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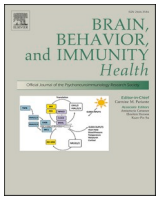

The beneficial effects of social support and prosocial behavior on immunity and health: A psychoneuroimmunology perspective

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A B S T R A C T

The COVID-19 pandemic emphasized the pivotal role of the social environment, prompting a surge in research on its impact on well-being and health. This article aims to examine the link between the social environment, the immune system, and health outcomes, with a particular focus on positive aspects like social support and prosocial behaviors that are under-explored. Different aspects of the social environment are examined: the negative effects of loneliness and adverse social conditions, contrasted with the benefits of social support and prosocial behaviors. While the mechanisms behind negative effects are partially studied, those driving the positive effects remain elusive. Understanding the mechanisms of lack of social connection and their effects will allow us to explore the benefits of social connections and whether they can reverse the adverse outcomes. Potential psychoneuroimmunology mechanisms are proposed, highlighting the promotion of a 'safe' state by the vagus nerve, oxytocin circuits, and the additional contribution of the reward pathways. This article reviews the need to bridge knowledge gaps, urging further research to study the causal effects of positive social interactions on immune response and health outcomes to raise clinical awareness and interventions. Such interventions may include integrating lonely individuals with prosocial activities, thereby improving their physical and mental health. There is growing potential to harness the power of social connections for the betterment of individual health and society as a whole.

"It is not good that the man should be alone" (Genesis 2:18).

1. Introduction

Throughout time, social bonds have been critical. Recently, the COVID-19 pandemic emphasized their pivotal role, making this issue a focal point of global and scientific attention (Lippke and Warner, 2023; Yu, 2023). Research on this topic surged, with studies like Wang et al. (2023) during the pandemic highlighting the detrimental effects of social distancing and loneliness on mental and physical health (Wang et al., 2023). However, there were also studies (albeit fewer) that exhibited the positive impacts of unity and prosocial behavior on well-being during the COVID-19 pandemic (Haller et al., 2022). Although the subject has made headlines recently, its significance has been studied for decades, showing that loneliness impacts immunity and health (Hawkley and Cacioppo, 2010; Uchino et al., 2018).

Social cues derived from the surroundings influence the brain, which then transmits signals downstream to the peripheral immune pathway through various mechanisms, such as the hypothalamic-pituitary-adrenal (HPA) axis, adrenergic signaling, and the vagus nerve. These processes alter different bodily functions and metabolism, such as increasing cortisol, epinephrine, and norepinephrine levels, which in turn modify the gene expression and function of immune cells (Cole, 2013; Garrido et al., 2022; Slavich et al., 2023). Despite decades of research showing how social stress influences the peripheral immune system through brain mechanisms (Leschak and Eisenberger, 2019; Slavich et al., 2023; Takahashi et al., 2018), the mechanisms by which positive social contexts, such as receiving support and engaging in prosocial behavior, impact the immune system remain elusive.

From an evolutionary perspective, being socially isolated increases vulnerability to outside threats, such as injuries and bacterial infections. Conversely, it reduces the risk of contracting viral infections from other counterparts. Adaptation to this environmental necessity results in a decreased antiviral response and an increased inflammatory response to promote healing (Leschak and Eisenberger, 2019; Smith and Bilbo, 2021). There is a growing body of evidence supporting this standpoint (Cacioppo et al., 2015; Cole et al., 2021; Leschak and Eisenberger, 2019; Slavich et al., 2023; Smith et al., 2020). One of the main tools to measure these immune responses to social contexts is the social genomics approach, a unique leukocyte gene transcription – the Conserved Transcriptional Response to Adversity (CTRA), which involves a shift towards upregulation of proinflammatory genes and downregulation of antiviral genes (Cole, 2013, 2019; Slavich et al., 2023). Although acute

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inflammation serves as an adaptive immune response to infection and injury, chronic inflammation is robustly associated with a wide range of diseases, such as cardiovascular disease, diabetes, and cancer, and significantly increases mortality risk (Furman et al., 2019).

The link between the social brain and the immune system is bidirectional; the brain constantly receives signals from the immune system and adjusts social behavior in response, and the signals from the social environment can shape the immune response (Smith and Bilbo, 2021). Infection leads to inflammation, resulting in "sickness behavior," which encompasses symptoms like lethargy, anorexia, and altered social behavior (Dantzer, 2021; Lasselin, 2021). This change in social interaction is complex; on the one hand, social withdrawal and isolation are essential to minimize infection spread and aid healing. On the other, there is a vital need for support and care from close ones or loved ones. Additionally, we have an inherent social ability to detect ill individuals through various cues, such as changes in walking patterns (gait) and facial expressions (Dantzer, 2021; Hansson et al., 2023; Regenbogen et al., 2017). Thus, we might choose to provide care and comfort or avoid or isolate ourselves to protect the group from infection. This decision may depend on whether the individual is a stranger or a loved one, affecting our social response and, in turn, influencing the feelings and actions of the ill individual (Dantzer, 2021; Muscatell and Inagaki, 2021).

Recently, Keely A. Muscatell (2021) coined the term "Social psychoneuroimmunology (PNI)" emphasizing the profound bidirectional connections between the social environment, the brain and the immune system (Muscatell, 2021). In this article I will explore the diverse influences of social contexts on immunity and health, with a specific emphasis on the less-explored positive aspects, such as receiving social support and engaging in prosocial behaviors, and the potential novel PNI mechanisms that may drive these effects. I will outline directions for future research to address the knowledge gaps, challenges and importance of building a strong social-PNI community (Fig. 1, Bio).

Fig. 1. Bio
Estherina Trachtenberg is a final year PhD candidate at Tel-Aviv University's Sagol School of Neuroscience, under the supervision of Prof. Shamgar Ben-Eliyahu and Dr. Inbal Ben-Ami Bartal. She obtained an MSc in medical science at the Technion – Israel Institute of Technology, in 2018, where she researched cognitive impairment in Hodgkin Lymphoma survivors, and prior to that worked as a registered nurse in hematology. In the clinic, Ms. Trachtenberg understood the importance of the impact of social environment on cancer patient recovery when noticing the difference in coping between patients with social support and those without social support or in isolation. Hence, in her PhD research, she investigates the effects of social context – positive and negative – on the immune system in rat models and in humans. Her rat studies include quantifying the effect of social isolation on cancer and immune function through neuro-immune pathways, and how helping behavior can mitigate these adverse effects in the context of isolation. In a human study initiated immediately after the first Covid-19 lockdown in Israel, Ms. Trachtenberg examined the effect of a prosocial environment on long-term health outcomes. A central aspect of her work focuses on the importance of volunteering, and she has been actively volunteering continuously for over a decade, with various organizations, including the founding of a non-profit organization. Ms. Trachtenberg takes an active part in several committees, such as the Communications Committee of the PNIRS. In the future, she plans to gain expertise in studying prosocial behavior in the context of immunity and to raise awareness of the importance of reducing loneliness.

2. The bad and the ugly sides of social PNI

The social environment profoundly influences health and immunity in both beneficial and detrimental ways (Table 1.). The negative impacts of certain social conditions characterize the 'bad' side of the spectrum, which is far more explored than the positive aspects. Loneliness, social isolation, and low socioeconomic status (adverse social experiences) are widely reported to impede health (Muscatell et al., 2020; Wang et al., 2023). Loneliness and social isolation are comparable to the effect of smoking 15 cigarettes a day (Xia and Li, 2018) and a risk factor for malignancy and mortality (Hawkley and Cacioppo, 2010; Holt-Lunstad et al., 2015; Lutgendorf et al., 2011, 2020; Wang et al., 2023). Vast evidence demonstrates that loneliness and social isolation, notably, have been associated with CTRA, which is a shift in gene expression towards increased proinflammatory and decreased antiviral immune response (Cole, 2013, 2019; Cole et al., 2015a, 2015b; Leschak and Eisenberger, 2019; Slavich et al., 2023). Furthermore, empirical evidence from recently published longitudinal studies, utilizing three markers of systemic inflammation in the plasma, demonstrates that social isolation has a robust association with systemic chronic inflammation (Matthews et al., 2024). As mentioned before, chronic inflammation has been linked with a greater risk of mortality in a variety of patients (Furman et al., 2019). This aligns with findings from a comprehensive meta-analysis that shows social isolation and loneliness are associated with increased mortality (Wang et al., 2023), suggesting that chronic inflammation could be the mechanism that explains these associations.

However, being alone is not inherently harmful. Prolonged solitude can benefit one's well-being, whether it's for spiritual reflection or spending time in nature (Petersen et al., 2021). This suggests that the subjective experience of being alone, characterized by feelings of a lack of belongingness and absence of a support network, is a key factor in loneliness. Conversely, the presence of others isn't always beneficial and can even become 'ugly'. Social environments can often harbor violence, threats, and discrimination. Lab-based experiments on acute social rejection have shown an increase in inflammatory response (Slavich et al., 2010), and a longitudinal study in young adults found that social rejection upregulates inflammatory gene expression (Murphy et al., 2013). Similarly, intimate partner violence, which is linked with heightened inflammation (Madison et al., 2023), thus underscores the significant negative consequences that arise when close bonds become violent rather than supportive.

The mechanisms underlying the adverse effects of loneliness, isolation, and social threats involve stress response pathways such as the HPA axis and the sympathetic nervous system (SNS), which activate peripheral immune responses (Cacioppo et al., 2015; Cole, 2013; Slavich, 2022). Other mechanisms, including the vagus nerve and oxytocin, may also play a role due to decreased activity. These aspects will be covered in later sections, which will discuss the positive aspects of social PNI. It is important to examine both negative and positive experiences, as they are interconnected. For instance, understanding the mechanisms behind

Table 1
Examples of key studies examining the different and complex sides of the social environment and their impacts on immunity and health outcomes.

Effect	Methodology	N	References
The good side – receiving support from others, kindness acts, volunteering			
Social support was significantly linked to lower inflammation levels.	Meta-analysis	41 papers	Uchino et al. (2018)
In cancer patients, social support was related to improved NK functions.	Cross-sectional	65 patients	Lutgendorf et al. (2005)
In cancer survivors, social support was associated with lower CRP levels.	Cross-sectional	15 – survivors 15 – controls	Muscatell et al. (2016)
Prosocial behavior directed towards specific others associated with improved CTRA.	Two randomized control trials (RCT)	159,182 adults	Nelson et al. (2016) Regan et al. (2022)
Volunteering may benefit mental health and reduce mortality risk.	Review and meta-analysis	40,5 papers	Jenkinson et al. (2013)
In older adults, 55+, volunteering was found to reduce mortality risk.	Meta-analysis	14 papers	Okun et al. (2013)
Stronger social relationships and social support are associated with reduced mortality risk.	Meta-analysis	148 papers	Holt-Lunstad et al. (2010)
In-person positive social connections, but not online ones, were associated with an improved CTRA.	Cross-sectional	142 young adults	Snodgrass et al. (2022)
The bad side – lack of social connection, inequality, and social related stress			
Social isolation was found to have a robust association with systemic chronic inflammation.	Cross-sectional and two longitudinal studies	6144 patients 881, 1448 adults	Matthews et al. (2024)
Loneliness and social isolation are associated with higher risk of mortality.	Meta-analysis	70 papers	Holt-Lunstad et al. (2015)
Social isolation was found to correlate with increased metastatic tumor and a poorer prognosis.	Two cross-sectional	68 patients 99 patients	Lutgendorf et al. (2011) Lutgendorf et al. (2020)
Loneliness and social isolation associated with CTRA, i.e., upregulated inflammatory and downregulated anti-viral gene expression.	Two longitudinal studies	141 older adults 108 older adults	Cole et al. (2015a), 2015b
Low socioeconomic status is associated with elevated proinflammatory markers.	Meta-analysis	43 papers	Muscatell et al. (2020)
The ugly side – violence, discrimination, and social related threat			
Social rejection is linked to upregulated inflammatory gene expression.	Longitudinal	147 adolescents	Murphy et al. (2013)
Domestic violence, i.e., intimate partner violence, may heighten inflammation.	Cross-sectional	214 adults	Madison et al. (2023)
Social rejection linked to increased inflammatory response.	Lab-based experimental	124 young adults	Slavich et al. (2010)

loneliness suggests that social connection likely operates through a reverse mechanism, thereby promoting positive outcomes. Moreover, our knowledge about social support is largely derived from understanding the consequences of its absence.

3. The 'good' side of social environment and its effect on the immune system and health outcomes

Humans often show kindness and support to both acquaintances and strangers (Preston, 2013; Wang et al., 2023). Across diverse populations, ranging from the healthy to those dealing with chronic illness, the beneficial effects of having a supportive environment have been consistently observed (Uchino, 2004). Social support is a comprehensive concept that captures an individual's perceived network of resources, offering various forms of support, such as informational, instrumental, and emotional (Zhou, 2014). An 85-year study at Harvard found that positive relationships were the primary psychological factor predicting a better and longer life (Waldinger and Schulz, 2023).

These issues have been studied for over 25 years. Uchino et al.'s comprehensive review in 1996 highlighted the link between social support and improved health outcomes. In their work, Uchino and colleagues analyzed 81 studies, mainly correlational, focusing on the cardiovascular, endocrine, and immune systems as potential avenues to explore the long-term health consequences of social support (Uchino et al., 1996). Two decades later, further evidence emerged linking higher levels of social support to reduced inflammation. A meta-analysis conducted by Uchino et al., in 2018 identified 41 studies, predominantly cross-sectional, demonstrating an association between social support and lower levels of proinflammatory cytokines, such as C-Reactive Protein (CRP) Interleukin-6 (IL-6), and Tumor Necrosis Factor-alpha (TNFa) (Uchino et al., 2018). These proinflammatory cytokines, acting as primary biomarkers, play a crucial role in mediating inflammation and are indicative of a wide range of adverse health conditions (Furman et al., 2019). Though foundational reviews have greatly enriched the field, there's a clear gap in longitudinal and causal studies needed to establish a direct link between social support and the immune system.

Furthermore, it's critical to underline that much of the evidence on the effect of social support on the immune system cited in the literature is driven by the **absence** of social support, with conclusions about the positive impact of social support being drawn from this deficit, like in a recent large sample study (N = 3647) presenting the absence of support linked with accelerated epigenetic aging (Rentscher et al., 2023). Rarely do studies directly find evidence of the presence of social support with its effect on immune parameters. For example, two studies conducted by Lutgendorf, Muscatell and their colleagues, showed that in cancer patients higher social support correlated with better NK function and tumor outcomes (N = 65), (Lutgendorf et al., 2005) and lower CRP levels (N = 30) (Muscatell et al., 2016). A recent study conducted during the COVID-19 pandemic (N = 142) which employed the CTRA expression, found that in-person positive social connections, but not online ones, were associated with an improved CTRA (Snodgrass et al., 2022).

Another dimension of the positive side is prosocial behavior, also known as acts of kindness, defined as **actions** that benefit others, whether familiar or strangers, by providing social or material support in times of need (Carter et al., 2017). Such behavior has been consistently linked to improved well-being and physical health. This association is highlighted in a review by Brown and Brown (2015) and further supported by an extensive meta-analysis of 201 studies conducted by Hui et al. (Brown and Brown, 2015; Hui et al., 2020). Additionally, observational evidence from two meta-analyses suggests that volunteering is associated with a lower mortality risk (Jenkinson et al., 2013; Okun et al., 2013). The link between prosocial behavior and improved health is mainly supported by correlative evidence across a broad health spectrum. Unlike the evidence for social support, which is associated with inflammatory biomarkers, among other effects, studies specifically examining the impact of prosocial behavior on the immune system are

limited.

In recent years, there has been a growing body of experimental and randomized control trials examining the effects of prosocial behavior. A large-sample longitudinal-experimental study with 473 participants demonstrated that acts of prosocial behavior—not self-focused acts—led to improved psychological flourishing and positive emotions (Nelson et al., 2016). Regarding the causal effect on immunity, a handful of studies have delved into how prosocial behavior affects CTRA gene expression. In a pioneering study by Nelson-Coffey et al. (2017), 159 participants were randomly assigned to perform acts of kindness towards others, towards the world in general, towards themselves, or control group. This study found that only prosocial behavior towards others improved CTRA, providing the first causal evidence linking acts of helping others with health benefits (Nelson-Coffey et al., 2017). Improvement in CTRA expression was characterized by a decrease in proinflammatory and an increase in anti-viral gene expression profiles compared to baseline, suggesting a more balanced and enhanced immune response (Cole, 2019). A recent study replicated the results from the 2017 study (N = 182), revealing that kind acts towards others significantly improved CTRA compared to control (Regan et al., 2022). Similarly, in a 9-month intervention study, 32 older adults who volunteered in a school exhibited a significant reduction in CTRA from baseline (Seeman et al., 2020). Together, these studies have opened an important window into understanding the impact of prosocial behavior on immune response and health, possibly shedding some light on the potential mechanisms driving this effect.

However, caring for others is not always beneficial; chronic caregiving can be stressful and is associated with increased CRP and CTRA expression (Black et al., 2013; Miller et al., 2008). On the other hand, a study with a large sample size comparing 3580 families of caregivers to 3580 non-caregivers found heightened stress and depression levels in the caregivers, but it also revealed a significant reduction in mortality rates (Roth et al., 2018). This suggests that, despite higher stress levels among caregivers, the reduced mortality rate could be attributed to the buffering effects of the rewards associated with helping. Such evidence underscores the complexity of social contexts and their influence on health. While there is a growing body of literature on the 'good' side of social aspects, including causal studies on prosocial behavior, the mechanisms underlying these positive effects remain elusive.

4. The potential PNI mechanisms in which the positive social context may impact the immune system and health outcomes

Several well-established neuroimmune pathways may play a role in influencing the immune system in social contexts. The HPA axis and the SNS, which activate stress response pathways, result in the activation of various immune responses. The SNS (i.e., epinephrine and norepinephrine) causes the mobilization of immune cells into the bloodstream and suppresses the transcription of antiviral type I interferon genes while it upregulates the transcription of inflammatory genes. Similarly, chronic activation of the HPA axis (i.e., cortisol) can also lead to increased expression of inflammatory genes (Cole, 2013; Schiller et al., 2021; Slavich, 2022). In turn, activation of the vagus nerve plays a crucial role in regulating immune function and suppressing inflammatory activity. Emerging research suggests it may also potentially upregulate antiviral activity (Pavlov and Tracey, 2012; Sloan and Cole, 2021). Oxytocin, another significant player, directly activates immune cells such as T cells, which express oxytocin receptors, and acts as an anti-inflammatory molecule in both the nervous system and peripheral tissues (Carter et al., 2020; Haykin and Rolls, 2021). But how does the positive social context (i.e., giving/receiving support) mediate changes through these mechanisms? In this section, PNI mechanisms that might shed light on these intricate pathways will be proposed.

First, promoting a 'safe' state – mitigation of the known stress pathways. As mentioned above, the vagus nerve plays a crucial role in regulating stress and suppressing inflammatory responses (Schiller et al., 2021; Sloan and Cole, 2021). Stephen Porges, in his Polyvagal Theory, explores the function of the ventral vagal complex, highlighting its role in the social engagement system. Inherently, we strive for safety, and this can be reached by successful social connections. This system is controlled by the head and face muscles, enabling the exchange of social cues and engagement that promote safety and downregulates sympathetic defense reactions (Porges, 2023). Also, according to the Social Safety Theory introduced by George Slavich, humans, as social beings, have evolved in such a way that our stress response promotes social safety and belongingness. Our brains are attuned to social cues that can modulate stress responses in systems like the HPA axis and the SNS. A safe social network can buffer these reactions by recognizing 'safe' cues, which then moderate signals within these stress arousal systems, leading to a reduced peripheral response (Slavich, 2022). By promoting a 'safe' state, the HPA response is attenuated, leading to the mitigation of negative stress-immune responses, such as the CTRA profile (increased proinflammatory and decreased antiviral gene expression). Additionally, the vagus nerve plays a key role in regulating these responses and contributes to the reduction of proinflammatory production (Cole, 2013; Sloan and Cole, 2021).

Empirical evidence supports these theories; an essential player in mediating HPA response is oxytocin, which is secreted in response to various affiliative social stimuli and can attenuate HPA axis responses. For instance, central and intracerebroventricular administration of oxytocin has been shown to reduce HPA activity (Hennessy et al., 2009). Moreover, oxytocin and corticotropin-releasing hormone (CRH) are co-localized in some neurons, regulating the HPA response (Carter et al., 2020; Carter and Kingsbury, 2022). In addition to its role in promoting a centrally 'safe' state, oxytocin can directly influence immune cells, resulting in reduced inflammation and improved wound healing (Carter and Kingsbury, 2022).

These theories emphasize the mechanisms through which social support is associated with reduced risk of mortality and morbidity (Holt-Lunstad et al., 2010). The attenuation of stress responses, alongside the activation of the vagus nerve and an increase in oxytocin levels, contribute to regulating chronically elevated cortisol levels and inflammation. This multifaceted physiological modulation can lead to a reduced risk of a wide array of diseases, including cancer, metabolic disorders, and cardiovascular diseases, which are often linked to chronic inflammation and glucocorticoid resistance (Furman et al., 2019). Furthermore, these theories highlight that social support is a foundational need, suggesting rethinking the hierarchical place of belonging/love in Maslow's pyramid of needs, placing it before safety needs (Oved, 2017).

Helping others and giving support also promote the 'safe' state. A study by Inagaki and Eisenberger (2016) demonstrates that giving support to others also reduced biological markers of sympathetic-related responses (Inagaki and Eisenberger, 2016). An fMRI study by the same authors showed that providing support was associated with reduced stress-related neuronal activities in various brain regions related to caregiving, and reward-related activity was also associated with giving support, underscoring the multi-faceted pathways that link prosocial behaviors to improved health outcomes (Inagaki et al., 2016).

Care behavior mechanisms are another angle in which prosocial behavior increases oxytocin levels (Marsh et al., 2021). In double-blind, placebo-controlled study designs, the administration of oxytocin in males increased altruistic behavior towards in-group subjects (De Dreu et al., 2010). A comprehensive meta-analysis supported the idea that intranasal oxytocin administration can elevate trust and response to social stimuli (Van IJzendoorn and Bakermans-Kranenburg, 2012). Collectively, oxytocin plays a crucial role in prosocial behavior through various mechanisms. As mentioned above, oxytocin also has immunomodulatory properties, providing another potential mechanism linking prosocial behavior to improved health.

The brain's reward circuits, and dopamine, are key systems associated with prosocial behavior in both human and animal models

(Ben-Ami Bartal et al., 2021; Wu and Hong, 2022), suggesting that this mechanism is unique to prosocial behavior. Specifically, in terms of how helping others can contribute to a favorable effect on immunity, prosocial behavior activates brain areas related to motivation and reward processing, such as the striatum and ventral tegmental area (VTA). These activations lead to positive outcomes that reinforce the behavior (Inagaki and Eisenberger, 2016). Beyond the intrinsic and extrinsic rewards of helping others, which manifest as feelings of joy and improved well-being and mental health, there is another significant mechanism that impacts immunity. Studies on mice conducted by Asya Rolls' research group demonstrate that direct chemogenetic activation of dopaminergic neurons in the VTA enhances peripheral innate immunity, boosting immune cells' response to tumors and bacterial infections (Ben-Shaanan et al., 2016, 2018). This may suggest that the dopamine-immune pathway is another potential PNI mechanism through which prosocial behavior can influence peripheral immunity. Mechanisms promoting a 'safe' state and increasing oxytocin and dopamine levels during acts of kindness suggest how prosocial behavior can enhance health outcomes. This is supported by evidence of improvements in the CTRA profile and a decreased mortality risk among volunteers and caregivers (Jenkinson et al., 2013; Regan et al., 2022).

The key PNI mechanisms that positively impact the immune system involve stress reduction pathways. These pathways are activated by enhancing 'safe' state signals through increased activity in the parasympathetic-vagal system and oxytocin levels and through regulation of the HPA axis and the SNS. On top of increasing the 'safe' mode, oxytocin can directly influence immune responses. This pathway likely represents the link in how social support mitigates the well-documented adverse effects of various life stressors. Additionally, helping behavior introduces another proposed mechanism: increased dopaminergic activity, which may directly influence peripheral innate immune functions (Fig. 2, visual illustration). However, much remains to be discovered about the complex mechanisms and the precise neuroimmune pathways through which dopamine and oxytocin facilitate their effects. Additionally, the role of serotonin—which is involved in various social behaviors and may also influence immune responses—is an area with limited literature and requires further exploration. Understanding the mechanisms behind these effects could shift the scientific community and policymakers' perspectives and efforts to invest more time and effort in these positive social aspects, which can improve public health outcomes and potentially reduce health-related costs.

5. Future directions

The 'positive' aspects of the social environment, which include caring for others, contributing to society, and being in a supportive environment, are crucial for public health. Three main points require addressing:

First, bridge the knowledge gap: There is an urgent need to study the causal effects of these social positives and explore their unique pathways. This can be achieved using animal models, as several validated prosocial behavior models exist across different species (Wu and Hong, 2022). For instance, the helping behavior test paradigm in rats, which revealed neurocircuitry similarities to empathy observed in humans (Bartal et al., 2011; Ben-Ami Bartal et al., 2021), is a potential method for investigating how helping behavior influences the immune system. Furthermore, this paradigm can be utilized to explore the immune implications for rats both providing and receiving support in stressful situations. In human research, experimental designs with immune challenges, such as endotoxin administration, can be implemented, alongside employing the latest wearable technology, such as smartwatches or Aura rings, for real-time data collection, enabling the accurate measurement of heart rate variability (HRV). This innovative approach facilitates comprehensive studies on the impacts of social aspects on both SNS responses and immunity.

Second, overcoming the challenge of studying the intricate effects of positive social contexts on immune function can be addressed by building on the previous point, which involves experimental studies and wide scientific network collaboration. It is essential to establish a coherent and validated paradigm that can be replicated by different researchers in the field, increase the sample size, and strengthen the causal evidence. This is a call to create a collaborative society that focuses on studying these social PNI aspects, which, when done collectively, can help overcome this challenge (Muscatell, 2021).

Third, there is a critical need to raise awareness about this topic in clinical settings as a public health matter. Physicians should incorporate social assessments into their routine evaluations, alongside inquiries about other risk and protective factors like smoking and physical activity. They should also inquire about social support and community involvement. Based on the responses, physicians can then tailor

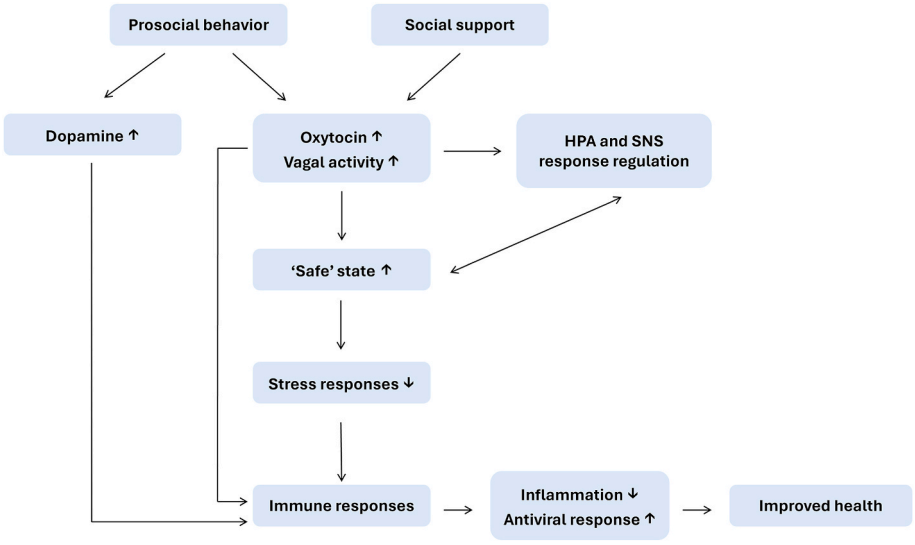

Fig. 2. The key PNI mechanisms that positively impact the immune system involve stress reduction pathways. These pathways are activated by enhancing 'safe' mode signals through increased activity in the parasympathetic-vagal system and oxytocin levels, and through regulation of the HPA axis and the SNS. In addition to increasing the 'safe' mode, oxytocin can directly influence immune responses. This pathway likely represents the link in how social support mitigates the well-documented adverse effects of various life stressors. Moreover, helping behavior introduces another proposed mechanism: increased dopaminergic activity, which may directly influence peripheral innate immune functions.

interventions to meet patients' social needs, such as involving the community in supporting them or encouraging participation in local volunteering. These interventions could help reduce the patient's risk of malignancy, morbidities, and mortalities. As supported by the literature mentioned above, suggesting interventions aimed at enhancing support and social integration is akin to recommending physical activities or a low-sugar diet. Raising awareness can be achieved by addressing the knowledge gaps mentioned in the previous points and by advocating for action from public health policymakers.

6. Conclusion

This article highlights the complexity of the social environment and its influence on immune systems and health outcomes, with a particular emphasis on the less-explored positive aspects and their proposed PNI mechanisms. There is still much to be done to harness the social context for the benefit of individual health and the broader society. However, there's no denying that we are witnessing an evolution in knowledge and initiatives aimed at fostering a healthier, more supportive society.

CRediT authorship contribution statement

Estherina Trachtenberg: Conceptualization, Methodology, Validation, Visualization, Writing – original draft, Writing – review & editing.

Declaration of competing interest

I declare no conflicts of interest.

Data availability

No data was used for the research described in the article.

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