

XVIIth Little Brain Big Brain: an extraordinary meeting in extraordinary times

Constanza Alcaino, Florencia Carbone, Peter H. Neckel & Naomi E. B. Tjaden



Little Brain Big Brain is a biannual meeting organized and attended by young investigators. Since its inception in 1989, this meeting has brought together promising junior researchers in neurogastroenterology. The XVIIth meeting featured the latest basic, clinical and industry research in the field in a special post-pandemic edition.

Little Brain Big Brain (LBBB) is a satellite meeting that usually precedes the Federation of Neurogastroenterology and Motility (FNM) congress. The format is simple: choose an isolated location, ask 30 talented young scientists to present their unpublished work and allow unlimited time for discussion¹. Historically, the meeting has launched the careers of attendees and resulted in fruitful collaborations and life-long friendships.

The COVID-19 pandemic left its first mark on LBBB in 2020, when the meeting was postponed and converted, along with the associated FNM2020 congress, to an online format. This mark almost became a permanent scar when FNM2022 was postponed to 2024. A 3-year gap for a dedicated young investigator meeting in a time where the training of junior researchers and clinicians was already suffering from a plethora of pandemic containment measures risked losing an entire generation of early-career neurogastroenterologists. As the designated LBBB2022 organizers, we decided to hold the XVIIth LBBB meeting as an extraordinary, stand-alone meeting in Heiligkreuztal, Germany.

Selection to improve diversity

We used LBBB2022 as a testing field to introduce more diversity and to promote scientific interdisciplinarity (Fig. 1). Applicant selection has always been solely based on scientific merit and innovation, but, at past meetings, participants from the Global North and from well-established laboratories tended to be over-represented. For the 2022 meeting, we used revamped selection criteria that involved double-blinding at the first stage, when reviewers scored completely anonymous intent letters. Measuring the exact effect of this change is difficult, but the overall feedback by reviewers and applicants was positive. In a second step, applicants with equal scores at the threshold for acceptance were re-assessed by the organizers with reference to CVs and support letters.

Although most successful applicants were still from higher income countries, we found that a double-blinded selection process led to a higher proportion of participants from Latin America, some of whom were affiliated with institutes in the Global South (Supplementary Fig. 1).

The double-blinded method also led to acceptance of participants with backgrounds other than neurogastroenterology, providing novel ideas and fresh discussion for our field (Supplementary Fig. 1). Overall, LBBB2022 hosted 30 participants (23 women and 7 men) from across the globe. The gender ratio and types of academic degrees held among the selected participants were similar to those among the total applicants (Supplementary Fig. 1), indicating that no severe bias was introduced by the new selection process. The meeting brought together scientists from across the world who study neurogastroenterology in three main areas: basic science models, clinical research and technology development. We discuss the highlights from the meeting in the following sections.

Basic science models

The cross-over between cell location, expression and function was a main driver of the scientific questions addressed in basic science talks. Topics included enteric nervous system (ENS) development, innervation of the gut wall, specialized nutrient-sensing epithelial cells and the microbial environment in the intestinal lumen. Work in mouse models dominated, including use of chemogenetic and optogenetic tools to target specific cell populations *in vitro* and *in vivo*. For example, in one study presented, the investigators were using a TRPV1-channelrhodopsin mouse model to optogenetically activate extrinsic sensory neurons while tracking recruitment of sensory-motor pathways in an *in vivo* model of colonic inflammation. In another study, a classical pharmacological approach was used to assess the analgesic effects of a pH-sensitive opioid analogue in a mouse model of acute colitis, in the hope of bypassing the adverse effects of opioid drugs².

Mucosal serotonin and enteroendocrine cells were also a hot topic of discussion – more than one-third of participants are studying how these cells modulate gut function in models of obesity, irritable bowel syndrome (IBS), visceral nociception, anxiety and depression. Two presentations provided many useful insights into transgenic zebrafish models in the study of the gut–brain axis and colorectal cancer, but also highlighted the challenges of translating findings in these models into human research.

The work presented also demonstrated that confocal microscopy remains one of the most commonly used techniques to characterize the ENS. In three imaging studies presented, high-quality confocal imaging was used to investigate epithelium innervation, enteric glia and glutamatergic neurons, providing a 2D architectural map and the potential to visualize and count the 3D components of single cells at incredible resolution. In another jaw-dropping study, sophisticated live confocal imaging of the intact gut of an anesthetized mouse showed simultaneous activation of neurons from the submucosal and myenteric plexus *in vivo*. Finally, the ENS sessions ended with a talk on changes in

Selection process

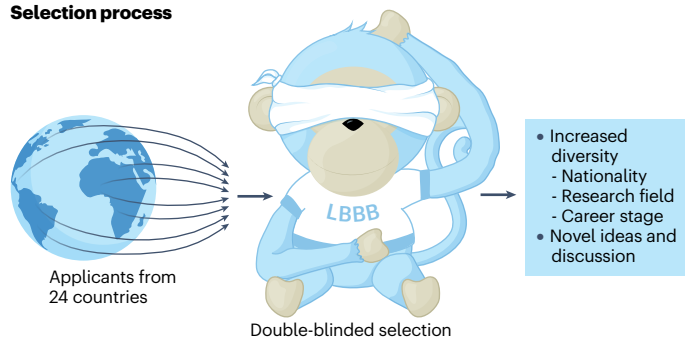


Fig. 1 | Overview of the selection process for Little Brain Big Brain 2022.

Applications were received from 24 countries across 5 continents. Applications were reviewed in a double-blind process to reduce the possibility of bias. This process resulted in a higher diversity of participants than in previous years, contributing to novel ideas and discussion at the meeting. Publ. note: Springer Nature is neutral about jurisdictional claims in maps.

myenteric neuronal function and neurotransmitter expression influenced by the light–dark cycle, suggesting that the circadian rhythm can induce ENS plasticity.

Clinical research and technology

Functional gastrointestinal disorders dominated the clinical research talks, with an interesting shift from pharmacological to dietary intervention. Two studies showed that elimination diets have a beneficial symptomatic effect in functional dyspepsia, and this effect was associated with restoration of duodenal mucosal integrity. Use of confocal laser endomicroscopy in patients with functional dyspepsia demonstrated acute positive reactions to various food antigens in the duodenum, suggesting involvement of atypical food-allergy-type reactions.

The gut microbiome and its influence on gastrointestinal health was discussed in depth. Several studies involved examination of how dysbiosis can trigger chronic inflammatory processes, increasing the risk of gastrointestinal symptoms and cancer. In one study, foods such as fermented dairy products, which contain specific strains of propionic bacteria, were carefully introduced to reduce the severity of colitis in a murine model of inflammatory bowel disease, highlighting the role of diet and gut bacteria in inflammation and barrier function.

Other work focused on the bidirectional microbiota–gut–brain axis. The gut microbiota can produce and modify neuroactive metabolites, thereby affecting brain function³, and some of the work presented indicated associations between circulating short-chain fatty acids, psychological stress and fear responses. Conversely, the psychological state of the host can determine infection responses, and, in another study, investigators looked at the effects of psychological distress levels on the risk of infection, susceptibility to barrier disruption and immune activation.

Technology development and industry talks focused on two main topics: identification of novel pharmacological targets and development of devices to modulate gut function. One presentation considered the use of a culture system to simulate distal colon function and study the risk of enteric infections, and another introduced the use of an ingestible neuromodulation device to electrically stimulate the ENS as a treatment for gastrointestinal disorders. Finally, participants

discussed the use of a commercially available postbiotic to acutely modulate ion transport and gastrointestinal motility. These novel approaches have important therapeutic potential in the treatment of gastrointestinal disorders.

Awards were presented to several participants of LBBB2022. Three participants were chosen by their peers to receive Best talk awards: Khalil Ramadi, Kristen Smith-Edwards and Ryan Hamnett. The Best participation award went to Adam Edwinston, and an Organizers Choice award was presented to Gisela Canedo-Marroquin, Nestor Jimenez-Vargas and Mabel Guzman. Winners were awarded a 1-year subscription to or invited to write an article for *Nature Reviews Gastroenterology & Hepatology*, and the Best speaker winners were awarded a podium presentation at the NeuroGASTRO 2023 meeting in Bucharest, Romania.

LBBB's future is bright in Bangkok

The XVIIIth LBBB will be held as a satellite meeting of FNM2024 in Bangkok, Thailand. The tradition of passing the Blue Monkey continues, and it is now in the hands of the LBBB2024 organizers: Alain Benitez, Ada Koo, Alyce Martin, Khalil Ramadi and Kristen Smith-Edwards. This meeting will continue to serve as a forum for intimate scientific collaborations and continue to advance the broadening field of neurogastroenterology. For more information about the legacy of the Blue Monkey, please visit the [LBBB website](#).

Constanza Alcaino ^{1,5} , Florencia Carbone ^{2,5} , Peter H. Neckel ^{3,5} & Naomi E. B. Tjaden ^{4,5}

¹Wellcome Trust-MRC Institute of Metabolic Science, University of Cambridge, Cambridge, UK. ²Translational Research Center for Gastrointestinal Disorders and University Hospital of Leuven, Leuven, Belgium. ³Institute of Clinical Anatomy and Cell Analysis, University of Tübingen, Tübingen, Germany. ⁴Division of Gastroenterology, Hepatology and Nutrition, Children's Hospital of Philadelphia, Philadelphia, PA, USA. ⁵These authors contributed equally: Constanza Alcaino, Florencia Carbone, Peter H. Neckel, Naomi E. B. Tjaden.

e-mail: caa62@medschl.cam.ac.uk; florencia.carbone@kuleuven.be; peter.neckel@uni-tuebingen.de; tjadenn@chop.edu

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Competing interests

The authors declare no competing interests.

Additional information

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