New Brain Nutrition: The Gut Brain Axis — An Important Key To Your Health

In this document, the scientists of New Brain Nutrition describe the latest research on the links between gut health and stress, depression and other psychological disorders, as well as basic executive functioning.

NEW BRAIN NUTRITION

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The European Union Horizon 2020
research programme No 728018

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The Gut-Brain Axis: How intestinal bacteria effect mental health

by *Prokopis Constanti, MSc* - May 17, 2018

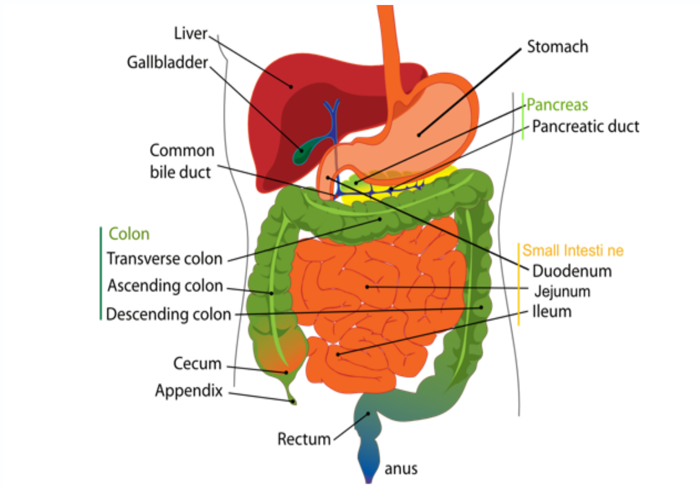
Recently, the idea that gastrointestinal microbiota are able to affect host behaviour is gaining momentum and it is based on studies conducted with animal models but also in humans with neurological disorders. However, the mechanisms that underlay this complex interplay between gut, brain and microbiota are not completely understood. Here we discuss recent findings on how microbial products could potentially affect the gut-brain axis.

Intestinal microbiota grow through the fermentation of undigested carbohydrates that end up in the large intestine. It was shown that absence of microbes or disruption of the microbiota, led to increased populations of impaired microglia cells in mice. Microglia cells are the primary effector cells for immune signalling to the central nervous system. The presence of a complex microbiota community, was shown to be essential for proper microglia maturation and function [1].

The main products of microbial fermentation in the gut are; acetate, propionate and butyrate, collectively known as short chain fatty acids(SCFA's). Their beneficial role in human physiology have been well described, and recently evidence suggests that these molecules are able to cross blood brain barrier [2]. Moreover, gut microbiota have been associated with the brain barrier integrity. Mice raised in absence of bacteria are reported to have reduced brain barrier integrity. Once colonized with either a butyrate or an acetate/propionate producing bacteria, significant improvements were reported in the barrier [3]. Notably the integrity of the blood-brain barrier from the germ free mice was able to be restored through the oral administration of butyrate. SCFA's are among the molecules having the privilege to cross the blood brain barrier and access the brain directly, their role should be studied in detail.

Recent studies also demonstrate that gut microbes regulate levels of intestinal neurotransmitters. The enteric nervous system interacts with a plethora of neurotransmitters (more than 30 have been identified so far.) Actually, the bulk of serotonin production ~90%, a neurotransmitter associated with mood and appetite is located in the gut. Specialized cells known as enterochromaffin cells are the main serotonin producers in the gut. In the absence of intestinal microbiota gastrointestinal serotonin levels are depleted. However, they can be restored by the addition of a specific spore forming consortium of intestinal bacteria. Specific bacterial metabolites have been reported to mediate this effect [4].

Other intestinal microbiota have been reported also to regulate the levels of the GABA neurotransmitter. Reduced levels of GABA have been associated with anxiety, panic disorder and depression. Bacterial GABA producers have been known to exist for years but it was not until 2016 that a gut bacteria was identified as GABA consumer [5]. For example, decreased levels of bacterial GABA producers were identified in a human cohort of depressed individuals. Studies in mice reinforce these findings. Intervention with the lactic acid bacteria *Lactobacillus rhamnosus* (JB-1) in healthy mice reduced anxiety related symptoms (accompanied by a reduction in the mRNA expression of GABA receptors in the Central Nervous System.) Lactic acid producing bacteria have also been reported to produce GABA in several food products such as kimchi, fermented fish and cheese [6].



Collectively, our gut microbiota encodes for ~100 times more genes than the human genome. The potential for some of these microbial genes to produce compounds able to interact with the nervous system and regulate critical pathways implicated in the gut brain axis is realistic and worth being explored.

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Prokopis Konstanti MSc performs PhD research in the group of Molecular Ecology at the Laboratory of Microbiology, Wageningen University (the Netherlands). He specializes in molecular analysis of microbial communities, and explores the role of microbes in human physiology focusing on the gut brain axis.

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The Information Super-Highway Between Your Gut and Your Brain

by Mariliis Vaht, PhD - November 15, 2018

Have you experienced drowsiness after eating a large meal? Has an important presentation made your stomach turn? Seeing a special someone made you feel butterflies in your stomach? If you have (and you most likely have), then you know how strong the connection between the brain and the gut is.

Scientists have found that many chronic metabolic diseases, type 2 diabetes, mood disorders and even neurological diseases, such as Parkinson's disease, Alzheimer's disease, amyotrophic lateral sclerosis (ALS) and multiple sclerosis, are often associated with functional gastrointestinal disorders (1). The importance of the association between the gut and the brain is gaining momentum with each new study. However, the way HOW the signaling between these two integral parts of the body exactly works hasn't been clear until recently.

It was thought for a long time that the only "communication channel" between the gut and the brain was the passive release of hormones stimulated by the consumed nutrients. Hormones entered the bloodstream and slowly notified the brain that the stomach is full of nutrients and calories. This rather slow and indirect way of passing messages takes from minutes to hours.

But now, a recent study (2) has elegantly proven that the gut can message the brain in seconds! Using a rabies virus enhanced with green fluorescence, the scientists traced a signal as it traveled from the intestines to the brainstem of mice, crossing from cell to cell in under 100 milliseconds – faster than the blink of an eye.

The researchers had also noticed that the sensory cells lining the gut were quite similar to the receptors in the nose and on the tongue (3). The effects, however, differ. In the mouth, the taste of fatty acids triggers signals to increase hunger, whereas in the small intestine, fatty acids trigger signals of satiety. This means that the discovered "gut feeling" might be considered as a sixth sense, a way of how the brain is being signaled when the stomach is full.

This new knowledge will help to understand the mechanism of appetite, develop new and more effective appetite suppressants and help those struggling with weight and problematic eating patterns.

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Mariliis Vaht, PhD is a Research Fellow of Neuropsychopharmacology at the Institute of Psychology, University of Tartu, Estonia. Her main focus of research: genetic and environmental factors in affective and anxiety disorders, drug use, and personality.

Early Life Nutrition and Gut Microbiota

by Yvonne Willemsen, MSc - January 2, 2019

This study will be performed in two cohorts which I will elaborate on in this current blog about early life nutrition and studying gut microbiota. The cohorts are called BIBO and BINGO.

BIBO stands for 'Basale Invloeden op de Baby's Ontwikkeling' (in English: basal influences on infant's development). Recruitment of this cohort started in 2006, and a total of 193 mothers and their infants were included. At age 10, 168 mothers and their children still joined the BIBO study; the attrition rate is thus low. The majority of the mothers are highly educated (76%). The number of boys (52%) and girls (48%) in this cohort are roughly equally divided. A unique aspect of the BIBO study is the number of stool samples collected in early life. Also, detailed information about early life nutrition has been recorded during the first six months of life (e.g. information on daily frequency of breastfeeding, formula feeding, and mixed feeding). Together, these stool samples and nutrition diaries provide important insights in the relations between early life nutrition and gut microbiota development. Data about children within the BIBO cohort will be collected at age 12,5 years and 14 years. At 12,5 years, the participants will be invited to the university for an fMRI scan (more information about the fMRI scan will be given in a future blog). At age 14, children's impulsive behavior will be assessed by means of behavioral tests and (self- and mother-report) questionnaires.

BINGO stands for 'Biologische INvloeden op baby's Gezondheid en Ontwikkeling' (in English: biological influences on infant's health and development). When investigating biological influences on infant's health and development, it is important to start before birth. Therefore, 86 healthy women were recruited during pregnancy. Recruitment took place in 2014 and 2015. One unique property of the BINGO cohort is the fact that not only mothers were recruited, but also their partners. The role of fathers is often neglected in research, and thus an important strength of this BINGO cohort. Another unique property is that samples of mothers' milk were collected three times during the first three months of life, to investigate breast milk composition. As for many infants their diet early in life primarily consists of breast milk, it is interesting to relate breast milk composition to later gut microbiota composition and development. Currently, 79 mothers and children, and 54 fathers are still joining the BINGO study. The average age of the participants at the time of recruitment was 32 years for mothers and 33 years for the father. Majority of the parents within this cohort are highly educated (77%) and from Dutch origin (89%). The number of boys (52%) and girls (48%) in this cohort are roughly equally divided. At age 3, children's impulsive behavior will be assessed by means of behavioral tests and mother-report questionnaires.

The Gut-Brain Axis: How intestinal bacteria effect mental health

by Yvonne Willemsen, MSc - April 4, 2018

The reason why I look at impulsive behavior is because mental disorders are the single largest contributors to disease burden in Europe. Impulsivity and compulsivity increase the risk of psychiatric disorders, especially Attention Deficit Hyperactivity Disorder, alcohol and drug abuse disorders, conduct disorder and antisocial disorders (including aggression). The urgency of addressing impulsivity and compulsivity is additionally strongly supported by the fact that these problems increase the risk for mortality.

My name is Yvonne Willemsen and I have started my PhD track at Radboud University in the Netherlands in October 2017. For my project I will assess the association between nutrition, gut microbiota composition and impulsive behavior in toddlers and young adolescents. In the following paragraphs, I will explain the first study that I am currently conducting.

Many previous studies have examined the association between nutrition and executive functions. Executive functions are cognitive processes in the brain that contribute to regulating thoughts and behaviors. Executive functions can be roughly divided into three core functions, namely: inhibitory control, working memory, and cognitive flexibility. Inhibitory control, which can be interpreted as the opposite of impulsivity, is necessary to suppress impulses. It is also an important core function of executive functions, as it supports working memory and cognitive flexibility. To date, studies have examined the association between nutrition and executive functions in general (1). Whether nutrition is related to inhibitory control specifically (in toddlers and young adolescents) is something that still needs to be investigated.

The next step of my study is to understand how nutrition is associated with inhibitory control. To explain a possible mechanism, we will look at the gut microbiota. The reason why the gut microbiota is a point of interest is because gut microbiota can secrete molecules that may influence brain function, and thus may influence inhibitory control (2). This connection between the gut and the brain is also known as the gut-brain axis. Gut microbiota composition can change according to nutritional intake, and can therefore play a role in the gut brain axis (3). To assess the association between nutrition, gut microbiota and behavior in toddlers and young adolescents, we will use questionnaires and different behavioural measures using the results of the BIBO and BINGO study.

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Yvonne Willemsen MSc does her PhD research at the Psychobiology lab, within the Developmental Psychology department of Radboud University in Nijmegen (the Netherlands). She is specialized in molecular nutrition and her main interest lies in nutrition and child health, especially the molecular mechanisms behind the associations between nutrition and gut microbiota.

Probiotics and ADHD

by Karina Rosales, MS, PhD - November 28, 2018

Maladaptive or uncontrolled impulsivity and compulsivity lead to emotional and social maladjustment, e.g. addiction and crime, and underlie psychiatric disorders. Recently, alterations in microbiota composition have shown to have implications for brain and social behaviors as we have been explaining in our lasts blogs. The microbiota-gut-brain axis may be involved in this process but the mechanisms are not fully identified (1). The supplementation of probiotics can modulate the microbial community and now has been suspected to contribute to ameliorating symptoms of a psychiatric disease with possible influence on social behaviors (2). To date, no randomized controlled trial has been performed to establish feasibility and efficacy of this intervention targeting the reduction of impulsivity and compulsivity. This gave us the idea to perform a study to investigate the effects of supplementation with probiotics, working with adults with Attention Deficit Hyperactivity Disorder (ADHD) and Borderline Personality Disorder (BPD) which in most cases present high levels of impulsivity, compulsivity and aggression.

We call our project PROBIA, which is an acronym of "PROBiotics for Impulsivity in Adults". This study will be performed in three centers of Europe including, Goethe University in Frankfurt, Semmelweis University in Budapest and Vall d'Hebron Research Institute (VHIR) in Barcelona, the coordinator of the clinical trial. We are planning to start recruiting patients in January of 2019 and obtain the results in 2021. In our study, we will explore the effects of probiotics by measuring the change in ADHD or BPD symptoms, general psychopathology, health-related quality of life, neurocognitive function, nutritional intake, and physical fitness. The effect of the intervention on the microbiome, epigenetics, blood biomarkers, and health will be also explored by collecting blood, stool, and saliva samples.

We are looking forward to having the results of this amazing study in order to understand the mechanisms involved in the crosstalk between the intestinal microbiome and the brain. If improvement effects can be established in these patients, new cost-effective treatment will be available to this population.

This was co-authored by Josep Antoni Ramos-Quiroga, MD PhD, psychiatrist and Head of Department of Psychiatry at Hospital Universitari Vall d'Hebron in Barcelona, Spain. He is also professor at Universitat Autònoma de Barcelona.

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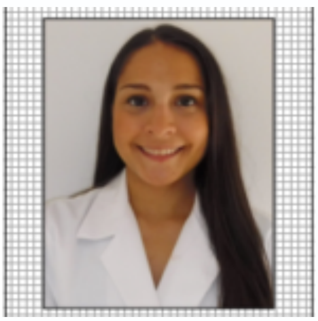

Karina Rosales Ortiz, MS PhD is a nutritionist who does research at the Department of Psychiatry, Vall d'Hebron Research Institute (VHIR), Barcelona, Spain. She is investigating the effects of food patterns on adults with attention deficit/hyperactivity disorder (ADHD).

Prebiotics and Probiotics in Mental Health

Psychobiotics: How Probiotics and Prebiotics Effect Mental Health

by Mariliis Vaht, PhD - November 9, 2018

Psychobiotics are helpful bacteria (probiotics) or support for these bacteria (prebiotics) that influence the relationship between bacteria and brain. The human digestive system houses around 100 trillion of these bacteria, outnumbering the human body cells 10:1. Probiotics provide a great deal of functions vital to our well-being, like supporting the digestion process and improving the absorption of nutrients. Based on the latest research, helpful gut bacteria that can also positively affect the brain – psychobiotics – benefit people suffering from chronic stress, poor mood, or anxiety-like symptoms (1).

There are 3 ways psychobiotics can affect your mental health:

- Brain chemicals like serotonin, dopamine, and noradrenaline can be produced in the intestines directly by gut microbiota.
- Battling with and protecting from stress by modifying the level of stress hormones.
- When an inflammation occurs, inflammatory agents are elevated throughout the body and brain and can cause depression and other mood and cognitive disorders. Psychobiotics can affect the brain by lowering inflammation.

Lactobacillus and *Bifidobacterium* are the most popular probiotics with respect to mental health (1).

Disruption of the balance of gut bacteria is quite common due to the use of different kinds of medications, antibiotics, artificial preservatives, poor food and water quality, herbicides, stress, and infections (2, 3, 4).

In order to support a healthy microbiota, one should start from eating a diverse range of foods rich in different plant sources. Foods that contain lots of fiber or are fermented also promote the growth of beneficial gut bacteria. Excessive consumption of sugar and artificial sweeteners should be minimized. Managing stress levels, exercising on a regular basis, not smoking and getting enough sleep are also important for keeping microbiota in good condition. When taking antibiotics, one should make sure to consume probiotics so the body can maintain the bacteria it needs to stay healthy.

For people needing help regarding mental health problems, psychobiotics may be a promising relief. Psychobiotics are well-adapted to the intestinal environment and naturally modulate gut–brain axis communications, thereby reducing the chance of adverse reactions.

It is possible that even simple prescribing of a particular diet may be sufficient to promote the selective proliferation of natural or therapeutically introduced psychobiotics (5). Further research focusing on the strain and dosage of psychobiotics, duration of treatment, and the nature of mental disorders will help to determine the most efficient ways of helping people to improve their mental health.

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How Prebiotics Reduce Aggression and Stress – The Animal Model

by Tunde Kilencz - November 8, 2018

A hot topic these days, that one can hear more and more information about is the microbiota-gut-brain axis, the bidirectional interaction between the intestinal microbiota and the central nervous system nowadays, this has become a hot topic. We are becoming increasingly aware that gut microbiota play a significant role in modulating brain functions, behavior and brain development. Pre- and probiotics can influence the microbiota composition, so the question arises, can we have an impact on our mental health by controlling nutrition and using probiotics?

Burokas and colleagues aimed to investigate this possibility in their study (2017), where the goal was to test whether chronic prebiotic treatment in mice modifies behavior across domains relevant to anxiety, depression, cognition, stress response, and social behavior.

In the first part of the study, the researchers fed mice with prebiotics for 10 weeks. They were administered the prebiotics fructo-oligosaccharides (FOS), galacto-oligosaccharides (GOS), a combination of both, or water. FOS and GOS are soluble fibers that are associated with the stimulation of beneficial bacteria such as bifidobacterium and lactobacillus.

Behavioral testing started from the third week including:

- the open field test (anxiety – amount of exploratory behavior in a new place),
- novel object test (memory and learning – exploration time of a novel object in a familiar context), and
- forced swimming test (depression-like behavior – amount of activity in the cylinder filled water).

Meanwhile, plasma corticosterone, gut microbiota composition, and cecal short-chain fatty acids were measured. Taken together, the authors found that the prebiotic FOS+GOS treatment exhibited both antidepressant and anxiolytic (anti-anxiety) effects. However, there were no major effects observed on cognition, nociception (response to pain stimulus), and sociability; with the exception of blunted aggressive behavior and more prosocial approaches.

In the second part, FOS+GOS or water-treated mice were exposed to chronic psychosocial stress. Behavior, immune, and microbiota parameters were assessed. Under stress, the microbiota composition of water-treated mice changed (decreased concentration of bifidobacterium and lactobacillus), which effect was reversed by treatment with prebiotics.

Furthermore, it was found that three weeks of chronic social stress significantly reduced social interaction, and increased stress indicators (basal corticosterone levels and stress-induced hyperthermia), whereas prebiotic administration protected from these effects.

After stimulation with a T-cell activator lectin (concanavalin A), the stressed, water-treated mice group presented increased levels of inflammatory cytokines (interleukin 6, tumor necrosis factor alpha), whereas in animals with prebiotics had these at normal levels.

Overall, these results suggest a beneficial role of prebiotic treatment in mice for stress-related behaviors and supporting the theory that modifying the intestinal microbiota via prebiotics represents a promising potential for supplement therapy in psychiatric disorders.

Watch YouTube Video: https://youtu.be/E479yto8pyk

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Hydrogen, Gut Microbes, and Inflammation

by Prokopis Constanti, MSc - January 4, 2019

Real time measurements of intestinal gases: a novel method to study how food is being digested

Researchers in Wageningen (The Netherlands), have been able to identify for the first time, how gut microorganisms process different types of carbohydrates by measuring in real time the intestinal gases of mice. This is not only a novel method to understand how food is digested but could also tell us more about the role of gut microorganisms in gut health.

Intestinal gases

The intestinal microbiota is a diverse and dynamic community of microorganisms which regulate our health status. The advancement of biomolecular techniques and bioinformatics nowadays allows researchers to explore the residents of our intestines, revealing what type of microorganisms are there. However, studying only the microbial composition of an individual provides limited insights on the mechanisms by which microorganisms can interact with the rest of our body. For example, far less is understood about the contribution of the gut microorganisms in the production of intestinal gases such as hydrogen, methane and carbon dioxide through the breakdown of food and how these gases affect the biochemical pathways of our bodies.

Intestinal gases consist mostly of nitrogen, and carbon dioxide, which originate primarily from inhaled air. Hydrogen and methane though, are produced as by-products of carbohydrate fermentation (break down), by intestinal microorganisms. However, not all carbohydrates are digested in the same way. For instance, food with simple sugars can be rapidly absorbed in the small intestine unlike complex carbohydrates such as fibers, which reach the colon where they are digested by the colonic microbiota.

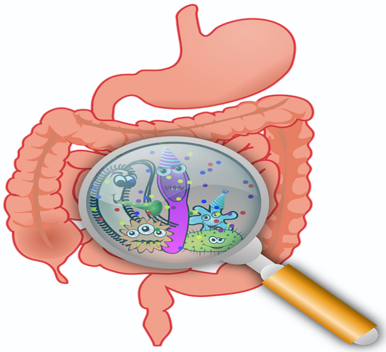
Measuring hydrogen in mouse intestines

To study these interactions and gain knowledge on how microorganisms process carbohydrates, the research team led by Evert van Schothorst from the Human and Animal Physiology Group of Wageningen University (WU) in collaboration with the WU-Laboratory of Microbiology fed mice two different diets with the same nutritional values but with different types of carbohydrates (1). The first diet contained amylopectin, a carbohydrate which can be digested readily in the small intestine while the second diet contained amylose, a slowly digestible carbohydrate that is digested by intestinal microorganisms in the colon.

Animals fed the easily digestible carbohydrates showed minimal production of hydrogen whereas the group fed with the complex carbohydrates presented high levels of hydrogen. Moreover, the two groups were characterized not only by distinct microbial composition (different types of bacteria present) but also distinct metabolic profiles (short chain fatty acids), suggesting that the type of carbohydrate strongly affects microbial composition and function.

The importance of hydrogen

Hydrogen consumption is essential in any anoxic (without oxygen) microbial environment to maintain fermentative processes. In the intestine it can be utilised through three major pathways for the production of acetate, methane and hydrogen sulphide. These molecules are critical mediators of gut homeostasis, as acetate is the most predominant short chain fatty acid produced in mammals with evidence suggesting a role in inflammationand obesity (2). Methane, which is produced by a specific type of microorganisms, called archaea, has been associated with constipation related diseases, such as irritable bowel syndrome(3) and also recently with athletes' performance (4)! Finally hydrogen sulphide is considered to be a toxic gas, although recent findings support the notion that it also has neuroprotective effects in neurodegenerative disorders such as Parkinson and Alzheimer diseases (5).



To the best of our knowledge, this is the first time that food-microbiota interactions have been studied continuously, non-invasively and in real time in a mouse model. Hydrogen is a critical molecule for intestinal health and understanding its dynamics can provide valuable information about intestinal function, and deviations in conditions such as Crohn's disease or irritable bowel syndrome (IBS).

Further reading

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High-Energy Food Addictions in People and Mice

by Bru Cormand, PhD - November 23, 2018

We know that high-energy food (rich in refined sugars and fats) is addictive and can lead to an eating addiction and obesity. Addiction is a very severe disorder with chronic and relapsing components. People who suffer from addiction show compulsivity, persistence to seek the reward (food), and high motivation to overconsume in some cases.

To study eating addiction, we have developed a mouse model that shows persistence to eat, high motivation for palatable food and resistance to punishment in obtaining the food. We have tested these three characteristics in several genetically identical animals and selected two extreme groups: Mice that are vulnerable to eating addiction and mice that are resilient to it.

Mice have more than 25,000 genes in their genome, and they can be turned on or turned off ('expressed' or 'not expressed') depending on certain needs or circumstances.

We are now investigating the activation status of a certain type of genes, the ones encoding the so-called microRNAs that are very important as they are involved in regulating the function of other genes. An alteration in the status of one of these genes can have numerous downstream consequences.

In particular, our studies highlighted several microRNA genes that are involved in multiple brain functions, like synaptic plasticity (variation in the strength of nerve signaling) or neuronal development. Now we will test these alterations in patients to try to find convergent abnormalities.

All this work is being done at the Department of Genetics, Microbiology & Statistics (Universitat de Barcelona) and at the Neuropharmacology lab at the Universitat Pompeu Fabra, both based in Catalonia.

Co-authored by Bru Cormand, Judit Cabana, Noelia Fernàndez

Bru Cormand, PhD, is an Associate Professor at the Department of Genetics, Microbiology & Statistics, University of Barcelona, Catalonia, He also is the Vice Dean of Research at the Faculty of Biology, where he leads the Neurogenetics research group. He has published more than 140 aricles on the genetic basis of both monogenic and multifactorial conditions, including ADHD, autism spectrum disorders and substance use disorders. He is principal investigator of several active research projects, where he uses diverse methodological approaches, from genomics and transcriptomics to cell and animal models or evolutionary insights.

ADHD and Obesity: Does One Cause the Other?

by Lin Li, MSc, PhD - December 14, 2018

Attention-deficit/hyperactivity disorder (ADHD) is a common neurodevelopment disorder characterized by inattention or hyperactivity–impulsivity, or both. It might seem paradoxical, but many studies indicate that individuals with a diagnosis of ADHD suffer from overweight and obesity. Therefore, it is important to understand the underlying mechanism that put individuals with ADHD at risk for obesity.

Evidence from within-individual study

A systematic review and meta-analysis (1) based on 728,136 individuals from 42 studies, suggested a significant association between ADHD and obesity both in children/adolescents and adults. The pooled prevalence of obesity was increased by about 70% in adults with ADHD and 40% in children with ADHD compared with individuals without ADHD. However, due to the lack of longitudinal and genetically-informative studies, the meta-analysis was unable to explain the exact direction of association and the underlying etiologic mechanisms. There are several potential explanations:

- ***ADHD causing obesity:*** The impulsivity and inattention components of ADHD might lead to disordered eating patterns and poor planning lifestyles, and further caused weight gain.
- ***Obesity causing ADHD***: Factors associated with obesity, for example dietary intake, might lead to ADHD-like symptoms through the microbiota-gut-brain axis.
- ***ADHD and obesity may share etiological factors***: ADHD and obesity may share dopaminergic dysfunctions underpinning reward deficiency processing. So the same biological mechanism may lead to both ADHD and obesity. This is difficult to investigate within individuals, but family studies can help to test this hypothesis.

We will further investigate these possibilities in the Eat2beNICE research project by using both perspective cohort study and twin studies.

Evidence from a recent within-family study

Recently, a population-based familial co-aggregation study in Sweden (2) was conducted to explore the role of shared familial risk factors (e.g. genetic variants, family disease history) in the association between ADHD and obesity. They identified 523,237 full siblings born during 1973–2002 for the 472,735 index males in Sweden, and followed them until December 3, 2009. The results suggest that having a sibling with overweight/obesity is a risk factor for ADHD. This makes it likely that biological factors (that are shared between family members) increase the risk for both ADHD and obesity.

Evidence from across-generation study

Given that both ADHD and obesity are highly heritable complex conditions, across-generation studies may also advance the understanding of the link between ADHD and obesity.

A population-based cohort study (3) based on a Swedish nationwide sample of 673,632individuals born during 1992-2004, was performed to explore the association between maternal pre-pregnancy obesity and risk of ADHD in offspring. The sibling-comparison study design was used to test the role of shared familial factors for the potential association. The results suggest that the association between maternal pre-pregnancy obesity and risk of ADHD in offspring might be largely explained by shared familial factors, for example, genetic factors transmitted from mother to child that contribute to both maternal pre-pregnancy obesity and ADHD.

Together, based on previous evidence from various study designs, there is evidence to suggest that the association between ADHD and obesity mainly is caused by shared etiological factors. However, future studies on different population are still needed to further test these findings.

New Brain Nutrition is the online learning platform of the Eat2beNICE project. This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 728018. This publication reflects only the author's view and the Commission is not responsible for any use that may be made of the information it contains.

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