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Negative parenting, epigenetic age, and psychological problems: prospective associations from adolescence to young adulthood

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Background: Epigenetic clocks are based on DNA methylation levels of several genomic loci and have been developed as indices of biological aging. Studies examining the effects of stressful environmental exposures have shown that stress is associated with differences between epigenetic age and chronological age (i.e., Epigenetic Age acceleration, EA). This pre-registered longitudinal study examined the long-term effects of negative parenting and psychological problems throughout adolescence (ages 13–17 years) on EA in late adolescence (age 17 years) and EA changes from late adolescence to young adulthood (age 25 years). Further, it examined how (change in) EA is related to changes in psychological problems from adolescence to young adulthood. **Methods:** We used data from a sample of 434 participants followed from age 13 to age 25, with saliva collected at ages 17 and 25. We estimated EA using four commonly used epigenetic clocks and analyzed the data using Structural Equation Modeling. **Results:** While negative parenting was not related to EA nor change in EA, (change in) EA was related to developmental indices such as externalizing problems and self-concept clarity. **Conclusions:** Declining psychological well-being during young adulthood was preceded by EA. **Keywords:** Adolescence; epigenetic age; epigenetics; longitudinal studies; mental health; parenting.

Introduction

Stress is thought to wear down the body and cause accelerated biological aging (Palma-Gudiel, Fañanás, Horvath, & Zannas, 2020; Wade, Fox, Zeanah, Nelson, & Drury, 2020). Such biological wear has been theorized to reflect environmental exposures, such as interpersonal stress, and to serve as a biological substrate that potentially sensitizes the individual to psychological maladjustment (Wade et al., 2020). DNA methylation (DNAm) is an epigenetic mechanism of transcriptional regulation that has been proposed to act as a biological substrate embedding stressful environmental exposures (Overbeek, Creasey, Wesarg, Huijzer-Engbrenghof, & Spencer, 2020; Szyf & Bick, 2013). Composite scores of DNAm across tens to hundreds of genomic loci have been developed as indices of biological aging—so-called 'epigenetic clocks'. In stressful contexts, a difference between chronological age and epigenetic age might arise, which is referred to as epigenetic age acceleration (EA). For example, an adolescent might be 17 years old, but their biological age might be 18.5 years, reflecting EA of 1.5 years. Increased EA is seen as biological wear of the body (Colich, Rosen, Williams, & McLaughlin, 2020; Oblak, van der Zaag, Higgins-Chen, Levine, & Boks, 2021).

Empirical studies have shown that EA is linked with both stressful conditions and psychological maladjustment. Negative parenting, including threat, exposure to violence (Colich et al., 2020; Jovanovic et al., 2017; Sumner, Colich, Uddin, Armstrong, & McLaughlin, 2019), and harsh parenting (Brody, Yu, Chen, Beach, & Miller, 2016), has been associated with increased EA. Also, psychological problems, including internalizing symptoms (Dammering et al., 2021; Sumner et al., 2019; Tollenaar et al., 2021) and externalizing problems (Raffington et al., 2021), have been associated with increased EA. However, such links have often been based on cross-sectional or retrospective data and EA has mostly been based on one single assessment of DNA methylation. These two limitations obscure our understanding of the nature of those links: Can EA *change* in response to environmental exposures? Is EA an outcome or a predictor of stress and psychological problems? In other words, does EA reflect past exposure to stressful environments, or does it reflect a developmental state that predicts future development?

To address these questions, we need to move to within-person, repeated assessments of EA (Aristizabal et al., 2020; Copeland, Shanahan, McGinnis, Aberg, & van den Oord, 2022), as repeated assessments of EA can help distinguish between *advanced age* and *true age acceleration* (Copeland et al., 2022). In this study, we use the term 'changes in EA' to refer to the difference between two repeated assessments of EA (a difference of difference). The main aim of this study was to examine the longitudinal links of

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negative parenting and psychological problems in EA and changes in EA, as well as the longitudinal associations of EA and changes in EA with changes in psychological problems.

There are only few studies with repeated assessments of EA, and they support the idea that EA changes both developmentally (Cerveira de Baumont et al., 2021; Marioni et al., 2019) and in response to exposures such as combat stress (Boks et al., 2015) and early life adversities (Copeland et al., 2022). Early life adversities were found to be prospectively associated with *changes* in EA from adolescence to young adulthood, but not with a single-point EA in adolescence (Copeland et al., 2022), showing that EA as an indication of biological age responds to environmental exposures. The only way to infer actual age acceleration is by using at least two timepoints such that each individual can serve as a control for themselves, and between-person differences are regressed out. Using repeated measures of the difference between chronological age and biological age allows to assess whether the body grows older at a faster pace biologically than chronologically. Therefore, the current study used two timepoints of EA to examine changes in EA from late adolescence to young adulthood.

So far, existing research on parenting predictors of EA has mainly focused on severe negative parenting, such as neglect and abuse. We know little about the prospective associations between EA and subtler, 'everyday' forms of negative parental behavior, such as psychological control, level of expressed emotion, and parent–child conflict intensity. Filling this gap is important, as such parental behaviors are more widespread in the population than neglect and abuse, and have significant implications for youth's psychological well-being (Michelson & Bhugra, 2012; Millman, Weintraub, & Miklowitz, 2018; Pinquart, 2017). It can, therefore, be expected that they also associate with EA. Thus, the current study conceptualizes negative parenting as consisting of parental psychological control, level of expressed emotion, and parent–child conflict intensity.

To understand whether EA is an outcome or a predictor of stress and psychological well-being, we need to examine the longitudinal associations between EA and psychological problems. There is a dearth of studies with repeated measures of psychological problems and EA. Tollenaar et al. (2021) found that internalizing symptoms during preschool significantly predicted EA at age 6 years, which was in turn significantly and prospectively associated with internalizing symptoms at ages 6–10 years. This study did not assess EA repeatedly, leaving it unclear whether changes in EA contribute to increasing problems, or vice versa. Thus, further research needs to examine the consequences of *changing* EA for health (Copeland et al., 2022), to clarify whether EA itself, or change in EA is more consequential for health. This study, therefore, investigated the longitudinal associations between repeatedly assessed EA and repeatedly assessed psychological problems.

In this study, we focused on adolescence and the transition from adolescence to young adulthood. Adolescence is characterized by important biological, cognitive, and psychosocial developments and is a formative period for future health, and for the life paths youth take. Several psychological problems of adulthood have their first appearance during adolescence (Solmi et al., 2022), while this developmental stage is also crucial for the development of the self (Branje, de Moor, Spitzer, & Becht, 2021). In this study, we included different aspects of psychological problems, namely, internalizing problems, externalizing problems, and (lack of) self-concept clarity. While externalizing and internalizing problems have been examined in the epigenetic literature, no study has examined associations with self-concept clarity. This is an important gap, as self-concept clarity has genetic (Drunen et al., 2021) and neural correlates (Van der Aar, Peters, Becht, & Crone, 2022), and plays an important role in the quality of close relationships (Becht et al., 2017) and internalizing problems (Van Dijk et al., 2014) in adolescence.

The present study

The present pre-registered study extended knowledge on associations between negative parenting, psychological problems, and EA in three ways. First, we examined the longitudinal associations of negative parenting and psychological well-being throughout adolescence with EA in late adolescence and with *change* in EA from late adolescence to young adulthood. Second, adding to literature investigating severe negative parenting aspects, such as abuse and neglect, this study focused on subtler, 'softer' negative parenting indicators, including parent–child conflict intensity, level of expressed emotion, and psychological control. Third, to elucidate the direction of effects between psychological problems and EA, we examined the bidirectional associations of EA and change in EA with psychological problems and change in psychological problems. The conceptual model of this study is shown in Figure 1. Several epigenetic clocks have been developed based on either chronological age (Horvath clock (Horvath, 2013); Hannum clock (Hannum et al., 2013)) or several biomedical health and lifespan indices [GrimAge (Lu et al., 2019); PhenoAge (Levine et al., 2018)]. Based on the frequency of their use, and in order to enhance comparability with existing research, we included four of the most commonly used epigenetic clocks (Horvath, PhenoAge, GrimAge, and Hannum) that have been around for some time, and most of which have been recently refined (Higgins-Chen et al., 2022). We conducted separate analyses for each clock. The research questions, research hypotheses, and analytic plan

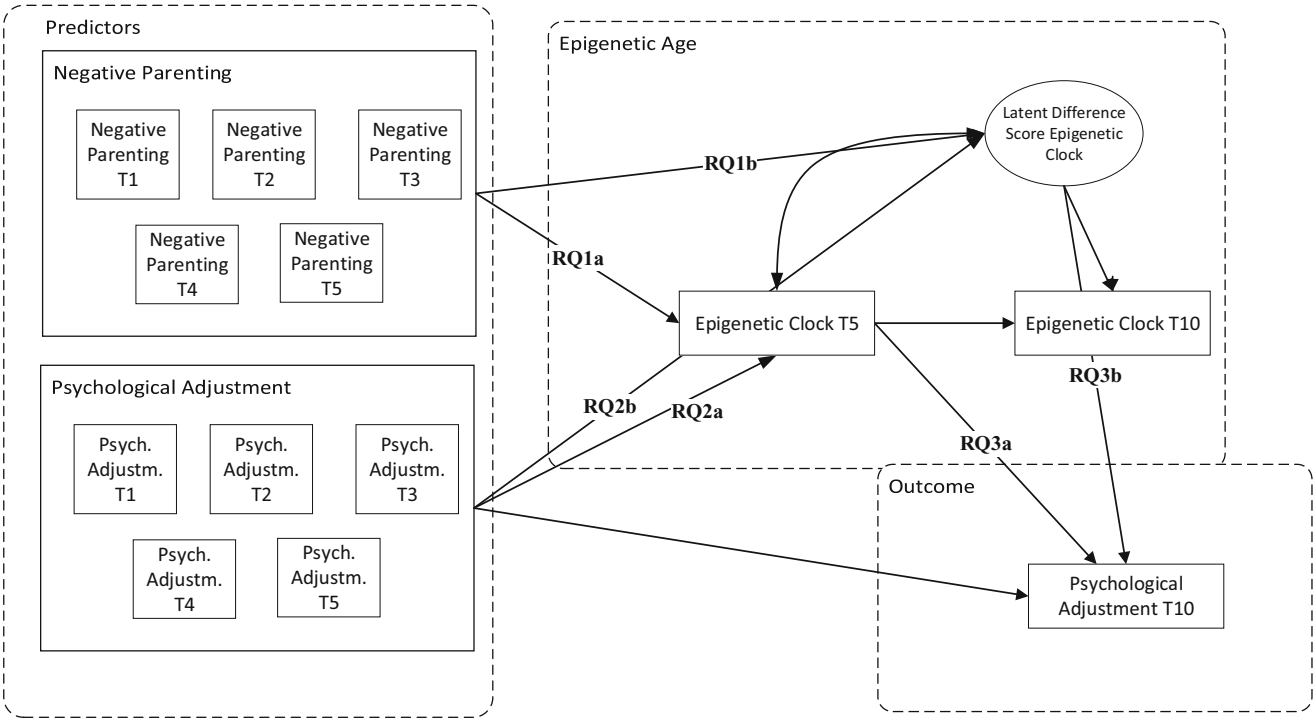

Figure 1 The analytic plan for this study

of this study were preregistered (https://osf.io/f6d39). The research questions (RQ) and respective hypotheses were the following:

RQ1. Does negative parenting during adolescence predict EA during late adolescence, and change in EA between late adolescence and young adulthood? We expected that negative parenting would reflect a stressful condition that positively predicts EA during late adolescence (Brody et al., 2016). We also hypothesized a positive effect of negative parenting on change in EA from late adolescence to young adulthood based on theory, even though some studies have found that more stressful conditions are associated with a decrease in epigenetic age (Boks et al., 2015; Clausing, Binder, & Non, 2021).

RQ2. Do psychosocial problems during adolescence predict EA during late adolescence and changes in EA from late adolescence to young adulthood? In line with evidence suggesting that DNAm is a mechanism in the development of psychopathology, and not vice versa (Barker, Walton, & Cecil, 2018), we expected higher levels of internalizing and externalizing symptoms during adolescence to be positively associated with EA during late adolescence but not with increases in EA during young adulthood. Regarding self-concept clarity our research question was exploratory.

RQ3. Does EA during late adolescence predict changes in psychological problems? Extrapolating from extant research, we expected both EA during late adolescence and changes in EA from late adolescence to young adulthood to be positively associated with internalizing symptoms during young adulthood (Barker, Walton, & Cecil, 2018; Smith et al., 2021; Tollenaar et al., 2021). Regarding externalizing problems, given inconsistent results showing either positive (Cicchetti & Handley, 2017; Raffington et al., 2021) or no significant effects (Tollenaar et al., 2021), we kept the research question exploratory. Regarding self-concept clarity, given the lack of studies, we made a tentative hypothesis based on findings involving cognitive functioning (Barker et al., 2018; Raffington, Tanksley, Sabhlok, et al., 2021; Wolf et al., 2016), that EA will negatively predict self-concept clarity.

Method

Participants

Data for this study came from the ongoing longitudinal Research on Adolescent Development And Relationships-Young study (RADAR-Y; Branje & Meeus, 2018). The original sample consisted of 497 adolescents (M_{age} = 13.03, *SD* = 0.47 at T1, 56.4% boys). The current study used data of the first 10 measurement waves. At Waves 1–5, adolescents took part in annual assessments, which included questionnaires on parenting, parent–adolescent relationship quality, and adolescent well-being. After Wave 5 (M_{age} = 17.03) a subsample of *N* = 415 adolescents provided saliva samples (T1 will be used from here on to refer to the first point of saliva collection). From Wave 7 onwards data collection took part every 2 years. At Wave 10 (M_{age} = 25.8) *N* = 247 adolescents provided saliva samples (T2). To increase power and given that analyses (see Analytic Plan) would apply robust methods to handle missing data, we included the 434 youth who provided saliva data at least once.

Measures

Negative parenting. Self-report questionnaires were used to assess Psychological Control, Parent–Adolescent

Negative Interactions, and Level of Expressed Emotion, as indicators of Negative Parenting. All three variables were assessed from Wave 1 to Wave 5. At each wave, each of the three measures was standardized, and then a mean score was calculated (for each year separately). These annual mean scores were then used as indicators in a Confirmatory Factor Analysis model (Kline, 2016).

Psychological Control was assessed with the Psychological Control Scale (Barber, 1996), consisting of 8 items, addressed on a 5-point Likert scale from 1 (*Does not describe my mother/father at all*) to 5 (*Describes my mother/father very well*). Adolescents addressed the items with respect to mother and father separately, and a mean score was computed for each wave, such that higher scores indicate higher parental Psychological Control. An example item is 'My mother/father often interrupts me'. Cronbach's alphas ranged from .75 to .87 across waves.

Parent–adolescent conflict intensity was assessed with the Negative Interactions subscale of the Network of Relationships Inventory-short form (De Goede, Branje, & Meeus, 2009; Furman & Buhrmester, 1985), which consists of 6 items addressed on a 5-point Likert scale, ranging from 1 (*Little or Not at all*) to 5 (*More is not possible*). Adolescents addressed the items with respect to mother and father separately, and a mean score for each wave was computed, such that higher scores indicate higher parent–adolescent conflict. An example item is 'How much do you and your mother/father get upset with or mad at each other?'. Cronbach's alphas ranged from .89 to .95 across waves.

Finally, Level of Expressed Emotion was assessed with the Dutch version of the Level of Expressed Emotion scale (Gerlsma & Hale, 1997). This scale consists of 38 items, which assess lack of emotional support (19 items), intrusiveness (7 items), irritation (7 items), and criticism (5 items; Hale et al., 2016). The items are addressed on a 4-point Likert scale, from 1 (*Untrue*) to 4 (*True*), and a mean score was used such that high LEE scores correspond to high levels of perceived parental lack of emotional support, intrusiveness, irritation, and criticism. Adolescents responded to the items with respect to their parents. Example items are ('My parents:') 'Accuse me of exaggerating when I say I'm unwell', and 'Are critical of me'. Cronbach's alphas for the total scale ranged from .81 to .95 across waves.

Psychological problems. Psychological problems consisted of three variables, assessed from Waves 1 to 5, and then at Wave 10, and analyzed in separate models. Specifically, internalizing problems were assessed using the Reynolds Adolescent Depression Scale—2nd version (Reynolds, 2002), which consists of 30 adolescent-reported items, addressed on a scale from 1 (*Almost Never*) to 4 (*Usually*), including items for negative self-evaluation (e.g., 'I feel I am bad'), dysphoric mood (e.g., 'I feel sad'), and somatic complaints (e.g., 'I feel tired'). A mean score was used, such that higher scores indicate more internalizing symptoms. Cronbach's alphas ranged from .90 to .95 across waves.

Externalizing problems were assessed with the Youth Self-Report scale (Achenbach, 1991; Verhulst, van der Ende, & Koot, 1997), which consists of 30 items assessing delinquency and aggression, self-reported by adolescents, on a scale from 0 (*Never*) to 2 (*Often*). A mean score was calculated, such that higher scores indicate more externalizing problems. Example items are 'I argue a lot', and 'I physically attack people'. Cronbach's alphas ranged from .88 to .91 across waves. T-scores based on the YSR norms ranged from 50 to 74 ($M_{T\text{-scores}}$ = 53.82–55.87 across W1–W5) for the delinquency subscale and from 50 to 89 ($M_{T\text{-scores}}$ = 52.58–53.20 across W1–W5) for the aggressive behavior subscale.

Self-Concept Clarity was assessed with the Self-Concept Clarity scale (Campbell et al., 1996), which consists of 12 self-reported items, addressed on a 5-point Likert scale from 1 (*Strongly disagree*) to 5 (*Strongly agree*). An example item is 'It is often hard for me to make up my mind about things because I don't really know what I want'. A mean score was calculated such that higher scores indicate *lower* self-concept clarity. Cronbach's alphas ranged from .83 to .91 across waves.

Epigenetic age. Epigenetic age was estimated from DNA derived from saliva using the Oragene DNA kit (DNA Genotek, Ottawa, ON, Canada). After bisulfite conversion using ZIMO kits, the saliva DNA samples were assayed using the Illumina 450K (T1), and Illumina EPIC (T2) bead chips (Illumina, San Diego, CA). Standard pre-processing steps were applied using functions of the R (R Core Team, 2020) bioconductor packages *meffil* (Suderman, Hemani, & Min, 2020), *minfi* (Hansen et al., 2022), and *ewastools* (Heiss & Just, 2018) for functional normalization and saliva-based cell-type adjustment. Extra quality control of the DNA methylation data included adjustment for cell-type composition for saliva using the Epidish function of the CellDMC package (Zheng, Breeze, Beck, & Teschendorff, 2018). In general, saliva is a very suitable resource for studies of behavioral phenotypes (Smith et al., 2015) and, except for the Hannum clock, the epigenetic clocks in this manuscript are calibrated on mixed tissue types (Harvanek, Boks, Vinkers, & Higgins-Chen, 2023). Epigenetic age was estimated based on four epigenetic clocks, including Horvath (Horvath, 2013), GrimAge (Lu et al., 2019), PhenoAge (Levine et al., 2018), and Hannum (Hannum et al., 2013), using newly developed principle component adjustment algorithms that increase the reliability of the epigenetic clocks (Higgins-Chen et al., 2022). The four epigenetic clocks were analyzed in separate models. Epigenetic age acceleration was calculated by regressing the chronological age on each epigenetic clock. Thus, the measure of EA indicated the difference between chronological age and epigenetic clocks.

Socioeconomic status. Socio-economic status was based on parents' job level (Statistics Netherlands, 1993). If at least one of the parents' jobs was classified as medium (e.g., police officer, physician's assistant) or high level (e.g., doctor, scientist, high school teacher), SES was deemed as medium/high (91%), whereas the rest of the sample was classified as low SES (9%, e.g., construction worker, janitor, truck driver).

Analyses

We examined the skewness of the distributions, to decide which estimators to use in the latent variable analyses. If the skew index γ was higher than 3, then the distributions were considered highly skewed, and Maximum Likelihood with Robust standard errors (MLR) was used to obtain more accurate parameter estimates (Kline, 2016). Otherwise, we relied on Maximum Likelihood (ML) estimation.

In addition, a series of Structural Regression Models were applied (Kline, 2016) using the *lavaan* package in R (Rosseel, 2012). In all following analyses smoking status, gender, and socioeconomic status were controlled for[1]. All analyses described below were applied to each epigenetic clock separately.

To answer RQ1, we performed the following steps. First, we estimated a Confirmatory Factor Analysis (CFA) of negative parenting, with the five repeated standardized measures of negative parenting loading on one latent factor. Second, EA at T1 was regressed on the latent negative parenting factor, to test whether prospectively and longitudinally assessed negative parenting during adolescence is associated with EA in late adolescence. Third, a Latent Change Score Model (LCSM; McArdle & Grimm, 2010) was applied on EA at T1 and T2, to estimate the latent change in EA capturing the within-person change in EA from age 17 to age 25 years. Finally, the latent change factor was regressed on the latent factor of negative

parenting, to test whether negative parenting is prospectively associated with change in EA.

To answer RQ2 on the prospective associations between psychological problems and EA, we applied similar steps as for parenting, separately for internalizing symptoms, externalizing symptoms, and self-concept clarity. First, each aspect was modeled as a latent variable using the mean scores of Wave 1 to Wave 5 as indicators. Second, EA at T1 was regressed on the latent variable, to examine the prospective effects of each index of psychological problems on EA during late adolescence. Third, the Latent Change Score of EA was regressed on the latent factor of each psychological problem indicator, to examine the prospective effects of psychological problems during adolescence on change in EA from late adolescence to young adulthood.

Finally, to answer RQ3 whether EA at T1 and change in EA between T1 and T2 predict changes in psychological problems from adolescence to young adulthood, observed mean scores of psychological problems at Wave 10 were regressed on the latent factor scores of psychological problems in adolescence (to control for autoregressive stability of each aspect) and on EA at T1, as well as on the latent change score of EA. This way, we tested whether EA at T1 and change in EA between T1 and T2 had a significant effect on psychological problems at Wave 10, controlling for earlier psychological problems. In separate models, we tested whether the potential effects of EA on psychological problems remained after controlling for negative parenting during adolescence, by adding the latent factor score of negative parenting as a predictor of Wave 10 psychological problems.

Results

Table 1 presents the means, standard deviations, and bivariate correlations of all study variables. Table S1 presents the means, standard deviations, and bivariate correlations of the unstandardized negative parenting variables. Figures 2–4 provide an overview of the study results.

Preliminary analyses

No variable showed severe skewness, with all gamma indices <1.5 (Kline, 2016). Therefore, all analyses were conducted with ML estimation. Table 2 presents the fit indices of all the analyses. The CFAs of negative parenting, internalizing symptoms, externalizing symptoms, and self-concept clarity had a very good fit, and the omega reliabilities of these four CFAs were .81, .86, .84, and .84, for negative parenting, internalizing symptoms, externalizing symptoms, and self-concept clarity, respectively, showing that the latent constructs of negative parenting and psychological problems were sound.

Negative parenting predicting epigenetic age acceleration and change in epigenetic age acceleration

The first RQ was whether negative parenting, repeatedly assessed from age 13 to 17 years, could predict EA at age 17, as well as change in EA from age 17 (T1) to age 25 (T2). As seen in Table 3, the effects of the latent variable of negative parenting on EA at T1 and change in EA from T1 to T2 were non-significant.

Psychological problems predicting epigenetic age acceleration and change in epigenetic age acceleration

The second RQ was whether psychological problems, including internalizing symptoms, externalizing symptoms, and low self-concept clarity, repeatedly assessed from age 13 to 17 years, had a significant effect on EA in late adolescence, or on change in EA from late adolescence to young adulthood. As seen in Table 4, no significant effects were found for internalizing symptoms and self-concept clarity. Therefore, most aspects of adolescent psychological problems included in this study were unrelated to EA in late adolescence, and to change in EA from late adolescence to young adulthood.

There were a few exceptions to this pattern: Externalizing symptoms predicted higher EA at age 17 years, based on one of the four clocks (GrimAge). In contrast, externalizing symptoms predicted a decrease in EA from T1 to T2 based on another clock (Hannum). Therefore, whereas externalizing symptoms throughout adolescence might contribute to EA during late adolescence, this association might be more complicated, as those symptoms might also decelerate EA in the longer term.

Epigenetic age acceleration and change in epigenetic age acceleration predicting psychological problems in young adulthood

The third RQ was whether EA at T1 or change in EA from T1 to T2 could predict psychological problems at Wave 10, thereby controlling for psychological problems throughout adolescence. Table 5 presents the parameter estimates of the final models, which controlled for the effects of sex, socioeconomic status, smoking, and negative parenting throughout adolescence.

Epigenetic age at T1 did not significantly predict changes in any of the psychological problems; as seen in the middle part of Table 5 all coefficients were non-significant. However, a relatively consistent pattern emerged regarding the predictive ability of change in EA. According to three out of four epigenetic clocks (except for Horvath), change in EA from age 17 to age 25 years significantly and positively predicted relative increases in externalizing symptoms over the same period from adolescence to young adulthood. Thus, a stronger change in EA was associated with stronger increases in externalizing symptoms. Furthermore, according to one out of four epigenetic clocks (Horvath), higher EA was associated with an *increase* in self-concept clarity from adolescence to young adulthood.

Table 1 Means, standard deviations, and correlations with confidence intervals

Variable	*M*	*SD*	1	2	3	4	5	6	7	8	9	10	11	12
1. Horvath2 T1	−0.02	3.82												
2. Horvath2 T2	−0.00	4.28	.36**											
3. GrimAge T1	0.01	2.02	−.28**	.06										
4. GrimAge T2	0.00	3.03	−.03	−.46**	.49**									
5. PhenoAge T1	0.03	5.03	−.43**	−.04	.63**	.22**								
6. PhenoAge T2	0.00	8.12	.08	−.57**	.13	.75**	.24**							
7. Hannum T1	0.02	3.05	.02	.07	.55**	.19**	.71**	.20**						
8. Hannum T2	0.00	4.89	.16*	−.44**	.14*	.71**	.16*	.92**	.29**					
9. negpar1	0.01	0.45	.03	−.08	−.00	.09	.00	.10	−.00	.06				
10. negpar2	0.02	0.45	−.11*	−.07	.03	.07	.06	.07	−.01	−.01	.47**			
11. negpar3	0.03	0.42	.02	.04	.01	.06	−.00	.07	−.02	.02	.41**	.48**		
12. negpar4	0.02	0.42	.02	−.10	−.05	.08	−.04	.09	−.03	.04	.36**	.48**	.60**	
13. negpar5	0.02	0.43	.03	−.04	−.09	.07	.00	.14*	−.00	.10	.28**	.44**	.50**	.58**
14. int1	1.63	0.40	.03	−.05	−.05	−.01	.03	.05	.01	−.04	.23**	.18**	.21**	.21**
15. int2	1.52	0.49	.05	−.01	−.08	−.05	.04	.05	.02	−.03	.17**	.28**	.31**	.18**
16. int3	1.54	0.52	.05	−.02	−.11*	−.08	−.00	.07	−.05	−.04	.15**	.19**	.39**	.28**
17. int4	1.56	0.54	.05	−.02	−.14**	−.07	.01	.11	−.06	.03	.19**	.21**	.32**	.31**
18. int5	1.55	0.52	.01	−.04	−.16**	−.07	−.03	.08	−.10	−.02	.19**	.21**	.32**	.27**
19. int10	1.72	0.48	.04	−.10	−.10	.03	−.03	.10	−.07	.06	.14*	.10	.26**	.28**
20. ext1	0.35	0.24	.03	.02	.14**	.04	.05	−.02	.06	−.06	.27**	.26**	.26**	.21**
21. ext2	0.32	0.27	−.00	−.01	.13*	.10	.04	.02	.07	−.04	.14**	.29**	.25**	.15**
22. ext3	0.33	0.25	.01	.06	.14**	.06	.00	−.09	.00	−.14*	.07	.16**	.34**	.20**
23. ext4	0.35	0.27	−.04	.06	.18**	.13	.03	−.04	.01	−.07	.11*	.19**	.28**	.22**
24. ext5	0.34	0.25	−.01	.01	.15**	.13	−.01	−.03	.01	−.08	.09	.13*	.24**	.19**
25. ext10	0.19	0.19	−.00	−.06	.10	.20**	−.01	.13*	−.03	.09	.16**	.17**	.28**	.33**
26. sc1	2.58	0.63	.01	.01	−.06	−.08	.04	.01	−.03	−.06	.18**	.15**	.15**	.17**
27. sc2	2.53	0.69	−.00	.07	.01	−.03	.05	.03	.04	−.02	.13*	.13**	.24**	.15**
28. sc3	2.50	0.74	.05	−.03	−.04	.00	.00	.08	.01	.00	.12*	.13*	.31**	.26**
29. sc4	2.52	0.80	.05	.01	−.12*	−.02	−.03	.08	−.04	.02	.12*	.15**	.27**	.26**
30. sc5	2.50	0.83	.07	.06	−.12*	−.04	−.05	.04	−.05	−.04	.08	.14**	.25**	.26**
31. sc10	2.45	0.84	.09	−.06	−.06	.04	−.03	.13	−.00	.08	.17**	.16**	.24**	.23**

M and *SD* represent mean and standard deviation, respectively. Negpar, Negative parenting; int, Internalizing symptoms; ext, externalizing symptoms; sc, self-concept clarity. Numbers in variable names represent wave of study.
*$p < .05$, **$p < .01$.

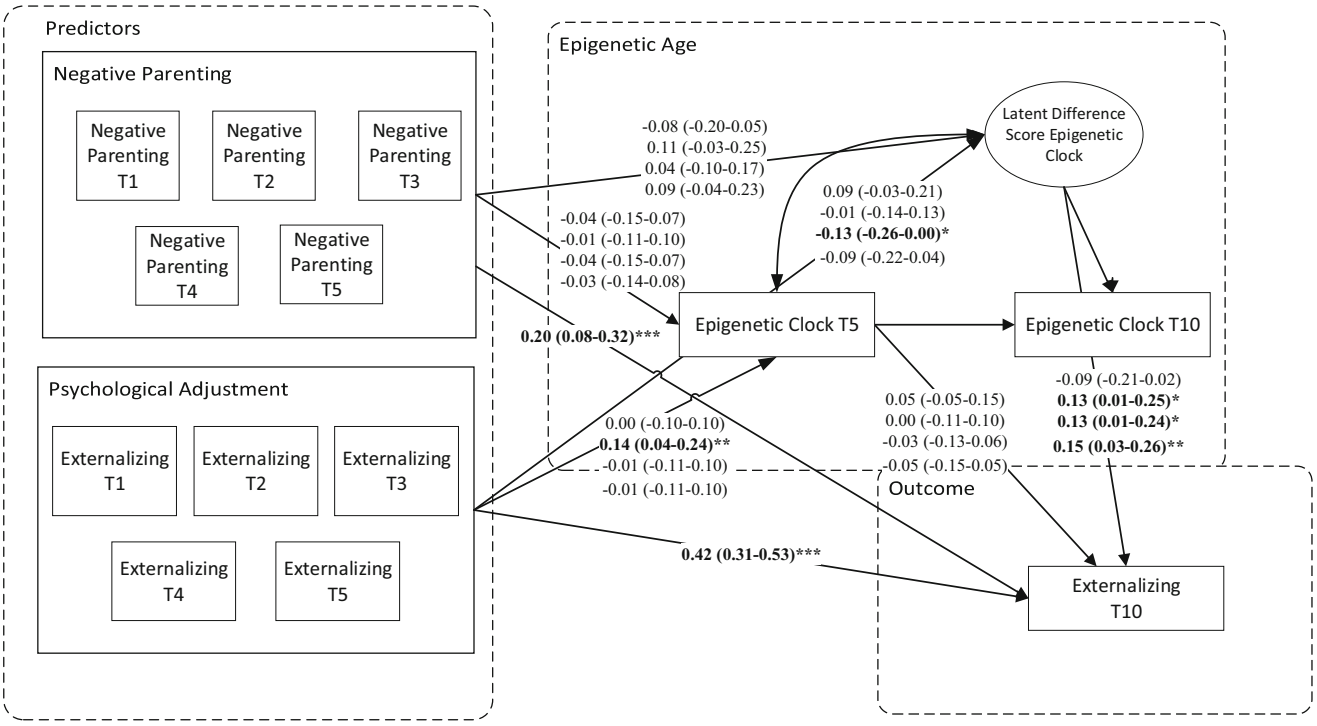

Figure 2 Standardized parameter estimates (95% CI) for the model including Externalizing Problems. From top to bottom, the estimates refer to separate models for each of the following epigenetic clocks: Horvath2, GrimAge, Hannum, and PhenoAge, respectively

13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
.17**																	
.27**	.56**																
.28**	.52**	.66**															
.34**	.51**	.62**	.71**														
.36**	.48**	.55**	.64**	.77**													
.21**	.38**	.38**	.41**	.47**	.51**												
.19**	.43**	.36**	.33**	.24**	.23**	.19**											
.15**	.31**	.42**	.35**	.27**	.27**	.15**	.64**										
.17**	.28**	.32**	.42**	.28**	.30**	.17**	.57**	.63**									
.27**	.21**	.29**	.30**	.31**	.26**	.18**	.52**	.58**	.76**								
.28**	.18**	.27**	.26**	.25**	.33**	.22**	.43**	.52**	.67**	.76**							
.31**	.26**	.20**	.23**	.24**	.37**	.49**	.37**	.41**	.44**	.46**	.50**						
.17**	.47**	.31**	.35**	.37**	.31**	.21**	.26**	.18**	.15**	.15**	.14**	.05					
.17**	.43**	.53**	.49**	.47**	.37**	.24**	.26**	.31**	.26**	.22**	.19**	.17**	.48**				
.23**	.40**	.49**	.60**	.56**	.45**	.31**	.21**	.25**	.27**	.24**	.23**	.21**	.50**	.67**			
.28**	.39**	.40**	.49**	.65**	.51**	.34**	.18**	.21**	.25**	.26**	.18**	.24**	.49**	.57**	.69**		
.27**	.35**	.39**	.48**	.58**	.60**	.35**	.21**	.26**	.27**	.23**	.26**	.24**	.44**	.54**	.64**	.75**	
.21**	.30**	.30**	.32**	.36**	.43**	.68**	.17**	.14*	.11	.14*	.22**	.43**	.24**	.32**	.36**	.43**	.45**

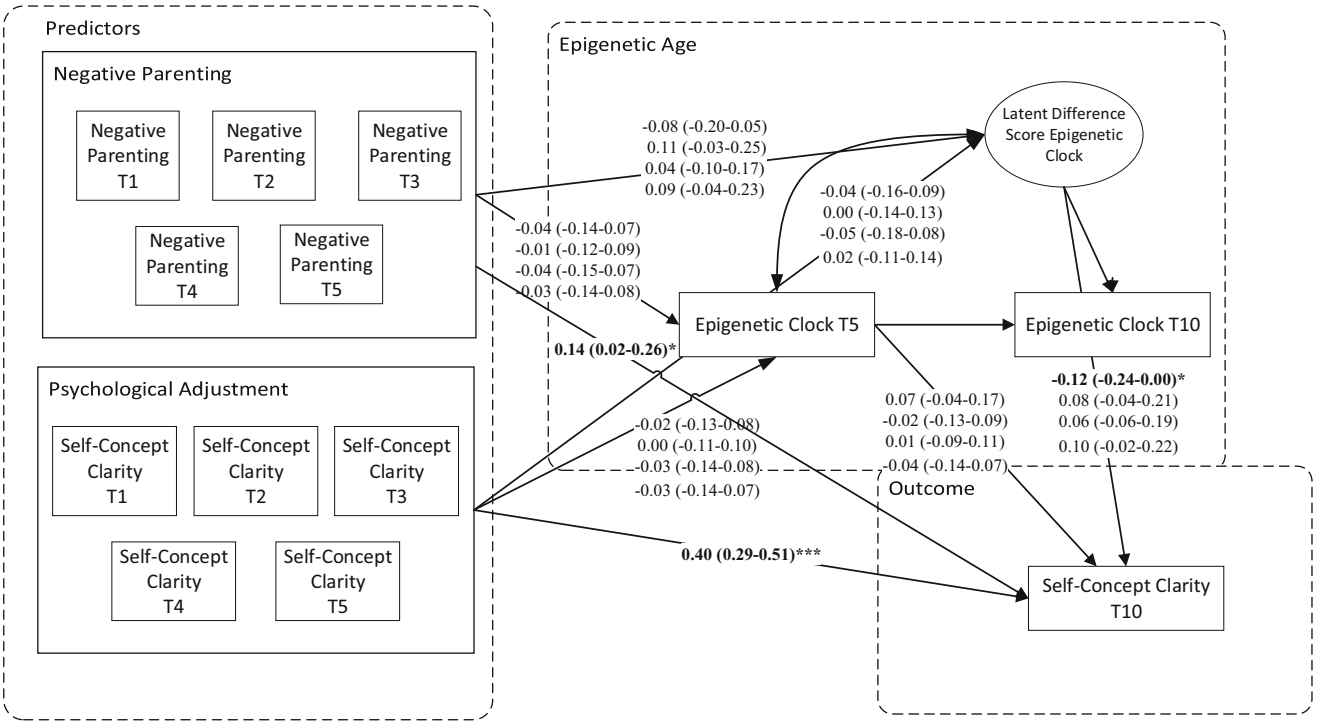

Figure 3 Standardized parameter estimates (95% CI) for the model including Self-Concept Clarity. From top to bottom, the estimates refer to separate models for each of the following epigenetic clocks: Horvath2, GrimAge, Hannum, and PhenoAge, respectively

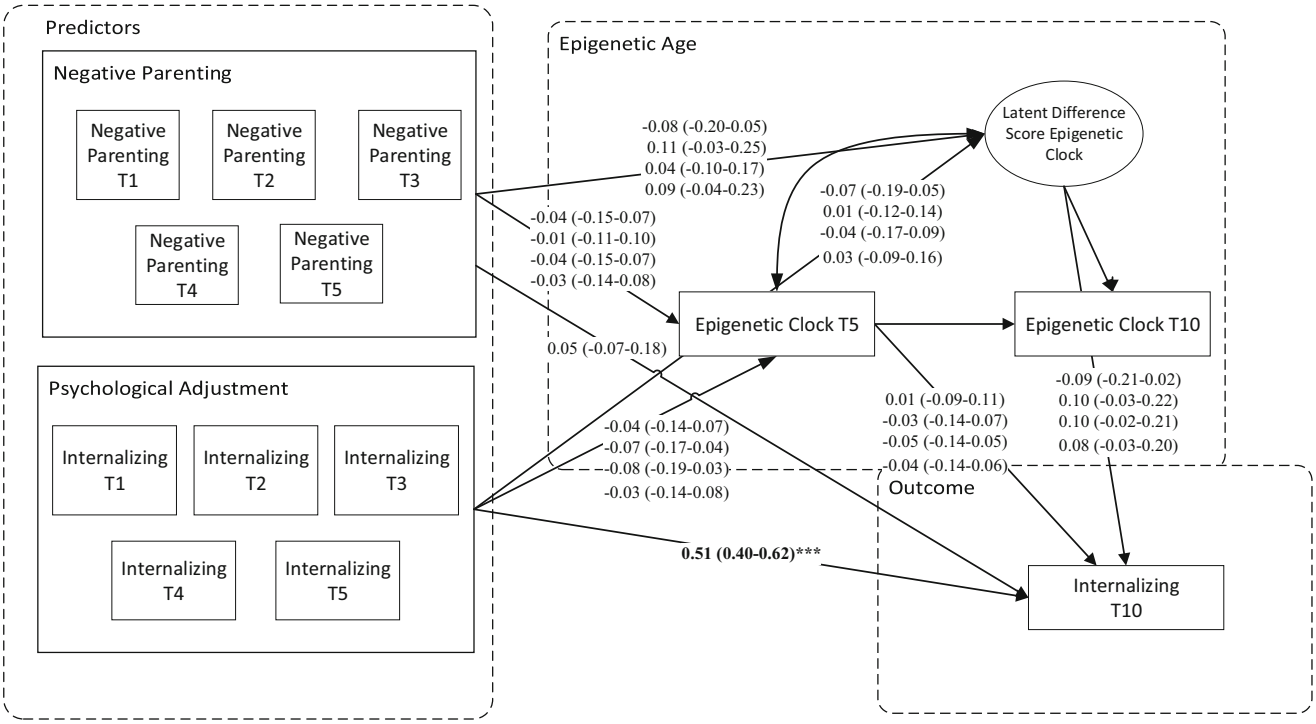

Figure 4 Standardized parameter estimates (95% CI) for the model including Internalizing Problems. From top to bottom, the estimates refer to separate models for each of the following epigenetic clocks: Horvath2, GrimAge, Hannum, and PhenoAge, respectively

A collateral finding (not included in our preregistered hypotheses) is also noteworthy: Negative parenting throughout adolescence was associated with a relative increase in externalizing symptoms and a decrease in self-concept clarity from adolescence to young adulthood. These findings testify to the long-term effects of negative parenting.

Discussion

This study examined longitudinal associations of negative parenting and psychological problems with epigenetic age acceleration (EA) and *change* in EA from late adolescence to young adulthood. In addition, longitudinal associations of EA and change in EA with changes in psychological problems from adolescence to young adulthood were analyzed. First, negative parenting and psychological problems throughout adolescence did not predict EA in late adolescence nor change in EA from late adolescence to young adulthood; an exception was the positive association of externalizing problems during adolescence with EA during late adolescence. Second, while EA during late adolescence did not predict changes in psychological problems from late adolescence to young adulthood, *change* in EA significantly predicted changes in externalizing problems and self-concept clarity.

Negative parenting throughout adolescence was not found to be prospectively related to EA during late adolescence nor with change in EA from late adolescence to young adulthood. As negative parenting was conceptualized as more 'everyday' parenting behaviors, this conceptualization might have explained the absence of significant results. Given the community-based, non-clinical sample of the present study, these findings imply that 'normative' parenting behaviors do not comprise strong stressful experiences to be biologically embedded and be reflected in EA. Even though negative repercussions for later adolescent development have been found for psychological control (Loeb, Kansky, Tan, Costello, & Allen, 2021), level of expressed emotion (Hale et al., 2016), and parent–adolescent conflict intensity (Zhang, Buchanan, Piehler, Gunlicks-Stoessel, & Bloomquist, 2022), and were also found in the current study, biological embedding of these experiences might entail different mechanisms not captured in this study, such as cardiovascular stress reactivity (Loeb et al., 2021).

Psychological problems throughout adolescence also were not found to be prospectively related to EA during late adolescence nor with change in EA from late adolescence to young adulthood, with one exception: higher externalizing problems throughout adolescence were positively associated with higher EA at age 17 years, according to the GrimAge only. Adolescents who reported more externalizing problems tended to show a larger epigenetic age than chronological age (higher EA) at age 17 years. Previous studies have found links between externalizing symptoms and *DNAm* (Barker, Walton, & Cecil, 2018; Carpentieri et al., 2021; Cicchetti & Handley, 2017). However, the only study we located that examined the links between externalizing symptoms and *EA* found a positive link with inflammation-

Table 2 Model fit indices for all study models

	χ^2	*df*	CFI	TLI	RMSEA
CFA					
Negative Parenting	30.386	5	0.959	0.918	0.112
Internalizing Symptoms	10.227	4	0.994	0.985	0.061
Externalizing Symptoms	1.5260	3	1	1.005	0.000
Self-Concept Clarity	4.0580	4	1	1	0.006
Research Question 1					
Horvath T1	63.722	24	0.940	0.917	0.062
GrimAge T1	55.819	24	0.952	0.935	0.055
Hannum T1	52.930	24	0.954	0.936	0.053
PhenoAge T1	56.359	24	0.949	0.930	0.056
Horvath LCS	75.040	32	0.938	0.918	0.056
GrimAge LCS	65.144	32	0.955	0.941	0.049
Hannum LCS	59.015	32	0.958	0.945	0.044
PhenoAge LCS	64.439	32	0.950	0.935	0.048
Research Question 2					
Int. – Horvath T1	80.569	23	0.949	0.927	0.076
Int. – GrimAge T1	82.677	23	0.948	0.926	0.077
Int. – Hannum T1	87.306	23	0.942	0.917	0.080
Int. – PhenoAge T1	82.912	23	0.946	0.923	0.077
Ext. – Horvath T1	83.414	23	0.947	0.924	0.078
Ext. – GrimAge T1	81.532	23	0.949	0.928	0.077
Ext. – Hannum T1	86.580	23	0.943	0.918	0.080
Ext. – PhenoAge T1	84.481	23	0.945	0.921	0.078
SCC – Horvath T1	58.695	23	0.966	0.951	0.060
SCC – GrimAge T1	69.449	23	0.957	0.938	0.068
SCC – Hannum T1	61.864	23	0.962	0.945	0.062
SCC – PhenoAge T1	64.106	23	0.960	0.943	0.064
Int. – Horvath LCS	85.297	31	0.953	0.936	0.064
Int. – GrimAge LCS	90.429	31	0.951	0.934	0.066
Int. – Hannum LCS	94.205	31	0.944	0.924	0.069
Int. – PhenoAge LCS	88.410	31	0.949	0.931	0.065
Ext. – Horvath LCS	90.974	31	0.948	0.930	0.067
Ext. – GrimAge LCS	95.902	31	0.947	0.928	0.069
Ext. – Hannum LCS	89.691	31	0.948	0.930	0.066
Ext. – PhenoAge LCS	90.599	31	0.947	0.929	0.067
SCC – Horvath LCS	67.538	31	0.966	0.954	0.052
SCC – GrimAge LCS	75.599	31	0.961	0.947	0.058
SCC – Hannum LCS	65.544	31	0.967	0.955	0.051
SCC – PhenoAge LCS	70.046	31	0.963	0.949	0.054
Research Question 3					
Horvath T1 – Int. T10	93.658	28	0.945	0.924	0.074
GrimAge T1 – Int.T10	97.119	28	0.943	0.92	0.075
Hannum T1 – Int. T10	101.183	28	0.940	0.916	0.078
PhenoAge T1 – Int. T10	95.723	28	0.944	0.922	0.075
Horvath T1 – Ext. T10	99.784	28	0.940	0.917	0.077
GrimAge T1 – Ext. T10	105.022	28	0.936	0.911	0.080
Hannum T1 – Ext. T10	103.509	28	0.937	0.913	0.079
PhenoAge T1 – Ext. T10	101.18	28	0.939	0.915	0.078
Horvath T1 – SCC T10	73.844	28	0.958	0.941	0.061
GrimAge T1 – SCC T10	85.520	28	0.948	0.927	0.069
Hannum T1 – SCC T10	78.008	28	0.954	0.936	0.064
PhenoAge T1 – SCC T10	79.795	28	0.953	0.934	0.065
Horvath LCS – Int. T10	126.688	40	0.931	0.910	0.071
GrimAge LCS – Int. T10	156.043	40	0.912	0.885	0.082
Hannum LCS – Int. T10	110.459	40	0.943	0.925	0.064
PhenoAge LCS – Int. T10	114.768	40	0.939	0.921	0.066
Horvath LCS – Ext. T10	135.151	40	0.925	0.902	0.074
GrimAge LCS – Ext. T10	165.276	40	0.905	0.877	0.085
Hannum LCS – Ext. T10	112.646	40	0.941	0.923	0.065
PhenoAge LCS – Ext. T10	119.878	40	0.935	0.916	0.068
Horvath LCS – SCC T10	110.125	40	0.939	0.921	0.064
GrimAge LCS – SCC T10	144.332	40	0.914	0.888	0.078
Hannum LCS – SCC T10	86.265	40	0.958	0.946	0.052
PhenoAge LCS – SCC T10	98.969	40	0.947	0.931	0.058
Horvath T1 – Int. T10 NegPar	226.211	81	0.926	0.909	0.064
GrimAge T1 – Int. T10 NegPar	220.922	81	0.928	0.912	0.063

(continues)

Table 2 (continued)

	χ^2	*df*	CFI	TLI	RMSEA
Hannum T1 – Int. T10 NegPar	222.020	81	0.928	0.912	0.063
PhenoAge T1 – Int. T10 NegPar	219.149	81	0.929	0.913	0.063
Horvath T1 – Ext. T10 NegPar	266.990	81	0.906	0.885	0.073
GrimAge T1 – Ext. T10 NegPar	263.794	81	0.907	0.887	0.072
Hannum T1 – Ext. T10 NegPar	259.199	81	0.909	0.889	0.071
PhenoAge T1 – Ext. T10 NegPar	259.640	81	0.909	0.889	0.071
Horvath T1 – SCC T10 NegPar	161.055	81	0.955	0.945	0.048
GrimAge T1 – SCC T10 NegPar	163.888	81	0.953	0.943	0.049
Hannum T1 – SCC T10 NegPar	153.826	81	0.959	0.949	0.046
PhenoAge T1 – SCC T10 NegPar	158.059	81	0.956	0.947	0.047
Horvath LCS – Int. T10 NegPar	265.453	97	0.916	0.899	0.063
GrimAge LCS – Int. T10 NegPar	284.571	97	0.909	0.890	0.067
Hannum LCS – Int. T10 NegPar	235.714	97	0.929	0.915	0.057
PhenoAge LCS – Int. T10 NegPar	242.180	97	0.926	0.911	0.059
Horvath LCS – Ext. T10 NegPar	307.312	97	0.896	0.875	0.071
GrimAge LCS – Ext. T10 NegPar	330.219	97	0.888	0.865	0.074
Hannum LCS – Ext. T10 NegPar	273.112	97	0.911	0.893	0.065
PhenoAge LCS – Ext. T10 NegPar	281.354	97	0.907	0.888	0.066
Horvath LCS – SCC T10 NegPar	204.005	97	0.941	0.929	0.050
GrimAge LCS – SCC T10 NegPar	229.018	97	0.930	0.915	0.056
Hannum LCS - SCC T10 NegPar	167.443	97	0.960	0.952	0.041
PhenoAge LCS – SCC T10 NegPar	182.173	97	0.952	0.943	0.045

All analytic models (except for the CFAs) controlled for sex, socioeconomic status, and smoking. T1, first wave of saliva collection (age 17); Int, Internalizing symptoms; Ext, Externalizing symptoms; SCC, Self-Concept Clarity; LCS, Latent Change Score; NegPar, Models controlling for negative parenting.

Table 3 Standardized parameter estimates for the final models addressing Research Question 1, on the effects of Negative Parenting from W1 to W5 on Epigenetic Age at T1 and change in Epigenetic Age from T1 to T2

Outcome	Horvath			GrimAge			Hannum			PhenoAge		
Predictors	*β*	95% CI	*p*	*β*	95% CI	*p*	*β*	95% CI	*p*	*β*	95% CI	*p*
					Epigenetic Age T1							
Sex	.26	0.17–0.36	.00***	−.29	−0.38 – −0.20	.00***	.05	−0.05–0.15	.34	.09	−0.01–0.19	.07
SES	−.02	−0.12–0.08	.71	.07	−0.03–0.17	.16	.02	−0.09–0.12	.76	−.01	−0.11–0.10	.89
Smoking	−.06	−0.19–0.06	.31	.20	0.08–0.31	.00***	.13	0.01–0.26	.03*	.22	0.10–0.35	.00***
Negative Parenting W1–W5[a]	−.04	−0.15–0.07	.46	−.01	−0.11–0.10	.91	−.04	−0.15–0.07	.46	−.03	−0.14–0.08	.62
					Epigenetic Age Change T1–T2							
Sex	.24	0.15 to 0.32	.00***	−.29	−0.38 – −0.21	.00***	.04	−0.05–0.14	.38	.10	0.01 to 0.19	.04*
SES	−.03	−0.12–0.06	.48	.08	−0.01–0.18	.08	.01	−0.09–0.11	.81	.01	−0.09–0.10	.91
Smoking	−.02	−0.12–0.09	.76	.21	0.10–0.32	.00***	.11	−0.01–0.22	.07	.19	0.07–0.31	.00***
Negative Parenting W1–W5[a]	−.08	−0.20–0.05	.24	.11	−0.03–0.25	.11	.04	−0.10–0.17	.57	.09	−0.04–0.23	.17

The results of several models are summarized here. In each model, the control variables were youth's sex, socioeconomic status, and smoking. Each epigenetic clock as well as the change thereof, were used as predictors in separate models.
*$p < .05$, ***$p < .001$.
[a]Negative Parenting was assessed as a latent factor comprised of psychological control, level of expressed emotion, and parent–adolescent conflict, repeatedly assessed from Wave 1 to Wave 5.

related methylation profiles, but not with epigenetic age (Raffington, Tanksley, Vinnik, et al., 2021). Thus, to the best of our knowledge, this is the first study showing the potential effects of preceding externalizing problems on EA.

Possibly, this effect of externalizing problems on EA might emerge because adolescents higher in externalizing symptoms are more prone to both psychological/behavioral (e.g., anger, aggression) and environmental (e.g., alcohol, drugs) toxic exposures, which might wear down the body. Another possible explanation is based on evolutionary theory suggesting that externalizing behaviors like aggression and risk-taking are linked with unpredictability in the environment and with a fast life history (Lu & Chang, 2019), which in turn has been linked to higher EA (e.g., Hamlat, Prather, Horvath, Belsky, & Epel, 2021). However, it is important to note that our sample was a rather well-off sample, consisting largely from middle/high SES families with likely not

Table 4 Standardized parameter estimates for the final models addressing Research Question 2, on the effects of Psychological problems from W1 to W5 on Epigenetic Age at T1 and change in Epigenetic Age from T1 to T2

Outcome	Horvath			GrimAge			Hannum			PhenoAge		
Predictors	*β*	95% CI	*p*	*β*	95% CI	*p*	*β*	95% CI	*p*	*β*	95% CI	*p*
Internalizing Symptoms												
Epigenetic Age T1												
Sex	.27	0.17–0.37	.00***	−0.27	−0.37 – −0.18	.00***	.07	−0.04–0.17	.20	.10	−0.01–0.20	.07
SES	−.02	−0.12–0.08	.74	0.07	−0.03–0.17	.15	.02	−0.08–0.12	.71	−.01	−0.11–0.10	.91
Smoking	−.06	−0.19–0.06	.32	0.20	0.08–0.32	.00***	.14	0.01–0.26	.03*	.22	0.10–0.35	.00***
Internalizing W1–W5[a]	−.04	−0.14–0.07	.50	−0.07	−0.17–0.04	.21	−.08	−0.19–0.03	.15	−.03	−0.14–0.08	.57
Epigenetic Age Change T1–T2												
Sex	0.24	0.15 to 0.33	.00***	−.29	−0.38 – −0.20	.00***	.05	−0.05–0.14	.34	.10	0.00 to 0.19	.04*
SES	−0.03	−0.12–0.06	.50	.09	−0.01–0.18	.08	.01	−0.08–0.11	.78	.01	−0.09–0.10	.91
Smoking	−0.02	−0.12–0.09	.78	.21	0.10 to 0.32	.00***	.11	−0.01–0.23	.07	.19	0.07–0.31	.00***
Internalizing W1–W5[a]	−0.07	−0.19–0.05	.23	.01	−0.12–0.14	.88	−.04	−0.17–0.09	.53	.03	−0.09–0.16	.59
Externalizing Symptoms												
Epigenetic Age T1												
Sex	0.26	0.17–0.35	.00***	−0.29	−0.38 – −0.20	.00***	0.04	−0.05–0.14	.39	.09	−0.01–0.19	.08
SES	−0.02	−0.12–0.08	.72	0.06	−0.04–0.16	.25	0.02	−0.09–0.12	.74	−.01	−0.11–0.10	.90
Smoking	−0.07	−0.19–0.06	.30	0.17	0.05–0.29	.01**	0.13	0.01–0.26	.04*	.22	0.10–0.35	.00***
Externalizing W1–W5[a]	0.00	−0.10–0.10	1.00	0.14	0.04–0.24	.01**	−0.01	−0.11–0.10	.87	−.01	−0.11–0.10	.92
Epigenetic Age Change T1–T2												
Sex	.24	0.15 to 0.32	.00***	−0.29	−0.38 – −0.20	.00***	.04	−0.05–0.14	.38	.10	0.01–0.19	.04*
SES	−.04	−0.13–0.06	.44	0.09	−0.01–0.18	.08	.02	−0.08–0.11	.76	.01	−0.09–0.11	.87
Smoking	−.03	−0.14–0.08	.61	0.21	0.10–0.32	.00***	.12	0.00–0.23	.05*	.20	0.08–0.31	.00***
Externalizing W1–W5[a]	.09	−0.03–0.21	.14	−0.01	−0.14–0.13	.91	−.13	−0.26–0.00	.05*	−.09	−0.22–0.04	.18
Self-Concept Clarity												
Epigenetic Age T1												
Sex	.27	0.17 to 0.36	.00***	−.29	−0.38–0.20	.00***	.05	−0.05–0.15	.32	.10	−0.01–0.20	.07
SES	−.02	−0.12–0.08	.73	.07	−0.03–0.17	.16	.02	−0.09–0.12	.74	−.01	−0.11–0.10	.91
Smoking	−.06	−0.19–0.06	.31	.20	0.08–0.31	.00***	.13	0.01–0.26	.03*	.22	0.10–0.35	.00***
Self-Concept W1–W5[a]	−.02	−0.13–0.08	.66	.00	−0.11–0.10	.93	−.03	−0.14–0.08	.56	−.03	−0.14–0.07	.54
Epigenetic Age Change T1–T2												
Sex	0.24	0.15–0.32	.00***	−0.29	−0.38 – −0.20	.00***	.05	−0.05–0.14	.33	.10	0.01–0.20	.04*
SES	−0.03	−0.12–0.06	.49	0.09	−0.01–0.18	.08	.01	−0.08–0.11	.79	.01	−0.09–0.10	.91
Smoking	−0.02	−0.12–0.09	.75	0.21	0.10–0.32	.00***	.11	−0.01–0.23	.07	.19	0.07–0.31	.00***
Self-Concept W1–W5[a]	−0.04	−0.16–0.09	.56	0.00	−0.14–0.13	.98	−.05	−0.18–0.08	.48	.02	−0.11–0.14	.81

The results of several models are summarized here. In each model, the control variables were youth's sex, socioeconomic status, and smoking. Each epigenetic clock as well as the change thereof, were used as outcomes in separate models.

*$p < .05$, **$p < .01$, ***$p < .001$.

[a]Each aspect of Psychological problems was assessed as a latent factor comprised of the respective mean observed scores, assessed from Wave 1 to Wave 5.

Table 5 Standardized parameter estimates for the final models addressing Research Question 3, on the effects of Epigenetic Age and change in Epigenetic Age on Psychological problems at Wave 10

Outcome	Internalizing W10			Externalizing W10			Self-Concept Clarity W10[a]		
Predictors	*β*	95% CI	*p*	*β*	95% CI	*p*	*β*	95% CI	*p*
Control variables									
Psychological problems W1–W5[b]	.51	0.40–0.62	.00***	.42	0.31–0.53	.00***	.40	0.29–0.51	.00***
Sex	−.03	−0.13–0.08	.62	−.04	−0.15–0.05	.31	.01	−0.09–0.12	.80
SES	−.02	−0.13–0.08	.65	−.05	−0.15–0.06	.42	−.01	−0.12–0.10	.90
Smoking	.03	−0.09–0.14	.64	.10	−0.02–0.22	.11	.02	−0.10–0.15	.74
Negative Parenting W1–W5[c]	.05	−0.07–0.18	.39	.20	0.08–0.32	.00***	.14	0.02–0.26	.02*
Epigenetic Clocks									
Horvath T1	.01	−0.09–0.11	.79	.05	−0.05–0.15	.30	.07	−0.04–0.17	.20
GrimAge T1	−.03	−0.14–0.07	.55	.00	−0.11–0.10	.99	−.02	−0.13–0.09	.72
Hannum T1	−.05	−0.14–0.05	.34	−.03	−0.13–0.06	.50	.01	−0.09–0.11	.82
PhenoAge T1	−.04	−0.14–0.06	.38	−.05	−0.15–0.05	.32	−.04	−0.14–0.07	.49
Epigenetic Clock Change									
Horvath LCS	−.09	−0.21–0.02	.12	−.09	−0.21–0.02	.11	−.12	−0.24–0.00	.05*
GrimAge LCS	.10	−0.03–0.22	.12	.13	0.01 to 0.25	.03*	.08	−0.04–0.21	.19
Hannum LCS	.10	−0.02–0.21	.10	.13	0.01 to 0.24	.03*	.06	−0.06–0.19	.31
PhenoAge LCS	.08	−0.03–0.20	.15	.15	0.03–0.26	.01**	.10	−0.02–0.22	.09

The results of several models are summarized here. In each model, the control variables were youth's sex, socioeconomic status, smoking, and the respective psychological problems aspect assessed from wave 1 to wave 5 (see further note). Each epigenetic clock as well as the change thereof, were used as predictors in separate models. In each of these models, the effects of the control variables changed only minimally; for the sake of space, only one estimate per outcome is presented here for each control variable.
*$p < .05$, **$p < .01$, ***$p < .001$.
[a]Self-Concept Clarity was reversed coded, such that higher scores indicate lower Self-Concept Clarity.
[b]In each model, predicting one of the Psychological problems aspects at W10, the respective aspect assessed as a latent factor from Waves 1–5 was used as a control variable. For example, for the models predicting Internalizing symptoms at W10, the latent factor of internalizing symptoms from W1 to W5 was used as a control variable.
[c]Negative Parenting was assessed as a latent factor comprised of psychological control, level of expressed emotion, and parent–adolescent conflict, repeatedly assessed from Wave 1 to Wave 5.

much unpredictability in their environment. A possible explanation for why the effect was only found for one clock might have to do with how the different clocks have been developed (trained). GrimAge is a mortality-based clock, which is designed to predict time-to-death, and not 'merely' chronological age, such as the Horvath and the Hannum clocks (Higgins-Chen, Boks, Vinkers, Kahn, & Levine, 2020; Oblak et al., 2021). Therefore, this finding might indicate that higher externalizing problems throughout adolescence may lead to more wear of the organism, leading to faster biological aging.

However, the explanation of the effects of externalizing symptoms on EA gets perplexed by the finding that externalizing symptoms also predicted *decreasing* EA from adolescence to young adulthood. Youth with higher externalizing problems throughout adolescence tended to show a decreasing difference between epigenetic age and chronological age. Given that only few past studies have examined predictors of changes in EA, this finding is difficult to interpret. One study also showed that the development of psychopathological symptoms (PTSD) after battle exposure was associated with *decreasing* epigenetic age (Boks et al., 2015) in the direct aftermath of the combat exposure. Some studies support the idea that the immediate effects of stressors may sometimes act in the opposite direction, decreasing biological wear (Epel et al., 2010). A speculative explanation may be that there is some adaptiveness in active externalizing coping with stressors. Alternatively, this finding might imply regression to the mean (decrease of high EA), or it might reflect the fact that youth's transition to adulthood and adult roles might go together with a decrease in the exposure to toxic experiences and, therefore, decreasing EA.

The most intriguing findings of this study are the longitudinal associations of change in EA with change in psychological problems during young adulthood. Notably, the significant effects involving externalizing symptoms were consistent across three of the four epigenetic clocks (GrimAge, PhenoAge, Hannum). The discrepancies between the results of the clocks are likely related to the fact that they are trained to capture different phenotypes and, therefore, probe different underlying biological mechanisms (Harvanek et al., 2023). Youth who age biologically at a faster pace are more prone to experience an increase in externalizing problems and, according to one clock, an increase in the clarity of self-perceptions from late adolescence to young adulthood. Research suggested that early life adversities had a prospective association only with change in EA, and not with single-timepoint EA (Copeland et al., 2022). Our results extend this finding by showing that change in EA is not only more responsive to exposures, but also more predictive of later adjustment. In addition, the fact that change in

EA was a significant predictor of young adult problems, even after controlling for earlier problems and negative experiences in the parent–adolescent relationship, indicates that change in EA is an independent biological risk factor for later psychological maladjustment (Tollenaar et al., 2021). A speculative reason for these findings might relate to cognitive functioning that has also been found to decay along with faster biological aging (Chouliaras et al., 2018; Horvath et al., 2018; Wolf et al., 2016). Declining neurocognitive abilities might be the reason for the increase in externalizing symptoms (e.g., lower self-control). This finding provides novel insights in the relevance of epigenetic clocks and suggests that the clocks are a risk factor for maladaptive development. This would explain the divergent relations with previous exposures and the more consistent relation with future development.

A collateral finding in this study was the long-standing effects of negative parenting in adolescence on psychological problems in young adulthood. Specifically, negative parenting repeatedly assessed from ages 13 to 17 years was a strong predictor of increases in externalizing problems and decreases in self-concept clarity from adolescence to young adulthood. Past research has attested to similar long-standing effects of negative parenting throughout adolescence (Loeb, Davis, et al., 2021; Loeb, Kansky, et al., 2021). Our findings add to that body of literature, stressing the need for early interventions aiming at improving the parent–adolescent relationship.

Limitations and strengths

This study has several limitations. First, the sample was relatively homogeneous regarding socio-economic and ethnic background and included mostly Dutch families of middle- to higher-SES. Our results might not replicate or might emerge even stronger in more varied samples including participants from lower SES strata, and/or ethnic minorities (Raffington, Tanksley, Vinnik, et al., 2021). Second, although we used contemporary algorithms for the most commonly used epigenetic clocks, the field is rapidly moving forward and newer adjustments such as clocks trained in specific (younger) populations may be a way to improve in the future (Dammering et al., 2021; McEwen et al., 2020). Relatedly, we used saliva to extract DNAm information; studies using blood samples might result in weaker or stronger effects. Third, even though our models and data provided enough power (>.90) to detect bad-fitting models (Moshagen & Erdfelder, 2016), power might have been limited to detect some of the specific target effects (e.g., Wang & Rhemtulla, 2021). Future longitudinal studies with repeated assessments of EA will benefit from larger sample sizes. However, this study has also several strengths, among which is the use of repeated measures of EA spanning a relatively large and developmentally crucial age period. Furthermore, several aspects of environmental exposures (negative parenting) and psychological outcomes were examined, broadening the scope of knowledge regarding the psychosocial determinants and outcomes of epigenetic age.

Conclusion

This pre-registered study used a repeated-measures, longitudinal design with pre-registered hypotheses to examine the predictors and outcomes of epigenetic age and changes in epigenetic age from adolescence to young adulthood. Focusing on 'subtle' aspects of negative parenting, and several aspects of psychological problems, we found no links between negative parenting and EA, yet significant associations between externalizing problems, self-concept clarity, and (changes in) EA. Most importantly, this study showed that changes in EA from adolescence to young adulthood can be an independent biological marker for declining mental health during young adulthood. This study, therefore, offers evidence that epigenetic clocks could be a useful tool in predicting future mental health.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article:

Table S1. Unstandardized negative parenting means, standard deviations, and correlations with confidence intervals.

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Key points

- EA is a biological marker reflecting the processes linked to biological aging. EA is based on the methylation level of tens or hundreds of cytosine-phosphate-guanine loci across the genome.
- EA is known to be associated with stress exposure, but it is less clear whether EA changes following stress exposure. The consequences of changes in EA for mental health are largely unknown.
- This study showed that EA is not associated with, nor changes following repeated exposure to negative parenting throughout adolescence.
- However, significant links between EA and mental health were found. Most importantly, changes in EA predict later changes in mental health.
- EA is a promising biological marker potentially involved in the development of psychological symptoms.

Endnote

1. During the revision process, all analyses were repeated including pubertal status at W1 as a control variable. Although pubertal status was significantly but weakly related to three of the clocks at W5 (~ age 17) (GrimAge, PhenoAge, Hannum, with standardized betas of .12–.19), no results changed substantively after controlling for pubertal status. As these analyses were not part of the pre-registered analytic plan and did not affect our conclusions, we report the analyses without pubertal status in our manuscript.

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