St. Joseph's Healthcare Hamilton

McMaster University HEALTH SCIENCES

Media Release

EMBARGOED until
Tuesday, April 4th 2017
at 11:00AM EDT

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Low-dose penicillin in early life induces long-term changes in behaviour, gut microbes and brain inflammation

Hamilton, Ont. (April 4, 2017) – In a landmark study, researchers at St. Joseph's Healthcare Hamilton and McMaster University have found that providing clinical (low) doses of penicillin to pregnant mice and their offspring results in long-term behavioural changes.

These changes include elevated levels of aggression and lower levels of anxiety, accompanied by characteristic neurochemical changes in the brain and an imbalance in their gut microbes. Giving these mice a *lactobacillus* strain of bacteria helped to prevent these effects.

The study was published in *Nature Communications* and was funded by the United States Office of Naval Research.

"In this paper, we report that low-dose penicillin taken late in pregnancy and in early life of mice offspring, changes behaviour and the balance of microbes in the gut. While these studies have been performed in mice, they point to popular increasing concerns about the long-term effects of antibiotics," says Dr. John Bienenstock, Director of the Brain-Body Institute at St. Joseph's Healthcare Hamilton and Distinguished Professor at McMaster University. "Furthermore, our results suggest that a probiotic might be effective in preventing the detrimental effects of the penicillin."

Other studies have shown that large doses of broad-spectrum antibiotics in adult animals can affect behaviour. But there haven't been previous studies that have tested the effects of clinical doses of a commonly-used, narrow-spectrum antibiotic such as penicillin on gut bacteria and behaviour.

"There are almost no babies in North America that haven't received a course of antibiotics in their first year of life," says Dr. Bienenstock. "Antibiotics aren't only prescribed, but they're also found in meat and dairy products. If mothers are passing along the effects of these drugs to their as yet unborn children or children after birth, this raises further questions about the long-term effects of our society's consumption of antibiotics."

A previous study in 2014 raised similar concerns after finding that giving clinical doses of penicillin to mice in late pregnancy and early life led to a state of vulnerability to dietary induction of obesity.

The research team will follow up their studies by analyzing the effects of penicillin on the offspring, if given only to the pregnant mothers. They also plan on investigating the efficacy of different types of potentially-beneficial bacteria in protecting offspring against the behavioural changes that result from antibiotic usage.

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– 30 –

Media Contacts:

Megan Bieksa
Senior Specialist, Media & Strategic Issues | Public Affairs Department
St. Joseph's Healthcare Hamilton
T: 905-975-2944 E: mbieksa@stjoes.ca
Twitter: @STJOESHAMILTON

Veronica McGuire
Media Relations, Faculty of Health Sciences, McMaster University
(905) 525-9140, ext. 22169
vmcguir@mcmaster.ca

More Information

About Dr. John Bienenstock

Dr. Bienenstock is the Director of the Brain-Body Institute at St. Joseph's Healthcare Hamilton* and has the title of Distinguished University Professor in the Department of Pathology and Molecular Medicine at McMaster University. He has received numerous international awards, is a fellow of the Royal Society of Canada, was named to the Order of Canada in 2002 and inducted into the Canadian Medical Hall of Fame in 2011.

His current research explores the ways in which non-pathogenic gut bacteria are involved in the functions of the brain including behaviour. He has published more than 500 peer reviewed articles and other publications, authored, edited and co-edited 8 books on mucosal immunology and allergy. He has supervised some 60 post-doctoral fellows and 10 doctoral students.

**The Brain-Body Institute (BBI) is a joint research initiative between St. Joseph's Healthcare Hamilton, and McMaster University and was created to advance the understanding of relations between the brain, the nervous system and bodily disorders. Scientists in this multidisciplinary Institute study the interaction and impact of environmental factors, including stress, early life experiences and early microbial exposure on the brain and nervous system. http://www.brain-body.ca/*

About Research at St. Joseph's Healthcare Hamilton

St. Joseph's Healthcare Hamilton is an academic health sciences centre fully affiliated with the Faculty of Health Sciences at McMaster University. The Research Institute of St. Joe's Hamilton oversees the work of over 155 researchers and their teams as they carry out studies that improve patients' quality of life within our hospital, across our province and around the world. In pursuit of this goal, the research enterprise at St. Joseph's Healthcare Hamilton attracts over $28 million annually in grants and research support funding. For more information, please visit www.stjoes.ca/research.

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About St. Joseph's Healthcare Hamilton

St. Joseph's Healthcare Hamilton is a regional leader in patient-centred care providing acute care, research, teaching, community and international outreach programs throughout our network. Since being founded by the Sisters of St. Joseph in 1890, our hospitals span three specialized campuses in the Greater Hamilton Area (Charlton Campus, West 5th Campus and King Street Campus), with St. Joseph's Villa Dundas providing long-term care and St. Joseph's Home Care providing personalized home care traversing the reach of our region. For more information about St. Joseph's Healthcare Hamilton, please visit www.stjoes.ca.

Journal Article Title & Abstract

Low-dose penicillin in early life induces long-term changes in murine gut microbiota, brain cytokines and behavior

Authors: Sophie Leclercq[1,2*], Firoz M. Mian[1], Andrew M. Stanisz[1], Laure B. Bindels[3], Emmanuel Cambier[4], Hila Ben-Amram[5], Omry Koren[5], Paul Forsythe[1,6], John Bienenstock[1,2*]

Affiliations:
[1] McMaster Brain-Body Institute at St Joseph's Healthcare Hamilton, 50 Charlton Avenue East T3304, Hamilton, Ontario, Canada, L8N 4A6.
[2] Department of Pathology and Molecular Medicine, McMaster University, 50 Charlton Avenue East, Hamilton, Ontario, Canada, L8N 4A6.
[3] Metabolism and Nutrition Research Group, Louvain Drug Research Institute, Université catholique de Louvain, Avenue E.Mounier 73, Brussels, Belgium, 1200.
[4] Faculty of Medicine, Université catholique de Louvain, Brussels, Belgium, 1200.
[5] Faculty of Medicine, Bar-Ilan University, Henrietta Szold 8, Safed, Israel, 1311502.
[6] Firestone Institute for Respiratory Health and Department of Medicine, McMaster University, 50 Charlton Avenue East, Hamilton, Ontario, Canada, L8N 4A6.

*To whom correspondence should be addressed: John Bienenstock or Sophie Leclercq.
McMaster Brain-Body Institute at St. Joseph's Healthcare Hamilton, T3304, 50 Charlton Avenue East, Hamilton, ON L8N 4A6, Canada. Email: bienens@mcmaster.ca or leclercs@mcmaster.ca

Abstract:
There is increasing concern about potential long-term effects of antibiotics on children's health. Epidemiological studies have revealed that early-life antibiotic exposure can increase the risk of developing immune and metabolic diseases, and rodent studies have shown that administration of high doses of antibiotics has long-term effects on brain neurochemistry and behavior. Here we investigate whether low-dose penicillin in late pregnancy and early postnatal life induces long term effects in the offspring of mice. We find that penicillin has lasting effects in both sexes on gut microbiota, increases cytokine expression in frontal cortex, modifies blood-brain barrier integrity and alters behavior. The antibiotic-treated mice exhibit impaired anxiety-like and social behaviors, and display aggression. Concurrent supplementation with *Lactobacillus rhamnosus* JB-1 prevents some of these alterations. These results warrant further studies on the potential role of early-life antibiotic use in the development of neuropsychiatric disorders, and the possible attenuation of these by beneficial bacteria.