



Characteristics of Intestinal Microbiota in Japanese Patients with Mild Cognitive Impairment and a Risk-Estimating Method for the Disorder

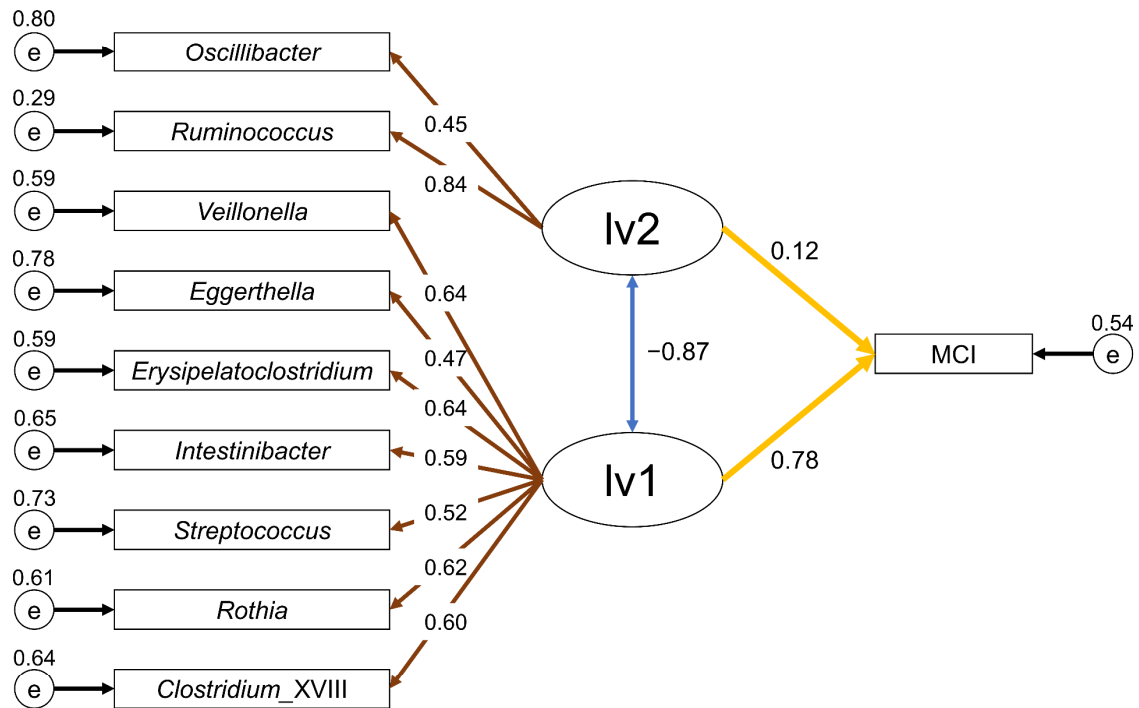
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Supplementary Figure S1. Constructed structural equation model for males and its values for each parameter. Ellipse (*lv1* or *lv2*), rectangle (MCI or taxa name) and circle (e) represent latent variables, observed variables, and residual terms, respectively. The values in the small circles, double-headed blue arrow, brown arrow, and yellow arrow represent residual variance, correlation coefficient, loading value, and path coefficient, respectively. The goodness-of-fit indices of the SEM were goodness-of-fit index (GFI) = 0.94, adjusted GFI (AGFI) = 0.88, and the root mean square error of approximation (RMSEA) = < 0.01. The detailed results are shown in Supplementary Table S4.

Supplementary Table S1. Exiting diseases in patients with MCI.

Disease	Male (n)	Female (n)
Arrhythmia	1	0
Arthralgia	0	1
Benign prostatic hyperplasia	1	0
Cataract	2	2
Cerebrovascular disease	1	0
Chronic gastritis	0	1
Chronic kidney disease	2	0
Constipation	1	4
Diseases of circulatory system	1	0
Dyslipidemia	2	2
Gout	1	0
Hashimoto's thyroiditis	1	1
Hypertension	4	4
Hypothyroidism	0	1
liver cirrhosis	1	0
Low back pain	1	1
Malaise and fatigue	0	1
Multiple myeloma	0	1
Osteoporosis	0	4
Overactive bladder	0	1
Periodontal disease	1	0
Pollinosis	1	1
Reflux esophagitis	1	0
Sensitivity to cold	0	2
Sleep disorder	0	1
Type 1 diabetes	0	1
Underweight	0	1

Supplementary Table S2. The male structural equation modeling output as shown in Figure 4a. NA, not available.

lhs ^a	op ^b	rhs ^c	est.std ^d	se ^e	z ^f	p-value ^g	ci.lower ^h	ci.upper ⁱ
lv1	=~	<i>Clostridium_XVIII</i>	0.57	0.19	2.98	<0.01	0.19	0.94
lv1	=~	<i>Rothia</i>	0.66	0.16	4.02	<0.01	0.34	0.98
lv1	=~	<i>Streptococcus</i>	0.57	0.18	3.23	<0.01	0.22	0.92
lv1	=~	<i>Intestinibacter</i>	0.59	0.20	3.02	<0.01	0.21	0.97
lv1	=~	<i>Erysipelatoclostridium</i>	0.61	0.20	3.11	<0.01	0.23	1.00
lv1	=~	<i>Eggerthella</i>	0.49	0.17	2.82	<0.01	0.15	0.83
lv1	=~	<i>Veillonella</i>	0.56	0.19	3.03	<0.01	0.20	0.93
MCI	~	lv1	0.69	0.20	3.45	<0.01	0.30	1.08
<i>Clostridium_XVIII</i>	~~	<i>Clostridium_XVIII</i>	0.68	0.21	3.18	<0.01	0.26	1.10
<i>Rothia</i>	~~	<i>Rothia</i>	0.57	0.21	2.65	0.01	0.15	0.99
<i>Streptococcus</i>	~~	<i>Streptococcus</i>	0.67	0.20	3.34	<0.01	0.28	1.07
<i>Intestinibacter</i>	~~	<i>Intestinibacter</i>	0.65	0.23	2.82	<0.01	0.20	1.10
<i>Erysipelatoclostridium</i>	~~	<i>Erysipelatoclostridium</i>	0.62	0.24	2.56	0.01	0.15	1.10
<i>Eggerthella</i>	~~	<i>Eggerthella</i>	0.76	0.17	4.47	<0.01	0.43	1.09
<i>Veillonella</i>	~~	<i>Veillonella</i>	0.68	0.21	3.28	<0.01	0.28	1.09
MCI	~~	MCI	0.52	0.28	1.88	0.06	-0.02	1.07
lv1	~~	lv1	1.00	0	NA	NA	1	1
<i>Clostridium_XVIII</i>	~1		<0.01	0.21	<0.01	1.00	-0.41	0.41
<i>Rothia</i>	~1		<0.01	0.23	<0.01	1.00	-0.45	0.45
<i>Streptococcus</i>	~1		<0.01	0.21	<0.01	1.00	-0.41	0.41
<i>Intestinibacter</i>	~1		<0.01	0.20	<0.01	1.00	-0.38	0.38
<i>Erysipelatoclostridium</i>	~1		<0.01	0.22	<0.01	1.00	-0.43	0.43
<i>Eggerthella</i>	~1		<0.01	0.20	<0.01	1.00	-0.40	0.40
<i>Veillonella</i>	~1		0	0.27	0	1.00	-0.52	0.52
MCI	~1		0	0	NA	NA	0	0
lv1	~1		0	0	NA	NA	0	0

^a Variable name that appears on the left-hand side of the formula

^b Operator indicates the following formula types: =~, latent variable definition; ~, regression; ~~ (residual) (co)variance; and ~1, intercept

^c Variable name that appears on the right-hand side of the formula

^d Standardized parameter estimates

^e Standard error for each estimated parameter

^f Z-value

^g p-value for testing the null hypothesis that the parameter value equals zero in the population

^h Lower 95% confidence intervals for standardized parameters

ⁱ Upper 95% confidence intervals for standardized parameters

Supplementary Table S3. The female structural equation modeling output as shown in Figure 4b. NA, not available.

lhs ^a	op ^b	rhs ^c	est.std ^d	se ^e	z ^f	p-value ^g	ci.lower ^h	ci.upper ⁱ
lv1	=~	<i>Ruthenibacterium</i>	0.65	0.13	4.92	<0.01	0.39	0.90
lv1	=~	<i>Enterocloster</i>	0.80	0.09	9.34	<0.01	0.63	0.96
lv1	=~	<i>Erysipelatoclostridium</i>	0.71	0.11	6.67	<0.01	0.50	0.92
lv1	=~	<i>Flavonifractor</i>	0.77	0.11	6.83	<0.01	0.55	0.99
lv1	=~	<i>Dysosmobacter</i>	0.62	0.14	4.53	<0.01	0.35	0.88
lv1	=~	<i>Eggerthella</i>	0.74	0.14	5.42	<0.01	0.47	1.00
lv1	=~	<i>Sellimonas</i>	0.58	0.15	4.00	<0.01	0.30	0.87
lv1	=~	<i>Bacteroides</i>	0.73	0.10	7.59	<0.01	0.54	0.91
lv2	=~	<i>Veillonella</i>	0.57	0.18	3.12	<0.01	0.21	0.94
lv2	=~	<i>Ligilactobacillus</i>	0.48	0.25	1.96	0.05	<0.01	0.96
lv2	=~	<i>Megamonas</i>	0.85	0.25	3.40	<0.01	0.36	1.34
MCI	~	lv1	0.52	0.18	2.94	<0.01	0.17	0.87
MCI	~	lv2	-0.52	0.22	-2.36	0.02	-0.95	-0.09
<i>Ruthenibacterium</i>	~~	<i>Ruthenibacterium</i>	0.58	0.17	3.43	<0.01	0.25	0.92
<i>Enterocloster</i>	~~	<i>Enterocloster</i>	0.36	0.14	2.68	0.01	0.10	0.63
<i>Erysipelatoclostridium</i>	~~	<i>Erysipelatoclostridium</i>	0.49	0.15	3.20	<0.01	0.19	0.79
<i>Flavonifractor</i>	~~	<i>Flavonifractor</i>	0.41	0.17	2.33	0.02	0.06	0.75
<i>Dysosmobacter</i>	~~	<i>Dysosmobacter</i>	0.62	0.17	3.69	<0.01	0.29	0.95
<i>Eggerthella</i>	~~	<i>Eggerthella</i>	0.46	0.20	2.31	0.02	0.07	0.85
<i>Sellimonas</i>	~~	<i>Sellimonas</i>	0.66	0.17	3.89	<0.01	0.33	0.99
<i>Bacteroides</i>	~~	<i>Bacteroides</i>	0.47	0.14	3.38	<0.01	0.20	0.74
<i>Veillonella</i>	~~	<i>Veillonella</i>	0.67	0.21	3.16	<0.01	0.25	1.08
<i>Ligilactobacillus</i>	~~	<i>Ligilactobacillus</i>	0.77	0.24	3.26	<0.01	0.31	1.23
<i>Megamonas</i>	~~	<i>Megamonas</i>	0.28	0.42	0.67	0.51	-0.55	1.11
MCI	~~	MCI	0.24	0.20	1.15	0.25	-0.17	0.64
lv1	~~	lv1	1.00	0	NA	NA	1.00	1.00
lv2	~~	lv2	1.00	0	NA	NA	1.00	1.00
lv1	~~	lv2	-0.41	0.17	-2.40	0.02	-0.75	-0.08
<i>Ruthenibacterium</i>	~1		<0.01	0.17	<0.01	1.00	-0.33	0.33
<i>Enterocloster</i>	~1		<0.01	0.16	<0.01	1.00	-0.31	0.31
<i>Erysipelatoclostridium</i>	~1		<0.01	0.16	<0.01	1.00	-0.31	0.31
<i>Flavonifractor</i>	~1		<0.01	0.16	<0.01	1.00	-0.31	0.31
<i>Dysosmobacter</i>	~1		<0.01	0.17	<0.01	1.00	-0.34	0.34
<i>Eggerthella</i>	~1		<0.01	0.17	<0.01	1.00	-0.33	0.33
<i>Sellimonas</i>	~1		<0.01	0.24	<0.01	1.00	-0.47	0.47
<i>Bacteroides</i>	~1		<0.01	0.19	<0.01	1.00	-0.38	0.38
<i>Veillonella</i>	~1		<0.01	0.17	<0.01	1.00	-0.34	0.34
<i>Ligilactobacillus</i>	~1		<0.01	0.32	<0.01	1.00	-0.64	0.64
<i>Megamonas</i>	~1		<0.01	0.52	<0.01	1.00	-1.02	1.02
MCI	~1		0	0	NA	NA	0	0
lv1	~1		0	0	NA	NA	0	0
lv2	~1		0	0	NA	NA	0	0

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^f Z-value

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^h Lower 95% confidence intervals for standardized parameters

ⁱ Upper 95% confidence intervals for standardized parameters

Supplementary Table S4. The male structural equation modeling output as shown in Supplementary Figure S1. NA, not available.

lhs ^a	op ^b	rhs ^c	est.std ^d	se ^e	z ^f	p-value ^g	ci.lower ^h	ci.upper ⁱ
lv1	=~	<i>Clostridium_XVIII</i>	0.60	0.18	3.35	<0.01	0.25	0.95
lv1	=~	<i>Rothia</i>	0.62	0.16	3.84	<0.01	0.31	0.94
lv1	=~	<i>Streptococcus</i>	0.52	0.19	2.76	0.01	0.15	0.88
lv1	=~	<i>Intestinibacter</i>	0.59	0.19	3.17	<0.01	0.23	0.96
lv1	=~	<i>Erysipelatoclostridium</i>	0.64	0.20	3.24	<0.01	0.25	1.02
lv1	=~	<i>Eggerthella</i>	0.47	0.17	2.77	0.01	0.14	0.81
lv1	=~	<i>Veillonella</i>	0.64	0.18	3.64	<0.01	0.29	0.98
lv2	=~	<i>Ruminococcus</i>	0.84	0.33	2.58	0.01	0.20	1.48
lv2	=~	<i>Oscillibacter</i>	0.45	0.18	2.54	0.01	0.10	0.79
MCI	~	lv1	0.78	1.05	0.74	0.46	-1.28	2.83
MCI	~	lv2	0.12	1.09	0.11	0.91	-2.02	2.26
<i>Clostridium_XVIII</i>	~~	<i>Clostridium_XVIII</i>	0.64	0.22	2.97	<0.01	0.22	1.06
<i>Rothia</i>	~~	<i>Rothia</i>	0.61	0.20	3.00	<0.01	0.21	1.01
<i>Streptococcus</i>	~~	<i>Streptococcus</i>	0.73	0.19	3.81	<0.01	0.36	1.11
<i>Intestinibacter</i>	~~	<i>Intestinibacter</i>	0.65	0.22	2.93	<0.01	0.21	1.08
<i>Erysipelatoclostridium</i>	~~	<i>Erysipelatoclostridium</i>	0.59	0.25	2.36	0.02	0.10	1.09
<i>Eggerthella</i>	~~	<i>Eggerthella</i>	0.78	0.16	4.81	<0.01	0.46	1.09
<i>Veillonella</i>	~~	<i>Veillonella</i>	0.59	0.22	2.65	0.01	0.15	1.03
<i>Ruminococcus</i>	~~	<i>Ruminococcus</i>	0.29	0.55	0.54	0.59	-0.78	1.37
<i>Oscillibacter</i>	~~	<i>Oscillibacter</i>	0.80	0.16	5.13	<0.01	0.50	1.11
MCI	~~	MCI	0.54	0.30	1.81	0.07	-0.04	1.13
lv1	~~	lv1	1.00	0	NA	NA	1.00	1.00
lv2	~~	lv2	1.00	0	NA	NA	1.00	1.00
lv1	~~	lv2	-0.87	0.16	-5.44	<0.01	-1.18	-0.56
<i>Clostridium_XVIII</i>	~1		<0.01	0.21	<0.01	1.00	-0.41	0.41
<i>Rothia</i>	~1		<0.01	0.23	<0.01	1.00	-0.45	0.45
<i>Streptococcus</i>	~1		<0.01	0.21	<0.01	1.00	-0.41	0.41
<i>Intestinibacter</i>	~1		<0.01	0.20	<0.01	1.00	-0.38	0.38
<i>Erysipelatoclostridium</i>	~1		<0.01	0.22	<0.01	1.00	-0.43	0.43
<i>Eggerthella</i>	~1		<0.01	0.20	<0.01	1.00	-0.40	0.40
<i>Veillonella</i>	~1		0	0.27	0	1.00	-0.52	0.52
<i>Ruminococcus</i>	~1		<0.01	0.21	<0.01	1.00	-0.41	0.41
<i>Oscillibacter</i>	~1		0	0.21	0	1.00	-0.41	0.41
MCI	~1		0	0	NA	NA	0	0
lv1	~1		0	0	NA	NA	0	0
lv2	~1		0	0	NA	NA	0	0

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