Using conversational artificial intelligence to dissect the psychoneuroimmunology of social safety and threat

Julian Packheiser[1,2], Sigrid Elsenbruch[3,4], Harald Engler[5,*], Dirk Scheele[1,2,*]

[1] Department of Social Neuroscience, Center of Medical Psychology and Translational Neuroscience, Medical Faculty, Ruhr University Bochum, Bochum, Germany

[2] Research Center One Health Ruhr of the University Alliance Ruhr, Ruhr University Bochum, Germany

[3]Department of Medical Psychology and Medical Sociology, Center of Medical Psychology and Translational Neurosciences, Ruhr University Bochum, Bochum, Germany

[4]Department of Neurology, Center for Translational Neuro- and Behavioral Sciences, University Hospital Essen, University of Duisburg-Essen, Essen, Germany

[5]Institute of Medical Psychology and Behavioral Immunobiology, Center for Translational Neuro- and Behavioral Sciences, University of Duisburg-Essen, University Hospital Essen, Essen, Germany

Author note

Julian Packheiser https://orcid.org/0000-0001-9805-6755

Sigrid Elsenbruch https://orcid.org/0000-0002-6528-2665

Harald Engler https://orcid.org/0000-0001-6329-1990

Dirk Scheele https://orcid.org/0000-0002-7613-0376

* *Shared last authorship*

Correspondence:

Julian Packheiser
Department of Social Neuroscience,
Research Center One Health Ruhr of the University Alliance Ruhr
Medical Faculty
Phone: +49 (0)234-32-22434
E-Mail: julian.packheiser@ruhr-uni-bochum.de

Dirk Scheele
Department of Social Neuroscience,
Research Center One Health Ruhr of the University Alliance Ruhr
Medical Faculty
Phone: +49 (0)234-32-28696
E-Mail: Dirk.Scheele@ruhr-uni-bochum.de

Abstract

Human health is profoundly shaped by the quality of our social environments, yet the mechanisms through which social experiences become biologically embedded remain poorly understood. Social Safety Theory (SST) proposes that perceived social safety and threat influence health through neuroendocrine and immune pathways, but it remains unclear which features of social interaction engage these pathways. Here, we argue that conversational artificial intelligence (AI) provides a powerful experimental tool to address this mechanistic gap. Synthetic agents allow researchers to systematically vary core social signals, including responsiveness, reciprocity, empathic cues, agency, and multimodal information, while holding other features of the interaction relatively constant. This controllability creates a unique opportunity to identify which social signals are necessary or sufficient to generate perceived safety or threat and to engage downstream biological responses. Building on SST, we propose a psychoneuroimmunological framework linking experimentally controlled features of synthetic social interaction to neuroendocrine and immune processes and derive testable hypotheses concerning perceived humanness, social-signal strength, and multimodal embodiment. By enabling the causal decomposition of social interaction, conversational AI could help reveal what makes an interaction biologically social and clarify the mechanisms linking social disconnection to health.

Introduction

Feeling socially connected is a fundamental human need. Social disconnection is commonly expressed as loneliness, the subjective discrepancy between desired and actual social relationships (Morr et al., 2022), and social isolation, characterized by small social networks and infrequent social interactions (Cacioppo et al., 2011). Both have emerged as major public health concerns (Cacioppo & Cacioppo, 2018). Despite unprecedented opportunities for communication across geographic distance, social disconnection remains widespread (Surkalim et al., 2022) and is associated with a broad range of adverse mental and physical health outcomes, including depression, anxiety, dementia, suicidality, cardiovascular disease, and type 2 diabetes (DeAngelis et al., 2026; Ezzatvar et al., 2025; Park et al., 2020). Large-scale meta-analyses further suggest that social disconnection rivals or even exceeds other well-established health risk factors such as smoking, obesity, or physical inactivity, in predicting pain symptomatology, morbidity and all-cause mortality (Holt-Lunstad et al., 2015; Piejka et al., 2026).

Despite these robust associations, how social disconnection manifests biologically and ultimately affects health remains poorly understood. Resolving this mechanistic gap is essential not only for understanding the consequences of loneliness, but also for developing scalable approaches to mitigate them. In this Perspective, we argue that conversational artificial intelligence (AI) offers a novel experimental tool for addressing this challenge. We proceed in three steps. First, we outline a mechanistic framework linking social disconnection to adverse health outcomes through alterations in social safety and downstream psychoneuroimmunological processes. Second, we examine which constituent features of human social interaction can be reproduced and independently manipulated in interactions with conversational AI. Third, we propose testable hypotheses about whether and how the exceptional parametrizability of synthetic social agents can be exploited to causally dissect which social signals generate safety or threat and how these signals translate into biological responses.

Social connectedness, social safety, and immune regulation

The pervasive associations between social disconnection and mental and physical health raise a fundamental question: through which biological pathways can social experiences influence such diverse health outcomes? One promising framework centers on social safety and social threat. Social connectedness is closely associated with feelings of safety, whereas loneliness

and social isolation can heighten perceptions of social threat (Best et al., 2021). Social Safety Theory (SST) provides an evolutionary and biological account of how these social experiences may become biologically embedded (Slavich, 2020). According to SST, the brain continuously monitors the social environment for cues of social safety or social threat with perceived social threat promoting neuroendocrine and inflammatory responses, whereas social safety may attenuate these processes. From an evolutionary perspective, such responses may have been adaptive because social conflict, exclusion, and isolation could increase vulnerability to physical injury and pathogen exposure. In contemporary environments, however, persistent perceptions of social threat may result in prolonged activation of these systems even in the absence of objective danger. Loneliness may be particularly relevant in this context because it may bias the perception of social environments toward threat, potentially linking chronic social disconnection to sustained immunological dysregulation (Slavich, 2020).

A growing psychoimmunological literature suggests that social connectedness plays a fundamental role in immune regulation and inflammatory functioning. Indicators of social safety, such as social support and perceived social integration, have been associated with lower systemic inflammation, more adaptive immune responses, and reduced physiological stress reactivity, whereas loneliness and social isolation have been linked to chronic low-grade inflammation and altered immune functioning(Granieri et al., 2026; Leschak & Eisenberger, 2019; Matthews et al., 2024). Social disconnection has further been associated with elevated circulating inflammatory markers (Matthews et al., 2024; Smith et al., 2020), altered antiviral responses (Cole, Levine, et al., 2015), and changes in gene expression profiles involved in inflammation and immune defense (Cole, Capitanio, et al., 2015). Importantly, however, the evidence is neither uniform nor specific. Meta-analytic evidence (Smith et al., 2020) suggests relatively modest and inconsistent associations between loneliness and pro-inflammatory cytokines such as interleukin (IL)-6 and tumor necrosis factor (TNF) α, whereas stronger and more consistent effects have been observed for objective social isolation, particularly with respect to elevated concentrations of the acute-phase protein C-reactive protein (CRP), a downstream marker of inflammation associated with increased risk for cardiovascular and metabolic disease (Olson et al., 2023). Despite rapidly growing interest in the interplay between social behavior and immune functioning (Flasbeck et al., 2026), substantial methodological heterogeneity, including variation in how social disconnection is

operationalized, which immune markers are assessed, and how health behavior, medication use, age, and socioeconomic status are controlled, continues to limit mechanistic inference.

Recent theoretical perspectives hypothesize that the chronicity of loneliness may represent a critical yet largely understudied moderator of health-related outcomes (Haihambo et al., 2025; Packheiser et al., 2025). While acute, transient loneliness may elicit adaptive social-threat and reaffiliation responses, prolonged or chronic loneliness may lead to persistent or dysregulated activation of these systems, thereby contributing to maladaptive inflammatory responses. However, this assumption has not yet been empirically tested. Consequently, the precise biological pathways through which social disconnection contributes to immune dysregulation remain incompletely understood (Smith et al., 2020). Moreover, social disconnection is strongly associated with conditions such as major depression and anxiety disorders (Cacioppo et al., 2006; Wolters et al., 2023), which are themselves accompanied by alterations in immune functioning (Hole et al., 2025). Establishing whether immunological changes are specifically attributable to social disconnection, or instead reflect broader dimensions of psychological distress, will therefore be essential for future mechanistic work.

Oxytocin represents one candidate pathway through which socially safe experiences could influence downstream biological processes. The oxytocin system is implicated in social bonding, affiliative touch, stress regulation, and immune functioning (Althammer et al., 2021), including the modulation of inflammatory responses and wound-healing processes (Schneider et al., 2026). Importantly, emerging evidence indicates that loneliness is associated with diminished oxytocin reactivity to positive social interactions. For example, lonely individuals exhibit reduced endogenous oxytocin responses following positive social contact, despite reporting similar subjective pleasantness as non-lonely individuals (Lieberz et al., 2021). In addition, administering intranasal oxytocin before a short-term group intervention enhanced reductions in state loneliness and promoted positive bonding among group members, although it did not augment intervention effects on more trait-like loneliness(Berger et al., 2024). Reduced oxytocin responsivity may therefore represent one mechanism through which chronic social disconnection becomes biologically embedded and contributes to adverse mental and physical health outcomes, potentially mediated via its broad anti-inflammatory effects (Mehdi et al., 2022).

Taken together, SST provides a compelling framework for understanding how social disconnection could affect health: diminished social safety and persistent social threat may engage neuroendocrine and immune pathways that, when chronically activated, contribute to adverse health outcomes. Consistent with this view, many interventions targeting loneliness seek either to recalibrate maladaptive interpretations of social situations through cognitive restructuring (Zagic et al., 2022) or to increase opportunities for positive social contact, both online and offline (Fokkema & Knipscheer, 2007; Käll et al., 2020). Yet interventions relying on human interaction partners are often resource-intensive, difficult to standardize, and inherently limited in the extent to which individual social signals can be manipulated independently.

Conversational AI creates a fundamentally novel and innovative experimental opportunity. Synthetic agents can generate socially meaningful interactions (Starke et al., 2024), and they allow researchers to systematically vary individual features of those interactions. Rather than viewing conversational AI solely as a scalable intervention for social disconnection, we propose using it as an epistemic tool to identify which components of social interaction generate perceptions of safety or threat and which of these components are sufficient to engage downstream biological responses. This approach first requires decomposing social interaction itself: Which signals make an interaction feel social? Which cues communicate safety or threat? How long must feelings of safety or threat persist to affect our health and well-being? Must these signals originate from a human agent, or is their perception sufficient? And can conversational AI manipulate these signals independently enough to reveal their causal contribution to psychoneuroimmunological functioning?

Decomposing social interactions

A minimal requirement of social interaction is the perceived presence of an interaction partner, either physically or digitally. Conversational AI readily fulfills this criterion: unlike human interaction partners, AI systems can be continuously available and immediately responsive (Stade et al., 2024). Yet social interaction involves more than mere presence. Humans value responsiveness, reciprocity, and the experience of being understood by others. These features may also have biological relevance. Longitudinal evidence suggests that greater perceived partner responsiveness is associated with smaller increases in systemic inflammation (Gouin et al., 2026), while partner responsiveness has been linked to reduced pro-inflammatory

reactivity in the context of an immune challenge (Lai et al., 2024). Conversational AI can reproduce some of these signals by generating highly responsive, context-sensitive, and validating responses, in some settings even outperforming physicians in perceived empathy and quality of communication (Ayers et al., 2023). Experimental evidence further suggests that conversational AI can elicit interpersonal experiences comparable to human interaction, but critically, these effects may depend on whether users believe that they are interacting with a human or an AI system (Kleinert et al., 2026).

Conscious awareness of interacting with an AI system represents a fundamental boundary condition of synthetic sociality. Conversational AI can simulate socially meaningful signals but lacks the intrinsic motivations, beliefs, intentions, and needs that characterize human agents (Bender et al., 2021). A central question is therefore whether social signals must originate from an intentional agent to engage social and biological systems, or whether their perceived social meaning is sufficient. Humans readily attribute human-like qualities to conversational AI, including empathy, awareness, and autonomous thought (Seok et al., 2025), and greater perceived empathy and humanness have been associated with stronger reliance on AI interaction partners (Mazhar et al., 2026). More broadly, humans can form meaningful parasocial bonds even with fictional characters despite the absence of genuine reciprocity (Nguyen et al., 2023). These findings suggest that objectively reciprocal agency may not be necessary for an interaction to acquire subjective social significance. This observation may also matter biologically. Perceived empathy during therapeutic encounters has been experimentally linked to improved immune-related outcomes and reduced infection risk (Rakel et al., 2011). Direct evidence that reciprocity itself modulates immune functioning remains scarce. However, reciprocal social interaction has been consistently linked to oxytocinergic signaling. In new romantic couples, plasma oxytocin concentrations were positively associated with interactive reciprocity, including social focus, positive affect, affectionate touch, and synchronized dyadic states (Schneiderman et al., 2012). Complementing this correlational evidence, synchronous dyadic interaction has been shown to increase endogenous oxytocin release, while intranasal oxytocin enhanced facial and vocal emotional expressiveness, suggesting a bidirectional association between oxytocin signaling and reciprocal social communication (Spengler et al., 2017). Given the immunomodulatory properties of the oxytocin system (P. Wang et al., 2015), these findings suggest a potential neuroendocrine mechanism through which reciprocity could influence immune functioning, although this

pathway needs to be tested directly. Whether the absence of genuine reciprocity and intentional agency in AI interactions limits their capacity to induce social safety and downstream biological responses therefore remains an important empirical question.

A further critical distinction between human and conversational AI interactions lies in their degree of symmetry. While human interactions can be highly asymmetrical, they are typically characterized by bidirectional initiative, with both partners actively shaping the course of the interaction in a dynamic and coordinated fashion (Jaegher & Di Paolo, 2007). In contrast, interactions with conversational AIs are generally structured more asymmetrically. Although they formally fulfill criteria of turn-taking, the contributions of the conversational AI are predominantly reactive and user-initiated (Shanahan, 2024). Human interaction partners, by comparison, initiate, guide, and pursue their own motivations during interactions (Chater et al., 2022). Whether such autonomous agency is necessary for an interaction to signal social safety remains unknown. SST emphasizes the perceived availability of responsive, supportive, and dependable others (Slavich, 2020), raising the possibility that these perceived properties, rather than genuine autonomy, may be sufficient to engage social-safety mechanisms. At the same time, contemporary therapeutic chatbots increasingly assume a more proactive role by guiding users through structured interventions such as cognitive-behavioral or mindfulness-based techniques (Farzan et al., 2025). Conversational AI therefore provides an unusual opportunity to experimentally vary the degree of perceived agency and initiative while holding other features of the interaction relatively constant.

Beyond these structural properties, human social interactions are inherently multimodal. Emotional understanding and perceived empathy are shaped not only by semantic content but also by vocal cues such as intonation, prosody, and inflection (Aziz-Zadeh et al., 2010; Regenbogen et al., 2012). This may be particularly relevant to social disconnection, as loneliness is associated with alterations in paralinguistic features of speech and can be predicted from automated speech analyses (Immel et al., 2026). Advances in text-to-speech technology increasingly allow artificial agents to produce emotionally expressive and controllable vocal signals (Liu et al., 2024), potentially strengthening their capacity to convey socially meaningful cues. Social vocalizations in human interactions have also been associated with increased oxytocin concentrations, suggesting a potential neuroendocrine pathway through which vocal signals could acquire biological relevance (Seltzer et al., 2010). Visual information provides another major source of social signals: facial expressions convey affective

states, attentional orientation, and trustworthiness and contribute substantially to perceived empathy (Drimalla et al., 2019). At present, most conversational AI interactions lack such visual feedback. However, emerging systems incorporating avatar-based interfaces aim to provide photorealistic, interactive representations that can express emotions through both facial and vocal channels (e.g., NVIDIA Omniverse avatars; Wu et al., 2026). These developments suggest that multimodal AI systems may increasingly approximate key aspects of face-to-face interaction.

In contrast to speech and visual modalities, tactile interaction remains largely absent from current conversational AI systems. Human social touch has been shown to exert powerful effects on physical and mental well-being (Packheiser et al., 2024) and to play an important role in social bonding and the reduction of loneliness (Packheiser et al., 2025). Some of these effects may involve immunological pathways. Evidence for this link comes from both correlational and experimental research. For example, a correlational study found associations between hugging behavior and proinflammatory cytokine levels (van Raalte & Floyd, 2021), whereas an experimental study demonstrated that individuals who received more frequent hugs were less susceptible to upper respiratory infection following controlled exposure to a respiratory pathogen (Cohen et al., 2015). Because tactile interactions involve close physical proximity and therefore increased risk of pathogen transmission (Thiebaut et al., 2021), these findings may indicate that social touch particularly engages antiviral immune responses. The absence of touch could consequently represent an important boundary condition for synthetic social interactions. Social robots may partially reproduce the benefits of human touch, although current evidence suggests that their effects are weaker than those of human-delivered touch (Packheiser et al., 2024). Advances in affective robotics may eventually allow tactile signals to be incorporated into AI-mediated interactions and, importantly, manipulated independently from other dimensions of social exchange.

Olfactory communication represents an even less explored dimension of human–AI interaction. Olfactory cues contribute to human social perception, familiarity, and interpersonal bonding (Ferdenzi et al., 2016; Maier et al., 2019), yet they are almost entirely absent from current artificial social agents. This modality may be particularly relevant to immune functioning because human body odors can convey information about sickness and immune activation (Anja Juran et al., 2023). Following experimental endotoxin exposure, for example, changes in human body odor can be detected by others and are associated with

cytokine responses to immune activation (Gordon et al., 2023). Conversely, familiar and pleasant body odors may facilitate affiliation and bonding (Blomkvist & Hofer, 2021; Croy et al., 2019). Initial attempts to introduce chemosensory signals into human–robot interactions have produced limited evidence, as for example, hexanal, an odor that has been shown to increase in interpersonal trust between humans (van Nieuwenburg et al., 2019), did not increase trust toward a robot (Croijmans et al., 2022), leaving the contribution of olfactory information to synthetic sociality largely unexplored.

Taken together, current conversational AI does not reproduce the full richness of human social interaction, but it can increasingly approximate, and, crucially, experimentally isolate, many of its constituent features (Figure 1). Advances in voice synthesis, embodied avatars, affective robotics, and potentially olfactory interfaces are progressively expanding the range of social signals that can be delivered by synthetic agents. Emerging approaches that equip AI systems with representations of internal states and embodied environments may further increase their capacity for adaptive and cooperative social behavior (Kadambi et al., 2026). The critical question, however, is not whether AI can perfectly reproduce human interaction. Rather, its scientific value may lie precisely in its imperfection and controllability: individual social signals can be added, removed, or parametrically varied to test which features are necessary or sufficient to generate social safety. Although many of these features have been linked, directly or indirectly, to immune functioning in human–human interactions, whether the same signals retain their biological potency when generated by a synthetic agent remains unknown. Addressing this question could reveal not only whether AI can evoke biologically meaningful social experiences, but also which components of human social interaction are sufficient to engage psychoneuroimmunological pathways in the first place.

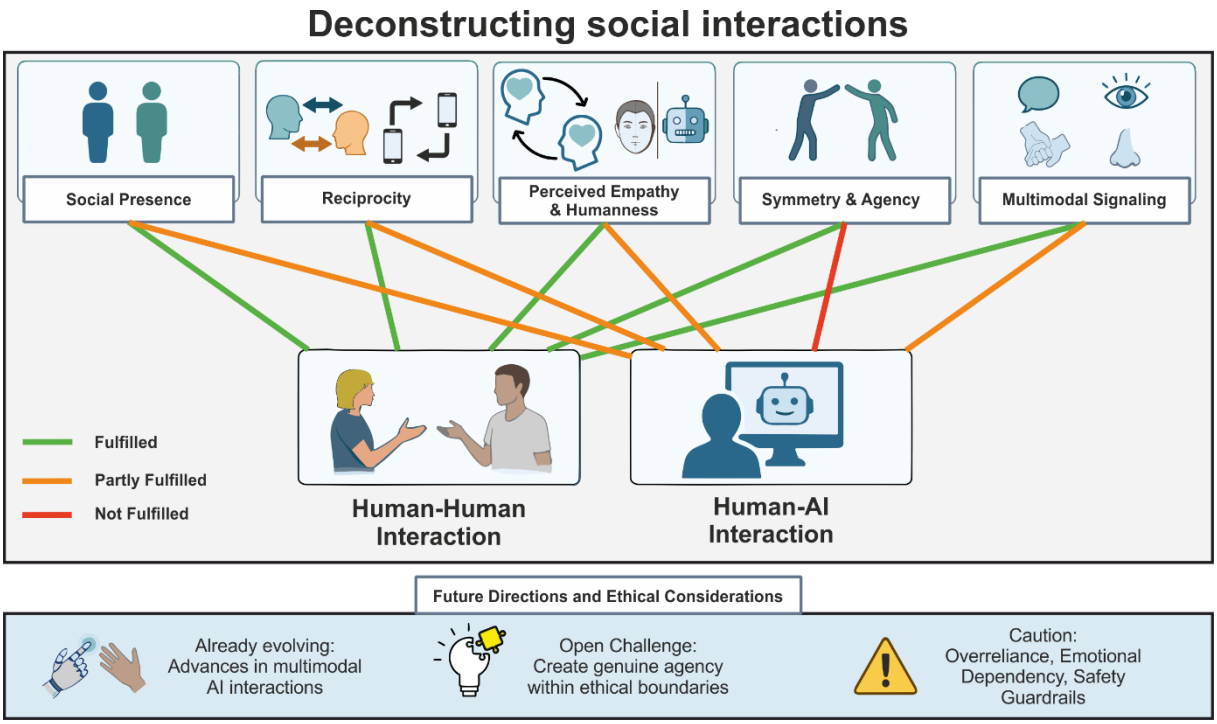

Figure1. Domains of social interactions (Social Presence, Reciprocity, Perceived Empathy and Humanness, Symmetry & Agency, Multimodal Signaling) and their presence in human-human or human-AI interactions. *For human–human interactions, all domains are generally well represented, although the availability and responsiveness of human interaction partners are naturally constrained.* In contrast, chatbots are always available and immediately respond if presence is demanded.

Toward a psychoneuroimmunological framework for human and synthetic social relationships

An emerging literature suggests that synthetic social interactions can reduce subjective social disconnection, at least in the short term(Fang et al., 2025; Folk & Dunn, 2026; Li et al., 2026; Y. Wang et al., 2025). We argue, however, that the scientific potential of conversational AI extends far beyond testing whether artificial companions can substitute for human interaction partners. Conversational AI provides a high level of control over the individual elements of social interaction. Responsiveness, reciprocity, perceived empathy, agency, and multimodal signaling can be systematically varied while other aspects of the interaction are held relatively constant, something that is difficult, if not impossible, to achieve in natural human–human interactions. This degree of controllability makes conversational AI a powerful epistemic tool for decomposing social interaction: it allows researchers to test which social signals are necessary or sufficient to generate perceptions of social safety or threat and how these signals are translated into downstream biological responses.

Realizing this potential requires moving beyond behavioral and self-report outcomes toward experiments that directly link controlled manipulations of synthetic social signals to neuroendocrine and immune responses. We propose that SST provides a useful

psychoneuroimmunological framework for this endeavor. If biological responses to social connection depend primarily on the perception of socially meaningful safety signals, rather than on the objective presence of another human being, then appropriately configured artificial agents should be capable of engaging at least some of the same pathways. Conversely, if genuine human agency or specific embodied signals are necessary, synthetic interactions should fail to reproduce these effects despite eliciting comparable subjective experiences. These competing possibilities generate a set of directly testable predictions (see Figure 2 for an overview):

H1: Synthetic social safety should engage immune-related pathways. Interactions with supportive conversational AI should increase perceived social safety relative to socially neutral or threatening AI interactions and produce corresponding regulatory changes in neuroendocrine and immune responses, such as attenuated stress-related and pro-inflammatory reactivity.Critically, these effects should extend beyond changes in subjective affect and could be tested using inflammatory responses to standardized immune challenges (Flasbeck et al., 2026) or, where ethically and practically feasible, susceptibility and symptom severity following controlled pathogen exposure (Cohen et al., 2015).

H2: Perceived humanness should moderate biological effects. If attribution of human agency contributes to social-safety signaling, identical interactions should elicit weaker subjective and biological responses when the interaction partner is explicitly identified as an AI rather than as a human (Kleinert et al., 2026). Such experimental dissociation of *interaction content* from *belief about the interaction partner* would provide a particularly stringent test of whether perceived humanness is necessary for biological social-safety responses.

H3: Individual social signals should exert parametrically dissociable effects. Systematically increasing or decreasing responsiveness, reciprocity, and perceived empathy should produce graded changes in perceived social safety and downstream neuroendocrine and immune responses. Factorial manipulation of these dimensions could further establish whether their effects are additive, interactive, or dependent on specific combinations of social cues.

H4: Multimodal embodiment should amplify, and potentially qualitatively alter, biological responses. Adding vocal, visual, tactile, or eventually olfactory signals should strengthen perceived social presence and amplify the social meaning of the interaction, thereby enhancing safety responses in supportive contexts and potentially threat responses in adverse

contexts.Tactile interaction may be particularly informative because physical contact and close proximity historically covary with pathogen exposure. We therefore hypothesize that adding an affective-touch component may engage host-defense pathways that are less strongly recruited by purely linguistic or audiovisual interactions.

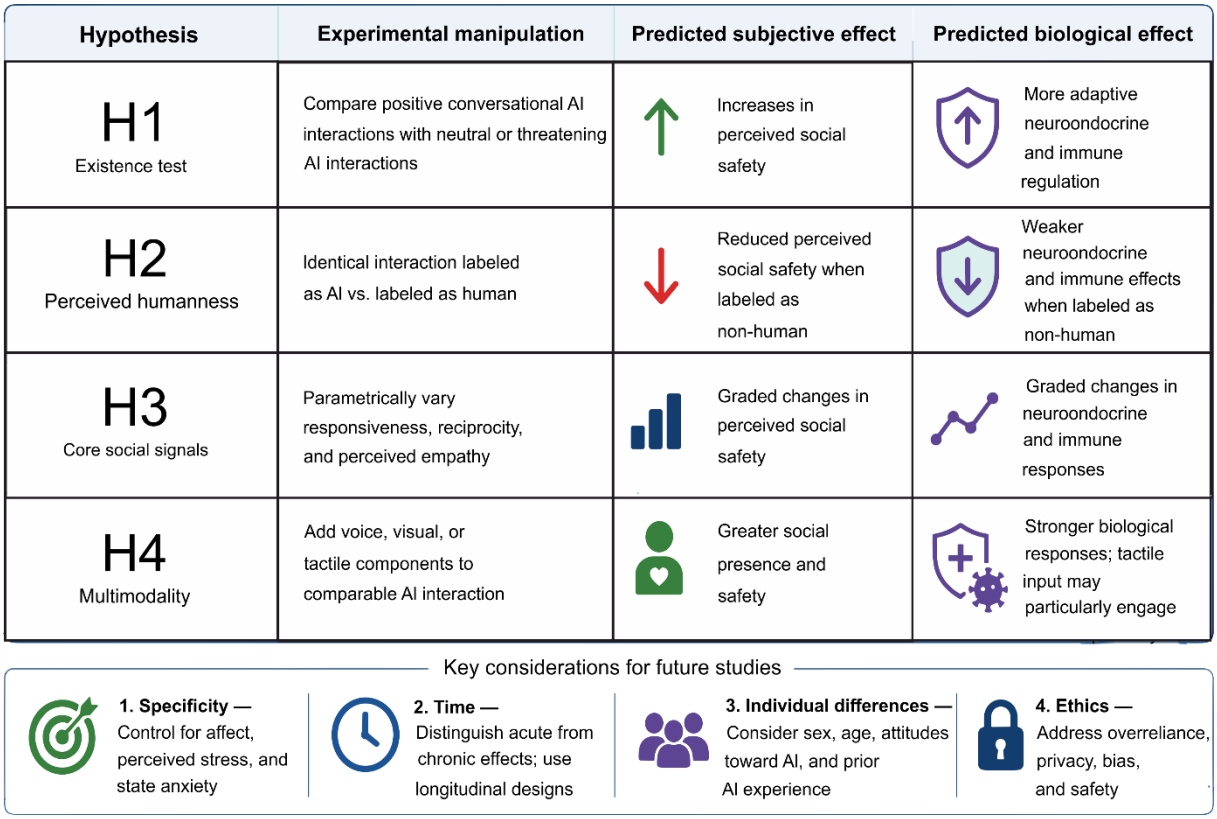

Figure 2. Testable hypotheses within a psychoneuroimmunological framework of human and synthetic social relationships. We propose that synthetic social interactions can engage social safety or threat systems and affect downstream neuroendocrine and immune processes, but that these effects depend on perceived humanness, the strength of core social signals, and the degree of multimodal embodiment. Future studies should additionally address specificity, chronicity, individual differences, and ethical risks.

Testing these predictions will require careful consideration of specificity. For example, changes in immune functioning following a socially supportive interaction could reflect social safety itself, but they could also arise indirectly through changes in positive or negative affect, perceived stress, or state anxiety. These variables should therefore be measured explicitly and incorporated into experimental models to determine whether social safety explains biological responses above and beyond more general changes in affective state. This issue is particularly important in research on social disconnection, where loneliness is associated with a broad range of psychological and health-related variables that may independently influence biological functioning (Piejka et al., 2026).

A second critical dimension is time. Although loneliness is associated with numerous adverse health outcomes, experimental evidence establishing a causal pathway from loneliness to biological dysfunction remains scarce, in part because loneliness itself is difficult to manipulate experimentally (Wiśniewska et al., 2025). Existing experimental studies largely concern transient states of loneliness, whereas theoretical accounts increasingly distinguish adaptive, short-lived loneliness from persistent or chronic loneliness, which may be particularly relevant to long-term health consequences (Haihambo et al., 2025). This distinction is also supported by immunological findings: impaired antibody responses to influenza vaccination, for example, have been associated particularly with persistent rather than transient loneliness (Pressman et al., 2005).

The same temporal distinction is crucial for synthetic relationships. An AI interaction that acutely reduces loneliness or increases social safety cannot be assumed to confer long-term health benefits. Indeed, longitudinal evidence suggests that greater reliance on conversational AI for companionship may under some circumstances predict increasing rather than decreasing loneliness over time (Folk & Dunn, 2026). Most evidence linking individual signals of social safety, such as responsiveness, reciprocity, or social contact, to immune functioning likewise concerns relatively acute responses. Future studies should therefore distinguish explicitly between acute state changes and longer-term biological embedding, ideally combining experimental manipulations with repeated assessments of social experience, neuroendocrine responses, and immune functioning. This would allow researchers to test whether repeated synthetic social experiences recalibrate social-safety systems over time or whether their acute benefits fail to translate into durable physiological adaptation.

Finally, the effects of synthetic social signals are unlikely to be uniform across individuals. Biological sex and gender may represent relevant moderators, as some neurocognitive and health-related consequences of loneliness appear to differ between men and women (Morr et al., 2022; Spreng et al., 2020) and social disconnection has been associated with sex-specific differences in inflammatory and immune-related outcomes (Davidsen et al., 2022; van der Velpen et al., 2024). Age is likely to be equally important, as age-related differences have been observed in both exposure to AI and attitudes toward AI-based technologies (Stein et al., 2024). More broadly, individual differences in anthropomorphism, trust in technology, prior AI experience, and expectations about artificial agents may determine whether identical synthetic signals are interpreted as socially meaningful. Such moderators are therefore not

merely nuisance variables: they provide an opportunity to identify the conditions under which synthetic signals acquire sufficient social meaning to engage biological social-safety systems.

Ethical and societal considerations

The same properties that make conversational AI potentially effective in fostering social connection also create important risks. Socially disconnected individuals may form strong attachments to artificial companions, potentially leading to overreliance, emotional dependence, or withdrawal from human relationships (Laestadius et al., 2024). This may be particularly relevant in chronic loneliness, which is associated with reduced interpersonal trust (Lieberz et al., 2021) and has been proposed to involve increased sensitivity to potential social threat (Hawkley & Cacioppo, 2010).

Artificial companions are typically highly available, responsive, and affirming, whereas human relationships inevitably involve disagreement, competing needs, and imperfect responsiveness. Repeated exposure to such interactions could therefore distort expectations about intimacy and reciprocity, particularly when AI systems display sycophantic tendencies by disproportionately affirming users' beliefs or behavior (Wiederhold, 2025; Cheng et al., 2026). Moreover, conversational AI can appear highly empathic without possessing genuine emotions or intentions, creating risks when users attribute excessive understanding or trustworthiness to these systems. Probabilistic outputs further necessitate robust safeguards, particularly in sensitive contexts such as mental health (Blease & Torous, 2023). Finally, synthetic relationships pose risks for privacy breaches, exposure of personal and sensitive data, or replacement of human professions, especially in the therapy sector (Starke et al., 2024). Their increasing social potency therefore strengthens the need for careful empirical evaluation and appropriate governance.

Conclusion

Conversational AI may transform not only efforts to address social disconnection, but also our understanding of how social experiences become biologically embedded. If synthetic interactions engage the same social-safety systems that regulate neuroendocrine and immune responses to human social cues, this would challenge the assumption that such effects require the physical presence or genuine intentionality of another person.

Crucially, conversational AI provides experimental control over individual social signals, including responsiveness, reciprocity, perceived empathy, agency, and multimodal cues, that is difficult to achieve in human interaction. Synthetic agents may therefore serve as an epistemic tool for identifying which features of social interaction are necessary or sufficient to generate social safety and downstream biological responses. Ultimately, this approach could reveal what makes a social interaction biologically "social" and capable of mitigating some of the health risks associated with social disconnection.

References

Althammer, F., Eliava, M., & Grinevich, V. (2021). Central and peripheral release of oxytocin: Relevance of neuroendocrine and neurotransmitter actions for physiology and behavior. *Handbook of Clinical Neurology*, *180*, 25–44. https://doi.org/10.1016/B978-0-12-820107-7.00003-3

Anja Juran, S., Tognetti, A., Lundström, J. N., Kumar, L., Stevenson, R. J., Lekander, M., & Olsson, M. J. (2023). Disgusting odors trigger the oral immune system. *Evolution, Medicine, and Public Health*, *11*(1), 8–17. https://doi.org/10.1093/emph/eoac042

Ayers, J. W., Poliak, A., Dredze, M., Leas, E. C., Zhu, Z., Kelley, J. B., Faix, D. J., Goodman, A. M., Longhurst, C. A., Hogarth, M., & Smith, D. M. (2023). Comparing Physician and Artificial Intelligence Chatbot Responses to Patient Questions Posted to a Public Social Media Forum. *JAMA Internal Medicine*, *183*(6), 589–596. https://doi.org/10.1001/jamainternmed.2023.1838

Aziz-Zadeh, L., Sheng, T., & Gheytanchi, A. (2010). Common premotor regions for the perception and production of prosody and correlations with empathy and prosodic ability. *PloS One*, *5*(1), e8759. https://doi.org/10.1371/journal.pone.0008759

Bender, E. M., Gebru, T., McMillan-Major, A., & Shmitchell, S. (2021). On the Dangers of Stochastic Parrots. In *Proceedings of the 2021 ACM Conference on Fairness, Accountability, and Transparency* (pp. 610–623). ACM. https://doi.org/10.1145/3442188.3445922

Berger, R., Hurlemann, R [Rene], Shamay-Tsoory, S., Kanterman, A., Brauser, M., Gorni, J., Luhmann, M., Schramm, E., Schultz, J., Philipsen, A., Lieberz, J., & Scheele, D. (2024). Oxytocin-Augmented Modular-Based Group Intervention for Loneliness: A Proof-Of-Concept Randomized Controlled Trial. *Psychotherapy and Psychosomatics*, *93*(3), 169–180. https://doi.org/10.1159/000538752

Best, T., Herring, L., Clarke, C., Kirby, J., & Gilbert, P. (2021). The experience of loneliness: The role of fears of compassion and social safeness. *Personality and Individual Differences*, *183*, 111161. https://doi.org/10.1016/j.paid.2021.111161

Blease, C., & Torous, J. (2023). Chatgpt and mental healthcare: Balancing benefits with risks of harms. *BMJ Mental Health*, *26*(1). https://doi.org/10.1136/bmjment-2023-300884

Blomkvist, A., & Hofer, M. (2021). Olfactory Impairment and Close Social Relationships. A Narrative Review. *Chemical Senses*, *46*. https://doi.org/10.1093/chemse/bjab037

Cacioppo, J. T., & Cacioppo, S. (2018). The growing problem of loneliness. *Lancet (London, England)*, *391*(10119), 426. https://doi.org/10.1016/S0140-6736(18)30142-9

Cacioppo, J. T., Hawkley, L. C., Norman, G. J., & Berntson, G. G. (2011). Social isolation. *Annals of the New York Academy of Sciences*, *1231*(1), 17–22. https://doi.org/10.1111/j.1749-6632.2011.06028.x

Cacioppo, J. T., Hughes, M. E., Waite, L. J., Hawkley, L. C., & Thisted, R. A. (2006). Loneliness as a specific risk factor for depressive symptoms: Cross-sectional and longitudinal analyses. *Psychology and Aging*, *21*(1), 140–151. https://doi.org/10.1037/0882-7974.21.1.140

Chater, N., Zeitoun, H., & Melkonyan, T. (2022). The paradox of social interaction: Shared intentionality, we-reasoning, and virtual bargaining. *Psychological Review*, *129*(3), 415–437. https://doi.org/10.1037/rev0000343

Cheng, M., Lee, C., Khadpe, P., Yu, S., Han, D., & Jurafsky, D. (2026). Sycophantic AI decreases prosocial intentions and promotes dependence. *Science (New York, N.Y.)*, *391*(6792), eaec8352. https://doi.org/10.1126/science.aec8352

Cohen, S., Janicki-Deverts, D., Turner, R. B., & Doyle, W. J. (2015). Does hugging provide stress-buffering social support? A study of susceptibility to upper respiratory infection and illness. *Psychological Science*, *26*(2), 135–147. https://doi.org/10.1177/0956797614559284

Cole, S. W., Capitanio, J. P., Chun, K., Arevalo, J. M. G., Ma, J., & Cacioppo, J. T. (2015). Myeloid differentiation architecture of leukocyte transcriptome dynamics in perceived social isolation. *Proceedings of the National Academy of Sciences of the United States of America*, *112*(49), 15142–15147. https://doi.org/10.1073/pnas.1514249112

Cole, S. W., Levine, M. E., Arevalo, J. M. G., Ma, J., Weir, D. R., & Crimmins, E. M. (2015). Loneliness, eudaimonia, and the human conserved transcriptional response to adversity. *Psychoneuroendocrinology*, *62*, 11–17. https://doi.org/10.1016/j.psyneuen.2015.07.001

Croijmans, I., van Erp, L., Bakker, A., Cramer, L., Heezen, S., van Mourik, D., Weaver, S., & Hortensius, R. (2022). No Evidence for an Effect of the Smell of Hexanal on Trust in Human-Robot Interaction. *International Journal of Social Robotics*, 1–10. https://doi.org/10.1007/s12369-022-00918-6

Croy, I., Mohr, T., Weidner, K., Hummel, T., & Junge-Hoffmeister, J. (2019). Mother-child bonding is associated with the maternal perception of the child's body odor.

Physiology & Behavior, *198*, 151–157. https://doi.org/10.1016/j.physbeh.2018.09.014

Davidsen, K., Carstensen, S., Kriegbaum, M., Bruunsgaard, H., & Lund, R. (2022). Do partnership dissolutions and living alone affect systemic chronic inflammation? A cohort study of Danish adults. *Journal of Epidemiology and Community Health*. Advance online publication. https://doi.org/10.1136/jech-2021-217422

DeAngelis, R., Burnside, L., Donnell, D. O., Hicken, M., Umberson, D., & Perry, B. (2026). Social connection and cognitive health: A review of concepts, measures, and research priorities. *Alzheimer's & Dementia : The Journal of the Alzheimer's Association*, *22*(5), e71517. https://doi.org/10.1002/alz.71517

Drimalla, H., Landwehr, N., Hess, U., & Dziobek, I. (2019). From face to face: The contribution of facial mimicry to cognitive and emotional empathy. *Cognition & Emotion*, *33*(8), 1672–1686. https://doi.org/10.1080/02699931.2019.1596068

Ezzatvar, Y., Caballero, Ó., Duclos-Bastias, D., Yáñez-Sepúlveda, R., & García-Hermoso, A. (2025). Loneliness and social isolation as risk factors for type 2 diabetes onset: A systematic review and meta-analysis. *Diabetes Research and Clinical Practice*, *223*, 112124. https://doi.org/10.1016/j.diabres.2025.112124

Fang, C. M., Liu, A. R., Danry, V., Lee, E., Chan, S. W. T., Pataranutaporn, P., Maes, P., Phang, J., Lampe, M., Ahmad, L., & Agarwal, S. (2025). *How AI and Human Behaviors Shape Psychosocial Effects of Extended Chatbot Use: A Longitudinal Randomized Controlled Study*. https://arxiv.org/pdf/2503.17473

Farzan, M., Ebrahimi, H., Pourali, M., & Sabeti, F. (2025). Artificial Intelligence-Powered Cognitive Behavioral Therapy Chatbots, a Systematic Review. *Iranian Journal of Psychiatry*, *20*(1), 102–110. https://doi.org/10.18502/ijps.v20i1.17395

Ferdenzi, C., Rouby, C., & Bensafi, M. (2016). The Social Nose: Importance of Olfactory Perception in Group Dynamics and Relationships. *Psychological Inquiry*, *27*(4), 299–305. https://doi.org/10.1080/1047840X.2016.1215207

Flasbeck, V., Engler, H., Marková, V., Schedlowski, M., & Brüne, M. (2026). Between care and contagion: Insights from the endotoxin model into the social facets of sickness. *Neuroscience and Biobehavioral Reviews*, *180*, 106486. https://doi.org/10.1016/j.neubiorev.2025.106486

Fokkema, T., & Knipscheer, K. (2007). Escape loneliness by going digital: A quantitative and qualitative evaluation of a Dutch experiment in using ECT to overcome loneliness among older adults. *Aging & Mental Health*, *11*(5), 496–504. https://doi.org/10.1080/13607860701366129

Folk, D., & Dunn, E. (2026). How Does Turning to AI for Companionship Predict Loneliness and Vice Versa? *Psychological Science*, *37*(4), 276–286. https://doi.org/10.1177/09567976261427747

Gordon, A. R., Lundström, J. N., Kimball, B. A., Karshikoff, B., Sorjonen, K., Axelsson, J., Lekander, M., & Olsson, M. J. (2023). Human scent as a first-line defense against disease. *Scientific Reports*, *13*(1), 16709. https://doi.org/10.1038/s41598-023-43145-3

Gouin, J.-P., Sánchez Carro, Y., Perezmontemayor Cruz, I., & MacNeil, S. (2026). Perceived partner responsiveness is associated with longitudinal changes in circulating inflammatory biomarkers among caregiving mothers in midlife. *Biological Psychology*, *206*, 109244. https://doi.org/10.1016/j.biopsycho.2026.109244

Granieri, A., Sauta, M. D., Cerutti, G., Luca, A. de, Ricco, C., Grimaldi, C., Gonella, M., & Franzoi, I. G. (2026). Loneliness, the immune system, and cardiovascular health: A systematic literature review. *British Journal of Health Psychology*, *31*(1), e70044. https://doi.org/10.1111/bjhp.70044

Haihambo, N., Layiwola, D.-M., Blank, H., Hurlemann, R [René], & Scheele, D. (2025). Loneliness and social conformity: A predictive processing perspective. *Annals of the New York Academy of Sciences*, *1547*(1), 5–17. https://doi.org/10.1111/nyas.15324

Hawkley, L. C., & Cacioppo, J. T. (2010). Loneliness matters: A theoretical and empirical review of consequences and mechanisms. *Annals of Behavioral Medicine : A Publication of the Society of Behavioral Medicine*, *40*(2), 218–227. https://doi.org/10.1007/s12160-010-9210-8

Hole, C., Dhamsania, A., Brown, C., & Ryznar, R. (2025). Immune Dysregulation in Depression and Anxiety: A Review of the Immune Response in Disease and Treatment. *Cells*, *14*(8). https://doi.org/10.3390/cells14080607

Holt-Lunstad, J., Smith, T. B., Baker, M., Harris, T., & Stephenson, D. (2015). Loneliness and social isolation as risk factors for mortality: A meta-analytic review. *Perspectives on Psychological Science : A Journal of the Association for Psychological Science*, *10*(2), 227–237. https://doi.org/10.1177/1745691614568352

Immel, D., Mallick, E., Linz, N., Barton, S., Hurlemann, R [René], & Scheele, D. (2026). Automatic speech analysis can predict loneliness. *Scientific Reports*, *16*(1). https://doi.org/10.1038/s41598-026-45965-5

Jaegher, H. de, & Di Paolo, E. (2007). Participatory sense-making. *Phenomenology and the Cognitive Sciences*, *6*(4), 485–507. https://doi.org/10.1007/s11097-007-9076-9

Kadambi, A., Aziz-Zadeh, L., Damasio, A., Iacoboni, M., & Narayanan, S. (2026). Embodiment in multimodal large language models. *Neuron*, *114*(11), 1908–1921. https://doi.org/10.1016/j.neuron.2026.03.004

Käll, A., Backlund, U., Shafran, R., & Andersson, G. (2020). Lonesome no more? A two-year follow-up of internet-administered cognitive behavioral therapy for loneliness. *Internet Interventions*, *19*, 100301. https://doi.org/10.1016/j.invent.2019.100301

Kleinert, T., Waldschütz, M., Blau, J., Heinrichs, M., & Schiller, B. (2026). Ai outperforms humans in establishing interpersonal closeness in emotionally engaging interactions, but only when labelled as human. *Communications Psychology*, *4*(1), 23. https://doi.org/10.1038/s44271-025-00391-7

Laestadius, L., Bishop, A., Gonzalez, M., Illenčík, D., & Campos-Castillo, C. (2024). Too human and not human enough: A grounded theory analysis of mental health harms from emotional dependence on the social chatbot Replika. *New Media & Society*, *26*(10), 5923–5941. https://doi.org/10.1177/14614448221142007

Lai, V. D., Paoletti-Hatcher, J., Wu-Chung, E. L., Mahant, I., Argueta, D. L., Brice, K. N., Denny, B. T., Green, C., Medina, L. D., Schulz, P. E., Stinson, J. M., Heijnen, C. J., & Fagundes, C. P. (2024). Perceived partner responsiveness alters the association between marital distress and well-being in dementia spousal caregivers. *Comprehensive Psychoneuroendocrinology*, *20*, 100271. https://doi.org/10.1016/j.cpnec.2024.100271

Leschak, C. J., & Eisenberger, N. I. (2019). Two Distinct Immune Pathways Linking Social Relationships With Health: Inflammatory and Antiviral Processes. *Psychosomatic Medicine*, *81*(8), 711–719. https://doi.org/10.1097/psy.0000000000000685

Li, R.-N., Folk, D., Singh, A., Ungar, L., & Dunn, E. (2026). Is a random human peer better than a highly supportive chatbot in reducing loneliness over time? *Journal of Experimental Social Psychology*, *125*, 104911. https://doi.org/10.1016/j.jesp.2026.104911

Lieberz, J., Shamay-Tsoory, S. G., Saporta, N., Esser, T., Kuskova, E., Stoffel-Wagner, B., Hurlemann, R [René], & Scheele, D. (2021). Loneliness and the Social Brain: How Perceived Social Isolation Impairs Human Interactions. *Advanced Science (Weinheim, Baden-Wurttemberg, Germany)*, *8*(21), e2102076. https://doi.org/10.1002/advs.202102076

Liu, J., Liu, Z., Hu, Y., Gao, Y., Zhang, S., & Ling, Z. (2024). *DiffStyleTTS: Diffusion-based Hierarchical Prosody Modeling for Text-to-Speech with Diverse and Controllable Styles*. https://arxiv.org/pdf/2412.03388

Maier, A., Scheele, D., Spengler, F. B., Menba, T., Mohr, F., Güntürkün, O., Stoffel-Wagner, B., Kinfe, T. M., Maier, W., Khalsa, S. S., & Hurlemann, R [René] (2019). Oxytocin reduces a chemosensory-induced stress bias in social perception. *Neuropsychopharmacology : Official Publication of the American College of Neuropsychopharmacology*, *44*(2), 281–288. https://doi.org/10.1038/s41386-018-0063-3

Matthews, T., Rasmussen, L. J. H., Ambler, A., Danese, A., Eugen-Olsen, J., Fancourt, D., Fisher, H. L., Iversen, K. K., Schultz, M., Sugden, K., Williams, B., Caspi, A., & Moffitt, T. E. (2024). Social isolation, loneliness, and inflammation: A multi-cohort investigation in early and mid-adulthood. *Brain, Behavior, and Immunity*, *115*, 727–736. https://doi.org/10.1016/j.bbi.2023.11.022

Mazhar, B., Niu, J., Ren, Y., & Ul Haq, I. (2026). Generative artificial intelligence as social actors: The mediating roles of empathy and autonomy in anthropomorphism-driven dependency. *International Journal of Information Management*, *89*, 103072. https://doi.org/10.1016/j.ijinfomgt.2026.103072

Mehdi, S. F., Pusapati, S., Khenhrani, R. R., Farooqi, M. S., Sarwar, S., Alnasarat, A., Mathur, N., Metz, C. N., LeRoith, D., Tracey, K. J., Yang, H., Brownstein, M. J., &

Roth, J. (2022). Oxytocin and Related Peptide Hormones: Candidate Anti-Inflammatory Therapy in Early Stages of Sepsis. *Frontiers in Immunology*, *13*, 864007. https://doi.org/10.3389/fimmu.2022.864007

Morr, M., Liu, X., Hurlemann, R [Rene], Becker, B., & Scheele, D. (2022). Chronic Loneliness: Neurocognitive Mechanisms and Interventions. *Psychotherapy and Psychosomatics*, *91*(4), 227–237. https://doi.org/10.1159/000524157

Nguyen, T. M., Khadadeh, M., & Jeong, D. C. (2023). Shippers and Kinnies: Re-conceptualizing Parasocial Relationships with Fictional Characters in Contemporary Fandom. In P. Lopes, F. Luz, A. Liapis, & H. Engström (Eds.), *Proceedings of the 18th International Conference on the Foundations of Digital Games* (pp. 1–12). ACM. https://doi.org/10.1145/3582437.3582476

Olson, M. E., Hornick, M. G., Stefanski, A., Albanna, H. R., Gjoni, A., Hall, G. D., Hart, P. C., Rajab, I. M., & Potempa, L. A. (2023). A biofunctional review of C-reactive protein (CRP) as a mediator of inflammatory and immune responses: Differentiating pentameric and modified CRP isoform effects. *Frontiers in Immunology*, *14*, 1264383. https://doi.org/10.3389/fimmu.2023.1264383

Packheiser, J., Hartmann, H., Fredriksen, K., Gazzola, V., Keysers, C., & Michon, F. (2024). A systematic review and multivariate meta-analysis of the physical and mental health benefits of touch interventions. *Nature Human Behaviour*, *8*(6), 1088–1107. https://doi.org/10.1038/s41562-024-01841-8

Packheiser, J., Ocklenburg, S., Hurlemann, R [René], & Scheele, D. (2025). Embracing the void: exploring the relationship between chronic loneliness and social touch. *Current Opinion in Behavioral Sciences*, *66*, 101590. https://doi.org/10.1016/j.cobeha.2025.101590

Park, C., Majeed, A., Gill, H., Tamura, J., Ho, R. C., Mansur, R. B., Nasri, F., Lee, Y., Rosenblat, J. D., Wong, E., & McIntyre, R. S. (2020). The Effect of Loneliness on Distinct Health Outcomes: A Comprehensive Review and Meta-Analysis. *Psychiatry Research*, *294*, 113514. https://doi.org/10.1016/j.psychres.2020.113514

Piejka, A., Elsenbruch, S., Icenhour, A., Okruszek, Ł., Scheele, D., & Packheiser, J. (2026). *A multivariate meta-analysis on the relationship between social connectedness and pain*. https://doi.org/10.64898/2026.03.24.26349176

Pressman, S. D., Cohen, S., Miller, G. E., Barkin, A., Rabin, B. S., & Treanor, J. J. (2005). Loneliness, social network size, and immune response to influenza vaccination in college freshmen. *Health Psychology : Official Journal of the Division of Health Psychology, American Psychological Association*, *24*(3), 297–306. https://doi.org/10.1037/0278-6133.24.3.297

Rakel, D., Barrett, B., Zhang, Z., Hoeft, T., Chewning, B., Marchand, L., & Scheder, J. (2011). Perception of empathy in the therapeutic encounter: Effects on the common cold. *Patient Education and Counseling*, *85*(3), 390–397. https://doi.org/10.1016/j.pec.2011.01.009

Regenbogen, C., Schneider, D. A., Finkelmeyer, A., Kohn, N., Derntl, B., Kellermann, T., Gur, R. E., Schneider, F., & Habel, U. (2012). The differential contribution of facial expressions, prosody, and speech content to empathy. *Cognition & Emotion*, *26*(6), 995–1014. https://doi.org/10.1080/02699931.2011.631296

Schneider, E., Hernández, C., Brock, R., Eckstein, M., Bodenmann, G., Heinrichs, M., Ehlert, U., Läuchli, S., & Ditzen, B. (2026). Intranasal Oxytocin and Physical Intimacy for Dermatological Wound Healing and Neuroendocrine Stress: A Randomized Clinical Trial. *JAMA Psychiatry*, *83*(2), 118–127. https://doi.org/10.1001/jamapsychiatry.2025.3705

Schneiderman, I., Zagoory-Sharon, O., Leckman, J. F., & Feldman, R. (2012). Oxytocin during the initial stages of romantic attachment: Relations to couples' interactive reciprocity. *Psychoneuroendocrinology*, *37*(8), 1277–1285. https://doi.org/10.1016/j.psyneuen.2011.12.021

Seltzer, L. J., Ziegler, T. E., & Pollak, S. D. (2010). Social vocalizations can release oxytocin in humans. *Proceedings. Biological Sciences*, *277*(1694), 2661–2666. https://doi.org/10.1098/rspb.2010.0567

Seok, J., Lee, B. H., Kim, D., Bak, S., Kim, S [Saeyeong], Kim, S [Sungtae], & Park, S. (2025). What Emotions and Personalities Determine Acceptance of Generative AI? Focusing on the CASA Paradigm. *International Journal of Human–Computer Interaction*, *41*(18), 11436–11458. https://doi.org/10.1080/10447318.2024.2443263

Shanahan, M. (2024). Talking about Large Language Models. *Communications of the ACM*, *67*(2), 68–79. https://doi.org/10.1145/3624724

Slavich, G. M. (2020). Social Safety Theory: A Biologically Based Evolutionary Perspective on Life Stress, Health, and Behavior. *Annual Review of Clinical Psychology*, *16*(Volume 16, 2020), 265–295. https://doi.org/10.1146/annurev-clinpsy-032816-045159

Smith, K. J., Gavey, S., RIddell, N. E., Kontari, P., & Victor, C. (2020). The association between loneliness, social isolation and inflammation: A systematic review and meta-analysis. *Neuroscience and Biobehavioral Reviews*, *112*, 519–541. https://doi.org/10.1016/j.neubiorev.2020.02.002

Spengler, F. B., Scheele, D., Marsh, N., Kofferath, C., Flach, A., Schwarz, S., Stoffel-Wagner, B., Maier, W., & Hurlemann, R [René] (2017). Oxytocin facilitates reciprocity in social communication. *Social Cognitive and Affective Neuroscience*, *12*(8), 1325–1333. https://doi.org/10.1093/scan/nsx061

Spreng, R. N., Dimas, E., Mwilambwe-Tshilobo, L., Dagher, A., Koellinger, P., Nave, G., Ong, A., Kernbach, J. M., Wiecki, T. V., Ge, T., Li, Y., Holmes, A. J., Yeo, B. T. T., Turner, G. R., Dunbar, R. I. M., & Bzdok, D. (2020). The default network of the human brain is associated with perceived social isolation. *Nature Communications*, *11*(1), 6393. https://doi.org/10.1038/s41467-020-20039-w

Stade, E. C., Stirman, S. W., Ungar, L. H., Boland, C. L., Schwartz, H. A., Yaden, D. B., Sedoc, J., DeRubeis, R. J., Willer, R., & Eichstaedt, J. C. (2024). Large language

models could change the future of behavioral healthcare: A proposal for responsible development and evaluation. *Npj Mental Health Research*, *3*(1), 12. https://doi.org/10.1038/s44184-024-00056-z

Starke, C., Ventura, A., Bersch, C., Cha, M., Vreese, C. de, Doebler, P., Dong, M., Krämer, N., Leib, M., Peter, J., Schäfer, L., Soraperra, I., Szczuka, J., Tuchtfeld, E., Wald, R., & Köbis, N. (2024). Risks and protective measures for synthetic relationships. *Nature Human Behaviour*, *8*(10), 1834–1836. https://doi.org/10.1038/s41562-024-02005-4

Stein, J.-P., Messingschlager, T., Gnambs, T., Hutmacher, F., & Appel, M. (2024). Attitudes towards AI: Measurement and associations with personality. *Scientific Reports*, *14*(1), 2909. https://doi.org/10.1038/s41598-024-53335-2

Surkalim, D. L., Luo, M., Eres, R., Gebel, K., van Buskirk, J., Bauman, A., & Ding, D. (2022). The prevalence of loneliness across 113 countries: Systematic review and meta-analysis. *BMJ (Clinical Research Ed.)*, *376*, e067068. https://doi.org/10.1136/bmj-2021-067068

Thiebaut, G., Méot, A., Witt, A., Prokop, P., & Bonin, P. (2021). "Touch Me If You Can!": Individual Differences in Disease Avoidance and Social Touch. *Evolutionary Psychology : An International Journal of Evolutionary Approaches to Psychology and Behavior*, *19*(4), 14747049211056159. https://doi.org/10.1177/14747049211056159

van der Velpen, I. F., Yaqub, A., Vernooij, M. W., Perry, M., Vernooij-Dassen, M. J. F., Ghanbari, M., Ikram, M. A., & Melis, R. J. F. (2024). Sex-differences in the association of social health and marital status with blood-based immune and neurodegeneration markers in a cohort of community-dwelling older adults. *Brain, Behavior, and Immunity*, *120*, 71–81. https://doi.org/10.1016/j.bbi.2024.05.031

van Nieuwenburg, D., Groot, J. H. B. de, & Smeets, M. A. M. (2019). The Subtle Signaling Strength of Smells: A Masked Odor Enhances Interpersonal Trust. *Frontiers in Psychology*, *10*, 1890. https://doi.org/10.3389/fpsyg.2019.01890

van Raalte, L. J., & Floyd, K. (2021). Daily Hugging Predicts Lower Levels of Two Proinflammatory Cytokines. *Western Journal of Communication*, *85*(4), 487–506. https://doi.org/10.1080/10570314.2020.1850851

Wang, P., Yang, H.-P., Tian, S., Wang, L., Wang, S. C., Zhang, F., & Wang, Y.-F. (2015). Oxytocin-secreting system: A major part of the neuroendocrine center regulating immunologic activity. *Journal of Neuroimmunology*, *289*, 152–161. https://doi.org/10.1016/j.jneuroim.2015.11.001

Wang, Y., Li, X., Zhang, Q., Yeung, D., & Wu, Y [Yihan] (2025). Effect of a Cognitive Behavioral Therapy-Based AI Chatbot on Depression and Loneliness in Chinese University Students: Randomized Controlled Trial With Financial Stress Moderation. *JMIR MHealth and UHealth*, *13*, e63806. https://doi.org/10.2196/63806

Wiederhold, B. K. (2025). Artificial Influence: Why AI Needs Guardrails for the Next Generation. *Cyberpsychology, Behavior and Social Networking*, *28*(10), 655–657. https://doi.org/10.1177/21522715251368264

Wiśniewska, M., Piejka, A., Wolak, T., Scheele, D., & Okruszek, Ł. (2025). Loneliness - not for the faint of heart? Effects of transient loneliness induction on neural and parasympathetic responses to affective stimuli. *Social Neuroscience*, *20*(6), 319–332. https://doi.org/10.1080/17470919.2025.2498384

Wolters, N. E., Mobach, L., Wuthrich, V. M., Vonk, P., van der Heijde, C. M., Wiers, R. W., Rapee, R. M., & Klein, A. M. (2023). Emotional and social loneliness and their unique links with social isolation, depression and anxiety. *Journal of Affective Disorders*, *329*, 207–217. https://doi.org/10.1016/j.jad.2023.02.096

Wu, F., Chen, K., & Dellinger, A. (2026). A Microservice-Based Implementation of Chinese Conversational Digital Avatars Using NVIDIA ACE. In R. Xu, Y. Wu, H. Chen, T. Jin, F. F. Dalimarta, & L.-J. Zhang (Eds.), *Lecture Notes in Computer Science. AI and Multimodal Services – AIMS 2025* (Vol. 16151, pp. 110–124). Springer Nature Switzerland. https://doi.org/10.1007/978-3-032-08557-3_9

Zagic, D., Wuthrich, V. M., Rapee, R. M., & Wolters, N. (2022). Interventions to improve social connections: A systematic review and meta-analysis. *Social Psychiatry and Psychiatric Epidemiology*, *57*(5), 885–906. https://doi.org/10.1007/s00127-021-02191-w