功能性磁振造影應用於中風個案抓握動作常見之影像分析與腦區關聯性分析方式

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目的：功能性磁振造影 (fMRI) 技術已逐漸應用於中風個案動作的研究上，除了可提供大腦可塑性的證據外，亦可為治療成效提供具體證明。本篇旨在介紹 fMRI應用於中風個案常見的影像分析方式及相關的連結形式，以更深入了解fMRI所能提供的資訊及可應用的層面。方法：使用搜尋引擎，共蒐集 39 篇相關文獻。使用分析方式包含：血氧濃度相依對比訊號的改變、側化指數、結構方程模式以及動態因果模式，功能性連結或效率性連結分析。結果：最近幾年的研究顯示結構方程模式以及動態因果模式分析的使用有上升的趨勢，說明腦區之間的因果關係分析日趨重要。結論：分析腦區之間的關聯性及因果關係有助於促進對於中風病患復原機制的了解，可以協助職能治療師更準確地選擇最適療法，提升治療效果，縮短療程。

關鍵詞：功能性磁振造影，中風，抓握任務

前　言

功能性磁振造影 (fMRI) 因其使用不具侵入性、造影取得快速，以及具有良好的空間解析度，目前已逐漸應用於中風個案的動作表現上 (Farr & Wegener, 2010; Richards, Stewart, Woodbury, Senesac, & Cauraugh, 2008)。造影資訊可提供大腦皮質可塑性的具體證據，並且可當作中風復健成效的證明。應用於職能治療領域上，除了可得知中風個案動作復原的過程以及預後因子外，還可提供臨床工作者辨別何種療法對何種動作表現的中風個案較為有效。過去研究發現，磁振造影時，執行抓握動作任務可得到較明顯的造影訊號 (Cramer et al., 2001; Ehrsson et al., 2000)。同時，由於抓握動作任務可適用於較廣泛的中風族群上 (Cramer et al., 1997)，已逐漸成為主要的磁振造影動作任務。磁振造影影像需後續的分析處理才能成為可解讀的結果，用於中風個案抓握動作的分析上。常見的分析處理方法有：血氧濃度相依對比訊號的改變 (Blood oxygen-level dependent, BOLD) (Ogawa, Lee, Nayak, & Glynn, 1990)、側化指數 (laterality index, LI) (Binder et al., 1996)、結構方程模式 (structural equation modeling, SEM) (Buchel & Friston, 1997)，以及動態因果模式 (dynamic causal modeling, DCM) (Friston, Harrison, & Penny, 2003)。較早之前的 fMRI 分析可提供與執行某動作相關的腦區圖，最近則由於 SEM 及 DCM 的分析方法使用，可提供各個相關腦區之間神經傳遞的因果連結，已成為近幾年較常使用的分析方式 (Rykhlevskaia, Gratton, & Fabiani, 2008; van den Heuvel & Hulshoff Pol, 2010)。透過了解神經傳遞間的因果連結，可得知執行特定某動作時各腦區所扮演的角色，以及某腦區受損後對其餘未受損腦區間訊息傳遞及行為表現的影響，而後進一步將此結果應用於臨床治療上。鑑

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於fMRI分析方法與所提供資訊愈來愈多元，本研究目的在於統計整理fMRI應用於中風個案抓握動作之常見分析方式以及各分析方式可提供之解讀資訊，供未來訂定中風個案fMRI分析之參考。

方　法

藉由 Medline、PubMed 等文獻搜尋引擎，輸入關鍵字為：stroke and grasp / grip / finger flexion and fMRI，且文獻需符合：(1)受試者包含中風個案，(2)使用的評估工具須包含fMRI，(3)執行的任務包含抓握，亦即需做出 finger flexion 的動作。依各篇文獻採用的分析方法分類整理。

結果與討論

共收集 39 篇文獻，依分析方法分類，血氧濃度相依對比訊號改變 27 篇，LI 10 篇，SEM 1 篇，DCM 1 篇，如表一。fMRI影像的分析方式主要依賴於數據的統計處理，得到的資料呈現除了可提供執行任務時所參與的大腦區域外，還可得知參與的腦區之間如何進行資訊的傳遞 (Friston, 2009)。各篇文獻的目標腦區皆包含雙側 M1 (primary motor cortex)、SMA (supplementary motor area) 及 PMC (premotor cortex)。另將 S1 與 M1 一同包含為 SMC 者 10 篇；將目標範圍設為全部腦區 20 篇；其他包含的目標腦區還有：小腦 (cerebellum) 5 篇、基底核 (basal ganglia) 1 篇、頂葉上端 (superior parietal cortex) 1 篇，以及額葉 (frontal cortex) 1 篇。而依據分析方式所得到的目標腦區連結，可分為功能性連結 (functional connectivity) 及效率性連結 (effective connectivity)。

分析方法

(1)血氧濃度相依對比訊號的改變 (BOLD signal change)：

血氧濃度相依對比訊號的改變，意指某些大腦區域在操作後活化大小的改變，即：（動作時或治療介入後造影活化量－休息時或治療介入前的活化量）。由此可得知某些大腦區域在動作時或治療介入後活化的差異。血氧濃度相依對比訊號改變是較簡易的分析方式，是早期或選取較多目標腦區時常見的分析方法 (Jaillard, Martin, Garambois, Lebas, & Hommel, 2005; Staines, McIlroy, Graham, & Black, 2001; Schaechter, Perdue, & Wang, 2008)。中風個案執行抓握動作時較健康成人活化較多大腦區域，而同一區域活

表一　中風後抓握任務 fMRI 分析方法分類

BOLD signal change	(Bestmann et al., 2010)、(Cramer et al., 2001)、(Feydy et al., 2002)、(Fujii & Nakada, 2003)、(Jaillard et al., 2005)、(Johansen-Berg et al., 2002)、(Kim et al., 2003)、(Kokotilo, Eng, McKeown, & Boyd, 2010)、(Loubinoux et al., 2007)、(Marshall et al., 2009)、(Michielsen et al., 2010)、(Mintzopoulos et al., 2008)、(Miyai et al., 2001)、(Nowak et al., 2008)、(Pariente et al., 2001)、(Rehme, Eickhoff, et al., 2011)、(Rehme, Fink, von Cramon, & Grefkes, 2011)、(Rocca et al., 2005)、(Schaechter et al., 2008)、(Staines et al., 2001)、(Takahashi, Der-Yeghiaian, Le, Motiwala, & Cramer, 2008)、(Tombari et al., 2004)、(von Lewinski et al., 2009)、(Ward, Brown, Thompson, & Frackowiak, 2003a)、(Ward, Brown, Thompson, & Frackowiak, 2003b)、(Ward, Brown, Thompson, & Frackowiak, 2004)、(Zarahn et al., 2011)
LI	(Foltys et al., 2003)、(Jang et al., 2003)、(Lee et al., 2010)、(Lin et al., 2010)、(Michielsen et al., 2011)、(Saleh et al., 2011)、(Schaechter et al., 2002)、(Stinear et al., 2007)、(Takahashi et al., 2008)、(Wu et al., 2010)
DCM	(Grefkes et al., 2008)、(Grefkes et al., 2010)、(Rehme, Eickhoff, et al., 2011)
SEM	(James et al., 2009)

化量較少，治療後則漸趨如健康成人的造影顯示 (Feydy et al., 2002; Miyai, Suzuki, Mikami, Kubota, & Volpe, 2001; Nowak et al., 2008)。依本文獻搜尋結果，多數中風個案會代償性的活化健側腦SMC、M1，而在患側腦中受損腦區活化下降，其他與運動相關但未受損腦區則會代償性增加活化 (Lee et al., 2010; Schaechter et al., 2008; Tombari et al., 2004)。

(2)側化指數 (laterality index, LI)：

側化指數以活化量爲依據，計算患側某些腦區對於健側對應腦區活化大小的改變。數值介於 1 至 -1 間，愈趨正值代表患側腦區活化量較健側腦區多，所計算的公式爲：

$$\frac{\text{患側某腦區活化量} - \text{健側對應腦區活化量}}{\text{患側某腦區活化量} + \text{健側對應腦區活化量}}$$

由側化指數可知動作時或治療介入後，患側腦區的活化量對照於健側腦的改變。LI 是依據血氧濃度相依對比訊號數據所加以計算出來的結果，相對於血氧濃度相依對比訊號改變所在意的前後測差別，LI 更注重患側腦相對於健側腦活化量的改變，因此常見於研究治療介入後，患側腦可塑性改變的文獻中。應用於中風個案的研究結果顯示，治療前與治療後，患側腦區的活化量相較於健側腦區增加 (Lin et al., 2010; Schaechter et al., 2002; Wu et al., 2010)。

(3)結構方程模式 (structural equation modeling, SEM)：

結構方程模式在統計學上強調變異數 (variance) 與共變異數 (covariance) 之間的結構關係，目的在於減少其間的不同 (Jezzar, Matthews, & Smith, 2002)。運用於fMRI的分析上可處理觀察數據間的因果關係，提供各大腦區域執行任務時連結方向的資訊，但需先有一假設的模式來當數據套入的基礎。此假設模式需以解剖學上的證據來當依據，分析時的假設模式中需有一起始的結點。模式中各節點的選定亦須符合解剖學上的知識 (Huettel, Song, & McCarthy, 2004; James et al., 2009)。SEM 的結果可知某腦區與其下層連結腦區間連結強弱的改變，應用至中風個案身上，可顯示患側某腦區與其下層腦區在前後測連結強弱的改變。本研究所收納的文獻使我們得知在積極介入後，患側腦之 PMC 可增加對健側腦 PMC 及患側腦 M1 的影響 (James et al., 2009)。

(4)動態因果模式 (dynamic causal modeling, DCM)：

動態因果模式最近幾年開始使用於 fMRI 上，在 fMRI 的應用主要在於檢視實驗操作下（例如：執行動作任務時）各個大腦區域間相互耦和 (coupling) 的情況，可提供區域間因果連結的資訊，並且可依所觀察的數據得到一個動態且具預測性的模型 (Friston, 2009)，而不需如結構方程模式分析時先預設一個模式。DCM 的結果強調的是提供一動態、預測性的腦區連結模型，但因其統計方法的繁複，無法如血氧濃度相依對比訊號改變將全腦區域當作目標腦區，收錄文獻中，DCM 選用的目標腦區個數至多爲 6 個。DCM 運用於中風個案上可知腦區間興奮及抑制連結強弱的改變，並且不需如 SEM 需作預先的模式 (Grefkes et al., 2008; Grefkes et al., 2010)。本研究收錄文獻中，DCM 的研究顯示中風個案在患手動作時，PMC 及患側腦 SMA 對患側腦 M1 的連結強度減弱，而健側腦M1 對患側腦M1 抑制加強，此現象會隨中風復原而改善 (Grefkes et al., 2008; Rehme, Eickhoff, Wang, Fink, & Grefkes, 2011)。

目標腦區的連結方式

(1)功能性連結 (functional connectivity)：

原始fMRI的造影訊號需經統計分析轉換爲可解讀的資訊，而分析的結果可得到各個目標腦區的連結方式。計算功能性連結以種子分析 (seed analysis) 爲最簡易的一種，分析時需先選擇目標腦區 (interest of region, ROI)，再將此目標腦區當作回歸子 (regressor)，計算在時間上相關的其他大腦區域。但種子分析只能選擇一個大腦區域當目標腦區，若需許多大腦區域當目標腦區，則可使用成分分析 (component analysis) (James et al., 2009)。由時間上相關的分析方式可

得知功能性連結 (functional connectivity)，了解其他腦區與目標腦區間相關性的強度。功能性連結是在執行某任務時，不同腦區在激活時間的相關性，例如：執行某任務時，腦區 A 和腦區 B 在時間序列上皆維持一致的相關，則可推論腦區 A 和 B 與此任務的執行有關，但此分析方式無法得知相關腦區間的因果連結方向 (Friston, Harrison, & Penny, 2003; James et al., 2009)。本研究收錄文獻中，功能性連結的文獻顯示：中風個案執行抓握任務時，SMC、M1、SMA 及 PMC 與抓握任務有關。

(2)效率性連結 (effective connectivity)：

依據功能性連結的資訊，再藉由 SEM 或 DCM 等高等統計方式則可得知效率性連結 (effective connectivity) (James et al., 2009)。效率性連結可了解某任務下相關腦區之間作用的方向及因果關係，了解一腦區如何影響另一腦區的活動 (Friston, 2009)。本研究收錄文獻中，效率性連結的文獻顯示：中風個案執行抓握任務下，腦區 SMA 及 PMC 與腦區 M1 有因果關係。

因此，依據血氧濃度相依對比訊號改變及 LI 的分析方式可得到腦區間的功能性連結，代表腦區間時序相關性的資訊，而 SEM 及 DCM 分析方式可得到腦區間的效率性連結，說明各腦區間的影響方向及因果關係。功能性連結可依時序顯示中風個案與健康成人抓握動作活化量及位置的不同，而效率性連結則可顯示中風後腦區間連結方向及強度的改變。

結　論

fMRI 在最近十年來逐漸應用於中風個案的動作表現上，提供神經活動的證據，使研究結果更具體。常見的應用於中風個案抓握動作的 fMRI 分析方法包括：血氧濃度相依對比訊號改變、LI、SEM及DCM。血氧濃度相依對比訊號改變適合觀察大範圍腦區的變化；LI 可用於比較治療前後患側腦區相較於健側腦區的活化增加量；SEM 可顯示患側某腦區與其下層腦區在治療前後連結強弱的改變；DCM 可顯示腦區間興奮及抑制連結強弱的改變，並且不需如 SEM 作預先的模式。目標腦區連結方式部分，功能性連結可依時序顯示中風個案與健康成人抓握動作活化量及位置的不同，而效率性連結則可顯示中風後腦區間連結方向及強度的改變。最近幾年的研究顯示 SEM 以及 DCM 的使用有上升的趨勢，說明腦區間的因果關係分析日趨重要。分析腦區間的關聯性及因果關係有助於了解中風後以及復原期間神經傳遞的機制，促進對於中風病患復原機制的了解，可以協助職能治療師針對病患特徵更準確地提供有效的療法，提升療效。

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Common Methods of Image Analysis and Functional Connectivity Analysis in Functional Magnetic Resonance Imaging for Grasping Tasks in Stroke Patients

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Objective: Functional magnetic resonance imaging (fMRI) has been increasingly used by studies investigated motor function in stroke patients. It can provide evidence of cortical plasticity and show actual effects of clinical intervention. The purpose of this review is to summarize common methods of image and functional connectivity analysis in fMRI in recent studies to enhance further understanding of the information able to be obtained from fMRI and possible application of fMRI in stroke patients. **Methods:** Two databases were searched for articles investigating cortical reorganization by functional MR imaging with grasping task from 2001 to 2011. Inclusion criteria were: using fMRI as an evaluating tool; including image processing and functional connectivity analysis; and including grasping task. **Results:** The use of structural equation modeling (SEM) and dynamic causal modeling (DCM)was increased in recent studies, indicating increasing attention to analysis of functional connectivity. **Conclusion:** Analyzing functional connectivity could enhance the understanding of the recovery mechanism after stroke and assists therapists to determine optimal therapy for each patient. Hopefully, the effectiveness of the therapy could be increased and the duration of rehabilitation could be shortened.

Key words: Functional magnetic resonance imaging, Stroke, Grasping task

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