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# Attachment and psychoneuroimmunology

Katherine B Ehrlich

In this review, I outline how attachment experiences in adulthood are thought to be related to the immune system. After a brief primer on the two branches of the immune system, I describe a theoretical model that explains how adults' attachment orientation could influence various immune processes. I then review recent findings documenting novel associations between attachment orientation and measures of the immune system, including inflammatory processes and cellular immunity. I conclude with a discussion about future directions focused on how we can advance our understanding about the role of attachment in shaping immune processes in ways that could shape our health over the lifespan.

## Address

University of Georgia, Department of Psychology and Center for Family Research, 125 Baldwin Street, Athens, GA 30602, USA

Corresponding author: Ehrlich, Katherine B ([kehrlich@uga.edu](mailto:kehrlich@uga.edu))

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## Introduction

*Psychoneuroimmunology* (PNI) is a term used to describe research on the interplay among psychological factors (e.g. behavior, relationships, cognitions, stress), neural and endocrine systems, and the immune system [1<sup>\*</sup>]. This interdisciplinary field has brought forth remarkable insights that highlight how the social world can 'get under the skin' to influence immune, neural, and neuroendocrine processes in ways that might have consequences for later health. For this selective review, I will focus on the *immunology* portion of PNI, but I encourage readers to read other reviews that focus on the neuroscience [2,3] and neuroendocrine [4] aspects of attachment.

In recent years, there has been interest in understanding links between attachment and various systems in the body (e.g. autonomic nervous system, neuroendocrine processes [5–7]). Further, there is compelling evidence that attachment experiences are related to measures of physical health [8]. Many PNI studies have examined the ways in which social relationships (e.g. social isolation and

loneliness, social support, conflict) are thought to influence measures of the immune system, including markers of inflammation and cellular immunity [9]. To date, only a handful of studies have examined how individuals' *attachment orientation* might influence immune processes, but there is growing interest in testing these links [10<sup>\*</sup>]. Attachment theory is particularly well suited to explain why certain qualities of close relationships could influence the immune system. Attachment theory describes how the availability of a responsive and dependable caregiver or relationship partner influences healthy development across the lifespan [11]. In the sections that follow, I begin with a brief overview of the immune system, and I describe a theoretical framework that outlines how attachment-related experiences can become biologically embedded in immune cells. Then, I review recent studies that have examined links between attachment orientation and immune processes in adulthood. I conclude with discussion of directions for future research.

## The immune system: a brief primer

The human immune system has evolved as a defense against bacteria, viruses, parasites, and other pathogens. The immune system is divided into two categories, including the innate and adaptive immune systems [12]. The innate immune system acts as the first line of defense against invaders that make their way past physical barriers (e.g. skin and mucous membranes), and it includes some white blood cells like macrophages that identify, contain, and eliminate bacteria and other pathogens. These cells produce and secrete cytokines, which are hormone-like messengers that play a critical role in the inflammatory response. The adaptive immune system, in contrast, includes cells that work to recognize and respond to specific infections (e.g. influenza). As such, the adaptive response is more complex and has a slower response time relative to the innate immune system. This system includes T cells and B cells, both of which help defend the body against infection (with the help of cytokines and antibodies) once the specific invader has been identified.

For both the innate and adaptive systems, regulation and balance are key to healthy functioning. For example, with regard to the innate immune system, the inflammatory response is essential for survival but it must be carefully regulated; otherwise, chronic inflammation can become persistent and contribute to the emergence of multiple diseases of aging [13<sup>\*\*</sup>,14]. Similarly, adaptive immune responses that are out of balance underlie many chronic diseases, such as allergies and asthma [15], and insufficient antibody production can result in risk for infection despite vaccination [16].

## A theoretical framework for attachment and the immune system

In the last several decades, evidence has emerged suggesting that social experiences can influence both adaptive immunity as well as systemic inflammation [17]. Some theoretical models highlight the importance of social experiences that take place early in development that might serve as ‘programming’ factors for the immune system [13<sup>\*\*</sup>,18]. In these models, exposure to chronic stressors incites a *proinflammatory phenotype*, which becomes embedded within key cells of the immune system: monocytes and macrophages. Across development, this proinflammatory phenotype can result in chronic, low-grade inflammation, which is increasingly recognized as a fundamental contributor to many of the chronic diseases of aging, including cardiovascular disease, diabetes, stroke, some cancers, and various autoimmune conditions [14,19–21]. Other researchers have emphasized how ongoing social experiences in adulthood, such as conflict in close relationships and ongoing stress, might shape immune processes [22]. It is likely that both early childhood relationships and current relationship experiences have important connections to immune functioning [23]. There has been less theoretical development regarding the notion that relationship experiences could influence adaptive immunity; however, findings suggest that chronic stressors are often associated with hyperactivation or suppression of the adaptive immune response [17,24].

As my colleagues and I have described previously [10<sup>\*</sup>], we argue that attachment is likely to play a role in shaping immune processes via two routes. First, we expect that direct links between attachment orientation and immunologic activity will emerge as researchers continue to study these processes. This hypothesis results from the understanding that insecure attachment is a risk for depressive symptoms as well as loneliness and problematic social relationships, all of which have been shown to be related to inflammatory activity and cellular immunity [25–29]. Second, we have argued that attachment orientation may serve as an important moderator of the already documented connections between psychosocial stressors and inflammation [24,30]. For example, attachment security may buffer against the heightened inflammatory consequences associated with low socioeconomic status [31]. Conversely, insecurely attached individuals who are also facing chronic or acute stressors may have greater inflammatory responses than securely attached individuals who are experiencing similar levels of stress.

## Evidence linking attachment and immune processes in adulthood

### Attachment and the innate immune system

A handful of studies have examined the association between self-reported attachment orientation and inflammation. Evidence for a link between attachment orientation and inflammation comes from a study that examined

inflammatory responses following a mildly stressful social interaction [32<sup>\*\*</sup>]. Couples participated in a laboratory discussion in which they were instructed to resolve conflict in their relationship. Attachment avoidance (but not anxiety) was positively associated with production of IL-6 following the conflict discussion.

Intriguing evidence linking adult attachment orientation to inflammatory response comes from a sample of patients undergoing coronary artery bypass graft surgery [33]. Patients reported on their attachment orientation prior to surgery, and researchers measured markers of circulating inflammation pre-surgery and post-surgery. Although attachment orientation was unrelated to post-surgery levels of two markers of inflammation (C-reactive protein and tumor necrosis factor- $\alpha$ ), attachment anxiety (but not avoidance) was related to higher levels of IL-6 after surgery when controlling for pre-surgery levels.

Other studies, however, have not found associations between attachment and inflammation. In a sample of 94 married couples composed of mostly White participants, Uchino and colleagues [34] did not find any links between attachment orientation and circulating levels of inflammation. Notably, however, this analysis examined the role of attachment after accounting for spouses’ feelings of ambivalence, which was correlated with attachment avoidance, so it is unclear whether attachment avoidance and anxiety were correlated with inflammation in that sample.

### Attachment and the adaptive immune system

One of the first studies to examine links between attachment orientation and the immune system studied these processes in a small sample of female nurses. Researchers measured both the frequency and function of natural killer (NK) cells, which play an important role in responding to virus-infected cells and tumor cells. Analyses revealed that attachment was not associated with the frequency of NK cells, but attachment avoidance was associated with lower NK cell cytotoxicity [35]. Follow-up analyses showed that this pattern was evident over a one-year period [36]. This lowered cytotoxicity, if sustained, could result in clinically significant health consequences (e.g. impaired response to viruses).

More recently, Fagundes and colleagues [37<sup>\*</sup>] examined links between attachment orientation and cellular immunity by studying Epstein–Barr virus (EBV) expression in patients who were being treated for cancer. EBV is a herpes virus often associated with infectious mononucleosis [38]. Although most adults test positive for EBV antibodies, the virus is typically inactive in healthy individuals. Nevertheless, latent infections can be reactivated, and greater EBV titers can be viewed as an index of immune dysregulation. In this sample, attachment

anxiety (but not avoidance) was positively associated with EBV titers, suggesting latent herpesvirus reactivation.

Additional evidence for a link between attachment and cellular immune response comes from Jaremka and colleagues [39<sup>••</sup>], who studied 85 married couples who were taking part in a larger study of marital relationships and wound healing. Couples took part in an overnight laboratory visit and returned the following day for an additional blood draw (three blood draws in total). Researchers examined the frequencies of several kinds of T cells, which are a class of lymphocytes that work to activate other immune cells and target and destroy infected cells. Researchers found that attachment anxiety (but not avoidance) was negatively associated with several types of T cells. These findings are particularly noteworthy because the T cells examined in this study play an integral part in the body's immune response to pathogens, so fewer available T cells may lead to a diminished ability to mount a defense.

### Conclusions and future directions

Compared to the robust literature on attachment and neuroendocrine functioning, only a handful of studies have examined links between adult attachment and various measures of the immune system. Nevertheless, a larger body of literature has identified links between attachment-relevant constructs (e.g. warmth, hostility, marital quality) and underlying biologic processes that could influence health [9,40–42]. This work, along with the emerging studies of attachment and measures of immune functioning, is beginning to yield new insights into the ways in which individuals' attachment experiences are associated with the immune system across the lifespan.

Because this area of research is still in its infancy, much more work is needed to address basic questions, such as the strength of the connection between attachment and measures of the immune system. Several studies have not found robust links between attachment orientation and inflammation [34] and others have found links between some indices of attachment but not others [37<sup>•</sup>,39<sup>••</sup>]. Indeed, these issues bring about two related questions: First, should we expect to find direct links between measures of attachment and the immune system? Second, should we expect both attachment avoidance and anxiety to be associated equally with immune measures? There are simply too few studies to make definitive conclusions at this time, but continued research will help identify the limits of attachment as a predictor of immune function.

Although the focus of this review has been on attachment and immune function in adults, it is important to keep in mind that these processes likely begin much earlier in development [13<sup>••</sup>]. In fact, the *fetal-programming model* argues that *in utero* experiences shape infant development

by exposing them to maternal signals about environmental conditions after birth [43]. Pregnancy brings a number of physiological adaptations, including critical changes to the immune system [44]. Some studies have considered the ways that mothers' stressful social relationships shape adverse pregnancy outcomes and underlying inflammatory processes [45<sup>•</sup>]. To what extent does maternal attachment insecurity shape inflammatory processes that shape pregnancy outcomes and influence the developing immune system of her child? These studies will help address questions about the intergenerational transmission of stress-health links.

Finally, future studies should consider the ways in which a dyadic approach to attachment and immune processes might yield new insights. For example, Actor-Partner Interdependence Models [46] can help uncover whether attachment orientations influence not only one's own immune functioning but also their partner's immune functioning. These analyses will help shed light on the extent to which attachment should be considered an intrapersonal versus interpersonal phenomenon in the context of PNI studies.

I look forward to the next generation of studies on attachment and immune functioning. These studies will help uncover the extent to which attachment experiences across the lifespan influence the immune system, and whether secure attachment can serve as a buffer against other risk exposures. Findings from these studies will offer new ideas about how the social world becomes biologically embedded in ways that might influence our physical health.

### Conflict of interest statement

Nothing declared.

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