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計畫期末執行進度報告

潛伏期（早期）精神分裂症之病理研究：
臨床病理與神經心理功能障礙

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一、研究計畫之背景及目的：

精神分裂症是慢性且病情嚴重之一種精神疾病。發展精神分裂症基礎病理研究與早期預防研究之新典範是重要之研究取向。

精神分裂症之病理範圍很廣，是屬一個病譜性之疾病。準備精神分裂症之診斷並不能涵蓋所有精神分裂症病譜之病理狀態。

本研究發展一套含有 33 項症狀之潛伏性精神分裂症診斷準則(TCLS)並發展對應之篩檢表(TSSLS)。應用回顧性之前瞻性研究設計，本研究發現以 TCLS 定義之潛伏期精神分裂症在追蹤治療過程中有 13.2%發展為嚴重之精神分裂症；只有 32.0%潛伏性精神分裂症患者合乎準精神分裂症之診斷準則。TCLS 所定義之潛伏性精神分裂症，發病年齡較早(17.5 ± 5.5 歲)，延遲 $20.2(\pm 6.1)$ 歲才尋求第一次之精神醫療。由 TCLS 所定義之潛伏型精神分裂症之臨床效度可由神經心理功能之障礙，如注意力、智力、執行功能、記憶力等之障礙予以引證。

關鍵詞:精神分裂症、潛伏型精神分裂症、早期預防、精神病理、神經心理功能、效度、診斷準則、篩檢表。

Abstract

Schizophrenia is a chronic and severe psychiatric illness. To develop a new paradigm for future basic psychopathological research on schizophrenia and early intervention research is an important step of schizophrenia research.

Schizophrenia was found to have a broad spectrum of pathology. Schizotypal disorder could not cover all spectrum pathology of schizophrenia. This study developed a set of Taita Criteria for Diagnosis of Latent Schizophrenia (TCLS) of 33 items and a corresponding screening schedule (TSSLS).

Using retrospective- prospective design, this study found that 13.2% of Latent Schizophrenia (LS) became schizophrenia in their treatment course; that 32.0 % of LS also fulfilled the criteria of schizotypal disorder. The cases of LS had very early mean age of onset at $17.5(\pm 5.5)$ years old. They delayed their first psychiatric visit for help until the mean age of $20.2(\pm 6.1)$ years old. The validity of the LS defined by TCLS were proved by having impaired neuropsychological functions, continuous performance test, Wisconsin Card Sort Test, VIQ, PIQ, FIQ and verbal paired test of memory.

Key words: Schizophrenia, Latent Schizophrenia, early intervention, psychopathology, neuropsychological functions, validity, diagnostic criteria, screening schedule.

二、源起與目的

Schizophrenia is a chronic and severe illness. The patients might become dependent on others and the family of the patients had high burden on taking care of the patients. Other than the clinical state of schizophrenia defined by current diagnostic criteria, there were several clinical states related to basic pathology of schizophrenia, such as schizotypal disorder, borderline schizophrenia, latent schizophrenia, Pan-neurosis. There is a lack of evidence to show that the schizotypal disorder could cover all these “latent” state of

schizophrenia. Clinically, many cases of this kind of pathology were diagnosed as neurotic disorders and received inappropriate treatment.

Cognitive impairments were found in the patients of schizophrenia as well as in the non-affected first degree relatives(Meehl,1989; Faraone, 1999). All these data induct the concept of spectrum of schizophrenia. For the purpose of basic psychopathological study as well as for developing early intervention measures. It is crucial to identify the cases of schizophrenia at latent state or at the subclinical state of spectrum.

This study was designed to develop a screening criteria of latent schizophrenia. The validity of there clinically identified cases of latent schizophrenia would be validated by neuropsychological studies.

三、結果

1. Establishment of Criteria and Screening Schedule of Latent Schizophrenia.
Based on literature of the psychopathology of latent schizophrenia (LS), borderline or pan-neurotic schizophrenia, this research group developed the Taita Criteria for Diagnosis of Latent Schizophrenia (TCLS). This TCLS included (1) Thought symptom (6 items), (2) perceptual symptom (6 items), (3) inappropriate behavior (6 items), (4) affect symptoms (6 items), (5) interpersonal interaction (5 items) and (6) specific neurotic symptoms (4 items). By excluding the diagnosis of schizophrenia, delusional disorder, major depressive disorder, and bipolar disorder. This research team develop the Taita Screening Schedule for Latent Schizophrenia (TSSLS). This TSSLS was revealed to have good inter-rater reliability.
2. Hypothesis Testing 1: Latent Schizophrenia (LS) is one component of schizophrenia spectrum. Some proportion of the cases of Latent Schizophrenia would become schizophrenia in the course of illness. This study checked the psychiatric medical charts of National Taiwan University form 1970 to 2002. Initially, 1778 medical charts had the clinical impression of latent schizophrenia. Available charts for review was 1454. Three criteria were used to obtain medical chart with enough information. Finally, 379 cases were available for study, 324(85.5%) out of 379 fulfilled the TCLS, 50(13.2%) cases became schizophrenia after follow-up for at least 6 months. Only 5(1.3%) cases could not fulfill the TCLS. This finding confirms this hypothesis.
3. Hypothesis Testing (2): The LS defined a broader spectrum of schizophrenia. Some proportion of LS will fulfill the criteria of DSM-IV or ICD-10 system of schizotypal disorder. 50 cases were interviewed face-to-face and the TCLS as well as schizotypal criteria were used for interview. Only 16(32.0%) out of 50 cases fulfill the diagnostic criteria of DSM-IV. This finding confirms this hypothesis.

4. Hypothesis Testing (3): The cases of LS has the characteristics of typical schizophrenia, but the severity is milder than that of schizophrenia. The cases of LS have mean age of onset at 16.1(\pm 6.7) . The function impairment started at age 17.9(\pm 5.5). The first psychiatric visit at age 20.2(\pm 6.1). The prevalence of criterion symptom categories of thinking, perception, inappropriate behavior, affect, interpersonal behavior and neurotic symptoms were similar in the case of in LS and schizophrenia. The mean social function of interpersonal relationship, achievement, time arrangement and family life were 4.0(\pm 1.5), 3.4(\pm 1.8), 4.0(\pm 1.9), 4.2(\pm 1.4), respectively. 74(50.3%) out of 147 cases of LS had a history of psychiatric admission. Apparently, the clinical condition was very similar to typical schizophrenia.

5. Hypothesis Testing (4): The LS has an impaired neuropsychological functions which were similar to these seen in schizophrenia.

As compared with the normal subjects, the LS had impaired masked continuous performance test as shown by the indicator of d' score (mean (sd): 3.3 (\pm 1.1) vs 0.9(\pm 1.6); $p < 0.006$). In Wisconsin Card Sort Test (WCST), the LS group had lower total correct score (93.7 \pm 20.7, $p < 0.05$) than normal controls; higher total error score (46.8 \pm 27.5 vs 34.3 \pm 20.7, $p < 0.05$); lower percentage of conceptual level response (52.9 \pm 28.7 vs 66.4 \pm 22.2, $p < 0.05$). There were higher scores of perseverative response (25.3 \pm 19.3 vs 18.5 \pm 13.2), higher scores of preservative errors (24.3 \pm 18.1 vs 16.9 \pm 11.2).

Verbal IQ and Performance IQ were lower in LS (108 \pm 13 vs. 117 \pm 15; and 97 \pm 15 vs. 113 \pm 14) in the LS than that of the normal controls. Weschler memory test of verbal paired test (hard) was more impaired than that in the normal (7.7 \pm 2.9 vs. 9.3 \pm 2.0, $p < 0.03$). In conclusion, the neuropsychological functions did impaired in the LS. The severity of impairment is not so severe as that of schizophrenia. These data support the validity of the concept of latent schizophrenia.

四、討論

The aims of this project had been achieved. The LS screening schedule with satisfactory reliability was developed. Some of (13.2%) those LS became aggravated and reach the clinical criteria of schizophrenia. About 32%, not 100% of the LS could fulfill the criteria of schizotypal disorder. This implied that the criteria of schizotypal disorder is too narrow for clinical reality. The study result assures that it is necessary to create a new set of clinical criteria for identifying LS for appropriate and early intervention of schizophrenia.

It is desirable to use the TSSLS for initial case screening in clinical setting. Neuropsychological test will enhance the specificity of the clinical diagnosis of LS for

early clinical intervention and management. Further study focus on neurobiological mechanisms and the early intervention became operable after these screening procedures.

五、計畫成果自評

The study results support the argument that the criteria of schizotypal disorder of DSM-IV or ICD-10 system were too narrow for clinical reality. The concept of LS needs to be noticed in clinical practice. Criteria of LS and the corresponding screening schedule need to be emphasized for academic and clinical purpose. This is the important contribution of this study. However, the control group of this study had higher education level. This might reduce the power of this comparison study on neuropsychological function between the LS and controls. However, the similarities of the neurological impairment between the LS schizophrenia justified the conclusion of this study.

六、潛伏型精神分裂症病理相關文獻：

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