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PSYCHOGERIATRIC NOTE

Faecal microbiota transplantation simultaneously ameliorated patient's essential tremor and irritable bowel syndrome

Essential tremor (ET) is a progressive, chronic, neurodegenerative disease. The aetiology of ET is not well understood. A previous study showed that dysfunction of the microbiota-gut-brain axis might lead to neurological disease,[1] and increasing evidence indicates a potential bidirectional relationship between gut microbiota and neurological disease. For example, gut microbiota is involved in motor deficits, microglia activation, and pathology, which play important roles in the development of Parkinson's disease.[2] Exchanging gut microbiota can reduce the expression of brain-derived neurotrophic factor in the brain.[3]

Faecal microbiota transplantation (FMT) is a microbiota-targeted therapy. Several case reports have described the therapeutic effects of FMT in patients with neuropsychiatric disorders, such as epilepsy, and autism.[4] However, the effect of FMT on ameliorating ET remains elusive. Here, we report the first case of using FMT to achieve remission of intestinal and neurological symptoms.

In May 2017, a 75-year-old woman with a 7-year history of ET was recruited by the Department of Gastroenterology at the First Affiliated Hospital of Guangdong Pharmaceutical University. A month before her recruitment, the patient had been diagnosed with irritable bowel syndrome (IBS) based on symptoms of abdominal pain and diarrhoea.

To confirm the patient's suitability for FMT, endoscopy was performed, and the results indicated chronic non-atrophic gastritis (moderate, antrum) and chronic rectal mucosal inflammation. Abdominal computed tomography did not indicate any organic lesion. Hydrogen- and methane-based breath tests were positive for small intestinal bacterial overgrowth, which indicated the dysbiosis of the intestinal microbiota. The patient's nutrition was generally balanced, and there was no vitamin deficiency. Based on these results and clinical symptoms, the patient was administered the first FMT course through a nasojejunal tube under anaesthesia on 31 May 2017 (dose: 200 mL once a day on three consecutive days) after the signing of the informed consent.

The stool was obtained from a young healthy donor who had undergone a comprehensive medical examination and psychological tests. After that, the fresh faecal microbiota was prepared within 2 h by using an automatic purification system (GenFMTer; FMT Medical, Nanjing, China) in our Intelligent Fecal Microbiota Separation Center and brought to the inpatient ward for immediate transplantation. The second day, the patient happily told the doctor that the frequency of defecation had significantly decreased and that she had experienced relief in her abdominal pain symptoms.

The patient subsequently began her second, third, and fourth FMT cycles on 31 July 2017, 9 October 2017, and 17 January 2018 after the signing of the informed consent (Fig. S1), respectively. Interestingly, the tremor of the head and upper limbs significantly decreased after the second cycle of FMT. Based on these promising clinical improvements, we encouraged her to stop clonazepam and undergo another two cycles of FMT treatments (i.e. the third and fourth cycles), which she did with informed consent. The improvement in ET after FMT was evidenced by a decrease in the Tremor Research Group Essential Tremor Rating Assessment Scale score from 5.5 to 1.0 (Table 1). Since the patient completed the fourth cycle, she has not experienced any recurrence of ET (Video S1).

The key clinical and laboratory parameters before and after the FMT are shown in Table 1. Our results showed that the IBS Severity Scoring System score dropped from 400 to 200 points after the second FMT treatment. Total bilirubin rose to a normal level after the first cycle of FMT and remained normal after the fourth. Indirect bilirubin increased to near the normal range after the second cycle of FMT. The albumin/globulin ratio, an indicator of liver function,

Table 1 Therapeutic evaluation of essential tremor and irritable bowel syndrome (IBS)

Parameter	Normal range	FMT cycles				
		Before FMT 27 May 2017	First 31 May 2017	Second 31 Jul 2017	Third 9 Oct 2017	Fourth 17 Jan 17, 2018
IBS-SSS score[†]	—	400	240	200	180	140
TETRAS score	—	5.5	4.5	2.0	1.5	1.0
BNP (pg/mL)	0–100	36.0	ND	ND	ND	ND
T-bil (μmol/L)	5–19	3.8	5.2	6.9	4.5	4.3
I-bil (μmol/L)	5–14	1.40	2.70	4.50	2.50	2.40
A/G ratio	1.2–2.4	1.12	1.46	1.24	1.37	1.42
ESR	0–20	ND	24.30	18.10	ND	60.00

[†] IBS-SSS severity categories: remission, 75–175; moderate: 175–300; and severe: >300.

A/G, albumin/globulin; BNP, brain natriuretic peptide; ESR, erythrocyte sedimentation rate; IBS-SSS, IBS Severity Scoring System; I-bil, indirect bilirubin; ND, not determined; TETRAS, Tremor Research Group Essential Tremor Rating Assessment Scale; T-bil, total bilirubin.

immediately increased to normal after the first cycle of FMT and remained normal through the all cycles, suggesting that FMT may improve liver function. The erythrocyte sedimentation rate was slightly elevated after the first cycle of FMT, but it returned to normal after the second cycle. This confirmed that gut microbiota can promote the induction of regulatory T cells and the secretion of anti-inflammatory cytokine.

Despite these results, the complex pathogenesis of ET remains unknown. It was previously shown that sensory cells of the gut known as enteroendocrine cells contain α-synuclein and synapses with enteric nerves, thus providing a connection from the gut to the brain.[5] Studies have also shown that tryptophan metabolites from gut microbiota can induce type I interferon through the blood–brain barrier and astrocytes; in turn, type I interferon can inhibit the inflammatory response of the central system by activating the aryl hydrocarbon receptor and the suppressor of cytokine signalling 2.[6] Based on these previous findings, we propose an underlying mechanism of the therapeutic effect of FMT for ET: FMT may increase beneficial bacteria and decrease pathogenic bacteria, inhibiting the production of inflammatory factors, repairing tight junction proteins, maintaining permeability, and preventing enteral inflammation and toxins from entering the blood–brain barrier (Fig. S2).[7] To further explore this proposal, we have successfully applied for funding from the provincial Natural Science Foundation for a study that will conduct 16S rRNA sequencing on subjects' faeces to improve and supplement relevant data (study title: 'Study on the efficacy and mechanism of fecal bacteria transplantation in the treatment of essential tremor').

In the present study, we provided evidence that FMT can significantly reduce ET symptoms, as well as ameliorate IBS. This finding has encouraged us to further explore the mechanism and efficacy of FMT in the treatment of ET.

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DISCLOSURE

None.

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SUPPORTING INFORMATION

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Figure S1. Time-line of faecal microbiota transplantation (FMT) in the treatment of essential tremor (ET).

Figure S2. Underlying mechanism of the therapeutic effect of faecal microbiota transplantation (FMT) for essential tremor (ET).

Video S1. The patient being followed up after the third faecal microbiota transplantation.