Identification of Gut Microbiome Signatures in Patients With Post-stroke Cognitive Impairment and Affective Disorder

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Stroke (ST), endangering human health due to its high incidence and high mortality, is a global public health problem. There is increasing evidence that there is a link between the gut microbiota (GM) and neuropsychiatric diseases. We aimed to find the GM of ST, post-ST cognitive impairment (PSCI), and post-ST affective disorder (PSTD). GM composition was analyzed, followed by GM identification. Alpha diversity estimation showed microbiota diversity in ST patients. Beta diversity analysis showed that the bacterial community structure segregated differently between different groups. At the genus level, ST patients had a significantly higher proportion of Enterococcus and lower content of Bacteroides, Escherichia-Shigella, and Megamonas. PSCI patients had a significantly higher content of Enterococcus, Bacteroides, and Escherichia-Shigella and a lower proportion of Faecalibacterium compared with patients with ST. Patients with PSTD had a significantly higher content of Bacteroides and Escherichia-Shigella and lower content of Enterococcus and Faecalibacterium. Parabacteroides and Lachnospiraceae were associated with Montreal cognitive assessment score of ST patients. Our study indicated that the characteristic GM, especially Bacteroidetes, could be used as clinical biomarkers of PSCI and PSTD.

Keywords: stroke, 16S ribosomal RNA sequencing, post-stroke cognitive impairment, post-stroke affective disorder, gut microbiota

INTRODUCTION

Stroke (ST) is the leading cause of death worldwide (Bonita et al., 2004). It can cause some neuropsychiatric diseases, including anxiety, depression, fatigue, apathy, personality changes, mania, and cognitive impairment. It is estimated that 1/3 of ST patients will develop neuropsychiatric disorders shortly after ST (Hackett and Pickles, 2014; Hackett et al., 2014). Post-ST cognitive impairment (PSCI) and post-ST affective disorder (PSTD) are the common complications of ST. The prevalence of depression and cognitive impairment within 3 months after ST are 25–31% and 10–47.3%, respectively (Aström et al., 1993; Jacquin et al., 2014). These two diseases usually coexist in ST patients and have a negative impact on the prognosis of the patient. Cognitive dysfunction is closely related to depression and interacts. Previous studies have shown that the cognitive function of ST patients after antidepressant treatment is normal, and vice versa, which suggest that they may have similar causes. In clinical practice, the limited use of scales and the inability to detect early symptoms have led to the failure of some patients with PSCI to receive correct diagnosis and treatment. Therefore, early evaluation and treatment of PSCI are important to prolong survival time after ST.
Gut microbiota (GM) disorders in neuropsychiatric diseases have been found in some studies (Bains et al., 2019; Nguyen et al., 2019). Recent studies have shown that there are significant differences in fecal microbial diversity in patients with Alzheimer’s disease (AD) (Zhuang et al., 2018). Jiang et al. found that the gut microbial structure of patients with active–severe depression has changed, among which, Bacteroidetes, Proteobacteria, Actinobacteria, and Enterobacteriaceae significantly increased, Firmicutes and Faecalibacterium decreased significantly (Jiang et al., 2015). The reduced proportion of Faecalibacterium leads to chronic low-grade inflammation of the intestinal blood–brain barrier, and is negatively related to the severity of depressive symptoms (Jiang et al., 2015). Recent studies have shown that compared with healthy controls, the composition of the intestinal flora of AD patients has changed (Liu et al., 2019). These reports suggest that the GM may be a crucial regulator of two-way communication between the gut and the brain.

More and more evidence show that intestinal flora can be used as a non-invasive diagnostic biomarker for schizophrenia and type 2 diabetes. It is worth noting that ST patients show obvious intestinal flora imbalance (characterized by a higher abundance of conditional pathogenic bacteria and a lower level of beneficial bacteria). In addition, in patients with PSCI, the abundance of Fusobacteria increases and short-chain fatty acids (SCFAs) decrease. However, the composition of the GM in PSCI and PSTD patients has not been evaluated. Therefore, the discovery of the characteristics of the gut microbial composition of PSCI and PSTD patients is of great significance for rehabilitation after ST. Herein, we aimed to investigate the GM composition in ST, PSCI, and PSTD patients. Besides, we also confirmed the characteristic GM of PSCI and PSTD and its potential as a biomarker for the diagnosis of the disease.

MATERIALS AND METHODS

Study Patients
The inclusion criteria for patients were as follows: (1) patients were 40–90 years; (2) patients were ischemic ST; and (3) patients were with infarcts in non-strategic brain regions. Exclusion criteria of patients were as follows: (1) patients with preexisting dementia history and infarct of strategic regions; (2) patients took antibiotics or probiotics (within 3 months); (3) patients with a restrictive diet, gastrointestinal surgery, recent infection, psychosis, severe life-threatening illnesses, communication deficits, and pregnancy. A total of 95 ischemic ST patients were enrolled from the first affiliated hospital of Shantou University, Medical College, which included 19 healthy controls (HC), 27 ST patients, 29 PSCI patients, and 20 PSTD patients. Clinical characteristics of studying subjects are shown in Table 1. The Ethics Committee of the First Affiliated Hospital of Shantou University Medical College approved the study protocol (2019), and all patients gave written informed consent.

Sample Collection and Processing
Fresh stool samples from all patients were obtained within 1 week of admission. Stool samples were collected and immediately transferred to the laboratory for repackaging within 15 min. Then 200 mg stool samples were put in a 2-mL sterile centrifuge tubes and labeled. All specimens were processed within 30 min and stored at −80°C. Stool genomic DNA was extracted as described in the previous study (Li et al., 2008; Shkporov et al., 2018). We put the stool sample in the lysis buffer, added VAHTS DNA cleaning beads, homogenized it in a vortex mixer for 3–5 min, purified with 200 mL of 80% ethanol, and eluted with 24 mL of elution buffer. A 2% agarose gel was used to evaluate the amount of extracted genomic DNA. A NanoDrop spectrophotometer (Thermo Fisher Scientific, USA) was used to determine the DNA purity and concentration. The A260/280 ratio was measured to determine the DNA purity. Then we stored the DNA at −20°C. We amplified the 16s ribosomal RNA gene region of V3–V4 after DNA extraction as described in the previous study (Bu et al., 2018). We performed the high-throughput sequencing on a MiSeq Benchtop Sequencer (Illumina, Singapore, USA).

Bioinformatics Analysis
Bacterial diversity was determined by alpha diversity and beta diversity. The Wilcoxon rank-sum test was used to identify significant differences in the α-diversity indices between the different groups. Beta diversity was analyzed by using Bray Curtis distances. The beta diversity was visualized via principal component analysis, principal coordinates analysis, and non-metric multidimensional analysis. Significant p-values associated with microbial clades and functions were identified by linear discriminant analysis effect size (LefSe; Qian et al., 2018). The Kruskal–Wallis test (alpha value of 0.05) and a linear discriminant analysis score >2 were the thresholds of the Lefse analysis. We used Phylogenetic Investigation of Communities by Reconstruction of Unobserved States (PICRUSt) to predict metagenomic functional information according to the operational taxonomic unit (OTU) table (Langille et al., 2013).

RESULTS

Alpha Diversity Analysis in ST vs. HC, PSCI vs. ST, and PSTD vs. ST Groups
To evaluate core taxonomic characteristics of ST, PSCI, and PSTD patients, we generated profiles of V3–V4 variable region of the 16s rRNA gene. In Figure 1, rank abundance distribution curves suggested increased richness in ST group and decreased richness in PSCI and PSTD groups compared with the ST group. The alpha diversity indices, coverage evenness, and SD values are shown in Figure 2. As seen from the Venn diagram, there were, respectively 887, 975, and 1,078 common OTUs between ST vs. HC, PSTD vs. ST and PSCI vs. ST groups (Figure 3).

Alterations in the Composition of Stool Microbiota Associated With ST at the Genus Level
In Figure 4, the relative proportions of dominant taxa at the genus level were assessed. We observed considerable variability in stool microbiota across samples. Bacteroides,
TABLE 1 | Clinical information of enrolled patients.

| Groups | Number | Gender | Age | MOCA score | MMSE score | Anxiety score | Depression scores | Hypertension | Diabetes |
|--------|--------|--------|-----|------------|------------|---------------|-------------------|--------------|----------|
| ST     | 1      | Female | 60  | 27         | 28         | 3             | 3                 | Yes          | No       |
|        | 2      | Female | 70  | 26         | 28         | 4             | 3                 | No           | No       |
|        | 3      | Male   | 59  | 26         | 27         | 3             | 0                 | No           | No       |
|        | 4      | Female | 61  | 25         | 26         | 5             | 2                 | Yes          | No       |
|        | 5      | Male   | 58  | 30         | 30         | 5             | 4                 | No           | No       |
|        | 6      | Male   | 64  | 28         | 30         | 0             | 0                 | Yes          | Yes      |
|        | 7      | Female | 67  | 26         | 27         | 2             | 0                 | Yes          | No       |
|        | 8      | Female | 69  | 26         | 27         | 4             | 4                 | Yes          | No       |
|        | 9      | Female | 66  | 26         | 28         | 3             | 0                 | No           | Yes      |
|        | 10     | Male   | 51  | 30         | 30         | 0             | 0                 | No           | No       |
|        | 11     | Male   | 74  | 27         | 27         | 1             | 0                 | Yes          | Yes      |
|        | 12     | Male   | 69  | 26         | 28         | 4             | 3                 | Yes          | No       |
|        | 13     | Male   | 54  | 29         | 30         | 6             | 3                 | No           | No       |
|        | 14     | Female | 38  | 30         | 30         | 3             | 4                 | No           | No       |
|        | 15     | Male   | 64  | 30         | 29         | 0             | 0                 | No           | No       |
|        | 16     | Female | 55  | 30         | 30         | 5             | 4                 | Yes          | No       |
|        | 17     | Female | 66  | 27         | 30         | 5             | 5                 | No           | No       |
|        | 18     | Male   | 62  | 29         | 29         | 2             | 1                 | No           | No       |
|        | 19     | Female | 73  | 26         | 29         | 6             | 5                 | Yes          | Yes      |
|        | 20     | Female | 61  | 26         | 28         | 4             | 2                 | No           | No       |
|        | 21     | Male   | 56  | 30         | 30         | 3             | 3                 | Yes          | No       |
|        | 22     | Male   | 74  | 26         | 26         | 2             | 5                 | Yes          | No       |
|        | 23     | Male   | 68  | 28         | 28         | 3             | 1                 | Yes          | No       |
|        | 24     | Male   | 45  | 30         | 30         | 6             | 2                 | No           | No       |
|        | 25     | Female | 74  | 26         | 27         | 0             | 0                 | No           | No       |
|        | 26     | Male   | 62  | 29         | 29         | 3             | 3                 | No           | No       |
|        | 27     | Female | 59  | 29         | 30         | 4             | 4                 | No           | No       |
|        | 1      | Female | 62  | 29         | 30         | 9             | 11                | No           | No       |
|        | 2      | Male   | 72  | 27         | 28         | 12            | 8                 | No           | No       |
|        | 3      | Male   | 54  | 30         | 30         | 13            | 14                | Yes          | Yes      |
| PSTD   | 4      | Female | 70  | 29         | 30         | 11            | 3                 | No           | No       |
|        | 5      | Female | 66  | 29         | 29         | 8             | 8                 | No           | No       |
|        | 6      | Female | 74  | 24         | 26         | 11            | 8                 | No           | No       |
|        | 7      | Male   | 77  | 26         | 28         | 2             | 8                 | No           | No       |
|        | 8      | Male   | 56  | 29         | 30         | 9             | 8                 | Yes          | No       |
|        | 9      | Female | 73  | 26         | 26         | 4             | 10                | Yes          | Yes      |
|        | 10     | Female | 58  | 29         | 30         | 8             | 5                 | Yes          | No       |
|        | 11     | Female | 69  | 28         | 28         | 8             | 8                 | Yes          | Yes      |
|        | 12     | Male   | 64  | 27         | 29         | 10            | 3                 | Yes          | Yes      |
|        | 13     | Male   | 54  | 30         | 30         | 8             | 3                 | No           | No       |
|        | 14     | Female | 77  | 24         | 25         | 10            | 5                 | Yes          | No       |
|        | 15     | Male   | 47  | 27         | 28         | 7             | 7                 | No           | No       |
|        | 16     | Female | 57  | 30         | 30         | 12            | 7                 | Yes          | No       |
|        | 17     | Male   | 61  | 27         | 28         | 12            | 9                 | No           | No       |
|        | 18     | Male   | 46  | 26         | 27         | 10            | 3                 | No           | No       |
| PSCI   | 19     | Male   | 55  | 29         | 30         | 8             | 6                 | Yes          | Yes      |
|        | 20     | Male   | 34  | 29         | 29         | 9             | 7                 | No           | No       |
|        | 1      | Female | 60  | 0          | 1           | 3             | 3                 | Yes          | Yes      |
|        | 2      | Male   | 56  | 0          | 4           | 0             | 2                 | No           | No       |

(Continued)
TABLE 1 | Continued

| Groups | Number | Gender | Age  | MOCA score | MMSE score | Anxiety score | Depression scores | Hypertension | Diabetes |
|--------|--------|--------|------|------------|------------|---------------|------------------|--------------|----------|
| 3      | Male   | 59     | 2    | 3          | 1          | 2             | Yes              | No           |          |
| 4      | Male   | 70     | 12   | 23         | 4          | 2             | No               | Yes          |          |
| 5      | Male   | 73     | 8    | 17         | 3          | 2             | Yes              | No           |          |
| 6      | Female | 62     | 12   | 20         | 4          | 3             | Yes              | Yes          |          |
| 7      | Female | 65     | 0    | 0          | 0          | 0             | No               | No           |          |
| 8      | Male   | 45     | 20   | 22         | 5          | 3             | Yes              | No           |          |
| 9      | Male   | 74     | 0    | 0          | 0          | 0             | No               | No           |          |
| 10     | Male   | 71     | 0    | 0          | 0          | 0             | No               | No           |          |
| 11     | Female | 66     | 0    | 4          | 1          | 1             | No               | No           |          |
| 12     | Male   | 80     | 0    | 2          | 2          | 0             | Yes              | Yes          |          |
| 13     | Male   | 74     | 2    | 7          | 5          | 3             | Yes              | No           |          |
| 14     | Male   | 54     | 0    | 3          | 6          | 4             | No               | No           |          |
| 15     | Female | 55     | 0    | 0          | 0          | 0             | Yes              | No           |          |
| 16     | Female | 72     | 5    | 17         | 4          | 2             | Yes              | Yes          |          |
| 17     | Female | 73     | 0    | 0          | 0          | 0             | Yes              | Yes          |          |
| 18     | Male   | 64     | 21   | 21         | 3          | 2             | Yes              | No           |          |
| 19     | Female | 72     | 16   | 18         | 4          | 2             | Yes              | No           |          |
| 20     | Male   | 70     | 5    | 12         | 3          | 3             | Yes              | Yes          |          |
| 21     | Male   | 58     | 2    | 8          | 0          | 0             | No               | No           |          |
| 22     | Male   | 64     | 17   | 20         | 0          | 0             | No               | No           |          |
| 23     | Male   | 57     | 2    | 6          | 5          | 3             | No               | No           |          |
| 24     | Male   | 57     | 5    | 12         | 3          | 0             | No               | Yes          |          |
| 25     | Male   | 52     | 10   | 18         | 5          | 2             | Yes              | No           |          |
| 26     | Male   | 60     | 0    | 1          | 0          | 0             | Yes              | No           |          |
| 27     | Female | 47     | 0    | 0          | 0          | 0             | No               | No           |          |
| 28     | Male   | 60     | 0    | 4          | 0          | 2             | Yes              | No           |          |
| 29     | Male   | 50     | 17   | 25         | 3          | 1             | Yes              | Yes          |          |

ST, stroke; PSTD, post-stroke affective disorder; PSCI, post-stroke cognitive impairment (PSCI); MOCA, Montreal Cognitive Assessment; MMSE, mini-mental state examination.

**FIGURE 1** | Rank-Abundance curve of the single sample in each group. X-axis and Y-axis means OUT from each sample and the relative abundance of OTUs, respectively. (A) ST vs. HC, (B) PSCI vs. ST, (C) PSTD vs. ST.

*Escherichia-Shigella*, *Megamonas*, and *Blautia* were the most predominant genera in the ST vs. HC group (Figure 4A). *Enterococcus*, *Bacteroides*, *Escherichia-Shigella*, and *Blautia* were the most predominant genera in the PSCI vs. ST group, whereas *Bacteroides*, *Escherichia-Shigella*, *Enterococcus*, and *Blautia* were the most predominant genera in PSTD vs. ST group (Figures 4B,C). At the genus level, ST patients had a significantly higher proportion of *Enterococcus* and a lower content of *Bacteroides*, *Escherichia-Shigella*, and *Megamonas*. By Wilcoxon rank-sum test, there was a significant increase in both the *Enterococcus* (P < 0.01) and *Lactobacillus* (P < 0.05) genus in the ST patients compared with the HC (Figure 5A). PSCI patients had a significantly higher proportion of *Enterococcus*, *Bacteroides*, and *Escherichia-Shigella* and lower content of *Faecalibacterium* compared with patients with ST. By Wilcoxon rank-sum test, there was a significant decrease in both the *Faecalibacterium* (P < 0.05) and *Subdoligranulum* (P < 0.05) genus in the PSCI patients compared with the ST patients.
FIGURE 2 | (A) Alpha diversity indices in ST vs. HC. (B) Alpha diversity indices in PSCI vs. ST. (C) Alpha diversity indices in PSTD vs. ST.
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FIGURE 3 | Venn diagrams of ST and HC groups (A), PSCI and ST groups (B), PSTD and ST groups (C).

FIGURE 4 | Distribution of the predominant bacteria at genus level of different groups. (A) ST vs. HC, (B) PSCI vs. ST, (C) PSTD vs. ST. The predominant taxa (>1% relative abundance) in each level are shown.

Alterations in the Composition of Stool Microbiota Associated With ST at the Species Level

In Figure 7, the relative proportions of dominant taxa at the species level were assessed. We observed considerable variability in stool microbiota across samples. *Escherichia coli* g__*Escherichia-Shigella*, *uncultured_bacterium* g__*Megamonas*, *Faecalibacterium prausnitzii*, and *Enterococcus faecium* g__*Enterococcus* were the most predominant species in the ST vs. HC group. *Enterococcus faecium* g__*Enterococcus*, *Escherichia coli* g__*Escherichia-Shigella*, *Faecalibacterium prausnitzii*, and *unclassified g__Blautila* were the most predominant species in PSCI vs. ST group, whereas *Escherichia coli* g__*Escherichia-Shigella*, *Enterococcus faecium* g__*Enterococcus*, *unclassified g__Blautila*, and *uncultured_bacterium* g__*Subdoligranulum* were the most predominant species in PSTD vs. ST group. At the species level, ST patients had a significantly higher proportion of *Enterococcus faecium* g__*Enterococcus* and a lower content of *Faecalibacterium prausnitzii* compared with patients with ST. Patients with PSTD had a significantly higher content of *Escherichia coli* g__*Escherichia-Shigella*, a lower content of *Enterococcus faecium* g__*Enterococcus*, and *uncultured_bacterium* g__*Subdoligranulum*.

Characteristics of Beta Diversity Analyses Between ST vs. HC, PSCI vs. ST, and PSTD vs. ST Groups

In Figure 8, beta diversity analysis was calculated based on partial least squares discriminant analysis (PLS-DA). PLS-DA, based on OTUs, showed a separation between the ST vs. HC, PSCI vs. ST, and PSTD vs. ST groups in the first two principal component scores, which accounted for 6.02 and 5.08%, 3.97 and 3.94%, 4.48 and 5.04% of the total variations, respectively. This indicated that ST may be a key factor that accounts for the changes in the structure of the stool microbiota.
FIGURE 5 | Bar charts of multi-species difference. (A) ST vs. HC, (B) PSCI vs. ST, (C) PSTD vs. ST. *0.01 < p < 0.05, **0.001 < p < 0.01.
Correlation Between GM Composition and MOCA Score and Its Subvariables

The Spearman rank correlation was used to confirm the correlation between Montreal cognitive assessment (MOCA) score and the GM. As shown in Figure 9, Faecalibacterium, Roseburia, Anaerostipes, and Agathobacter were positively related to the MOCA score. Parabacteroides, Escherichia-Shigella, Enterococcus, UCG.002, Lactobacillus, and Bacteroides showed a negative correlation. Furthermore, we also investigated the correlation between GM and the MOCA subitems.
Parabacteroides (P < 0.05), Eubacterium_hallii_group and Anaerostipes were found to be positively associated with diabetes_mellitus. Unclassified_f__Lachnospiraceae, Roseburia, and Lachnoclostridium were negatively correlated with age.

DISCUSSION

The gut–brain axis (GBA) is a two-way communication network between the brain and the gastrointestinal tract (Tan et al., 2020). GBA is regulated by the central nervous system, autonomic nervous system, enteric nervous system, and hypothalamic–pituitary–adrenal axis (Carabotti et al., 2015). Acute ischemic ST induces dysbiosis of the microbiome, and these resultant changes in the GM affect neuroinflammatory processes and ST outcomes (bottom-up signaling). After ST, up to 50% of patients will experience dysphagia, constipation, gastrointestinal bleeding, and fecal incontinence (Harari et al., 2004; Schaller et al., 2006; Camara-Lemarroy et al., 2014). Gastrointestinal complications after ST lead to the delayed outcome, increased mortality, and progressive neurological dysfunction. It is shown that impaired intestinal flora could also be a risk factor for ST, which affects the prognosis after ST (Li et al., 2019; Zeng et al., 2019).

Differences in microbiota composition are found between models and controls after ST. There are significant differences in the microbiota in all parts of the gastrointestinal tract, even at the phylum level. Growth of Bacteroides phylum after ischemia was confirmed in monkeys (Chen et al., 2019). The abundance of Bacteroides phylum also increased 3 days after the ischemic ST in mice, which is regarded as a feature of post-ST disorders (Singh and Roth, 2016). In contrast, a clinical study of stool samples collected 2 days after admission showed that patients with acute ischemic ST had decreased Bacteroidetes portal protein levels (Yin et al., 2015). In the study of monkeys after focal cerebral ischemia, the relative abundance of Prevotella increased, indicating that this type may be related to the inflammatory response after ST. Herein, we detect the GM composition of ST, PSCI, and PSTD patients. Although the bacterial diversity of GM in PSCI and PSTD patients was similar to that of ST patients, the microbial composition was distinct. At the genus level, ST patients had a significantly higher proportion of Enterococcus and a lower content of Bacteroides, Escherichia-Shigella, and Megamonas. PSCI patients had a significantly higher proportion of Enterococcus, Bacteroides, and Escherichia-Shigella and a lower content of Faecalibacterium compared with patients with ST. PSTD patients had a significantly higher proportion of Bacteroides and Escherichia-Shigella and a lower content of Enterococcus and Faecalibacterium.
Among the population at high risk of ST, the microbiota alpha diversity index did not change significantly. However, conditional pathogens were found to be enriched in people at high risk of ST, and the abundance of butyrate-producing bacteria was low (Zeng et al., 2019). Faecalibacterium is considered to be the main source of butyrate (Machiels et al., 2014). Butyric acid is a SCFA, which plays an important role in maintaining the integrity of the intestinal barrier (Bourassa et al., 2016; Gopher et al., 2017). It is considered as a therapeutic target for brain dysfunction. Chronic intestinal dysbiosis may also affect the production of SCFAs (Chen et al., 2019). In our results, patients with PSCI and PSTD had a lower content of Faecalibacterium compared with patients with ST. We speculated that the reduction of Faecalibacterium leads to the reduction of butyrate content, which further damages the intestinal barrier and produces proinflammatory cytokines, thus aggravating the disease progression.

Cerebral ischemic ST also causes GM dysbiosis. Bacteroides plays a crucial role in the health of the host and can trigger endogenous infections or colitis when the normal microecological balance of the host is impaired (Wexler, 2007). Escherichia_Shigella can produce strong endotoxins, increase the intestinal permeability, and cause endotoxemia. Enterococcus is an important pathogen of nosocomial and postoperative infections, including the urinary tract and pelvic cavity infections (Sáez-Llörens et al., 1991; Watt et al., 2009). Our results showed that PSCI patients had a significantly higher content of Enterococcus, Bacteroides, and Escherichia-Shigella compared with ST patients. PSTD patients had a significantly higher content of Bacteroides and Escherichia-Shigella compared with ST patients. These results indicated that these opportunistic pathogens may play crucial roles in the progression of ST into PSCI and PSTD.

In the correlation analysis between MOCA score and the GM, we found that Parabacteroides were significantly positively associated with diabetes_mellitus. Unclassified_f_Lachnospiraceae was remarkably negatively correlated with age. Increased abundance of Parabacteroides is found in patients with ischemic ST compared with healthy individuals (Li et al., 2019). In patients with depression/anxiety, the content of Parabacteroides has changed (Roy et al., 1992; Cheung et al., 2019). In addition, the relative abundance of Parabacteroides is positively correlated with gastrointestinal tract (GI) symptoms in elderly patients with type 2 diabetes mellitus (Li et al., 2020). Lachnospiraceae plays an important role in modulating GI motility (Yano et al., 2015). It is found that Lachnospiraceae dynamically changed with age and positively correlated with anxiety and cognition levels (Duan et al., 2019; Tengler et al., 2020; Liu et al., 2021). The abundance of Lachnospiraceae is significantly decreased in the age-matched PSCI patients (Ling et al., 2020). Moreover, Lachnospiraceae had a potential diagnostic value for patients with acute ischemic ST (Xiang et al., 2020). This suggested that Parabacteroides and Lachnospiraceae are associated with MOCA score of ST patients. However, there are limitations to our study. Firstly, the sample size in each group is small. More stool samples of patients are further needed. Secondly, the deeper mechanism research is not investigated. Further, the animal model is needed in the study.

DATA AVAILABILITY STATEMENT

The datasets presented in this study can be found in online repositories. The names of repository and accession number (PRJNA734105) can be found in the SRA dataset (https://www.ncbi.nlm.nih.gov/bioproject/PRJNA734105).

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by The First Affiliated Hospital of Shantou University Medical College. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

YH and WH conceived and designed the experiments. YH and ZS performed the experiments and conducted the statistical analyses. All authors contributed to the article and approved the submitted version.

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