SUPPLEMENTAL MATERIAL

Table S1. Metabolic parameters changes between baseline and 12-week after treatment in both groups.

	Control group (n=23)			GLP-1 group (n=24)			P value
	0-week	12-week	P value*	0-week	12-week	P value†	
Body-mass index —kg/m²	24.7 ± 1.8	24.8 ± 1.9	0.8488	28.1 ± 2.2	27.2 ± 2.5	0.001	0.001
Fasting blood glucose — mmol/L	8.56 ± 3.33	7.24 ± 3.32	0.0172	9.63 ± 3.50	7.93 ± 2.63	0.0447	0.433
HbA1c — %	8.71 ± 2.14	7.69 ± 2.09	0.0084	9.54 ± 1.99	7.44 ± 1.55	<0.001	0.643
Blood pressure — mmHg							
Systolic	128 ± 11	125 ± 12	0.3816	129 ± 11	126 ± 10	0.3280	0.866
Diastolic	80 ± 8	78 ± 8	0.4011	81 ± 8	79 ± 8	0.3910	0.786
TC —mmol/L	5.09 ± 1.49	4.59 ± 1.30	0.0141	4.58 ± 1.35	4.42 ± 1.61	0.6569	0.696
TG —mmol/L	1.75 ± 1.10	1.51 ± 0.89	0.3250	3.14 ± 2.28	2.79 ± 2.88	0.6112	0.049
HDL-c —mmol/L	1.23 ± 0.27	1.13 ± 0.23	0.0312	0.95 ± 0.14	1.19 ± 0.34	0.0046	0.538
LDL-c —mmol/L	2.81 ± 0.95	2.59 ± 1.05	0.1465	2.80 ± 0.87	2.73 ± 0.81	0.7490	0.614

Data are mean ± SD. The body-mass index is the weight in kilograms divided by the square of the height in meters. SD = standard deviation; HbA1c=Glycated Hemoglobin;

TC= total cholesterol; TG=triglycerides; HDL-c: high density lipid-cholesterol; LDL-c: low density lipid-cholesterol.

Table S2. Mean OxyHb concentration during VFT in relevant channels after GLP-1 treatment.

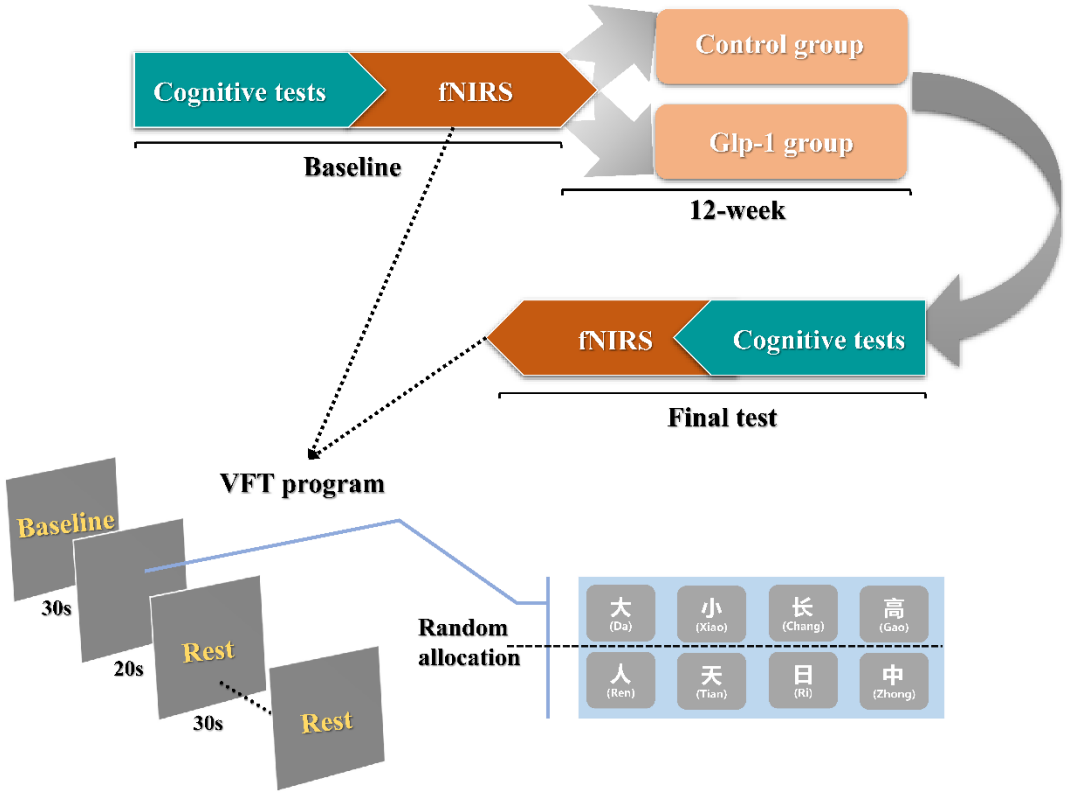
channel	Area	0-week	12-week	Pvalue
Ch2	DLPFC	-0.0589 [-0.1052, 0.1081]	0.1852 [0.0426, 0.2771]	0.0016
Ch8	DLPFC	-0.0491 [-0.1619, 0.0416]	0.1521 [0.0607, 0.2757]	0.0086
Ch13	OFC	-0.0463 [-0.1662, 0.2294]	0.2248 [0.1136, 0.4036]	0.0229
Ch17	DLPFC	-0.0628 [-0.2092, 0.0844]	0.1722 [0.0366, 0.3289]	0.0150

Data are median with interquartile range. DLPFC: dorsolateral prefrontal cortex. OFC: orbitofrontal cortex.

Table S3. Correlations of metabolic parameters and cognitive assessments with the mean OxyHb concentration in significant channels during VFT after liraglutide treatment.

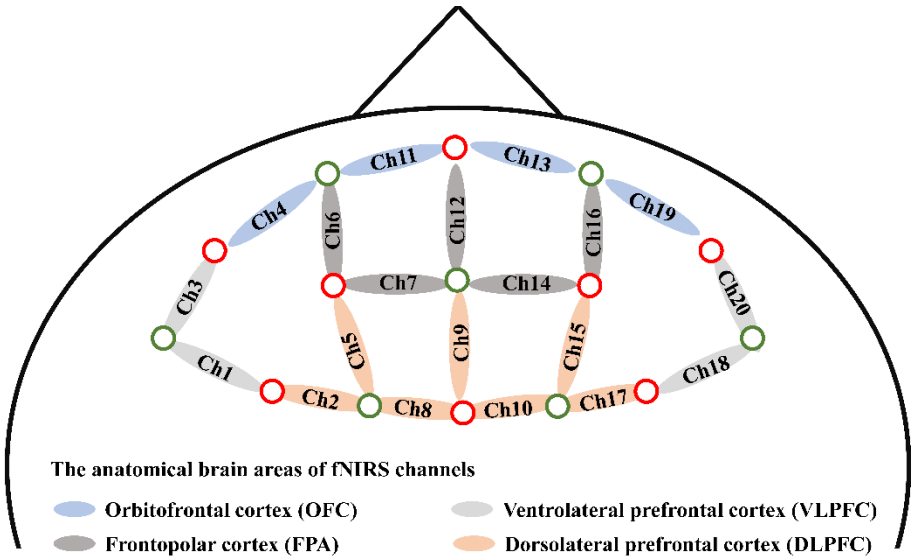
	Ch13	Ch15
BMI	r = 0.1859, *P* = 0.2108	r = 0.1423, *P* = 0.3399
Fasting blood glucose	r = 0.1437, *P* = 0.3354	r = 0.0375, *P* = 0.8024
HbA1c	r = -0.0102, *P* = 0.9458	r = -0.0190, *P* = 0.8993
Blood pressure — mmHg		
Systolic	r = -0.0715, *P* = 0.6332	r = 0.0425, *P* = 0.7765
Diastolic	r = 0.0071, *P* = 0.9622	r = 0.0384, *P* = 0.7977
TC	r = 0.0947, *P* = 0.5267	r = 0.1207, *P* = 0.4192
TG	r = 0.3987, *P* = 0.0055	r = 0.4163, *P* = 0.0036
HDL-c	r = 0.2016, *P* = 0.1741	r = -0.0297, *P* = 0.8427
LDL-c	r = 0.0960, *P* = 0.5208	r = 0.1118, *P* = 0.4543
Digit Span Test (DST)- forwards	r = -0.0024, *P* = 0.9872	r = 0.0333, *P* = 0.8239
Digit Span Test (DST)- backwards	r = 0.1639, *P* = 0.2710	r = 0.1742, *P* = 0.2417
Total Learning	r = -0.0200, *P* = 0.8940	r = 0.1291, *P* = 0.3869
Long-Delay Free Recall (LDFR)	r = 0.0738, *P* = 0.6985	r = 0.4303, *P* = 0.0176
Recognition	r = 0.2608, *P* = 0.1041	r = 0.2746, *P* = 0.0864
Animal Naming Test (ANT)	r = 0.2262, *P* = 0.1263	r = 0.2438, *P* = 0.0986
Clock Drawing Test (CDT)	r = -0.0442, *P* = 0.7681	r = -0.1494, *P* = 0.3163
Trail Making Test (TMT)	r = 0.0346, *P* = 0.8192	r = -0.1288, *P* = 0.3934
Minimum Mental State Examination (MMSE)	r = 0.3056, *P* = 0.0367	r = 0.3120, *P* = 0.0328
Memory and executive screening (MES)- Memory	r = -0.0308, *P* = 0.8374	r = 0.0172, *P* = 0.9089
Memory and executive screening (MES)-Executive	r = -0.0610, *P* = 0.6839	r = -0.0373, *P* = 0.8036
Memory and executive screening (MES)-Total	r = 0.0384, *P* = 0.7977	r = 0.0349, *P* = 0.8159

Figure S1. Experiment design.



All patients were performed cognitive tests and fNIRS at baseline and at 12 weeks after treatment. Each block of the VFT consisted of a 30-s pre-task baseline and a 20-s VFT, then followed by a 30-s resting period. The designated word was selected and presented in a random order from the following two groups of four words: “Da,” “Xiao,” “Chang,” “Gao”, or “Ren,” “Tian,” “Ri,” and “Zhong”.

Figure S2. The configuration of the fNIRS probe array arrangement in the OFC region during the experiment (front view), which consists of 8 emitters (red) and 7 detectors (green) in the arrangement resulted in a total of 20 channels.



The anatomical brain areas of fNIRS channels were listed as following: orbitofrontal cortex (OFC): channels 4, 11, 13 and 19; ventrolateral prefrontal cortex (VLPFC): channels 1, 3, 18, and 20; dorsolateral prefrontal cortex (DLPFC): channels 2, 5, 8, 9, 10, 15, and 17; and frontopolar cortex (FPA): channels 6, 7, 12, 14, and 16.

Figure S3. Flowchart of participant enrollment and follow-up during 12 weeks.