Dysregulation of **Leptin**-modulated Corticostriatal Circuitry and Altered Dietary Decision-Making Behavior in **Bipolar** Disorder

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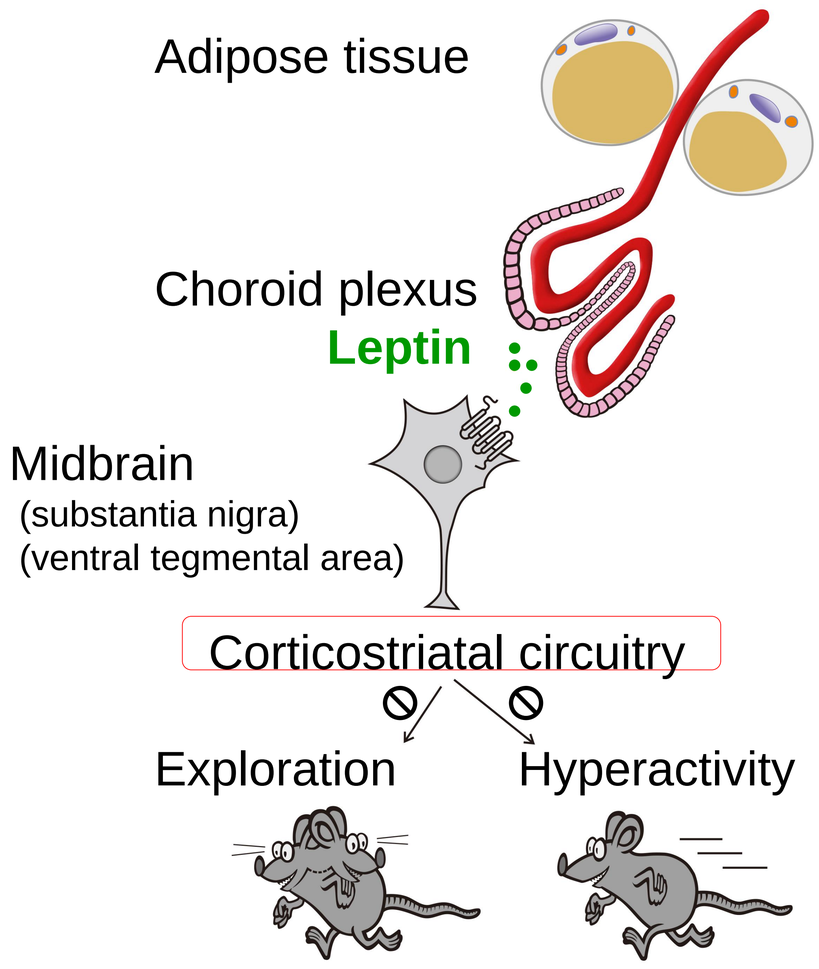
Introduction

The dopamine hypothesis is a key theory in **bipolar disorder (BD)**. Beyond the dopaminergic neurons, **leptin** modulate rewarding effects and behaviors.



Leptin is an adipokine that plays a key role in the **metabolism**. The corticostriatal circuitry is essential in **dietary decision-making** and the motivation of neuropsychiatric disorders.

We **aimed** to investigate whether the **corticostriatal connectivity** was associated with the **leptin** and dietary decision-making in controls, BD I and BD II patients.

Methods

- Fasting plasma **leptin**: commercial immunoassay kits.
- **Functional connectivity**: resting-state functional MRI, seeded at caudate (Di Martino, 2008).
- **Taiwan Food Craving Inventory** (Yen et al., 2010).
- Correlations between aforementioned measurements.

Results

Table 1	BD I patients (*n*=28)	BD II patients (*n*=36)	Controls (*n*=66)	*p* value
Age, year	38.4 ± 13.49	35.47 ± 12.05	32.36 ± 9.85	0.154
Gender, female	16 (57%)	22 (61%)	38 (58%)	0.930
Body mass index	25.23 ± 4.35	26.21 ± 5.77	24.93 ± 5.41	0.516
HAMD score	3.71 ± 5.44	5.00 ± 4.93	1.59 ± 1.91	0.003
YMRS score	2.00 ± 3.80	1.18 ± 1.78	0.02 ± 0.13	< 0.001
Leptin (ng/ml)	20.86 ± 21.03	20.41 ± 17.84	18.00 ± 13.64	0.791
Food craving	39.39 ± 13.35	45.64 ± 11.81	41.33 ± 12.07	0.146
salty	9.04 ± 3.20	10.76 ± 3.12	9.78 ± 3.36	0.132
sweet	12.13 ± 4.81	13.41 ± 5.48	12.03 ± 3.64	0.410
carbohydrate-rich	10.65 ± 4.01	12.21 ± 2.98	10.39 ± 3.39	0.069
fast	7.63 ± 3.73	9.09 ± 3.67	9.14 ± 6.01	0.181

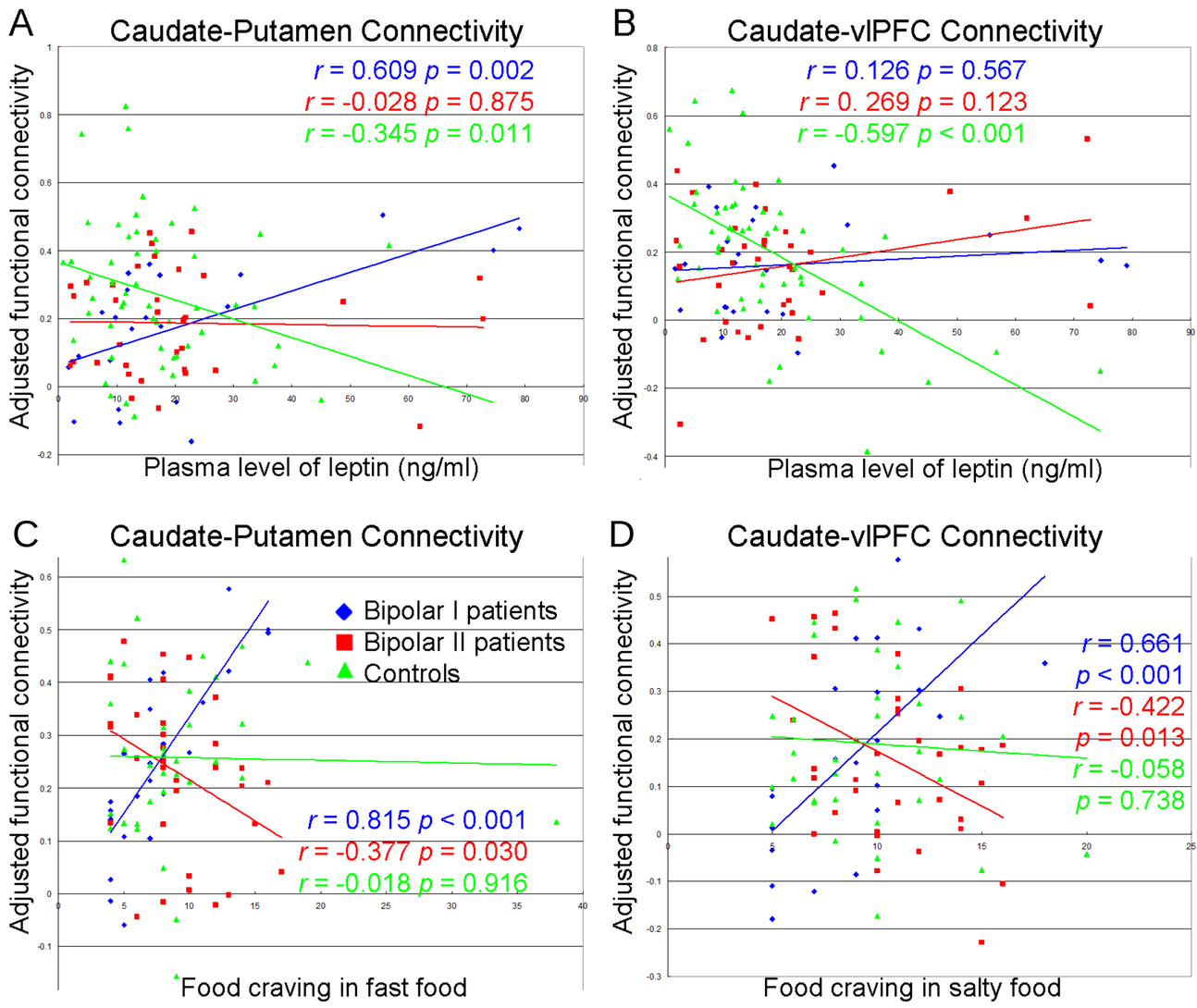


Figure 1. **(A, B)** Negative correlations between **leptin** level and the **corticostriatal circuitry** were absent in BD patients, while a reverse correlation was noted in the BD I. Furthermore, such leptin-modulated circuitry was correlated with **(C)** fast food and **(D)** salty food preferences only in the BD I patients. The scatterplots disclose the relationship between the caudate-seeded functional connectivity and leptin and food craving scores, respectively. The corresponding correlation coefficients (*r*) and *p* values are provided. Significance was thresholded at the uncorrected voxel level *p*=0.001, followed by the FWE-corrected cluster level *p*=0.05.

Discussion

- **Leptin** suppresses the **reward circuitry** only in healthy controls (Fig. A and B).
- Altered **leptin feedback regulation** in corticostriatal circuitry in BD (Fig. A and B).
- **Unhealthy food craving** was correlated with corticostriatal circuitry in **BD I** (Fig. C and D), which may partially explain the **high morbidity of metabolic diseases** in BD patients, especially in BD I.
- There was no significant difference in the plasma **leptin** level (Table 1), which was in line with a previous meta-analysis (Fernandes et al., 2016).

Funding: This work was supported by the Ministry of Science and Technology, Taiwan (MOST 107-2314-B-006-082, MOST 107-2320-B-006-016, MOST 107-2320-B-006-071, MOST 107-2628-B-006-005-, MOST 108-2320-B-006-047-MY3, MOST 108-2321-B-006-026-MY2, and MOST 108-2628-B-006-004-) and National Cheng Kung University Hospital (NCKUH-10703005 and NCKUH-11004018).
Disclosure: The authors declare no conflict of interest.