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The contribution of attenuated selection *in utero* to small-for-gestational-age (SGA) among term African American male infants

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ABSTRACT

Natural selection conserves mechanisms allowing women to spontaneously abort gestations least likely to yield fit offspring. Small gestational size has been proposed as an indicator of fitness observable by maternal biology. Previous research suggests that exposure to ambient stress in utero results in more "culling" of small fetuses and therefore lower rates of small-for-gestational-age (SGA). However, African American women persistently have higher rates of SGA than non-Hispanic white women, despite experiencing more ambient stress. This paper tests whether attenuation of the stress response among highly stressed African American women, as suggested by the weathering hypothesis, may help to explain this apparent inconsistency. We apply time-series modeling to over 2 million African American and non-Hispanic white male term births in California over the period of January 1989 through December 2010. We test for the parabolic (i.e., "U" shaped) relationship, implied by an attenuated stress response, between unusually strong labor market contraction and the rate of SGA among African American term male infants, and a linear relationship among non-Hispanic whites. We find the hypothesized parabolic relationship among term male African American infants. As expected, we find a linear relationship between unexpected layoffs and the rate of SGA among term male non-Hispanic whites. These results are robust to sensitivity analyses. These results may help to explain the high rates of SGA among term male African American infants, despite greater maternal exposure to ambient stress during pregnancy.

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Introduction

Much literature argues that natural selection conserves mechanisms that allow women to spontaneously abort gestations least likely to yield fit offspring (Baird, 2009; Forbes, 1997; Møller, 1997; Stearns, 1987; Trivers & Willard, 1973; Wells, 2000). This "selection in utero" implies that somewhere in the biology of pregnant women is a means to estimate the ratio of likely grandchildren (a result of fit offspring) to maternal investment required to sustain offspring from gestation through reproductive age (Baird, 2009; Forbes, 1997; Møller, 1997; Stearns, 1987; Wells, 2000). Relatively low ratios presumably put a gestation at greater risk of spontaneous abortion (Wells, 2000).

This literature further argues that the ratio falls when ambient stressors threaten maternal and infant well-being because stressed mothers have fewer resources to invest in offspring that need more investment to survive (Catalano et al., 2012b). The maternal stress response, in other words, adjusts the grandchildren/investment ratio of a gestation to reflect changing environments. Gestations that would yield live births in relatively benign times may, therefore, end in spontaneous abortion during stressful times (Baird, 2009).

The argument for selection *in utero* implies that male fetuses should exhibit greater risk of spontaneous abortion than females. This elevated risk arises from the fact that sons, despite receiving greater maternal investment, more likely die before completing their reproductive years than do daughters (Clutton-Brock, 1991; Helle, Lummaa, & Jokela, 2002; Powe, Knott, & Conklin-Brittain, 2010). In fact, male infants experience higher mortality than any other sex-by-single-year age group under the age of 60 in every society for which we have reliable statistics (Human Mortality Database).

Observed data support the argument for selection *in utero*, particularly against males. Fewer than 30% of conceptions yield live births, with males on average predominating among the spontaneous abortions (Boklage, 1990; Byrne & Warburton, 1987;

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Catalano, Margerison-Zilko, et al., 2012; Catalano, Saxton, et al., 2012; Hassold, Quillen, & Yamane, 1983; Roberts & Lowe, 1975). The ratio of male to female fetal deaths rises during stressful times while that of male to female live births (i.e., the secondary sex ratio) falls (Catalano, 2003; Catalano & Bruckner, 2005; Catalano, Zilko, Saxton, & Bruckner, 2010). Males from birth cohorts with low secondary sex ratios have lower infant mortality rates, die less frequently between infancy and reproductive age, and live longer than those from high sex ratio cohorts, suggesting that less fit gestations were not conserved (Catalano & Bruckner, 2006; Catalano, Saxton, Bruckner, Goldman, & Anderson, 2009).

Selection *in utero* requires indicators of fetal fitness detectable by maternal biology. Wells (2000) suggests that these indicators include fetal size because small-for-gestational-age (SGA) increases the risk of fetal death, small male infants experience the highest death rates of any other age by sex group throughout reproductive life, and males of small stature appear less successful in mate finding than larger males (Leger et al., 1997; Ma & Finch, 2010; Sear, 2010).

Consistent with selection against SGA fetuses, Catalano, Goodman, et al. (2012) report that weekly birth cohorts of term males have fewer SGA members if exposed *in utero* to unexpectedly poor economies, a known population stressor (APA, 2012). The analyses focused on term infants (i.e., those with gestations of at least 37 completed weeks) because medical interventions have increasingly yielded preterm live births from pregnancies that, through most of human evolution, would have ended in spontaneous abortion or stillbirth. Following this logic, term SGA births may result from a relaxed selection filter and vary inversely with the strength of a population stressor. These results not only support the argument that ambient stressors may trigger selection *in utero*, but may also shed light on disparities in SGA between African American and non-Hispanic white women.

Rates of SGA among term infants have declined over time, but are persistently higher among African American women than non-Hispanic white women (Ananth, Balasubramanian, Demissie, & Kinzler, 2004; Kramer, Ananth, Platt, & Joseph, 2006; Margerison-Zilko, Catalano, Hubbard, & Ahern, 2011). In 2000, 16% of African American term infants were SGA, compared to 9% of white term infants, down from 21% and 12%, respectively, in 1975 (Ananth et al., 2004). An extensive literature describes mechanisms thought to connect stress to adverse pregnancy outcomes (Giscombé & Lobel, 2005; Hobel, Goldstein, & Barrett, 2008; Rich-Edwards & Grizzard, 2005; Shannon, King, & Kennedy, 2007). This literature posits that the higher levels of cumulative life stress and prenatal stress reported by African American women compared to their non-Hispanic white counterparts could help explain the persistent racial disparities in birth outcomes (Giscombé & Lobel, 2005; Hobel et al., 2008; Lu & Chen, 2004; Rich-Edwards & Grizzard, 2005; Shannon et al., 2007).

The racial disparity in rates of SGA would appear inconsistent with selection *in utero* if, as the literature suggests, African American women experience more ambient stressors than non-Hispanic white women (Hatch & Dohrenwend, 2007; Lu & Chen, 2004) and report more experiences of financial stress (Vines, Ta, Esserman, & Baird, 2009). According to the selection *in utero* argument, higher stress levels should lead to greater "culling" of SGA male fetuses and, therefore, lower rates of SGA among male term infants.

The literature on the embodiment of cumulative stress suggests mechanisms that may reconcile selection *in utero* with endemically high levels of SGA among African American infants. As argued in the seminal work of Selye (1946, 1956), and developed in much contemporary literature (Ellis & Boyce, 2008; McEwen, 1998), natural selection conserved the stress response to protect human fitness from environmental threats. The capacity to mount and

sustain a stress response, however, has limits. Each episode diminishes some fraction of remaining capacity, which may also decline with aging. Successive responses therefore decline in either or both generality or intensity implying that some benefits of the stress response also diminish with use and age (Selye, 1956).

The relatively high stress loads persistently born by African American women – particularly their experiences of racism, discrimination, and the intergenerational transfer of financial disadvantage – could accelerate depletion of their stress response consistent with the "weathering hypothesis" (Geronimus, Hicken, Keene, & Bound, 2006). African American women, on average, would therefore have less capacity with which to respond to stressors than would other, less stressed, women of the same chronological age. While both groups might respond equivalently to relatively low doses of environmental challenge, an increasingly virulent stressor would exhaust capacity among African American women before doing so among others. The "benefits" of the stress response would, therefore, decline first among African Americans. Selection in utero against SGA fetuses might, for example, become less effective. That is, whatever mechanism operates to induce spontaneous abortion of fetuses deemed least likely to survive to reproduction in stressful environments may fail to operate at high levels of ambient stress among African Americans due to response attenuation. This circumstance could help explain, post hoc, the much noted endemically high rate of SGA among African American

Beyond offering *post hoc* explanations of observed rates of SGA, lessened selection *in utero* would predict, *a priori*, a "U" shaped (i.e., parabolic) relationship between ambient stressors and the rate of SGA among African American term male infants. Rising doses of ambient stressors would induce greater spontaneous abortion among the disproportionately male population of fetuses with low grandchildren to investment ratios, leading to lower rates of SGA. At some level of rising dose the stress response would, however, diminish among African American women and selection *in utero* against their SGA male fetuses would abate. Stress-induced selection against non-Hispanic white SGA male fetuses would continue unabated. The incidence of SGA among African American infants, therefore, would rise above that of non-Hispanic whites even if both groups experience the same high level of ambient stressors.

We determine whether the above prediction proved accurate for 312,045 term African American male infants born in California over the 1146 weeks starting January 1, 1989. More specifically, we test the hypothesis that temporal variation in the rate of SGA among African American, but not non-Hispanic white, male infants will exhibit a parabolic dose response to a known population stressor — unexpected increases in job loss due to slackening demand for labor.

We focus on disemployment (i.e., involuntary job loss) as a population stressor because (1) the incidence of stressful job and financial experiences reportedly increase when the labor markets contract (Catalano & Dooley, 1983; Dua & Smyth, 1993; Larson, Wilson, & Beley, 1994; Leigh, 1985; Minchin, 2009); (2) stressful job and financial experiences reportedly increase the risk of experiencing other stressors less intuitively associated with the labor market (Catalano, Dooley, & Rook, 1987; Rook, Dooley, & Catalano, 1991; Vinokur, Price, & Caplan, 1996); (3) job loss and insecurity among workers increases the stress levels reported by their partners (Howe, Levy, & Caplan, 2004; Rook et al., 1991); and (4) job loss creates strife between partners (Rook et al., 1991; Vinokur et al., 1996). Catalano, Goodman, et al. (2012) report, moreover, that contracting labor markets predict falling rates of SGA among male term births in California.

We use time-series analysis to determine whether the rate of SGA among term male infants differs from its expected value in

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