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# **Urine metabolomics reveals early biomarkers in diabetic cognitive dysfunction**

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## Supporting Information

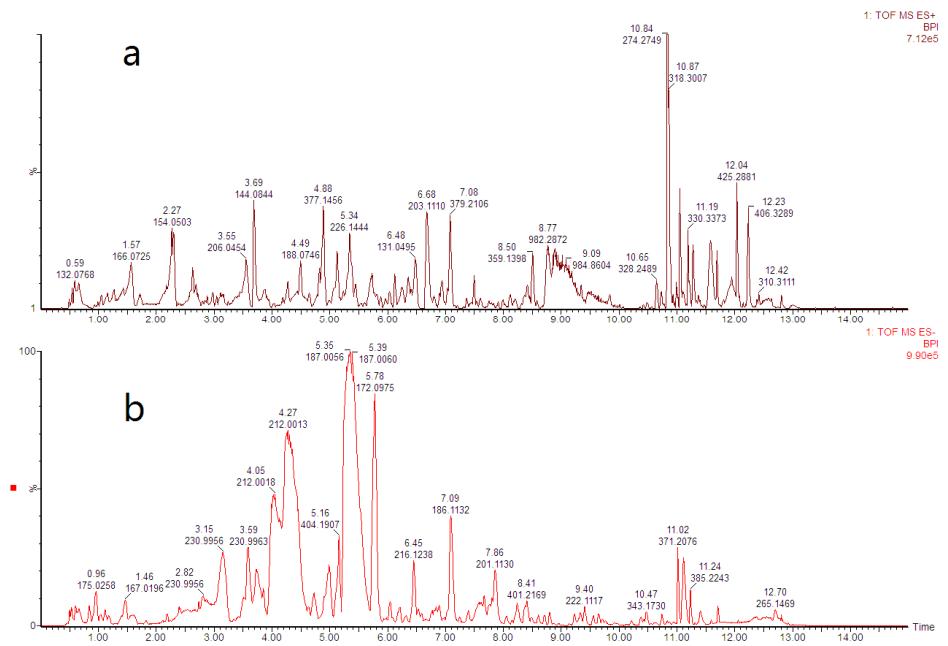


Fig. S1 The positive and negative ion mode analysis of urine samples .a. ESI+; b. ESI-

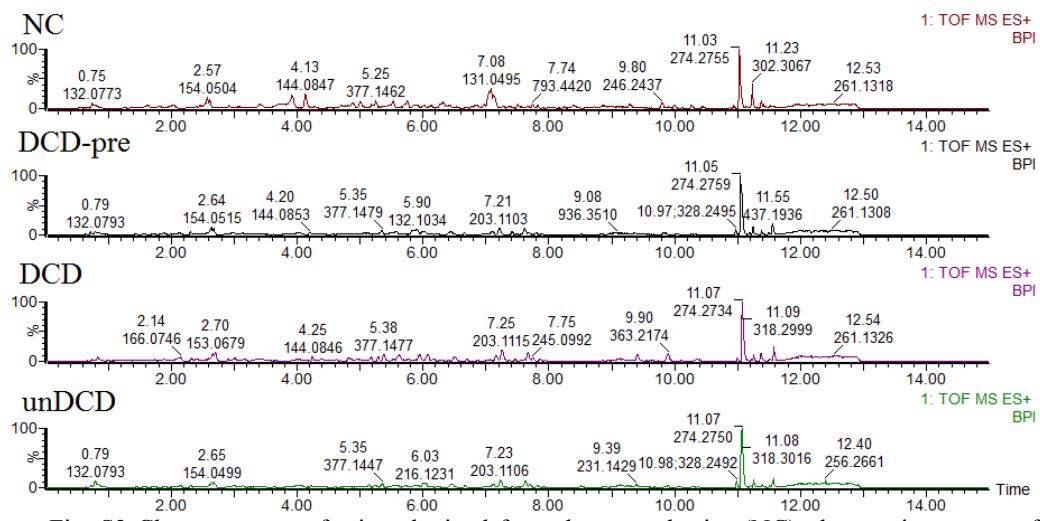


Fig. S2 Chromatogram of urine obtained from the control mice (NC), the previous stage of the diabetic cognitive dysfunction mice (DCD-pre), diabetes cognitive dysfunction mice (DCD) and diabetes without cognitive dysfunction group (unDCD) respectively. (TIF)

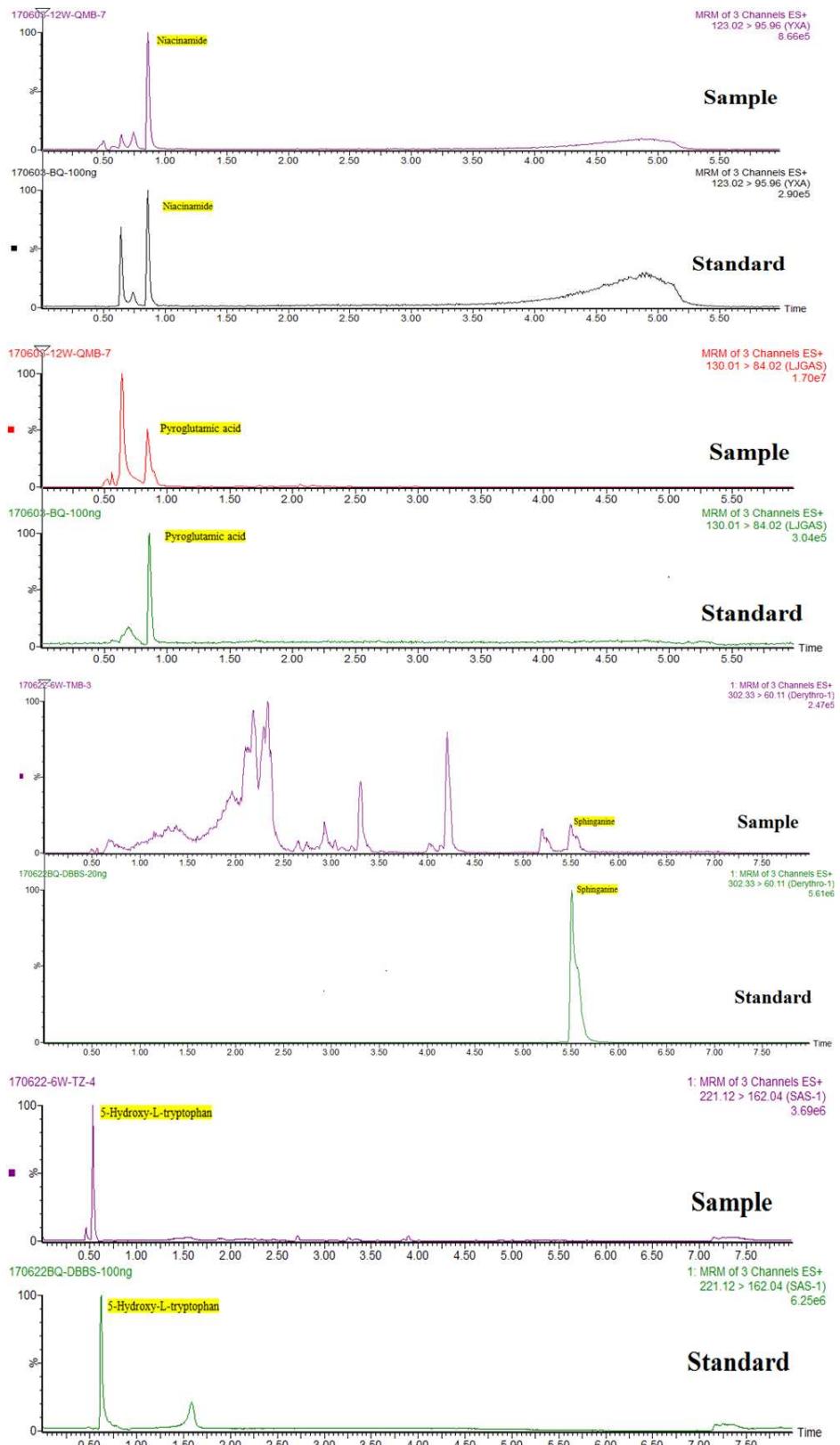


Fig. S3 The comparison results of the chromatogram of niacinamide, pyroglutamic acid, sphinganine, 5-Hydroxy-L-tryptophan.

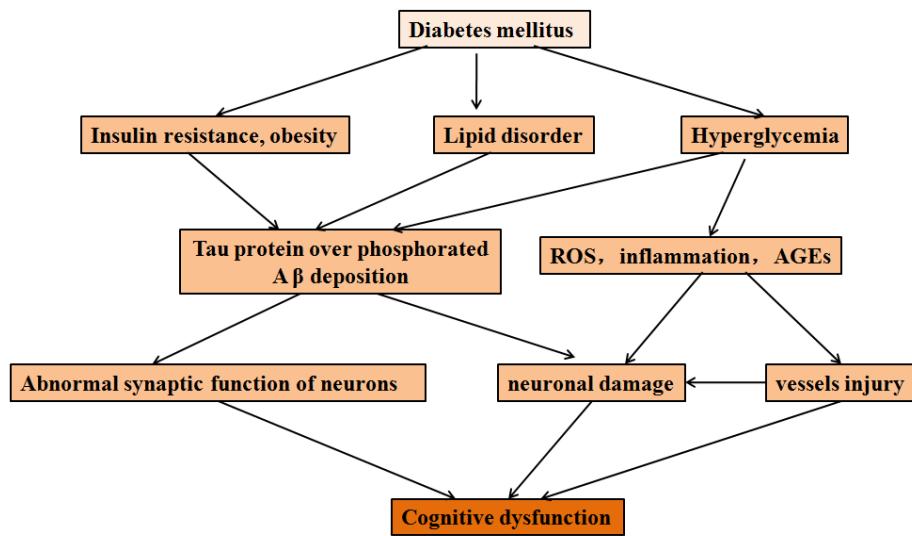


Fig. S4 The pathogenesis of diabetes cognitive dysfunction. (TIF)

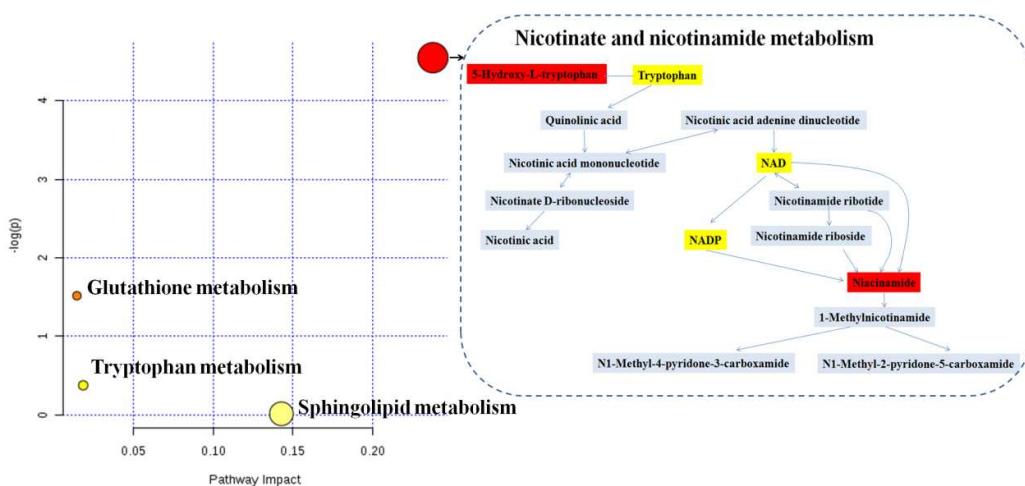


Fig. S5 The results of metabolic pathway analysis from MetPA database

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Table S1 The ESI-MS/MS parameters of four metabolites (PDF)

Compound name	Precursor ions(m/z)	Daughter ions(m/z)	Cone voltage (V)	Collision energy (V)
Niacinamide	123.0200	95.9600	28	12
5-Hydroxy-L-tryptophan	221.1200	162.0400	16	16
Pyroglutamic acid	130.0100	84.0200	28	20
Sphinganine	302.3300	60.1100	48	16

Table S2 The results of SVM between DCD-pre and DCD mice at 6<sup>th</sup> week.(PDF)

	Evaluation index	DCD-pre/unDCD
Construction of 11 characteristic ions	Model parameter	c=1.3195,g=0.78786
	Forecast accuracy	Accuracy=83.3333%
Construction of residual ions after removal C <sub>5</sub> H <sub>7</sub> NO <sub>3</sub>	Model parameter	c=1.3195,g=0.75786
	Forecast accuracy	Accuracy=63.3333%
Construction of residual ions after removal C <sub>10</sub> H <sub>9</sub> NO	Model parameter	c=1.3195,g=0.43528
	Forecast accuracy	Accuracy=63.3333%
Construction of residual ions after removal C <sub>9</sub> H <sub>8</sub> O <sub>3</sub>	Model parameter	c=1.3195,g=0.78786
	Forecast accuracy	Accuracy=83.3333%
Construction of residual ions after removal C <sub>8</sub> H <sub>15</sub> NO <sub>4</sub>	Model parameter	c=1.3195,g=0.43528
	Forecast accuracy	Accuracy=63.3333%
Construction of residual ions after removal C <sub>8</sub> H <sub>10</sub> N <sub>4</sub> O <sub>3</sub>	Model parameter	c=1.3195,g=0.25
	Forecast accuracy	Accuracy=83.3333%
Construction of residual ions after removal C <sub>9</sub> H <sub>14</sub> N <sub>4</sub> O <sub>3</sub>	Model parameter	c=4,g=0.43528
	Forecast accuracy	Accuracy=83.3333%
Construction of residual ions after removal C <sub>18</sub> H <sub>39</sub> NO <sub>2</sub>	Model parameter	c=2.2974,g=1.3195
	Forecast accuracy	Accuracy=63.3333%
Construction of residual ions after removal C <sub>8</sub> H <sub>3</sub> N	Model parameter	c=1.3195,g=1.3195
	Forecast accuracy	Accuracy=63.3333%
Construction of residual ions after removal C <sub>6</sub> H <sub>14</sub> N <sub>4</sub> O <sub>3</sub>	Model parameter	c=1.3195,g=0.0272
	Forecast accuracy	Accuracy=83.3333%
Construction of residual ions after removal C <sub>11</sub> H <sub>12</sub> N <sub>2</sub> O <sub>3</sub>	Model parameter	c=0.75786,g=0.75786
	Forecast accuracy	Accuracy=63.3333%
Construction of residual ions after removal C <sub>6</sub> H <sub>6</sub> N <sub>2</sub> O	Model parameter	c=1.3195,g=4
	Forecast accuracy	Accuracy=63.3333%

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Note: DCD-pre, unDCD, NC, respectively, on behalf of previous stage of the diabetic cognitive dysfunction group, diabetes without cognitive dysfunction group and normal control group; c, the complexity of the model, g said the kernel function parameters.

Table S3. Results from pathway analysis with MetPA.(PDF)

No.	Pathway name	Total	-log(p)	Hits	Raw p	Holm p	FDR	Impact
1	Nicotinate and nicotinamide metabolism	13	4.5484	1	0.010585	0.042338	0.042338	0.2381
	Glutathione metabolism	26	1.5163	1	0.21953	0.65859	0.43906	0.01431
3	Tryptophan metabolism	40	0.37557	1	0.6869	1	0.91586	0.01826
4	Sphingolipid metabolism	21	0.013026	1	0.98706	1	0.98706	0.14286

Note: **Total** is the total number of compounds in the pathway; the **Hits** is the actually matched number from the user uploaded data; the **Raw p** is the original p value calculated from the enrichment analysis; the **Holm p** is the p value adjusted by Holm-Bonferroni method; the **FDR p** is the p value adjusted using False Discovery Rate; the **Impact** is the pathway impact value calculated from pathway topology analysis.