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I am submitting herewith a thesis written by Tobey Lewis Nichols entitled "Differential Susceptibility Effects of Maternal Sensitivity in Childhood on Small for Gestational Age (SGA) Adults' Wealth." I have examined the final electronic copy of this thesis for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Science, with a major in Child and Family Studies.

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Differential Susceptibility Effects of Maternal Sensitivity in Childhood on Small for Gestational
Age (SGA) Adults' Wealth

A Thesis Presented for the
Master of Science
Degree
The University of Tennessee, Knoxville

Tobey Lewis Nichols
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Abstract

Small for gestational age (SGA) birth has been shown to have adverse consequences on health and is considered as a developmental vulnerability. However, in-utero protection of the brain may not increase vulnerability but rather result in higher individual susceptibility to environmental experiences. The aim was to test if individuals born SGA are more susceptible to both negative and positive environmental experiences assessed by sensitive parenting in childhood compared to those born appropriate for gestational age (AGA). The target outcome was economic success in young adulthood. 438 participants (SGA n = 109, AGA n = 329) were studied as part of the Bavarian Longitudinal Study, a prospective, geographically defined investigation of neonatal at-risk children in South Germany. Maternal sensitivity was observed during a standardized mother-child interaction task, and IQ was defined as a K-ABC MPC Score at age 6 years. At age 26, participants' wealth was assessed as a comprehensive composite score. Comparative analysis confirmed that individuals born SGA were more susceptible to the positive effects of sensitive parenting after controlling for gestational age and IQ at age 6 years. This means, if maternal sensitivity was lower than average, SGA adults did worse than AGA adults, but with high sensitivity in childhood they were significantly more successful than their AGA peers at 26 years of age. It appears that adverse uterine conditions resulting in SGA birth may alter susceptibility to environmental experiences in a for-better-or-for-worse way. Increasing parental sensitivity is a likely avenue to improve life outcomes for SGA individuals.

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1. Introduction

Intrauterine growth restriction (IUGR), is an adaptation to adverse pre-conceptual and prenatal conditions such as malnutrition, poor placental supply, or maternal stress; protecting the development of vital organs (i.e., the brain) while constraining the fetus from reaching its potential size. These unfavorable conditions in utero lead to prenatal programming during developmental periods of high organ plasticity, impacting behavioral functioning and health in later life (Barker, 2007; DeWolff & van Ijendoorn, 1997; Gluckman, Hanson, Cooper, & Thornburg, 2008; Lucas 1994). IUGR is associated with small for gestational age (SGA, <10th percentile weight for gestational age) birth, low birth weight (LBW, <2500g), preterm birth (<37 weeks gestational age), and increased perinatal mortality and morbidity, indicating that weight for gestational age is an important indicator of perinatal outcomes (Lucas, 1994; Pollak & Divon, 1992; Raikkonen & Pesonen).

In addition to poor health outcomes, those born SGA are at increased risk to score lower than appropriate for gestational age (AGA) born peers in math, reading, and fine motor skills at age 5 (Li et al., 2017). Mild cognitive deficits in children born SGA result in lower academic achievement and a higher likelihood of being recommended for special education than those born AGA (Strauss, 2000). However, SGA birth at term may have few long-term effects on executive functions and attentional control (Kulseng et al., 2006), indicating the brain's potential to compensate and catch up after IUGR. Others have found that SGA individuals continue to show higher rates of learning difficulties in adolescence (O'Keeffe, O'Callaghan, Williams, Najman, & Bor, 2003) and lower IQ scores in young adulthood (19-20 years of age) compared with AGA peers (Løhaugen et al., 2013).

The early adverse outcomes of those born at neonatal risk become building blocks for reduced life chances, economically impacting both the individual and society (D'Onofrio et al., 2013). Direct costs associated with neonatal care, follow up treatment and special educational needs, and indirect financial burdens affect families, government agencies, and nonprofit organizations (Petrou, 2003; Petrou, Johnson, Wolke, & Marlow, 2013). These costs add up over a life time resulting in a significant economic impact. In 2006, preterm birth was estimated to cost 2.946 billion British pounds over childhood alone (US\$ 4.567 billion) in England and Wales (Mangham, Petrou, Doyle, Draper, & Marlow, 2009). But the long shadow thrown by neonatal risk continues into adulthood, with premature adults being less economically independent and productive than their term born peers (Heinonen et al., 2013; Männistö et al., 2015; Saigal et al., 2016). In the British Birth Cohort Study of 1970, adults born SGA were found to have similar educational attainment and worked a similar number of hours, but on average had lower weekly incomes compared with those born AGA (Strauss, 2000). A recent Swedish study found that those born SGA were more likely to retire early and receive a disability pension (Helgertz & Vagero, 2014). Moreover, SGA adults may have an increased risk for psychiatric disorders (Indredavik et al., 2010), which also negatively affects their overall societal functioning. Considering the cascading nature of early adversities and their impact on societal functioning in adulthood, it is important to not only study adverse consequences of SGA birth but also environmental factors that may promote life-course success.

Sensitive parenting is an important environmental predictor for later success. Maternal sensitivity predicts positive developmental outcomes in early and late childhood (Belsky et al., 2014; DeWolff & van Ijzendoorn, 1997). Children who receive sensitive parenting, regardless of

temperament in infancy, score better in math, reading, vocabulary, social skills, and work habits (Pluess & Belsky, 2010). For those born at neonatal risk, sensitive parenting might be especially important: Children born preterm and VLBW who experienced sensitive parenting from their mothers demonstrated better academic outcomes and lower perceived behavior problems than preterm/ VLBW children that did not experience sensitive parenting from their mothers (Boyce, Cook, Simonsmeier, & Hendershot, 2015). Maternal sensitivity protects against the adverse effects of VP/VLBW birth (Wolke, Jaekel, Hall, & Baumann, 2013), positively affecting attention regulation (Jaekel, Wolke, & Chernova, 2012) and academic performance throughout childhood and adolescence (Treyvaud et al., 2016; Wolke et al., 2013). For those born SGA, early maternal sensitivity reduced deficits in cognitive abilities and motor skills compared to their AGA peers, while parental intrusiveness widened the developmental gap between the two groups (Li et al., 2017).

Maternal sensitivity may represent a key environmental factor for children born SGA because the adverse and scarce conditions they faced in utero in association with IUGR may lead to an increased adaptability to the environment after birth (i.e., being able to survive in unpredictable conditions) (Wadhwa, Buss, Entringer, & Swanson, 2009). Thus, compared with AGA infants, those born SGA may be programmed for a higher susceptibility to be affected by the environment (Pluess & Belsky, 2011). Accordingly, differential susceptibility theory (DST) proposes that those that have been traditionally viewed as vulnerable to environmental influences in the diathesis-stress framework (Zuckerman, 1999) are in fact more susceptible to environmental impacts, for-better-or-for-worse (Belsky & Pluess, 2009). According to the diathesis-stress framework, individuals born SGA (i.e., those who carry the risk factor) would be

predicted to perform worse than those born AGA given below average environmental factors (e.g., low sensitive parenting). When given an above average environment, those born SGA would do as well as their AGA peers. While DST also predicts that those born SGA (i.e., those who carry the susceptibility factor) would perform worse than their AGA peers given a below average environment, the difference is that DST predicts better average performance of SGA compared with AGA individuals given an above average environment (e.g., high parental sensitivity). DST postulates that those born AGA are relatively unaffected by environmental variations while the outcomes of those born SGA are more variable.

Investigations of DST among children born LBW, VLBW (Jaekel et al., 2015), and VP (Hadfield, O'Brien, & Gerow, 2017) found these populations to be more vulnerable to environmental factors, not more susceptible. However, an investigation of DST among those born with mild perinatal adversity, late preterm or SGA at term, found that when receiving harsh parenting this population had lower hair cortisol levels at age 6, supporting susceptibility among those born with mild perinatal adversity (Windhorst et al., 2017). Similarly, among those in the lowest 30th percentile of early literacy, children born with mild perinatal risk outperformed their peers born term and AGA, after both groups had received a computerized reading literacy intervention with adaptive feedback, suggesting that those born late preterm and SGA are more susceptible to environmental cues (van der Kooy-Hofland, van der Kooy, Bus, van Ijzendoorn, & Bonsel, 2012).

Accordingly, preterm and LBW children may be programmed for high susceptibility to their environments but their frequent neurodevelopmental deficits may limit their resources to profit from environmental stimulation. SGA children, on the other hand, are born across the full

range of gestational age while their brains have been protected from intra-uterine adversity, thus they may be highly susceptible and less constrained by neurodevelopmental limitations than those born preterm. We propose that there are two competing forces, increased susceptibility versus limited neurobiological resources, that decide the level of developmental plasticity an individual grows up with. Although those born SGA, on average, experience less favorable long-term outcomes than their AGA peers, we hypothesize that the adverse intrauterine conditions that lead to protection of the brain by down regulating weight gain may result in high individual susceptibility to environmental experiences.

The aim of this present study was to investigate the relationship between sensitive parenting in childhood and adult wealth for individuals born SGA compared to those born AGA in the Bavarian Longitudinal Study (BLS). We applied confirmatory-comparative modeling to test our hypothesis that SGA individuals are more susceptible (not more vulnerable) to the long-term effects of sensitive parenting than their AGA peers.

2. Methods

Participants and Design

Data were collected as part of the Bavarian Longitudinal Study, a geographically defined whole-population sample of children born in Southern Bavaria (Germany) between January 1985 and March 1986 who required admission to a children's hospital within the first 10 days of life ($n=7,505$; 10.6% of all live births). Additionally, 916 healthy term control infants were identified at birth from the same period and hospitals. Written informed consent was obtained from parents within 48 hours of child birth and from adult participants at the 26 years follow up. Original ethical approval was given by the University of Munich Children's Hospital, ethical approval for the adult follow up was given by the University Hospital Bonn Ethical Board (reference #159/09). Regular neurological and psychological test batteries and parental interviews were used to assess participants' development throughout childhood and into adulthood. Complete details of inclusion criteria and dropout rates are provided elsewhere (Eryigit Madzwamuse, Baumann, Jaekel, Bartmann, & Wolke, 2015; Gutbrod, Wolke, Soehne, Ohrt, & Riegel, 2000; Wolke, Dipl, & Meyer, 1999). At age 6 and 26 years, participants were assessed for one whole day by trained psychologists, pediatricians, and research nurses who were blind to their background characteristics.

At the age 26 year assessment, $n=109$ SGA and $n=329$ AGA of the original participants took part. The participating adults did not differ from the original participants in terms of SGA births, gender, and neonatal complications but those with complete longitudinal data were more often of higher socioeconomic status (SES) (see Table 1). Characteristics of the final sample can be seen in Table 2.

Measures

Biological variables at birth. Gestational age was determined from maternal reports of the last menstrual period and serial ultrasounds during pregnancy. Birth weight was documented in the birth records. Infants were classified as SGA if they weighed less than the sex specific 10th percentile for their respective gestational age according to national standard weight charts (1985-1986) (Riegel & Betke, 1995).

Maternal sensitivity. At age six, maternal sensitivity was observed and rated during a structured dyadic cooperation task using a standardized coding system, the “Assessment of Mother-Child-Interaction with an Etch-a-Sketch (AMCIES) (Jaekel et al., 2012). Raters received extensive training, bimonthly feedback, and frequent refreshers. Rating scales consisted of three subscales for the mother (Verbal Control, Non-Verbal Control, and Criticism, all reverse-coded) and one subscale for mother-child joint behavior (Harmony) (Jaekel, Pluess, Belsky, & Wolke, 2015; Wolke et al., 2013). These were used to create a single index of Maternal Sensitivity (Cronbach’s $\alpha=.58$). The AMCIES coding system has established high inter-rater reliabilities (Jaekel et al., 2012). For a subsample ($n=565$), the in vivo rated scores used for the current study could be compared with video-rated scores of Maternal Sensitivity (Wolke et al., 2013) and showed excellent convergence (intraclass-correlation coefficient of .76, $p<0.001$, for two master raters).

IQ. At age 6, children’s intelligence was assessed with the German version of the Kaufman Assessment Battery for Children, K-ABC Mental Processing Composite (MPC) score (Kaufman & Kaufman, 1983; Melchers & Preuss, 1991).

Table 1. Longitudinal study participants' characteristics compared to the original participants at birth

	Original participants not assessed longitudinally n = 7983	Final longitudinal sample n = 438	t/χ^2, p
SGA	25.5%	24.9%	0.10, .750
Child Sex (% male)	53.6%	49.3%	3.10, .078
Family SES at birth (n,%)			
high	1395 (20.1%)	123 (28.1%)	40.11, <.001
middle	2557 (36.9%)	191 (43.6%)	
low	2986 (43.0%)	124 (28.3%)	
OPTI	-4.23 (2.98)	-4.59 (4.83)	1.55, .122

Data are presented as M (SD) for interval scaled and percentages for categorical variables.

Table 2. Study participants' descriptive characteristics according to SGA versus AGA birth (N = 438)

	SGA
	n = 109
Birth weight (g)	1473.77 (680.04)
Gestational age (weeks)	33.34 (3.98)
Child sex (% male)	50.50%
Family SES (1 = low, 6 = high)	3.42 (1.51)
IQ at 6 years	88.82 (14.62)
Maternal Sensitivity at 6 years ^a	-.10 (.78)
Wealth score at age 26 years ^a	-.53(1.26)

Data are presented as M (SD) for interval scaled and percentages for categorical variables.

^a z-standardized according to healthy term participants' scores

Adult wealth score. Wealth was a composite score derived from a life-course interview and questionnaires at age 26 years. Critical responses that indicated poor economic success included 'no own income', or 'social benefits' (please see Table 3 for details) and were summed into a comprehensive wealth index score. Scores were reverse coded for analysis (i.e. higher scores indicated higher wealth).

Analytic Approach

Analyses were conducted using SPSS 23 (SPSS Inc., Chicago, IL). Descriptive characteristics are reported according to SGA versus AGA birth status. Maternal sensitivity and adult wealth scores were z-standardized according to the healthy term born participants in the sample. All reported tests are two-tailed using $\alpha = .05$. All models are control for gestation age and IQ at age 6. Exploratory regression models were used to identify the main effects for gestational age and maternal sensitivity (model 1). For model 2, an interaction effect between SGA birth and maternal sensitivity was added. Confirmatory model testing was performed by fitting data to four different reparametrized regression models. This method systematically varies parameters in order to test how well DST versus diathesis stress explain the data (Belsky, Pluess, & Widaman, 2013).

Both DST and diathesis stress models predict that a below average environment (i.e. low maternal sensitivity) will result in lower adult wealth for SGA adults compared with their AGA peers. However, DST predicts that an above average environment (i.e., high sensitivity) will result in significantly higher adult wealth for SGA adults compared with AGA peers who received similarly high levels of sensitivity in childhood. In contrast, diathesis stress predicts that an above average environment will result in SGA adult wealth equal to AGA peers (i.e.,

Table 3. Description of indicators for wealth in adulthood

Wealth	SGA (n = 109)	AGA (n = 329)
Receives social benefits ^a	3.7%	0.6%
Receives allowance from parents or others ^a	13.8%	20.7%
Being unemployed at present or in the past or being without occupation ^a	46.8%	34.7%
Working less than 17 hours per week, excluding students ^a	0.9%	0.9%
Having had more than five jobs ^a	4.6%	5.2%
Lives at parents'/grandparents' house, in a home, or in a sheltered accommodation ^a	37.6%	30.4%
None, secondary school or profession oriented educational qualifications ^a	58.7%	38.6%
Sometimes or often fails to pay debts or meet other financial responsibilities ^b	4.7%	3.0%
Relative poverty (lower threshold net income: €981) (Grabka, Goebel, & Schupp, 2012) ^a	27.5%	28.9%
Health limits work or leisure activities <u>OR</u> has just about enough money to be unable to afford things one needs ^c	35.2%	28.4%

^a Derived from life course interviews

^b derived from Young Adult Self Report (YASR) (Achenbach, 1997)

^c derived from the London Handicap Scale.

catch-up growth). In addition, each theoretical model has a strong and a weak version: Strong DST (3a) and strong diathesis stress (3c) models predict that individuals born AGA are not affected by the environment (i.e. a regression line with a slope of 0). In contrast, weak DST (3b) and weak diathesis stress (3d) models predict that those born AGA are influenced by the environment but to a lesser degree than those born SGA. Finally, results of each model were compared to determine which model provides the best fit to the data. All regression models were adjusted for IQ at age 6 years.

3. Results

On average, SGA adults were born at a lower gestational age and birth weight, experienced lower maternal sensitivity, were more likely to suffer from cognitive impairment, and obtained lower adult wealth scores than AGA adults (see Table 2). Maternal sensitivity at age 6 predicted higher wealth at age 26 ($\beta = .23$, $p = .002$) for both AGA and SGA adults (Model 1). Adding the interaction effect between SGA birth and maternal sensitivity (Model 2) revealed that the positive effect of sensitivity on adult wealth was stronger among SGA compared to AGA adults, ($\beta = .44$, $p = .004$).

As seen in Figure 1, the economic outcomes at 26 years of those born AGA that experienced below average maternal sensitivity did not significantly differ from those born AGA that experienced above average maternal sensitivity. However, those that were born SGA did worse than their AGA peers when experiencing below average maternal sensitivity but did increasingly better than AGA peers when experiencing above average levels of maternal sensitivity.

Differential Susceptibility Versus Diathesis Stress Model Fitting

For Model 3 data was fit to four reparametrized regression models to compare the fit of strong and weak DST (Models 3a and 3b, respectively) and strong and weak diathesis stress (Models 3c and 3d, respectively) in adults born SGA versus AGA. Model fit values indicate that the DST models (Model 3a and 3b) were a better fit for the data than the diathesis stress models (Models 3c and 3d) (see Table 4).

Both DST strong and weak models, showed similar fit, but the amount of variance explained by the two models was not significantly different, suggesting that the more

parsimonious DST strong (Model 3a) as the best fit. Confirmatory model testing indicates that the relationship between maternal sensitivity and adult wealth supports that those born SGA are more susceptible to maternal sensitivity compared to those born AGA.

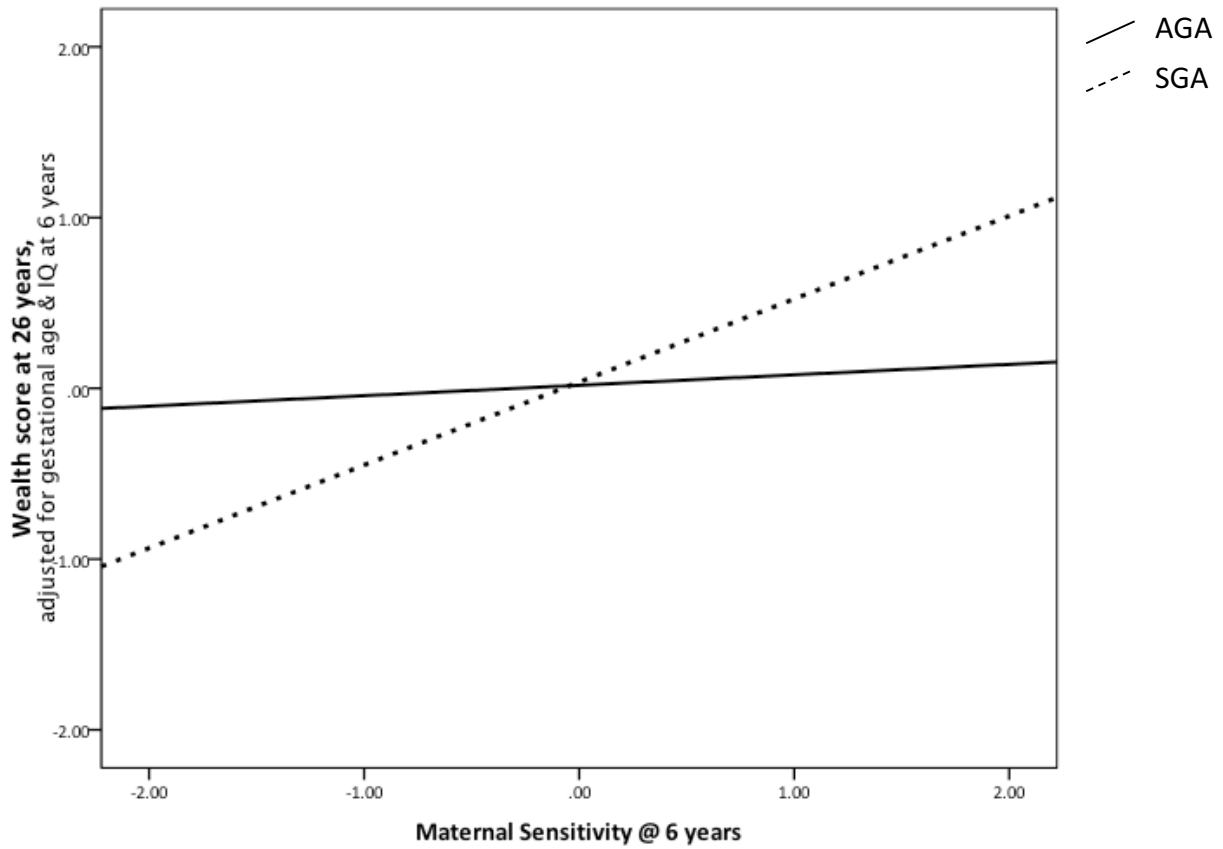


Figure 1. Differential susceptibility of SGA versus AGA children to sensitive parenting in childhood on adult wealth ($N = 438$)

Table 4. Results of alternate regression models for effect of maternal sensitivity at age 6 years on SGA versus AGA individual's economic scores at 26 years (N = 438)

Standard parameterization			Reparametrized regression equation				
Parameter	Model 1	Model 2	Parameter	Differential Susceptibility		Diathesis Stress	
				Strong: Model 3a	Weak: Model 3b	Strong: Model 3c	Weak: Model 3d
Economic Outcomes							
B₀ (Intercept)	-3.14 (.47)	-3.08 (.47)	B₀	-3.18 (-.41)	-3.11 (.43)	-3.09 (.41)	-2.69 (.46)
B₁ (sensitivity)	.23 (.08)	-.35 (.22)	B₁	.00 (-)	.09 (.09)	.00 (-)	.18 (.08)
B₂ (SGA groups)	-.04 (.12)	-.03 (.11)	C	.06 (.22)	.06 (.26)	--	--
B₃ (interaction)	--	.44 (.15)	B₃	.52 (.13)	.53 (.13)	.21 (.08)	.32 (.09)
R²	.175	.191	R²	.189	.191	.172	.181
F vs. 1	--	8.368	F vs. 3b	0.950	--	5.125	5.245
df	--	432	df	432	--	432	432
p	--	.004	p	.330	--	.006	.022
	--	--	F vs. 3c	9.300	5.125	--	4.956
	--	--	df	432	432	--	432
	--	--	p	.002	.006	--	.0265
AIC	-14.029	-20.432	AIC	-21.469	-20.432	-14.161	-17.008
BIC	-11.914	-18.266	BIC	-19.354	-18.266	-15.031	-12.088

AIC, Akaike information criterion; BIC, Bayesian information criterion. Tabled values are parameter estimates with their standard errors in parentheses. Significant parameter estimates are marked bold. F versus 1 stands for an F test of the difference in R² for Model 2 versus Model 1. F versus 3b stands for an F test of the difference in R² for a given Model versus Model 3b.

4. Discussion

This is the first study to show that individuals born SGA are more susceptible, not more vulnerable, to the long-term effects of sensitive parenting compared to their AGA peers. Confirmatory model testing showed that maternal sensitivity played a significant role in predicting the wealth outcomes of adults born SGA, while wealth of those born AGA was relatively unaffected by maternal sensitivity. SGA children who had received lower than average maternal sensitivity fared worse than AGA peers, but SGA children who had experienced higher than average rates of maternal sensitivity were more economically successful in adulthood than their AGA peers. These findings support the conclusion that individuals born SGA are more susceptible, for better-or-worse, to environmental influences than those born AGA, not more vulnerable as traditionally thought.

Consistent with past studies, the adults born SGA in our study on average showed lower wealth in adulthood compared to their AGA peers. SGA born individuals' lower composite wealth scores indicate that they may need more social stimulation and support than their AGA peers. This could be the result of the early developmental deficits of those born SGA accumulating into academic difficulties (Li et al., 2017) and later economic impacts such as lower weekly earnings (Strauss, 2000). Understanding what environmental factors, such as maternal sensitivity, act as protective factors for those born SGA is an important step in supporting their life-course outcomes.

As we predicted, above average maternal sensitivity was positively associated with wealth among SGA born adults. Although, given average or below average maternal sensitivity those born SGA demonstrated lower wealth in early adulthood. While maternal sensitivity

works to better later life outcomes for those born with a neonatal risk (Boyce, et al, 2015), average maternal sensitivity may not be enough to foster the best possible outcomes for those born SGA. This may be because SGA born individuals may require a higher level of support and scaffolding than AGA peers to help overcome their developmental impairments (Jaekel, 2016).

Traditionally, SGA birth has been viewed as a developmental deficit, seeing the individual born SGA as vulnerable to environmental experiences. However, adverse intra-uterine conditions could program them to be more adaptive to uncertain environments (Pluess & Belsky, 2011). Differential susceptibility has been tested among other at-risk neonatal groups, such as VLBW and LBW (Jaekel et al., 2015) and diathesis stress was a better statistical fit to explain long-term outcomes, possibly resulting from the neurocognitive impairments often faced by those born VLBW and LBW overpowering the conflicting effect of their potentially increased susceptibility. However, those born SGA do not experience the same severity of cognitive impairments (Gutbrod et al., 2000) allowing high susceptibility and developmental plasticity. While previous studies have supported DST among SGA children born at term SGA, it may be difficult to confirm strong environmental effects among SGA born preterm because of the severity of complications associated with preterm birth (Li et al., 2017). However, our results support susceptibility across the full gestational range of those born SGA.

Implications

With limited resources to invest, it becomes increasingly important to identify what groups of individuals will benefit most from intervention. The findings of this study point towards prioritizing investments in childhood interventions that help support and teach sensitive parenting practices for mothers of infants born SGA.

Strengths and Limitations

This is the first study to utilize competitive confirmatory model testing to confirm differential susceptibility among individuals born SGA in a large sample of neonatal at-risk children across the full gestational age range assessed prospectively from birth to adulthood. Those lost to follow-up did not differ from adult participants with regard to the rate of SGA birth, sex, and neonatal risk, however, as in most other longitudinal studies low SES families were less likely to continue participation studies (Hille, Elbertse, Gravenhorst, Brand, & Verloove-Vanhorick, 2005). Our study used quality assessments such as our maternal sensitivity assessment, a reliable comprehensive observational measure with an excellent intraclass-correlation coefficient (Cicchetti, 1994), and a comprehensive composite wealth score at age 26. Given significant changes in neonatal and obstetric care over the past three decades there is room to wonder if our results are generalizable to neonatal at-risk children born today. However, so far there is little evidence that increased survival rates have led to higher quality of survival (Moore et al., 2012). Indeed, comparison of Bavarian Longitudinal Study findings with more recent cohorts have shown that the underlying processes and mechanisms do not differ between cohorts as a function of time (Wolke, Baumann, Strauss, Johnson, & Marlow, 2015; Wolke et al., 2015). This suggests that the findings presented here are valid and important.

5. Conclusion

Individuals born SGA are more susceptible to sensitive parenting in childhood than their AGA peers. If maternal sensitivity was lower than average, SGA adults fared worse economically but when sensitive parenting was above average, they did much better economically in young adulthood. It appears that intrauterine malnourishment alters susceptibility to environmental experiences in a for-better-or-for-worse way. Increasing parental sensitivity is an important avenue to interventions aimed at improving life-long outcomes of children born SGA.

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Vita

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