# 探討甲基安非他命精神病中 **AKT1** 所扮演之角色

# Study the Role of AKT1 in Methamphetamine Psychosis


## 中文摘要

物質濫用在各個研究領域都是相當重要的問題。臨床研究也證實物質濫用所導致的主要神經精神疾病具有許多相似的共通點，不過其詳細的致病機轉到目前爲止仍然不明。甲基安非他命 (methamphe- tamine) 濫用就是一個物質濫用最好的例子。臨床發現，甲基安非他命濫用者所產生的症狀不盡相同。一部份的病人在甲基安非他命濫用的過程中，並不會產生任何精神病的症狀；不過，一部份的病人則會迅速地造成精神病。而造成此差異的詳細機轉至今仍不清楚。先前的研究指出，精神分裂的患者，其周邊血液淋巴球內 Akt1 的表現量都顯著地降低。而在缺乏 Akt1 的老鼠投予安非他命時，即會喪失「測試驚嚇反應」(prepulse inhibition, PPI) 的能力。這些發現暗示較低的 Akt1 可能在安非他命誘導的精神病中扮演了風險因子 (risk factor) 的角色。在本研究中，我們發現與甲基安非他命濫用或成癮組的個案相較，甲基安非他命精神病組個案之 Akt1 基因表現量之背景值有意義地較低。不過在 Akt1 基因多型性分析以及西方墨點法中，並未發現各組之間有顯著的差異。本研究之重要發現爲，甲基安非他命精神病組個案之 Akt1 基因表現量背景值有意義地較低。因此，我們認爲 Akt1 基因表現量對於甲基安非他命濫用之個案可以視爲一重要的風險因子 (risk factor)。

## 英文摘要

Substance misuse is an important issue in many research areas including the criminology, sociology, behavioral psychology, neurology, and biological psychiatry. Many clinical manifestations of substance misuse have similar features with the symptomatology of primary neuropsychiatric disorders. The detailed pathogenesis of many neuropsychiatric disorders remains obscure. It is reasonable to assume that through the understanding of the clinical manifestations and pathophysiology of substance misuse is a way to explore the underlying pathophysiology of psychiatric disorders. Methamphetamine (MAP) misuse is also a good example to the above-mentioned relationship. The clinical manifestations for MAP abusers are variable. Some patients appear never to develop psychotic symptoms during the course of MAP abuse; however, others rapidly become psychotic. The findings of Emamian et al (2004) are the most promising. They showed Akt1 level was significantly lower in the peripheral lymphocytes and frontotemporal cortex of schizophrenia patients. Akt1 levels were not affected by antipsychotics treatment. Another interesting finding was that amphetamine could impair prepulse inhibition in Akt1 knockout mice. These data suggest that low Akt1 might be a risk factor for

amphetamine-induced psychosis. They also showed specific Akt1 gene TC halpotype polymorphism was found to be associated with the low Akt1 level. In this study, we found the akt1 gene level of MAP psychosis subgroup was significantly lower than it of MAP dependence subgroup of MAP abusers. However, in Akt1 polymorphism analysis, we did not find any significant difference in Akt1 genotype and allele frequency, and there was no significant difference found in Western blotting as well. Most important finding in our study is that Akt1 gene level is a risk factor for MAP abusers.