

Is there a link
between gut
microbiota and
altered brain function
in mental illness...



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'Trust Your Gut: Is There a Link Between Gut Microbiota and Altered Brain Function in Mental Illness?'

Summary:

Emerging research into the microbiome-brain-gut axis has suggested there may be a link between gut microbiota and mental health conditions, with certain bacteria affecting brain function, and more specifically, mood and behaviour. Therefore, this could indicate that gut microbiota is a crucial factor in the link between diet and mental disorders (Dash et al., 2015). This could therefore provide potential treatments for these conditions through the normalisation of the composition of gut microbiota using probiotics and changes to diet.

What Is the Aim of The Exhibit?

The aim of my poster is to investigate the question of whether there is in fact a tangible link between gut health and mental health, and how this relates to various strategies to manage mental disorders. Changes to unhealthy diet, and treatments with both probiotics and antibiotics, could prove crucial in managing and reducing the risk of mental disorders such as anxiety and OCD. I will use my exhibit piece to present this information clearly, as well as to raise the awareness of mental illness, to my audience of fellow university students in a concise and informative way. The structure of the poster would closely mirror the structure of this dissertation, with the subheadings acting as key sections within the exhibit.

Why Is This Topic Important for My Audience?

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The Institute for Public Policy Research (2017) has found that in the UK, 19 per cent of 16 to 24-year-olds report having a mental health condition, which is up from 15 per cent in 2003. There have also been a staggering number of student suicides, with the number increasing by 79 per cent between 2007 and 2015 (from 75 to 134). Sadly, this number is only set to rise and therefore the need to further understand the causes of mental illnesses, such as anxiety and depression, has never been more vital. This is especially true for universities, who need to understand how best to distribute their limited resources to those most in need in order to prevent these tragic consequences. Hence, I feel this topic is important for my audience and have chosen to present a poster showing the findings of the most recent research in this area as I feel it is an engaging method of presentation. The exhibit method has also been selected in order to raise more awareness for mental health amongst students and suggest causes of and preventative measures against mental illness.

What Is The ' Brain-Gut' Axis?

The ' brain-gut axis' is a " bi-directional communication system, comprised of neural pathways, such as the enteric nervous system, vagus, sympathetic and spinal nerves, and humoral pathways" (Bercik, Collins and Verdu, 2012 p. 405). Though research on the link between gut microbiota and brain function is limited in human subjects, there have been numerous animal studies on the topic. Mice that have been raised in a germ-free environment are very useful in these studies, as they allow the effect of microbiota on brain and body development to be assessed more objectively (Foster and Neufeld, 2013). It has also been found that infections significantly change <https://assignbuster.com/is-there-a-link-between-gut-microbiota-and-altered-brain-function-in-mental-illness/>

gut function, including changes to the metabolism of kynurenine and tryptohan pathways, as well as in pro-inflammatory cytokines. These alterations have been linked with symptoms of anxiety and depression (Bercik and Collins, 2014).

How Does the Gut Influence the Brain?

Normal gut microbiota is crucial for normal brain development and behaviour, with environmental influences, like exposure to various microbiota early in life, having a huge effect on the brain's function later (Heijtz et al., 2011). Changes in bidirectional brain-gut microbiota interactions are believed to be associated with many gastrointestinal disorders, as well as brain and mood disorders. Research by Mittal, Ellman and Cannon (2008) has found that microbial pathogen infections during the crucial perinatal period has been linked with neurodevelopmental disorders, such as schizophrenia. This indicates that gut microbiota has a significant impact on the brain's development, and infections early in life could be a cause of altered brain function, leading to mental illnesses later.

Furthermore, research by Lyte, Varcoe and Bailey (1998) has shown that during the early phase of acute infection with *Campylobacter jejuni*, mice display altered anxiety-like behaviours. There have also been links between microbiota and memory and cognition, with diet being a key factor in this link. Li et al. (2009) found that mice given food with a higher content of ground beef for three months had higher diversity of gut microbiota, than mice on standard rodent food. This long-term dietary manipulation affected working memory, and reduced anxiety-like behaviour in mice and the speed

in which they looked for food. These studies indicate that gut microbiota could have a significant impact on cognition and behaviour, as well as other physiological responses which have been researched in more depth previously.

There has also been evidence that gut microbiota influences the function of the central nervous system (CNS), which is a crucial pathway of communication between the gut and brain. Dysfunctional gut microbiota can be detrimental to the body and brain and can contribute to CNS disorders (Rees, 2014). Gut microbiota has been shown to be vital in normal healthy homeostasis and effects the risk of mood disorders and stress, including anxiety (Foster and Neufeld, 2013).

The dysregulation of the brain-gut axis can have serious consequences for the body, with many conditions resulting from this. Mayer (2011) has found that disruptions in brain-gut interactions are correlated to eating disorders, such as anorexia nervosa, as well as gut inflammation and other gastrointestinal (GI) disorders. There is also a clear link between these GI disorders, like irritable bowel syndrome, and stress related psychiatric symptoms like anxiety (Kennedy et al., 2012). The high co-morbidity shows that many gut-related conditions are also accompanied by mental distress, thus emphasising how crucial the brain-gut axis is for our overall health and demonstrates clearly the link between them. Research has also shown that microbiota is key in regulating brain function, as both IBS and depression symptoms respond independently to antibiotics (Dinan and Cryan, 2013).

Compelling new evidence from Valles-Colomer et al., (2019) has found that in people with depression, regardless of whether they were taking antidepressants or not, two bacteria groups of *Coprococcus* and *Dialister* are reduced. Further to this, the presence of both *Faecalibacterium* and *Coprococcus* were linked to people without depression and was associated with higher quality of life. The ability for subjects to synthesise the dopamine metabolite *3, 4-dihydroxyphenylacetic acid* was correlated positively with a better quality of mental health. This study clearly demonstrates the link between gut microbiota and a person's mental health. However, it is important still to note that these results are merely correlations and there is still no firm evidence that the reduction or presence of certain microbiota directly causes depression or other mental illnesses. For example, diet could play an important role in impacting a person's microbiota and in turn their mental well-being.

The dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis has also been linked to depression, with HPA reactivity directly correlating to gut microbiota (Sudo et al. 2004). Right from birth the HPA axis is programmed by gut microbiota, which also impacts stress reactivity throughout life (Foster and Neufeld, 2013). This emphasises the effect of gut microbiota on stress, with Allen et al., (2012) finding that environmental stressors in life, such as social disruption, significantly impacted the stability of intestinal microbiota and affected host health. Further evidence of this has been found in a study involving mice subjected to chronic restraint stressor, who showed a significant difference in the community structure of microbiota compared to non-stressed mice (Bailey et al., 2011).

The HPA axis and sympathetic nervous system also help to balance levels of different stress hormones, including cortisol and noradrenaline (De Kloet, Joels and Holsboer, 2005). Research has also found a link between OCD and an increase in activity of the HPA axis, as increased levels of corticotrophin releasing hormone were found in patients with the condition (Altemus et al., 1992). There is evidence that gut microbiota could be a cause of OCD, with Swedo et al., (1998) finding that children who had group A *beta-hemolytic streptococcal* (GABHS) infections at a very early age went on to experience a sudden onset of acute OCD symptoms immediately afterwards. This important discovery clearly indicates the effect gut microbiota has on the brain, especially in terms of when infection alters healthy microbiota. With this in mind, there could be the potential for antibiotics to be an avenue of treatment for patients with OCD, if it was directly caused by GABHS infection.

The Effects of Diet on Microbiota and Mental Health:

Diet is vital in the regulation of gut microbiota and any dramatic changes to diet can quickly have a significant impact on both microbiota and subsequently host health, including brain function, as the diversity of microbiota alters. The Western diet is high in sugar, fats and salt and has been linked to an abundance of *Collinsella* in humans with a high-fat diet, with this bacterium being associated with obesity (Sandhu et al., 2016). This indicates a strong relationship between host health and gut microbiota, with diet being the mediating factor between them. These diet-induced changes in the microbiota-gut-brain axis are also associated with increases in both depression and anxiety-like behaviour due to a Western diet.
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Therefore, a potential solution to this could be to change to a Mediterranean style diet which is higher in fibre and vegetables and lower on meat consumption and sugars, as well as being low-fat compared to a Western diet. Research by Sánchez-Villegas et al., (2009) provides strong support for the significant impact diet has on microbiota and mental health, finding a Mediterranean diet increases monoamine neurotransmitter turnover, helping to regulate mood and depressive episodes. Furthermore, a Mediterranean diet is high in vitamin B, which is associated with the synthesis of neurotransmitters such as dopamine and serotonin. Therefore, this type of diet could act as a natural antidepressant which boosts mood and increases the abundance of useful bacterium like *Prevotella*, which is high in people with a Mediterranean diet (Sánchez-Villegas et al., 2009).

The evidence of the effect diet has on host health and gut microbiota could prove crucial in the development of potential treatments for mental health conditions, like depression and the management of its symptoms.

Probiotic Treatments for Depression:

Further to changes in diet, more research has been done on potential treatments of depression using probiotics to change gut microbiota. Probiotic studies are often also carried out in order to support the relationship between bacteria and the brain. Messaoudi (2011) found that taking a combination of two probiotics; *Lactobacillus helveticus* R0052 and *Bifidobacterium longum* R0175, for 30 days significantly reduced participants' scores on the hospital anxiety and depression scale (HADS) in the general population. The fact that a probiotic, which alters the

composition of microbiota in the gut, can significantly influence mental health symptoms, provides strong evidence for the brain-gut link. There is also an opportunity to take this research further and focus more on probiotics in order to help manage the psychiatric symptoms of mental illnesses and potentially prevent them entirely.

This is supported by further research conducted by Desbonnet et al., (2010) who used a rat maternal separation model, finding that the probiotic *Bifidobacterium infantis* helped to return the immune system back to its normal state and reverse behavioural deficits, such as anxiety, caused by the maternal separation. Furthermore, the study found that basal noradrenaline levels in the brainstem were restored as a result of the probiotic treatment. These findings help provide evidence that that *Bifidobacterium* has a significant effect on neuronal development and that there is scope for probiotics to be used as a treatment for mood disorders.

Another probiotic study using mice was conducted by Bravo et al., (2011) who investigated how alterations to GABA, the main CNS inhibitory neurotransmitter, would impact host health. The mice were treated with *Lactobacillus rhamnosus* which was shown to reduce stress-induced corticosterone and anxiety and depression-related behaviour, as well as changing the expression of both GABA_A and GABA_B receptors in the brain. However, these behavioural and neurochemical changes were not found in vagotomised mice, indicating the importance of the vagus nerve in mediating the effects of microbiota such as *Lactobacillus rhamnosus*. This study further supports the link between gut microbiota and altered brain

function in mental illnesses, with probiotics helping to demonstrate this through experimental methods.

Problems with Studying the Role of Microbiota in The Gut-Brain Axis:

Although the relationship between gut microbiota and brain and behavioural development seems to be very convincing, there are still challenges regarding exactly how this relates to the causes of mental health. Most of the evidence we do have comes from animal studies, rather than on human subjects who have a more diverse microbiota, meaning more research would be needed before firm conclusions could be drawn. Furthermore, it may be the case that the influence of microbiota on the central nervous system is due to their metabolism profile and not a specific bacterium. For example, diet and stress are just some of the environmental factors which can affect these metabolic characteristics and potentially influence mental health, rather than microbiota (Bercik, Collins and Verdu, 2012). However, research has shown the impact both diet and stress have on gut composition, meaning it could be a circular explanation.

Conclusions:

Whilst it is clear there are links between mental health conditions and gastrointestinal pathology, the challenge of causality is still significant. At present it is impossible to know whether the differences in gut microbiota that are correlated with various mental illnesses, are in fact the cause of the disease or merely another symptom of it. More research would also need to be done on human subjects, with randomised control trials being conducted to further our understanding of the influence specific bacteria has on the

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brain. Further to this, it is important to continue investigating the potential of novel treatments to manage the symptoms of mood disorders, for example using probiotics as well as changes to diet.

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