
Article:
Robinson, J.M. and Breed, M.F. (2020) The Lovebug Effect : is the human biophilic drive influenced by interactions between the host, the environment, and the microbiome? Science of The Total Environment, 720. 137626. ISSN 0048-9697

https://doi.org/10.1016/j.scitotenv.2020.137626

Journal Pre-proof

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PII: S0048-9697(20)31137-2

DOI: https://doi.org/10.1016/j.scitotenv.2020.137626

Reference: STOTEN 137626

To appear in: *Science of the Total Environment*

Received date: 2 February 2020

Revised date: 27 February 2020

Accepted date: 27 February 2020

Please cite this article as: J.M. Robinson and M.F. Breed, The Lovebug Effect: Is the human biophilic drive influenced by interactions between the host, the environment, and the microbiome?, *Science of the Total Environment* (2020), https://doi.org/10.1016/j.scitotenv.2020.137626

Discussion

The *Lovebug Effect*: Is the Human Biophilic Drive Influenced by Interactions between the Host, the Environment, and the Microbiome?

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Word count: 6,350; **Figures:** 4; **Tables:** 1

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Keywords: Lovebug Effect; Microbiome; Evolution; Holobiont; Nature Connectedness; Hologenome

Abstract

Psychological frameworks are often used to investigate the mechanisms involved with our affinity towards, and connection with nature—such as the Biophilia Hypothesis and Nature Connectedness. Recent revelations from microbiome science suggest that animal behaviour can be strongly influenced by the host's microbiome—for example, via the bidirectional communication properties of the gut-brain axis. Here, we build on this theory to hypothesise that a microbially-influenced mechanism could also contribute to the human biophilic drive – the tendency for humans to affiliate and connect with nature. Humans may be at an evolutionary advantage through health-regulating exchange of environmental microbiota, which in turn could influence our nature affinity. We present a conceptual model for microbially-influenced nature affinity, calling it the *Lovebug Effect*. We present an overview of the potential mechanistic pathways involved in the *Lovebug Effect*, and consider its dependence on the hologenome concept of evolution, direct behavioural manipulation, and host-microbiota associated phenotypes independent of these concepts. We also discuss its implications for human health and ecological resilience. Finally, we highlight several possible approaches to scrutinise the hypothesis. The *Lovebug Effect* could have important implications for our understanding of exposure to natural environments for health and wellbeing, and could contribute to an ecologically resilient future.

1 Introduction

Despite considerable attention given to the mechanistic pathways involved in biophilia (our innate tendency to affiliate with nature or our 'biophilic drive') and nature connectedness (the degree to which humans are emotionally connected to nature), some of the potential biological mechanisms that lead to our biophilic drive remain elusive. Furthermore, associations between the microbiome and the human biophilic drive have not, to our knowledge, been explored.

Here we hypothesise that a microbially-influenced mechanism contributes towards the tendency for humans to affiliate with natural environments. Our hypothesis partially stems from microbiome research which suggests that microbial interactions through the gut-brain axis and other pathways (e.g., via olfactory dynamics) can have a significant influence on host behaviour (Heijtz et al. 2011; Leitão-Gonçalves et al. 2017; Farzi et al. 2018; Huang et al. 2019). Furthermore, we detail how humans are host to a diversity of microbes. Collectively (the host plus associated microbes) this is termed a 'holobiont' or metaorganism, and it could potentially form a unit of selection via effects on host phenotypes.

Microbial interactions may influence our affinity towards and connection with nature, thus enhance our evolutionary fitness through health-regulating microbial exchange. It is important to note that the mechanisms set out in this paper are not intended to replace current perspectives on biophilic tendencies. This is a multidimensional proposition, adopting a predominantly biological framework whilst recognising exogenous social and environmental influences. With this, our aim is to add a new perspective to the already standing frameworks to better understand the complexities behind biophilic tendencies.

Building on this newly proposed mechanism to nature affinity, we also hypothesise that an additional pathway to nature connectedness may exist – one also mediated by microbial communities. Indeed, "*nature connectedness may result from specific interactions with nature*" (Lumber, Richardson and Sheffield (2018, p.2). We propose that a microbially-influenced affinity for natural environments could also form one of the converging pathways to explain nature connectedness.

We refer to this collective microbially-influenced mechanism as the *Lovebug Effect.* This translates to 'microbio-philia', from 'philia'– a Greek word for '*love'* or 'attraction' and '*bug*' as a colloquial term for microorganism. This hypothesis builds on the ecological approach to describe humans as dynamic ecosystems, openly interacting with the wider environment (Robinson, Mills, and Breed, 2018; Mills et al. 2019). We present a conceptual overview, predominantly of the biological and evolutionary pathways, that could potentially mediate behaviours associated with microbially-influenced nature-affinity. We discuss this concept in relation to broader socioecological implications using two interconnected examples—namely, public health and ecological resilience. We conclude by setting out a number of possible experimental approaches that could be taken to start testing the *Lovebug Effect* hypotheses.

Including a microbial perspective with the established theories associated with the Biophilia Hypothesis and nature connectedness has the potential to contribute towards a new appreciation for the microbial world, which could ultimately benefit human and planetary health.

2. Biophilia and nature connectedness

The Biophilia Hypothesis (Wilson 1984) proposes that humans have an innate tendency to affiliate with the natural world, and this is suggested to be mediated by a number of evolved survival-based biopsychological responses to environmental stimuli such as the drive to acquire nutrients, and materials for shelter (Kellert, 2016). Indirect support for this hypothesis arrives from research demonstrating links between 'exposure' to environmental features (e.g., urban parks, waterbodies, and woodlands) and enhanced physical health and psychological wellbeing (Li et al. 2009; Carrus et al. 2015; Gascon et al. 2017; Berto et al. 2018; Lyu et al. 2019).

Further support for biophilia comes from research into evolutionary predispositions that manifest as 'phobic' responses to biotic stimuli. These particular stimuli are considered to be threatening to human survival, such as an aversion to aposematic signals including triangular shapes or body forms associated with predators (Gullone, 2000; Souchet and Aubret, 2016; Prokop, Fančovičová and Kučerová, 2018). The fear responses (referred to as '*biophobia'*) are modulated in part by the autonomic nervous system (e.g., the sympathetic 'fight or flight' response) and are thought to have evolved in a world where humans were at a heightened threat of predation and/or poisoning by phyto–or–zootoxins. Although biophobic responses are converse to their biophilic counterparts, they represent the same overarching evolutionary framework (Figure 1).

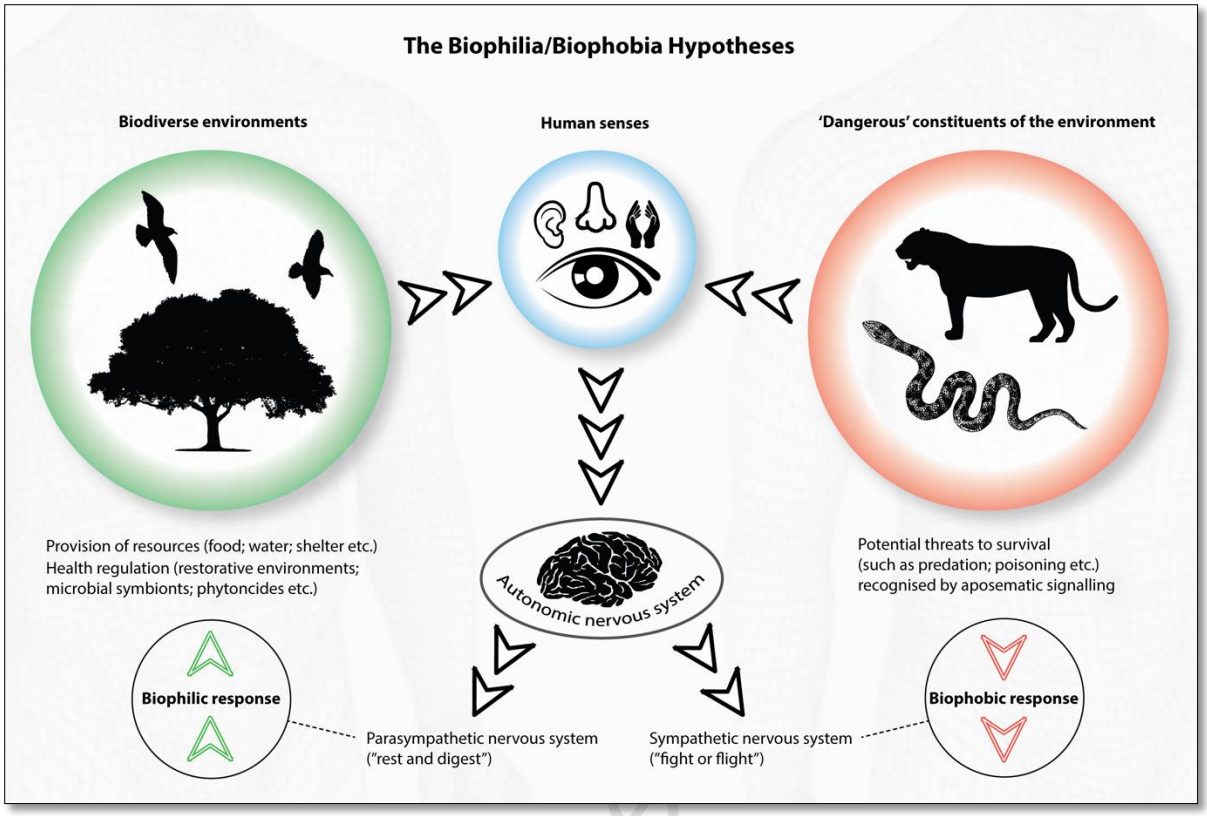

Figure 1. Human Biophilia and Biophobia Hypotheses – showing human behavioural responses to different environmental stimuli, modulated in part by the autonomic nervous system. In general, nature provides health-regulating opportunities and resources for survival. However, some natural features also pose a danger to humans and elicit biophobic responses.

Lumber, Richardson and Sheffield (2017) investigated the mechanisms by which humans connect with nature emotionally—that is, 'nature connectedness'—using the Biophilia Hypothesis as a conceptual framework. The authors point out that nature connectedness and Biophilia are distinct constructs, whereby:

- Biophilia is primarily based on increasing survival opportunities (e.g., via health promoting interactions; resource provision etc.); and,
- Nature connectedness is a recognition that humanity is deeply embedded within nature itself.

The authors noted that nature connectedness is also an "*act of self-realisation of the similarity between other aspects of nature and the individual*" (Schultz et al., 2004 in Lumber, Richardson and Sheffield, 2018, p.15).

Psychological frameworks have been developed to systematically examine how our innate tendencies to affiliate with the natural world are expressed—for example, via the nine values of Biophilia, which range from Ecological-Scientific values (e.g., an attraction to learn about nature to meet life's physical and mental requirements, pertinent to evolutionary fitness) to Aesthetic values (e.g., seeking beauty in nature to provide sensory pleasure and the associated wellbeing benefits) (Delavari-Edalat and Abdi, 2010). Furthermore, seven conceptual themes have been identified with significant implications for the "formation and maintenance" of the connection that humans have with the rest of the natural world (Lumber, Richardson and Sheffield, 2018 p.2). Examples of these themes include "investigating nature through scientific enquiry", "noting nature through artistry", and "engaging with wild nature" (Lumber, Richardson and Sheffield, 2018 p.2).

As mentioned earlier, some of the potential biological mechanisms that lead to our biophilic drive remain elusive. To this end, we will now discuss the *Lovebug Effect*, that is, microbially-influenced nature affinity as a potential mechanism to help explain the human biophilic drive (or the tendency to affiliate with natural environments).

3. Microbially-influenced nature affinity - the *Lovebug Effect*

The *Lovebug Effect,* as a developing conceptual model, describes microbially-mediated nature affinity. We propose that within this model, several mechanistic pathways could be involved, either independently or as a multidimensional process. For example, the *Lovebug*

Effect could be viewed from a metacommunity perspective, where the internal and external microbiomes, the host and abiotic factors interact and influence the host phenotype. Indeed, the current explanation of biophilia is based on psychological traits, but we propose there could be an external manipulator, i.e., the microbiome. Therefore, the biophilic drive is not only 'self' controlled, but additionally influenced by external forces. Hereby the host is also a controlling/selecting factor, as animals can shape their microbial community by selecting favourable microbial communities. Based on this approach, horizontal transmission of microbes is likely to be an important aspect.

Another perspective is that the health and wellbeing of humans, physically and psychologically, relies on microbial communities. These communities are strongly influenced by environmental factors, such as food, but also interactions with our surrounding. These interactions could be biotically driven, i.e., contact with other macro and microscopic organisms. This could lead to horizontal transmission. They could also be abiotically driven, e.g., temperature influencing communities in the environment, but also within an organism (e.g., seasonal fluctuation of microbes in invertebrates is known) (Ferguson et al. 2018).

The *Lovebug Effect* could involve direct host manipulation by microbes, which may have important effects on both the host and the resident microbes. A mechanistic overview of this potential pathway is described further in Section 4. However, there could also be other evolutionary pathways involved – such as selected behavioural traits (e.g., to spend time in biodiverse environments) in the host that benefit both the host and the resident microbes collectively (i.e., as a holobiont). Indeed, holobionts have been defined as "*biomolecular networks composed of the host plus its associated microbes […] and their collective genomes*

forge a hologenome" (Bordenstein and Theis, 2015). We discuss the holobiont and the hologenome concept of evolution in more detail in Sections 4.2. and 4.3.

Figure 2 (below) sets out an initial overview of the *Lovebug Effect* conceptual model. Process 1 describes how the human host is exposed to environmental microbiota which can subsequently colonise the host. Interactions between the microbiota and the host give rise to a number of potential benefits such as immunoregulation, leading to adaptive advantages. Human-microbiota associations are then selected for, and this could be on the integrated activities of both the host and all of its associated microbes (i.e., changes in the hologenome). Human-microbiota feedbacks then lead to either direct manipulation or selected behavioural traits, providing the biophilic drive towards natural environments.

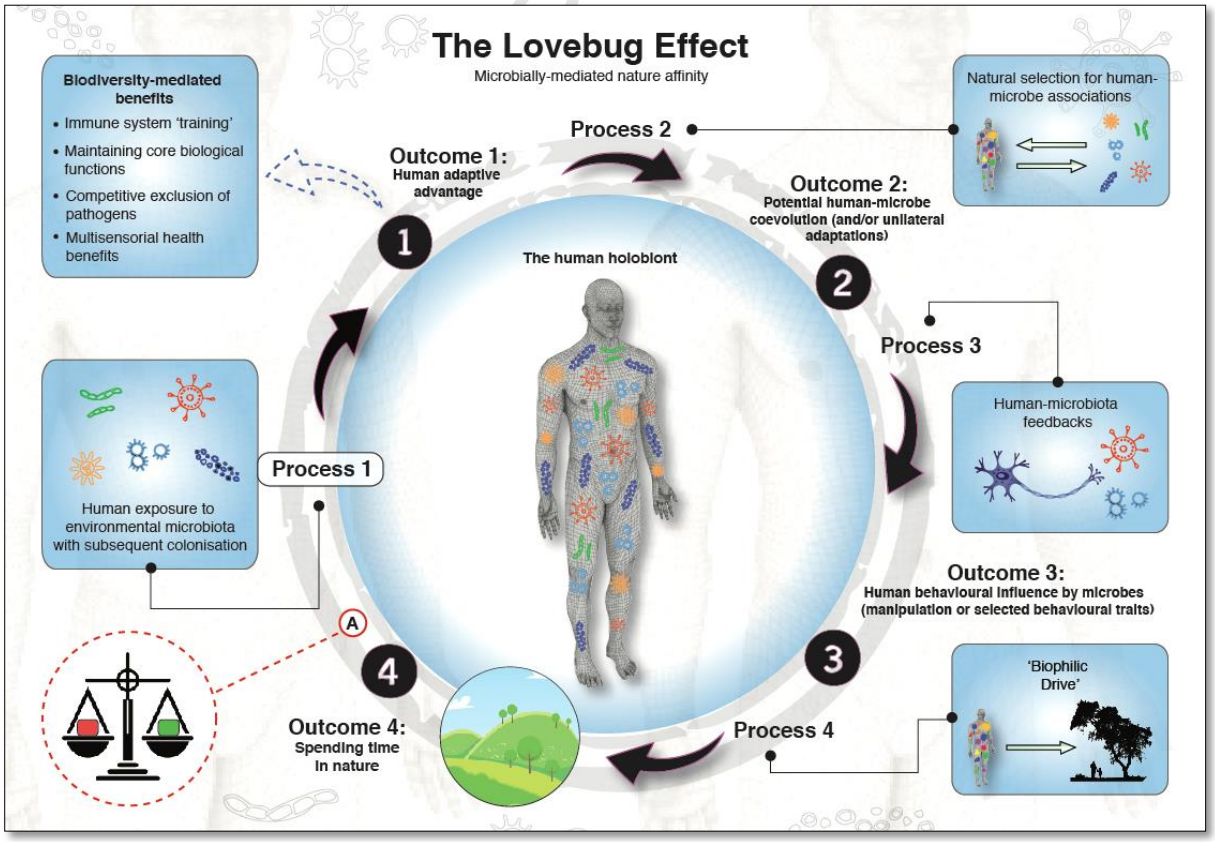

Figure 2. The *Lovebug Effect* - microbially-mediated nature affinity. This hypothesis proposes that our biophilic drive towards natural environments could be influenced by coevolution, biodiversity-mediated benefits and potentially unilateral adaptations. Arrows relate to processes and numbers in circles relate to outcomes. In the absence of anthropogenic impacts, the *Lovebug Effect* continues while subject to a stable pressure-benefits counterbalance. 'A' represents anthropogenic pressures, further defined in Figure 4.

A mechanistic overview of potential host-microbe behavioural manipulation and holobiont adaptation

The microbiome—that is, the consortium of microorganisms and their genetic material in a given environment—and in particular, the microbiome of the gastrointestinal (GI) tract, can have a considerable influence on host behaviour, mood, and neurological conditions such as depression (Heijtz et al. 2011; Farzi et al. 2018; Huang et al. 2019). Several mechanisms have been proposed as potential mediators of this process, including the presence of a bi-directional communication system, modulated by the vagus nerve. The vagus nerve is an extensive cranial nerve that links the brain stem to several peripheral organs across the body, and importantly for the current topic, to the GI tract (Ueno and Nakazato, 2016; Breit et al. 2018).

The microbiome of the GI tract has been suggested to 'hijack' this communication infrastructure to relay information to the brain, and thus influence host behaviour (Forsythe, Bienstock and Kunze, 2014; Vuong et al. 2017; Davidson et al. 2018). Although the mechanisms are not yet fully understood, it is now thought that an array of metabolites produced by microbiota within the gut can initiate the release of peptides and hormones via enteroendocrine cell activation and/or stimulate the vagal afferent fibres that form one of the

gut-brain signalling pathways (Lach et al. 2018; Fülling, Dinan and Cryan, 2019). Microbiota within the gut can also produce neurotransmitters such as serotonin (as well as dopamine, noradrenaline and gamma-aminobutyric acid or 'GABA'), which can directly activate the vagus afferents that connect the gut to the brain (Strandwitz, 2018; Fülling, Dinan and Cryan, 2019).

There are other proposed pathways involved in microbially-influenced host behavioural responses, such as through the synthesis of neuroactive molecules that affect the central nervous system (CNS). These microbially-synthesised molecules include 5-hydroxytryptamine (5-HT), catecholamines, and acetylcholine, and can be transported in the systemic circulatory system to penetrate the blood-brain barrier (Petra et al. 2015). Furthermore, some bacteria are known to release factors that alter peripheral immune cells to stimulate interaction with the blood-brain barrier (Logsdon et al. 2018).

Pasquaretta et al. (2018) suggested that a microbially-mediated pathway to decision-making may also exist, involving active manipulation of host behaviour to select particular food items that favour the nutrient requirements of their microbial symbionts. This is supported by research involving the model fruit fly *Drosophila melanogaster*, which showed that commensal bacteria, and specifically *Acetobacter pomorum* and *Lactobacillus sp.,* work synergistically to become 'potent modulators of feeding decisions' – a process that is influenced by the availability of dietary amino acids (Leitão-Gonçalves et al. 2017). Furthermore, Yuval (2017) pointed out that in the invertebrate holobiont, microbial symbionts are known to influence breeding and ultimately speciation (Sharon et al. 2010; Shropshire and Bordenstein, 2016; Simon et al. 2019).

It has also been suggested that host sociability could be influenced by the microbiome, that is, by mediating host behavioural responses and increasing inter-host transmission of microbes (Stilling et al. 2014; Wong et al. 2015; Sherwin et al. 2019). This could potentially increase dispersal and evolutionary fitness as a consequence (Archie and Tung, 2015).

Interestingly, several animal studies support the idea that microbially-influenced behavioural change may be partially governed by olfactory system interactions. For example, both adults and larvae of *D. melanogaster* have been shown to be attracted to volatile compounds of *Saccharomyces cerevisiae* and *Lactobacillus plantarum* but repelled by *Acetobacter malorum* (Qiao et al. 2019). Casadei et al. (2019) showed that microbiota trigger widespread transcriptional responses in the olfactory organs of zebrafish and mice. Studies also suggest that microbiota may influence the structure of the olfactory epithelium, and as Karsas, Lamb and Green (2019) pointed out, human twin studies indicate that the genotype of an olfactory gene (OR6A2) could be related to microbiota (Goodrich et al. 2016; Bienenstock, Kunze, and Forsythe, 2017).

4.1. The extended phenotype

The idea of behavioural manipulation at the metaphorical hand of a mutualistic, commensal or parasitic organism, is by no means a novel concept. Indeed, the central theorem of the extended phenotype (Dawkins, 1989) suggests that the continuity of genes that influence host behaviour tend to be maximised as a result of the behaviour itself—regardless of whether the genes are of host origin (or of the residing microbes).

Take the classic example of host behavioural manipulation by the protozoan *Toxoplasma gondii*. This organism is a microscopic eukaryote (an obligate intracellular parasite), that,

based on current knowledge, can only undergo gametogenesis in the intestines of species in the Felidae family, the definitive hosts (Poirotte et al. 2016). However, *T. gondii* oocysts (zygote-containing sacs) are shed in the felid's faeces where they subsequently sporulate to become infective (Zulpo et al. 2018). Environmental materials contaminated with the infective oocysts are consumed by intermediate hosts—typically rodents and birds (Krücken et al. 2017; Amouei et al. 2018). These intermediate hosts are characteristic prey items of cats, and the maintenance of this virtuous loop is essential for the protozoan's continuity—that is, *T. gondii's* survival is highly dependent on the cat becoming infected by feeding on infected prey (Vyas, 2015). It is this survival pressure that is suggested to have resulted in *T. gondii* evolving mechanisms to acutely manipulate the behaviour of the intermediate host (e.g., rodents). Such behavioural transpositions manifest as reduced innate aversion to the definitive host (the cat), and potentially even a 'fatal attraction' towards the definitive host, thus enhancing the transmission of parasite genes into future generations (Vyas, 2015; Hughes and Libersat, 2019). Although there are still several intermediary manipulation factors to uncover, it is thought that *T.gondii* infection in the intermediate host initiates testosterone production to cause hypomethylation of the medial amygdala, which then leads to loss of innate aversion to their predatory counterparts (Vyas, 2015; Tan and Vyas, 2016; Herbison, Lagrue and Poulin, 2018).

It is important to note that we use the *T. gondii* example to further highlight that a mechanistic pathway for microbially-influenced behavioural manipulation is possible. There are other examples of host manipulation involving viruses (e.g., family *Baculoviridae*), helminths (Hamblin and Tanaka, 2013; Poulin and Maure, 2015), and geometrid moths *Thyrinteina eucocerae* (Libersat et al. 2018). However, we also acknowledge that these examples lack evidence to show that the specific interactions benefit the host in such a way

that host behaviour is selected for (although in the *T. gondii* example, the feline is likely to benefit from catching the rodent prey more efficiently). Therefore, more research is needed to identify whether co-evolutionary relationships that benefit the host and their microorganisms exist.

In a recent randomized controlled study, Liddicoat et al. (2019) identified that a soil-derived anaerobic spore-forming butyrate-producer (*Kineothrix alysoides*) was supplemented to a greater extent in the gut microbiomes of mice exposed to trace-levels of higher biodiversity aerobiome treatment (Figure 3). The relative abundance of *K. alysoides* in the gut of these mice was associated with reduced anxiety-like behaviours. These results are relevant to the *Lovebug Effect*, where the authors suggest that their findings point to an intriguing hypothesis that biodiverse soils may supply butyrate-producing microorganisms to the mammalian gut microbiome with potential implications for behavioural regulation.

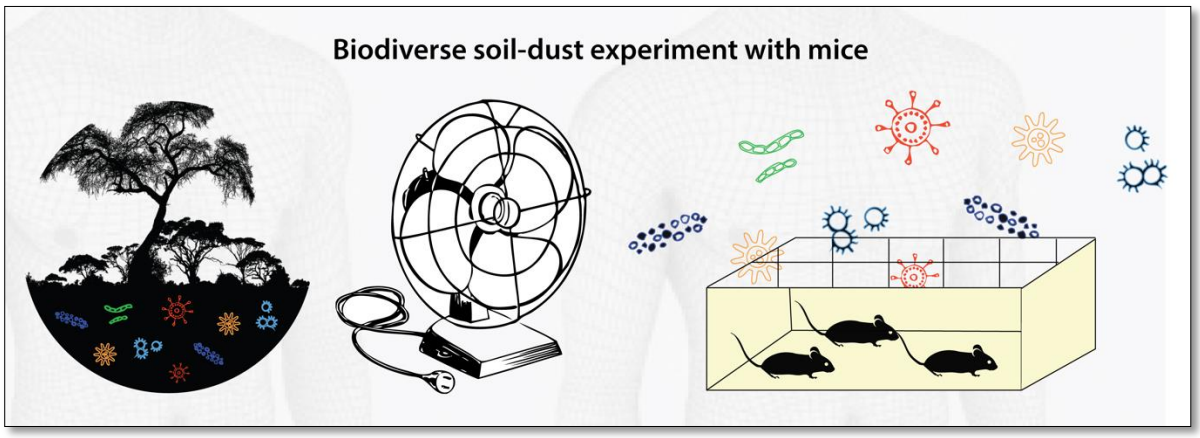

Figure 3. Using fans, germ-free mice were exposed to trace-levels of biodiverse soil dust in controlled conditions (Liddicoat et al. 2019).

Indeed, the idea that intake of microbes from the environment, e.g., due to breathing, is an important factor in health and is supported in other cases. For example, one study suggests

that closed air cycles in hospitals are harmful to humans mainly due to the lack of microbial diversity and the accumulation of harmful microbes (Arnold, 2014). As such, exposure to microbial diversity is likely to be an important factor in health.

4.2. (*Co)evolution*

Direct host-manipulation is one potential mechanism for microbially-mediated behavioural change. However, Johnson and Foster (2018) suggested that behavioural effects may arise more often as a result of selection on the microorganisms to proliferate in the host, and on the host to depend on their microbial symbionts. The authors suggested that microbial symbionts may preferentially benefit from local manipulation (i.e., changes to the immediate environment) rather than global manipulation (i.e., direct neurological manipulation). This is due to the higher energy investment required to set the neurochemically-intensive global manipulation process in motion, which would potentially leave these organisms vulnerable to competitive exclusion by other species with lower levels of investment. However, this local manipulation by the agency of microbiota could still have considerable downstream effects on host behaviour via the central nervous system.

Human physiology may have adapted to utilise microbiota, thus detecting and responding to certain strains and species assemblages (Johnson and Foster, 2018). Conceptually, this idea has parallels with the Old Friends Hypothesis, which posits that humans are dependent on a diversity of microbiota for immune system 'training', development and function (Rook et al., 2014) – factors which may affect brain function, and thus, behaviour (Rook and Lowry, 2008). Indeed, humans may have evolved a dependency on microbiota for 'normal' brain function, such that disturbance to the gut microbiome could impact human behaviour. Johnson and Foster (2018) suggested that evolved dependencies could be a simple indirect driver of microbially-influenced behaviour change. Disrupting this relationship through the

loss of microbial species or change to microbial communities in the host may translate to cognitive perturbation. Furthermore, functional redundancy is thought to exist in the gut microbiome (i.e., phylogenetically differentiated microbiota that share similar functional roles and may modulate host dependence) (Louca et al. 2018). Therefore, this could mean that the loss of, or impairment to, important functional *traits* resulting from functionally-important core microbial assemblages (as opposed to specific microbial *species*) may also be important drivers of impairment in host behaviour (Johnson and Foster, 2018).

4.3. The hologenome concept of evolution

This coevolution narrative could be explicitly linked to the hologenome concept of evolution (Rosenberg and Zilber-Rosenberg, 2016). Although some aspects of this concept are controversial, it is suggested that the holobiont could operate as a functional system, interacting with the environment as a unique biological entity through its collective traits (Roughgarden et al. 2018). Furthermore, it has been argued that the genome of the microbiome can be altered rapidly via environmental microbial exchange, horizontal gene transfer and DNA mutations (Rosenberg and Zilber-Rosenburg, 2018), leading to changes in the holobiont that could potentially be reproduced in future generations (Roughgarden et al. 2018; Collens, Kelley, and Katz, 2019). Selection at the level of the holobiont may be physiological and developmental (Roughgarden et al. 2018), and thus microbially-influenced regulation and development of behaviour could also be viewed from this multidimensional perspective.

A key criticism of the hologenome concept of evolution is the apparent lack of evidence to support vertical transmission of the gut microbiome. Indeed, with the exception of births delivered through caesarean section, it is thought that the main initial colonization of

microbiota in humans arrives through contact with the mother's vaginal microbiome (Houghteling, Pearl, and Walker, 2015; Dreyer and Leibl, 2018). As such, it would seem that multiple temporally-distinct microbiomes coevolving with the host to produce a given behaviour would be required for the transmission of microbially-mediated traits. However, Rosenberg and Zilber-Rosenberg (2019) suggested that there is some evidence to support vertical transmission. For example, supporting studies provided by the authors demonstrate that individuals can maintain the same *Helicobacter pylori* strains as their ancestors, even when they have migrated to different geographical locations (Achtman et al. 1999; Falush et al. 2003), and subsequent supporting studies were also provided (e.g., Ochman et al. 2010; Goodrich et al. 2016; Moeller et al. 2016). However, the authors do indicate that more robust quantitative data are still needed.

Collens, Kelley, and Katz (2019) argued that the hologenome concept of evolution could be an epigenetic phenomenon due to the influence that symbionts can exert on gene expression and patterns of inheritance in host genomes. The authors suggested that the influence of the symbiont on the host genome is outside the Mendelian view of gene transmission and that hologenome interactions can lead to changes in host gene expression without host DNA sequence modification. Examples to support this view are reported for humans, where the gut microbiome can influence epigenetic patterns via the modulation of DNA methylation (Cureau et al. 2016). Furthermore, evidence also supports reciprocal miRNA-mediated epigenetic interactions between the host and the microbiome. This mechanism is supported by studies that report on the interactions between host miRNA secretion and bacterial gene expression in mice (Williams et al. 2017).

It is also worth considering the effect of non-microbially mediated host physical and mental health factors as additional ecological pressures that may influence the functional and compositional dynamics of the microbiome (Alverdy et al. 2017; Karl et al. 2018). Any changes to the host microbiome resulting from health-related impacts could have cascading effects on host–microbiome behaviour. As such, there may be additional complex feedback systems to consider.

The *Lovebug Effect*: other potential evolutionary pathways and the natural environment as a restorative domain

Hitherto, we have discussed some of the mechanistic pathways, and hologenome-centric and coevolutionary frameworks, that could potentially be involved in host behavioural adaptation and manipulation by the agency of microbes (see Process and Outcome 3, Figure 2). However, there are other microbially-influenced processes that could contribute to nature affinity without the need to meet the criteria of vertical transmission of microbial genomes and direct manipulation.

Indeed, to explain the *Lovebug Effect*, it is important to discuss the fundamental ecological factors associated with microbially-mediated nature affinity in humans. As mentioned above, the portfolio of pathways that influence a human's desire to affiliate with nature must be recognised – some of which include complex psychosociocultural factors. However, from a microbially-mediated perspective, we propose that a biophilic drive towards natural environments (Process 4 in Figure 2) is not only influenced by (co)evolutionary processes between the host and symbionts, but also by interactions with biodiversity that could influence heritable human phenotypes. For example, via regulatory mechanisms that improve

human health and do not require vertical transmission of microbial genomes or direct manipulation (Outcome 1 and Process 2 in Figure 2). Such microbially-influenced pathways are also relevant to the biophilia and nature connectedness conceptual frameworks.

For example, life-course exposures that could potentially disrupt the human holobiont ecosystem if left unchecked could include factors that influence immune dysfunction and homeostatic imbalance, human-specialised pathogens, and other health-related disorders (both physical and mental phenomena). These 'normal' pressures could be counterbalanced, in part, by interactions between the host and the wider biotic community – i.e., natural environments (as conceptualised in Figure 2). These environments are potentially rich reservoirs of macro and microbial diversity and other biogenic compounds, such as phytoncides, which are linked to human health (Li et al. 2009; Moore, 2015). Exposure to a diversity of environmental microbiota is critical for immune system 'training' to protect against known and novel infectious agents, and to potentially remove pathogens through competitive exclusion whilst maintaining core biological functions (Rook et al. 2014; Mills et al. 2019). As such, these interactions form part of an important survival mechanism, and one that relates strongly to the Biophilia Hypothesis. It is also plausible that these complex interactions contribute to a person's nature connectedness, that is, the individual's sense of their relationship with nature (McMahan et al. 2018; Richardson et al. 2018). This could transpire indirectly through the immersive psychological effects and multisensorial experiences of being in nature—experiences that could potentially be influenced by a microbially-mediated biophilic drive – i.e., the process we term the *Lovebug Effect*.

Alternatively, aspects of nature connectedness could be influenced by the transfer of microbiota or microbial by-products from the environment to the human body, which in

theory, could influence regulatory pathways in both cognitive and affective domains. Indeed, some of the natural smells humans enjoy (such as the earthy scents of changing seasons and musky emissions following a period of rain) are in fact volatile organic compounds (e.g., geosmin) produced by microbes. For example, petrichor is a term used to describe the musky smell produced when rain combines with the spores of actinomycetes bacteria in soil (Dwivedi et al. 2011).

It is also important to mention that stress could have a negative impact on the composition and metabolic activity of gut microbiota (Dantzer et al. 2018; Karl et al. 2018). Indeed, several studies have elucidated the negative impacts of host-related stressors on microbiota. For example, stress-induced reductions of the non-spore forming *Lactobacilli* has been highlighted in humans and non-human primates (Bailey and Coe, 1999; Knowles et al. 2007). To this end, there could be potential fitness costs to certain individuals and/or communities of microbiota in the gut and other body sites. It is essential to acknowledge here that gut microbiota have emerged as important mediators of stress responses in humans (Dinan and Cryan, 2012; Foster, Rinaman and Cryan, 2017; Hantsoo et al. 2019). Moreover, stress could have negative (and positive) consequences for reproductive fitness and success in humans and other animals through a range of primary and secondary pathways (e.g., downstream lifestyle choices) that could, for example, elicit immune-endocrine disequilibria (Nakamura, Sheps and Arck, 2008; Mumby et al. 2015; MacLeod et al. 2018; Roychoudhury et al. 2019; Zhou, Cai and Dong, 2019).

Consequently, we argue that spending time in stress-ameliorating environments—for example, in calming natural surroundings that facilitate psychological restoration or eudaimonia—could potentially confer positive indirect effects on the human microbiome. To

this end, natural environments may provide additional salutogenic stimuli that drive the adaptive evolution of behaviours that benefit the host and its microbial symbionts via stress reduction pathways.

Discussion

6.1. The *Lovebug Effect*: 'big picture' implications and interventions

Unravelling the mechanisms of the *Lovebug Effect* could have far-reaching implications for researchers, practitioners, the general public, and from a biocentric perspective—the wider environment. This is relevant to nature-based health interventions and nature-based solutions, whereby the management of public health and ecosystems are often considered concurrently, giving rise to important co-benefits (Robinson and Breed, 2019). Augmenting our understanding of the factors that shape the human tendency to affiliate with nature could also help to strengthen our appreciation for planetary health—a relatively recent philosophical framework that describes the inextricable and multiscale links between human and environmental health (Prescott and Logan, 2017; Gabrysch, 2018; Prescott and Logan, 2019).

Mental health conditions such as depression and anxiety, and noncommunicable diseases (NCDs) such as asthma, diabetes, and inflammatory bowel disease are on the rise, which coincides with a global megatrend in biodiversity loss (Haahtela et al, 2013; Haahtela, 2019). It is thought that the key factors driving these megatrends include industrialisation, population growth and the ongoing increase in urbanisation (Pathway A in Figure 4) (Rodriguez et al. 2011; von Hertzen et al. 2011; Rook, 2014; Sartorius et al. 2015; Den Braver et al. 2018). These additional anthropogenic pressures could perturb the cycle of the *Lovebug Effect* by exacerbating 'normal' ecological pressures, and thus contribute to dysbiotic drift—that is, a non-random, industrial urban lifestyle-driven, push towards 'life in

distress', microbial imbalance, and socioeconomic disadvantage (Prescott et al. 2018). Furthermore, a ratcheting down effect or the 'extinction of nature experience' (Soga and Gaston, 2016; Lin et al. 2018), along with reduced availability of, and access to biodiverse environments could theoretically compound this effect. This in turn could lead to a degeneration of the *Lovebug Effect*.

As the *Lovebug Effect* could be a potent mechanistic pathway to the survival benefits associated with the Biophilia Hypothesis and the psychological wellbeing benefits of nature connectedness (and associated pro-environmental behaviours), the implications of its degeneration for public health and ecological resilience could be considerable. Nevertheless, there is a range of anthropogenic interventions that could be implemented to help alleviate these pressures, thus allowing the *Lovebug Effect* to be restored (Pathway B in Figure 4).

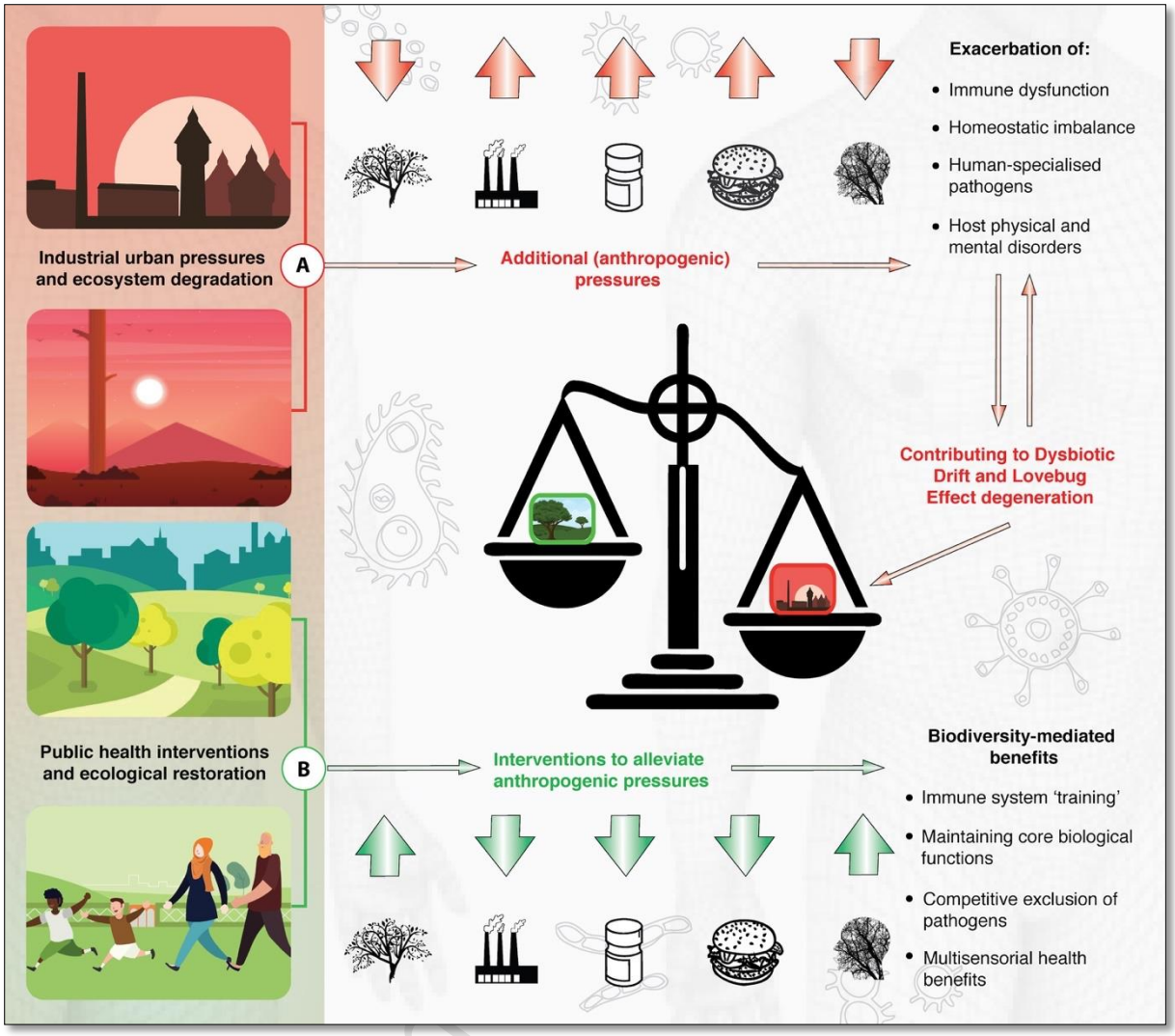

Figure 4. Pathway **(A)**: Anthropogenic pressures and ecosystem degradation could lead to a 'dysbiotic drift' and degeneration of the *Lovebug Effect*. This contributes to an increase in noncommunicable diseases and to a 'ratcheting down effect' (risk of extinction of nature experience and reduced exposure to biodiversity). Pathway **(B)**: Holistic public health and ecological restoration interventions could potentially alleviate these pressures, allowing the restoration of the *Lovebug Effect* in areas of nature deficit or to continue at a stable level in areas with sufficient supply of biodiversity.

6.2. Holistic approaches for public health and ecological restoration

Anthropogenic pressures that could disturb the *Lovebug Effect* are deeply ingrained in complex sociopolitical structures, and are therefore systemic by nature—that is, there are

unlikely to be specific isolated factors that would alleviate these issues. Holistic approaches are needed to address social inequalities, loss of biodiversity (including diverse microbial communities), inaccessibility to good quality natural environments, pollution, inappropriate use of antibiotics, ultra-processed diets and extinction of nature experience (as represented in Pathway A in Figure 4). From this perspective, initiatives that explicitly consider multidimensional co-benefits could be valuable. Examples of these integrated approaches include:

- Ecological restoration initiatives (Pathway B in Figure 4), i.e., restoring degraded ecosystems along with their ecosystem services, typically through active management methods (Vaughan et al. 2010; Matzek et al. 2019) with integrated public health evaluations;

- Schemes that aim to empower communities, improve sustainable development, and provide ecological education and opportunities at the 'grass roots' level - such as community gardening projects (Kim, 2017; Othman et al. 2018);

- Green prescribing (prescribed nature-based activities such as biodiversity conservation, therapeutic horticulture and nature walks), which has potential to enhance human and environmental health (Robinson and Breed, 2019; Shanahan et al. 2019).

Including a microbial model with the psychological frameworks associated with the Biophilia Hypothesis and nature connectedness has the potential to contribute towards a new appreciation for the microbial world, which could ultimately benefit human health. Indeed, it

has recently been argued that access to beneficial microorganisms is a facet of public health, and inequitable microbial exposure may compound health inequalities (Ishaq et al. 2019; Robinson and Jorgensen, 2020). Developing and integrating a microbe-centric view (Cavicchioli, 2019) is crucial in the face of existential risks such as global biodiversity loss and the climate crisis which ultimately affect human health through the vast array of health-supporting ecosystem services—many of which are microbially-supported (Rashid et al. 2016; Cavicchioli et al. 2019). To achieve this, it will be imperative to address the rise of 'germaphobia' — the perception that all microbes are bad and must be eliminated to maintain healthy living environment for humans (Timmis et al. 2019).

At this stage, the *Lovebug Effect* is a hypothesis that requires robust scrutiny. The following section aims to provide an alternative view, counter-arguments, and a starting point for researchers to test the hypothesis.

6.3. Challenges and next steps for the *Lovebug Effect*

As with any newly proposed hypothesis, it is imperative to take a critical view of the conceptual merits and potential pitfalls of the *Lovebug Effect*. To this end, one could easily question why in certain circumstances, some people appear to exhibit a disinclination towards biodiverse environments (Qiu et al. 2013; Hand et al. 2017) – a notion that could be used more broadly to challenge the Biophilia Hypothesis. Furthermore, it is important to also remember there is always a risk of false-consensus cognitive biases.

To counterbalance this perspective, one could point to the importance of anthropogenically-driven changes in life history traits and sociocultural norms in reducing the multiplexity of interactions and connections between humans and the rest of nature (Soga and Gaston, 2016;

Colléony et al. 2017; Cox and Gaston, 2018). In other words, could the addition of recent pressures be overriding one's innate and adaptive desire to affiliate with nature? Fattorini et al. (2017) pointed out that some children's preference for less natural and biodiverse environments are likely driven by cultural conditioning, and their innate nature-affinity will fail to flourish if inadequately stimulated.

If the *Lovebug Effect* is fundamentally driven by natural selection, then a degree of natural variation would be expected. Perhaps affinity to nature is beneficial only under certain circumstances (e.g., in certain ecological contexts or life history stages, but not others). If the associated benefit varies spatially and/or temporally, it would lead to variation in selection for this effect, resulting in variation in the trait itself. This has parallels with the concept of adaptive evolution in natural ecosystems, where, for example, adaptive variation in flowering times of plants varies spatially (e.g., later bud-burst in higher latitudes) and through time (e.g., optimal flowering can vary season-to-season) (Blackman, 2017; Cole and Sheldon, 2017). There is no single universally optimal flowering time. On an individual level, the optimisation of this process will depend considerably on location and prevailing environmental conditions. Therefore, the *Lovebug Effect* could fit this evolutionary framework even with high degrees of inter-individual variation in the levels of biophilic drive.

An important line of enquiry, which from a correlative perspective could be investigated with relative ease, is whether an individual's *nature connectedness* is influenced by microbiota (or vice versa). A first step could be to associate the human microbiome with people's Nature Connectedness Index scores via the validated, six-item survey with a seven-point response scale (Richardson et al. 2019). Questions that may arise include: is low or high microbial

diversity associated with low or high nature connectedness, and do particular—dominant or diminutive levels of —microbial taxa associate with nature connectedness?

To start testing the *Lovebug Effect* in general, we suggest that researchers explore our eight-step model (see Figure 2) in pairs of process-outcomes, using observational and experimental models for each stage, as follows (summarized in Table 1):

Stage 1. Human exposure to environmental microbiota with subsequent colonisation

For Stage 1, experiments should build on several recent and active studies that investigate human–environmental microbial exchange. For example, Grönroos et al. (2018) demonstrated that short-term direct contact with soil and plants leads to increases in skin microbial diversity. Nurminen et al. (2018) suggested that exposure to nature-derived microbiota associates with gut microbial diversity in the short-term. Ottman et al. (2019) showed that direct soil exposure modifies the gut microbiota in a mouse model. Liddicoat et al. (2019) observed the presence of aerobiome-mediated gut microbiota modulation via exposure to trace-levels of soil dust.

It should be noted that examples of long-term colonisation by environmental microbiota during the adult life stage are limited. Several studies on probiotics show varied results for allochthonous bacterial persistence in the gut (Maldonado-Gómez et al. 2016; Zmora et al. 2018; Xiao et al. 2019). A recent study demonstrated that bile-resistant *Lactobacillus johnsonii* 456 (LBJ 456) can persist in the gut for at least a month following a week-long course (Davoren et al. 2019). Determining the colonisation potential for different body sites

and across different life stages will be an important focus point for researchers investigating the *Lovebug Effect*.

Due to the dynamism of the gut microbiome during the human weaning phase—approximately 0-3 years of age (Yang et al. 2016; Moore and Townsend, 2019)—it is likely that there will be enhanced opportunities for colonisation by environmental microbiota during this period. Therefore, understanding the microbial influences during this key phase of gut microbiome colonisation should be of early interest in these Stage 1 studies.

Additional randomized controlled trials such as those conducted by Liddicoat et al. (2019) would be a useful framework for testing the *Lovebug Effect*. Detailed experiments to investigate the exposures of different types of microbiomes are needed (e.g., aerobiomes, rhizospheres, phyllospheres), while also studying dose-responses patterns (e.g., compositional changes, durations of effects, longitudinal changes to gut microbiota) and downstream impacts on host phenotypes (e.g., physiology and immune responses).

Stage 2. Selection for human–environmental microbiota associations (does colonization result in health outcomes?)

Experiments for this stage would build on the Old Friends Hypothesis (Rook, 2014). Researchers should aim to identify whether human associations and subsequent colonization (covered in Stage 1) with environmental microbiota can result in improved health outcomes in humans (e.g., via immunoregulation). This idea fits with the hologenome concept of evolution, and perhaps neurological manipulation, but also with more traditional theories of evolution. For example, associations could potentially benefit both the host and the

symbionts—and vertical transmission of microbial genomes could, in theory, contribute to this process. However, interactions with environmental microbiota could also improve health outcomes in humans in a way that adaptively leads to selection for the behavioural traits in humans that maximise exposure to natural environments. As such, these adaptive phenotypes could subsequently be inherited in future generations without vertical transmission of microbial genomes.

Initial studies could include exposing mice to environmental microbiota (as per Stage 1), determining colonization, and examining metabolite production and markers of immunomodulation. Genome-wide association studies combined with microbiome and metabolite characterisation (e.g., short chain fatty acids) could be used to determine the genetic basis of microbiome interactions and metabolic diseases. For example, Sanna et al. (2019) provided evidence of a causal effect of the gut microbiome on metabolic traits (and Type II diabetes) using bidirectional Mendelian randomization analyses.

Karsas, Lamb and Green (2019) pointed out that microbiota may modulate physiology. This is supported by a study that presented evidence for microbial modulation of olfactory epithelium physiology (François et al. 2016). As alluded to earlier, microbially-influenced behavioural changes may be partially governed by olfactory system interactions. Therefore, further investigations into host and bacterial gene associations (e.g., genes related to olfaction such as OR6A2) (Goodrich et al. 2016; Chang and Kao, 2019) could also offer insight into the *Lovebug Effect*.

Stage 3. Human-microbiota feedbacks

Unravelling the complexities involved in the microbiota-gut-brain axis is an active area of research (Cryan et al. 2019). To explore the *Lovebug Effect*, researchers should conduct environmental microbiome exposure studies (initially using germ free mouse models), followed by fine-scale investigations into the transfer and influence of different microbial taxa with a focus on cognitive and behavioural changes. There is a wide range of validated tests available for the behavioural phenotyping of mice, including protocols for testing basic motor and sensory function, learning and memory, social behaviour, anxiety and depression, impulsivity and personality (Carola et al. 2002; Bailey and Crawley, 2009; Kaidanovich-Beilin et al. 2011; Wolf et al. 2016).

These studies should also integrate functional molecular biology approaches to elucidate the potential biological mechanisms involved in microbially-mediated behavioural change. For example, researchers could focus on immune system responses, tryptophan metabolism, vagal and enteric nervous system activity, while analysing the activity of the microbial metabolites involved in the microbiota-gut-brain axis, such as peptidoglycans, short-chain fatty acids, and branched chain amino acids (BCAAs).

Stage 4. Biophilic Drive

To begin investigating the potential existence of microbial influences on the biophilic drive, researchers could extend the tests in Step 3 with a focus on the response variable being an increased desire for time spent in biodiverse or natural environments. Using randomized controlled trials and mouse models, choice chamber experiments could be designed, whereby two or more microhabitats (initially soil-based) are created with different levels of biodiversity. The experimental mice can then be exposed to and thereby inoculated with

different individual strains and assemblages of microbiota (testing a range of diverse microbial communities, pathogens, and microbially-derived metabolites). This should be followed by behavioural tests to determine whether the treatments influence decision making in the mice. There are various other approaches that could be taken, for example, exposing mice to different habitats over varying periods of time, and assessing microbial and molecular effects with subsequent behavioural phenotyping.

Ideally, these types of studies should eventually be modified and scaled up to humans. However, there will be important challenges associated with this process. For example, controlled environments are difficult to create in human studies and there are many potential confounding factors to consider. Some noteworthy, potential confounders of microbiome studies include lifestyle, health, exposures, and psychosocial biases. Overcoming such confounders requires large sample sizes and carefully selected groups.

Other approaches that could be useful for the *Lovebug Effect* include studying the human microbiome composition, structure and dynamics alongside tests for nature connectedness, such as the Nature Connectedness Index (Richardson et al. 2019) and other validated psychosocial instruments. Determining whether spending time in natural environments influences the human microbiome and whether this subsequently correlates to levels of nature connectedness could be an important study for the *Lovebug Effect.* A starting point could be to simply investigate relationships between nature connectedness scores and human microbiome composition (e.g., diversity, individual strains, relative abundances) across different body sites. This could raise questions such as: does a higher level of nature connectedness result in a more diverse human microbiome? Is this a result of a desire to spend time in nature that subsequently increases microbial diversity?

This line of enquiry could be enhanced by longitudinal cohort studies investigating microbiome dynamics from birth with subsequent assessments of nature connectedness and pro-environmental behaviours. Perhaps a study investigating potential relationships between these behaviours throughout the life course with explicit consideration for birth mode (i.e., caesarean section vs. vaginal delivery) could also bring important insights. Furthermore, it is plausible that a parent who is more connected to nature is more likely to expose their children to natural environments during the critical window of microbiome development (0-3 years). As such, studying potential associations between a person's microbiome and their parents' nature connectedness could also be a valuable approach.

7. Conclusions

Here we propose the *Lovebug Effect* as a microbially-mediated pathway to help explain the human biophilic drive – the tendency to affiliate and connect with nature. The *Lovebug Effect* is supported by the hologenome concept of evolution. However, the effect would still be relevant in the absence of this evolutionary framework. There are evolutionary processes related to nature affinity that could be microbially-influenced that do not need to meet the criteria of vertical transmission of microbial genomes or direct host manipulation. The pathways discussed in this paper tie together the presence of evolutionary pressures and the mechanisms to microbially-mediated behavioural change (direct or indirect). The foundations have been set to start testing the *Lovebug Effect*, which could extend the portfolio of pathways to nature affiliation. Investigating the *Lovebug Effect* could have implications for the way the Biophilia Hypothesis and nature connectedness are studied in the future. Finally,

from a broader perspective, the *Lovebug Effect* could also have implications for the way public health and ecological restoration is approached.

Competing or Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential competing or conflict of interest.

Author Contributions

J.M.R and M.F.B contributed to the conception and design of the hypothesis and the article; J.M.R and M.F.B wrote the first draft of the manuscript; J.M.R and M.F.B contributed to manuscript revision, read and approved the submitted version.

Acknowledgements

J.M.R. is undertaking a PhD through the White Rose Doctoral Training Partnership (WRDTP), funded by the Economic and Social Research Council (ESRC). M.F.B. is supported by the Australian Research Council.

Data Accessibility Statement

There is no data used in this manuscript.

Figure Legends

Figure 1. The Biophilia (and Biophobia) Hypothesis – showing human behavioural responses to different environmental stimuli, modulated in part by the autonomic nervous system. In general, nature provides health-regulating opportunities and resources for survival. However, some natural features also pose a danger to humans and elicit biophobic responses.

Figure 2. The *Lovebug Effect* - microbially-mediated nature affinity. This hypothesis proposes that our biophilic drive towards natural environments could be influenced by coevolution, biodiversity-mediated benefits and potentially unilateral adaptations. Arrows relate to processes and numbers in circles relate to outcomes. In the absence of anthropogenic impacts, the *Lovebug Effect* continues while subject to a stable pressure-benefits counterbalance. 'A' represents anthropogenic pressures, further defined in Figure 4.

Figure 3. Using fans, germ-free mice were exposed trace-levels of biodiverse soil dust exposure in controlled conditions (Liddicoat et al. 2019).

Figure 4. Pathway **(A)**: Anthropogenic pressures and ecosystem degradation could lead to a 'dysbiotic drift' and degeneration of the *Lovebug Effect*. This contributes to an increase in noncommunicable diseases and to a 'ratcheting down effect' (risk of extinction of nature experience and reduced exposure to biodiversity). Pathway **(B)**: Holistic public health and ecological restoration interventions could potentially alleviate these pressures, allowing the restoration of the *Lovebug Effect* in areas of nature deficit or to continue at a stable level in areas with sufficient supply of biodiversity.

Table 1. Suggested approaches to start testing the hypotheses of the *Lovebug Effect*.

Stage	Process	Outcome	Test
Stage 1	Human exposure to environmental microbiota with subsequent colonisation	Human adaptive advantage via colonising environmental microbiota-mediated benefits	Molecular epidemiology of humans in nature (human-environmental microbiota colonisation studies) and controlled trials with mouse model. Follow-up trials of humans, and assess for longitudinal changes to gut microbiota. Cross-sectional study of mice and humans, exploring the association between health outcomes of exposure to environmental microbiota. Dose-response effects studies in mouse models where dose can be quantity (quantum of microbiota) or quality (e.g., biodiversity – high vs low). Additional randomized controlled trials such as those used by Liddicoat et al. (2019) would be beneficial. Detailed randomised controlled trials to test the exposures of different types of microbiomes and body sites, whilst studying compositional changes, durations of effects, longitudinal changes to gut microbiota, and downstream impacts on host phenotypes. Importantly, these tests should be applied at different life stages with early life microbial dynamics as a key consideration.
Stage 2	Natural selection for	Human-microbiota co-	Expose mice to environmental microbiota (as per Stage 1), determining colonization, and examining

	human-microbiota associations	evolution (and/or unilateral adaptations)	metabolite production and markers of immunomodulation. Genome-wide association studies, microbiome sequencing and metabolite production examined to determine causal relationships between microbiome interactions and metabolic diseases. Further explorations into host and bacterial gene associations e.g., those that influence host olfaction. Study health of people in different environments through time. Ancient DNA combined with proxies for health (e.g., health at death, indicators of good/ill health such as bones). Develop mathematical models to simulate evolutionary processes and outcomes.
Stage 3	Human-microbiota feedbacks	Human behavioural manipulation by microbiota	Environmental microbiome exposure experiments (initially using germ free mouse models), followed by fine-scale investigations into the transfer and influence of different microbial taxa with a focus on cognitive and behavioural changes. Functional molecular biology approaches should be included. Focus on immune system dynamics, tryptophan metabolism, vagal and enteric nervous system activity, whilst analysing the activity of the microbial metabolites involved in microbiota-gut-brain axis processes. Case-control trials commencing in mouse models and moving to humans.

Stage 4	Biophilic Drive	Spending time in 'nature'	Extend tests in Step 3 with a focus on the outcome being an increased desire for time in biodiverse environments. Randomised controlled trials with choice chamber experiments for mice. Two or more microhabitats created with different levels of biodiversity. The mice can then be inoculated with different individual strains and assemblages of microbiota. This should be followed by behavioural tests to determine whether the treatments influence decision making in the mice. Other approaches that could be taken include exposing the mice to the different habitats over varying periods of time, and assessing microbial and molecular effects with subsequent behavioural phenotyping. Study the human microbiome composition, structure and dynamics alongside tests for nature connectedness, such as the Nature Connectedness Index (NCI) and other validated psychosocial frameworks. This approach could be taken to study microbiome–nature connectedness associations for individuals, but also between the microbiome of individuals and their parents' degree of nature connectedness.

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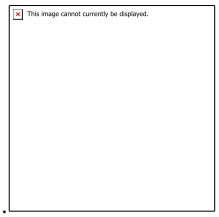
Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Graphical abstract

148. 

Highlights

- Animal behaviour can be strongly influenced by the host's microbiome
- A microbially-influenced mechanism could contribute to the human biophilic drive
- We present a conceptual model for microbially-influenced nature affinity
- This conceptual model is called the *Lovebug Effect*
- The Lovebug Effect could have implications for ecological resilience and human health