins, or neurogenesis (49). Here, we found that slower reaction time at age 16 years was a significant predictor of still being a current smoker at age 36 years. Although it is impossible to be certain of the direction of the effect between smoking and poorer mental health in our study, the finding that 17% of the effect of reaction time at aged 16 years on HADS anxiety scores was mediated through current smoking could plausibly reflect the anxiogenic impact of long-term nicotine intake. Smoking is highly likely to contribute to allostatic load, but in this study, we found no evidence that allostatic load mediated the association between reaction time and HADS anxiety score. Smoking did not have a mediating role in the association between reaction time and HADS depression score.

Our study has some limitations. First, a recent review of more than 50 studies found that the factor structure of the HADS varied across studies and populations, with the number of factors ranging from one to four (50). The authors subsequently suggested that it might be more appropriate to view the HADS as an assessment of emotional distress given that it does not provide good separation between symptoms of anxiety and depression (51). In view of this, our findings using the anxiety and depression subscales need to be viewed with caution. Second, our measure of physical activity—number of brisk walks per week—may not adequately capture the extent or intensity of physical activity among our participants at age 36 years, although it is worth noting that it was significantly inversely related to HADS subscale scores. Third, we were unable to adjust for substance abuse in adolescence, which might potentially confound associations between reaction time and later symptoms of anxiety and depression. Finally, we had no data on intelligence in adolescence so we were not able to use our study sample to investigate the suggestion that faster processing speed might help explain links between higher intelligence and reduced risk of anxiety and depression (10). Reaction time is moderately correlated with intelligence (16), and there is some evidence that it accounts, to a very large extent, for the association between higher intelligence and lower mortality (52). The extent to which it explains associations between intelligence and mental health needs to be investigated in future studies.

In this prospective study of adolescents, we found that those with slower processing speed, as indexed by longer choice reaction time, reported higher levels of anxiety and depression 20 years later. Effect sizes were modest. Part of the effects of reaction time on later levels of anxiety or depression was mediated through smoking or allostatic load, respectively, although the latter's role ceased to be statistically significant after adjustment for covariates. Further prospective studies of the relation between reaction time and mental health outcomes in other samples are needed to gauge whether reaction time is a true risk factor for mental disorders and to confirm the mediating roles played by smoking and allostatic load.

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