Journal Pre-proof

Recurrent depression in childhood and adolescence and low childhood socioeconomic status predict low cardiorespiratory fitness in early adulthood

Georgios Nikolakaros , Tero Vahlberg , Lauri Sillanmäki ,
Andre Sourander Principal Investigator

Please cite this article as: Georgios Nikolakaros , Tero Vahlberg , Lauri Sillanmäki , Andre Sourander Principal Investigator , Recurrent depression in childhood and adolescence and low childhood socioeconomic status predict low cardiorespiratory fitness in early adulthood, *Journal of Affective Disorders* (2019), doi: https://doi.org/10.1016/j.jad.2019.11.029

Highlights

- Cardiorespiratory fitness (CRF) is a major determinant of health
- We studied 1647 Finnish male army conscripts
- Low socioeconomic status in childhood was associated with low adult CRF
- Childhood depression recurring in adolescence was associated with low adult CRF
- Childhood conduct problems affected adult CRF through obesity and smoking

TITLE

Recurrent depression in childhood and adolescence and low childhood socioeconomic status predict

low cardiorespiratory fitness in early adulthood

Authors: Georgios Nikolakaros[1,2], Tero Vahlberg[3], Lauri Sillanmäki[4] and Andre Sourander[,4,5]

[1]Department of Clinical Neurophysiology, HUS Medical Imaging Center, Helsinki University

Central Hospital, Finland

[2]Sleep Disorders Outpatient Clinic, Department of Psychiatry, Helsinki University Central Hospital,

Finland

[3]Department of Clinical Medicine, Biostatistics, University of Turku, Finland

[4]Research Center for Child Psychiatry, University of Turku, Finland

[5]INVEST Research Flagship, University of Turku, Finland (Principal Investigator)

Address correspondence to:

Georgios Nikolakaros, MD

Department of Clinical Neurophysiology

HUS Medical Imaging Center, Helsinki University Central Hospital

Stenbäckinkatu 9, PL 100, 00029 HUS, Finland

Phone: +358947182010, Fax: +358947175500

email: georgios.nikolakaros@gmail.com

ABSTRACT

Background: Cardiorespiratory fitness (CRF) strongly influences health, but very little is known about the childhood determinants of adult CRF. Our longitudinal study investigated whether childhood psychopathology and socioeconomic status (SES) were related to adult CRF in 1647 Finnish male military conscripts.

Methods: Childhood psychopathology was assessed at the age of eight using the Rutter and Children's Depression Inventory questionnaires. Parental education and family structure were used to assess childhood SES. In late adolescence, depressive symptoms were assessed with the Beck Depression Inventory and smoking with a questionnaire. CRF in early adulthood was examined with the Cooper's 12-minute run test.

Results: General linear models showed that low parental education (p=0.001), depressive symptoms in childhood (p=0.035) and late adolescence, smoking, underweight, and overweight/obesity (all p<0.001) independently predicted lower CRF. The interaction between depressive symptoms in childhood and adolescence was significant (p=0.003). In adolescents with depressive symptoms, childhood depressive symptoms (p=0.001) and overweight/obesity (p<0.001) predicted lower CRF. In adolescents without depressive symptoms, conduct problems in childhood

predicted lower CRF in the initial models, but the effect disappeared after taking into account smoking and body mass index. Mediational analysis confirmed these results.

Limitations: We lacked data on physical activity and only studied males at three time-points.

Conclusions: Recurrent depression in childhood and adolescence and low SES in childhood predict lower adult CRF. Conduct problems in childhood predict lower CRF, but the effect is mediated by overweight/obesity and smoking. Psychiatric treatment for children and adolescents should promote physical activity, particularly for children with low SES.

Keywords: adolescent; child; cardiorespiratory fitness; conduct disorder; depressive symptoms; socioeconomic factors

INTRODUCTION

Cardiorespiratory fitness (CRF) is the ability of the circulatory, respiratory, and muscular systems to supply oxygen during sustained physical activity (Lee et al., 2010). CRF in late adolescence (Crump et al., 2016), young adulthood (Carnethon et al., 2003), and middle age (Kennedy et al., 2018) have been shown to be strong predictors of future health. CRF is partially determined by genetic factors (Bouchard et al., 2011). During adulthood, physical activity, obesity, underweight, smoking, and socioeconomic status (SES) have been associated with CRF (Lakoski et al., 2011; Nikolakaros et al., 2017; Ombrellaro et al., 2018).

Childhood psychopathology can have profound effects on adult health (Duarte et al., 2010; Goodwin et al., 2009; Sourander et al., 2009). Childhood depression may recur (Rao and Chen, 2009), and it may coexist with conduct disorder (Ingoldsby et al., 2006).

Five cross-sectional studies have reported that childhood psychopathology, mostly depressive symptoms, were associated with lower CRF during childhood and adolescence (Esmaeilzadeh, 2015; LaVigne et al., 2016; Rieck et al., 2013; Shomaker et al., 2012; Yeatts et al., 2017). Depressive symptoms in obese adolescents were associated with lower CRF (Shomaker et al., 2012). Another study of adolescents aged 10-14 found that higher CRF was associated with less depressive symptoms in both sexes and with less internalizing symptoms in males (LaVigne et al., 2016). Esmaeilzadeh, 2015 showed that CRF was associated with depressive symptoms in subjects aged 7-11 years. Rieck et al., 2013 reported that high CRF was associated with a lower level of depression in adolescents aged 11-15. Yeatts et al., 2017 showed that high CRF was associated with less depressive symptoms in adolescents with high levels of neuroticism. One longitudinal study found that high baseline CRF prevented the onset of new depressive symptoms in adolescents over a one-year period (Ruggero et al., 2015). Another longitudinal study of adolescents found that CRF decreased with increasing levels of depressive symptoms over a period of four years (Olive et al., 2016). To our knowledge, there has been only one previous study that has examined childhood determinants of CRF in adults. That study found no association between parental SES during childhood and CRF during military service (Stea et al., 2009).

The existing literature suggests that there is an association between depression and CRF during adolescence, but there are no existing studies on the effects of childhood and adolescent psychopathology on adult CRF. Such an association is plausible for two reasons. Firstly, childhood psychopathology has been associated with the development of somatic (Duarte et al., 2010; Goodwin et al., 2009) and psychiatric (Sourander et al., 2009) morbidity in adulthood. Secondly, childhood depression has been shown to have a bidirectional association with physical activity (Stavrakakis et al., 2012), and physical activity has been shown to be a strong predictor of CRF (Lakoski et al., 2011). Given the salient effects of CRF on mortality and morbidity, understanding any associations between CRF and factors during childhood and adolescence is of major public health importance.

Our population-based study of young Finnish male military conscripts has previously shown that smoking in late adolescence and body composition in young adulthood were associated with CRF in young adulthood (Nikolakaros et al., 2017). The present study extended that assessment to examine any associations between CRF in early adulthood and psychopathology, namely depressiveness, neuroticism, and conduct problems and SES in childhood and depressive symptoms in late adolescence. We measured CRF with Cooper's 12-minute run (12MR) test (Cooper, 1968), a widely used objective measure of CRF (Hamari et al., 2010; Nikolakaros et al., 2017). We took into account the effects of smoking in late adolescence and body composition at the time of the CRF assessment by including them as covariates in the models. Our first research hypothesis was that childhood psychopathology and SES would predict adult CRF. Our second research hypothesis was that the recurrence of childhood depression in late adolescence would be associated with a more profound effect.

METHODS

This investigation was a part of our longitudinal population-based ''From a Boy to a Man'' study (Sourander et al., 2004), which belongs to the Finnish Psychiatric Birth Cohort Consortium (PSYCOHORTS, www.psycohorts.fi). The study is focusing on a large cohort of Finnish children and assessing adult health-related outcomes in relation to child psychopathology. The initial cohort comprised 2964 subjects, a representative sample of Finnish males born in 1981. The present study gathered information on the study subjects at three time-points: at the age of eight years, in late adolescence, and in early adulthood. At eight years of age (first assessment of the study subjects) mental health was evaluated by questionnaires filled in by the children, their parents, and their teachers. The parents completed the 31-item parent version of the Rutter questionnaire (Rutter, 1970) and the teachers completed the 26-item teacher version. The children completed the

Children's Depression Inventory (CDI) (Kovacs, 1992) in the classroom and were asked to answer the questions based on how they felt at that point and in the previous two weeks. This questionnaire was developed from the Beck Depression Inventory (BDI) (Beck et al., 1961). The original CDI includes 27 items. However, we omitted the question about suicide for ethical reasons. The parent and teacher information was combined by adding the individual domain-specific scores to generate Rutter emotional, conduct, and hyperactivity total scores, in line with previous studies (Duarte et al., 2010). The parents' educational level (either parent having completed upper secondary education versus lower) and family structure (the child living with both biological parents versus other) were used to evaluate the children's SES.

In Finland, military service is mandatory for young adult men, who are called up around the age of 18 (late adolescence). At the call-up, 2216 subjects were administered the BDI and a questionnaire on their smoking habits. This provided five smoking categories: no smoking, occasional smoking, smoking 1–5 cigarettes per day, smoking 6–10 cigarettes per day, and smoking 11 or more cigarettes per day (Nikolakaros et al., 2017).

Of these 2216 subjects, 1882 began their military service during early adulthood (third assessment). In Finland, all conscripts undergo a 12MR test and have their height and weight measured at the beginning of service (Nikolakaros et al., 2017). We obtained the height, weight, and the 12MR test values from the Finnish military. The subjects' body mass index (BMI) was calculated using the standard weight/height^2 formula. The 12MR test measures the distance covered by running for 12 minutes (Cooper, 1968), and it has been reported to have good overall reliability in estimating CRF in young healthy men. However, it might underestimate CRF at low values and overestimate CRF at high values (Penry et al., 2011). Conscripts were instructed to perform the 12MR with a maximal effort and to progressively increase their running speed. They also received safety instructions that stated that they could voluntarily stop the test. The accuracy of the measurements was ± 10 meters (Hamari et al., 2010; Santtila et al., 2006).

The final study cohort consisted of 1647 subjects. Figure 1 shows the selection of the study subjects. Similar to our previous study (Nikolakaros et al., 2017), we excluded 20 subjects with a 12MR score of fewer than 1200 meters to reduce the effect of lack of motivation. Performing 1200 meters in the 12MR test can be achieved with brisk walking, without any attempt to run. We compared the 1647 young adults whose data were analyzed with the 1075 who were not included in the study and found that the study subjects had significantly more depressive (mean 7.9 versus 7; p<0.001), conduct (mean 3 versus 2.3; p<0.001), hyperactive (mean 2.3 versus 1.7; p<0.001), and emotional (mean 2.5 versus 2.1; p<0.001) symptoms.

Of the subjects with a childhood depressive symptom score of 0-50 %, 37/921 (4%) were depressed in late adolescence. The respective figures for subjects with a childhood depressive symptom score of 50-90 % and 90-100 % were 48/542 (8.9%) and 29/158 (18.4%). The difference was statistically significant (X^2 (2, $N = 1621$) = 46.54, p<0.001). The 1647 subjects we studied had a mean age of 19.52 years (SD = 0.81) at the time of the CRF and BMI assessments. The mean 12MR score was 2523.6 meters (SD = 347.6). In correlation analysis of the childhood psychopathology variables, the Pearson correlation coefficients were less than 0.66, and the collinearity statistics (tolerance values) were greater than 0.30, suggesting no collinearity.

Statistical analyses

We used general linear models and mediational analysis. The 12MR test score in young adulthood, at the beginning of the subject's military service, was the outcome variable for CRF, and smaller values represented lower CRF. The predictor variables from the first assessment at eight years of age comprised the four child psychopathology variables (the combined parent/teacher emotional, conduct, and hyperactivity scales and the child depressive symptom scale), the parents' educational

level, and family structure. The mental health symptom scales were used as continuous for the hypothesis testing, as recently recommended (Blackford, 2017). These continuous variables were standardized, so that the regression coefficients could be interpreted as the difference in the 12MR score that corresponds to a change of one standard deviation in the scale.

The four mental health scales were categorized into three groups: less than the 50th percentile indicated the absence of mental health problem or a low level, the 50th to 90th percentile was a moderate level, and above the 90th percentile indicated a high level. The cut-off points were based on the distribution of the scores in the initial cohort at eight years of age (Duarte et al., 2010). Models with these categorical predictor variables were used in supplementary analyses as single predictor models to facilitate clinical interpretation (Blackford, 2017) and for interaction analyses (see below).

Predictor variables from the second evaluation in late adolescence, during the military call-up process, comprised two dichotomous variables: regular smoker versus other and depressed if the BDI score was at least eight versus non-depressed if it was less than that. This BDI cut-off value was the 90th percentile of the BDI distribution and depicted a marked level of depressive symptoms (Rønning et al., 2011). The predictor variable from the third assessment in young adulthood, at the beginning of the military service, was BMI categorized as underweight (<18.5), normal weight (18.5–24.9), and overweight/obese (≥25). The BMI categorization used was compatible with the World Health Organization guidelines.

The first step to examine our first hypothesis, that childhood psychopathology and SES would predict adult CRF, was to run single general linear regression predictor models. The subsequent multiple predictor analyses used stepwise backward selection with retaining criterion p<0.05 in models containing all the childhood predictors that were significant in the single predictor analyses. These were: child psychopathology, parental education, and family structure. We then added the predictors from the late adolescence evaluation (smoking and BDI) and young adulthood (BMI).

To examine our second research hypothesis, which was that the effect of childhood depression on CRF in young adulthood would be modified by the presence of depression in late adolescence, we added the interaction term of the childhood and adolescence depressive symptom variables as a predictor. This interaction term was significant, and the interaction between depression in childhood and depression in late adolescence was further explored by performing separate analyses in subgroups defined by one of the predictors (Corraini et al., 2017; Nikolakaros et al., 2017). Specifically, we performed single and multiple predictor subgroup analyses according to whether subjects had a marked level of depressive symptoms in late adolescence or not (effect modification, (Corraini et al., 2017)).

To examine whether the effect of childhood depression on CRF in young adulthood was modified by the presence of conduct problems during childhood, we constructed a model that contained three predictors: the childhood depressive symptoms score, the childhood conduct problems score, and their interaction term.

The mediational analysis was performed with the SAS CAUSALMED procedure. We tested predictors that were significant in the general linear models. Mediation effects for the possible mediators were tested one at a time, and we included the other predictors as covariates. Models with non-significant direct and indirect effects were interpreted as evidence for no mediation. Models with significant direct and indirect effects were interpreted as evidence for partial mediation. Finally, models with non-significant direct and significant indirect effects were interpreted as evidence for complete mediation.

The subject's age at the time of the 12MR test was included as a covariate in all of the models. We used Bonferroni correction for multiple comparisons. Statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) and IBM SPSS Statistics version 23 (IBM Corp., Armonk, NY, USA). A two-tailed $p<0.05$ was considered statistically significant.

Ethics

The Joint Commission on Ethics of Turku University and Turku University Central Hospital approved the research plan. Permission to use the military register data was obtained from the Finnish Defense Forces. The study subjects and their parents provided written permission for the study.

RESULTS

Childhood predictors

In the single predictor models of childhood factors, low parental education, family structure, childhood depressive symptoms, childhood conduct problems, and childhood hyperactivity predicted a lower 12MR score (Table 1, Models A). Low parental education, childhood depressive symptoms, and childhood conduct problems remained significant in the multiple predictor analysis (Table 1, Model B). A single predictor model was also used with childhood depressiveness as a categorical variable: compared with subjects with a low level of depressive problems, subjects with a moderate level of depressive symptoms had a mean 12MR test score that was non-significantly decreased by 38.6 meters (p=0.10), and subjects with a high level of depressive symptoms had a mean 12MR test score that was significantly decreased by 109.3 meters (p=0.001).

Childhood, late adolescence, and early adulthood predictors

In the single predictor models, all the late adolescence and young adulthood predictors (depressive symptoms, smoking, and BMI) were highly significant (p<0.001). Table 2 shows the results of the multiple predictor models, with backward selection, which started with the predictors that remained significant after all the previous steps. Low parental education, childhood depressive symptoms, depressive symptoms and smoking in late adolescence, and BMI (both underweight and

overweight/obesity) in early adulthood remained significant and independently predicted a lower 12MR score.

Interaction analyses

1. Interaction between depressive symptoms in childhood and depressive symptoms in late adolescence

The interaction term was significant in the model that contained the interaction between depressive symptoms in childhood and depressive symptoms in late adolescence in addition to the variables that remained significant in earlier multiple predictor models. The p-values for the interaction term in models with the continuous and categorical childhood depressive symptoms variable were 0.002 and 0.003, respectively. The effect of parental education was virtually unchanged.

Exploring the interaction between childhood and late adolescence depressiveness: Table 3 shows the results of the analyses in the subjects without depressive symptoms in late adolescence. In the single predictor models, the following predicted a lower 12MR score: low parental education, childhood depressive symptoms, childhood conduct problems, smoking in late adolescence, and BMI (both underweight and overweight/obesity). Only parental education and childhood conduct problems remained significant in the multiple predictor models of the childhood variables. When smoking and BMI were added to the final model, parental education, smoking, and BMI (both underweight and overweight/obesity) remained significant.

Table 4 shows the results in subjects with depressive symptoms in late adolescence. In the single and multiple predictor models, only childhood depressive symptoms and overweight/obesity in young adulthood predicted a lower 12MR score.

2. Interaction between childhood depressive symptoms and childhood conduct problems

The interaction term was not significant (p=0.51) in the model that contained childhood depressive symptoms, childhood conduct problems, and their interaction term.

Mediational analyses (Figure 2)

In the whole study population, the effect of childhood hyperactivity problems was completely mediated by childhood conduct problems and depressive symptoms. The effect of the family structure was totally mediated by childhood conduct problems. The effect of childhood depressiveness was partially mediated by depression in adolescence. Lastly, the effect of childhood conduct problems was totally mediated by smoking, overweight/obesity, and parental education,

In the subjects that were not depressed in adolescence, the effect of childhood depressiveness was completely mediated by childhood conduct problems. In turn, the effect of childhood conduct problems was completely mediated by smoking, overweight/obesity, and parental education. There was no mediation of effects in the subjects that were depressed in adolescence.

DISCUSSION

In this population-based study of young men assessed as healthy for military service, we have

shown, for the first time, that childhood psychopathology and SES predict adult CRF. Depressive

and conduct symptoms at the age of eight and depressive symptoms in late adolescence predicted

lower CRF in young adulthood. The effect of childhood depressive symptoms was much stronger in

subjects who were also depressed in late adolescence. In this group, the effect of childhood

depressive symptoms was independent of SES, other child psychopathology measures, smoking in

late adolescence, and underweight/overweight/obesity in early adulthood. Low SES in childhood

was associated with low CRF in early adulthood.

The general linear models and the mediational analysis suggested several paths leading from

childhood psychopathology and SES to adult CRF. The following paths were the most consistent

across analyses: firstly, a direct path that started from parental education. Secondly, a direct path

that started from childhood depression. Thirdly, indirect paths that started from childhood

depression and passed through childhood conduct problems and separately through adolescent

depression. Finally, an indirect path started from childhood conduct problems and passed through

smoking in adolescence and being overweight/obese in adulthood to reach lower adult CRF.

The main finding of our study was that childhood depressive symptoms that recurred in late adolescence independently predicted low CRF in early adulthood. It has previously been shown that childhood depression predicts adverse adult outcomes, including an increased risk of psychiatric disorders, criminality, and lower academic achievement (Rao and Chen, 2009). Most depressed children recover, but there is a high risk of relapse (Haavisto et al., 2004; Kovacs et al., 2016; Rao and Chen, 2009). The recurrence of childhood depression is difficult to predict (Rao and Chen, 2009). However, a recent study reported that the persistence of childhood depression into late adolescence was associated with autistic traits, particularly when subjects had experienced bullying (Rai et al., 2018). We have previously shown that the recurrence of childhood depressive symptoms in late adolescence is predicted by adverse life events in childhood, and it may lead to poor adaptive functioning in late adolescence (Rønning et al., 2011).

In adults, several longitudinal studies have demonstrated that high CRF protects from depression (Åberg et al., 2012; Becofsky et al., 2015; Dishman et al., 2012; Lindwall et al., 2014; Schuch et al., 2016; Shigdel et al., 2019; Sui et al., 2009; Willis et al., 2018). The reciprocal relationship is more relevant to the present study, and, to our knowledge, there have not been any studies that have examined the effects of depression on later CRF in adults.

In children and adolescences, cross-sectional studies have suggested associations between childhood psychopathology and CRF (Esmaeilzadeh, 2015; LaVigne et al., 2016; Rieck et al., 2013; Shomaker et al., 2012; Yeatts et al., 2017). In a prospective study with a one-year follow-up, high CRF protected subjects from developing depression in middle school, particularly girls (Ruggero et al., 2015). Exercise interventions improved depressive symptoms in adolescents (Carter et al., 2016). High CRF has been shown to enhance the physical and mental health of children and adolescents (Ortega et al., 2008). Concerning the etiological direction relevant to the present study, we are aware of only one previous longitudinal study that examined the effect of psychological

factors on future CRF. Olive et al. followed 676 children from the age of eight until the age of 17 and found that depressive symptoms had a significant detrimental effect on CRF for girls, with a similar trend for boys (Olive et al., 2016).

Depression may prevent the development of high CRF by reducing the subject's physical activity (Motl et al., 2004; Olive et al., 2016; Rottenberg et al., 2014). In children and adolescents, mood problems have been associated with low levels of physical activity (Kantomaa et al., 2008; Sallis et al., 2000), and physical activity has been shown to promote CRF (Ortega et al., 2008). Taken together with previous findings on the association between mood problems and CRF/physical activity, our results suggest that recurring depressive symptoms in childhood and adolescence may compromise the development of a healthy CRF level through young adulthood by means of a prolonged mood-related reduction in physical activity. A second possible etiological path that has been suggested is direct neuroendocrine dysfunction, namely chronic hyperactivity of the hypothalamic–pituitary–adrenal axis or the locus coeruleus-norepinephrine system (Hollenberg et al., 2003; Olive et al., 2016).

Childhood depression may co-occur with conduct problems, particularly among children with lower cognitive abilities (Riglin et al., 2016) and those facing psychosocial adversity (Simic and Fombonne, 2001). Co-occurring childhood depression and conduct disorder have been shown to predict lower academic adjustment and social competence in adolescence (Ingoldsby et al., 2006). In our study, the interaction between childhood depressive and conduct symptoms in predicting CRF in early adulthood was not significant. This means that there was no modifying effect of conduct symptoms on the association between childhood depressive symptoms and CRF in early adulthood in the whole study population. In the subgroup with depressive symptoms in childhood but not in late adolescence, the association between childhood depressive symptoms and CRF became non-significant after we took conduct symptoms into account. In turn, conduct symptoms

became non-significant when we took smoking in late adolescence and BMI in early adulthood into account. These results suggest that there is no direct association between non-recurring childhood depressive symptoms and adult CRF. Conduct problems in childhood may be associated with adult CRF, and this association may be mediated by adaptation of an unhealthy lifestyle, i.e., smoking and overweight/obesity.

In previous studies of the same study population, childhood conduct problems predicted both overweight/obesity (Duarte et al., 2010) and smoking (Niemelä et al., 2009). In another study, the accumulation of cardiovascular risk factors was associated with the severity of asymptomatic atherosclerosis in young people (Berenson et al., 1998). Thus, our results expand previous findings on the accumulation of important cardiovascular risk factors in children with conduct problems. These results should be taken into account when health promotion interventions are being devised for children with conduct problems.

Childhood psychopathology increases the risk for psychiatric disease later in life (Rao and Chen, 2009; Sourander et al., 2009), and low CRF in early adulthood predicts future psychiatric morbidity (Åberg et al., 2014). Therefore, our results suggest that the persistence of psychiatric symptoms into adulthood might be a complex phenomenon that is partly mediated by childhood psychopathology causing low CRF.

Cross-sectional studies on the association between SES and CRF during childhood and adolescence have produced conflicting results. Some studies have found evidence that supported a detrimental effect of low SES on CRF (Freitas et al., 2007; Jiménez-Pavón et al., 2010; Jin and Jones-Smith, 2015; Kristensen et al., 2006), whereas another study did not find any clear association (Sandercock et al., 2017). To our knowledge, there has only been one previous longitudinal study on the association between SES in childhood and CRF in young adults. Stea et al., 2009 examined 750

Norwegian conscripts and reported that there was no significant association between parental education during childhood and CRF in young adulthood. In contrast, when we looked at subjects who were not depressed in late adolescence, we found a clear association between parental education when the subjects were eight years of age and CRF in early adulthood. In this subgroup, the association between SES and CRF was independent of smoking, BMI, and childhood psychopathology. The differences between our results and the study carried out by Stea et al. could be due to the latter study having less statistical power. Other previous research has suggested an association between childhood SES and CRF later in life. Firstly, it has been shown that low SES in childhood predicts physical inactivity in adolescence (Sherar et al., 2016) and adulthood (Matthews et al., 2019; Pinto Pereira et al., 2014). Secondly, socioeconomic differences in CRF may emerge early in life (Kristensen et al., 2006).

A recent meta-analysis has suggested that school-based physical activity programs improve CRF in children (Pozuelo-Carrascosa et al., 2018). The association between low SES in childhood and low CRF in early adulthood suggests the need to take SES into account when designing health interventions to enhance physical activity in childhood and adolescence. Such interventions may be more effective if they include support for both family- and community-based activities, because low SES may prevent the children of deprived families from participating in family-based activities. Parental support and parental high physical activity have been shown to enhance the adoption of a physically active lifestyle by a child, particularly in families with a low SES (Kwon et al., 2016; Lounassalo et al., 2019; Rovio et al., 2018).

Limitations and strengths

Our study has several limitations. Firstly, we did not have data on CRF during childhood or adolescence or data on physical activity. Thus, we were not able to assess the continuity of CRF from childhood to early adulthood or assess possible mediating or modifying effects of physical

activity. Secondly, we only had information on male subjects. Thirdly, we only had information on CRF for subjects that were judged to be fit for military service. Some subjects with psychiatric problems in late adolescence were not included because their military call-up assessments showed they were not fit for military service. Those subjects were more likely to have had high childhood psychopathology scores (Duarte et al., 2010). Thus, our study may have underestimated the effects of childhood psychopathology on CRF. Fourthly, we only had information on childhood and adolescent depressive symptoms at two time-points. This means that we may have missed episodes of depressiveness, such as in early adolescence. Fifthly, our study may have not had enough power in subjects with depressive symptoms in late adolescence, and significant effects of parental education and conduct problems in childhood and smoking in late adolescence cannot be excluded with confidence in this group. Sixthly, we did not have information on the subjects' education, which has been shown to be an independent determinant of adult CRF (Ombrellaro et al., 2018). Thus, we were not able to examine potentially important pathways from childhood psychopathology and SES to adult CRF with regard to the educational level attained by the subjects. Finally, to enhance statistical power, we used a relatively low symptom threshold for depressive symptoms in late adolescence. However, it has been shown that even mild depressive symptoms in childhood and adolescence are associated with adverse adult outcomes (Duarte et al., 2010; Pine et al., 1999).

Our study also has strengths. The original sample of eight-year-olds is highly representative of the Finnish population. The assessment of childhood psychopathology was thorough, and it was carried out with widely accepted instruments. The assessment of CRF in the conscripts was also carried out in a standardized and consistent way.

Conclusions

This study has shown, for the first time, that psychopathology and lower SES during childhood predict lower CRF in young adulthood. Depressive symptoms that occur in both childhood and late adolescence may confer a particularly increased and independent risk of having low CRF as a young adult. Given the salient contribution of CRF to health, our results highlight the importance of treating child and adolescent psychopathology to avoid long-term adverse effects on CRF and physical and psychological health. Psychiatric treatment of children and adolescents should include an assessment of their physical activity and fitness, especially in children at high risk of recurrent depression. Relevant health interventions should take into account the child's SES.

Contributors

GN conceptualized and designed the study, reviewed the literature, designed and carried out statistical analyses, and drafted the initial manuscript. TV designed and supervised statistical analyses. LS designed and carried out statistical analyses. AS conceptualized and designed the study. All authors reviewed and revised the manuscript and approved the final manuscript as submitted.

Role of the funding source

Acknowledgements

Figure legends

Representative sample of Finnish 8-year-old males (N = 2964). The Rutter and Children's Depression Inventory questionnaires were administered. Parental education and family structure were also assessed.

242 subjects were excluded because their Finnish Personal Identification Number was unavailable.

2722 subjects underwent the Beck Depression Inventory during military call-up at the age of 18 years. Smoking was also assessed.

506 subjects with no data on the Beck Depression Inventory were excluded.

34 subjects with no data on smoking were excluded.

300 subjects who were found unfit for military service were excluded.

1882 subjects began their military service. Weight and height were measured, and the 12-minute run test was administered.

215 subjects with missing body mass index or 12-minute run test values were excluded.
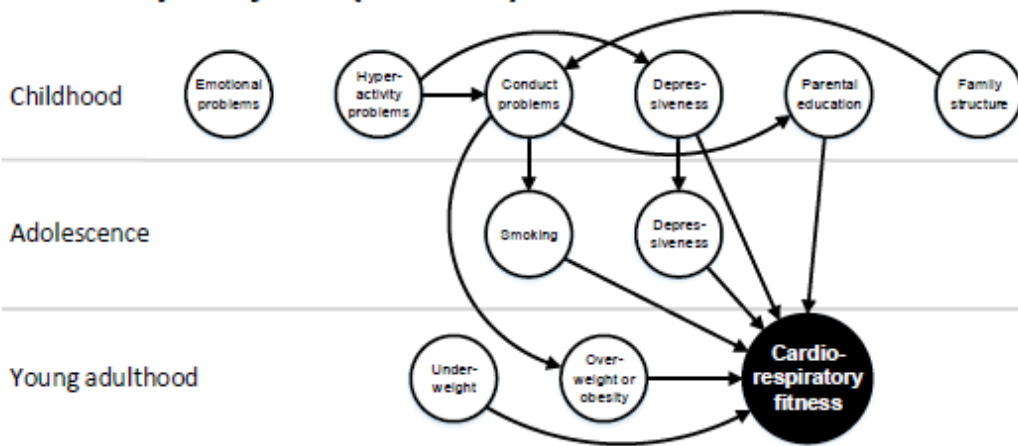
20 subjects with a 12-minute run test score < 1200 meters were excluded.

Data from 1647 subjects were analyzed.

FIGURE 1. Flow chart showing the selection of the study subjects.

All study subjects (N=1647)

Non-depressed in late adolescence (N=1528)
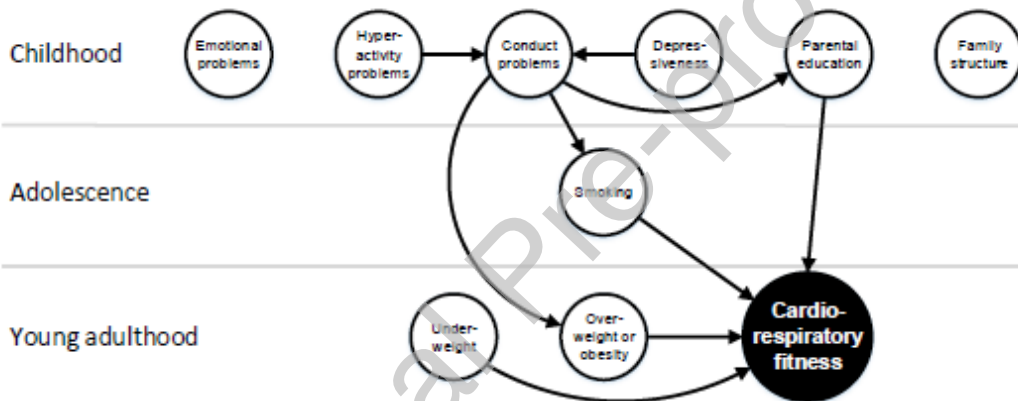
Depressed in late adolescence (N=115)
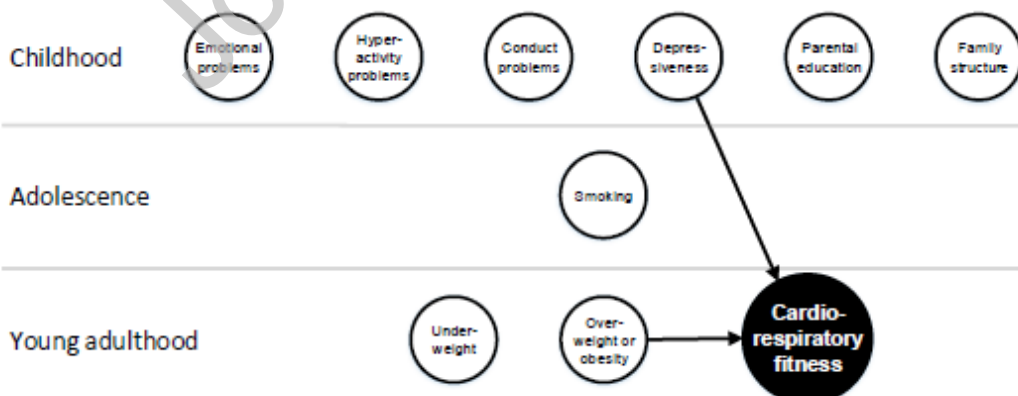
FIGURE 2. Mediational analysis of childhood psychopathology and socioeconomic status, adolescence depression and smoking, and body mass index in young adulthood as predictors of cardiorespiratory fitness in young adulthood. The whole study population (upper part), subjects that were not depressed in adolescence (middle), and subjects that were depressed in adolescence (lower part).

REFERENCES

Åberg, M.A.I., Nyberg, J., Torén, K., Sörberg, A., Kuhn, H.G., Waern, M., 2014. Cardiovascular fitness in early adulthood and future suicidal behaviour in men followed for up to 42 years. Psychol. Med. 44, 779–788. doi:10.1017/S0033291713001207

Åberg, M.A.I., Waern, M., Nyberg, J., Pedersen, N.L., Bergh, Y., Åberg, N.D., Nilsson, M., Kuhn, H.G., Torén, K., 2012. Cardiovascular fitness in males at age 18 and risk of serious depression in adulthood: Swedish prospective population-based study. Br. J. Psychiatry 201, 352–359. doi:10.1192/bjp.bp.111.103416

Beck, A.T., Ward, C.H., Mendelson, M., Mock, J., Erbaugh, J., 1961. An Inventory for Measuring Depression. Arch Gen Psychiatry 4, 561–571. doi:10.1001/archpsyc.1961.01710120031004

Becofsky, K.M., Sui, X., Lee, D., Wilcox, S., Zhang, J., Blair, S.N., 2015. A Prospective Study of Fitness, Fatness, and Depressive Symptoms. Am. J. Epidemiol. 181, 311–320. doi:10.1093/aje/kwu330

Berenson, G.S., Srinivasan, S.R., Bao, W., Newman, W.P., Tracy, R.E., Wattigney, W.A., 1998. Association between Multiple Cardiovascular Risk Factors and Atherosclerosis in Children and Young Adults. N. Engl. J. Med. 338, 1650–1656. doi:10.1056/NEJM199806043382302

Blackford, J.U., 2017. Leveraging Statistical Methods to Improve Validity and Reproducibility of Research Findings. JAMA Psychiatry 74, 119–120. doi:10.1001/jamapsychiatry.2016.3730

Bouchard, C., Rankinen, T., Timmons, J.A., 2011. Genomics and Genetics in the Biology of Adaptation to Exercise, in: Comprehensive Physiology. John Wiley & Sons, Inc., Hoboken, NJ, USA, pp. 1603–1648. doi:10.1002/cphy.c100059

Carnethon, M.R., Gidding, S.S., Nehgme, R., Sidney, S., Jacobs, D.R., Liu, K., 2003. Cardiorespiratory Fitness in Young Adulthood and the Development of Cardiovascular Disease Risk Factors. JAMA 290, 3092–3100. doi:10.1001/jama.290.23.3092

Carter, T., Morres, I.D., Meade, O., Callaghan, P., 2016. The Effect of Exercise on Depressive Symptoms in Adolescents: A Systematic Review and Meta-Analysis. J. Am. Acad. Child Adolesc. Psychiatry 55, 580–590. doi:10.1016/j.jaac.2016.04.016

Cooper, K.H., 1968. A Means of Assessing Maximal Oxygen Intake. Correlation Between Field and Treadmill Testing. JAMA 203, 201–204. doi:10.1001/jama.1968.03140030033008

Corraini, P., Olsen, M., Pedersen, L., Dekkers, O., Vandenbroucke, J.P., 2017. Effect modification, interaction and mediation: an overview of theoretical insights for clinical investigators. Clin. Epidemiol. 9, 331–338. doi:10.2147/CLEP.S129728

Crump, C., Sundquist, J., Winkleby, M.A., Sundquist, K., 2016. Interactive effects of physical fitness and body mass index on risk of stroke: A national cohort study. Int. J. Stroke 11, 683–694. doi:10.1177/1747493016641961

Dishman, R.K., Sui, X., Church, T.S., Hand, G.A., Trivedi, M.H., Blair, S.N., 2012. Decline in Cardiorespiratory Fitness and Odds of Incident Depression. Am. J. Prev. Med. 43, 361–368. doi:10.1016/j.amepre.2012.06.011

Duarte, C.S., Sourander, A., Nikolakaros, G., Pihlajamaki, H., Helenius, H., Piha, J., Kumpulainen, K., Moilanen, I., Tamminen, T., Almqvist, F., Must, A., 2010. Child Mental Health Problems and Obesity in Early Adulthood. J. Pediatr. 156, 93–97. doi:10.1016/j.jpeds.2009.06.066

Esmaeilzadeh, S., 2015. The association between depressive symptoms and physical status including physical activity, aerobic and muscular fitness tests in children. Environ. Health Prev. Med. 20, 434–440. doi:10.1007/s12199-015-0484-0

Freitas, D., Maia, J., Beunen, G., Claessens, A., Thomis, M., Marques, A., Crespo, M., Lefevre, J., 2007. Socio-economic status, growth, physical activity and fitness: The Madeira Growth Study. Ann. Hum. Biol. 34, 107–122. doi:10.1080/03014460601080983

Goodwin, R.D., Sourander, A., Duarte, C.S., Niemelä, S., Multimäki, P., Nikolakaros, G., Helenius, H., Piha, J., Kumpulainen, K., Moilanen, I., Tamminen, T., Almqvist, F., 2009. Do mental health problems in childhood predict chronic physical conditions among males in early

adulthood? Evidence from a community-based prospective study. Psychol. Med. 39, 301–311. doi:10.1017/S0033291708003504

Haavisto, A., Sourander, A., Multimäki, P., Parkkola, K., Santalahti, P., Helenius, H., Nikalakaros, G., Kumpulainen, K., Moilanen, I., Piha, J., Aronen, E., Puura, K., Linna, S.L., Almqvist, F., 2004. Factors associated with depressive symptoms among 18-year-old boys: A prospective 10-year follow-up study. J. Affect. Disord. 83, 143–154. doi:10.1016/j.jad.2004.06.008

Hamari, A., Toljamo, T., Nieminen, P., Kinnula, V.L., 2010. High frequency of chronic cough and sputum production with lowered exercise capacity in young smokers. Ann. Med. 42, 512–520. doi:10.3109/07853890.2010.505933

Hollenberg, M., Haight, T., Tager, I.B., 2003. Depression decreases cardiorespiratory fitness in older women. J. Clin. Epidemiol. 56, 1111–1117. doi:10.1016/S0895-4356(03)00167-7

Ingoldsby, E.M., Kohl, G.O., McMahon, R.J., Lengua, L., 2006. Conduct Problems, Depressive Symptomatology and Their Co-Occurring Presentation in Childhood as Predictors of Adjustment in Early Adolescence. J. Abnorm. Child Psychol. 34, 602–620. doi:10.1007/s10802-006-9044-9

Jiménez-Pavón, D., Ortega, F.B., Ruiz, J.R., España-Romero, V., Artero, E.G., Moliner-Urdiales, D., Gómez-Martínez, S., Vicente-Rodríguez, G., Manios, Y., Béghin, L., Répasy, J., Sjöstrom, M., Moreno, L.A., González Gross, M., Castillo, M.J., 2010. Socioeconomic status influences physical fitness in European adolescents independently of body fat and physical activity: The Helena study. Nutr. Hosp. 25, 311–316. doi:10.3305/nh.2010.25.2.4596

Jin, Y., Jones-Smith, J.C., 2015. Associations Between Family Income and Children's Physical Fitness and Obesity in California, 2010–2012. Prev. Chronic Dis. 12, 140392. doi:10.5888/pcd12.140392

Kantomaa, M.T., Tammelin, T.H., Ebeling, H.E., Taanila, A.M., 2008. Emotional and behavioral problems in relation to physical activity in youth. Med. Sci. Sports Exerc. 40, 1749–1756. doi:10.1249/MSS.0b013e31817b8e82

Kennedy, A.B., Lavie, C.J., Blair, S.N., 2018. Fitness or Fatness: Which Is More Important? JAMA 319, 231–232. doi:10.1001/jama.2017.21649

Kovacs, M., 1992. Children's Depression Inventory (CDI) manual. Toronto: Multi-Health Systems.

Kovacs, M., Obrosky, S., George, C., 2016. The course of major depressive disorder from childhood to young adulthood: Recovery and recurrence in a longitudinal observational study. J. Affect. Disord. 203, 374–381. doi:10.1016/j.jad.2016.05.042

Kristensen, P.L., Wedderkopp, N., Møller, N.C., Andersen, L.B., Bai, C.N., Froberg, K., 2006. Tracking and prevalence of cardiovascular disease risk factors across socio-economic classes: A longitudinal substudy of the European Youth Heart Study. BMC Public Health 6, 20. doi:10.1186/1471-2458-6-20

Kwon, S., Janz, K.F., Letuchy, E.M., Burns, T.L., Levy, S.M., 2016. Parental characteristic patterns associated with maintaining healthy physical activity behavior during childhood and adolescence. Int. J. Behav. Nutr. Phys. Act. 13, 58. doi:10.1186/s12966-016-0383-9

Lakoski, S.G., Barlow, C.E., Farrell, S.W., Berry, J.D., Morrow, J.R., Haskell, W.L., 2011. Impact of body mass index, physical activity, and other clinical factors on cardiorespiratory fitness (from the Cooper center longitudinal study). Am. J. Cardiol. 108, 34–39. doi:10.1016/j.amjcard.2011.02.338

LaVigne, T., Hoza, B., Smith, A.L., Shoulberg, E.K., Bukowski, W., 2016. Associations between physical fitness and children's psychological well-being. J. Clin. Sport Psychol. 10, 32–47. doi:10.1123/jcsp.2014-0053

Lee, D., Artero, E.G., Sui, X., Blair, S.N., 2010. Mortality trends in the general population: the importance of cardiorespiratory fitness. J. Psychopharmacol. 24, 27–35. doi:10.1177/1359786810382057

Lindwall, M., Gerber, M., Jonsdottir, I.H., Börjesson, M., Ahlborg, G., 2014. The relationships of change in physical activity with change in depression, anxiety, and burnout: A longitudinal study of Swedish healthcare workers. Heal. Psychol. 33, 1309–1318. doi:10.1037/a0034402

Lounassalo, I., Salin, K., Kankaanpää, A., Hirvensalo, M., Palomäki, S., Tolvanen, A., Yang, X., Tammelin, T.H., 2019. Distinct trajectories of physical activity and related factors during the life course in the general population: a systematic review. BMC Public Health 19, 271. doi:10.1186/s12889-019-6513-y

Matthews, K.A., Jennings, J.R., Lee, L., Pardini, D., 2019. Depressive Symptoms During Childhood and Cardiovascular Risk Factors in Black and White Men. Psychosom. Med. 81, 176–183. doi:10.1097/PSY.0000000000000652

Motl, R.W., Birnbaum, A.S., Kubik, M.Y., Dishman, R.K., 2004. Naturally occurring changes in physical activity are inversely related to depressive symptoms during early adolescence. Psychosom. Med. 66, 336–342. doi:10.1097/01.psy.0000126205.35683.0a

Niemelä, S., Sourander, A., Pilowsky, D.J., Susser, E., Helenius, H., Piha, J., Kumpulainen, K., Moilanen, I., Tamminen, T., Almqvist, F., 2009. Childhood antecedents of being a cigarette smoker in early adulthood. The Finnish 'From a Boy to a Man' Study. J. Child Psychol. Psychiatry 50, 343–351. doi:10.1111/j.1469-7610.2008.01968.x

Nikolakaros, G., Vahlberg, T., Auranen, K., Sillanmäki, L., Venetoklis, T., Sourander, A., 2017. Obesity, Underweight, and Smoking Are Associated with Worse Cardiorespiratory Fitness in Finnish Healthy Young Men: A Population-Based Study. Front. Public Heal. 5, 206. doi:10.3389/fpubh.2017.00206

Olive, L.S., Telford, R.M., Byrne, D.G., Abhayaratna, W.P., Telford, R.D., 2016. Psychological distress leads to reduced physical activity and fitness in children: the Australian longitudinal LOOK study. J. Behav. Med. 39, 587–598. doi:10.1007/s10865-016-9723-0

Ombrellaro, K.J., Perumal, N., Zeiher, J., Hoebel, J., Ittermann, T., Ewert, R., Dörr, M., Keil, T., Mensink, G.B.M., Finger, J.D., 2018. Socioeconomic Correlates and Determinants of Cardiorespiratory Fitness in the General Adult Population: a Systematic Review and Meta-Analysis. Sport. Med. - Open 4, 25. doi:10.1186/s40798-018-0137-0

Ortega, F.B., Ruiz, J.R., Castillo, M.J., Sjöström, M., 2008. Physical fitness in childhood and adolescence: A powerful marker of health. Int. J. Obes. 32, 1–11. doi:10.1038/sj.ijo.0803774

Penry, J.T., Wilcox, A.R., Yun, J., 2011. Validity and reliability analysis of Cooper's 12-minute run and the multistage shuttle run in healthy adults. J. Strength Cond. 25, 597–605. doi:10.1519/JSC.0b013e3181cc2423

Pine, D.S., Cohen, E., Cohen, P., Brook, J., 1999. Adolescent depressive symptoms as predictors of adult depression: Moodiness or mood disorder? Am. J. Psychiatry 156, 133–135. doi:10.1176/ajp.156.1.133

Pinto Pereira, S.M., Li, L., Power, C., 2014. Early-Life Predictors of Leisure-Time Physical Inactivity in Midadulthood: Findings From a Prospective British Birth Cohort. Am. J. Epidemiol. 180, 1098–1108. doi:10.1093/aje/kwu254

Pozuelo-Carrascosa, D.P., García-Hermoso, A., Álvarez-Bueno, C., Sánchez-López, M., Martinez-Vizcaino, V., 2018. Effectiveness of school-based physical activity programmes on cardiorespiratory fitness in children: A meta-Analysis of randomised controlled trials. Br. J. Sports Med. doi:10.1136/bjsports-2017-097600

Rai, D., Culpin, I., Heuvelman, H., Magnusson, C.M.K., Carpenter, P., Jones, H.J., Emond, A.M.,

Zammit, S., Golding, J., Pearson, R.M., 2018. Association of Autistic Traits With Depression From Childhood to Age 18 Years. JAMA Psychiatry 75, 835–843. doi:10.1001/jamapsychiatry.2018.1323

Rao, U., Chen, L.A., 2009. Characteristics, correlates, and outcomes of childhood and adolescent depressive disorders. Dialogues Clin. Neurosci. 11, 45–62. doi:10.1016/j.bbi.2008.05.010

Rieck, T., Jackson, A., Martin, S.B., Petrie, T., Greenleaf, C., 2013. Health-related fitness, body mass index, and risk of depression among adolescents. Med. Sci. Sports Exerc. 45, 1083–1088. doi:10.1249/MSS.0b013e3182831db1

Riglin, L., Thapar, A., Shelton, K.H., Langley, K., Frederickson, N., Rice, F., 2016. Profiling depression in childhood and adolescence: the role of conduct problems. J. Child Psychol. Psychiatry 57, 481–490. doi:10.1111/jcpp.12465

Rønning, J.A., Haavisto, A., Nikolakaros, G., Helenius, H., Tamminen, T., Moilanen, I., Kumpulainen, K., Piha, J., Almqvist, F., Sourander, A., 2011. Factors associated with reported childhood depressive symptoms at age 8 and later self-reported depressive symptoms among boys at age 18. Soc. Psychiatry Psychiatr. Epidemiol. 46, 207–218. doi:10.1007/s00127-010-0182-6

Rottenberg, J., Yaroslavsky, I., Carney, R.M., Freedland, K.E., George, C.J., Baji, I., Dochnal, R., Gádoros, J., Halas, K., Kapornai, K., Kiss, E., Osváth, V., Varga, H., Vetró, Á., Kovacs, M., 2014. The association between major depressive disorder in childhood and risk factors for cardiovascular disease in adolescence. Psychosom. Med. 76, 122–127. doi:10.1097/PSY.0000000000000028

Rovio, S.P., Yang, X., Kankaanpää, A., Aalto, V., Hirvensalo, M., Telama, R., Pahkala, K., Hutri-Kähönen, N., Viikari, J.S.A., Raitakari, O.T., Tammelin, T.H., 2018. Longitudinal physical activity trajectories from childhood to adulthood and their determinants: The Young Finns

Study. Scand J Med Sci Sport. 28, 1073–1083. doi:10.1111/sms.12988

Ruggero, C.J., Petrie, T., Sheinbein, S., Greenleaf, C., Martin, S., 2015. Cardiorespiratory fitness

may help in protecting against depression among middle school adolescents. J. Adolesc. Heal.

57, 60–65. doi:10.1016/j.jadohealth.2015.03.016

Rutter, M., 1970. Education, health and behaviour. London: Longmans.

doi:10.1017/S0033291700044858

Sallis, J.F., Prochaska, J.J., Taylor, W.C., 2000. A review of correlates of physical activity of

children and adolescents. Med. Sci. Sports Exerc. 32, 963–975. doi:10.1097/00005768-

200005000-00014

Sandercock, G.R.H., Lobelo, F., Correa-Bautista, J.E., Tovar, G., Cohen, D.D., Knies, G., Ramírez-

Vélez, R., 2017. The Relationship between Socioeconomic Status, Family Income, and

Measures of Muscular and Cardiorespiratory Fitness in Colombian Schoolchildren. J. Pediatr.

185, 81-87.e2. doi:10.1016/j.jpeds.2016.12.058

Santtila, M., Kyröläinen, H., Vasankari, T., Tiainen, S., Palvalin, K., Häkkinen, A., Häkkinen, K.,

2006. Physical fitness profiles in young Finnish men during the years 1975-2004. Med. Sci.

Sports Exerc. 38, 1990–4. doi:10.1249/01.mss.0000232023.28984.78

Schuch, F.B., Vancampfort, D., Sui, X., Rosenbaum, S., Firth, J., Richards, J., Ward, P.B., Stubbs,

B., 2016. Are lower levels of cardiorespiratory fitness associated with incident depression? A

systematic review of prospective cohort studies. Prev. Med. (Baltim). 93, 159–165.

doi:10.1016/j.ypmed.2016.10.011

Sherar, L.B., Griffin, T.P., Ekelund, U., Cooper, A.R., Esliger, D.W., van Sluijs, E.M.F., Andersen,

L.B., Cardon, G., Davey, R., Froberg, K., Hallal, P.C., Janz, K.F., Kordas, K., Kriemler, S.,

Pate, R.R., Puder, J.J., Sardinha, L.B., Timperio, A.F., Page, A.S., 2016. Association between

maternal education and objectively measured physical activity and sedentary time in

adolescents. J. Epidemiol. Community Health 70, 541–548. doi:10.1136/jech-2015-205763

Shigdel, R., Stubbs, B., Sui, X., Ernstsen, L., 2019. Cross-sectional and longitudinal association of

non-exercise estimated cardiorespiratory fitness with depression and anxiety in the general

population: The HUNT study. J. Affect. Disord. 252, 122–129. doi:10.1016/j.jad.2019.04.016

Shomaker, L.B., Tanofsky-Kraff, M., Zocca, J.M., Field, S.E., Drinkard, B., Yanovski, J.A., 2012.

Depressive symptoms and cardiorespiratory fitness in obese adolescents. J. Adolesc. Heal. 50,

87–92. doi:10.1016/j.jadohealth.2011.05.015

Simic, M., Fombonne, E., 2001. Depressive conduct disorder: Symptom patterns and correlates in

referred children and adolescents. J. Affect. Disord. 62, 175–185. doi:10.1016/S0165-

0327(99)00201-3

Sourander, A., Klomek, A.B., Niemelä, S., Haavisto, A., Gyllenberg, D., Helenius, H., Sillanmäki,

L., Ristkari, T., Kumpulainen, K., Tamminen, T., Moilanen, I., Piha, J., Almqvist, F., Gould,

M.S., 2009. Childhood Predictors of Completed and Severe Suicide Attempts. Findings From

the Finnish 1981 Birth Cohort Study. Arch. Gen. Psychiatry 66, 398–406.

doi:10.1001/archgenpsychiatry.2009.21

Sourander, A., Multimäki, P., Santalahti, P., Parkkola, K., Haavisto, A., Helenius, H., Nikolakaros,

G., Piha, J., Tamminen, T., Moilanen, I., Kumpulainen, K., Aronen, E.T., Linna, S.-L., Puura,

K., Almqvist, F., 2004. Mental Health Service Use Among 18-Year-Old Adolescent Boys: A

Prospective 10-Year Follow-up Study. J Am Acad Child Adolesc Psychiatry 43, 1250–1258.

doi:10.1097/01.chi.0000134493.88549.e2

Stavrakakis, N., De Jonge, P., Ormel, J., Oldehinkel, A.J., 2012. Bidirectional prospective

associations between physical activity and depressive symptoms. The TRAILS study. J.

Adolesc. Heal. 50, 503–508. doi:10.1016/j.jadohealth.2011.09.004

Stea, T.H., Wandel, M., Mansoor, M.A., Uglem, S., Frølich, W., 2009. BMI, lipid profile, physical fitness and smoking habits of young male adults and the association with parental education. Eur. J. Public Health 19, 46–51. doi:10.1093/eurpub/ckn122

Sui, X., Laditka, J.N., Church, T.S., Hardin, J.W., Chase, N., Davis, K., Blair, S.N., 2009. Prospective study of cardiorespiratory fitness and depressive symptoms in women and men. J. Psychiatr. Res. 43, 546–552. doi:10.1016/j.jpsychires.2008.08.002

Willis, B.L., Leonard, D., Barlow, C.E., Martin, S.B., DeFina, L.F., Trivedi, M.H., 2018. Association of midlife cardiorespiratory fitness with incident depression and cardiovascular death after depression in later life. JAMA Psychiatry 75, 911–917. doi:10.1001/jamapsychiatry.2018.1467

Yeatts, P.E., Martin, S.B., Petrie, T.A., 2017. Physical fitness as a moderator of neuroticism and depression in adolescent boys and girls. Pers. Individ. Dif. 114, 30–35. doi:10.1016/j.paid.2017.03.040

TABLE 1. Childhood predictors of cardiorespiratory fitness in 1647 male conscripts. Single and multiple predictor general linear models.

Childhood factor	N	Models A (single predictor)				Mod
		Mean 12MR test score (meters)	Mean 12MR test score difference	95% CLs for the mean difference	P	Mean 12MR test score (meters)
Parental education						
Either parent upper secondary	561	2578				2569.7
Both less than upper secondary	1024	2497	–81	–45.5 , –116.4	<0.001	2502.8
Family structure						
Two biological parents	1376	2531.4				
Other	224	2481.9	–49.4	–0.6 , –98.3	0.047	
Depressive problems (CDI)						
1 SD unit = 5.6 points			–38.9	–22.2 , –55.7	<0.001	
Emotional problems						
1 SD unit = 1.84 points			–13.8	3.1 , –30.7	0.11	
Hyperactivity problems						
1 SD unit = 2.17 points			–25.7	–8.8 , –42.6	0.003	
Conduct problems						
1 SD unit = 2.7 points			–38.1	–21.3 , –54.9	<0.001	

Models A include one predictor at a time (single predictor analysis).

Model B initially included all predictors that were significant in single predictor models (Models A). With backward selection, the hyperactivity scale predictor was removed first with a p-value of 0.79. Next, the family structure predictor was removed with a p-value of 0.19. The model shown comprises the predictors that remained significant.

The subject's age at the time of the 12MR test was included as a covariate in all the models.

CLs = Confidence Limits, CDI = Children's Depression Inventory

TABLE 2. Predictors of cardiorespiratory fitness among 1647 male conscripts in childhood, late adolescence, and early adulthood. Multiple predictor general linear model (backward selection).

Predictor	N	Mean 12MR test score (meters)	Mean 12MR test score difference	95% CLs for the mean difference	P
Parental education					
Either parent upper secondary	554	2421.3			
Both less than upper secondary	1007	2363.8	−57.4	−24.6, −90.2	0.001
Childhood depressiveness (CDI)					
1 SD unit = 5.6 points	1561		−17.2	−1.2, −33.1	0.035
Depressiveness in late adolescence					
BDI < 8 (not depressed)	1453	2451.2			
BDI ≥ 8 (depressed)	108	2333.9	−117.4	−55.4, −179.3	<0.001
Regular smoking in late adolescence					
No	1035	2455.1			
Yes	526	2330	−125.1	−91.8, −158.5	<0.001
Body mass index in early adulthood					<0.001
Normal (18.5 - 25)	1131	2533.9			
Underweight (<18.5)	93	2399	−135	−54.0, −215.9	<0.001
Overweight/obese (≥25)	337	2244.8	−289.2	−242.6, −335.7	<0.001

The conduct problems scale was removed from the model with a p-value of 0.17. The model shown comprises the predictors that remained significant.

The subject's age at the time of the 12MR test was included as a covariate.

CLs = Confidence Limits, CDI = Children's Depression Inventory, BDI = Beck Depression Inventory

TABLE 3. Cardiorespiratory fitness of 1528 male conscripts who were not depressed (Beck Depression Inventory score <8) in late adolescence. Single and multiple predictor general linear models.

		Models A (single predictor)				M
Predictor	N	Mean 12MR test score (meters)	Mean 12MR test score difference	95% CLs for the mean difference	P	Mean 12MR test score (meters)
Parental education						
Either parent upper secondary	527	2588				2482.1
Both less than upper secondary	946	2508.2	−79.8	−43.6, −116.0	<0.001	2421.2
Childhood depressiveness (CDI)						
1 SD unit = 5.6 points			−26.3	−8.6, −44.0	0.004	
Childhood conduct problems						

	N	Mean 12MR test score (meters)	Mean 12MR test score difference	95% CLs	P	Model B
1 SD unit = 2.7 points			−34.2	−16.8, −51.6	<0.001	
Regular smoking in late adolescence						
No	1031	2583.9				2522.2
Yes	497	2433.1	−150.8	−115.0,−186.6	<0.001	2381
Body mass index in early adulthood					<0.001	
Normal (18.5 – 25)	1113	2605.4				2590.7
Underweight (< 18.5)	86	2470.7	−134.7	−49.0,−220.4	0.001	2461.6
Overweight/Obese (≥25)	329	2312.8	−292.6	−244.5,−340.6	<0.001	2302.7

Models A include one predictor at a time (single predictor analysis).

Model B initially included all childhood predictors that were significant in single predictor analysis (Models A). With backward selection, the childhood depressiveness variable was removed first with a p-value of 0.078. Next, body mass index and smoking were added to the model, and at that stage, the conduct problems variable was removed with a p-value of 0.21. Model B includes the predictors that remained significant.

The subject's age at the time of the 12MR test was included as a covariate in all the models.

CLs = Confidence Limits, CDI = Children's Depression Inventory

TABLE 4. Cardiorespiratory fitness of 115 male conscripts who were depressed (Beck Depression Inventory score ≥8) in late adolescence. Single and multiple predictor general linear models.

Predictor	N	Mean 12MR test score (meters)	Models A (single predictor)			Mo
			Mean 12MR test score difference	95% CLs for the mean difference	P	Mean 12MR test score (meters)
Parental education						
Either parent upper secondary	33	2415.9				
Both less than upper secopndary	76	2360.1	−55.9	−103.4,−215.1	0.49	
Childhood depressiveness (CDI)						
1 SD unit = 5.6 points			−99.1	−40.5,−157.6	0.001	
Childhood conduct problems						
1 SD unit = 2.7 points			−18.5	−5.0, −41.9	0.12	
Regular smoking in late adolescence						
No	59	2401.5				
Yes	56	2341.1	−63.1	−80.0,−206.3	0.38	
Body mass index in early adulthood					<0.001	
Normal (18.5 – 25)	79	2476.2				2465.9
Underweight (< 18.5)	9	2255.6	−172.0	−142.0,−486.0	0.56	2299.8
Overweight/Obese (≥25)	27	2106.4	−350.4	−153.5,−547.2	<0.001	2120.5

Models A include a single predictor at a time.

Model B first included childhood depressiveness, the only childhood predictor that was significant in the single predictor analyses. Next, body mass index was added to the model. Both childhood depressiveness and body mass index remained significant in the final model (Model B).

The subject's age at the time of the 12MR test was included as a covariate in all the models.

CLs = Confidence Limits, CDI = Children's Depression Inventory

Conflict of interest

All authors declare that they have no conflicts of interest.