INTERLEUKIN 1 BETA AS A PREDICTOR OF LIFE HISTORY STRATEGY AND IMPULSIVITY IN HUMANS

by

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ABSTRACT

Previous research shown that early-life environmental conditions serve as a predictor of a variety of related phenotypes later in life such as impulsivity, present focus, risky sexual behavior, and health-related risk taking. Within the context of life history theory (LHT), these traits are indicative of differences between life history strategies (LHS) in different individuals. Although a link between ecologically-dependent mortality threats and life history tradeoffs have been identified, no previous research has considered the role that internal factors could play in LHS development. The present research identified interleukin 1 beta (IL-1β) as a potential indicator of overall somatic condition and sought to identify a relationship between serum IL-1β levels and LHS. Participants provided whole blood samples and completed questionnaires to assess impulsivity and present focus. Data collected indicated higher IL-1β levels were correlated with a faster LHS. These results suggest internal factors, in some cases unrelated to the external environment, may calibrate LHS and affect behavior throughout life.

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Background

Life History Theory

Life history theory (LHT) is based on the understanding within evolutionary biology that the most basic goals of an organism are the pursuit of survival and reproduction. This chance of successfully reproducing is known as biological fitness and can vary greatly between members of the same species due to differences between them.

LHT posits that each organism has a limited amount of energy available to be spent to maximize biological fitness. This energy must be effectively budgeted between biological processes such as growth, maintenance, and reproduction. In other words, the body must "decide" when and where to allocate its limited energy in order to give the organism the best chance of reaching maturity and having offspring. Furthermore, energy priorities are not only determined by species—energy allocation varies between individuals of the same species and changes within individuals throughout life. For example, age of onset of puberty can vary greatly between people, and research has shown that as puberty begins and investment in development of secondary sex characteristics increases, energy investment in some facets of the immune system decreases (Del Giudice, Kaplan, & Gangestad, 2015).

To most efficiently use the energy available to increase biological fitness, organisms adopt a life history strategy (LHS) that best fits individual circumstances. These strategies exist on a continuum from slow to fast, referring to the speed at which the organism will progress through life. Fast strategists are characterized by a shorter lifespan and usually reach sexual maturity relatively early. They often have a smaller body size and have a large number of offspring. On the other hand, slow strategists tend to have longer lifespans and invest more energy in growth before reproduction, leading to increased body size and later onset of puberty.

Slow strategists often have fewer offspring, but are better equipped to invest heavily in their care.

These strategies are easily observable when comparing two different species. For example, an elephant, which may have five calves over the course of its seventy-year lifespan, certainly has a much slower life strategy than a mouse, which could have dozens of pups over during its two years of life. However, the reasons for differences in strategy among individuals of the same species are less intuitive. These differences in LHS between individuals of the same species—humans—will be the main topic of discussion in this paper. Humans clearly have a slow life strategy when compared to most other species, but this relative interspecies difference will not be further discussed here. All further references to slow or fast strategists will be in relation to the average human.

Differences in the LHS of humans also exist to provide each individual with the greatest biological fitness. The primary determinant of one's strategy is mortality risk. Individuals with a high mortality risk due to any number of causes would most effectively use their energy to mature quickly in order to reproduce. If a person is at an increased risk of dying, delaying reproduction in favor of growth and development is not evolutionarily advantageous. These fast strategists also tend to be more present-focused, impulsive, and willing to take risks in order to receive a reward sooner rather than later. In the opposite scenario, delaying reproduction in favor of growth and development is adaptive for individuals with a lower mortality risk. With a less salient threat of death, the individual can invest more in him/herself first in order to be better equipped to care for offspring later. Understandably, human slow strategists tend to be more future-oriented, less impulsive, and more willing to delay gratification for a later reward.

Previous research has revealed the role that environmental factors in early childhood can play in calibrating LHS. Early life conditions are used to predict conditions later in life, and so an organism can make predictive adaptive responses to adjust the LHS to best fit the environment predicted for adulthood (Nettle, Frankenhuis, & Rickard, 2013). Children raised in a harsh or unpredictable environment have been shown to develop a faster life strategy (Brumbach, Figueredo, & Ellis, 2009; Hampson et al., 2016). Interestingly, research has shown that children raised in harsh environments also tend to begin puberty at an earlier age than those raised in more benign environments (Rickard, Frankenhuis, & Nettle, 2014). During development, the body becomes calibrated to a faster life strategy due to increased mortality risk associated with life in a harsh environment. Clearly, external factors play a role in the development of a life history strategy.

Although the link between external, environmental factors and differences in LHS in humans has been identified, researchers are only beginning to consider the role that internal factors might also play in LHS development. Recently published findings revealed that harsh environments in childhood may have effects on LHS that are mediated by health status, suggesting that internal factors are involved in LHS development (Chua et al., 2017). As noted earlier, LHS is largely dependent on mortality risk, and the internal environment of an organism reasonably serves as a major determinant of mortality risk along with the external environment. These internal factors are broadly referred to as somatic integrity and include age, health, genetics, and history of biological stress. Low somatic integrity would include conditions such as old age, poorly adaptive genes, and high levels of stress. Because somatic damage is indicative of a heightened mortality risk, these factors influencing somatic integrity are likely related to the development of LHS. Our research sought to determine the existence of this relationship.

Interleukin 1 Beta

In order to understand how somatic integrity could be related to LHS, a means for quantifying somatic integrity had to be identified. Recent discoveries have shown that the immune system, in addition to its roles in defense and maintenance, also behaves as a sort of interoceptive sensory system. In other words, the immune system constantly senses the somatic state of the body and relays this information to the central nervous system (CNS) so that behavior and biological processes can be adjusted. We hoped to identify a biological signal that the body could potentially be using to inform the CNS of somatic damage in order to shape behavior.

Our attention turned to cytokines, proteins produced by immune cells as part of the innate immune response. Cytokines are known to act as autocrine, paracrine, and endocrine signaling molecules, and are typically found in picomolar concentrations, in contrast to hormones, which tend to circulate in the nanomolar range. During infection or injury, concentrations of cytokines can increase greatly to encourage inflammation and signal immune cells to activate and travel to the site of the damage.

Recent studies have found that physical and psychological stress in early life may encourage a proinflammatory state of the immune system that can persist throughout life. In fact, early childhood stressors are believed to trigger long-lasting modifications within immune cells to encourage production of cytokines and reduce the sensitivity of immune cells to inhibitory signals (Miller, Chen, & Parker, 2011; Fagundes, Glaser, & Kiecolt-Glaser, 2013). These findings suggest increased cytokine production could potentially be a means of transducing early childhood external stressors into lifelong biological changes that could in turn influence behavior (Bilbo, 2009). These long-term changes in cytokine production can be seen as adaptive for a fast-

life strategist because increased cytokine production means a stronger and more responsive innate immune system at the cost of potential autoimmune diseases and diseases of inflammation in later life.

Although there are dozens of different cytokines in humans, interleukin 1 beta (IL-1β) became the focus of this study for several reasons. First, previous research has revealed that IL-1β is the major regulator of inflammation in humans. IL-1β has been implicated as the primary culprit for inflammation in a variety of autoimmune and autoinflammatory diseases, including diabetes mellitus type II, rheumatoid arthritis, osteoarthritis, cyropyrin-associated autoinflammatory syndromes (CAPS), urate crystal arthritis (gout), and many more (Dinarello, 2011). In addition, IL-1β levels are known to increase with age, and research has shown that IL-1β production increases during both physical and psychological stress (Brydon et al., 2005; Goshen & Yirmiya, 2009). As IL-1β plays a central role in inducing certain autoinflammatory diseases, increases with age, and is released in response to stress, we believed IL-1β could serve as an indicator of somatic damage.

Furthermore, research has shown that IL-1β is able to affect a variety of CNS processes. Although most circulating IL-1β is unable to directly affect the brain due to the blood-brain barrier, peripheral IL-1β is able to induce IL-1β expression in the brain with signals via vagal afferents (Dantzer et al., 1998). Receptors for IL-1β are present in several different brain regions, and IL-1β is known to alter neurotransmitter release as well as neurogenesis within the CNS (Farrar et al., 1987; Donzis & Tronson 2014).

Unsurprisingly, IL-1β can cause behavioral changes as well. Since the late 1980's, IL-1β has been known to affect the hypothalamic-pituitary-adrenal (HPA) stress response and can directly cause hormone release from the pituitary gland (Bernton et al., 1987). In the 1990's, IL-

1β was shown to induce fever and sickness behaviors—lethargy, depression, and loss of appetite (Kent et al., 1992; Dantzer & Kelley, 2007). Since that time, the effects of the cytokine on behavior continued to be revealed. Research discovered that IL-1β even plays a role in modulating aggression and hostility (Zalcman & Siegel, 2006).

Because IL-1β seems to be a good overall indicator of somatic integrity and possesses the ability to influence the CNS in a variety of ways, we chose to focus on the relationship between IL-1β levels and observed behavioral differences in humans. Specifically, we predicted that elevated IL-1β levels, indicative of greater somatic damage and heightened mortality risk, would be correlated with a faster life history strategy as seen through increased present-focus and impulsivity.

Methods

Participants

This study gathered data from 130 young adults (65 male, 65 female). The participants were college students recruited from the psychology department of Texas Christian University or individuals from the surrounding community in Fort Worth, TX. To be eligible to participate in the study, participants had to meet a series of requirements meant to minimize differences on IL-1β levels due to activity. Participants were required to (1) be non-obese (body mass index less than 30 kg/m^2), (2) be a non-smoker, (3) have no history of chronic medical conditions or psychiatric disorders, (4) have no history of disease in the past two weeks, (5) not drink alcohol, exercise, or take anti-inflammatory medications for the 48 hours before the study session, (6) not eat or drink the morning of the session, and (7) not be taking contraceptive medication. Additionally, females were scheduled to attend sessions four to nine days after the onset of their menstrual period.

Written consent forms were obtained from all participants prior to the study sessions. Community participants were compensated for their time with a gift card, and TCU participants were given the choice between the gift card or credit toward a psychology course as compensation.

Procedure

Each study session was held at 7:30am to control for circadian fluctuations in IL-1β levels. Participants were brought to our computer lab where they first completed a computer-based questionnaire including three measures of present focus and impulsivity. After completing the questionnaires, the participants were taken one by one to the wet lab for a blood draw. Using venipuncture, a trained phlebotomist drew 75 mL of whole blood for later analysis to quantify IL-1β levels.

Measuring Present Focus and Impulsivity

Three self-report measures will be used to evaluate participant impulsivity and temporal focus. These characteristics should reflect the tendency of individuals to favor either present or future rewards. This tendency is an important facet of LHS, as fast strategists favor instant gratification while slow strategists are more inclined to delay gratification for a larger payout later.

The first self-report measure was the Barratt Impulsivity Scale (BIS-11) that is a commonly used scale to assess impulsivity (Patton et al., 1995). The BIS-11 consists of a series of statements, and the participant rates on a numerical scale how strongly they feel that the statement applies to them. Items on the BIS-11 include statements like “I act on the spur of the moment” or “I am restless at the theater or lectures.” High scores on the BIS-11 indicate higher levels of impulsivity.

The next measure was the Delayed Gratification Index (DGI), which serves to evaluate present focus (Hoerger et al., 2011). The DGI is similar to the BIS-11 in that it is a series of statements where the participant rates on a numerical scale how strongly they feel that the statement applies to them. DGI items include statements like "I can resist junk food when I want to" and "I worked hard in school to improve myself as a person." High scores on the DGI indicate less present focus—in other words, increased future orientation.

The final psychological assessment was the Future Orientation Scale (FO). This measure assesses future orientation (Steinberg et al., 2009). The FO includes a series of paired statements about opposite personality types. An individual would read both statements and then select which statement is most applicable to him/herself and how strongly the statement fits. For example, one item might include the statements "I think about all possible outcomes before a decision" and "it's not necessary to think about every little possibility." High scores on the FO indicate increased future orientation.

Measuring IL-1β Levels

With whole blood samples obtained from each participant, in vivo IL-1β levels were measured to assess general inflammatory activity. Using an enzyme-linked immunosorbent assay (ELISA), serum levels of IL-1β were quantified.

Factors Affecting IL-1β Levels

To control for factors that could influence participant IL-1β levels, several steps were taken. Using self-report measures, we collected data for participant age, gender, ethnicity, amount of sleep, and amount of physical activity. Additionally, participant body mass index was calculated after direct body measurements with a weight scale and stadiometer. Each of these

factors is known to affect inflammation, so the data collected were used to control for the factors during statistical analysis.

Results

After analyzing the psychological measure scores and the quantified serum IL-1β levels obtained from each participant, a relationship between present focus and IL-1β was observed. Our results supported our hypothesis, and all three psychological measures were correlated with the IL-1β levels in our participants. As expected, higher scores on the BIS-11, indicative of higher impulsivity, were correlated with increased serum IL-1β. This was indicated by a moderately strong, positive correlation between BIS-11 and serum IL-1β ($r = 0.42$, $p < 0.01$). Higher scores on the DGI and the FO scales, indicative of less present focus, were correlated with decreased serum IL-1β. These inverse correlations between serum IL-1β and both the DGI ($r = -0.37$, $p < 0.01$) and the FO ($r = -0.34$, $p < 0.05$) are also moderately strong relationships. All findings were statistically significant.

Additionally, after controlling for factors known to influence inflammation (gender, amount of sleep, ethnicity, age, body mass index, amount of physical activity) the correlations between the measures of present focus and IL-1β remained.

Discussion

The results of the study supported our hypothesis that increased serum IL-1β levels are correlated with increased impulsivity and present focus, typical of a fast life strategy. As age, genetics, stress, or disease, reduce the perceived somatic integrity of the body, the immune system may be increasing production of this cytokine. This evidence suggests that IL-1β may modulate LHS by acting as a biological signal to inform the CNS of somatic damage.

A number of biological mechanisms could be responsible for producing the changes in IL-1β production because there are a variety of factors that influence the immune system and somatic integrity; however, a likely candidate is epigenetic changes to immune cells that may occur during stress and injury, especially during development. Modifications to the DNA of cytokine-producing cells have the potential to alter the expression IL-1β in the long-term.

The ways in which IL-1β may affect behavior are unknown. Possibilities include long-term neuronal changes such as altered synaptic connections and neurogenesis in specific areas of the brain as well as changes to neurotransmitter levels. IL-1β is known to affect all of these processes through action on IL-1β receptors in the brain. The effects of these receptors are not fully understood, but further research on their intracellular effects and studies on large-scale effects of IL-1β on the brain would shed light on the ways that IL-1β may able to affect behavior.

Additionally, further research may consider how different variants of the IL-1β allele may alter the observed relationship between the cytokine and LHS. Variations within the IL-1β gene in some individuals may enhance or diminish the effect of IL-1β on the CNS or perhaps make the gene less responsive to the intracellular signals altering IL-1β expression after stress or injury.

Overall, these findings are significant for the study of LHT and understanding the ways human behavior may be shaped by health and stress. This study has led to many new questions regarding the function of cytokines in behavior. Understanding the impacts of early life external and internal factors on traits later in life is important for the health of people around the world, particularly those who spend their formative years in harsh environments.

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