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Original article

Genetic and environmental factors in pain symptoms and self-harm, and their association. A twin study

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ABSTRACT

Individuals who self-harm are often insensitive to pain, and consequently pain sensitivity has been proposed as a barrier for self-harm. It is unclear how pain and self-harm interplay in real life settings, and to what extent genetics and environmental factors contribute to the etiology of both.

This study was registry based using classical twin design. A cohort of 16 948 Swedish twin pairs born between 1992 and 2010, was prospectively assessed for pain symptoms at ages 9 and 18, and followed up for later self-harm until 2016 and a maximum age of 24.

The relative contributions of genetic and environmental factors to each phenotype were estimated using univariate twin models. Logistic regression models assessed their association, and conditional models adjusted for familial confounding.

Genetics and non-shared environment contributed to pain and self-harm to a moderate degree at both age 9 and age 18, while the contribution of shared environment was small for both pain and self-harm at both ages. At age 18 the pain symptoms group had higher odds for later self-harm (odds ratio 1.59, 95% CI 1.06–2.41, p = .003), and pain seemed to be partially in the causal pathway as it was not explained by familial confounding. This study adds to the evidence of pain symptoms as a predictor for self-harm.

1. Introduction

Self-harm behaviors are intentional acts of, for example, cutting, carving, poisoning or burning oneself with or without suicidal intent, (Moran et al., 2024) with a global prevalence of 17.7 % for 10- to 19-year-olds (Moloney et al., 2024). Beginning typically at 13–16 years, self-harm behaviors may progress into suicide attempts (Duarte et al., 2020; Hamza et al., 2012) and are considered to be the strongest predictor of subsequent suicide (Geulayov et al., 2019). It is often hard to distinguish between self-harm with or without suicidal intent as the behaviors overlap and intention fluctuates (Kapur et al., 2013). The Lancet commission on self-harm recommends defining self-harm as self-harming behavior regardless of intention (Moran et al., 2024), and we will follow that recommendation.

Self-harm behaviors are common among patients with borderline personality disorder but also in individuals with depression, excessive drinking, eating disorders, anxiety, and ADHD (Hawton et al., 2013; King et al., 2008; Moran et al., 2024; Reichl and Kaess, 2021). Adults and adolescents who self-harm consistently display group-level higher pain thresholds (the minimum pressure/cold/heat intensity required to experience pain) than healthy controls, in clinical and community settings (Cummins et al., 2025; Koenig et al., 2016, 2017b; Lalouni et al., 2022; Pontén et al., 2025). This lower sensitivity to painful stimuli has been proposed to be a potential biomarker of self-harm in both adults and young people, (Cummins et al., 2021; Lalouni et al., 2022) and to enable self-harm behaviors (Hooley and Franklin, 2018).

Some individuals who self-harm report no pain during the act, increasing the risk of suicide attempts (Ammerman et al., 2016).

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Continued exposure to painful and fearful stimuli is posited to contribute to the acquired capability for suicide in the Interpersonal Theory of Suicide (Van Orden et al., 2010). It is however unclear whether a lower sensitivity to pain exists before the onset of self-harm behaviors, is a consequence of self-harm practice, or a combination of both.

The definition of pain is "An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage" according to the International Association of the Study of Pain (IASP (2020)), underlining the subjectivity of the human pain experience. A complex interplay between sensory, affective, and cognitive neural processes shapes our perception of pain, which is ultimately a property of the brain (Melzack, 2001; Melzack and Katz, 2006). Our ability to perceive pain is an adaptive mechanism that keeps us safe from tissue damage (Fordyce, 1984; Melzack, 2001). However, pain perception varies substantially between individuals with potential genetic contributions to both low and high pain sensitivity (Cox and Srivastava, 2024), and within individuals depending on context and mood (Carlino and Benedetti, 2016; Coghill, 2010).

The theoretical understanding of non-suicidal self-harm behaviors is dominated by the Benefits and Barriers model. In short, the model states there are powerful benefits of self-harm behaviors: emotional regulation, communication, affiliation, and self-punishment; in theory available to everyone. But most do not access these benefits because of the existing barriers: awareness, aversion, positive self, social norms, and pain (Hooley and Franklin, 2018).

Evidence suggests genetics partly explain the variance of self-harm, but findings concerning the degree to which this is the case are mixed. Genome-wide association studies have reported up to 13 % of variation explained (Campos et al., 2020; Russell et al., 2021; Sun et al., 2025), while twin studies have estimated the genetic influence on self-harm to be up to 55 % (Maciejewski et al., 2014; Ohlis et al., 2025).

In a cross-sectional study by Lalouni et al., individuals with self-harm exhibited lower pain sensitivity and more efficient central pain inhibition, assessed with the test conditioned pain modulation (Ramaswamy and Wodehouse, 2021), compared to healthy controls (Lalouni et al., 2022). These findings were not related to the duration and frequency of self-harm, indicating it was not a practice effect. Few longitudinal studies have investigated this phenomenon, but Koenig et al. showed in a small experimental study in 2016 that adolescent self-harm patients had higher pain thresholds than healthy controls at study start, but also experienced increased pain thresholds one year later, while the healthy controls reported lowered pain thresholds (Koenig et al., 2017a), indicating a practice effect of repeated self-harming. Boyne & Hamza recently showed in an observational study that lower pain sensitivity could predict higher self-harm frequency four months later in a community sample (Boyne and Hamza, 2024), while self-harm practice did not predict subsequent lower pain sensitivity, indicating no effect of practice on pain sensitivity. Taken together, evidence suggests low pain sensitivity may be at least partially a result of genetic predisposition, precedes self-harm behaviors, and may indeed act as an enabler for self-harm.

On the other hand, self-harm behaviors are also prevalent in clinical chronic pain samples, particularly among adolescents (Chen et al., 2023; Torino et al., 2025). Chronic pain patients consistently display higher pain sensitivity compared with healthy controls, as shown in a meta-analysis comparing pain thresholds between patients and controls (Amiri et al., 2021) and in a study comparing pain tolerance between patients and controls (Skogberg et al., 2022).

Mechanistic studies have also provided evidence for plasticity in the pain system in both humans and animal models, where persistent unintentional exposure to pain, or other stressors, may be associated with heightened pain sensitivity (Harte et al., 2018; Latremoliere and Woolf, 2009), while intentional pain exposure in clinical chronic pain samples, has led to improvements and has been associated with changes in central pain processing mechanisms (Jensen et al., 2012; Yoshino et al., 2018).

Pain sensitivity and self-harm thus seem to be influenced by genetic factors to an unclear degree, may change over time, and evidence concerning the nature of their relation is inconclusive.

Twin studies are a robust way to estimate the genetic and environmental influences on traits at a certain point in time, and this design has to the best of our knowledge not been used to longitudinally investigate the association between pain and self-harm in children and young adults.

The aim of this study was thus to characterize the genetic and environmental contributions to pain symptoms and self-harm, and their relationship. The purpose was to better understand the role of pain in self-harm behavior.

Using data from the Swedish Twin Registry with prospectively collected data of twins aged 9/12 and 18+ years old, we investigated childhood pain symptoms in relation to self-harm in adolescents and young adults.

The research questions were:

- What are the relative genetic and environmental contributions to pain symptoms?
- What are the relative genetic and environmental contributions to self-harm?
- Are pain symptoms associated with self-harm and is this association due to unmeasured familial confounding? (genetic or non-genetic)

We hypothesized that there would be a genetic contribution to both pain symptoms and self-harm, and that pain symptoms during childhood would be associated with a decreased likelihood of self-harm later in life.

2. Methods

2.1. Study design

This was a classical twin study using prospectively collected longitudinal data from Swedish registries. Twin models compare the within-pair resemblance between monozygotic (MZ) twins, who share all segregating DNA, with dizygotic (DZ) twins, who share 50 % of DNA on average. Details on the twin design are provided in Rijsdijk & Sham (Rijsdijk and Sham, 2002).

2.2. Participants

Participants were part of the Child and Adolescent Twin Study in Sweden, CATSS, a nationwide population-based longitudinal study. All twins born in Sweden are identified via the Swedish Birth Registry, and those twins born from July 1992 and onwards are invited to participate in CATSS at age nine (earlier cohorts at age 12) (Anckarsäter et al., 2011). Follow-ups occur at ages 15, 18, and 24. CATSS is linked with nationwide Swedish registers (see below). This study used data from twins born 1992–2010, included in CATSS at ages 9/12 (response rate 69 %) and 18 (response rate 55 %) until 2019, with linked registry data up to 2016. Participants were aged 24, at the oldest, at the end of available follow-up.

The CATSS has ethical approval from the Karolinska Institute Ethical Review Board: CATSS-9/12 Dnr: 03–672 and 2010/507–31/1, and CATSS-18 Dnr: 2010/1410/31/1.

2.2.1. Exclusion and inclusion criteria

Inclusion criteria for CATSS are: a) twins born in Sweden, and b) twins have turned nine years old, and c) parents have agreed to participate in the twin registry.

Exclusion criteria for this study were: a) unclear zygosity for either twin, and/or b) missing CATSS data from co-twin, and/or c) either twin had emigrated/died, and/or d) one or both twins had protected identity.

2.3. Variables

Age was calculated from birth date extracted from official records, and the date parents completed the surveys. For analyses, birth years were grouped: 1992–1995, 1996–2000, 2001–2005, and 2006–2010.

Sex assigned at birth was collected from parental report and linkage with the Medical Birth Register. Ethnicity data were unavailable.

Zygosity was determined through DNA or parental report of twin resemblance when no genotype data existed. Only twins classified with 99 % confidence using parental report were included.

As anxiety and depression often co-occur with both chronic pain and self-harm, clinical diagnoses from the National Patient Register were used as co-variates. ICD-10 codes F40-F42 (phobias, anxiety, OCD) and F32-F33 (depressive disorders) were used and dichotomized regardless of when they were diagnosed during follow-up.

2.3.1. Pain

Pain was used as a proxy for pain sensitivity, and data were prospectively collected from parental reports in CATSS. At age 9/12, parents completed a screening about their children's health conditions and asked about aches and pains: Would you say that your child: a) neither has aches nor pains?, b) has moderate aches or pains?, c) has severe aches or pains?, d) don't know, e) don't want to answer), and recurring headaches: How often does your child have recurring headaches? a) less than once a month, b) 1–3 times a month, c) 1–3 times a week, d) almost daily. A twin was considered to have pain if severe aches or pains were reported, and/or recurring headaches 1–3 times weekly or almost daily.

At age 18, parents completed the Adult Behavior Checklist (ABCL), which included 3 pain items: Physical problems without known medical cause: Aches or pains (not stomach or headaches); Headaches; Stomach-aches. Answering options were a) not true, b) somewhat or sometimes true, c) very true or often true. See supplemental information for a complete overview of questions and answering options. A twin was considered to have pain if any aches, headaches, or stomach-aches were reported to be very true or often true. The pain variable was dichotomized. Cutoffs were conservatively chosen to include only more severe cases of pain and exclude milder pain complaints.

2.3.2. Self-harm

Self-harm data were prospectively collected from parental ABCL reports at age 18, self-report from the Lifetime History of Aggression (LHA) form at age 18, and the Swedish National Patient Register (NPR), that records all specialist inpatient care in Sweden since 1987, and outpatient care from 2001. A twin was classified as engaged in self-harm if parents reported lifetime/last 4 weeks self-harm attempts, and/or the twins themselves reported having self-harmed four times or more, and/or if NPR records showed ICD-10 codes X60-X84 (deliberate self-destructive actions) or Y10-Y34 (self-destructive actions with unclear intent). All data resources include self-harm with and without suicidal intent. See supplemental information for an overview of parental and self-report questions and answering options.

Self-harm was treated as an outcome and thus had to occur after the report of pain sensitivity in everyone's timeline to be included in analyses. The self-harm variable was dichotomized. Cutoffs on the LHA were conservatively chosen to include only more severe cases of self-harm.

2.4. Statistical methods

Univariate twin models assessed relative contributions of genetic and environmental factors to pain sensitivity and self-harm using liability threshold models for binary data. These models assume a continuous distribution of liability underlying categorical data and estimate the proportions of variance in liability to each phenotype explained by additive genetic influences (A), shared environment (C), and nonshared environment (E). For details on the twin design, see Rijsdijk & Sham (Rijsdijk and Sham, 2002).

To test for phenotypic associations between pain sensitivity and self-harm, we used logistic regression models implemented as generalized estimating equations to account for dependent observations (i.e., twins). Pain sensitivity was the exposure, and self-harm the outcome. Models were initially unadjusted for covariates, then adjusted for sex and birth year. We further adjusted for anxiety and depression diagnoses. This adjustment was not pre-registered and should be considered exploratory.

Conditional logistic regression models were then fitted to adjust for familial confounding – to test if the association between pain sensitivity and self-harm could be explained by shared familial influences (genetic and shared environmental factors that contributed to both phenotypes).

Finally, bivariate twin models estimated whether genetic and environmental influences on both phenotypes were correlated and explained their association.

95 % Confidence intervals (CI) were reported, and results were considered statistically significant if the CI excluded zero for estimates from the twin model, and 1 for odds ratios.

3. Results

3.1. Participants

There were 34 378 participants in CATSS at age 9. Of those, 435 individuals were removed for missing zygosity, and 47 whose co-twin did not participate. The sample thus included 16 948 twin pairs at age 9, and 4 932 pairs at age 18, all followed in national registries until

Table 1
Descriptive data.

	Overall	MZ	DZ	F	M
Age 9					
Pairs, N (%)	16,948	5183 (30.6)	11,765 (69.4)	NA	NA
Female ind, N (%)	16,749 (49.4)	5382 (51.9)	11,367 (48.3)	NA	NA
Pain, N (%)	545 (1.6)	139 (1.5)	406 (1.9)	273 (1.6)	272 (1.6)
Aches, N (%)	199 (0.6)	53 (0.5)	146 (0.6)	90 (0.5)	109 (0.6)
Headaches, N (%)	362 (1.2)	92 (1.0)	270 (1.3)	194 (1.2)	168 (1.0)
Self-Harm after 9, N (%)	1672 (4.9)	476 (4.6)	1196 (5.1)	1139 (6.8)	533 (3.1)
Anxiety disorders, N (%)	346 (1.0)	100 (1.0)	246 (1.0)	198 (1.2)	148 (0.9)
Depression, N (%)	650 (1.9)	184 (1.8)	466 (2.0)	401 (2.4)	249 (1.5)
	Overall	MZ	DZ	F	M
Age 18					
Pairs, N (%)	4932	1517 (30.8)	3415 (69.2)	NA	NA
Female ind, N (%)	5133 (52.0)	1694 (55.8)	3439 (50.4)	NA	NA
Pain, N (%)	487 (5.1)	149 (5.1)	338 (5.2)	369 (7.2)	118 (2.5)
Aches, Pains, N (%)	150 (1.6)	39 (1.3)	111 (1.7)	125 (2.4)	25 (0.5)
Headache, N (%)	240 (2.5)	76 (2.6)	164 (2.5)	176 (3.4)	64 (1.4)
Stomach-aches, N (%)	196 (2.1)	62 (2.1)	134 (2.0)	148 (2.9)	48 (1.0)
Self-Harm after 18, N (%)	941 (9.5)	292 (9.6)	649 (9.5)	689 (13.4)	252 (5.3)
Anxiety disorders, N (%)	120 (1.2)	40 (1.3)	80 (1.2)	65 (1.3)	55 (1.2)
Depression, N (%)	267 (2.7)	81 (2.7)	186 (2.7)	188 (3.7)	79 (1.7)

MZ, monozygotic; DZ, Dizygotic; F, female; M, male (independent of zygosity).

2016. See Table 1. 31 % were monozygotic (MZ) (5183 pairs at age 9, and 1517 at age 18), and 69 % dizygotic (DZ) (11,765 pairs at age 9, and 3415 at age 18). Among MZ twins, 52–56 % were female (5382 individuals at age 9, and 1684 at age 18). Of DZ twins 50.4 % were same sex, and 49.6 % were opposite sex.

Pain was reported by 545 individuals (1.6 %) at age 9, and 487 (4.9 %) at age 18. Self-harm was reported by 1672 (4.9 %) after age 9 and by 941 (9.5 %) at age 18. Pain was equally prevalent between sexes at age 9, at age 18 pain symptoms were almost three times more common in females than males. Self-harm was about 2 times more common in females.

Anxiety disorders were diagnosed in 346 individuals (1 %) who had participated at age 9, and 120 (1.2 %) who had participated at age 18. Depression was diagnosed in 650 (1.9 %) who participated at age 9, and in 267 (2.7 %) who participated at age 18.

Descriptives including birth year cohorts, and split by sex and zygosity, are available in supplemental Tables 1 and 2.

3.2. Relative contribution of genetic and environmental factors to pain

At age 9, the correlation for pain was 0.52 (CI 0.35–0.67) between MZ twins and 0.29 (CI 0.17–0.41) between DZ twins, and at age 18, correlations were 0.53 (CI 0.38–0.66) for MZ twins and 0.35 (CI 0.23–0.46) for DZ twins, suggesting genetic influences. The MZ correlations were below 1, indicating non-shared environmental influence.

At age 9 the heritability of pain (A) was estimated at 0.46 (CI 0.04–0.66), shared environmental (C) at 0.06 (CI 0.00–0.35) and non-shared environmental (including measurement error) (E) at 0.48 (CI 0.34–0.65); A and E showed statistically significant contributions.

At age 18, the genetic contribution to pain (A) was 0.36 (CI 0.00–0.65), shared environment (C) was 0.17 (CI 0.00–0.43), and non-shared environment (E) was 0.47 (CI 0.34–0.62). Only E showed a statistically significant contribution.

3.3. Relative contribution of genetic factors to self-harm

The correlation for self-harm after age 9 was 0.57 (CI 0.50–0.64) between MZ twins and 0.35 (CI 0.29–0.41) between DZ twins. After age 18, the correlation was 0.50 (CI 0.39–0.60) for MZ twins and 0.22 (CI 0.13–0.31) for DZ twins, suggesting genetic influence. Again, the MZ correlation was below 1, suggesting non-shared environmental influences.

The heritability of self-harm (A) after age 9 was estimated at 0.44 (CI 0.25–0.62), shared environment (C) at 0.13 (CI 0.00–0.27) and non-shared environment (E) at 0.43 (CI 0.36–0.50). After age 18, genetic contribution to self-harm (A) was 0.49 (CI 0.39–0.57), shared environment (C) was estimated at 0 (CI 0.00–0.15), and non-shared environment (E) at 0.51 (CI 0.43–0.61).

See Fig. 1 for all ACE estimates and Table 2 for model fit.

3.4. Association between pain and self-harm

Among participants with pain at age 9, a significantly larger proportion, 7.16 %, later reported self-harm, compared to 4.93 % among those without pain ($p = .018$). At age 18, participants with pain had significantly higher prevalence, 21.97 %, of later self-harm versus 8.99 % for non-pain individuals ($p < .001$).

After adjusting for sex and birth year, the odds ratio (OR) for later self-harm when reporting pain at age 9 was 1.36 (CI 0.97–1.92), indicating that odds for self-harm were higher in the pain group, but this was not statistically significant ($p = .078$). See Fig. 2 for all ORs. Adjusting for familial confounding, the OR was 1.24 (CI 0.70–2.20), and also not significant ($p = .470$). When adjusting for anxiety and depression, the OR was 1.31 (CI 0.92–1.96), and also not significant ($p = .139$). Thus, the slightly greater odds for self-harm in the pain symptoms group at age 9 was not significant, and was only marginally attributable to anxiety, depression, and familial confounding.

At age 18, after adjusting for sex and birth year, the OR for later self-harm when pain was reported was 2.33 (CI 1.85–2.95, $p < .001$), indicating a more than doubled odds of self-harm. Adjusting for familial confounding reduced this to 1.59 (CI 1.06–2.41, $p = .003$). When adjusting for anxiety and depression, the OR was 2.08 (CI 1.62–2.67, $p < .001$), suggesting the increased odds was partly attributable to causal factors beyond anxiety, depression, and familial confounding. See Fig. 2.

Bivariate results showed a phenotypic correlation between pain at age 9 and later self-harm of 0.03 (CI −0.04–0.09), and between pain at age 18 and later self-harm of 0.24 (CI 0.18–0.30). No further analyses were conducted as the phenotypic correlation for age 9 was insignificant and still small at age 18 – hence it was not feasible to decompose the correlation into genetic and environmental components. See Table 3.

4. Discussion

This study found moderate genetic and non-shared environmental contributions to pain symptoms and self-harm in a large twin sample, and that pain symptoms in adolescence were associated with higher

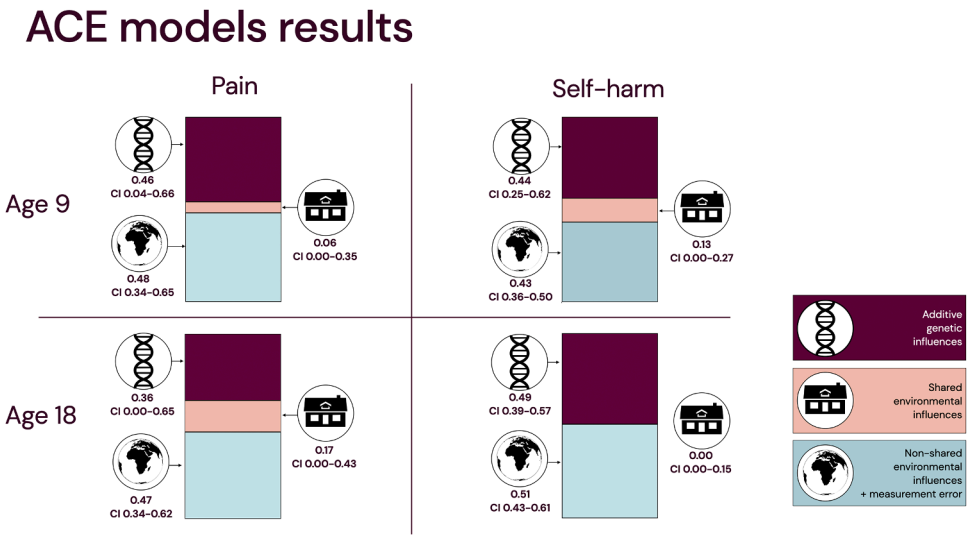

Fig. 1. ACE model estimates for the additive genetic, shared environment and non-shared environmental influence on pain and self-harm, at ages 9 and 18, with point estimates and 95% confidence intervals.

Table 2
ACE model fit estimates.

Pain, age 9										
Model	Comparison	Parameters	−2LL	df	ΔX^2	Δdf	*p*	A (95 % CI)	C (95 % CI)	E (95 % CI)
Fully Saturated	NA	6	5421.20	30,800	NA	NA	NA	NA	NA	NA
ACE	Fully Saturated	4	5429.25	30,804	8.05	4	0.090	0.46 (0.04–0.66)	0.06 (0.00–0.35)	0.48 (0.34–0.65)
AE	ACE	3	5429.43	30,805	0.19	1	0.666	0.54 (0.40–0.66)	NA	0.46 (0.34–0.60)
CE	ACE	3	5433.86	30,805	4.61	1	0.032	NA	0.36 (0.26–0.45)	0.64 (0.55–0.74)
E	ACE	2	5478.10	30,806	48.85	2	<0.001	NA	NA	1.00 (1.00–1.00)
Pain, age 18										
Model	Comparison	Parameters	−2LL	df	ΔX^2	Δdf	*p*	A (95 % CI)	C (95 % CI)	E (95 % CI)
Fully Saturated	NA	6	3746.07	9473	NA	NA	NA	NA	NA	NA
ACE	ACE	4	3770.02	9477	23.95	4	<0.001	0.36 (0.00–0.65)	0.17 (0.00–0.43)	0.47 (0.34–0.62)
AE	AE	3	3771.45	9478	1.43	1	0.231	0.57 (0.45–0.68)	NA	0.43 (0.32–0.55)
CE	CE	3	3773.60	9478	3.58	1	0.058	NA	0.41 (0.32–0.68)	0.59 (0.50–0.68)
E	E	2	3839.93	9479	69.91	2	<0.001	NA	NA	1.00 (1.00–1.00)
Self-harm, any time										
Model	Comparison	Parameters	−2LL	df	ΔX^2	Δdf	*p*	A (95 % CI)	C (95 % CI)	E (95 % CI)
Fully Saturated	NA	6	13,796.54	33,890	NA	NA	NA	NA	NA	NA
ACE	Fully Saturated	4	13,874.60	33,894	78.06	4	<0.001	0.43 (0.24–0.61)	0.15 (0.01–0.28)	0.42 (0.36–0.50)
AE	ACE	3	13,879.34	33,895	4.74	1	0029	0.61 (0.56–0.67)	NA	0.39 (0.33–0.44)
CE	ACE	3	13,894.47	33,895	19.88	1	0	NA	0.43 (0.38–0.47)	0.57 (0.53–0.62)
E	ACE	2	14,185.52	33,896	310.92	2	0	NA	NA	1.00 (1.00–1.00)
Self-harm, after age 9										
Model	Comparison	Parameters	−2LL	df	ΔX^2	Δdf	*p*	A (95 % CI)	C (95 % CI)	E (95 % CI)
Fully Saturated	NA	6	12,962.65	33,890	NA	NA	NA	NA	NA	NA
ACE	Fully Saturated	4	13,045.28	33,894	82.63	4	<0.001	0.44 (0.25–0.62)	0.13 (0.00–0.27)	0.43 (0.36–0.50)
AE	ACE	3	13,048.81	33,895	3.53	1	0.060	0.61 (0.55–0.67)	NA	0.39 (0.33–0.45)
CE	ACE	3	13,064,42	33,895	19.14	1	<0.001	NA	0.42 (0.38–0.47)	0.58 (0.53–0.62)
E	ACE	2	13,323.15	33,896	277.87	2	<0.001	NA	NA	1.00 (1.00–1.00)
Self-harm, after age 18										
Model	Comparison	Parameters	−2LL	df	ΔX^2	Δdf	*p*	A (95 % CI)	C (95 % CI)	E (95 % CI)
Fully Saturated	NA	6	6081.60	9858	NA	NA	NA	NA	NA	NA
ACE	Fully Saturated	4	6124.15	9862	42.54	4	<0.001	0.49 (0.39–0.57)	0.00 (0.00–0.15)	0.51 (0.43–0.61)
AE	ACE	3	6124.15	9863	0	1	1	0.49 (0.39–0.57)	NA	0.51 (0.43–0.61)
CE	ACE	3	6139.01	9863	14.87	1	<0.001	NA	0.32 (0.25–0.39)	0.68 (0.61–0.75)
E	ACE	2	6211.37	9864	87.23	2	<0.001	NA	NA	1.00 (1.00–1.00)

A: Additive genetic influence; C: Shared environment: E: Non-shared environment and measurement errors.

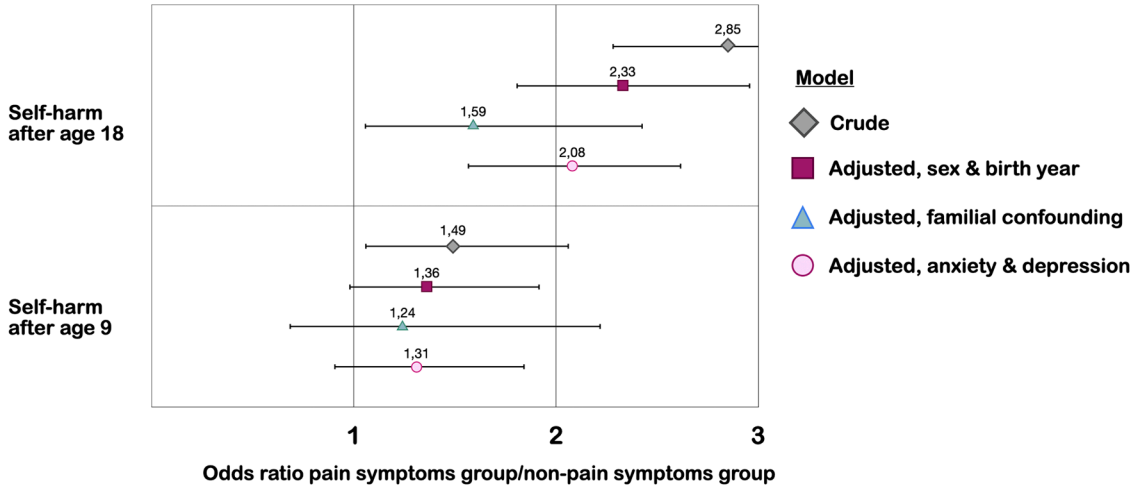

Fig. 2. Odds ratios (ORs) and 95% confidence intervals for later self-harm, for children and adolescents with and without pain at ages 9 and 18.

odds for self-harm later in adolescence and early adulthood.

Our first hypothesis (a genetic contribution to pain) was partially confirmed with heritability estimated at 46 % at age nine and 36 % at age 18. These estimates align with previous twin studies suggesting 22–60 % heritability for pain symptoms (Nielsen et al., 2008; Norbury et al., 2007). The non-shared environment was estimated to explain nearly half of the variation at both 9 and 18 years, while shared environment had no to very modest contribution. While genome-wide association studies have identified common gene variants, pain symptoms likely involve numerous genes as well as contextual factors (Melzack, 2001).

The second hypothesis: a genetic contribution to self-harm was confirmed with heritability estimated at 44 % at age nine and 49 % at age 18. Non-shared environment showed a contribution of 43 % at age 9 and 51 % at age 18. Previous studies vary widely, from suggesting purely

Table 3
Phenotype correlations pain sensitivity – self-harm.

Exposure	Outcome	rPH (95 % CI)	MZ CTCT (95 % CI)	DZ CTCT (95 % CI)
Pain Age 9	Self-Harm After Age 9	0.03 (−0.04–0.09)	0.03 (−0.09–0.14)	−0.02 (−0.10–0.06)
Pain Age 9	Self-Harm, Any Time	0.02 (−0.04–0.08)	0.01 (−0.09–0.12)	−0.04 (−0.11–0.04)
Pain Age 18	Self-Harm After Age 18	0.24 (0.18–0.30)	0.20 (0.09–0.30)	0.15 (0.07–0.23)
Pain Age 18	Self-Harm, Any Time	0.22 (0.16–0.28)	0.19 (0.08–0.29)	0.13 (0.05–0.20)

rPH, phenotype correlation; MZ, monozygotic; DZ, dizygotic; CTCT, cross-twin cross trait.

environmental factors (Jang et al., 1996) to approximately 55 % genetic influence (Maciejewski et al., 2014), while a recent genome-wide study estimated ≈10 % SNP heritability for self-harm behaviors (Campos et al., 2020). Taken together, self-harm etiology is complex, and this study adds evidence on the importance of genetic influence *and* non-shared environment.

The third hypothesis (that pain symptoms during childhood would be associated with a decreased likelihood of self-harm later in life) was not confirmed. Instead, the results indicate the opposite: earlier pain symptoms were associated with two-fold increased odds of later self-harm beyond age 18. This association was only marginally affected by co-morbid anxiety and/or depression, and familial confounding, indicating pain is partially in the causal pathway to self-harm.

In the "Benefits and barriers" model (Hooley and Franklin, 2018) pain sensitivity is considered a barrier for engaging in self-harm, but the association between pain and self-harm may be more complex. Chronic pain patients show high pain sensitivity yet engage in self-harm at elevated rates (Chen et al., 2023), while self-harm patients have on a group level higher pain thresholds (Boyne and Hamza, 2024; Koenig et al., 2016; Lalouni et al., 2022). From a behavioral perspective, the *function* of pain can be considered distorted in both groups, as perceived pain may not act as a barrier, but instead be positively reinforced. Besides being a way to regulate emotions, a meta-analysis including both young and adults, and both clinical, self-referred and community samples reported that individuals who self-harm often describe the pain when self-harming as a punishment that they “deserve”, and/or that self-harming can distract from and be a means to take control over other painful experiences (Edmondson et al., 2016). In this sense, our results do not contradict the Benefits and Barriers model; instead, it shows that pain need not always be on the barrier side but can also function as a perceived benefit for some individuals, under some circumstances.

Also, abdominal pain in adolescence has been found to predict severe mental health disorders in adulthood (Bohman et al., 2012) and chronic pain in adolescence is related to suicidal ideation, independent of depression (Van Tilburg et al., 2011). A study of 8-year-old children showed that headache and abdominal pain predicted suicides and suicide attempts by age 24 in boys but not in girls (Luntamo et al., 2014). So, potential other explanations include shared risk factors (maladaptive coping, adverse childhood experiences, opioid dysfunctions), or a shift from pain sensitivity to insensitivity through repeated exposure. The relationship between pain and self-harm seems to play a pivotal role and warrants further investigation through experimental designs with long-term follow-up, in particular studies investigating pain sensitivity before the onset of self-harm behaviors would add important pieces of the puzzle.

Clinically, our findings emphasize the importance of pain as a significant risk factor for later self-harm.

4.1. Strengths and limitations

Our study's strength lies in the prospectively collected data in a large population-based twin sample with longitudinal follow up from age 9 to 24 and registry linkage. Also, both the pain and self-harm variables had conservative cut-offs to increase clinical validity.

Limitations include that only persons born in Sweden are invited to participate in the twin registry, no ethnicity data were available, and we did not control for other diagnoses or medication use. Another limitation is measuring pain via parental reports of aches and pains, rather than direct assessment. While recurring pain consistently correlates with higher pain sensitivity (Fontanillas et al., 2022; Nielsen et al., 2008) other factors, such as catastrophizing (Sullivan et al., 2001) or parents under-reporting children’s pain (Chambers et al., 1998), may also play a role.

4.2. Conclusions

The genetic influence on pain symptoms may explain around a third up to nearly half the variation in childhood and adolescence. For self-harm, the genetic influence was estimated to explain almost half of the variation, and non-shared environment also seems to play a large part. Pain symptoms in adolescence were associated with increased odds of self-harm later in life, and this relationship seems to be partially causal.

Trial registration

Open Science Framework, https://osf.io, registration nr: sx6gp, https://doi.org/10.17605/OSF.IO/SX6GP

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CRediT authorship contribution statement

Jenny Rickardsson: Writing – review & editing, Writing – original draft, Visualization, Project administration, Investigation, Funding acquisition, Conceptualization. **Mark J. Taylor:** Writing – review & editing, Writing – original draft, Validation, Methodology, Formal analysis, Data curation. **Paul Lichtenstein:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Henrik Larsson:** Writing – review & editing, Investigation, Data curation. **Sebastian Lundström:** Writing – review & editing, Investigation, Data curation. **Karin Jensen:** Writing – review & editing, Funding acquisition, Conceptualization. **Maria Lalouni:** Writing – review & editing, Writing – original draft, Conceptualization.

Declaration of competing interest

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Supplementary materials

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