The master puppeteer? – Impact of microbes on brain and behaviour

For the longest time microbiology & neuroscience used to be studied independently and with limited overlap. Recently, however, research on the *microbiome* and its interaction with our organs, including the brain, is increasingly gaining momentum. With more evidence finding comprehensive microbiome-gut-brain communication, questions have been raised as to the extent to which microbes influence brain physiology and behaviour. In fact, we usually call microbes that do have a largely accepted role in behavioural manipulation parasites. In addition to several single-celled parasites, many parasitic viruses have been described to infect the brain and induce marked changes in brain physiology, cognition, and behaviour.

While these cases are fascinating, however, other types of symbiosis are less well understood. Indeed, there is now a rapid increase in awareness of the importance of the ‘normal/healthy’ microbiome (also sometimes incorrectly called “gut flora”) in shaping our behaviour. In fact, the microbiome and its ability to influence our behaviour is a very exciting area in both, scientific literature and the popular press. However, there has been much lurid media coverage and pseudoscientific discussions in social media, which may have lead to the impression that our behaviour is exclusively driven by the composition of our microbiome.

Therefore, it is important to try and clarify whether a certain microbial interaction partner is rather beneficial or rather malignant for us. In fact, in many cases it turns out to be a very challenging exercise to determine where a given microorganism is located on the spectrum between “really good for us (mutualism)” and “really bad for us (parasitism)”. This is further complicated by the

long evolutionary history that intimately connects us with our microbes.

The term ‘manipulation’ is probably an overstatement and our best guess as to why a ‘normal/healthy’ microbiome would influence our behaviour has undoubtedly been forged in an evolutionary tug-of war between microbes and host. It is also hard not to think about this process as unidirectional and simplified and we therefore often impose intentions on the microbes, which they clearly don’t have. Another limitation is that we often forget that, at all times, our evolution has occurred in the presence of, and most likely also in dependence of, microbial life. Therefore, humans and animals have never lived in a sterile environment and will never be able to live, develop nor evolve in a germ-free way outside laboratory isolators.

In summary, it is tempting to speculate as to why such a crucial relationship has evolved. However, from the perspective outlined here the question *“Who is master and who is slave?”* is just the wrong question to ask. Especially from a healthcare point of view it is much more intriguing to ask the questions *to what extent* microbes influence our lives and *how* is this achieved on the molecular level so that we can harness our symbionts in the most efficient way in both, health and disease.

In a recent conceptual minireview we discuss current hypotheses on host-microbe interaction and argue that novel experimental approaches and theoretical concepts, such as the hologenome theory, are necessary to include transgenerational epigenetic inheritance of the microbiome into evolutionary theorie.

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