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Genes and Circuits for Memory(記憶的基因與網路)

Ann-Shyn Chiang

Brain Research Center, National Tsing Hua University, Taiwan
Institute of Biotechnology, National Tsing Hua University, Taiwan

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Why you can quickly learn a new telephone number but often forget it soon after dialing the number? Is mass learning or spaced learning more effective for establishing long-term memory? How often do you forget someone's name and then retrieve it again after thinking of his or her face image? Why an aged person can learn normally but often forget easily in a few hours or days while he still has an intact memory of his childhood experience? Post-genomics neuroscientists promise to reveal these mystery human brain capabilities through understanding genes and circuits involved in learning and memory.

Thousands of genes operate in the brain circuits, each at a different time and space, controlling complex behavior. NMDA receptors are membrane proteins acting as key coincidence detectors during learning and memory in human brain. Recently, we reported that NMDA receptors play a similar role in fly learning and memory as in human. This leads to the conclusion that flies and human may share common basic molecular mechanisms involved in learning and memory. Here, I summarize our recent progress in (1) the development of new imaging methods to visualize brain circuits expressing specific genes, (2) the analysis of information flow among memory circuits, (3) the generation of a new database archive gene expression circuitry, (4) molecular and behavior verification of memory circuits, (5) establishment of fly models for studying human brain neurodegenerative diseases.

Related publications:

1. Xia S, Miyashita T, Fu TF, Lin WY, Wu CL, Pyzocha L, Lin IR, Saitoe M, Tully T, Chiang AS (2005) NMDA receptors mediate olfactory learning and memory in *Drosophila.* Curr. Biol. 15, 603-615. (IF: 11.91)
2. Agrawal N, Pallos J, Slepko N, Apostol BL, Bodai L, Chang LW, Chiang AS, Thompson LM, Marsh JL (2005) Identification of combinatorial drug regimens for treatment of Huntington's disease using *Drosophila* Proc. Natl. Acad. Sci. USA 102, 3777-81 (IF: 10.272)
3. Iijima K, Liu HP, Chiang AS, Konsolaki M, Zhong Y (2004) A *Drosophila* model of Alzheimer's disease: dissecting the pathological roles of Ab42 and Ab40. Proc. Natl. Acad. Sci. USA 101, 6623-6628. (IF: 10.272)
4. Chiang AS, Blum A, Barditch J, ChenYH, Chiu SL, Regulski M., Armstrong JD, Tully T, Dubnau J (2004) *radish* encodes a phospholipase-A2 and defines a neural circuit involved in anesthesia-resistant memory. Curr. Biol. 14, 263-272. (IF: 11.91)
5. Tamura T, Chiang AS, Ito N, Liu HP, Horiuchi J, Tully T, Saitoe M (2003) Aging specifically impairs amnesiac-dependent memory in *Drosophila*. Neuron 40, 1-20. (IF: 15.30)
6. Dubnau J, Chiang AS, Grady L, Barditch J, Gossweiler S, McNeil J, Smith P, Buldoc F, Scott R, Certa U, Broger C, Tully T (2003) The *staufen*/*pumilio* pathway is involved in *Drosophila* long-term memory. Curr. Biol. 13, 286-296. (IF: 11.91)

為甚麼人家告訴你一個新的電話號碼你可以馬上記得，但是撥完話不到幾分鐘就再也記不起來了呢？密集式的讀書學習效果比較好，還是間斷穿插式的讀書學習效果比較好呢？你會經常忘記朋友的姓名，而過一會兒想一想他的長相又記起他的姓名了嗎？老年人對多年前發生的事通常是記憶深刻，但卻經常忘了昨天的事，這是甚麼原因呢？後基因體時代的腦科學研究藉由尋找參與學習與記憶的基因，正逐步解開人類大腦的神秘面紗。

數以千計的基因在不同的時間及空間參與腦內迴路的運作，調控整合複雜的行為。NMDA (N-methyl-D-aspartate) 受體是膜蛋白的一種，在人腦處理學習與記憶的過程裡，擔任偵測共發事件的關鍵角色。我們最近的研究報導了 NMDA 受體在果蠅腦處理學習與記憶的過程中，扮演著與在人腦中相似的角色，所導致的結論是，果蠅與人類在學習與記憶的過程中，可能使用同樣的基本分子機制。在這裡，我彙整了我們最新的進展：1) 發展新的生物影像方法來觀察特定基因在腦內迴路的表現；2) 分析在記憶迴路中訊息的傳遞方向及次序；3) 建立一個全新的腦神經迴路基因表現資料庫；4) 以分子生物與行為來驗證記憶迴路；5) 建立研究人類腦神經病變的果蠅模式系統。