出國報告(開會)

第 14 屆歐洲自殺及自殺行爲會議
心得報告

服務機關：國防醫學院三軍總醫院
姓名職稱：黃三原、三總精神醫學部主任
派赴國家：以色列特拉維夫
報告日期：101 年 9 月 19 日
出國時間：101 年 9 月 1 日至 9 月 9 日

摘要

自殺是一個複雜的精神及社會性問題；而談到自殺，首先要先了解幾個名詞，何謂自殺意念、自殺行爲、自殺企圖、自我傷害、作態性自殺及非自殺性自我傷害(NSSI)。由於自我傷害與自我殺害相關的名詞非常多，故有許多的爭議存在；到底自殺企圖與非自殺性自我傷害是否應該列爲一個診斷，在與會學者裡面，仍存在著許多爭議。但在歐洲及美洲各地學者經過一個辯論性的討論會議中，大多數學者認爲自殺企圖與非自殺性自我傷害是一種症狀或是一種人格特徵，不應該直接將其納入 DSM-V 的診斷當中；否則太多的診斷與分類反而造成全世界的不一致性，也會造成分類與治療上的困擾。

在有關自殺的四天的會議中，自殺會議的主軸在強調如何預防自殺，從公共衛生的議題到社會支持、心理因素及生物標誌等相關議題作分析探討，進而討論如何降低自殺率、如何運用藥物進行介入性預防、如何運用限制性方法預防自殺及最新自殺相關生物標誌的研究及美國軍人相關自殺研究之經驗分享。

本次會議本人申請一個口頭會議報告和兩個壁報展示，從基因、人格特質及腦影像學等研究與世界各國學者作分享。在與會 43 個國家中，本人榮幸在壁報展示中獲得此次會議的第一名，並從美國哥倫比亞大學著名教授 John Mann 手中接受此獎牌(附件一)，讓本人深深覺得這幾年在研究上的努力沒有白費，但日後的研究及提攜後進仍需更加努力，才能使中華民國讓世界都看得到。另外在會議中，大會將參與 43 個國家中的國旗標示在顯著的地方(附件二)，可見得大會的用心與尊重。雖然我們國家到國外參與國際會議，大多以台灣名稱參加，無法展現自己國家的國旗；但在第一天的會場中即見到自己國家的國旗，心中有無比的激動，更顯示大會的周全設計與人性化安排。

目次

本文

目的:

本人本次至以色列參加第十四屆自殺及自殺行爲會議之主要目的在學習目前世界有關於自殺防治、自殺研究、及相關自殺治療之方法與經驗，並與國外相關學者做學術與經驗分享。另外，並學習國際性會議的安排與佈置，以利將來本人若有機會承辦一些國際性會議，作事先的觀摩與學習。

過程：

由於台灣到以色列無直飛班機，必須由三地或四地的班機轉接方能到達，故國人大多由香港或曼谷轉機，且經濟艙票價由四萬到八萬元不等。另外由於軍人過境香港轉機，有不得在香港停留超過四小時之規定，所以本次在訂票、轉機、時間掌握與經費節省須事先準備，亦從其中學到不少學術以外的奧妙。本次以色列之行，本人選擇過境香港、曼谷(過境在機艙待一小時不可下飛機)、約旦阿曼，再到目的地以色列拉特維夫。近幾年出國至歐洲或中東不管是直飛或轉機皆要在曼谷停留一下，從中發現不管國內或國外航空公司由原本出發地不到一半之乘運量，在曼谷轉乘後會增加至九成多，可見曼谷機場不管紅衫或黃衫軍如何霸佔抗議皆無法改變其重要性，令人感慨我們不斷改建的桃園國際機場何時才能趕上曼谷機場的不可取代性。

本人於 101 年 9 月 2 日上午總算順利到達一個由全球六大洲多種民族構成的國家以色列特拉維夫。進到會場的第一天，就看到大會布置 43 個參與國的國旗於顯目的地方，當然本人也看到自己國家的國旗，內心無比的興奮，且深深覺得大會的用心佈置與人性化的安排，且重視每個國家的參與，給予本人深刻的印象。

101 年 9 月 3 日大會安排主題式的自殺議題教育。首場由美國哥倫比亞大學 John Mann 教授演說未來十年自殺研究議題要如何進行，除了自殺相關生物因子分析之外，社會環境、個人體質因素皆須考慮。在自殺生物標的相關研究中，雖

在自殺基因影像研究上已進行多年，但仍存在著許多爭議。目前更先進的功能性核磁共振腦部造影及正子造影，雖發現這些研究工具可輔助自殺病因之探討，但仍需日後加以佐證。第二個教育主題由英國心理學家 Dr. Rory O’ Connor 針對從心理歷程探討自殺危險性，Dr. Rory O’ Connor 提出一個 Integrated Motivational-Volitional Model(IMV) theory，認爲自殺行爲的過程由三階段構成；第一階段爲動機前期(pre-motivational-phase):主要探討自殺背景議題，如個體的體質(diathesis)、環境壓力(environment)及生活事件(life events)等的誘發因子；第二階段爲動機期(motivational-phase)主要探討自殺意念與自殺強度的形成，其過程如當一個人遇到挫折或羞辱之後，就威脅到個體本身的自我調適，若自我調適失敗就會進入自殺的圈套之中，在此圈套中個體進入動機性的調整，若此動機性的自我調整失敗則形成自殺意念與增強自殺強度；且雖有自殺意念與強度，但最後一關，也就是第三階段是行動期(volitional phase)，此期仍有決定自殺意念之調整，像是可控制性、衝動性等，若調整失敗才會出現自殺之行爲。且自殺行爲之執行又受自殺方法的可進性、可用性及媒體傳播影響。

在接下來兩天會議中，本人聽取有關歐洲自殺防治的議題，依據世界衛生組織(WHO)2008 年的報告，全世界自殺死亡人數一百萬人，而歐洲約佔了五萬八仟人，這些數據比 2003 年 WHO 統計的數據高出一、二十倍。而自殺最主要的危險因子在於憂鬱症，所以改善憂鬱症的治療及照顧是一個有效預防自殺的方法。接下來本人從大會中學習到歐洲 OSPI 計畫(optimizing suicide prevention programs and their implementation in Europe)，此計畫內容分爲五大主題：第一爲初始照顧(primary care)，第二是公共政策的提醒，第三是社區促進者(例如學校老師、警察)，第四爲要提供高危險群的自我幫助及如何求助，第五爲要限制一些可能容易取得的致命性的自殺方法；而這些目標都不僅僅是一位精神科醫師可以達成的，需要有開業醫師、家庭醫師、政府政策執行者、社區守門員(如警察、老師和公共衛生護士)才能一起執行防治的工作。

另外以色列學者 David Brent 認爲應將年輕族群的自殺分爲自殺行爲、自殺

意念、自殺合併藥酒癮、自我傷害等議題做探討。其中亦提出爲何自殺的預防無法成功，共提出三大點：第一點爲錯誤時間與錯誤地點的預防，一般在醫院及急診室最高自殺死亡時間爲出院後一個月內，故在此黃金時期內，應做一到兩次的評估；第二爲錯誤的後續預防方法，兩個成功的介入預防應該設立個案管理及教育訓練在社區大眾參與者與健康照顧提供者；第三爲錯誤的治療目標，預防的模式應該更勝於疾病的治療，一般青少年應該加強其保護因子的重要性，如家庭支持度、正向情感與情感修復、避免物質濫用和良好的睡眠，當這些重要的保護因子失去平衡時就容易造成青少年的自我傷害及自殺。

本人本次會議共發表三篇文章(附件三、四、五)。第一篇文章探討在憂鬱症中多巴胺轉換器對人格特質的影響：研究結果顯示在憂鬱症患者中的 DAT1 基因多型性雖有頃向影響人格特質，但其較正後之統計數值並無意義，故我們對 DAT1 基因在漢民族憂鬱症患者中的是否會影響仍需做進一步的亞型分析。第二篇文章探討憂鬱症中血清素轉換器與 SLC6A4 基因多型性之關連性：研究結果顯示血清素轉換器或許可以成爲發展憂鬱症的生物標記，但我們仍需更多的研究證據支持此結果。第三篇文章探討 F-18 正子照影的血清素轉換器與憂鬱性自殺的關連性：研究結果顯示沒有自殺行爲的憂鬱症患者中的血清素轉換器明顯低於有自殺行爲的憂鬱症患者和正常人組；以及人類中腦內血清素轉換器、自殺量表分數和憂鬱量表分數在不同性別上有很大的差異存在。

心得及建議：

1.政府部門的重視與國家優點的展現

在進到會場的第一天，本人就看到大會布置 43 個參與國的國旗於顯目的地方，當然也看到自己國家的國旗，內心無比的興奮，且深深覺得大會的用心佈置與人性化的安排，且重視每個國家的參與，這也讓我啓發日後本國及本人如何籌辦世界型會議、如何展現自己國家的優勢，從中學習到一些思緒，希望日後本人可以靈活運用；同時，本人建議日後若國內有舉辦如此大型會議，希望能受到政府相關部門之重視。

2.研究經費的不足與爭取

在歐洲腦部影像大型整合性計劃中，歐洲國家花費了十億歐元（約等同於四百五十億台幣）進行五年有關精神疾病之腦部機轉研究。反觀我們國家五年五百億的計畫僅分配給幾個重點發展大學，且還要再細分給各學科部門，經費實在有限；故日後本國之研究發展，應朝向幾個重要議題做整合性之研究發展，方仍與國際學術機構一較長短。歐洲國家花費了約五億在自殺防治作業上面，但我國目前軍方並沒有獨立自殺防治作業，且關於自殺防治研究之經費實在有限，我國對於自殺之重視仍有很大進步空間。

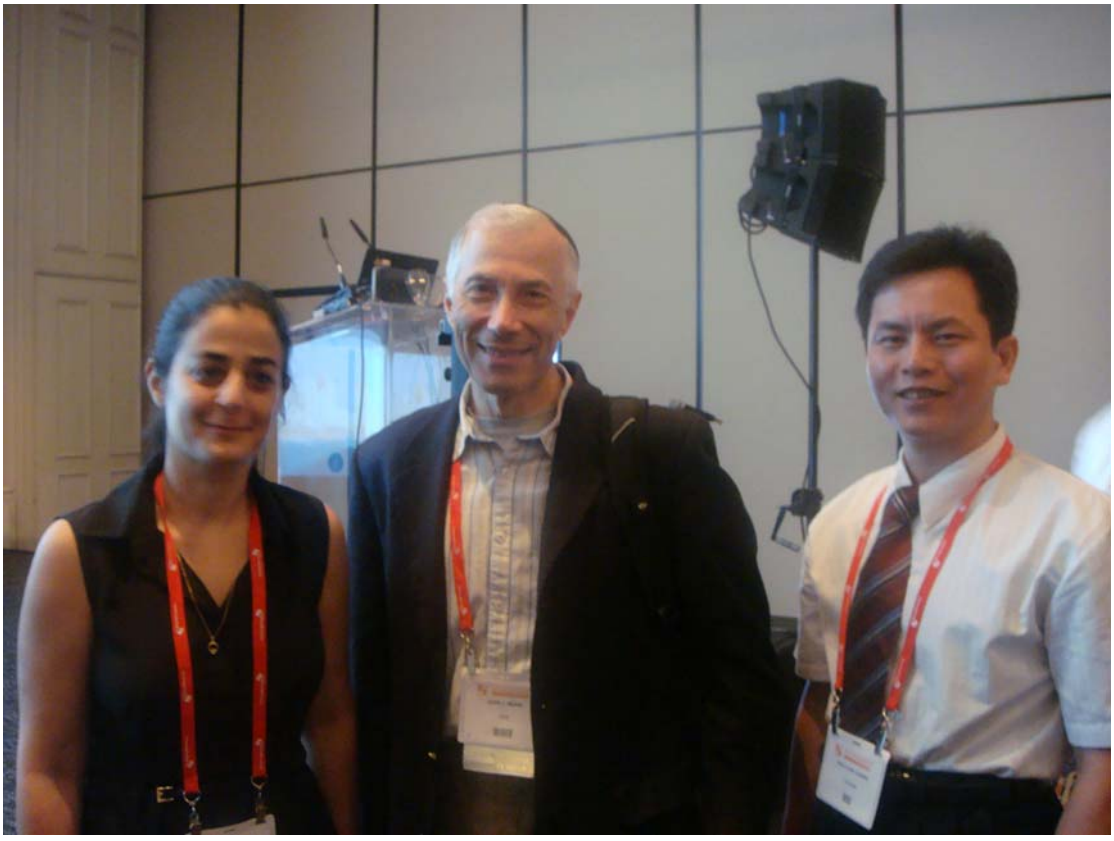
3.自殺防治需要大家一起協助

歐洲 OSPI 計畫分爲五大主題：第一爲初始照顧，第二是公共政策的提醒，第三是社區促進者，第四爲要提供高危險群的自我幫助及如何求助，第五爲要限制一些可能容易取得的致命性的自殺方法；而這些目標都不僅僅是一位精神科醫師可以達成的，需要有開業醫師、家庭醫師、政府政策執行者、社區守門員(如警察、老師和公共衛生護士)才能一起執行防治的工作。

此次會議旅程使我獲益良多，不只是與國外學者學術交流，還有見識到以色列台拉維夫當地的風俗民情、地方政府對於研究大量投入的人力和資源，這些都是值得我們國家深思的議題。

附錄

附件一



附件二


We are honored to have
you here in Tel Aviv
ESSSB14 2012
all over the world

附件三

Dopamine transporter gene possibly affects personality traits in patients with early-onset major depressive disorder

San-Yuan Huang [1]*; Chang-Chih Huang [1]; Ru-Band Lu [2] ; Mei-Chen Shih [1]; Che-Hung Yen

[1] Department of Psychiatry, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, ROC
[2] Institute of Behavior Medicine, College of Medicine, National Cheng Kung University, Tainan, Taiwan, ROC

Introduction

Comorbid personality pathologies may affect the outcome of patients with major depression (MD). The dopamine transporter gene DAT1 (SLC6A3) has been suggested to play a role in both depression and specific personality traits. The aim of this study was to assess five polymorphisms of the DAT1 gene (rs2550948, rs2975226, rs6347, rs27072 and 3′ VNTR) to determine whether this gene influences personality traits in patients with MD or its subgroups.

Methods

The DAT1 polymorphisms were analyzed in 463 unrelated Han Chinese MD patients. The personality traits novelty seeking (NS) and harm avoidance (HA) were examined using the Tridimensional Personality Questionnaire. The patients were also divided into four clinical subgroups based on differences in their sex (male or female) and age at disease onset (early or late).

Results

The genotype distributions and allelic frequencies for all the patients with MD and their subgroups are summerized in Table 1. There was no association between the DAT1 and either novelty seeking or harm avoidance in the total MD sample or the sex-based subgroups (Table 2). However, early-onset MD patients with the G/G genotype of rs2550948 and the T/T genotype of rs2975226 had lower novelty seeking scores than patients with the other genotypes ($P_{corrected}$ = 0.05 for rs2550948 and $P_{corrected}$ = 0.005 for rs2975226, see Table 3).

Conclusion

Our results support that DAT1 polymorphisms do not influence the personality traits of all MD patients or the sex-based subgroups of these patients. However, we suggest that DAT1 promoter variants may affect specific personality traits in the early-onset subgroup of depressed patients in the Han Chinese population.

Table 1. Genotype distributions and allelic frequencies of the polymorphisms in the *SLC6A3 (DAT1)* gene with major depression (MD) in a Han Chinese population.

Variant	Allele Frequency [a] (%)		Genotype (%)															
	1	2	Total MD (n=463)			MD, male only (n=190)			MD, female only (n=273)			p [c]	MD, early onset (n=162)			MD, late onset (n=301)			p [d]
			1/1	1/2	2/2	1/1	1/2	2/2	1/1	1/2	2/2		1/1	1/2	2/2	1/1	1/2	2/2	
rs2550948	G (85.1)	A (14.9)	337 (72.8)	114 (24.6)	12 (2.6)	128 (67.4)	58 (30.5)	4 (2.1)	209 (76.6)	56 (20.5)	8 (2.9)	0.046	121 (74.7)	37 (22.8)	4 (2.5)	216 (71.8)	77 (25.6)	8 (2.7)	0.824 [e]
rs2975226	T (84.3)	A (15.7)	331 (71.5)	119 (25.7)	13 (2.8)	125 (65.8)	60 (31.6)	5 (2.6)	206 (75.5)	59 (21.6)	8 (2.9)	0.054	117 (72.2)	41 (25.3)	4 (2.5)	214 (71.1)	78 (25.9)	9 (3.0)	0.980 [e]
rs6347	A (89.4)	G (10.6)	369 (79.7)	90 (19.4)	4 (0.9)	150 (78.9)	37 (19.5)	3 (1.6)	219 (80.2)	53 (19.4)	1 (0.4)	0.440 [e]	126 (77.8)	34 (21.0)	2 (1.2)	243 (80.7)	56 (18.6)	2 (0.7)	0.596 [e]
rs27072	C (74.9)	T (25.1)	255 (55.1)	184 (39.7)	24 (5.2)	98 (51.6)	79 (41.6)	13 (6.8)	157 (57.5)	105 (38.5)	11 (4.0)	0.259	77 (47.5)	72 (44.4)	13 (8.0)	178 (59.1)	112 (37.2)	11 (3.7)	0.020

Variant	Allele Frequency [a] (%)		Genotype (%)									
			Total MD (n=463)		MD, male only (n=190)		MD, female only (n=273)		p	MD, early onset (n=162)		MD, late onset (n=301)		p
	1	2	1	2	1	2	1	2		1	2	1	2	
3′-VNTR [b]	10R (91.0)	Non10R (9.0)	381 (82.3)	82 (17.7)	157 (82.6)	33 (17.4)	224 (82.1)	49 (17.9)	0.872	134 (82.7)	28 (17.3)	247 (82.1)	54 (17.9)	0.860

Table 2. Association analysis between *SLC6A3 (DAT1)* gene polymorphisms and specific personality traits in patients with major depression (MD).

Variants	Genotype [a]		Total MD (n=463)					
	1	2	Novelty seeking			Harm avoidance		
			1	2	p	1	2	p
rs2550948	G/G	G/A&A/A	14.05 (±5.56)	14.66 (±5.07)	0.143	19.87 (±5.26)	20.76 (±5.76)	0.166
rs2975226	T/T	T/A&A/A	14.02 (±5.56)	14.92 (±5.13)	0.105	19.76 (±5.25)	21.00 (±5.85)	0.050
rs6347	A/A	A/G&G/G	14.24 (±5.30)	14.40 (±6.02)	0.796	20.13 (±6.07)	20.04 (±6.49)	0.899
rs27072	C/C	C/T&T/T	14.12 (±5.49)	14.46 (±5.41)	0.505	19.70 (±6.16)	20.62 (±6.13)	0.110
3′ VNTR [a]	10R	non10R	14.22 (±5.40)	14.54 (±5.71)	0.631	20.10 (±6.08)	20.16 (±5.54)	0.943
Variants	Genotype [a]		MD, male only (n=190)					
	1	2	Novelty seeking			Harm avoidance		
			1	2	p	1	2	p
rs2550948	G/G	G/A&A/A	13.89 (±5.41)	15.69 (±5.23)	0.031	19.77 (±6.57)	22.27 (±5.63)	0.011
rs2975226	T/T	T/A&A/A	13.78 (±5.35)	15.83 (±5.30)	0.013	19.59 (±6.54)	22.51 (±5.61)	0.003
rs6347	A/A	A/G&G/G	14.45 (±4.97)	14.56 (±6.88)	0.917	20.90 (±6.14)	19.43 (±7.14)	0.194
rs27072	C/C	C/T&T/T	14.08 (±5.43)	14.90 (±5.38)	0.297	20.00 (±6.45)	21.22 (±6.27)	0.189
3′ VNTR [a]	10R	non10R	14.40 (±5.10)	14.61 (±5.56)	0.900	20.63 (±6.34)	20.39 (±5.63)	0.847
Variants	Genotype [a]		MD, female only (n=273)					
	1	2	Novelty seeking			Harm avoidance		
			1	2	p	1	2	p
rs2550948	G/G	G/A&A/A	14.14 (±5.68)	14.09 (±4.82)	0.949	19.93 (±5.11)	19.30 (±5.58)	0.456
rs2975226	T/T	T/A&A/A	14.16 (±5.69)	14.04 (±4.83)	0.881	19.86 (±6.08)	19.54 (±5.74)	0.699
rs6347	A/A	A/G&G/G	14.10 (±5.53)	14.28 (±5.36)	0.828	19.61 (±5.96)	20.50 (±6.00)	0.327
rs27072	C/C	C/T&T/T	14.18 (±5.54)	14.11 (±5.44)	0.999	19.82 (±5.96)	20.16 (±6.00)	0.390
3′ VNTR [b]	10R	non10R	14.05 (±5.57)	14.49 (±5.11)	0.615	19.74 (±5.87)	20.00 (±6.54)	0.781

Table 3. Association analysis between *SLC6A3 (DAT1)* gene polymorphisms and specific personality traits in subgroup of MD patients (Early-onset and late-onset).

Variants	Genotype [a]		MD, early-onset [c] (n=162)					
	1	2	Novelty seeking			Harm avoidance		
			1	2	p	1	2	p
rs2550948	G/G	G/A&A/A	13.88 (±5.84)	17.32 (±4.44)	0.001	20.82 (±6.11)	22.68 (±5.42)	0.069
rs2975226	T/T	T/A&A/A	13.71 (±5.76)	17.47 (±4.64)	0.0001	20.66 (±6.12)	22.93 (±5.34)	0.022
rs6347	A/A	A/G&G/G	14.60 (±5.31)	15.31 (±6.99)	0.575	21.66 (±5.72)	20.00 (±6.76)	0.143
rs27072	C/C	C/T&T/T	14.65 (±5.72)	14.85 (±5.74)	0.827	20.44 (±6.33)	22.06 (±5.58)	0.086
3′ VNTR [b]	10R	non10R	14.45 (±5.35)	16.21 (±7.10)	0.137	21.57 (±5.76)	19.93 (±6.92)	0.247
Variants	Genotype [a]		MD, late-onset [c] (n=301)					
	1	2	Novelty seeking			Harm avoidance		
			1	2	p	1	2	p
rs2550948	G/G	G/A&A/A	14.14 (±5.43)	13.71 (±4.95)	0.524	19.34 (±6.32)	19.84 (±5.75)	0.533
rs2975226	T/T	T/A&A/A	14.18 (±5.46)	13.61 (±4.89)	0.396	19.27 (±6.28)	20.00 (±5.88)	0.353
rs6347	A/A	A/G&G/G	14.06 (±5.30)	13.84 (±5.33)	0.784	19.34 (±6.11)	20.07 (±6.38)	0.420
rs27072	C/C	C/T&T/T	13.89 (±5.38)	14.20 (±5.19)	0.628	19.38(±6.07)	19.63 (±6.31)	0.736
3′ VNTR [b]	10R	non10R	14.09 (±5.43)	13.67 (±4.67)	0.593	19.31 (±6.11)	20.28 (±6.40)	0.295

附件四

2012 ESSSB 14 in Israel

Association study of Serotonin transporter availability and SLC6A4 gene polymorphism in patient with major depression.

San-Yuan Huang[1], Kai-Jen Ho[2], Wen-Sheng Huang[3], Pei-Shen Ho[2], Mei-Chen Shih[1]

1. Department of Psychiatry, Tri - Service General Hospital , **National Defense Medical Center,** Taipei, Taiwan, R.O.C.,
2. Beitou Armed Forces Hospital, Taipei, Taiwan, ROC ,
3. Department of Nuclear medicine, Tri - Service General Hospital , National Defense Medical Center, Taiwan, R.O.C

Introduction

The serotonin transporter (SERT) is an important target to evaluate the pathophysiology of major depression (MD). Brain imaging has been used to evaluate SERT expression in living individuals, with inconsistent results. The aim of this study was to explore whether SERT availability of brain is different in patient with MD and healthy individuals. The effects of the serotonin transporter gene (SLC6A4) on SERT availability were also investigated.

Objective

- **1. To measure the difference in brain SERT availability between MD patients and healthy controls using [123I]ADAM during depressive episode.**
- **2. To analysis the relationship between SERT availability and severity of depression.**
- **3. We hypothesised that brain SERT availability was affected by different polymorphisms of SLC6A4.**

Materials and methods

Subjects:

A total of 52 individuals were enrolled in this study. Fourty subjects with MD and twelve age-matched healthy subjects were recruited.

SPECT procedure and analyses

1. SPECT studies with [^{123}I]ADAM were performed within the first week of admission.
2. MRIs were co-registered to each SPECT image using the fusion modality of PMOD software. ROIs were marked in reference to the corresponding MRI. VOIs were counted after each ROI was drawn in each slice.

Genotyping of SLC6A4 :

Two single nucleotide polymorphisms (SNPs) (rs6354 in exon 2 and rs25531 in the promoter region), and two variable number tandem repeats (VNTR) (STin2 in intron 2, 5-HTTLPR in the promoter region) were selected for genotyping.

Table 1. Demographic, clinical characteristics and triallelic genotype reclassification of depressive and healthy subjects

	Pure MD (N=40)	Healthy controls (N=40)	Statistic	*p*-value
Male: Female	13:27	8:4	χ^2=4.776	0.048 [a]
Age, years: mean±S.D.	36.47±12.6	32.0±9.9	Z= - 0.968	0.333 [b]
Marital status(% married)	42.5	41.7	χ^2=0.003	0.959 [c]
Education, years: mean±SD	12.6±3.6	15.7±4.2	Z= - 3.014	0.003 [b]
Smoker : Non-smoker	19:21	5:7	χ^2=0.126	0.722 [c]
Cigarettes per day	5.6±7.2	8.3±11.1	Z= - 0.356	0.721 [b]
Lorazepam, mg/day: mean±S.D.	0.67±0.21			
HDRS, mean±S.D.	28.9±6.5			
Triallelic genotype reclassification				
S'S': S' L' [d]	29:11	7:5	χ^2=0.870	0.478 [a]
STin2				
12/12:non-12 repeated	30:10	7:5	χ^2=<0.001	1.000 [a]
rs6354 TT: Non-TT	34:6	9:5	χ^2=3.936	0.100 [a]

a Chi-square test with Fisher's exact test;; b Kruskal-Wallis test;; c Mann-Whitney test
d S' S' included LG/LG, LG/S, S/S; S'L' included LA/LG , LA/S

Results

- **In MD patients, the mean specific uptake ratio (SUR) values in the thalamus differed significantly between MD patients and controls ($p<0.05$). Genetic variants of SLC6A4, age, gender, severity of depression, and smoking behaviour did not influence SERT availability ($p>0.1$).**

Table 2. Specific uptake ratio in brain regions of healthy controls, Pure MD and MD/ALC subgroups

Brain area	Healthy controls n = 12	Total MD n = 40	*Z*	*p*-value[a]
Striatum	1.10±0.35	1.00 ± 0.40	- 1.409	0.159
Thalamus	1.32±0.54	1.00 ± 0.42	- 2.101	0.036
Midbrain	1.86±0.46	1.63 ± 0.65	- 1.481	0.139
Pons	1.39±0.34	1.20 ± 0.42	- 1.762	0.078

All entries for brain specific uptake ratio in this table presented as mean ± S.D.
[a]*p* value of Mann-Whitney U test

Figure 1. Depression Severity and SERT availability

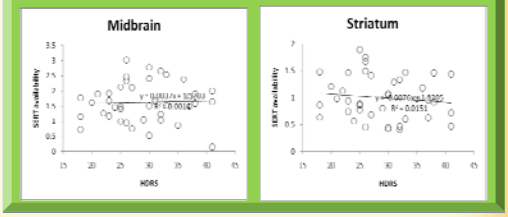


Figure 2. SUR of 123I-ADAM in examined brain regions of S' S' homozygotes (grey boxes) versus L' S' heterozygotes (white boxes) of the 5- HTTLPR in healthy controls, pure MD and MD/ALC.

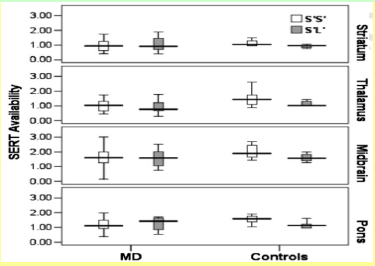


Figure 2: SUR of [123I]ADAM in the examined brain regions of 5-HTTLPR S'S' homozygotes versus S'L' heterozygotes in MD patients and healthy subjects. Horizontal lines indicate group medians. Boxes indicate interquartile range.

Conclusions

- **SERT availability might be a useful biomarker of the development of MD; however, a larger sample size is needed to provide more concrete evidence.**

附件五

2012 ESSSB 14 at Israel

An association study between 4-[^{18}F]-ADAM serotonin transporter PET imaging and depressive suicide

Yi-Wei Yeh, MD[1] ; San-Yuan Huang, MD, PhD[1]*
[1]Department of Psychiatry, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan

Background

◆The serotonergic system play an important role in the pathophysiology of major depressive disorder (MDD) and suicide. Previous imaging studies of serotonin transporter (SERT) revealed controversial results in relationship among depression, suicide , and SERT in distinct brain regions.
◆The aims of this study was to examine whether the SERT availability in different brain regions is a susceptibility factor for MDD and the development of suicidal idea in MDD.

Materials and Methods

Participants

There were total of 23 patients with diagnosis of MDD, age 19-54, recruited from a medical center and 20 control from the same community.

◆Included criteria:
1.18-65 years old male or female
2.Drug- naïve MDD met DSM-IV criteria
3.Normal controls had no prior and current psychiatric history and no psychiatric family history

◆Excluded criteria:
1.Impaired hepatic or renal function
2.Pregnant or prepare pregnancy
3.Alcohol or other substance abuse
4.Under using antidepressant, mood stabilizer or antipsychotics.

Measures

Psychiatric screening and diagnosis of MDD:
◆Chinese version of the Schedule of Affective Disorder and Schizophrenia-Lifetime (SADS-L)
◆Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision (DSM-IV-TR)
Severity of depression:
◆21-item Hamilton Rating Scale for Depression ($HRSD_{21}$)
Severity of suicidal intent:
◆Beck Scale for Suicide Ideation (BSS)

Protocol

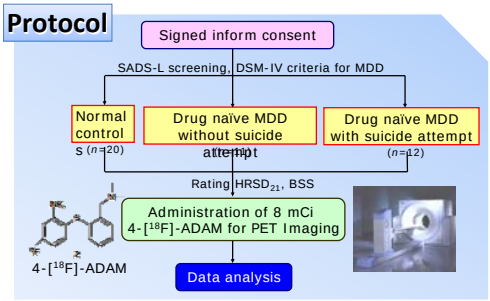
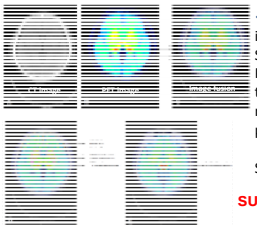


Image reconstruction



◆PET/CT images were reconstructed in the axial plane (panel A.B.C) and SERT availability was measured by PMOD v3.0 software to demarcate the region-of-interest (ROI) on the midbrain, thalamus, striatum, and prefrontal cortex (PFC) (panel D.E).

Specific uptake ratio (SUR) :

$$SUR = \frac{\text{Target region} - \text{Cerebellum}}{\text{Cerebellum}}$$

Result

Table 1. Demographic data of MDD patients and controls.

	MDD patients		Healthy controls	
	No suicide attempt(n=11)	Suicide attempt (n=12)	(n=20)	p-value
Male : Female	5 : 6	7 : 5	11 : 9	0.812[a]
Age (years): mean ± S.D.	31.55 ± 10.64	30.75 ± 10.39	32.05 ± 6.53	0.922[b]
Education (yrs): mean ± S.D.	14.00 ± 2.68	13.42 ± 2.07	16.80 ± 2.29	**<0.001**[b]
BMI (kg/m^2): mean ± S.D.	22.66 ± 2.34	21.47 ± 2.70	22.74 ± 3.60	0.469[b]
Smoker: non-smoker	3 : 8	7 : 5	3 : 17	0.050[a]
Daily smoking amount: mean ± S.D.	6.36 ± 11.20	13.05 ± 715.08	2.00 ± 5.23	0.021[b]
$HRSD_{21}$, mean ± S.D.	22.45 ± 6.47	28.42 ± 4.81	0.40 ± 0.99	**<0.001**[b]
BSS, mean ± S.D.	8.55 ± 7.35	26.00 ± 6.92	0	**<0.001**[b]

[a] Chi-square test or Fisher exact test [b] One-Way ANOVA

Table 2. Compared four brain regions' SUR in MDD patients with/without suicide and healthy controls at 2 hr after administration of 4-[^{18}F]-ADAM.

Brain region	Healthy Controls (C) (n = 20)	MDD without S (WS) (n = 11)	MDD with S (S) (n = 12)	p-value [a]	Multiple comparison between two group	p-value after correction
Midbrain	1.24 ± 0.22	0.93 ± 0.36	1.08 ± 0.42	0.052		
Thalamus	1.16 ± 0.17	0.76 ± 0.26	0.95 ± 0.36	**0.002***	WS < C	**<0.001***
Striatum	0.95 ± 0.04	0.64 ± 0.21	0.82 ± 0.28	**0.002***	WS < C	**<0.001***
PFC	0.38 ± 0.12	0.29 ± 0.15	0.42 ± 0.14	0.050		

[a] Compared among three groups using Kruskal-Wallis test *Significant after Bonferroni correction

Table 3. The effect of age, gender, BMI, daily smoking amount, $HRSD_{21}$ score, suicidal attempt, and brain regions on SUR in MDD patients using GEE model

	Estimated coefficients	Standard error	Wald χ^2	p-value
Age (years)	0.012	0.493	16.260	**<0.001*****
BMI (kg/m^2)	-0.033	0.016	4.462	**0.035***
Daily smoking amount	0.122	0.038	10.554	**0.001****
$HRSD_{21}$ score	-0.014	0.006	5.380	**0.020***
Male v.s. Female	0.218	0.086	6.454	**0.011***
Suicide attempt v.s. without suicide	0.235	0.068	12.008	**0.001****
Thalamus v.s. midbrain	-0.149	0.048	9.512	**0.002****
Striatum v.s. midbrain	-0.271	0.060	20.327	**<0.001*****
Prefrontal cortex v.s. midbrain	-0.650	0.082	62.125	**<0.001*****

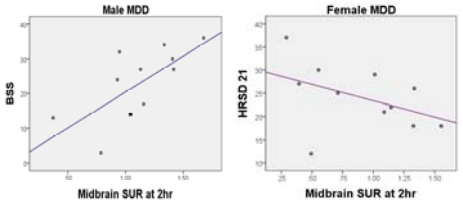
*p<0.05, **p<0.01, ***p<0001

Table 4. Correlation between the score of the $HRSD_{21}$ & BSS with SERT availability after controlling age and BMI.

SERT availability	Total MDD (n = 20)		Male MDD (n = 12)		Female MDD (n = 11)	
	r	p value	r	p value	r	p value
$HRSD_{21}$						
Midbrain	-0.126	0.588	0.265	0.459	**-0.859**	**0.003***
Thalamus	-0.024	0.917	0.158	0.662	-0.736	0.024
Striatum	0.141	0.543	0.327	0.356	-0.558	0.119
PFC	0.214	0.351	0.131	0.718	0.144	0.712
BSS						
Midbrain	0.266	0.243	**0.853**	**0.002***	-0.423	0.256
Thalamus	0.401	0.071	0.694	0.026	-0.016	0.967
Striatum	0.486	0.026	0.772	0.009	-0.071	0.856
PFC	**0.673**	**0.001***	0.672	0.033	0.423	0.256

*Significant after Bonferroni correction

Figure 1. Midbrain SUR at 2hr had a positive linear correlation with BSS in male MDD and a negative linear correlation with $HDRS_{21}$ in female MDD



Conclusion

◆MDD patients without suicide attempt had a significant lower SERT availability than MDD patients with suicide attempt and healthy controls.
◆Gender different correlation was found among midbrain SERT availability, BSS and $HRSD_{21}$ score.