Supplementary materials

Psychological data analysis

The following equation was used to calculate psychophysical parameters:

$$p(x) = l + \frac{1 - 2l}{1 + \exp\left(-\frac{\ln(21/4)}{\sigma} \times (x - \mu)\right)}$$

where l is subject's lapse rate, μ is the midpoint or perceived reference point, and σ is the detection/discrimination threshold around the midpoint corresponding to the necessary shift from μ for reliable reporting (>84%) and always has one target value (Figure 1D). This function was adjusted to the data using Bayesian fitting (1). In addition, we defined the sensitivity index of the psychophysical function curve as the slope between the two points corresponding to 75% and 50% of the maximum value of the psychophysical function curve.

In vivo electrophysiology

Mice were anesthetized with isoflurane and fixed on a stereotaxic device using ear rods. Anesthesia was maintained with isoflurane and oxygen mixed gas, and the body temperature of each mouse was maintained with an adaptive temperature regulation system. Through a craniotomy, a small hole (0.25 mm^2) was opened above the V1 (~3.5 mm posterior to the bregma and ~2.5 mm lateral to the midline, within 800 μm below the pial surface) and dLGN (~2.5 mm posterior to the bregma and ~2.1 mm lateral to the midline, 2.5–3.0 mm below the pial surface). Subsequently, linear electrodes (A1×32, poly2, electrode array width -50 μm; site area -177 $μm^2$; NeuroNexus, Ann Arbor, MI, USA and ASSY-37-32-5, 8.3 mm; Acute 32 channel assembly; LOTUS BIOCHIPS, Diagnostic biochips, USA) were implanted to record neural signals.

Electrophysiological data analysis

The method for calculating orientation bias (OB) has been described elsewhere (2; 3). These methods have been used to calculate the orientation sensitivity of lateral geniculate nucleus (LGN) relay cells (4; 5) and the primary visual cortex (V1) (6). This is a global measurement that is influenced by all of the data points on the tuning curve and was calculated using the following equation:

$$\mathrm{OB} = \left| \frac{\sum_K R_K e^{i2\theta_k}}{\sum_K R_K} \right|$$

where R_K is the average response of neurons after removing the baseline of stimuli whose orientation is θ_K (radius). OB values ranged from 0 to 1, OB equal to 0 means that the neuron has no selectivity for any orientation, and OB equal to 1 means that the neuron only responds to a specific orientation.

The neuronal orientation response data were fit with a double von Mises transformation (7):

$$f(R \mid \theta_1, \theta_2, k_1, k2, R_0) = \frac{e^{k_1 \cos(R-\theta_1)}}{2\pi I_0(k_1)} + \frac{e^{k_2 \cos(R-\theta_2)}}{2\pi I_0(k_2)} + R_0$$

Here, $I_0(k)$ is the modified Bessel function of order 0 and R represents the stimulus angle. As can be seen in the equation; θ_1 and θ_2 (radius) represent the optimal direction and null direction of a neuron, respectively. The difference between θ_1 and θ_2 is π; k_1 and k_2 are concentration parameters at θ_1 and θ_2, respectively, and R_0 is the response baseline. The half-width at half-height (HWHH) of the fitted function was used to describe the bandwidth, which was calculated as follows:

$$HWHH = 0.5 \times arccos[(\ln 0.5 + k) / k]$$

The orientation selectivity index (OSI) was used to measure orthogonal/optimal response (8; 9). The OSI values were defined as follows:

$$OSI = \left(1 - \frac{R_{vertical}}{R_{optimal}}\right) \times 100\%$$

Here, $R_{vertical}$ is the neuron's response to vertical orientation, and $R_{optimal}$ is its response to the optimal orientation. OSI values ranged from 0 to 1. An OSI equal to 1 implies the strongest orientation selectivity, while 0 implies the weakest orientation selectivity.

The signal-to-noise ratio (SNR) was defined as the ratio between the neuron's visually evoked response (R_{evoked}) to the optimal stimulus and the neuron's spontaneous response ($R_{\text{spontaneous}}$) (10; 11).

$$\text{SNR} = \left(\frac{R_{\text{evoked}}}{R_{\text{spontaneous}}}\right)$$

Oral glucose tolerance and insulin tolerance tests

As previously described (12), for the oral glucose tolerance test (OGTT), after fasting overnight, mice were administered glucose (20% glucose solution) by gavage at a dose of 1 g/kg body weight. Blood was collected from the tail vein and BG concentration was measured prior to glucose administration (0 min) and then again at 15, 30, 60, and 120 min after administration . For the insulin tolerance test (ITT), the mice fasted for 5 h (18:00–22:00), during which only water was provided. The mice were intraperitoneally administered insulin (Sigma, St. Louis, MO, USA) at a dose of 0.75 U/kg body weight. Blood was collected from the tail vein at 0, 15, 30, 45, and 60 min post administration, and BG concentration was measured at each timepoint . The area under the curve (AUC) was calculated to quantitatively evaluate insulin resistance and glucose clearance activity (13). The OGTT and ITT were both performed after 8 weeks of HFD administration and at two weeks after the model was successfully established.

High-Performance Liquid Chromatography (HPLC) Analysis of Amino Acids

V1 tissues and a 1:1 (V:V) 10% formic acid methanol-ddH2O solution were placed in a high throughput tissue grinder with glass beads and shaken at 55 Hz. The mixture was centrifuged for 5 min at 15400 × g at 4°C. The supernatant was then maintained at -70°C until determination of free amino acids by HPLC.

Chromatographic column: ACQUITY UPLC BEH C18 column (2.1×100 mm, 1.7 μm, Waters Corporation, USA). The column temperature was 40℃, and the mobile phases were A-10% methanolic water (containing 0.1% formic acid) and B-50% methanolic water (containing 0.1% formic acid). The gradient elution conditions were 0~1 min, 20~100% B; 1~7 min, 100% B; 7~7.5 min, 100~20% B; 7.5~11 min, 20% B. The flow rate was 0.4 mL/ min.

Mass spectrometry conditions: electrospray ionization (ESI) source, positive ionization mode. The ion source temperature was 500°C, the ion source voltage was 5500 V, the collision gas pressure was 6 psi, the curtain gas pressure was 30 psi, and the atomization gas and auxiliary gas pressures were both 50 psi. Scanning was performed using multiple reaction monitoring (MRM).

Establishment of a type 2 diabetes mouse model

We established a diabetic mouse model to investigate whether diabetes damages the visual center. The weights of HFD mice were significantly higher than that of the control mice (Figure S4A), and the BG concentration in HFD mice was significantly higher than that of the controls (Figure S4B). The results of OGTT (Figure S4C) showed that HFD mice had significantly higher BG concentrations than the controls. At the same time, the ITT (Figure S4D) showed that BG levels remained higher in the HFD mice at all timepoints. Analysis of total AUCs of the OGTT and ITT data (Figures S4E and S4F) indicated that the AUCs were significantly greater for HFD mice than controls in both tests.

We subsequently induced diabetes in obese mice using streptozotocin (STZ), as previously described (14; 15). The BG concentration was significantly higher in the diabetic group than in the control group (Figure S4G). OGTT and ITT of diabetic mice (Figures S4H and S4I) indicated that BG concentrations were higher than those of the controls at each timepoint, and the AUC of the diabetic group was significantly higher than that of the control group (Figures S4J and S4K). The diabetic mice exhibited sustained hyperglycemia, glucose intolerance, and insulin resistance, consistent with the clinical manifestations of diabetes.

Table S1 List of primary antibodies used in Western blot analyses.

Protein	Product	Dilution	Source
GluA2	Abcam ab20673	1:200	Rabbit
GluA3	Abcam ab40845	1:1000	Rabbit
GluN1	Abcam ab109182	1:1000	Rabbit
GluN2A	Abcam ab124913	1:1000	Rabbit
Phospho-mTOR	Cell Signaling Technology 5536T	1:1000	Rabbit
mTOR	Cell Signaling Technology 2983T	1:1000	Rabbit
β-Actin	Cell Signaling Technology 4967S	1:1000	Rabbit

Table S2 Statistical significance, power and effect size.

Duration	2 weeks			4 weeks		
	effect size (d)	Power (1-β)	P value	effect size (d)	Power (1-β)	P value
V1						
OB(SU)	0.137	0.966	0.0003	0.528	1.000	<0.0001
OB(MU)	0.202	0.934	0.0019	0.203	0.835	<0.0001
OB(LFP)	0.425	1.000	<0.0001	0.343	1.000	<0.0001
Spontaneous	0.099	0.774	0.0562	0.033	0.180	0.7004
Peak	0.296	1.000	<0.0001	0.285	1.000	<0.0001
SNR	0.201	0.999	<0.0001	0.351	1.000	<0.0001
Average	0.156	0.989	0.0004	0.392	1.000	<0.0001
LGN						
OB(SU)	0.037	0.169	0.7456	0.180	0.899	0.0154
OB(MU)	0.099	0.302	0.4499	0.361	0.996	0.0002
OB(LFP)	0.015	0.070	0.9853	0.525	1.000	<0.0001
Spontaneous	0.126	0.461	0.2478	0.091	0.199	0.6974
Peak	0.139	0.461	0.1750	0.647	1.000	<0.0001
SNR	0.007	0.059	0.9967	0.151	0.315	0.4599
Average	0.131	0.721	0.0555	0.306	0.999	<0.0001
RS & FS						
Firing rate(RS)	0.214	1.000	<0.0001	0.139	0.845	0.0076
Firing rate(FS)	0.053	0.142	0.8305	0.049	0.109	0.9065

OB(RS)	0.145	0.950	0.0008	0.588	0.999	<0.0001
OB(FS)	0.068	0.164	0.8345	0.470	0.990	0.0017

Table S3 Statistical significance, power and effect size.

	effect size (d)	Power(1 - β)	P value
Threshold	0.673	0.846	0.0002
Bias	0.290	0.309	0.4430
Lapse	0.422	0.505	0.0006
Sensitivity Index	1.059	0.995	<0.0001

Table S4 Electrophysiological recordings of the number of control and diabetic mice, and the number of neurons recorded in V1 and dLGN.

	Control Group		Diabetic Group	
Duration, weeks	2	4	2	4
V1				
No. of mice	12	10	11	10
No. of puncture	38	22	42	21
No. of neurons	1113	933	996	822
dLGN				
No. of mice	12	10	11	10
No. of puncture	42	46	35	43
No. of neurons	628	597	520	359

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