

Why inflammation and the activities of the immune system matter for social and personality psychology (and not only for those who study health)

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Abstract

A growing body of research finds that the activities of the immune system—in addition to protecting the body from infection and injury—also influence how we think, feel, and behave. Although research on the relationship between the immune system and psychological and behavioral outcomes has most commonly focused on the experiences of those who are ill or experiencing an acute immune response, we propose that the immune system may also play a key role in influencing such outcomes in those who are healthy. Here, we review theory and research suggesting that inflammation—a key component of the immune response to pathogens and stressors—may play an important modulatory role in shaping emotions, motivation, cognition, and behavior, even among those without symptoms of illness. Moreover, because inflammation occurs in response to a number of everyday social experiences (e.g., loneliness and stress), we propose that it may be an important mediator of many psychological and behavioral outcomes that are of interest to social and personality psychologists. We close by discussing potential opportunities for researchers looking to incorporate psychoneuroimmunology (PNI) into their area of inquiry.

1 | INTRODUCTION

Researchers have long known about the critical role that the immune system plays in protecting the body from infection and injury. More recently, however, researchers have also begun to uncover an important role for the immune

system in regulating motivational, emotional, and behavioral processes (e.g., Dantzer & Kelley, 2007; Inagaki, Muscatell, Irwin, Cole, & Eisenberger, 2012; Lasselin et al., 2017; Shields, Kuchenbecker, Pressman, Sumida, & Slavich, 2016). For example, research finds that inflammation—a major component of the immune system's response to pathogens and stressors—influences a wide range of neurobiological, cognitive, and behavioral outcomes (e.g., Dantzer, 2001; Dantzer & Kelley, 2007; Eisenberger et al., 2010; Hennessy, Deak, & Schiml, 2014; Jewett & Krueger, 2012; Moieni & Eisenberger, 2018).

Despite the growing interest in the impact of inflammation on cognition and social behavior, we propose that the extant literature has focused too narrowly on outcomes observed among those who are ill or experiencing an acute immune response. Because inflammatory signaling plays a vital role not only in eliminating pathogens but also in coordinating the activities of the nervous system (Blalock, 1984; Blalock & Smith, 2007; Dantzer, 2001; Goshen & Yirmiya, 2009; Kipnis, 2018), this form of communication likely has a hand in modulation of a wide range of neural, psychological, and behavioral outcomes, even among those without overt symptoms of illness. Moreover, because inflammation occurs in response to a number of everyday social experiences (e.g., in response to loneliness: Jaremka et al., 2013; stress: Segerstrom & Miller, 2004; and diet: Galland, 2010), it may be an important mediator of many psychological processes and behaviors that are of interest to researchers in social and personality psychology.

In the following article, we review literature providing evidence that the immune system impacts how we think, feel, and behave. We then discuss research suggesting that the immune system plays an important role in everyday brain functioning and detail the implications this may have for outcomes of interest to social and personality psychologists. Finally, we close with suggestions for areas of research that are poised to yield much empirical fruit from incorporating insights from psychoneuroimmunology (PNI) into their own line of research.

2 | INFLAMMATION IMPACTS HOW WE THINK, FEEL, AND BEHAVE

The immune system is the primary mechanism through which the body protects and defends itself from the ubiquitous threats posed by illness, injury, and neoplastic growth (Janeway, Travers, Walport, & Shlomchik, 2005; Matzinger, 2012; Sompayrac, 2015). When immune cells are stimulated, they secrete a complex array of signaling proteins—such as cytokines—which regulate the host organism's immune response, helping clear/prevent infections and heal injuries (Dinarello, 1999; Janeway et al., 2005; Thomson & Lotze, 2003).

In addition to directing the activities of the immune system, cytokines also have the ability to influence activities of the nervous system (Banks, 2005; Benveniste, 1992; Rothwell & Hopkins, 1995). Cytokines are able to communicate with the brain through three major pathways: (a) active transport across the blood–brain barrier (e.g., saturable transport systems), (b) passive transport (e.g., via circumventricular organs), and (c) through the activation of visceral nerve fibers in the periphery (e.g., vagal afferents) that prompt *de novo* cytokine synthesis inside the brain by cells such as microglia (Banks, 2005; Benveniste, 1992; Rothwell & Hopkins, 1995).

The idea that cytokines have the ability to alter neurotransmission is something that was first captured by research demonstrating a causal role of cytokines in orchestrating sickness behavior. Sickness behavior is a cytokine-induced motivational state characterized by a constellation of physical, psychological, and behavioral tendencies—such as fatigue, anhedonia, weakness, and social avoidance—that commonly occur in the context of an acute immune response (Aubert, Vega, Dantzer, & Goodall, 1995; Dantzer, 2001; Dantzer & Kelley, 2007). Although sickness behavior was originally believed to be a maladaptive byproduct of pathogen presence, it is now understood to reflect an adaptation by the host organism that functions to reduce bodily damage and conserves energetic resources for the immune response and recovery at times when the body is ill, injured, or in poor condition (Dantzer, 2001; Dantzer & Kelley, 2007; Medzhitov, Schneider, & Soares, 2012).

In addition to playing an important role in orchestrating sickness behavior, a growing body of research suggests that proinflammatory cytokines may also contribute to behavioral and psychological outcomes as diverse as mood

(D'Acquisto, 2017), feelings of social connection (Eisenberger, Inagaki, Mashal, & Irwin, 2010), how we perceive others (Inagaki et al., 2012), and our valuation of rewards (Draper et al., 2018; Eisenberger, Berkman, et al., 2010). Although this research is still in its infancy, it has already begun to offer novel insights into the role that the immune system may play in the development of psychological disorders, as well as in contributing to day-to-day fluctuations in social perception and behavior. We turn to this literature now.

2.1 | Mood

Several researchers have now proposed that proinflammatory cytokines may play a role in the pathogenesis of depression (Capuron & Miller, 2011; Dantzer, O'Connor, Freund, Johnson, & Kelley, 2008; Dooley et al., 2018; Miller & Raison, 2016; Raison & Miller, 2011). Consistent with this hypothesis, research finds that patients with major depressive disorder have higher levels of inflammation in their peripheral blood and cerebrospinal fluid than do healthy controls (Berk et al., 2013; Raison & Miller, 2011). Others find that experimental manipulations (i.e., endotoxin administration) that increase levels of inflammation *in vivo* (i.e., within the body; vs. *in vitro*: outside the body) also increase depressed mood in otherwise healthy subjects (Reichenberg et al., 2001). More recent work employing a similar experimental paradigm has expanded on this finding, revealing that the relationship between elevated levels of inflammation and depressed mood was mediated by increased feelings of social disconnection in response to the immunological threat (Eisenberger, Inagaki, et al., 2010). This finding suggests that changes in social perception may play an important role in the impact of inflammation on depressive symptoms.

2.2 | Interpersonal processes and social perception

Separate studies provide additional support for the possibility that inflammation influences social perception. Specifically, this research suggests that inflammation impacts how we register threats and opportunities in our environments, biasing our perceptions in ways that would help promote the avoidance of harm and help facilitate recovery in the face of illness or injury. For example, research finds that experimentally induced inflammation leads to greater activity in brain regions associated with anxiety, fear, and social rejection in response to socially threatening experiences (Inagaki et al., 2012; Muscatell et al., 2015; Slavich, Way, Eisenberger, & Taylor, 2010) but not to non-socially relevant threats (e.g., pictures of guns; Inagaki et al., 2012). These results provide evidence that inflammation may lead to the over-perception of the magnitude of social threats at times when the danger posed by those threats is particularly pronounced.

In addition to promoting vigilance toward negative social experiences, research also finds that inflammation increases one's sensitivity to positive social experiences. For example, in one study, participants received either endotoxin—which elicited an inflammatory response—or placebo (Muscatell et al., 2015). After enough time had passed to allow inflammation to rise, participants underwent functional magnetic resonance imaging (fMRI) while receiving positive, negative, and neutral feedback from confederates about an interview they had given prior to the imaging procedure. Results revealed that those who received endotoxin (compared to the placebo) had greater neural activity in threat-related brain regions when receiving negative feedback (i.e., bilateral amygdala and dorsal anterior cingulate cortex), as well as greater activity in brain regions associated with reward (i.e., ventral striatum and ventromedial prefrontal cortex) when receiving positive feedback. Others find that individuals who have been administered endotoxin (compared to those receiving placebo) report a greater desire to be around others who provide them with social support and exhibit more activity in the brain's reward centers when viewing photographs of such people (Inagaki et al., 2015). Together, this research suggests that inflammation may increase sensitivity to social cues, both positive and negative.

2.3 | Reward sensitivity

Lastly, research indicates that the activities of the immune system may play a powerful—if not yet well understood—role in the motivation and preference for appetitive stimuli, such as money and food (Dooley et al., 2018; Draper et al., 2018; Eisenberger, Berkman, et al., 2010; Gassen, Prokosch et al., 2019; Gassen, Makhanova et al., 2019; Lasselin et al., 2017). For example, fMRI research in humans finds that inflammation predicts lesser ventral striatum activity in response to monetary reward cues (Eisenberger, Berkman, et al., 2010), as well as decreased functional connectivity in the brain's neural reward circuitry (Felger et al., 2016). Each of these patterns is consistent with the idea of sickness-induced anhedonia, which is a well-known phenomenon in the animal literature (Dantzer, 2001; Dantzer & Kelley, 2007). However, more recent work suggests that the impact of inflammation on reward sensitivity in humans may be highly nuanced and variable across contexts. For example, some research finds that inflammation is associated with reduced effort to receive rewards but not sensitivity to the reward's magnitude (Draper et al., 2018). Still others find that inflammation can actually increase motivation to work for rewards, as long as rewards are highly probable and of high value (Lasselin et al., 2017). Together, this research provides evidence that inflammation may influence several aspects of choice behaviors, although the precise nature of this role is still somewhat uncertain.

3 | BEYOND SICKNESS: INFLAMMATION AS A MEDIATOR OF PSYCHOLOGICAL AND BEHAVIORAL OUTCOMES AMONG THE NON-SYMPTOMATIC, HEALTHY

In addition to their role coordinating sickness behavior, proinflammatory cytokines may also play a vital role in regulating the activities of the nervous system in the absence of an acute immune response (Bilbo & Schwarz, 2009, 2012; Blalock, 1984; Blalock & Smith, 2007; Gadani, Cronk, Norris, & Kipnis, 2012; Kipnis, 2018; Kipnis, Gadani, & Derecki, 2012; Lopes, 2017; Maier & Watkins, 1998; Vitkovic, Bockaert, & Jacque, 2000). There are cytokine receptors present in virtually all neural cell types (Bartfai & Schultzberg, 1993; Conti et al., 2008; Kronfol & Remick, 2000; Vitkovic et al., 2000), and much research finds that modifying the action of cytokines leads to changes in the central nervous system. For example, research finds that such actions have implications for sensory function (Chen et al., 2017; Miller, Jung, et al., 2009), sleep (Fang, Wang, & Krueger, 1998; Jewett & Krueger, 2012), learning (Gonzalez, Schiöth, Lasaga, & Scimonelli, 2009; Goshen et al., 2007; Huang & Sheng, 2010; Jones, Lebonville, Barrus, & Lysle, 2015; Takemiya, Fumizawa, Yamagata, Iwakura, & Kawakami, 2017), the stress response (Goshen & Yirmiya, 2009), temporal focus (Gassen, Makhanova, et al., 2019; Gassen, Prokosch, et al., 2019), and even social behavior (Hennessy et al., 2014; Lisboa et al., 2018; Moon et al., 2015; Yim et al., 2017). The impact of cytokines on the activities of the nervous system is therefore unlikely to be limited to the impact they have on organisms' behaviors when they are sick.

For example, proinflammatory cytokines such as interleukin-17, interleukin-6, and interleukin-1beta (IL-1 β) each help regulate the excitability of sensory neurons (Chen et al., 2017; Miller, Jung, et al., 2009; Zhong, Dietzel, Wahle, Kopf, & Heumann, 1999). Others find that the presence of IL-1 β —although it leads to learning and memory impairments when levels are acutely elevated (Gonzalez et al., 2009; Oitzl, Van Oers, Schöbitz, & de Kloet, 1993)—is necessary at low levels for learning and memory to occur at all (Goshen et al., 2007; Huang & Sheng, 2010; Jones et al., 2015; Takemiya et al., 2017). Still others find that mice genetically modified to lack the anti-inflammatory cytokines interleukin-4 or interleukin-10 (compared to control mice not lacking these cytokines) display increased anxiety (Moon et al., 2015) and dysregulated sleep (Toth & Opp, 2001), respectively. Accordingly, rather than being something that matters only in terms of understanding the behavior of the acutely ill, the elderly, and those with clinical disorders, cytokines may be important mediators of numerous psychological and behavioral outcomes, including a number that are not directly related to health.

The idea that the activities of the immune system should play an important role in the everyday functioning of an organism's nervous system is also well supported by theoretical models in the evolutionary sciences (e.g., Higginson, Fawcett, Houston, & McNamara, 2018; McNamara & Houston, 1996; Näslund & Johnsson, 2016; Rands, Pettifor, Rowcliffe, & Cowlshaw, 2004; Schuck-Paim, Pompilio, & Kacelnik, 2004). These models (called state- or condition-dependent models) predict that organisms should adjust development and behavior in ways that take into account the physiological condition of the body (Higginson et al., 2018; Houston, McNamara, & Thompson, 1992; Luttbeg & Sih, 2010; Näslund & Johnsson, 2016; Rickard, Frankenhuys, & Nettle, 2014), exhibiting one set of developmental or behavioral contingencies when the organism is in good condition and another when in poor condition.

Although these evolutionary biological models have been largely mechanistically agnostic (i.e., they do not specify the mechanisms through which the body is able to communicate information about its condition to the brain), given the ability of cytokines to direct the activities of the nervous system, they seem to be a likely candidate for playing this role. Indeed, prominent researchers in the field of psychoneuroimmunology (PNI) have proposed just such a role for cytokines, suggesting that the immune system acts as a sixth (e.g., Blalock & Smith, 2007) or seventh sense (Kipnis, 2018). According to this perspective, the immune system—just like the body's other sensory organs—provides the brain with important information about the body's condition, which is used to compute psychological and behavioral choices that are likely to optimize survival given its internal, physical condition.

Although the proposal that the immune system may be an important player in guiding the activities of a healthy nervous system is relatively new, a growing body of research has begun to find hints of immune system involvement in a variety of outcomes that are observed both in sickness and in health. For example, research suggests that the activities of the immune system may have a hand in calibrating psychological outcomes as diverse as personality (Segerstrom, 2000; Vedhara et al., 2015), pathogen avoidance motivation (Fessler, Eng, & Navarrete, 2005; Fleischman & Fessler, 2011; Gangestad & Grebe, 2014; Gassen et al., 2018), disgust sensitivity (Bradshaw, Gassen, Prokosch, Boem, & Hill, under review), the desire for immediate versus delayed rewards (Gassen et al., 2018; Gassen, Makhanova, et al., 2019; Gassen, Prokosch, et al., 2019), learning (Ziv et al., 2006; Derecki et al., 2010), and mood (Raison & Miller, 2011).

In one line of research inquiry, for example, researchers have begun to investigate the possibility of a bidirectional relationship between the activities of the immune system and pathogen avoidance motivations (e.g., Ackerman, Hill, & Murray, 2018; Bradshaw et al., under review; Fessler et al., 2005; Fleischman & Fessler, 2011; Gassen et al., 2018). According to this perspective, the immune system and the nervous system work together to help keep people safe from illness and disease, with pathogen avoidance motivations changing in response to changes in immunological activity and vice versa. Consistent with this hypothesis, research finds that disgust sensitivity is elevated during pregnancy when the maternal immune system is downregulated (Fessler et al., 2005), among those with relatively low levels of basal inflammatory activity (Gassen et al., 2018) and among those randomly assigned to take 325 mg of aspirin (which suppresses inflammatory activity; Amann & Peskar, 2002; Morris et al., 2009) when compared to those in the placebo group (Bradshaw et al., under review). Similar relationships between immunological activity and pathogen avoidance behaviors have been observed in many species of non-human animals, as well (e.g., bees: Richard, Holt, & Grozinger, 2012; birds: Yorinks & Atkinson, 2000; goats: Takeuchi, Kikusui, & Mori, 1995; non-human primates: Ghai, Fugere, Chapman, Goldberg, & Davies, 2015), suggesting that pathogen avoidance motivation is higher in the context of reduced immune activation.

Although this research is not yet at a point where one can conclude that there exists a cause and effect relationship between the activities of the immune system and pathogen avoidance psychology, it represents an important first step in having established that there is a relationship between these variables. Rigorously controlled, experimental research is needed to determine whether the demonstrated links between immunological activity and pathogen avoidance motivation are causal and also to examine which specific neural and immunological mechanisms create these links. Future research in this field holds promise to provide novel insights into the complex physiology underlying personality, learning, and social behavior, as well as provide clues to the adaptive function of relationships between behavioral and immune traits (Lopes, 2017).

4 | WHY THIS MATTERS FOR SOCIAL AND PERSONALITY PSYCHOLOGY

We have proposed that the activities of the immune system may play an important role in what people think, feel, and do, even outside the context of illness (e.g., Gassen et al., 2018; Gassen, Makhanova, et al., 2019; Gassen, Prokosch, et al., 2019; Kipnis, 2018; Maier & Watkins, 1998; Vitkovic et al., 2000). Although the immune system does not typically weigh heavily in the minds of researchers in personality and social psychology, incorporating mechanistic insights from PNI into the study of person–situation interactions has much to offer researchers in these areas. This is because inflammation, in addition to being associated to behavioral tendencies (Filiano et al., 2016) and personality traits (Segerstrom, 2000; Vedhara et al., 2015), also changes in important ways in response to threats and opportunities in the environment.

For example, research in the area of affective immunology finds that inflammation increases in response to stress (Kiecolt-Glaser et al., 2003; Miller et al., 2008; Segerstrom & Miller, 2004; Steptoe, Hamer, & Chida, 2007), loneliness and social isolation (Jaremka et al., 2013; Jaremka, Fagundes, Glaser, et al., 2013; Moons & Shields, 2015; Pressman et al., 2005; Shivpuri et al., 2011), pathogen cues (Schaller, Miller, Gervais, Yager, & Chen, 2010), and situations that evoke anxiety (Moons & Shields, 2015). These patterns are reasoned to occur because each denotes a context that historically would have been associated with a sharp increase in one's risk of predation, wounding, and infection (for a discussion, see, e.g., D'Acquisto, 2017; Jaremka, Fagundes, Glaser, et al., 2013; Moieni et al., 2015). For example, one study found that experimentally inducing anxiety—which is an affective response to threat—led to increases in mucosal interleukin-1 β and IFN- γ , two cytokines with proinflammatory properties (Moons & Shields, 2015). Others find that loneliness—which often occurs when one is lacking in social support—plays a powerful modulatory role in inflammatory signaling, potentiating the impact of stress and immunological challenges on the release of proinflammatory cytokines (Jaremka, Fagundes, Glaser, et al., 2013; Moieni et al., 2015; Uchino et al., 2018).

Inflammation—in short—is not something that occurs strictly in the face of an acute immune response. Instead, it is something that also occurs—although at lower levels—when healthy bodies are preparing for the possibility of illness or injury. Given that many of the situations that people find themselves in during their daily lives are associated with changes in the probability of illness and injury, it is likely that inflammation has important implications for a wide variety of motivational, emotional, cognitive, and behavioral processes that occur in the absence of an acute immunological event. It may prove to be an important mediator of social behavior among the healthy, leading to coordinated psychological and behavioral changes that, historically, would have helped promote survival and reproductive success in the face of threats. Accordingly, psychological states as diverse as stress, shame, fear, loneliness, and excitement, as well as situational cues as diverse as discrimination, pathogen presence, crowding, danger, and social rejection, may all have important implications for behavior that operate through changes in circulating levels of proinflammatory cytokines. See Figure 1 for examples of predictors and outcomes that may be linked through the activities of the immune system.

Examining the patterns of psychological and behavioral changes that regularly occur in the context of inflammation may provide social psychologists new insight into the processes that generate situationally contingent behavioral patterns. For example, research in PNI suggests that inflammation can have an impact on people's feelings of social isolation (Eisenberger, Inagaki, et al., 2010) and may reduce motivation to exert effort for rewards (Draper et al., 2018). Therefore, one possibility for generating new lines of research would be to consider whether either of these global psychological changes might also drive behaviors observed in response to situational antecedents of inflammation (e.g., exposure to pathogen cues, stress, or situations evoking fear or shame). We may find, for example, that those living in pathogen dense ecologies—which is a context that favors increased inflammatory activity (Gassen, Makhanova et al., 2019; Schaller et al., 2010)—may exhibit decreased reward motivation relative to what is observed among those living in areas of the world with a lesser pathogen burden. This is, as far as we know, the first theoretical model to make this prediction, which could help account for some of the observed variability in gross domestic product around the world (see, e.g., Nikolaev & Salahodjaev, 2017).

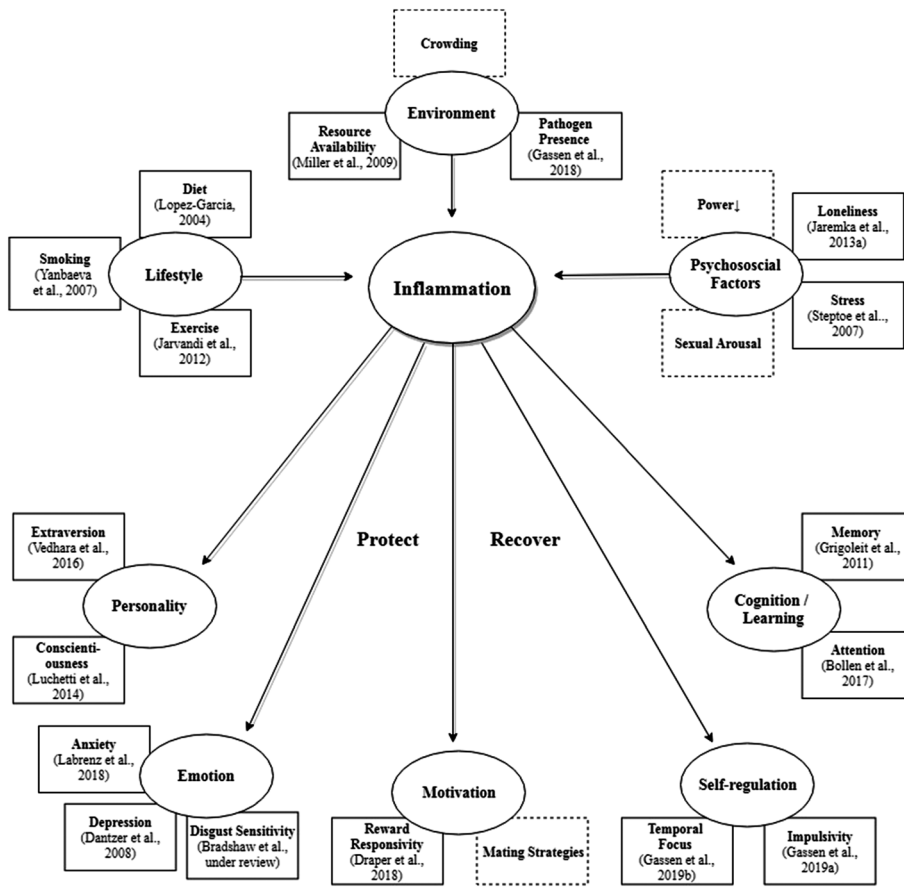


FIGURE 1 Pathways through which the social environment impacts inflammation which, in turn, may influence personality, emotion, motivation, cognition, and behavior, even among healthy individuals. These outcomes are predicted to occur because they would help (a) protect the body from infection (outcomes on the left-hand side of the figure) or (b) expedite its recovery (outcomes on the right-hand side of the figure). Boxes outlined with dashed lines represent variables predicted to be related to inflammation but for which sufficient evidence examining such a relationship is currently lacking

Another possibility to consider is whether individual differences in one's tendency to exhibit an exaggerated inflammatory response to such situational cues may have an important moderating effect on behavior. For example, disparate lines of research indicate that growing up in conditions of low socioeconomic status (SES) promotes (a) the development of an exaggerated inflammatory response to immunological stimulation (Miller, Chen, et al., 2009; Miller & Chen, 2007) and (b) the tendency to act impulsively in response to stress (Griskevicius et al., 2013; Griskevicius, Tybur, Delton, & Robertson, 2011). Given recent empirical work linking heightened inflammatory activity to decision making characterized by impulsivity (Gassen, Makhanova, et al., 2019; Gassen, Prokosch, et al., 2019), it is possible that signaling by the immune system may play a mechanistic role linking one's early life environments with how they respond to stressors in adulthood. Incorporating insights from psychoneuroimmunology into research on individual differences in stress reactivity therefore has the potential of bridging these previously disconnected bodies of research, raising the possibility that differences in the magnitude of the inflammatory response may play an important role in differential susceptibility to other stress-induced behavioral changes that are often disproportionately represented in the poor (e.g., Griskevicius et al., 2011; Griskevicius et al., 2013). These are but a few of the research questions that arise when we consider the important role that the immune system may play in mediating how individuals' feelings and behaviors change in response to their environments.

In addition to offering new possibilities to researchers interested in social behavior, examining the linkages between the activities of the immune system and psychological processes can provide new insights into individual differences and psychopathologies. For example, considering the evidence linking people's pathogen avoidance psychology to the activities of their immune systems (e.g., Fessler et al., 2005; Gassen et al., 2018), it is possible that pathologies marked by excessive fear of contamination may be driven by unusually low levels of basal immunological activity (see, e.g., Gray & Bloch, 2012). This could account for the tendency of conditions like obsessive compulsive disorder (OCD) to be more prevalent among those living in more affluent environments. Perhaps OCD is the result of too little contact with elicitors of inflammation (e.g., microbes), a possibility that would open up new treatment strategies.

5 | DISCUSSION

Throughout the current article, we have reviewed theory and research suggesting that the activities of the immune system—inflammation, in particular—may play a key role in regulating how people think, feel, and behave (e.g., Dantzer & Kelley, 2007; Inagaki et al., 2012; Lasselin et al., 2017; Shields et al., 2016). Although relationships between inflammation and behavior are often studied in the context of illness (i.e., sickness behavior; Dantzer, 2001) or pathology (e.g., depression; Miller & Raison, 2016), there is a growing body of theoretical (Blalock & Smith, 2007; D'Acquisto, 2017; Kipnis, 2018; Lopes, 2017; Shields, Moons, & Slavich, 2017) and empirical evidence suggesting that inflammation also influences a wide range of psychological processes, such as development (Bilbo & Schwarz, 2009, 2012), pathogen avoidance motivation (e.g., Gassen et al., 2018), self-regulation (e.g., Gassen, Makhanova, et al., 2019; Gassen, Prokosch, et al., 2019), and learning (e.g., Goshen et al., 2007; Huang & Sheng, 2010; Jones et al., 2015). This research, when juxtaposed with that which finds that the social environment also impacts inflammation (e.g., Chen, Miller, Kobor, & Cole, 2011; O'Connor & Irwin, 2010; Segerstrom & Miller, 2004), suggests that the activities of the immune system may be a key mechanism that mediates relationships between environments and behavior, even among the healthy.

Although integrating insights from PNI into social psychological research has the potential to yield much conceptual and empirical fruit, there are several challenges that confront such an integration. The biggest challenge facing researchers stems from how to measure the activities of the immune system and how to interpret those measures. Although immunological activity is incredibly complex and can be measured in multiple ways (e.g., examining Th1/Th2 balance and conducting functional assays of specific cell populations, such as neutrophils or natural killer cells), much of the research on neural-immune interactions has focused on inflammatory activity. However, even this very limited way of measuring immunological activity is itself very complex. There are many different types of cytokines (and other inflammatory factors), some of which are largely proinflammatory (e.g., IL-1 β , tumor necrosis factor-alpha), some of which are largely anti-inflammatory (e.g., interleukin-10), and still others that can be either depending on context (e.g., interleukin-6; Del Giudice & Gangestad, 2018; Janeway et al., 2005; Thomson & Lotze, 2003). Adding to this complexity is the fact that inflammation—both in terms of its causes and consequences—is likely to vary depending on the ecological context and nature of sample in which it's measured (i.e., inflammatory activity in Westerners caused by excess adiposity may differ in its effects on behavior from inflammatory activity observed in samples of people living in pathogen-dense regions of the world) and likely influences behavior via multiple pathways. For example, in addition to its direct effects on the nervous system, inflammation might also indirectly influence behavior by interacting with hormones and their receptors (e.g., Goshen & Yirmiya, 2009; Sun, Hedger, & Risbridger, 1993). Finally, future research may find that certain relationships between the activities of the immune system and outcomes relevant to social and personality psychology are non-linear. This possibility is consistent with research finding that relationships between biological factors (e.g., hormones and glucose levels) and behavior (e.g., memory) often follow an inverted-U shape (Gold, Vogt, & Hall, 1986; Joëls, 2006).

Despite these complexities, incorporating measures of inflammation in social psychological research presents both new opportunities for studying how individual and situational factors influence behavior. In particular,

experimental studies that employ ecologically valid manipulations to elicit increases in inflammation in otherwise healthy participants (e.g., social stress, dietary modifications, or physiological doses of antigens) and measure multiple markers of inflammation may provide a useful first step in establishing whether changes in immunological activity alter cognitive functioning and social behavior. Moreover, longitudinal studies might also help determine whether changes in behavior map onto natural fluctuations in inflammatory markers over the course of hours, days, weeks, or even longer time scales.

Integrating PNI into social psychological research has already yielded many novel findings regarding the biological mechanisms underlying emotions, motivation, cognition, and behavior. Experimental design, statistical rigor, and other insights from social psychology, too, have enriched the field of PNI. Moving forward, those studying relationships between the immune system and the social behavior will face several challenges, including situating findings from PNI into current social psychological and evolutionary biological theories (e.g., state-dependent decision making; Higginson et al., 2018; Näslund & Johnsson, 2016; McNamara & Houston, 1996), establishing causal pathways using experimental designs (e.g., endotoxin; Eisenberger, Berkman, et al., 2010; Eisenberger, Inagaki, et al., 2010) and finding suitable outlets for publication. In overcoming these challenges, however, such research is positioned to transform our understanding of human psychology and behavior.

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