

# **Under the skin**

**Early-life stress exposure and the co-occurrence of mental and physical health problems**

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# PREFACE

*“In the depth of winter, I found there was, within me, an invincible summer.”* Albert Camus  
– Summer (1954)

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### Note

This is a work in progress. Stay tuned :)

## Aknowledgements

TODO

# INTRODUCTION

Dear reader,

oh my good why does this not update

This an that (Fraser et al., 2013; R Core Team, 2021)

See Chapter [1](#) for additional discussion.

## References

## **Part I**

# **PART 1: The role of ELS in the development of mental and physical health**

# 1 ELS and adolescent psycho-physical health

Adapted from:

**Differential effects of pre- and postnatal early-life stress on internalizing, adiposity and their comorbidity**

**Defina, S.**, Woofenden, T., Baltramonaityte, V., Pariante, C. M., Lekadir, K., Jaddoe, V. W., Serdarevic, F., Tiemeier, H., Walton, E., Felix, J. F., & Cecil, C. A. M., *on behalf of the EarlyCause Consortium*. (2023). JAACAP\*. [DOI](#)

## Abstract

Objective: Depression and obesity are two highly prevalent and often comorbid conditions. Exposure to early-life stress (ELS) has been associated with both depression and obesity in adulthood, as well as their preclinical manifestations during development. However, it remains unclear whether: *(i)* associations differ depending on the timing of stress exposure (prenatal vs postnatal) and *(ii)* ELS is a shared risk factor underlying the comorbidity between the two conditions.

Method: Leveraging data from two large population-based birth cohorts (ALSPAC: n=8428 (52% male participants); Generation R: n=4268 (48% male participants)), we constructed comprehensive cumulative measures of prenatal (in utero) and postnatal (from birth to 10 years) ELS. At age 13.5 years we assessed: a) internalizing symptoms (using maternal reports); b) fat mass percentage (using dual-energy X-ray absorptiometry); c) their comorbidity, defined as the co-occurrence of high internalizing and high adiposity.

Results: Both prenatal (*total effect* [95%CI] = 0.20 [0.16; 0.22]) and postnatal stress ( $\beta$  [95%CI] = 0.22 [0.17; 0.25]) were associated with higher internalizing symptoms, with evidence of a more prominent role of postnatal stress. A weaker association (primarily driven by prenatal stress) was observed between stress and adiposity (prenatal: 0.07 [0.05; 0.09]; postnatal: 0.04 [0.01; 0.07]). Both pre- (OR [95%CI] = 1.70 [1.47; 1.97]) and postnatal stress (1.87 [1.61; 2.17]) were associated with an increased risk of developing comorbidity.

Conclusion: We found evidence of *(i)* timing and *(ii)* shared causal effects of ELS on psycho-cardiometabolic health in adolescence, but future research is warranted to clarify how these associations may unfold over time.



## 1.1 Introduction

In summary, this book has no content whatsoever (Elsenburg et al., 2017; Wiklund et al., 2008). But I shall write it anyway cause. Cause I kind of do have no choice so, checking justification works

## 1.2 Methods

## 1.3 Discussion

## References

- Elsenburg, L. K., Wijk, K. J. E. van, Liefbroer, A. C., & Smidt, N. (2017). Accumulation of adverse childhood events and overweight in children: A systematic review and meta-analysis [Journal Article]. *Obesity (Silver Spring)*, 25(5), 820–832. <https://doi.org/10.1002/oby.21797>
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## 2 Lifestyle factors, ELS and adolescent psycho-physical health

Adapted from:

The role of lifestyle factors in the association between early-life stress and adolescent psycho-physical health: Moderation analysis in two European birth cohorts

**Defina, S.**, Woofenden, T., Baltramonaityte, V., Tiemeier, H., Fairchild, G., Felix, J. F., Cecil, C.A.M., & Walton, E. (2024). *Preventive Medicine*. DOI

### Abstract

### 2.1 Introduction

In summary, this book has no content whatsoever (Boyd et al., 2012; Fraser et al., 2013). But I shall write it anyway cause. Cause I kind of do have no choice so, checking justification works

### 2.2 Methods

### 2.3 Discussion

### References

### References

Boyd, A., Golding, J., Macleod, J., Lawlor, D. A., Fraser, A., Henderson, J., Molloy, L., Ness, A., Ring, S., & Davey Smith, G. (2012). Cohort profile: The 'children of the 90s'—the index offspring of the avon longitudinal study of parents and children [Journal Article]. *International Journal of Epidemiology*, 42(1), 111–127. <https://doi.org/10.1093/ije/dys064>

Fraser, A., Macdonald-Wallis, C., Tilling, K., Boyd, A., Golding, J., Davey Smith, G., Henderson, J., Macleod, J., Molloy, L., Ness, A., Ring, S., Nelson, S. M., & Lawlor, D. A. (2013). Cohort profile: The avon longitudinal study of parents and children: ALSPAC mothers cohort [Journal Article]. *Int J Epidemiol*, 42(1), 97–110. <https://doi.org/10.1093/ije/dys066>

## 3 ELS and intracortical myelination

Adapted from:

Early-life stress exposure and intracortical myelination in childhood: a population-based neuroimaging study

**Defina, S.**, Manzoni, D., Tiemeier, H., Brouwer, R.M., Cecil, C.A.M., & Muetzel R.L. (*in preparation*)

### Abstract

#### 3.1 Introduction

In summary, this book has no content whatsoever (Boyd et al., 2012; Fraser et al., 2013). But I shall write it anyway cause. Cause I kind of do have no choice so, checking justification works

#### 3.2 Methods

#### 3.3 Discussion

### References

### References

Boyd, A., Golding, J., Macleod, J., Lawlor, D. A., Fraser, A., Henderson, J., Molloy, L., Ness, A., Ring, S., & Davey Smith, G. (2012). Cohort profile: The 'children of the 90s'—the index offspring of the avon longitudinal study of parents and children [Journal Article]. *International Journal of Epidemiology*, 42(1), 111–127. <https://doi.org/10.1093/ije/dys064>

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## 4 ELS and cardiac morphology

Adapted from:

Early-life stress exposure and heart morphology in childhood: a prospective population-based study

Defina, S., Kamphuis, A., Gaillard, R., & Felix, J. F. (*in preparation*)

### Abstact

#### 4.1 Introduction

In summary, this book has no content whatsoever (Boyd et al., 2012; Fraser et al., 2013). But I shall write it anyway cause. Cause I kind of do have no choice so, checking justification works

#### 4.2 Methods

#### 4.3 Discussion

### References

## **Part II**

# **PART 2: Reciprocal relationships between mental and physical health problems**

## References

- Boyd, A., Golding, J., Macleod, J., Lawlor, D. A., Fraser, A., Henderson, J., Molloy, L., Ness, A., Ring, S., & Davey Smith, G. (2012). Cohort profile: The 'children of the 90s'—the index offspring of the avon longitudinal study of parents and children [Journal Article]. *International Journal of Epidemiology*, 42(1), 111–127. <https://doi.org/10.1093/ije/dys064>
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# 5 Longitudinal psycho-physical co-development

Adapted from:

Longitudinal co-development of depressive symptoms and cardio-metabolic risk factors from childhood to young adulthood

Defina, S., Cecil, C.A.M., Felix, J.F., Walton, E., & Tiemeier, H. (*under revision*)

## Abstact

### 5.1 Introduction

In summary, this book has no content whatsoever (Boyd et al., 2012; Fraser et al., 2013). But I shall write it anyway cause. Cause I kind of do have no choice so, checking justification works

### 5.2 Methods

### 5.3 Discussion

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# DISCUSSION

See Chapter 1 for whatever whatever.

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