# 社團法人台灣成癮科學學會 2009 年年會暨學術研討會

#### 學術研討會摘要集



#### 台灣成癮科學學會 TAIWANESE SOCIETY OF ADDICTION SCIENCE

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主辦單位:社團法人台灣成癮科學學會

合辦單位:國家衛生研究院 行政院衛生署管制藥品管理局

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### 美沙冬替代療法治療海洛因成癮之成效及影響治療持續性之相關因子探討

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目的:以較全面的方式探討美沙多維持療法的實施成效,分爲三個部分:(一)以文獻回顧的方式探討各國實施替代療法的成效。(二)使用國際通用之評估工具Opiate Treatment Index、留置率(retention rate)、生理及社會生活評估等方式探討本院實施替代療法之成效。(三)分析影響個案治療持續性(retention in treatment)的相關因子,探討個案流失之可能因素,作爲改善之參考。

方法:本研究之研究對象爲在本院接受替代療法之病患,預定收案人數約 600 人。首先以文獻探討的方式來瞭解各國實施替代療法的成效。採用國際通用之評估工具Opiate Treatment Index,(已完成中文版之製作與信效度檢測)。於開始接受治療時、接受治療三個月、六個月時、一年、一年六個月時,以Opiate treatment index及相關問卷與統計資料,評估受試者在物質使用行爲、犯罪行爲、身體健康狀況、生活功能(含職業功能、收入與家庭生活等)、尿液非法藥物篩檢及血液傳染疾病相關危險行爲等相關療效指標上的變化,並參照本院過去的相關研究成果,來探討美沙多維持療法之成效。分析比較持續治療、退出治療個案及退出後再返回個案(re-entry)此三組之間的差異,探討影響個案治療持續性的相關因素,作爲改善之參考。

結果:本研究在兩年間收案各為 331 人及 614 人,分別分析其OTI分數變化情形及治療存活分析以評估受試者治療效果。發現在治療滿三個月,其物質使用行為、高危險行為、身體健康情形、社會功能都有顯著進步。尿液藥物篩檢顯示嗎啡陽性率在治療後比治療前顯著下降。治療保護因子有:受到補助、高於60mg/d的治療劑量。

結論:依照減害的標準,替代療法療效顯著。而在本研究的個案身上也可以發現相同的結果。雖然尿液嗎啡陽性率仍高,但是實際上藥物使用的頻率已經大幅下降,受到毒品控制而造成社會心理功能障礙已經改善。

# 影響美沙冬替代療法留置(存)率之相關因素與介入策略之探討 Exploring the factors affecting retention rate on methadone maintenance treatment and the intervention strategies

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目的:台灣自 2006 年引進「美沙冬替代療法」。國外許多研究指出:延長 治療時間有助於毒品成瘾者的戒治成效,個案持續接受替代療法的時間越長, 其未來的預後越好。目前尚無本土替代療法留存率相關因素的研究,本研究目 的在探討影響不同時段之留存率的相關因素。

方法:以 2006 年 4 月起至 2008 年 7 月止,加入嘉南療養院替代療法之個案,排除服用 Suboxone 藥物、重複收案、轉院治療等。統計三個月、六個月、九個月及一年之留存率,並進行相關因素分析。

結果:在治療留存率方面,治療滿 90 天、180 天、270 天、360 天的留存率,分別為 81.4%、65.5%、49.8%、39.2%;治療未滿 30 天即退出者約佔 7%。若排除緩起訴身份之個案,則在滿 90 天、180 天、270 天、360 天的留存率分別為 79.9%、63.5%、48.6%、40.5%。而與留存率有相關的因素包括:(一)司法壓力:緩起訴身分個案的留存率較高。(二)教育程度:高中以上學歷的個案留存率較高。(三)性別:女性個案的留存率較高。(四)婚姻關係:目前仍保有婚姻關係之個案的留存率較高。(五)年齡:41歲以上的個案之留存率較佳。(六)成癮問題嚴重度:曾有安非他命濫用史、有酒精使用疾患或其他藥物濫用的個案之留存率較差。在滿意度與留存率的關連性方面,並未達統計學上的顯著,但在等待看診的時間項上,滿意度分數較高者留存狀況略佳。

討論:影響替代療法留存率之相關因素包括個案的司法身分、教育程度、性別、婚姻關係、年齡、成癮問題嚴重度。針對可能提早退出的個案,及早辨識、積極介入,如配合個案管理模式、提供心理社會介入、加強其他成癮物質之戒治服務、提升服務滿意度、結合司法力量,可以有助於提高治療留存率,降低流失,以提升成效。服務機構對本身方案的留存率之定期評估、提出可行的介入策略行動,可改進服務成效。

接受美沙多維持治療的海洛因使用者之醫囑配合度、預後和預測因子:一追蹤研究

Medical Adherence to and Prognosis of Methadone Maintenance Treatment and Their Predictive Factors in Heroin Users: A Prospective Study

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目的:本三年追蹤研究目的在於調查:(1)接受美沙多維持療法的海洛因使用者之醫囑配合度高低;(2)預測醫囑配合度高低的因子;(3)在進入美沙多治療後社區適應、犯罪程度、憂鬱嚴重度、海洛因依賴的嚴重程度、使用海洛因所造成的害處、生活品質等預後指標的變化,以確定美沙多治療的成效爲何。

方法:在本研究第一年中,共完成 358 位至門診尋求美沙冬治療的海洛因成癮者個案的初次收案,之後以每三個月一次進行追蹤訪談。本報告先以描述性統計分析個案在 3 個月和 6 個月後追蹤時自治療流失的百分比,再以t test和 $x^2$  test檢驗持續治療組和流失組之間各因子的差異,最後以t test比較基礎收案時和 6 個月追蹤時各預後指標的變化是否達到差異。

結果:3個月和6個月後追蹤時,分別有29.0%和43.3%的個案自美沙冬治療中流失。若基礎點收案時平均每月花費在購買海洛因的金額較高、決策平衡問卷中自覺使用海洛因壞處較少、自覺使用海洛因所造成的害處較輕、從住處到接受美沙冬治療之醫院所需要時間較多者,較易在3個月內停止接受美沙冬治療。若平均每月花費在購買海洛因的金額較高、先前曾經嘗試戒除海洛因的次數較少者,較易在6個月內停止接受美沙冬治療。比較收案時和6個月後追蹤的資料顯示:海洛因成癮者在接受美沙冬治療6個月後,社區適應和自覺生活品質程度有顯著提升,而犯罪嚴重程度、憂鬱嚴重度、海洛因依賴的嚴重程度、自覺使用海洛因所造成的害處則有顯著降低。

**討論**: 宜於一開始收案時就注意具有流失高危險因子者自治療中流失的危險性。本研究再次支持美沙多治療的有效性。

#### Factors influencing the maintenance of Methadone Maintenance Therapy in Drug-Addicted Patients

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**Aims:** The effectiveness of methadone maintenance therapy (MMT) is highly associated with the length of patients' stay in the program. This study aims to examine factors influencing the maintenance in MMT program.

#### Method:

#### Subject and Procedure

Study subjects include patients with heroin dependence currently engaged in a MMT program operated by a medical center in Southern Taiwan. Subjects who participated in the MMT under deferred indictment or likely to be unwillingly terminated (e.g., imprisonment) were excluded.

Early termination was defined as staying in MMT less than 6 months.

Drug use section of Opiate Treatment Index (OTI) and Severity of Dependence Scale (SDS) were applied to assess the patterns substances use including heroin and intensity of psychological dependence of heroin accordingly; the Methadone Ambivalence Scale (MAS) and the Brief "Opinions About Methadone" Scale (OAM) were applied to assess attitudes toward MMT. In addition, Family APGAR Index, the Brief version of Situational Confidence Questionnaire(SCQ) and the Mini-International Neuropsychiatric Interview (M.I.N.I.) were employed to evaluate family factors, subjective confidence in keeping abstinence, and psychiatric comorbidity, respectively. Respondents' medical record was reviewed to obtain more information regarding treatment.

#### Statistic Analysis

Univariate analysis was conducted by *t*-test and Chi-square test, and significant factors were further included in multivariate logistic regression analysis.

**Results**: Altogether, 217 participants of MMT were recruited into the present study. 73 (28.2%)of them were classified as early termination. The risk factors for early termination in univariant analysis included poorer family function, no funds for MMT, motivation coming form lack of money for heroin use, negative HIV serostatus, less hesitance to methadone, viewing methadone substitution treatment only as a procedure of dexotification, co-use of hypnotics, comorbidity with alcohol

dependence, more confidence of abstinence in urges and temptations for heroin, comorbidity with major depressive disorder, a concurrent major depressive episode, and suicide tendency. In addition, higher severity of heroin dependence before MMT might be potential risk factors influencing adherence. However, only two significant (the financial reasons to engage into MMT and viewing methadone substitution treatment as a procedure of detoxification) and one borderline significant (comorbidity with alcohol dependence)risk factors were demonstrated for early termination in multivariate logistic regression analysis.

**Conclusion:** The opinions toward methadone and the motivation to engage into MMT are the crucial factors influencing adherence of MMT. Besides, comorbidity with alcohol dependence also has impact on coordination with therapy.

#### 分別以美沙冬和丁基原啡因爲藥癮戒治替代療法之成本效益分析

### Methadone versus Buprenorphine maintenance: a cost-effectiveness analysis

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**目的**:比較美沙冬和丁基原啡因對海洛因成癮者在減害治療上的成本效益 並探討國內外實施藥癮戒治替代療法之成本效益。

方法:在相同之治療環境下,將符合 DMS-IV-TR 鴉片類成癮之診斷個案, 以隨機分組方式分使用美沙冬或丁基原啡因組(採用 suboxone 製劑)。分別蒐集 兩組之直接成本與間接成本,並以戒斷率做爲效益指標來進行成本效益分析。

結果: 1.在成本方面,服藥滿三個月的 methadone 替代療法平均一個個案花費為 18,303 元, suboxone 替代療法平均一個個案花費為 28,135 元;服藥滿六個月的 methadone 替代療法平均一個個案花費為 31,950 元, suboxone 替代療法平均一個個案花費為 49,604 元。 2.在效益方面,服藥滿三個月 methadone 替代療法的戒斷率為 24.4%, suboxone 替代療法的戒斷率為 15.1%;服藥滿六個月 methadone 替代療法的戒斷率為 18.7%, suboxone 替代療法的戒斷率為 14.7%。 3.成本效益分析結果,服藥滿三個月之 ICER 值為-105,720,服藥滿六個月之 ICER 值為-441,350。

討論:不論是 methadone 或 suboxone 替代療法,對於個案在海洛因的戒斷上皆具有效益。methadone 替代療法之成本花費較 suboxone 替代療法爲便宜,但在效益也就是戒斷率上來看,兩者是不具差異性。臺灣本土施行替代療法的時間尚短,成本效益之相關性研究可說是少之又少,本研究成果可視爲一個初步的成本效益研究報告,未來仍有待專家學者進行更多樣本數及其他醫療經濟學方面深入的探討。另外,對於替代療法藥物在使用上的安全性(死亡率及藥物交互作用方面等)亦是未來需要關注與研究的議題。

### 台灣北部地區美沙多替代療法實施背景、成效及成本效益:三年期追蹤研究

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目的:美沙多療法是針對海洛因成癮者的替代療法,過去五年來台灣地區 因爲愛滋病毒在藥癮族群的快速感染而引進美沙多治療做爲減少愛滋感染的方 案之一;然而美沙多治療在台灣地區是否能有效的減少海洛因藥癮者的生理、 心理與社會三方面的傷害、以及協助藥癮者預防愛滋,依舊缺乏實證資料說明, 因此本研究主要目的是探討美沙多療法對於海洛因藥癮者的效益與成本爲何?

方法:本研究爲三年期計畫,第一年共有三個目標:(1)依據文獻及專家會議,建立美沙多療法各項成效指標;(2)依據建立之評估指標,編制與發展相對應的測量工具,並分析其初步的信效度;(3)收取至少500位美沙多療法受試者參與本研究。之後兩年的研究,再採用三年期縱貫型追蹤設計,每六個月追蹤評量一次,檢視美沙多替代療法之成效;以及根據3年追蹤研究,評估美沙多成本效益。

結果:本研究蒐集國內外相關文獻,以及諮詢相關專家意見,研究群會議訂定美沙多療法之成效指標,應包含留置率、犯罪率、海洛因的再使用率、生活品質、死亡率,以及經濟就業等六項。500位受試者收樣主要來源爲台北市市立聯合醫院昆明院區、台北縣板橋醫院、署立基隆醫院、與宜蘭縣羅東博愛醫院;第一年(97年)年度最後共計收案505人,439名男性,66名女性。生理篩檢資料中,HIV陽性者占12%,C型肝炎者約佔74.9%,尿液中檢驗出含有嗎啡者占64.5%。教育程度以國中三年級最多,超過一半的個案只完成到9年義務教育。參與美沙多治療後,較治療前工時增加,有工作者也增多,但工資略微減少。

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#### 藥癮戒治個案社區追蹤模式前瞻性研究:第一年

### Cohort study of community follow-up of heroin addicts: First year study

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目的:海洛因成癮是慢性腦部疾患,患者常合併其他合法或非法藥物使用、以及情緒障礙等精神疾病。儘管海洛因成癮帶來強烈的戒斷症狀以及渴癮導致強迫性用藥行為,個案卻很少求診,且長期追蹤成效極低。對於藥物成癮的治療,有賴於對於成癮個案危險因子的瞭解。而前瞻性的追蹤,對澄清個案的病程與治療反應的瞭解非常重要。目前有關海洛因成癮的個案社區追蹤,由各縣市毒品危害防制中心接受法務部勒戒及戒治出所個案列案後進行轉介,由精神科醫院社區個案管理師進行社區追蹤。而社區的海洛因成癮個案來源另有美沙冬門診自願就診個案,也列入醫院社區個案管理師之追蹤。

方法:本研究採前瞻性世代研究法設計,針對不同來源的海洛因成癮患者進行社區追蹤服務,並研究一年時間內個案的治療持續率(retention in treatment)、尿液檢查毒品陽性率的比例,並分析造成海洛因成癮復發相關的危險因子。

結果: 社區追蹤者資料收集不易。若以美沙冬個案爲其中子群體之統計,海洛因成癮的身體共病性達 34.5%,精神疾病共病性達 26.3%,病史中併用安非他命者達九成以上,併用酒精也達九成以上。若以美沙冬個案爲其中子群體初步統計個案平均年齡約爲 40.9歲,教育年數 9.4年。有司法前科者 53.3%,而有藥酒癮家族史者 14.3%。全部個案在社區關懷服務方案結束時失聯比例約爲 20%,八個月後電話追蹤個案,失聯的比例達到六成。接受追蹤研究的意願約佔全部的一成。追蹤結果發現,個案一年死亡率約爲 3%,入監率約爲 16%。全部個案中,鴉片類藥物等物質濫用比例及精神醫療使用率的數字,目前仍在分析中。個案的衝動性人格明顯,與藥物治療與否無關。個案的神經心理功能沒有明顯障礙,但衝動指標量測顯示個案接受美沙冬藥物治療時,衝動指標SSRT 明顯降低。

**結論**:針對上述指標的前瞻性追蹤,可望釐清相關影響治療的危險因子與 保護因子。

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#### 運用個案管理模式對美沙冬替代療法之影響

#### The Effects of Harm Reduction Program for the Case Management

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**目的**:本研究計畫的目的在探討參與自費美沙多替代療法之海洛因成癮個案,運用個案管理模式對替代療法的成效,並探討其相關影響因素,可做爲未來建立美沙多之照護模式之參考。

方法:本研究計畫以追蹤南部某精神專科教學醫院參加自費美沙多替代療法的個案爲對象,收案人數約107人,收集個案的基本資料,包括性別、年齡、教育程度、婚姻狀態、職業類別、居住地、初次使用毒品年齡、使用方式、毒品使用量、每月毒品花費及海洛因戒治經驗,並建立個案管理卡記錄,包括門診次數、返診出席狀況、每日出席服藥記錄。將自費接受美沙多替代療法個案以接受個案管理介入評估前、後分爲對照組及實驗組,在接受個案管理評估前3個月與接受個案管理模式介入評估後1~3個月、4~6個月的平均服藥出席率、再返診率進行比較,並以服務滿意度問卷及生活品質問卷量表的前、後測,做爲個案管理模式介入後服務之滿意度與生活品質改善的指標。

結果:個管模式介入前,三個月內注射毒品頻率對於個案持續的參與美沙冬替代療法在統計上有顯著關係( $\rho$ =.05)。個案管理模式對美沙冬替代療法之服藥出席率與再返診率,經過個案管模式後 6 個月雖無顯著的差異( $\rho$ >.05),但整體而言,服藥出席率及再返診率仍然有提升。參與美沙冬替代療法的自費個案在個案管理模式介入後 6 個月,其生活品質在四個範疇裡,呈現明顯的改善( $\rho$ <.05),尤其是在生理範疇方面,更呈現大幅的改善( $\rho$ <.01)。而服務滿意程度上面,在個案管理模式介入後,較個案管理模式未介入前,滿意程度有明顯的提升。

討論:個管模式除提升參與美沙多替代療法個案之服藥出席率及再返診率外,亦提升個案之生活品質與醫療服務滿意度,並探討影響參與美沙多替代療法之個案長時間參與治療的因素與個管模式介入前,三個月內注射毒品頻率有關。建議個案在參與美沙多替代療法時,需觀察個案在三個月內注射毒品的頻率,以期掌握個案在後期能持續性地參與美沙多替代療法,並針對個案在服藥期間能有穩定的工作與住所,希能幫助個案規律的出席服藥及門診。

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#### 排除社會型態下危險他者之社會復歸:藥癮戒治者之社會支持接納 系統之研究

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**目的**:本文針對藥瘾者之社會支持接納與藥物濫用處遇措施系統的建構之探討,並對於藥瘾/毒品政策下的藥瘾者社會情境進行分析,期待可以作爲提供臺灣藥瘾政策之參考。

方法:本文採紮根理論研究方法,訪談藥廳者 17 名(8 位愛滋病者),了解 其社會脈絡以及觀察藥廳者社會支持網絡之機制、去除標籤化的相關措施與整 合的功能。另以文獻分析法蒐集相關犯罪學與社會學原典著作及論文資料,作 為探究與詮釋現象的基礎,以得到兼具統合性與原創性的發現。

**結果**:藥癮者「思茫」濫用藥物引發其在物質的、情緒的、尊重的、友伴的社會支持系統崩潰,籌錢用藥導致家庭關係的惡化,家庭成員亦成爲受害者,在藥癮朋友相牽之下而成爲治安所欲控制之對象。如藥癮者因注射海洛因而感染愛滋病時,藥癮者等於犯罪者的社會烙印上再加上一層。

討論:在鉅觀的藥廳/毒品政策觀察發現,能動者在這過程中扮演結構性社會排除的推手,尤其傾重刑罰/保安處分之政策運用,更致藥廳者社會復歸之路難上加難。藥廳/毒品政策對於藥廳者已發生社會排除的結構條件與壓力,建議未來應避免排除性政策之規劃,增加社會資本的投資,除美沙多維持療法外,更應提供其他藥廳醫療資源,以符合藥廳者實際戒廳需求,刑罰之處罰應爲最後手段。

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#### 藥廳戒治個案管理及追蹤輔導模式研究

### Case Management and Follow Counseling Models in Drug Addiction Abstention Research

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**目的**:面對國內毒品氾濫及藥癮者持續高復發的情形,政府近年來積極運用個案管理及追蹤輔導工作模式,來進行藥癮戒治者的整合性、連續性及社區化的服務;我國毒品危害防制中心及替代療法之執行都尙屬起步階段,有必要對於個案管理及追蹤輔導等措施的實際運作及成效進行評估,故本研究將探討藥癮戒治者之持續意願、服務需求及其成效。

方法:本研究將以問卷調查及焦點團體兩項方法進行資料收集,分別針對受戒治服務者及提供戒治服務者進行研究。問卷調查採用 SPSS 統計套裝軟體進行研究資料統計分析,包括前測回收 473 份問卷,後測回收 337 份問卷,前後測均完成者共計 243 份;焦點團體部分,本研究共計召開兩場實務工作焦點團體會議,總計 20 位中部地區相關藥癮戒治服務機構人員參與,進行錄音逐字稿分析,實際討論目前相關實務工作經驗並作為未來藥癮戒治工作改善建議。

結果:(一)調查問卷部分:結果分析顯示,接受治療者之健康生活品質(SF-36)依然低於一般台灣民眾,但經這段療程後,健康生活品質改善雖未達顯著水準,但整體而言平均值皆有上升。(二)焦點團體部份,歸納以下結果分析:(1)以個案管理工作整合藥癮戒治服務團隊;(2)不同機構間的個案管理工作權責有待協調整合;(3)政府政策是推動個案管理工作的重要主導力量;(4)藥癮個案聯繫追蹤困難需要更多配套機制及技巧;(5)加強各機構間垂直委任關係互動緊密;(6)法制化毒品危害防制中心的組織定位。

**討論**:根據研究結果顯示藥癮個案在治療期間健康生活品質皆獲得穩定漸進的改善,減害計畫亦發揮功能讓持續接受服務治療者的情況日漸穩定,團隊服務的成效也獲得個案的肯定。未來建議加強各機構間個案管理工作的統合,並建構更具持續性、多元性的藥癮治療政策,同時法制化及強化毒品危害防制中心的功能。

#### 美沙多維持療法患者之家庭負荷與接受多家屬團體心理治療效果之 探討

### Family burden and therapeutic effect of multiple familial group therapy of heroin addicts in MMT

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**Objectives:** The purpose of this study was to extend our knowledge how social support and family functioning affect subjects with heroin dependence in MMT and the associations between social support and family functioning in variant domains.

**Method**: We enrolled patients who met DSM-IV criteria of heroin dependence, which were with stable dose of methadone for at least one month. All subjected were interviewed by professional workers (including psychiatrists, psychologists, social workers) for clarify severity of symptomatology and comorbid Axis I disorder through Mini-Interview. Characteristics data of heroin addicts and primary caregivers were also evaluated under structured interview. Heroin addicts were surveyed by Beck Depression Inventory (BDI), WHOQOL-BREF, Beck Anxiety Inventory (BAI), Social Support Rating Scale (SSRS), Family Emotional Involvement and Criticism Scale (FEICS). After well inform concerning, we included subjects who willing to enter our multiple-familial group therapy. Excluded criteria were patient or primary who suffered psychiatric illness and physical illness could not tolerant the process of group therapy. 11 subjects were enrolled and 8 sessions with specialized agendas, closed, psychoeducative group therapy would be performed. We measured the atmosphere and therapeutic factors among group therapy and Beck Depression Inventory (BDI), Short-Form Life Quality Rating Scale (WHOOOL-BREF), Beck Anxiety Inventory (BAI), Social Support Rating Scale (SSRS), Family Emotional Involvement and Criticism Scale (FEICS) were be retested again for evaluating the therapeutic effects of group therapy.

For bivariate analyses, correlation analysis was used to examine the association between all continuous variables. Social support, family function, depression, and anxiety symptoms and different kinds of substances using were analyzed using ANOVA. All variants were analyzed by SPSS 13.0

Results: 2 families could not completed the course of group therapy due to acting out self-harm and agitated behaviors. These 2 heroin subjects who asked for quit could not tolerant the criticism from their family members. However, the other 6 subjects completed the course and the scores of BDI, BAI decreased and the scores of WHOQOL-BREF increased significantly. Family Intimacy increased after group therapy, but critics increased, either. This phenomenon suggested that self-disclosure and family interaction increased after treatment. However, this may need further management after group therapy for conducting to the appropriate communication. On the other side, patients' emotional support increased after group therapy. In conclusion, multiple-familial group therapy did actual benefit to heroin addicts and their family members. Nevertheless, the group members still should be prepared for

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preventing early drop-out.

**Discussion:** These data suggested that heroin addicts struggle their life with poor family function and social support even in MMT. Their primary caregivers came from lower socioeconomic status and could not afford to assist their family to quit heroin. Under the consideration of lengthening the duration of heroin abstinence and decreased the psychosocial stressors among their families, we should investigate more resources in heroin addicts' families to establish stronger supportive networks in MMT. For promoting motivation of these individuals, forensic psychiatric services or the closed connection among abstinence organization and network should be considered.

### Effects of Stress Inoculation Training Program on Heroin Abusers' Craving and Intention of Relapse

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**Objective:** This study was to investigate the effects of The Stress Inoculation Training Program (the SIT) on those heroin abusers' coping strategy, irrational beliefs in drug using, drug craving, and relapse intentions.

**Method:** Twenty male imprisoned heroin abusers were sampled from the Drug Treatment Center in Kaohsiung and twenty female heroin abusers enrolled from Tainan Detention Center. A 2x2 pretest and post-test experiment design was used in this study. There were two experiment groups and two control groups, ten subjects were assigned randomly into each group with their gender. The experiment group received a Stress Inoculation Training Program with twelve two-hour sessions, twice a week. The effects of the SIT were assessed by the followed scales: The Scale of Beliefs about Drug Use, the Scale of Coping with Drug Abuse, the Scale of Craving, and the Scale of Intention about Relapse.

Results: (1) Effects of the SIT had been found on the heroin abusers' coping strategy. It showed that the SIT can effectively increase the frequency in using the problem-focused coping strategies in stress situation for male and female heroin abusers, however, the enhancement had found in emotion-focused strategies for the female heroin abusers only. (2) Effects of the SIT had been found on the heroin abusers' irrational beliefs in drug use. It suggested that the SIT can reduce the male heroin abusers' self-devaluation with dependency on drugs in irrational beliefs only, however, it also reduces significantly the female heroin abusers' relapse intentions that activated by their negative emotion, and exposure in drug use. (3) Based on the comparison of T-scores of pre-test and post-test for the subjects of treatment group, it showed that those male heroin abusers who had a higher

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self-esteem and self-strength, their craving in drug and their beliefs that depend on drugs use had been reduced; and their coping strategies in the stressful situation had improved after the treatment. Those male heroin abusers who had a higher reflectivity, their beliefs that depend on drugs use had been reduced after the treatment. Furthermore, the subjects who take negative coping strategies could get the best benefits from this program. In contrast, the female heroin abusers who tended to have a higher reflectivity and a higher self-strength, their relapse intentions had been reduced, and they also more tend to use the problem-focused strategies to cope their stresses after the treatment. However, the subjects who had a higher negative emotion, had a higher craving and had more irrational beliefs in drug using could get the best benefits from this program. (4) In the follow-up of the SIT, the subjects of the experiment group had a positive appraisal for their experience of the SIT, i.e., their interpersonal relationships, confidence in their abstinence, and skills in stress management, and knowledge of drugs harm.

**Conclusion:** The effects of the SIT had been validated in the relapse prevention for the male and female drug abusers respectively in this study. However, the subjects' craving had been also activated by the cues of which illicit drug use mentioned frequently in the SIT program. Hence how to debrief the sensitivity of those cues of drug-using will be taking a considerate assessment in the further.

#### 藥癮戒治之轉向處遇制度與可行性之探討-以藥物法庭爲例

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目的:近年來毒品犯人數不斷攀升,且累再犯比例已趨近8成,顯示以刑罰處遇毒品施用者並無法達到戒癮成效。由於藥癮者戒治不易,在現階段缺乏醫療專業與社區配套措施下,藥癮者累再犯比率高,已對矯正機構形成沈重負擔。而醫療戒癮與社區、民間戒癮機構由於缺乏強制力,僅能對有戒癮意願者提供協助,其成效亦受限。美國佛羅里達州自1989年開始設立毒品法庭(Drug Courts),由法官、觀護人與社區機構通力合作,監控與協助藥物濫用者進行戒毒。加州亦自1991年開始設置毒品法庭,由法院監督與其他戒治機構整合的戒治計畫,以促進藥癮者長期戒治,減少毒品的使用與再犯,其對毒品法庭的評估指出,毒品法庭方案對戒治成本、戒治效益、犯罪人再犯比例、監禁比例等方面皆有明顯成效。因此,醫療、社區處遇與刑事司法體系之藥癮戒治結合模式,應當可做爲我國藥癮戒治之參考。

方法:本研究分析國外現行對毒品使用者之司法轉向制度,以國內藥癮戒治體系現況與藥物濫用者之需求爲基礎,評估對藥物濫用者之司法轉向處遇在國內實施之可行性。主要以質性訪談與座談會方式實施,藉由邀請國內藥癮戒治體系機關方案主要執行者參與座談,以瞭解國內藥癮戒治問題,藥癮戒治體系之成效與困境、藥癮戒治各環節體系之資源提供與戒治資源需求、戒癮體系銜接整合問題、藥癮戒治體系與刑事司法體系整合之可能性,據以研擬適合我國國情與毒品問題、藥癮戒治體系與刑事政策之司法矯正系統與藥癮治療系統統整模式。

結果:以統整的方式結合社區處遇的治療與持續的司法監督,才能有效達到藥癮戒治成效。目前我國毒品危害防治條例已具備轉向制度,但藥物法庭的概念並不僅止於轉向而已,藥物法庭強調的是司法系統和戒癮體系之間的協調,不同於傳統刑事司法的轉向處遇將監督權委外,在藥物法庭計畫裡裡,法官需協調觀護人、個案管理人和處遇供應者以掌管處遇的過程,並確保可以提供充足的治療方案,且當有違法的事件發生時,能提供立即予以制裁。藥物法庭之設立目的乃藉由法庭來管理藥廳者之戒治,結合社會、社區與醫療資源,促使藥廳者能夠回歸社會正常生活,而非僅將藥廳者由司法處遇體系轉介至藥廳戒治體系,藥廳者之戒治仍爲藥物法庭之核心目標。因此藥物法庭的設置概念與我國現有的少年法院理念與設置概念更爲相近,若能以少年法庭之概念設立藥物法庭,當能更有效處理毒廳問題,提供有效的司法監督與醫療戒癮、社區合作關係。

**討論**:藥物法庭之目的乃在協助藥癮者戒癮並回歸社會,依據藥癮者之狀態,給予合適有效的戒治處遇,並引進社區與醫療支援,協助藥癮者戒癮並回

歸社會,藥癮戒治之實務工作雖有專業團體負責,但藥物法庭仍須掌握藥癮者之戒癮進度、監督藥癮者用藥情形,以及藥癮戒治體系的專業能力。毒品危害防制條例修訂後的緩起訴附帶戒癮命令是我國目前已實施的藥癮者司法轉向制度,但實質上緩起訴附帶戒癮命令與藥物法庭的核心概念仍有相當大的差距,包含個案的診斷評估,以及戒癮管理。

緩起訴附帶戒癮命令制度將司法監督權委外,將個案轉由醫療院所實施戒 癮治療,欠缺司法監督力量的介入與配合,其本質與藥物法庭制度強調司法與 戒癮的共同合作並不相同。且緩起訴制度亦欠缺對個案的篩選與戒癮方案的擇 定欠缺專業性之評估,亦需發展個案的調查篩選與監督執行環節。

國外藥物法庭制度乃適用於有藥物濫用問題之犯罪人,其單純藥物濫用者多由醫療體系與社區治療體系所承接。然我國法令規定仍視施用毒品行為為犯罪行為,而由刑事司法體系處理藥物濫用問題,因此我國藥癮治療多由刑事司法體系承接。與國外藥物法庭制度相較之下,我國欠缺社會資源的協助,包含戒癮機構、安置收容中心、社政、勞政、衛生等政府與民間單位之共通合作。藥癮治療的轉向制度需有良好的社會資源相關環節才能順利實施,但相關的社會資源網絡亦需有足夠的個案來源才有發展專業資源的需求,兩者是互利共生,亦需共同成長。因此需逐漸試辦藥物法庭轉向方案,並扶植社會相關資源的發展,以建構完善的藥物法庭戒癮體系。

#### 國際間毒品先驅化學物質管理制度規範及總體影響之研究

### Research in International Precursors Control Regulation and Total Influence

陳荔形1

Robert Lih-Torng Chen<sup>1</sup>

目的:在國際毒品先驅化學物質管理準則下,我國對於全球相關管制規範應如何因應,為本研究之主要目的。本研究將檢視國際間毒品先驅化學物質的管理制度規範,更進一步介紹目前以及未來國際間對該類物質管理趨勢,著重於國際麻醉藥品管制局之管理制度以及相關「活動」與「專案」的因應措施,提出我國未來毒品先驅化學物質管理制度之作爲。

**方法:**本研究在研究方法上,兼採「文獻探討法」、「歷史研究法」、「比較分析法」以及「訪談分析法」。

**結果**:本研究建議管理機關單一化,各國的管制大多皆由單一機關爲之, 且多數爲衛生單位,因此本研究建議應修法使管制藥品原料及先驅化學品工業 原料統一由管制藥品管理局管理。

**討論:**加強國際合作,透過區域性組織、非政府組織及學術單位之交流來 與國際接軌。

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#### 美沙冬替代維持療法-網絡服務計畫模式

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背景:2005年雲林縣內毒癮愛滋病患暴增,毒癮者相關犯罪頻繁,2006年 10月以醫院爲治療核心開辦美沙冬替代維持療法,然縣境近海鄉鎭精神醫療缺乏,患者規則就醫困難;本案整合醫療、公衛體系、矯正機關、社政、教育及就業等有限資源,營造有利於病患治療的客觀環境。

方法:以『標竿學習』『外展社區給藥點模式』『人員教育訓練』『區域網絡會議』『區域資源整合』方式進行機構網絡建構;推動『新生活護照』,強調病患自主健康管理,鼓勵家屬成爲治療伙伴。

成果:縣內毒癮愛滋病新增通報數降到 47 人(年度);本院治療中病患穩定維持在 200 人(±),平均出席率 77%,退出率為 28.75%,整體轉診人數 230 人,縣內佔 159 人,每月在衛生所服藥者約有 70 人;持續治療 1 年以上的有 117 人;54%病患自陳海洛因使用降至 4 次/月以下(尿液陽性率 41.83%);治療一季後,有工作比例提高 24%。

討論:本模式在創造適合醫療的外在環境,獲『健康促進醫院創意計畫獎』 肯定及『2008|SNQ』認證,凸顯醫療匱乏地區,以網絡服務模式可以獲致最大 綜效。網絡間不強調醫療競爭,營造伙伴關係,交流經驗提昇治療能力,降低 危險,以『新生活護照』作爲醫、病、家屬及機構間溝通的橋樑,回歸到案主 『自主健康管理』的核心價值。現階段病患工作不穩定性尚難克服,預期團體 心理治療、職能治療等專業介入,及善用就業與社團資源,應能獲致改善。持 續有高度生活危機的病患,加強團體心理治療、個案管理照護,降低對周遭環 境及病患自身危害。

#### 保護管束戒癮團體成效研究

### Outcomes of Group Psychotherapy on Parole Subject with Substance Abuse

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目的:根據法務部統計(2006),有毒品前科之再犯人數比例,從民國86年至91年,由58.8%上升爲65.6%;而觀察勒戒期間再度違反毒品危害防制條例之再犯者亦達43.9%;經戒治出所後再犯比率亦達36.7%。因此,地檢署觀護人室嘗試與醫療單位合作,以團體治療搭配原本的觀護制度,期能改善毒品的再犯情形。而本研究目的則爲探討保護管束結合戒癮治療團體方案之處遇成效。

方法:對於士林地檢署甫出監有吸食毒品前科,保護管束時間在一年以上者,以隨機分配分為兩組,有效樣本中實驗組有9案,對照組有12案。研究者在團體前後一個月,以生活品質量表及觀護期間採尿與犯罪行為評估資料工具,對兩組進行施測。實驗組除提供團體治療,並在每次團體後藉由團體療效因素量表來搜集成員在團體中的反應。團體爲配合觀護制度安排每月進行一次。團體設計以心理動力團體爲團體進行的架構。

結果:實驗組十個月後的再犯罪率為 0.00%,對照組的再犯罪率為 33.33 %。而生活品質方面,在一為藥廳者而設計的量表中,參與團體組的生活品質主觀滿意分數顯著高於非參與團體組。但另一方面,若以為一般人而設計的生活品質量表上,則剛好有相反的結果。

**討論**:此整合觀護與團體治療的方案,就降低犯罪率而言,結果優於無團體治療介入組,相較於過去衛教式的團體模式毒品再犯率 30%,此團體亦出現較佳的表現。在生活品質量表的表現上,推測是對藥廳者的生活品質界定內容與一般人的界定有所不同所致。

#### 受保護管束人海洛因及安非他命藥癮治療團體

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目的:藥癮患者之治療,在臨床上夙爲難題。通常除藥癮外,他們也會合併其它精神科診斷,而人格違常亦是常見。藥癮患者常常易衝動、暴力、自傷、對治療缺乏合作及呈現多種社會心理問題,例如婚姻問題、家庭解組、社會及職業功能不佳、犯罪及觸法等。針對曾服刑之藥癮患者之治療,屬司法心理治療之範疇,其施行須細密思考,方可確保安全及療效。本次團體治療以假釋、緩刑中受保護管束人爲對象組成輔導團體,針對成癮藥物的認識及影響、藥物濫用與藥癮問題、愛滋病認識、家庭婚姻問題、及生活休閒與適應等,以精神醫療專業團隊知能,進行團體諮商與治療,希望協助成員正確認識藥物,培養拒絕誘惑的高危險情境與阻斷再犯的能力,藉以遠離毒品避免再犯。

方法:經臺灣士林地方法院檢察署以委託辦理方式,由台北榮總精神部承辦一年的團體方案,從 2006年2月起由地檢署轉介個案來醫院評估,共篩選14位個案進入團體(男性13人,女性1人)。4月起,每月進行一次,每次2小時,共計有8次。地點由地檢署安排。團體由兩位治療者共同主持(含一精神科醫師與一觀護人),治療團隊全體成員亦在團體內,全程錄影,以供記錄和討論,錄影帶遵循保密之治療倫理原則,並不外流。參與治療之成員簽名同意錄影。每次團體結構設計爲:前45分鐘以不同主題進行衛教,接著團體互動75分鐘,採支持性和認知行爲導向的治療策略,強調復發預防。承辦第1年,經成員正向反應,第2年即2007年,延用類似團隊治療模式續辦一年。

結果:2006年第一次團體共14人進入團體,13人爲男性,只有1名女性。團體中期有2人離開團體,一爲HIV陽性反應並再度用海洛因被警查獲;另一人則吸食安非他命。在團體過程中另有二位成員涉及法律案件但與毒品無關。另有一成員有輕微安非他命精神症。2007年第二次團體共13人進入團體,皆爲男性。於團體過程中,陸續有3人再犯,另有1人假釋期滿而離開團體。每次團體出席率因成員須向觀護人報到尙穩定,但時有遲到現象。二次團體結束前成員的回饋,半數以上皆肯定從團體過程中,獲得藥物和AIDS相關知識、對自己心理問題有進一步的了解、對自己的行爲更有控制能力、並知道在面對藥癮問題時,自己並不孤單、情緒有得到支持且更有信心。多數表示,團體討論並分享比單純上課好接受。成員並反應這樣的團體最好在出獄前或出獄後半年

內進行較好。

討論: 1. 兩次團體相較,第二次團體成員出獄後不到一年,在 8 個月的療程中,團體有 13 位,3 人 DROPOUT,第 4 人也坦承用藥,所以再度用藥的比例為 4/13(30%)。可見出獄後的第一年,再犯的風險甚大。 2. 衛教的安排,佔去不少時間,團體之互動時間遂變少,殊爲可惜。 3. 如再度進行如是團體,依這 2 年經驗,對安全的顧慮應可較放心,宜精簡治療團隊,並將主題集中在預防再犯和減害。帶團體方式,可考慮依主題,每次用簡答問卷,順其答覆帶話題。

#### 家庭支持對於藥物濫用者藥物渴求及復發意向之影響研究

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目的:檢視相關的文獻與報導,藥物濫用者能夠順利重返社會、戒除使用毒品的行為,家庭扮演極爲關鍵的角色。相關研究指出,受戒治人在所期間,有無親屬接見與出所之後再犯毒品罪之比率有顯著關係。假若家人的探望可以視爲家屬對於身在牢中親人支持的型態之一,則可進一步假設家人支持對於藥物濫用者復發的意向可能會有影響。因此家庭支持對藥物濫用者的藥物渴求及復發意向會有何種的影響是本研究的研究目的。

方法:本研究將採用問卷調查的方式進行,研究樣本選定以南部某戒治所為取樣的單位,並針對於戒治所內約600受戒治人進行全面性的施測,無意願參與研究者則排除取樣。問卷填答採用自填試問卷,家庭支持量表部分改編自余雅惠(2006)的家庭支持量表,受試者就自己對家庭內情感性支持、訊息性支持及實質性支持之家庭支持狀況感知程度,透過量表分數表示。用藥物的渴求信念程度,採用林瑞欽與黃秀瑄(2003)用藥渴求信念量表(craving beliefs questionnaire)加以測量,量表只有一個渴求因素。復發意向量表採用由林瑞欽與黃秀瑄(2003)所編修之復發預測量表(relapse prediction scale)加以測量。量表計39題,量表計有情緒引發、毒品接觸引發、情境引發等三個因素。分析部分將以單因子變異數分析檢驗個人基本特性資料與家庭支持度、用藥渴求及復發意向,兩兩變項之間的關係。以皮爾森積差相關分析檢視家庭支持、用藥渴求與復發意向三個變項之間的關聯性情形。以多元逐步迴歸分析,探討家庭支持用藥渴求對於復發意向之預測解釋力。

**預計研究成果**:研究結果將可以讓研究者及相關的實務工作者更清楚知道,引起藥物濫用復發心理因素(用藥渴求)及環境因素(家庭支持)間的相關性,提供藥物濫用處遇實務工作者在設計家庭支持方案上作爲參考,以協助藥物濫用者與其家庭獲得更有效之戒癮策略與方法。

## 接受美沙冬替代療法之成癮患者社會參與概況之探究一以桃園療養院個案爲例

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目的:許多研究報告及實務工作者均指出,海洛因成癮者多有人際與社會 疏離的問題,其形成的原因除了成癮者個人特質、家庭問題或偏差次文化之外,還包括:(1)刑罰對海洛因成癮者的長時間監禁,中斷了原有的人際與社會關係;(2)受到使用毒品及有關行為的標籤化影響,使成癮者與他人間產生了心理上的隔閡;(3)毒品次文化之拉力——成癮者在其中較容易生存與獲得部份人際歸屬的滿足;(4)成癮者在生理與心理上對海洛因的依賴,阻礙了成癮者拓展與走入其他人際社群的機會...等等。自95年政府實施戒治醫療整合計畫及美沙冬替代計畫以來,臨床實務上發現,一旦海洛因成癮者想戒除時,接踵而來要面對的便是如何修復或重建人際與社會關係之問題,也發現其社會參與情況並不踴躍,有些人即使有工作,也缺乏適當休閒興趣、人際互動及社區參與,此將影響其社會資源的運用、生活壓力的調適及自我概念的提升,而難以跳脫社會邊緣人的困境,此勢必影響美沙冬替代療法之成效,因此擬探討接受美沙冬替代療法之成癮者,其在社會生活適應部分之狀況及困難,據以研擬相關治療輔導措施,協助其重返主流社會場域,預防其再繼續使用毒品。

方法:以在桃園療養院接受美沙冬治療之成癮者,治療一週以上爲研究對象,共計 1111 位。資料蒐集包括:(1)設計社會參與自塡問卷,隨機調查 439 位(2)由門診電腦檔案查閱受試個案基本資料(包括年齡、性別、教育程度)、使用毒品年齡、美沙冬治療時間、每週服用美沙冬次數、是否曾使用其他毒品等事項。資料分析使用 SPSS 進行統計分析。

結果:在基本特性分析中,第一次接觸毒品年齡以21歲至25歲(31.7%)最多;16至20歲(19.1%)、26至30歲(19.6%)次之。經濟來源完全自給自足(62%),有負債(48.1%),覺得入不敷出(31.2%)。接受替代療法前已有工作佔58.8%,而接受替代療法後有工作者則提高至82.9%。人際關係方面,仍與有使用毒品的朋友往來者佔52.2%,與接受美沙冬的朋友往來的有53.7%,完全沒有朋友佔26.65%。目前仍感到有困難問題不知如何處理的人有45.1%,其中以有經濟問題(54.6%)最多,其他依序爲情緒(29.5%)、家庭(28.4%)、工作(27.3%)、健康(24.6%)、法律(20.8%)、兩性情感(19.1%)、婚姻(10.9%)及人際問題(6%)曾經使用其他毒品、已感染HIV病毒、有案待審理或執行以及喝藥劑量較高的成癮患者,較不易完全脫離使用毒品的交友圈,亦可能爲中斷治療及復發的高危

險群。主觀感受治療後之社會參與變異狀況以經濟生活(76.8%)及穩定工作(81.1%)為最多。

討論: 研究結果顯示,接受治療的持續性與工作的持續性有關,而工作的持續性會影響經濟能力,間接也與人際往來、休閒生活有連帶關係,且較年輕的成癮患者來接受治療後,投入政黨/政治活動與公益/志願服務的時間/頻率亦明顯增加,因此若能及早接受治療,並維持治療的持續性,則較可以使原本受阻滯的社會發展重新啟動,故政策上應促進成癮患者接受替代療法以取代刑罰。在實務工作方面,對於有特殊需求的個案,應提供更多的諮商與諮詢服務,並增進成癮者提高工作能力與工作收入的可能性。

#### 強制團體治療於毒品緩起訴個案之應用

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**目的:**本研究的目的在評估毒品緩起訴個案參與強制團體治療的效果,了解毒品犯個案中斷治療及完成治療的可能原因,並評估此強制團體治療模式持續應用的可能性。

方法:研究針對 41 位被判緩起訴的毒品犯,進行四個梯次,每梯次爲期 24 週的強制團體治療,比較完成團體組與未完成團體組之間的差異。

結果:完成團體治療與中途退出治療的毒品犯在統計資料上顯示性別、年齡、毒品前科、非毒品前科、使用毒品的種類與時間長短、以及教育程度各變項間無顯著差異。團體過程中,無法完成團體者其缺席次數,遲到次數,以及尿液毒品篩檢呈陽性反應的比例,與完成團體者之間達統計上的差異。而持續使用毒品者,較無法維持規律的工作。

結論:從基本資料(demographic data)以及過去的犯罪史與毒品使用史,無法預期強制治療的結果。完成團體的毒品犯在減少毒品使用行為上有明顯的效果。團體治療過程中缺席、遲到、工作情形、與毒品陽性反應,可以預期毒品犯是否無法完成治療。此外,以毒品犯個案在團體中生活分享的內容來看,規律的生活作息、與家人關係良好或有改善,以及家人若積極與治療人員聯繫,皆有助於毒品犯完成團體治療且減少再次使用毒品的機率。

海洛因成癮減害藥物維持治療(於台灣施行)提前終止個案終止原因 探討

To Investigate the Drop-out Causes between the Maintenance Treatment for the Heroin Depender by the Methadone or Buprenorphine in Taiwan

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目的:海洛因對人體危害及社會成本之付出,相當明確。國外成癮者減害治療已實施數十年,成效及相關文獻研究甚豐,然我國直至 2006 年才開始試辦,相對缺乏我國本土相關資料。無論國內外之研究大都著重於其治療效果上之差異與影響,較少著墨提前終止個案之探討,因此本研究試圖比較國人接受兩種替代療法藥物之治療過程提前終止個案資料差異,進行分析進而探討終止原因之相關因素,提供本土性之資料,以供未來毒品防治政策推動之參考。

方法:以南部某精神專科醫院於 2006 年 4 月至 12 月期間參與海洛因成癮者減害治療計畫,由精神科專科醫師初診評估符合鴉片類成癮診斷(DSM-IV-TR),且使用海洛因時間長達一年以上者,以抽籤方式決定處方藥物種類 Methadone(M)或 Suboxone(S),進行前瞻性追蹤研究。研究對象需遵守服藥規定(每日服藥、定期回診、完成指定檢驗項目,若無法來院服藥需事先請假)。個案服藥缺席達十四天者,經醫師同意退出並停止其服藥資格。研究期間共收案 150 人,追蹤累積服藥達九個月,退出 91 人,留置 59 位。追蹤收集分析兩組個案相關資料,進而探討終止原因之相關因素。

**結果**:研究期間收案150人,扣除服藥缺席41人(45.1%)、入獄26人(28.6%)、轉緩起訴8人(8.8%)、自行退出7人(7.7%)、轉他院3人(3.3%)、協商完治與因病退出各2人(2.2%)、違反服藥規定與轉自費各1人(1.1%),累積服藥滿九個月留置爲59人(39.3%),其中M組38人,S組21人;退出91人,其中M組32人,S組59人。M與S兩組個案人口學資料、非法物質使用經驗、自陳疾病及初診傳染病上均未達統計上顯著性差異(α=0.05)。而在初診傳染率方面,兩組個案具C型肝炎的比例均達九成以上,說明C型肝炎爲藥癮者的高傳染病。

M 與 S 兩組退出原因分析,服藥缺席、入獄、轉緩起訴、自行退出、轉他

院、協商完治與因病退出、違反服藥規定等均未達統計上顯著性差異(α=0.05)。 但其中服藥缺席(M組 31.3% S組 52.5% p-value 0.051)及因病退出(M組 6.3% S組 0.0% p-value 0.052) 雖未達統計上顯著性差異,但兩組差異明顯,是否有其藥物特性差異之傾向值得進一步研究。

討論:海洛因成癮會造成生理及心理依賴,特別是心理依賴往往不是短期的解毒治療能改善或消除的,此部份更是導致海洛因成癮者再犯的重要原因。藉由提供美沙多(Methadone)及丁基原啡因(Buprenorphine)予海洛因成癮者每日使用,減少海洛因成癮者注射使用毒品及共用針具行爲所引發的愛滋等傳染疾病的擴散,進而緩減相關的社會問題,此爲台灣成癮科學研究重要且迫切之課題。

本研究結果對接受兩種替代療法藥物之治療過程提前終止個案資料差異,進行分析並探討終止原因之相關因素,均未達統計上顯著性差異,唯在兩組初診傳染率方面具 C 型肝炎比例均達九成以上,說明 C 型肝炎為藥癮者的高傳染病。而在退出原因部份,其中服藥缺席及因病退出雖未達統計上顯著性差異,但兩組差異明顯,是否有其藥物特性差異之傾向,值得進一步研究。另本研究收案僅九個月,是否足夠看出兩組差異,亦值得繼續追蹤。

但本研究就爲台灣地區同時施行美沙多和丁基原啡因兩種替代藥物爲減害維持治療之早期試辦醫院,藉此分析比較兩種藥物在台灣減害治療提前終止個案之探討,提供本土性資料之目的,是值得鼓勵的。海洛因成癮者減害治療我國直至 2006 年才開始試辦,本土相關資料之建立甚爲缺乏,還需相關研究繼續投入。

#### 成人海洛因和安非他命使用行為復發之前置情境和相關因子研究 Relapse Antecedents for Heroin and Methamphetamine Use and Related Factors in Taiwanese Adults

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目的:物質使用行爲具有高度的復發性,而海洛因和安非他命由於具有高度成癮性、會導致生理心理健康受損,對於個人、家庭、社會造成嚴重的負面影響,有必要深入了解海洛因和安非他命使用行爲復發的議題並發展介入策略。本研究即針對國內成人海洛因和安非他命使用行爲復發的常見前置情境和影響個案做歸因的相關因子進行調查,以作爲未來擬定介入策略、進行治療之依據。

方法:本研究擬定「海洛因和安非他命使用行為復發前置情境問卷」,自高雄第二監獄附設觀察勒戒處所中篩選具有符合「曾經嘗試戒除使用該類毒品且維持六個月時間以上未使用但再次使用」之復發定義的海洛因使用者 150 人和安非他命使用者 126 人進行訪談,評估其對於復發前置情境,以及情境種類與個人社會人口學、毒品使用型態、心理健康狀況、毒品使用態度的關連性。

結果:無論是在海洛因或安非他命使用者,「負向情緒狀態」和「人際互動壓力」皆爲最常被歸因的復發前置情境,「自我測試控制力」和「正向情緒狀態」則皆爲較不常被歸因的前置情境;而海洛因使用者比安非他命使用者較常歸因「渴求」爲自己復發的前置情境。同時,有多種社會人口學資料、毒品使用特徵、心理健康狀況和對於使用毒品的態度會與個案對於自己毒品使用行爲復發前置情境的歸因有關。

**討論**:建議依據本研究的結果對於毒品使用者進行包括覺察危險情境、改變認知期待、發展應對技巧的認知行為心理治療,以及對具有會容易做某種復發情境歸因的相關因子者做持續的追蹤監測。

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### Excess death in community reentry: a longitudinal study on the first-time drug offenders in Taiwan

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**Objective**: The purpose of this study was to assess possible excess risk of death and associated sociodemographic and judiciary determinants among the first-time adult drug-involved offenders over the 3 years after release from correctional facilities.

**Method**: A total of 29914 male and 5589 female adults who had served sentence at least one day in correctional facilities for illegal drug-related offenses were identified from the judiciary records of the Ministry of Justice, Taiwan. The underlying causes of death were defined by the International Classification of Diseases, Ninth Revision.

**Findings**: The all-cause standardized mortality ratios (SMRs) for the first-time drug offenders were approximately 3~4, and the cause-specific estimates were even greater than 10 for suicide, homicide, and mental disorders. The hazard of death was gradually increasing till the 10th~15th month after release. Age of 30 or older and the engagement of higher-ranked schedule substance were associated with 2-fold risk of death. Drug-offenders with subsequent re-imprisonment were less likely to die (aHR=0.19~0.42); an estimated 45%~71% excess in mortality was observed in actual drug-using offenders, as indexed by having the experience of receiving observational detoxification or rehabilitation as sentence.

**Conclusions**: Our evidence offers support that sociodemographic and judiciary factors might be associated with differential risk of drug-offenders' premature death in the community reentry and reintegration. This information may have values in the design of policies or intervention to address the healthcare and social welfare needs of drug offenders while transitioning from correctional setting to community.

#### 美沙冬治療藥物監測及其代謝的性別差異 Methadone Therapeutic Drug Monitoring and Gender Metabolic Differences

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目的:美沙冬(methadone)是目前國內廣泛使用於成癮治療的藥物,有鑑於 長期服用美沙冬可能帶來的副作用,以及治療效果的評量,分析病人服用美沙 冬的穩定期間而中濃度,並評量其治療效果成為重要的課題。

方法:本實驗室以高壓色層分析儀設立了美沙多藥物血中濃度監測的分析方法,並開始與臨床醫師合作收集服用美沙多超過一星期以上的病人血液檢體,分析血液中有效的 R-methadone and S-methadone,及其 inactive 代謝物 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine (EDDP),由於催化 methadone 到 EDDP 需經由代謝酵素 CYP-450 的同工酵素 CYP2B6,2C19,and 3A4,因此,本實驗室未來將以 single nucleotide polymorphism (SNP)的基因鑑定方法,研究服用美沙多的病人的代謝狀況與藥效乃至副作用之間的關係。實驗室同時量測 Sprague-Dawley (SD) Rat 母鼠懷孕期間使用嗎啡,美沙多或 buprenorphine 下對幼鼠肝臟 CYP-450 的同工酵素表現量和活性的影響。嗎啡的母鼠實驗較先進行。

結果:在七位服用美沙冬的病人部分發現病人服用的美沙冬劑量可以差異達 20 倍,其 R-methadone 血中濃度有 8 倍的差異存在。動物實驗方面,目前分析有 13 週大(相當於人的青壯期)幼鼠,雄性與雌性老鼠各 15 隻,發現雄性老鼠肝臟的 CYP-450 的同工酵素表現量仍受嗎啡母鼠的影響,酵素的活性則仍在分析階段,雌性幼鼠的表現量在控制組,注射環境毒素 Lipopolysaccharide (LPS)組,嗎啡組,嗎啡和 LPS 組沒有差異。

**討論**:建議研究收案時病人服用美沙多劑量以及因爲藥物間交互作用可能 使得血液中美沙多濃度升高或下降的其他藥物,需特別作註記以利未來研究結 論的分析。其次,美沙多或者嗎啡類成癮藥物在性別間代謝的差異影響是我有 興趣更進一步觀察的方向。

#### 物質成癮的表現型與基因關聯研究初報

### Addiction-related phenotypes and genetic association: a preliminary report

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**目的:**海洛因成癮的成因包括基因、發展、心理及環境因素。以往研究顯示物質成癮的遺傳率介於 0.4~0.6 之間。針對個案物質使用的行爲之外進行表現型的探討有助於進一步的遺傳關聯研究。

方法:研究收集國內高度成癮物質使用的個案約 280 名,進行臨床資料收集、精神疾病共病性評估、衝動性評估、神經心理測驗評估等,並採集 DNA,與正常對照組進行 OPRM1、DRD2、ENO2、OPRL1 的基因關聯研究。

**結果**:以 OPRM1、DRD2 進行 tag SNP genotyping,統計無顯著差異;以 ENO2 與 OPRL1 進行 tag SNP genotyping,顯示統計達到顯著差異(包括 ENO2 的 rs11064464、rs3213433、rs10849541 以及 OPRL1 的 rs6090043, rs2229205)。

**結論**:物質成癮的臨床表現型顯示出個案相當程度的異質性。進行遺傳關聯研究,應對此部分進行個案分群,以便應用基因關聯研究法時,增加研究結果的可靠性。

# Study of Cardio-physiology and Heredity in Heroin Addiction and Methadone Maintenance Treament (CHHAMMT Study)

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**Background:** Heroin is the most popular illegal substance of abuse in Taiwan. Methadone has been introduced to actively prevent heroin use and reduce the harms associated with it. During withdrawal, the HPA axis is hyper-activated, evident with the rise of cortisol level, and use of methadone normalizes the activation. Strangely, blockage of cortisol synthesis also causes withdrawal-like symptoms. The oxymoron may imply that lower cortisol level and high sensitivity to cortisol induction are susceptible to heroin addiction. High level of cortisol causes lower vagal activity and this increases the risk of cardiac problems. Although methadone normalizes the hyper-activated HPA function, it also induces QT interval prolongation in many heroin addicts, probably via a non-cortisol pathway. inherited response pattern of HPA axis may determine the susceptibility of heroin addiction and heroin induced cortisol boost, with the price of abnormal cardio-physiology. Additional hints linking abnormal cardio-physiology to heroin addiction come from the studies investigating the use of α2-adrenegic agonists in treating heroin withdrawal symptoms. Furthermore, whole genome scan studies indicated that two genes that related to resting heart rates, namely, ankyrin-B and myozenin 2, may involve in the development of heroin addiction.

**Aims:** We propose to study: (1) prevalence rates of cardiac abnormality in heroin addicts of different methadone maintenance treatment (MMT) history and, time-dosage effects of heroin and methadone on cardio-physiology and (2) role of candidate genes in cardio-physiology, addiction behavior and methadone treatment outcomes. We plan to recruit 300 heroin addicts who enter the MMT for the first time, and 600 sex and age matched controls in 4 years.

**Expected Results:** Current literatures have not been able to compare the cardiac abnormality caused by heroin and methadone on an equal basis. This study should provide further information explaining the role of cardio-physiology in heroin addiction and methadone treatment outcomes, and the contribution of genes.

### Molecular Genetic Study on Addiction 成癮之分子遺傳研究

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**Objective:** There is high relapsed rate in addiction, and so far there are no biomarkers available to predict the risk of relapse. In addition, there is no effective medicine to treat the complication of addiction and to prevent its relapse. The goal of our study is to identify the genetic underpinnings of addiction that can help treat and prevent the relapse of addiction.

**Methods:** We use molecular and functional genomic methods to identify the risk genes of addiction, including candidate genes analysis, differentially expressed genes analysis, and comparative proteomics analysis. In addition, we also use several behavioral modalities in rodents to study the molecular basis of addiction, and screening for new medicine to treat addiction.

**Results:** We have identified several candidate biomarker genes from our current studies. Their potential use in clinical practice needs further evaluation. In addition, we also found several genes that are related to the pathogenesis of addiction in our animal models.

**Conclusion:** The clinic-oriented approaches in our laboratory would help increase our understanding about the pathogenesis of addiction, and also help develop new medicine to treat and prevent addiction in the future.

## Pentoxifylline and Clenbuterol Ameliorate Methamphetamine-Pentoxifylline and Clenbuterol Ameliorate Methamphetamineinduced Cognitive Deficits

Pentoxifylline 和 Clenbuterol 改善甲基安非他命引起的認知缺失

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慈濟大學

**Background**: Methamphetamine (METH) is a potent and highly addictive psychostimulant. Chronic use of methamphetamine (METH) results in long-term cognitive deficits which might be related to microglial activation. Pentoxifylline, an inhibitor of phosphodiesterase and a non-selective antagonist of adenosine receptor, and clenbuterol, a  $\beta 2$  adrenergic receptor agonist, exhibit neuroprotective activity and inhibit the production of microglial activation.

**Objective:** The purpose of the study is to evaluate the therapeutic effect of pentoxifylline and clenbuterol on METH-induced behavioral deficits in mice.

**Methods**: Male ICR mice were either treated with METH (4×5 mg/kg, s.c., 2hr apart) or METH (2.5 mg/kg, s.c.) every other day for 8 injection. Novel object recognition test (NORT) was examined. Subsequently, pentoxifylline (10 mg/kg, i.p.) or clenbuterol (1mg/kg, i.p.) was given acutely or subchronically for seven days. NORT was examined again.

**Results**: Both METH treatment regimens produced significant cognitive impairment in NORT. Acute administration of pentoxifylline and clenbuterol did not affect the cognitive deficits induced by both METH treatment regimens, whereas subchronic administration of pentoxifylline and clenbuterol for 7 days ameliorated the cognitive deficits and the effects were lasted for at least 1 week.

**Conclusion:** These findings suggest that pentoxifylline and clenbuterol might have the therapeutic potential for treating cognitive deficits in METH abusers.

### 美沙冬對海洛因成癮個案衝動性改善之探討

# Decreased Impulsivity of Heroin Dependence Subjects in Methadone Maintenance Treatment

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目的:研究顯示衝動性與物質濫用及其他精神疾病相關。本研究針對美沙 冬門診之海洛因成癮個案,以巴氏衝動性量表(以下簡稱BIS)、及測量衝動性之 兩種神經心理測驗—Stop signal task (簡稱SST)及Immediate memory task /Delay Memory task (簡稱I/DMT),評估美沙冬對於海洛因成癮個案的衝動性之影響。

方法:實驗組爲在美沙多替代療法門診中,符合DSM-IV海洛因成癮診斷之98名男性個案,分別以BIS, SST, I/DMT評估其衝動性。測驗結果經適當品管指標篩選後選取60名個案,另以相同方式及標準,在戒治所及看守所附設勒戒所中篩選強迫戒癮之海洛因成癮男性共99名爲對照組。兩組之臨床資料及施測結果以SPSS統計軟體建檔並分析。

結果:兩組之教育年數無統計差異,但年齡達統計差異(雙尾t檢定,p=0.01)。以BIS 分數測量衝動性格,兩組分數在統計上無顯著差異(雙尾t檢定,p=0.989)。在SST方面,實驗組之mean reaction time (MRT) 及 stop-signal reaction time (SSRT) 均短於對照組,且達統計上之顯著差異(p<0.001)。在I/DMT方面,實驗組之IMT平均反應速度(response latency)比對照組短(p<0.001),DMT平均反應速度亦達統計上之顯著差異(p<0.05)。另外,實驗組之post error slowing (PES) 比對照組長,但未達統計上之顯著差異。

討論:和處於強迫戒癮狀態的對照組相比,服用美沙冬之海洛因成癮個案, 其衝動指標SSRT 明顯較短,代表服用美沙冬後在某些衝動行為的抑制上有改善,由於實驗組之MRT 短於對照組,故可排除其衝動抑制來自於藥物鎮靜效果。而實驗組之IMT/DMT平均反應速度較短,亦可再度佐證其衝動抑制並非來自於藥物鎮靜效果,且此衝動抑制並非局限於單一衝動指標。此發現在臨床上之意義,值得進一步探討。

### 美沙冬替代療法個案的尿液監測

# The drug monitor in patients treated by methadone maintenance therapy

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**目的:**本研究的目的是探討接受替代療法的海洛因成癮個案使用其他非法物質或醫療用藥品的情形。

方法:本研究為一橫斷性研究,選擇台灣南部專科醫院接受替代療法的海洛因成癮個案為研究對象,建立個案基本資料,並以初診時留取的尿液為分析對象,以 BIO-RAD REMEDI<sup>TM</sup> HS Drug profiling system 廣譜藥毒物分析系統套裝試劑分析個案尿液中含有的藥物成分。

**結果**:本研究共收案 278 名,篩檢各種非法及合法藥物使用的盛行率,發現以嗎啡類物質最高佔 88.8%,安非他命類佔 19.8%,Tramadol 佔 11.5%,抗精神病藥物 9.0%,其他物質的使用也高達 55.8%。

**討論**:根據研究結果顯示使用海洛因的個案其合併使用其他物質的比例相當高,此部分與國外文獻的結果相當類似。美國合併使用中樞神經興奮劑者主要以古柯鹼爲主,而本國合併使用的中樞神經興奮劑則以安非他命類爲多。

# DECREASED STRIATAL MONOAMINE RESPONSES TO FLUOXETINE CHALLENGE IN RATS EXPOSED TO PRENATAL LPS AND MORPHINE

(孕期 LPS 以及嗎啡對子代 SSRI 反應的影響)

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**Objective**: Selective serotonin reuptake inhibitors (SSRIs) are of new generation antidepressants. SSRIs (e.g. fluoxetine) increase the extracellular level of serotonin by inhibiting its reuptake into the presynaptic neurons. SSRIs have been used to treat conditions such as clinical depression, anxiety, panic disorder, obsessive-compulsive disorder, etc. Prenatal bacterial endotoxin LPS is known to cause losses of both dopamine and serotonin neurons in the nigra and dorsal raphe nucleus, and prenatal opioid was also known to decrease brain serotonin levels. Thus, we hypothesize that animals prenatally exposed to LPS or opioid will have altered responses to fluoxetine challenge. In the current study, we investigated the postnatal effects of prenatal LPS and opioid exposures on the brain monoamine responses using fluoxetine challenge

**Method**: Twenty four gravid female rats were divided into four groups and injected with saline, LPS (10,000 units/kg at E10.5), morphine hydrochloride (2 to 4 mg/kg with 1 mg/kg increment per week from E3 to E21), or combination of LPS and morphine. Twenty three adult rats were randomly selected from each of 23 litters for striatal microdialysis and HPLC monoamine analysis. For collection of samples, probes were inserted into striata and fixed to the skull with dental cement. Twenty four hr later, samples were collected 40 min before and 160 min after fluoxetine injection (5mg/kg) at 20 min interval.

**Results**: Prenatal exposures were found to decrease striatal dopamine metabolite (HVA plus Dopac) levels ( $F_{3,275}$ =5.937,P=0.001) and serotonin metabolite (5-HIAA) levels ( $F_{3,275}$ =7.369,P<0.001) following fluoxetine challenge.

**Conclusion**: Results suggest that prenatal environmental toxin LPS and opioid (morphine) were able to adversely affect offspring dopamine and serotonin systems. The clinical implication of the current study could be rather significant.

回目次

### 精神科門診病人的吸菸率

### Prevalence of Tobacco Smoking among Psychiatric Outpatients

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**目的**:有許多的原因精神科醫師應該瞭解其病人的吸菸狀況,因爲吸菸改善情緒,戒菸使情感和認知功能惡化,使用菸品減低藥物的療效,也使很多精神作用藥物的副作用加劇,亦影響精神疾病的病程,讓人縮減壽命。國外的研究顯示精神疾病病人的吸菸率高,一些疾患尤甚。本研究探討幾種常見的精神疾病如精神分裂症、重鬱症、酒精依賴、海洛因依賴門診病人的吸菸率與相關的因素。

方法: 研究樣本爲台灣中部一家醫學中心精神科門診,年齡爲 18 歲及以上的病人,單一診斷需符合美國精神醫學會出版的精神疾病診斷與統計手冊第四版的教科書修正版的精神分裂症、重鬱症、酒精依賴、海洛因依賴的診斷標準。經過精神科與專科醫師進行會談及精神狀態檢查,填寫問卷與量表,再將資料作成紀錄整理,以電腦軟體 SPSS/PC+ 作統計分析。

結果:共完成 1045 位符合條件的病人的會談調查,男性為 732 人 (70.0%),女性為 313 人 (30.0%)。精神分裂症、重鬱症、酒精依賴、海洛因依賴的病人數目分別為 233 人、301 人、211 人、300 人;吸菸率分別為 31.8%、30.9%、84.8%、94.7%,男性的吸菸率遠高於女性,大多數的病人明瞭吸菸有害健康,多數有戒菸的想法。

**結論**:精神分裂症及重鬱症病人的吸菸率和一般人無差異,然而物質依賴病人的吸菸率則遠高於一般人,應設法解決此問題。

# Elder heroin addicts under methadone maintenance therapy in central Taiwan

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**Background**: Heroin addict is a chronic disorder and easily recurrent relapse. Heroin addict in elder adults is a growing problem. Methadone maintenance therapy could reduce or eliminate the use of heroin. It also improved health, criminal and social economic problems. However, there is limited data associated with elder adults. Here, we reported elder heroin addicts treated with methadone in central Taiwan.

**Method**: We enrolled heroin addict elder adults, which over 50 year-old, receiving methadone maintenance treatment in the four hospitals in the central Taiwan since November 2006 to October 2008. We collected their demographic data. We tried to investigate the relative factors associated with retention rate.

**Result :** We collected 228 heroin addict patients, who are older than 50 years old and joined methadone treatment program. There are 8 female patients and 220 male patients in the sample. More than half (53%) are occupied. Most of them used heroin since their thirties age or forties. The average years of heroin use is 14.86 years. Most of them used heroin by vein injection and smoking. 15 patients in the sample are HIV carriers. 40% patients kept the methadone treatment, 58% patients dropped out, and 2% patients had incomplete data. In the drop-out patients, we lost contact with them mostly (72%). Some of them (14%) stopped methadone treatment by their own asking. We found that female elder adults have higher retention rate than males. We found there's no relationship between retention rate and heroin using style, or occupational status, or education level or marriage status. Longer heroin users had more criminal record and higher heroin using dosage.

Conclusion: Though the reliability of data from these patients should be careful. But elder heroin addicts and treatment with methadone maintain therapy is public health problem and growing problem. They are different with young adults in metabolism, comorbidity, and economic status. Further studied in this population is need.

# **Prenatal Morphine Exposure Accelerated Postnatal Tolerance Development in Rats**

(孕期嗎啡暴露加速子代嗎啡耐受性的形成)

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**Objective**: Abuse of addictive substances is a serious problem which has significant impacts on health, economy, public safety and society. Uses of heroin in young women at reproductive ages have drawn much attention around the country. In this study, an animal model was established by prenatal exposure of female rats to morphine. The offspring of exposed rats were studied for development deficiency and possible mechanisms.

**Method**: Female pregnant Sprague-Dawley rats received morphine hydrochloride, 2 to 4 mg/kg (1 mg/kg increment per week), subcutaneously, twice a day from E3 to E21. These animals were allowed for normal delivery. The offspring were tested for the anti-nociceptive effect by tail-flick test. Rats were put in a restrainer for 5 min for adaption before the tail-flick test. The I.R. (Infrared) intensity of tail-flick machine was set at 45, and the cut-off time was 10 sec. Rats were subjected to the tail-flick procedure once a day. The measurement procedure was performed before morphine injection (10 mg/kg) and every 30 min after for a total of 3 hr.

**Result :** There were no obvious behavioral abnormality and body weight change being noted during the growing period (8-12 weeks) in prenatally morphine-exposed offspring. However, when the male offspring received morphine hydrochloride injection twice a day for a duration of 4 days, the prenatally morphine-exposed animals developed faster morphine tolerance as evidenced by the anti-nociceptive response determined by tail-flick tests ( $F_{1,18}$ =16.14, p<0.001). At the 4<sup>th</sup> day (7<sup>th</sup> injection) after daily administration of morphine hydrochloride, the area under curve (AUC) in tail-flick test showed 35 % decrease (t-test, p<0.001) in prenatally morphine-exposed animals relative to prenatally saline-exposed animals. The female offspring also exhibited similar results.

**Conclusion:** The data suggest that the prenatal exposure of morphine affects neural development in the brain. The results also indicate a non-reversible toxicological effect of morphine on the animals even when they reached their adulthood.

# Systemic Increase of Oxidative DNA Damage Correlates with Alcohol Withdrawal Severity in Patients with Alcohol Dependence

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**Objective:** Free radicals that induced lipid peroxidation and DNA damage have been implicated in some neurodegenerative disease, including Parkinson's disease and Alzheimer's dementia. Alcohol withdrawal is also associated with the mechanism of neurotoxicity. This study aims to investigate the status of systemic oxidative damage by measuring plasma malondial dehyde (MDA) level and 8-hydroxydeoxyguanosine (8-OHdG). We also explored the correlation between early alcohol withdrawal severity and these two oxidative stress markers.

**Method**: Eighty-four inpatients fulfilled the DSM-IV-TR criteria for alcohol dependence and sixty-three healthy controls were enrolled. Serum MDA level and 8-OHdG were measured within 24 hours of alcohol detoxification. The severity of alcohol withdrawal was evaluated by Chinese version of Clinical Institute Withdrawal Assessment-Alcohol revised (CIWA-Ar-C) every 8 hours. Average and highest scores of CIWA-Ar-C at the first day were recorded as the baseline withdrawal severity. We compared the differences of MDA and 8-OHdG levels between groups, and examined the correlation between baseline withdrawal severity and oxidative stress markers.

**Results**: Compared to controls, serum MDA and 8-OHdG levels were significantly elevated in alcoholic patients. MDA levels improved, but not 8-OHdG, after one-week detoxification. After controlling other significant variables, 8-OHdG was significantly correlated with the average ( $\beta = 0.48$ , p = 0.005) and highest ( $\beta = 0.49$ , p = 0.005) CIWA-Ar-C scores at the first day of detoxification.

**Conclusion**: Alcoholic patients encountered high oxidative stress. Notably, the 8-OHdG levels maintained significantly elevated despite the MDA had reduced following early withdrawal. Our data also demonstrated a significant correlation between 8-OHdG levels the severity of alcohol withdrawal symptoms.

**Key words**: oxidative stress, malondialdehyde, oxidative DNA damage,

8-OHdG, alcohol withdrawal

回目次

### 身體質量指數在海洛因濫用者(合併HIV感染或無HIV感染)之分佈 Body Mass Index distribution in Heroin Addicts with HIV or without HIV infection

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目的:藥廳者通常會花較多時間及金錢去尋找及使用毒品,因而忽略對自身之健康照顧;較少注意本身之身體質量指數(Body Mass Index簡稱BMI)。因此,本研究目的在分析海洛因濫用者BMI之分佈。另外進一步探討BMI與美沙冬劑量之潛在相關性。

方法:回溯分析274位來自美沙多維持療法門診病患,診斷符合DSM-IV鴉片類物質依賴。分析初診時記錄之身高和體重,BMI值計算方式爲體重(公斤)除以身高(公尺)平方。BMI值大於24,定義爲體重過重(overweight)。以臺灣地區一般族群爲控制組(National Nutrition and Health Survey in Taiwan, 1993-1996),22.9%男性和20.3%女性屬於體重過重。並同時分析美沙冬之起始劑量、維持劑量以及和BMI之相關性(partial correlation,已校正性別、HIV、HCV等因子)。

**結果**: 其中 218 位爲男性,56 位爲女性,平均年齡 34.4(SD:5.8)歲。BMI 平均值 22.9(SD: 3.1),美沙冬起始劑量平均值 38.9mg/day (SD: 5.5)和 BMI 之相關性 (partial correlation coefficient, r= 0.146, p=0.016)及維持劑量平均值 62.9mg/day (SD: 24.5)和 BMI 之相關性 (r= 0.162, p=0.008)。HIV 感染組 (n=89),BMI 平均值 23.0 (SD: 3.4)。在非 HIV 感染組 (n=185),BMI 平均值值 23.0 (SD: 2.9)。兩組並無統計上之顯著差異(independent samples test, p=0.69)。HIV 感染組有 15.7% 病患 BMI 低於 20(BMI 最低值: 16.7)。有 28.2%男病患 (n=71)和 44.4% 女病患 (n=18)BMI 高於 24(BMI 最高值: 33.7)。在非 HIV 感染組有 16.8%病患 BMI 低於 20 (BMI 最低值: 17.5)。有 39.5%男病患 (n=147)和 15.8%女病患 (n=38)BMI 高於 24(BMI 最高值: 33.3)。

討論:從以上資料顯示,初診 BMI 値和美沙多之起始劑量、維持劑量皆呈現統計上有意義之正相關,也許可當作臨床上美沙多劑量給予之參考指標之一。在 HIV 感染組,有 15.7% BMI 低於 20,即符合消瘦徵候群(wasting syndrome)定義之一;這也顯示可能潛在營養不良、免疫力不佳及感染之危險。因此當 BMI 過低之藥癮者進入戒癮治療之同時,營養之相關衛教是必要的介入。BMI 高於24 之體重過重藥癮者,在 HIV 感染組之女病患,是一般族群之2.2 倍。在非 HIV 感染組之男病患是一般族群之1.7 倍。因屬於代謝徵候群(metabolic syndrome)之高危險族群;適當運動及飲食之相關衛教也需一起納入戒癮治療計畫之內,以增進病患持續就醫之意願及減少未來相關醫療支出。

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### 台灣北部地區物質濫用/依賴者心理防衛模式之探討

### An Exploration of Defense Styles among Substance Abusers/Dependants in Northern Taiwan

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**Objective**: Researches have shown that defenses mature with age and the maturity of defense style is related to physical and psychological health. Defense mechanisms and the strategies of personal existence were found influential in substance misuse. The psychological defense styles of substance abusers and dependants were assessed and compared with those of the control group. Differences of defense styles among sub-groups of different drug choices were also probed as well in the present study.

**Methods**: 1069 participants, age range from 19 to 60, involved in the present study in between Oct. 2005 and Sept. 2007. 370 students (22.2± 4.2 years old) from 2 colleges and one university in northern Taiwan participated for the control group. 652 substance users (31.8± 8.2 years old) in a detention center and 47 participants (36.3± 9.8 years old) who went for out-patient addiction treatment in a psychiatric hospital in northern Taiwan were assessed using Defense Style Questionnaire as that was performed for the control group. The 2-week test-retest reliability of Chinese edition Defense Style Questionnaire was 0.87. Factor analysis was done for the questionnaire and was comparable to the original one. SPSS was used for data management and analysis.

**Results:** There were significant differences in demographic variables between groups of control, detention center and out patient participants (OPD), especially in variables of age, years of education, and frequency and duration of substance use (p<0.01). Age of the OPD group participants was significantly greater than that of the detention center and control group, as the control group was the youngest. The OPD group held significantly greater frequencies and longer duration of substance use than that of the detention group ( $4.5 \pm 3.4$  vs.  $1.9 \pm 2.6$  times/per day;  $113.8 \pm 105.3$  vs.  $20.1 \pm 37.7$  months). The outpatients reported more immature and neurotic

defense styles and was significantly greater than the ones in detention center (p<0.01). Participants in detention center applied neurotic defense styles more than that of the controls (p<0.01) significantly. There were also significant differences in sub-groups of heroin, amphetamine, combine usage of heroin and amphetamine, and other substance users (marijuana, ketamine, MDMA), particularly in variables of age, education, and tendencies of using mature defense styles (p<0.01). Other substance users reported more mature defense styles than that of the other sub-groups (p<0.01).

**Conclusion:** The results of present study not only indicated that defenses mature with age and are related to substance use, but also showed that the more immature defense styles performed, the severer of substance use, the worse life function of the substance users are. In order to improve the efficiency of substance addiction treatment, it is beneficial to assess clients' defense styles and formulate related treatment programs to enhance the development of defenses. Therefore, the more mature defenses will be performed and better strategies of personal existence can be applied to adapt varieties of life stressors.

# Explore The Role of MAPK Signaling In Methamphetamine-Induced Place Preference: Acquisition, Extinction And Reinstatement By Stress

MAPK 訊號在壓力所引起的甲基安非他命復犯行爲中所扮演的角色

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**Objective:** Drug abuse and reinstatement has become a severe social problem in nowadays society, it is important to delineate the downstream mechanism in order to provide valid solution. Stress is a well-known social factor which can trigger addiction relapse, but the involvement of stress-induced cellular events and its neural circuitry links with drug relapse remain unclear. According to above information, we attempt to establish an animal model of conditioned place preference to paired methamphetamine (METH) that can reinstate the METH relapse by physical stress after extinction training and explore the downstream molecular mechanism.

**Methods**: Conditioned place preference is one of the effective ways to distinguish drug addiction. The C57BL/6J mice purchased from National Animal Breeding Center were injected with METH then placed into drug-paired compartment for 30 minutes followed by second day of saline injection but placed in vehicle-paired compartment. Those 4 cross-pairing sessions complete an acquisition training, another 4 cross-pairing without METH injection was considered to be extinction training. To initiate METH relapse, extinction-trained mice were stressed by various stressors. Some animals after extinction were implanted bilaterally with cannulas into ventral tegmental area (VTA; A: -0.36cm, L:±0.05, V: -0.4cm). After 5 days recovery, mice received CRF2R antagonist infusion were exposure to stressor followed by preference test. Animals of acquisition, extinction and relapse group were scarified after behavioral test, VTA and nucleus accumbens were dissected out and frozen in liquid nitrogen immediately. Tissue samples were analyzed by western blot or immunohistochmistry for phosphor-p44/42 determination.

**Results**: After extinction session, several stressors were tested and we found that physically restrained animals exhibited maximal ability to reinstate METH preference. Pretreatment with CRF2R antagonist prior to restraint tended to inhibit the stress-induced METH reinstatement. In preliminary results, phospho-ERK1/2 signals were only detected in the nucleus accumbens of stress-induced relapsed animals, not observed in non-relapsed animals.

**Conclusion:** We demonstrate that stress could reinstate animals' drug preference after extinction. In addition, inhibition CRF2 receptor in the VTA tends to attenuate drug reinstatement. These results suggest CRF2 receptors in the VTA appear to play a role in stress-induced drug reinstatement, while the activation of MAPK in the nucleus accumbens could be viewed as a marker for drug reinstatement.

北台灣某戒治所藥癮戒治個案接受醫療戒治合併社區追蹤出所後的再犯率分析初探

Impact of psychiatric intervention and Community Case management on Relapse among subjects discharged from one Drug Abstinence Center in northern Taiwan—a preliminary study

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**目的:**海洛因成癮個案之完全戒癮,有賴於生理、心理及環境因素因素的完整處理。法務部某戒治所個案於強制戒治期間,接受兩家精神專科醫院醫療團隊的醫療處遇,於出所回到社區後接受社區個案管理與追蹤服務。本研究欲瞭解個案接受醫療處遇後出所後再犯毒品罪的比例。

方法:研究收集民國 95 至 97 年間,北台灣法務部某戒治所接受強制戒治 約一年期間接受醫療處遇後出所回到社區者,進行電話追蹤與服務,以每三個 月定期電話追蹤的方式聯繫個案,並針對個案之現況訪談瞭解個案可能需要的 轉介服務提供諮詢與轉介。處遇名單由法務部統計室比對於民國 97 年 1 月至 11 月中毒品再犯名單。以卡方分析失聯 6 個月以上與持續接受追蹤的個案再犯毒品罪的比例差異。

結果:接受醫療處遇與社區追蹤並有再犯資料比對成功的名單中,民國 95 年共 68 人,民國 96 年共 101 人,民國 97 年共 353 人。以失聯 6 個月與否將個案分成兩群,並統計一年內再犯毒品罪接受司法偵察與否將個案分成兩群,進行卡方分析。三年間再犯差異的 p 值分別為 0.021, 0.001,及 0.019,失聯後再犯毒品罪的勝算比分別為 3.94, 4.96 及 3.20。

結論:由於資料取得之限制,本研究無法比對出所後兩週內即失聯以及戒 治期間未接受醫療處遇個案之再犯資料,資料亦無法扣除確實死亡的個案。但 以同樣方式進行處遇與追蹤服務,失聯個案由於成癮復發而再犯毒品罪的勝算 比高達 3.2~4.9 倍。顯示失聯爲個案成癮復發的高危險群,但醫療系統無法進 一步提供協助。建議針對此群個案應有司法系統的積極介入。 北台灣某戒治所藥癮戒治個案出所後的個案管理服務需求分析 Need for case management among subjects discharged from one Drug Abstinence Center in northern Taiwan

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目的:海洛因成癮復發率高,其影響層面也遍及生理、心理及環境因素。個案之完全戒癮,有賴於上述因素的完整處理。個案於法務部戒治所強制戒治期間,接受醫療處遇,於出所後回到社區,若有個案管理服務,不僅可追蹤其動態,評估處遇成效,也可提供後續治療及服務內容的修正。本研究欲瞭解個案出所後接受電話追蹤以及對戒癮、醫療、社福、心理諮詢及就業輔導等服務之轉介的使用率與成功率。

方法: 研究針對北台灣法務部某戒治所接受強制戒治約一年後出所者,進行社區電話追蹤服務,以每三個月定期電話追蹤的方式,確定個案聯繫的比率,並針對個案之現況,訪談瞭解個案可能需要的轉介服務,提供諮詢與轉介。

結果:民國 97 年全年出所人數共 959 人,其中有 547 人直接回到社區。其中由戒治所方面電話取得聯繫者共 437 人。於戒治所內接受處遇的 353 名個案轉由醫院個案管理師進行電話追蹤與個案管理。於一年追蹤期間內未失聯的 323 名個案中,48 人轉介戒癮治療,25 人轉介精神科或內外科治療,10 人轉介社會福利資源介入,9 人轉介諮商服務,9 人接受勞工局、更生保護會或職訓局就業諮詢。自覺暫不需任何協助者有 187 人。總計成功追蹤保持聯繫的個案中,對於轉介的使用率為 30.65%,而轉介後確實得到幫助的比例為 67%。就業轉介成功的比例僅約 22%。

結論:以個案管理方式進行追蹤以及資源轉介,服務的使用率高達三成。 建議將工作分為兩階段,在第一階段聯繫並確認個案的轉介需求後,宜有第二 階段的個案管理加強轉介的成功率,尤其是就業輔導的面向。

回目次

### 美沙冬替代療法初診補助金額減少對初診個案數的影響

The influence of reduced government subsidization on utilization of methadone maintenance therapy by fresh cases

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目的:美沙冬替代療法從94年8月開始在國內試辦並推廣後,行政院衛生署疾病管制局除針對藥癮愛滋個案提供掛號費以外所有的補助外,對於非愛滋個案,初期也提供藥費與初診醫療檢驗費用的補助。根據 Lu Ann Aday 的 Expanded Behavioral Model,就醫的經濟障礙是預測病人使用醫療服務困難度的一個操作型指標。本研究嘗試分析在國家政策改變,對於美沙冬替代療法經費補助減少的情況下,對於海洛因毒癮患者進入美沙冬替代療法的影響。

方法:以中部某公立區域級綜合教學醫院的美沙多特別門診個案爲統計分析對象。收集民國 97 年 1 月至 98 年 2 月,共 14 個月所有初診個案數,排除已結案後重接案的個案,只計算從未接受美沙多替代療法的 fresh cases,因此這些個案都必須接受初診的醫療檢驗。1 月至 7 月加入的初診個案,不論是否爲愛滋或非愛滋藥癮個案,都有接受「初診醫療檢驗費」4600 元之補助。從民國 97 年 8 月 1 日起,則取消對於非愛滋藥癮個案之「初診醫療檢驗費」之補助,改由個案自付。比較取消補助前後,各 7 個月份的初診個案數是否有所變化。

結果:97年1月至98年2月共14個月的資料收集期間,某醫院除了初診補助費用取消外,其他美沙冬個案就醫相關流程制度,例如門診時間與次數、服藥時間、其他費用如掛號、診察費、給藥費等費用,都維持不變。97年1月至7月有初診補助時,某醫院的美沙冬特別門診初診個案,單月最高89人(97年2月),最低48人(97年6月),平均67.6人。8月至12月取消初診補助後,單月最高35人(98年2月),最低28人(97年8月),初診個案平均31.8人。每月平均初診個案數有明顯下降,不到原先之1/2。初診人數變化幅度最大的,爲97年7月的53人降到同年8月的28人,降幅達47.2%。正是補助從有變成無的兩個相鄰月份。

討論:在醫療體系提供的其他服務內容與流程不變的情況下,初診補助取消之後,個案須自付的醫療檢驗費用,雖然只有第一次門診需增加4600元。然而已經使得約一半原先有意願加入美沙多替代療法的海洛因毒癮患者,因此裹足不前。可見經濟因素對於這群患者使用替代療法的困難度,有非常重要的影響。政府如果要擴大替代療法的涵蓋面,除了增加醫院與給藥處等的就醫方便性外,經費補助也是必要投入的重點項目。

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# CB2 cannabinoid receptor: identification of novel human promoter elements, isoforms, and tissue expression patterns

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**Introduction**: Cannabinoids, endocannabinoids and marijuana activate two well-characterized cannabinoid receptors (CBRs), CB1-Rs and CB2-Rs. The expression of CB1-Rs in the brain and periphery has been well studied but neuronal CB2-Rs have received much less attention than CB1-Rs. Many studies have now identified and characterized functional glial and neuronal CB2-Rs in the central nervous system. However, many features of CB2-R gene structure, regulation and variation remain poorly characterized in comparison to the CB1-R.

#### Methods:

#### Molecular Genetic studies

Isoform-specific expression analyses: exon-specific primers and fluorescent FAM-labeled minor-groove binding (MGB) probes were designed across two alternatively spliced exons using Primer Express software.

The cDNA templates synthesized from total RNA of human tissues or mouse tissues were amplified using ABI Prism 7900HT Sequence Detection System with a default cycling program. Pre-developed human or mouse GAPD and beta-actin provided a control.

#### **Behavioral Studies**

The experimental and control mice of C57BL/6 strain, were pre-exposed to the forced swim test (FST), used in screening anti-depressants, prior to the day of the test. The experimental animals were treated daily for 7 days with the mixed cannabinoid agonist, WIN55212-2 (2 mg/kg). On test days animals were treated with either cannabinoid agonist or antagonists for 30 mins before assessment of the performance of the mice in FST for 5-mins.

Six mice per group were sacrificed and non-injected BTBR mice tissue parts included for analysis. Vehicle= (V1-V6), WIN55212-2 (2 mg/kg) = (W1-W6) and untreated BTBR = (B1-B6).

**Results**: Both human and mouse CB2 genes contain upstream and downstream promoters that produce two alternatively spliced isoforms, CB2A and CB2B. Human CB2A isoform is expressed in various brain regions while CB2B is more limited in peripheral tissues. Human CB2 gene (90kb) is four times larger than mouse CB2 gene (23 kb). Human CB2A is prominently expressed in testis and CB2B prominently in spleen. Mouse CB2A and CB2B are both expressed prominently in spleen. Mouse CB2A is expressed more highly in brainstem and CB2B is expressed more highly in striatum. Mouse CB2A is upregulated in the cerebellum of BTBR mice and by the treatment with the mixed cannabinoid agonist WIN55212.

**Conclusion:** These results provide much improved information about CB2 gene structure and its human and rodent variants that should be considered in developing CB2-R-based therapeutic agents.

# Clinical Treatment of Opioid-Induced Hyperalgesia—A Case Report.

### 鴉片類藥物造成疼痛過敏之臨床治療—個案報告

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**Background**: Opioids, intended to abolish pain, can unexpectedly produce hyperalgesia, particularly during rapid opioid escalation. Recent studies have shown that neural plasticity associated with the development of opioid tolerance may activate a pronociceptive mechanism that could counteract the analgesic effects of opioids. Thus, exposure to opioids could lead to two seemingly unrelated cellular processes (ie, the development of opioid tolerance and opioid-induced pain sensitivity). Their converging effects may be part of the mechanisms leading to the reduced opioid analgesic efficacy in chronic opioid therapy. Once diagnosed or provisionally considered, treatment strategies could include opioid dose reduction, opioid rotation, use of agents with NMDA receptor antagonism, and a properly timed coxib. Opioid switching could be a therapeutic option in a condition of opioid-induced tolerance or hyperalgesia, but conversion ratios between opioids are difficult to apply in this context and require strict surveillance and expertise. We present a case report in which switching from high dose oral morphine to antidepressant duloxetine was effective.

Case Report: Mr. L is a 34 years old male suffered form right humeral open fracture and right brachial plexus injury. After open reduction internal fixation and augment injectable bone graft treatment, he still refractory pain. His morphine use increased gradually in pain clinic. His mood which disturbed by pain very much was dysphoria so he took pills for suicide. He admitted to out psychiatry ward for unstable affect and repeated self-harm in recent one week.

In pain clinic, his opioid drugs were morphine 960 mg per day (slow release 60 mg 4#/Q6H) and morphine as needed. In two weeks treatment period, his morphine dose was reduced to 160 mg per day (30 mg 1#/QID and 10 mg 1#/QID). The other medication combination was duloxetine 120 mg per day (30 mg 2#/BID) and clonidine 0.6 mg (0.075 mg 2#/QID). In the meantime, the pain was under control.

**Discussion**: Experimental evidence suggests that opioid tolerance and opioid-induced hyperlagesia might limit the clinical utility if opioids in controlling chronic pain. The differential diagnosis of opioid-induced hyperalgesia and its implications in clinical pain management are discussed.

Duloxetine, a serotonin-norepinephrine reuptake inhibitor, was proved effectively in relieving neuropathic pain in many clinical trials.

According to this case report, switching from opioid to antidepressant duloxetine in patients with chronic pain might be the possible way to balance between analgesia and adverse effects.

# 胚胎期暴露於嗎啡類藥物對微膠質細胞之氧化壓力的影響 Microglial Oxidative Stress in Prenatal Exposure of Opiate

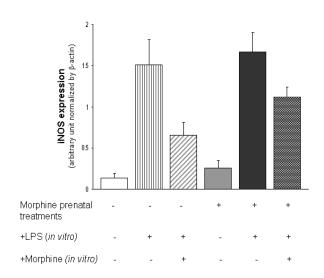
謝奉勳、林兆東 Feng-Shiun Shie, Zaodung Ling

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目的: 嗎啡類藥物具有破壞腦細胞功能及造成行爲變異之作用。近年研究發現,膠質細胞與腦細胞間的互動異常可能和嗎啡類藥物引發之腦細胞功能異常有關。其中,經由微膠質細胞活化產生的一氧化氮及其衍生物不僅會毒害腦細胞,也可能是造成嗎啡成癮的重要因素。因此,瞭解一氧化氮的生物特性在細胞間互動扮演的角色,可以進一步釐清嗎啡成癮及腦細胞毒性發生的機制。本研究的重點在於探討胚胎期若接受嗎啡類藥物的暴露是否會增加微膠質細胞之氧化壓力,進而改變腦細胞對嗎啡類藥物或毒物的敏感度。本研究的終極目的是希望能從此研究幫助瞭解嗎啡成癮的機制,並提供治療成癮有用的訊息。

方法: 我們利用胚胎期與新生動物之嗎啡類藥物模型,並測試初代微膠質細胞之一氧化氮的生成及其相關的訊號傳遞。

**結果:** 胚胎期若接受嗎啡類藥物會增加初代微膠質細胞之 iNOS 表現。可是,若只有在初代培養同時接受嗎啡類藥物及 LPS 的刺激, iNOS 的表現反而會被抑制。



**討論**: 結果顯示,胚胎期若接受嗎啡類藥物的暴露似乎會長期地改變微膠質細胞之免疫功能而增加其氧化壓力。

回目次

### 應用唾液檢體篩檢海洛因成癮個案的可行性初探

Saliva as screening tool for heroin dependence subjects in methadone clinic: a pilot study

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**目的:**海洛因成癮的門診追蹤需要瞭解個案的成癮物質使用情形,目前以個案自我陳述以及尿液篩檢爲主流。本研究期望應用唾液檢體進行成癮物質篩檢,探討與自述與尿液篩檢方法的差異。

方法:研究收集國內美沙冬門診個案 27 名,經臨床診療後記錄個案成癮物質使用情形、以 ELISA 方式進行尿液篩檢、另同時使用唾液檢體由 Draeger Drug Test 5000 儀器使用 ELISA 以數位判讀方式進行成癮物質篩檢。

結果: 27 名書面同意參加研究的個案中,有 4 名因儀器/篩檢套件無法讀取而沒有檢驗結果。3 名個案於檢驗中放棄唾液採檢。其餘 20 名個案中,尿液與唾液同時呈陽性反應者共 10 名,同時呈陰性反應者共 5 名;尿液檢驗陽性而唾液檢驗陰性者 5 名;沒有唾液檢驗陽性而尿液檢驗陰性者。27 名個案中,尿液檢驗與自述海洛因使用的結果完全相符。比對唾液篩檢結果的 20 名個案,檢驗的敏感性爲 66.67%,而特異性達 100%。唾液檢驗爲陰性的 5 名個案中,自述最後一次使用海洛因的時間,有 3 名爲 24 小時內,2 名爲 48 小時內。

**結論:**此初步結果顯示以唾液檢體作爲篩檢成癮物質的方法,有待進一步 驗證其敏感度以及臨床應用的可行性。

# Dosage patterns and demographic in methadone treatment among mid Taiwan: 1 year survey

### 中部地區一年美沙酮劑量及使用方式分析

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**OBJECTIVE:** To examine the extent to which mid-taiwan methadone dosage patterns distribution, 2007-2008. DATA SOURCE: Data were collected from a 4 methadone maintenance treatment hospital representative sample of outpatient treatment facilities in 2007-2008.

**STUDY DESIGN:** Random-effects multiple regression analysis was used to examine unit characteristics associated with below recommended doses. DATA COLLECTION: Data regarding the proportion of patients who received maintenance dosages more than 180 day were collected from data.

**PRINCIPAL FINDINGS:** 1,400 patients receive methadone maintenance treatment. The current age of treatment is mostly (94%) age between 20 to 40. Only small portion (31%) use heroin only and mostly (62%) use 1 more other substance, 3.6% use 2 more other substance, and 2.6% use 3 more substance. The methadone use pattern maybe clustered into 4 groups: stay in low dose, stay in medium dose, stay in high dose, and dose increase to 90 mg and return to low dose.

**CONCLUSIONS:** Base on the methadone use pattern subtypes; there maybe further phenotype existed for heroin addiction. Further larger sample and prospective study will be needed.