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Early childhood SES and Major Depressive Disorder (MDD) in Later-life

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Abstract

The objective of this paper was to explore the effect of early childhood SES on the predisposition for Major Depressive Disorder (MDD). Taking into account that there are both genetics and social determinants of MDD, the analysis here presented attempts to extrapolate the role of each, essentially testing the hypotheses at the interaction between social sciences and natural studies: epigenetics. The hypothesis of this paper is that childhood SES has an essential role in later life predisposition for MDD. I tested this conjecture using a revised version of the KHB analysis in order to actually capture the relative mediation of the regressors. In particular, I sought to explain three outcomes: a) childhood SES has long-lasting effect on MDD outcomes in later life; b) The persistence of early disadvantages is not fully mediated by midlife social outcomes; c) Regardless of differences in genetic predisposition (proxied by neuroticism), the effect of childhood SES on MDD in later life persists. I find positive results on the persistence of the effect of early childhood disadvantage on MDD outcome in later-life, at age 50 and more.

INTRODUCTION

Major Depressive Disorder (MDD) is often referred as the 'common cold' of psychiatry, with disturbing consequences both at the micro and macro level. Most importantly, MDD has been consistently observed as the foremost risk for poor health. The Global Burden of Disease Study, which systematically gathers the epidemiological data about different indicators of population health, identified that MDD was the third cause of global health burden in 2017. At the individual level, MDD shapes health outcomes and increases the risk for suicide and heart diseases (Ferrari, Charlson, Norman, Patten, et al. 2013).

In epidelomogical research, it is well-documented that the prevalence of MDD is socially confounded and substantively varies between and within countries. Between country variation is mainly explained by differences in exposure to conflict and violence (Ferrari, Charlson, Norman, Flaxman, et al. 2013) Lim et al. 2012). At the individual level, among various risk factors, early childhood adversity shapes MDD outcomes (Gilman et al. 2002) (Sadowski et al. 1999). However, the exact mechanism which links early childhood experiences and MDD remains uncovered. There is some evidence that maternal attachment abates the impact of adversity, but this is consistent only for those children who are biologically sensitive to context[1] (Bakermans-Kranenburg et al. 2008). On the other hand, recent evidence indicates the plausible epigenetic path as the bridging mechanism between early childhood adversity and MDD (Essex et al. 2013). Though it calls for a test, whether early disadvantage becomes 'embodied' and shapes the propensity of major depressive disorder or the effect of early deprivation is fully mediated by later-life social outcomes.

The work here presented is the very first attempt to bridge multidisciplinary perspectives of allostatic load (AL) and differential susceptibility theory (DST) for examining propensity of MDD in later-life. The concept of allostatic load denotes accumulated biological burden which aggravates as a result of permanent exposure to social adversity. On the other hand, differential susceptibility theory (DST) highlights that individuals differ in their resilience and are not equally affected by the environment, conversely, they are differentially susceptible to stressors. Bridging these two perspectives is a well-suited theoretical solution for disentangling the true confounders of major depressive disorder. In addition, this multidisciplinary perspective opens a new avenue for future research. The proposed framework is reasonable for identification of

[1] Indexed by DRD 4 7-repeat allele

gene-environment interaction patterns, if the effect of early SES holds after accounting for later-life social outcomes and differential susceptibility to depression it will indicate that the mechanism through which early SES shapes the propensity of depression might be biological 'embodiment' of early disadvantage.

Drawing on the concept of allostatic load (AL) I argue that early childhood material deprivation increases the biological burden of the organism in such a way that is not compensable over the life-course and shapes the propensity of experiencing major depressive disorder in later-life. Early childhood is a sensitive period when the brain is vulnerable to environmental influences, that is why it is reasonable to argue that early material deprivation constitutes a distinct risk for MDD outcome. Hence, the first aim of the study is to uncover the long-lasting effect of early SES on the propensity of MDD. I introduce a composite measure of early childhood SES, which I constructed by Principal Component Analysis. The childhood SES variable includes the direct measures of deprived living conditions, indirect measures of parental cultural capital (the number of books), father's occupation and measures of cognitive dis/advantage at age 10 (math and language position). In social stratification research it is well-documented that early childhood cognitive dis/advantage is the best proxy for early adversities. , so that, including the measures of early cognitive performance and parental cultural capital comprehensively reflects all the possible components of early dis/advantage. However, allostatic load aggravates across entire life-course, so that, mid-life social burden substantially increases AL. Hence, second aim of the paper is to identify if the effect of early disadvantage holds after accounting for the possible mediators such are: educational attainment and occupational position at age 35. I use these two variables as the sociological proxies of mid-life adversities. But, differential susceptibility theory (DST) highlights that individuals are not equally susceptible to environmental stressors and the response to the same contextual stimuli differs by biological reactivity to stress. I do not have the direct measures of differential susceptibility but, one dimension of the Big-Five personality traits, namely neuroticism might be used as the measure of differential susceptibility to depression since it has been recently identified that neuroticism and depression have same genetic confounding (they share two genetic loci) (Okbay et. all 2016). Hence, the third aim of the paper is to test if the effect of early disadvantage holds after accounting for genetic predisposition to depression, proxied by neuroticism.

I do find the evidence for long-lasting effect of childhood SES on MDD outcome in later-life, medium and high childhood SES background individuals have statistically significant lower propensity of experiencing MDD at age 50 and more. In addition, the effect holds in box sex. Educational attainment and occupational position at age 35 significantly mediate the effect of early dis/advantage, but the effect of early childhood SES holds after accounting these life-course trajectories. Adding neuroticism into the model does not neutralize the effect of early SES. The findings are suggestive that the mechanism through which early deprivation constitutes a distinct risk for MDD outcome in later-life might be biological 'embodiment', but the findings call for a further multidisciplinary test.

LITERATURE REVIEW

MAIN PREDICOTRS OF MAJOR DEPRESSIVE DISORDER (MDD)

The aetiology of Major Depressive Disorder has been widely examined in clinical research. The most frequently explored predispositions to MDD are genetics and gender. Mounting evidence demonstrates that MDD is genetically confounded disease. Approximately 30-40% of predisposition to MDD is explained by genetic factors (Sullivan, Neale, and Kendler 2000) (Mitjans and Arias 2012)(McGuffin and Katz 1989) (Tsuang and Faraone 1990). Evidence suggests that women are more likely to experience MDD compared to men (Hyde, Mezulis, and Abramson 2008)(Weissman et al. 1993)(Kessler et al. 1993). However, what shapes the higher prevalence of depression in women is still unclear. The mechanisms of genetic heritability have been tested separately by sex. Nonetheless, the evidence is inconclusive: Some studies demonstrate that the genetic factors shaping the risk for MDD are equally heritable among men and women (Kendler and Prescott 1999) (Lyons et al. 1998) (McGuffin et al. 1996). Conversely, other studies have also demonstrated the evidence for gender differences in heritability, with women having higher heritability of depression (Kendler, Gatz, et al. 2006) (Bierut et al. 1999) (Silberg et al. 1999). That is why it has become typical to examine the propensity of MDD separately by sex. Generally, there is evidence for the similarity of MDD predictors among females and males. Indeed, separate sex models evinced that females and males show similar pathways of genetic endowments, except one difference: low-self-esteem has been found to be a crucially significant pathway in men, while in women it was not (Kendler, Gardner, and Prescott 2002) (Kendler, Gardner, and Prescott 2006).

Besides genetics and gender, the third widely recognized predictor of MDD is personality traits. However, it is disputed across the disciplines whether personality traits are genetically confounded or influenced by contextual factors. Among the various measures of personality differences, the Big-Five model is the most widely accepted, since it captures the main domains of self (McCrae 1989). In addition, there is evidence that neuroticism and MDD share same genetic loci (Okbay et al. 2016a). However, it has not been tested whether this genetically confounded dimension of the Big-Five has the same effect on the propensity of depression when it interacts with different environment, more precisely if the predisposition to depression indexed by neuroticism expresses itself regardless contextual experiences.

In addition to abovementioned biological factors, such as genetics, gender and neuroticism, significant amount of the variance in the prevalence of depression is explained by emotionally traumatic childhood events (Chapman et al. 2004) (Jacobson, Fasman, and DiMascio 1975). The link between early material deprivation and MDD is only partially examined (Ritsher et al. 2001). Most importantly, the evidence on whether the effect of early deprivation is mediated in later-life or it encompass a specific risk for MDD (which is not compensable across the life-course) is scant.

Some studies suggest the possible mechanisms through which early childhood deprivation becomes biologically 'embodied' and shapes the health outcome. One of the plausible channel for 'embodiment' is epigenetic change, which occurs when genes and environment interact (Bagot and Meaney 2010). Empirical evidence demonstrates that low socioeconomic status in teenage years induces changes in the expression of serotonin transporter gene (Swartz, Hariri, and Williamson 2017) (Zhao et al. 2013).

Even though, that the importance of early deprivation for later-life outcomes has been widely recognized, the link between childhood SES and depression remains elusive. Individuals from low childhood socioeconomic background are more likely to experience major depressive disorder (Gilman et al. 2002) (Sadowski et al. 1999). However, the literature has failed to test whether the effect of early childhood SES holds across entire life-course, after accounting for the plausible mediators. The present research attempts to address the following two gaps: first, providing a test on whether the effect of early childhood disadvantage holds after accounting for the plausible mediators of the risk for MDD. Second, furnishing evidence on whether the effect of early childhood SES holds after accounting for genetic confounding of MDD.

THEORETICAL FRAMEWORK

LONG-LASTING CONSEQUENCES OF CHILDHOOD SES

The long-lasting consequences of childhood SES on different social outcomes is well-documented. The origin effect shapes destination (Duncan et al. 1998) (Duncan, Ziol-Guest, and Kalil 2010) (Jonsson et al. 2009). Social mobility researchers have already identified several channels of social inequality reproduction. Educational attainment is the primary channel through which origin affects destination. But, even after the expansion of access to education, parents' social class still significantly shapes life-course outcomes. Even though the strength of origin effect varies across countries (is mediated by institutional context), the main effect remains significant (Breen and Luijkx 2004) (Breen and Jonsson 2005) (Breen and Karlson 2014). Research has documented that origin affects not only destination, rather it shapes cognitive skills (Ericsson et al. 2017) and health outcomes (Elo 2009). The significant part of origin effect emerges in early childhood, for instance has shown, that early childhood material deprivation and maternal depression predicts cognitive development at age three (Kiernan and Huerta 2008).

EXISTING FRAMEWORKS FOR EXAMINING MDD OUTCOME

Three different conceptual frameworks of examining MDD outcome might be differentiated. The first framework focuses on the primacy of sensitive periods and highlights that the timing of deprivation is decisive. The relative power of the effect of deprivation is higher if the timing coincides with early developmental phase, when the formation of brain occurs (Heim and Binder 2012). The second framework can be characterized as the model of risk accumulation, when MDD is shaped by the sum of different events across entire life-course, rather than by singular adverse experiences. The final framework is more individualized and examines unique individual experiences of adversity (Colman and Ataullahjan 2010) (Côté et al. 2009).

The presented research is based on the first and the second frameworks: drawing on the sensitive periods approach, I theorize that early childhood psychosocial deprivation, proxied by factor variable of early childhood SES (before the age 10) encompass a distinct risk for MDD which is not compensable across the life-course. However, considering the perspective of accumulated disadvantage, I expect that the effect of early SES will be mediated by life-course social outcomes, namely educational attainment and mid-life occupational position. I use education and occupation as the proxies for life-time social burden.

CHILDHOOD SES AND ALLOSTATIC LOAD

Drawing on the concept of allostatic load (AL), which was introduced by (McEwen and Stellar 1993) I hypothesize that early childhood material deprivation becomes 'embodied' and increases the allostatic load of the organism across the entire life-course. Allostasis is a process when the organism physiologically adjusts to the context based on the environmental stimuli received from that context, maintaining the allostatic state is a necessary condition for the survival of every organism. AL is characterized as the physiological burden, which emerges in the process of maintaining stability under the condition of exposure to permanent adversity, more precisely, allostatic load accumulates as a result of constantly threatening environment and is mediated by the neural and endocrine systems. However, the response, which influences the neural and endocrine systems activates itself after detecting the treat, so that the individual perception of what is safe or threatening shapes the neural and hormonal responses (McEwen and Wingfield 2003).Though, the link between subjective perceptual factors and the hormonal responses is bidirectional.

Based on the theoretical premises of AL, I theorize that the effect of early childhood SES might have two pathways shaping socially patterned risk for MDD: a. material deprivation (being poor) which has direct impact on functioning via the lack of resources b. perception of deprivation (feeling poor) which aggravates changes in neural and hormonal systems. Both factors together generate accumulated disadvantage, namely allostatic load. The allostatic load substantially differs from biological risk, it can be characterized as the aggravated burden which has severe consequences for health, while each individual component of AL does not have statistically significant effect on health outcome, separately (Ganzel, Morris, and Wethington 2010). In recent neuroendocrinological research several indices of AL has been proposed and demonstrated that they predict different health outcomes (McEwen 2003) (Juster, McEwen, and Lupien 2010) (Danese and McEwen 2012) (Zsoldos and Ebmeier 2016). Though, the persistent effect of AL accumulated in early childhood on MDD outcome is still underexplored.

IMPACT OF CONTEXTUAL FACTORS AND DIFFERENTIAL SUSCEPTIBILITY

I proposed that regardless adversities accumulated in mid-life, the effect of early disadvantage remains significant and increases the risk for MDD in later-life. However, individuals differ in resilience and the 'embodiment' of adversity is mediated by the individual characteristics. The interaction between the contextual effects and individual characteristics has been primarily examined from the perspective of differential susceptibility theory (DST). The individual response to the same contextual stressor is mediated by stress reactivity (Belsky 1997b) (Belsky 1997a). Hence, DTS perspective focuses on identifying physiological markers of stress reactivity and highlights that some individuals are easily influenced by both negative and positive contextual experiences, while others remain unaffected (Ellis et al. 2011). Though, the markers of differences in resilience are not fully uncovered. Some evidence suggests that the variation in context sensitivity depends on dopamine-related genes[2], which shapes the responsiveness to reward and punishment, however genes interact with the contextual effects, children who were susceptible/sensitive[3] to environmental stimuli and whose mothers were using penalty without explanation showed more prosocial behavior, compared to their counterparts with the same marker of context sensitivity (Bakermans-Kranenburg and van Ijzendoorn 2007). In fact, DTS perspective is a strong theoretical starting point against biological determinism and for testing the interactions between genetic predispositions and contextual experiences.

BRIDGING AL AND DST PERSPECTIVES

The present research is the very first attempt to bridge two different perspectives of allostatic load and differential susceptibility theory to examine MDD outcome in later-life. However, the proposition is more heuristic, since I do not have the direct measures of allostatic load, neither the markers of differential susceptibility to stress. However, drawing on the premise that allostatic load could be proxied by sociological measures of dis/advantage, such are: childhood SES, years of education and occupational attainment. Hence, the first aim of the study is to uncover the long-lasting effect of early SES on the propensity of MDD. The SHARELIFE data gives us unique opportunity to test the effects of early SES and mid-life mediators together. Beside constructing the sociological proxy of allostatic load, I address the genetic confounding of MDD by examining the effect neuroticism on depression outcome in later-life. This analytical decision has its limitations and strengths, at the same time. Accounting for the effect

[2] DRD2, DRD4
[3] They had the DRD4 7-repeat allele

of neuroticism does not capture all the genetic predispositions to MDD. Nonetheless, using the measure of neuroticism allows me to explore two different theoretical purposes: 1. to proxy the genetic confounding of MDD expressed via Neuroticism 2. to test if neuroticism has the same effect on the risk for MDD regardless early childhood socioeconomic background.

PROPOSED MEDIATORS: EDUCATIONAL AND OCCUPATIONAL ATTAINMENT

The variation in the prevalence of MDD is socially patterned not only by early adversities but by mid-life outcomes. I differentiate two mediating channels of the effect of childhood SES: occupational position and educational attainment. Occupational position shapes mental well-being through different pathways: a. the first pathway is occupational conditions, specifically some occupations encompass higher risk for physical injury and constitute psychological burden. b. the second pathway is the imbalance between job demand and control. It is empirically observed that demanding jobs with low level of control, when the employee does not have autonomy to direct their own action have negative effect on well-being (Theorell, Karasek, and Eneroth 1990) c. the third pathway is disproportionate effort-reward schemas d. the last path is job insecurity and uncertainty (Ferrie et al. 1998).

All abovementioned models demonstrate that occupational attainment shapes mental health outcome, but they focus on establishing the link between occupational attainment and subjective well-being or life satisfaction, while the clinical symptoms of depression substantively differ from life-satisfaction. Disentangling the relative explanatory power of different occupational channels or explaining the possible pathways on how occupation shapes the depression outcome is beyond the scope of the presented research. But, based on the existing evidence it is reasonable to argue that occupational position might have mediating effect on early childhood disadvantage. I hypothesize, that occupational position at age 35 (at the proxy for lifetime occupational attainment) mediates the effect of early childhood SES on the risk for MDD. Occupational status at age 35 could be used as the lifetime proxy of occupational attainment since in the SHARELIFE data occupational positions at different ages (at age 25,35, 45 or 55) are highly correlated and the occurrence of job change is relatively rare.

HYPOTHESIS

In the theoretical framework I proposed a broad conceptual model to test the effect of early childhood SES on the depression outcome. Hence, I formulate the following hypothesis:

H1: Early childhood SES is the significant predictor of MDD outcome in later-life.

H2: The effect of early childhood SES is not fully mediated my mid-life social outcomes, such are: educational and occupational attainment.

H3: The effect of early childhood SES holds after accounting for genetic predisposition to MDD expressed via neuroticism.

DATA AND VARIABLES

I use the SHARELIFE data, which is the third wave of the Survey of Health, Aging and Retirement in Europe 4. The SHARE is a cross-sectional panel study which includes information on various socio-economic variables and health status of European population at age 50 and more. The study covers 14 European countries (participating in all waves of SHARE): Austria, Germany, Sweden, Netherlands, Spain, Italy, France, Denmark, Greece, Switzerland, Belgium, Czech Republic, Poland, Ireland. The third wave of the SHARE is the most relevant setting to test the long-lasting effect of childhood SES on depression outcome in later life, since the wave 3 includes retrospective information about the entire life-course of the person since he/she was born up until the time of the interview. The number of respondents participating in the wave 3 is 28 492. In addition, wave 7 includes information on Big-Five Personality Traits. I use neuroticism as the proxy for genetic confounding of MDD (Major Depressive Disorder). Several genome wide association studies have identified the same genetic loci for depression and neuroticism (Bartels and Boomsma 2009). To shed some light on possible paths how neuroticism interacts with childhood SES and affects the propensity of MDD in later-life, I merge the waves 3 and 7 data at the individual level (N=13 966). Since the neuroticism has been already identified as the time-invariant trait, this analytical decision is unproblematic.

[4] I use the data release 6.1.1.; release time: 19th June 2018 and the wave 7, which includes information on Big Five Personality Traits , the data release 7.0.0. release time: 3rd April 2019.

VARIABLES

MAJOR DEPRESSIVE DISORDER (DV)

In the SHARELIFE data set, the symptoms of MDD are measured by EURO-D scale, which captures the following dimensions: feelings of depression, pessimism, wishing death, guilt, irritability, tearfulness, fatigue, sleeping problems, loss of interest, loss of appetite, concentration problems and loss of enjoyment. I use a dichotomized EURO-D scale. The suggested cut-off point for depression outcome is more than three symptoms, which has been validated in the EURODEP study (Prince et al. 1999). However, I have chosen the lower cut point, if a person reports at least three or more symptoms I treat it as MDD outcome, choosing the lower cut-off point increases the robustness of the results.

CHILDHOOD SES

I constructed the index of early childhood SES (before the age 10) using Principal Component Analysis. In the second step, based on the index, I have generated three categories of childhood SES: a. Low SES (0) <percentile 40 b. Medium SES (1) >= percentile 40 & >= percentile 80 c. High SES (2) >= percentile 80. The childhood SES index includes math and language position at age ten, because early cognitive scores are best proxies for parental social class (Sullivan, Ketende, and Joshi 2013a) (Duncan, Magnuson, and Votruba-Drzal 2014).The components of the childhood SES index are described in Table 1

Table 1: Description of the components of childhood SES

Variable	Description	Response categories /generated variables
Childhood SES	1. **Features of accommodation** when ten: a. fixed bath b. cold running water supply c. hot running water supply d. inside toilet e. central heating . 2. **Breadwinner's occupation** at the age of ten 3. **Number of books** when ten 4. **Rooms per person ratio** - 4.a. number of rooms in house when ten divided by 4.b. people living in house when ten. 5. **Math position** at age ten. 6. **Language position** at age 10	1. As the proxy of household wealth, I have created an ordinal variable Features of Accommodation as the sum of the features of accommodation. 2. I have created a factor variable of SES index including a) **Features of Accommodation b) Breadwinner's occupation** at age ten c) **The number of books** at home when the respondent was 10 years old d) **Rooms per person ratio** e) Math and Language position at age ten.

CONTROLS

The main predictors of MDD might be grouped as the following: genetics, stress and chronic illness. Individuals with certain chronic conditions are more likely to experience MDD. Though the link between chronic illness and MDD is bidirectional (Egede 2007). However, this reverse causality cannot bias the results, since I am interested in the long-lasting impact of childhood SES, if it remains significant after controlling for chronic conditions that will indicate that childhood SES creates a distinct risk for MDD. Besides the impact of chronic illness, the prevalence of MDD significantly depends on biological sex. The most obvious path between sex and MDD is hormonal, reproductive hormones impact the mood regulation process among females. However, hormonal changes do not affect all woman equally (Asthana et al. 2009; Schmidt and Rubinow 2009; Miller et al. 2010; Ben Dor et al. 2013; Epperson, Wisner, and Yamamoto 1999). I control all models for gender, age and country effects. In addition, I control all full models for chronic conditions.

MODEL SPECIFICATION

I estimate the effect of early childhood SES on the propensity to MDD in later life by a revised version of KHB model, which has been recently proposed (Breen, Karlson, and Holm 2018). The research puzzle includes not only identifying the long-lasting effect of childhood SES on MDD but – disentangling how much of the effect is mediated by other predictors. The mediation analysis is the best available methodological solution to identify the true effect of the independent variables when the outcome (DV) is binary. In nested nonlinear probabilistic model, the amount of change in the coefficients across different specifications might be driven by rescaling effect, since the variance of the residual/error is not constant across different models. The KHB approach solves this problem by holding the residual constant (Karlson, Holm, and Breen 2012). I follow all the steps of a revised version of KHB model.

First, I run the multivariable logistic regression model on the binary outcome of MDD including all mediators and controls. I check the linearity of all continuous covariates. The smoothed scatterplot[5] of years of education indicates that it is nonlinear that is why I added the

[5] Lowess smooth method is the graphical presentation of the lowess smooth of the outcome versus the covariate

logarithmic transformation of years of education into the models. The full model includes early childhood SES, years of education, occupational position at age 35, neuroticism and controls for heart disease, stroke and other chronic conditions, excluding obesity.

In the second step of the analysis, I save the linear predictor, namely κ from the full multivariable logistic regression model. The linear predictor is a continuous variable which captures the propensity of MDD outcome.

$\kappa = h^{-1}(pr(Y=1)) = b_0 + b_1$childhood_ses $+ b_2$years of Education$+ b_3$job at age 35 $+ b_4$neuroticism$+ b_5$controls (final Model)

In the third step, I fit four OLS models, using the linear predictor as the dependent variable:

$\kappa = \alpha_0 + \alpha_1$childhood_ses $+ x_1$controls $+ \varepsilon$ (Model 1)

$\kappa = \beta_0 + \beta_1$ childhood SES $+ \beta_2$ years of education $+ z_2$controls$+ \varepsilon$ (Model 2)

$\kappa = \mu_0 + \mu_1$ childhood SES $+ \mu_3$years of education $+ \mu_4$ job at age 35 $+ \nu_1$controls$+ \varepsilon$ (Model 3)

$\kappa = \varphi_0 + \varphi_1$ childhood SES $+ \varphi_3$years of education $+ \varphi_4$ job at age *35* $+ \varphi_5$neuroticism $+ \lambda_1$controls$+ \varepsilon$ (Model 4)

These specifications allow us to disentangle the effects of childhood SES and mediators.

TESTING THE INTERACTIONS

In addition, to identify if the effect of childhood SES varies by different levels of neuroticism, I test the interaction between early SES and neuroticism, separately by sex. The model specification is the following:

$Y = b_0 + b_1$childhood_ses $+ b_2$years of Education$+ \beta_3$job at age *35* $+ \beta_4$childhoods SES * neuroticism $+ (X_1$controls)

RESULTS

Table 2 shows the estimated association between Major Depressive Disorder (MDD) and the possible covariates using a revised version of KHB[6] (Latent Index Approach). The index is the

[6] The new version of KHB model is often referred as Latent Index Approach

latent continuous variable capturing the propensity of being depressed. Model 1 (baseline model) demonstrates that individuals from medium and high childhood SES background have statistically significant lower propensity of experiencing major depressive disorder in later-life, compared to low childhood SES category. Model 4 (final model) shows that the effect of early childhood SES declines after including mediators, however it remains significant. The decrease in propensity of experiencing MDD in later-life for higher childhood SES categories indicate that early SES has gradational effect on the propensity of MDD.

In addition, the final model (Model 4) demonstrates that the mid-life social outcomes such are: educational and occupational attainment, significantly decrease the propensity of MDD; however, they do not neutralize the effect of early disadvantage. This latter finding falls in line with the hypothesis that the childhood SES encompass a specific risk for the MDD outcome in later-life. As it is suggested in the previous research, I estimated all models, separately by sex. Table 3 and 4 shows the estimates for separate sex models. The effect of early SES on MDD holds in females and males. Besides, identifying the long-lasting consequences of early SES, the research puzzle included testing if the early SES effect remains significant after accounting for differential susceptibility to MDD, proxied by neuroticism. The findings from the final model indicate that regardless neuroticism the early SES effect holds. However, this finding should be interpreted cautiously, since neuroticism does not capture all the effect of genetic predisposition to MDD.

Table 2: Estimates for the propensity of MDD using Latent Index Approach (LI) for both sex

VARIABLES	(Model 1) LI	(Model 2) LI	(Model 3) LI	(Model 4) LI
Low Childhood SES (reference)				
Medium Childhood SES	-0.217***	-0.149***	-0.138***	-0.119***
	(0.0127)	(0.0125)	(0.0126)	(0.00734)
High Childhood SES	-0.426***	-0.294***	-0.271***	-0.229***
	(0.0159)	(0.0160)	(0.0164)	(0.00957)
Log(Years of Education)		-0.368***	-0.339***	-0.325***
		(0.0134)	(0.0141)	(0.00825)
Occupation at age 35			-0.0138***	-0.0104***
			(0.00219)	(0.00128)
Neuroticism				0.425***
				(0.00311)
Constant	-0.607*	0.0165	0.00197	-0.999***
	(0.362)	(0.349)	(0.348)	(0.203)
Observations	9,681	9,681	9,681	9,681

Standard errors in parentheses.*** p<0.01, ** p<0.05, * p<0.1 All models are controlled for country, gender and age effects. The final model is controlled for heart disease, stroke and chronic conditions

Table 3: Estimates for the propensity of MDD using Latent Index Approach (LI) in females

VARIABLES	(Model 1) LI	(Model 2) LI	(Model 3) LI	(Model 4) LI
Low Childhood SES (reference)				
Medium Childhood SES	-0.208***	-0.124***	-0.118***	-0.0898***
	(0.0182)	(0.0177)	(0.0178)	(0.0107)
High Childhood SES	-0.567***	-0.406***	-0.394***	-0.320***
	(0.0228)	(0.0228)	(0.0233)	(0.0140)
Log(Years of Education)		-0.450***	-0.432***	-0.399***
		(0.0197)	(0.0208)	(0.0125)
Occupation at age 35			-0.00814***	-0.00715***
			(0.00308)	(0.00185)
Neuroticism				0.418***
				(0.00441)
Constant	0.389	1.033**	1.006**	-0.548*
	(0.530)	(0.505)	(0.505)	(0.303)
Observations	5,068	5,068	5,068	5,068
	0.535	0.579		

Standard errors in parentheses.*** p<0.01, ** p<0.05, * p<0.1 All models are controlled for country, gender and age effects. The final model is controlled for heart disease, stroke and chronic conditions

Table 4: Estimates for the propensity of MDD using Latent Index Approach (LI) in Males

VARIABLES	(Model 1) LI	(Model 2) LI	(Model 3) LI	(Model 4) LI
Low Childhood SES (reference)				
Medium Childhood SES	-0.246***	-0.195***	-0.179***	-0.170***
	(0.0177)	(0.0176)	(0.0178)	(0.0100)
High Childhood SES	-0.237***	-0.137***	-0.105***	-0.0985***
	(0.0220)	(0.0224)	(0.0232)	(0.0131)
Log (Years of Education)		-0.278***	-0.244***	-0.245***
		(0.0183)	(0.0193)	(0.0109)
Occupation at age 35			-0.0171***	-0.0114***
			(0.00321)	(0.00181)
Neuroticism				0.437***
				(0.00440)
Constant	-1.809***	-1.255***	-1.216**	-1.460***
	(0.491)	(0.481)	(0.479)	(0.270)
Observations	4,613	4,613	4,613	4,613

Standard errors in parentheses.*** p<0.01, ** p<0.05, * p<0.1 All models are controlled for country, gender and age effects. The final model is controlled for heart disease, stroke and chronic conditions

Table 5 shows the mediated percentages for each proposed mediator, separately by childhood SES category. The hypothesized possible mediators are educational attainment, occupation at age 35 and neuroticism. Educational attainment mediates the effect of early SES by 31% in medium and high socioeconomic background group. In addition, occupational attainment at age 35 mediates early SES effect by 7-8%, respectively in medium and high socioeconomic background categories. The remaining unmediated effect of early childhood SES indicates that

education and occupation are not the only channels that create advantage for medium and high childhood SES groups.

Table 5: The Effect of the Mediators and Mediated Percentages

	Medium childhood SES	High childhood SES
Mediated Percentage:	Both sex	
Educational Attainment	31%	31%
Occupational Position	7%	8%
	Females	
Educational Attainment	40%	28%
Occupational Position	4%	3%
	Males	
Educational Attainment	20%	42%
Occupational Position	8%	23%

Note: standard errors are in parenthesis .

In order to shed some light on the pattern if childhood SES has the same effect on propensity to MDD for different levels of neuroticism, I tested the interactions between childhood SES and neuroticism, separately by sex, but interaction effect was not significant.

DISCUSSION

The work here presented was the first attempt of examining socially patterned risk for Major Depressive Disorder (MDD) through interdisciplinary perspective by bridging two different theoretical frameworks of allostatic load (AL) and differential susceptibility (DST). I theorized that early childhood material deprivation creates a distinct risk for the occurrence of MDD in later-life and the effect is not fully mediated by the proposed life-course outcomes such are: educational attainment and mid-life occupational position. I found the evidence that early childhood SES has long-lasting consequences on the propensity of major depressive disorder. Though, mid-life social outcomes significantly mediate the effect of early SES on the risk for MDD, the remaining unmediated effect indicates that low childhood SES constitutes a specific risk for experiencing major depressive disorder in later-life, at age 50 and more.

Furthermore, the research puzzle included identifying if the early SES effect was present after accounting for the genetic predisposition to depression, proxied by neuroticism, since it is already known that genetic predisposition to MDD varies. To address the confounding effect, I included neuroticism into the final model, since it shares the same genetic loci with MDD and could be used as the proxy for biological predisposition. I found that neuroticism does not neutralize the effect of early disadvantage. In general, the results are in agreement with the

previous evidence that early childhood SES significantly shapes the MDD outcome (Gilman et al. 2002) (Sadowski et al. 1999). However, the long-lasting effect of early childhood SES while accounting for genetic propensity of MDD has not been examined. I found the evidence, that early SES effect is present in later-life, at the age of 50 and more, even after considering differences in predisposition. The findings suggest that the possible mechanism through which early SES shapes MDD outcome in later-life might be biological 'embodiment'.

Bridging the two different perspectives of allostatic load and differential susceptibility theory opens a new avenue for future research to identify which specific components of early disadvantage shape the propensity to MDD. However, the work here presented has several limitations, it uses retrospective information about childhood material deprivation, which could be potential source for recall bias or coloring. Furthermore, MDD outcome is constructed based on the current symptoms of major depressive disorder while the information about recurrent MDD episodes could have been better measure. In addition, neuroticism does not proxy all the genetic confounding of MDD that is why the history of parental depression should be considered.

Furthermore, the plausible channel linking early SES and MDD might be parent-child relationship and rearing practices. In social stratification research, it is well-established fact that parenting styles differ by socioeconomic status and they produce different cognitive outcomes (Ermisch 2008) (Chan and Koo 2011) (Sullivan, Ketende, and Joshi 2013b). However, the link between the parenting-style and depression remains elusive. The components of parenting-styles that shape MDD outcome are not identified, except maternal attachment and warmth. In social stratification research it has been already examined that parenting-styles, especially intellectually stimulating activities shape cognitive development of a child. Additionally, parenting-styles encompass SES gradient, parents from low socioeconomic background are more likely to follow natural growth approach without participating in enriching activities. But, without empirical examination it is not reasonable to theorize that the distribution of maternal attachment or warmth is stratified by socioeconomic background. The SHARELIFE data does not include the variables capturing parent-child relationship dynamics. However, findings demonstrated that even without considering the patterns of maternal attachment and warmth the effect early childhood SES, which is the proxy for material deprivation in early life (at age 10) holds.

The ideal setting for examining the effect of early childhood SES on propensity of Major Depressive Disorder in later-life would be longitudinal cohort study which follows individuals from the time when they were born across the entire life-course and gathers information not only about socioeconomic variables but about various as well.

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