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注意力缺失/過動疾患兒童之執行功能(1/2)

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摘要

注意力缺失/過動疾患(ADHD)是一種盛行於兒童的精神疾患，會長期的影響學業成績、社會功能及職業成就。雖然已有大量的文獻研究此族群的執行功能，但其中對於執行功能的定義卻不盡相同，且此族群本身的異質性也使得在描述認知模式上更加困難。本研究的主要目標是意圖了解 ADHD 三種亞型(注意缺失型、過動-衝動型、混合型)中的執行功能是否不同，著重於執行功能中的 1)抑制，2)工作記憶，3)計畫/策略使用，4)持續性注意力，5)自我監控/心智轉換。第二個目的是建立適用於台灣文化的測驗，因為使用西方的測驗與常模可能會受中西方社會差異的影響。本研究的第一年參考了已發行的英文測驗並發展台灣適用的執行功能測驗。目前本研究已有兩個抑制能力、三個工作記憶、三個計畫/策略使用、兩個持續性注意力、及三個自我監控/心智轉換的測驗。本研究正在收集 30 位國小學生的前測資料，從前測中會淘汰不適合測 4-12 歲兒童能力的測驗。本研究會用 CIDI 的結構性晤談判別 ADHD 亞型及紀錄共病問題的存在，已有兩位研究助理經過 CIDI 之訓練。研究第二年將進行正式實驗階段，預計使用 60 位 ADHD 的兒童(三種亞型各 20 位)。比較 ADHD 亞型間的執行功能差異對醫學文獻有重要的貢獻，亞型間的差異可支持 DSM 診斷系統並推測各亞型之不同的潛在神經因素。實務貢獻在於發展出可幫助臨床工作者辨識且解釋 ADHD 兒童認知模式的測驗。

關鍵詞：注意力缺失/過動疾患；執行功能；神經心理學；認知模式；注意力缺失/過動疾患亞型

Abstract

Attention-Deficit/Hyperactivity Disorder (ADHD) is one the of most prevalent childhood psychiatric disorders. This is a chronic condition that impairs academic performance, social functioning, and occupational achievement. The primary aim of this study is to focus on the executive function of children with ADHD. Although ample evidence points to executive dysfunction among this population, the literature is fraught with vague definitions of executive function. Furthermore, the heterogeneity in this population has made description of its cognitive profile difficult. It is more promising to target ADHD subtypes. The present study focuses on: 1) inhibition; 2) working memory; 3) planning/strategy use; 4) sustained attention; 5) self-monitoring/set shifting, and attempts to examine whether the Inattentive, Hyperactive/Impulsive, and Combined subtypes of ADHD differ in these abilities. A secondary goal is to develop tests of these functions that are appropriate to Taiwan's culture and language. This is direly needed as the lack of standard translations makes comparison of findings across clinics and research groups difficult, and referencing western norms could be inappropriate due to subtle differences in social standard between the east and the west. During the first year of the study, we have reviewed published instruments and have developed a battery including two inhibition, three working memory, three planning/strategy use, two sustained attention, and three self-monitoring/set shifting measures. Data from 30 pilot subjects are currently being collected. From this pilot data measures inappropriate to measuring functions of 4-12 year old children will be eliminated from the final battery. This study will use the CIDI to classify ADHD subtype and to document presence of comorbid disorders. Two research assistants have gone through training to administer this structured interview. The experimental stage will take place during the second year of the study. A total of 60 children subjects diagnosed with ADHD will be recruited with 20 subjects each in the Inattentive, Hyperactive/Impulsive, and Combined subtype groups. Comparison of executive functions of different ADHD subtypes will be a significant contribution to the psychiatric and neuropsychological literature. Differences between subtypes will provide further support for the current DSM diagnostic system, and will suggest that each subtype may have a different underlying neuropsychiatric disturbance. This study will also contribute to the clinical practice of child psychology by developing instruments that could help in elucidating the cognitive profiles of children with ADHD, and by obtaining control data against which deviant cognitive levels could be compared.

Key words: Attention-Deficit/Hyperactivity Disorder; executive function; neuropsychology; cognitive profile; ADHD subtypes.

前言

Attention-Deficit/Hyperactivity Disorder (ADHD) is one of the most prevalent childhood disorders requiring psychological intervention. The number of cases referred to medical settings for treatment seems to be on the rise. The Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (APA, 1994) estimated the prevalence rate to be between 3-5% in school-aged children. By the year 2000, the estimated prevalence rate has risen to 3-7% in school-aged children (APA, 2000). The goal of this study is to elucidate the executive function of children with different ADHD subtypes, and to establish some data on executive function using instruments appropriate to Taiwan's culture.

文獻探討

There is ample evidence suggesting that children with ADHD have deficits of executive functioning (Boucugnani & Jones, 1989; Seidman et al., 1997; Shue & Douglas, 1992; see Pennington & Ozonoff, 1996 for review). These neuropsychological data are consistent with development in neuroimaging and neurochemistry literatures (Swanson et al., 1998). However, which executive functions are impaired among individuals with ADHD remain unclear.

Barkley (1996) conceptualizes that in the core of executive functioning is a deficit in behavioral inhibition. This core deficit has sequalae for the development of executive functions such as working memory, self-regulation of affect, internalization of speech, and reconstitution of behavior. Specifically, being able to inhibit inappropriate responses buys an individual time to allow for other cognitive processes to be engaged. For Barkley, executive functions include both behavioral inhibition and those four cognitive processes on which behavioral inhibition can influence.

According to Denckla's (1996) conceptualization, executive function comprises processes subserving nonautomatic behaviors with supraordinate goal(s). Executive function includes intention, working memory, sustaining set maintenance, self-monitoring, and goal-oriented planning. Intention comprises four subcomponents. These include initiating a response, sustaining a response, inhibiting extraneous responses, and shifting from one response to another.

Attempts to specify the components of executive function have met with myriads of descriptions. However, many have been differences in semantics rather than in substance. For example, Barkley's term "reconstitution" refers to analyzing the situation, generating multiple plans of action, and synthesizing a behavioral set in the service of reaching a goal. This definition inherently must include Denckla's idea of intention to act and goal-oriented planning. Thus rather than getting lost in specific definitions of each and every component of executive function, this study will only focus on those most relevant to ADHD: 1) the inhibition of inappropriate responses, 2) working memory, 3) planning/strategy use, 4) sustained attention, and 5) self-monitoring/response shifting.

Those familiar with ADHD children will note the variability existent within the ADHD population. The most current Diagnostic Statistical Manual delineates three different subtypes of ADHD: Hyperactive-Impulsive, Inattentive, and a Combined type (APA, 2000). Given the heterogeneity of the behavioral phenotype, one would surmise that underlying neuropsychological underpinning might differ as well, which should have consequences in cognitive functioning. Indeed, recent research has begun to look at cognitive profiles of subtypes of ADHD.

Based on Cohen's model of attention, Lockwood et al. (2001) examined sensory selection, response selection, capacity/focus, and sustained attention in children with ADHD. They found that the Inattention subtype of ADHD performed worse on tasks requiring sensory selection, as predicted given the "sluggish" tempo reported among this population (McBurnett et al., 2001). However, a major weakness of this study was that it was a retroactive study. The clinical tests they categorized as tapping sensory selection included Digit Span, copy of the Rey Complex Figure, Trail Making A, and recognition score of a story memory task. While all of these tasks required subjects to selectively attend to a sensory modality, their scores also reflect the integrity of other complex cognitive processes, such as memory, hand-eye coordination, and organizational skills. Thus it is not clear if the Inattention subtype of ADHD has worse selective attention or weakness with other cognitive processes as well.

Nigg et al. (2002) looked at inhibition, planning, and set shifting of the Inattentive and Combined subtypes of ADHD. Although both subtypes performed worse than controls, there were no differences between the two subtypes. The lack of differences could be due to several factors. One, the authors predicted that the Inattentive subtype would have more problems with mental inhibition, whereas the Combined subtype would have more problems with motor inhibition and planning. It is not clear why the authors focused on mental inhibition for the Inattentive group and not on sustained attention, such as traditionally measured by the continuous performance test. It may be that if the authors had looked at other measures of sustained attention, the results would have been slightly different. Two, the subtypes of ADHD chosen to be the focus of this study were not the ideal groups. The current DSM-IV Text Revision (DSM-IV-TR; APA, 2000) delineate three subtypes: Hyperactive-Impulsive (HI), Inattentive (IA), and Combined, which meet both the criteria for HI and IA. The ideal groups to compare would be the HI and the IA. The reason that the authors chose to look at the Combined and IA groups may be because of an epidemiological phenomenology that challenges researchers in this field.

Barkley (1996) posited that at the core of executive function difficulty of children with ADHD is impulsivity. This impulsivity prevents the proper development of other functions, such as sustained attention. Thus according to Barkley's model, children will exhibit impulsive symptoms first, then as they grow older, symptoms of inattention will emerge as

these children fail to develop age-appropriate cognitive processes. In other words, the HI subtype will grow into the Combined subtype, and the age of onset for the two subtypes will differ. The HI subtype will have a younger age of onset, while the Combined subtype will be older when given this diagnosis. Data from the DSM-IV field trials appear to support Barkley's prediction. The HI group's average age at assessment was younger than the Combined group's by almost three years. The Combined group's age at assessment was younger than the IA group's by one year. These differences were all statistically significant (Lahey, et al., 1994). In studies comparing ADHD subtypes, the trend that the IA group is older than the HI or the Combined group is seen as well (Chhabildas, Pennington, & Wilcutt, 2001; Faraone, Biederman, Weber, & Russell, 1998).

If this phenomenon indeed exist, then it may not be appropriate to control for equivalent age between ADHD subtype groups. If in striving for equivalent age between different ADHD subtypes, studies may be limited to school-aged children, because toddlers and pre-schoolers are not expected to have age-inappropriate inattentive symptoms that interfere with their social functioning; thus few may meet criteria for the IA subtype. If limited to school-aged children, children who were previously diagnosed as the HI subtype may have developed enough inattentive symptoms to meet criteria for the Combined type; thus few children meeting the HI subtype remain. This may have been the situation encountered by Nigg et al. (2002). They aimed to match the groups on age. The average age for the Inattentive group was 124 months, 115 months for the Combined group, which are well into the school age.

The present study aims to compare executive function of the HI, IA, and Combined subtypes of ADHD. Age will not be matched between groups for the reason described above. Five areas of executive functioning will be focused: 1) the inhibition of inappropriate responses, 2) working memory, 3) planning/strategy use, 4) sustained attention, and 5) self-monitoring/response shifting. These have been measured operationally using tasks such as the continuous performance test (CPT; Connors, 1995; Gordon, 1988), the Stop task (Logan et al., 1984), Stroop test (Golden, 1978), Go-No Go (Golden et al., 1991), the Wisconsin Card Sorting Test (WCST; Heaton, 1981; Kongs et al., 2000), Trailmaking Test (Reitan & Wolfson, 1985), Tower of London (Krikorian et al., 1994), sentence span, and digit span. A major problem is that most of these tasks are inappropriate for direct application in Taiwan due to language differences. For example, the Stroop and the Trailmaking tests both require a high level of familiarity with the alphabet and English vocabulary. Thus more culture-free tests such as the Color Trails Test (Williams et al., 1995) and the attention subtests of the Leiter International Performance Scale-Revised (Leiter-R; Roid & Miller, 1997) will be more appropriate for Taiwan. A second problem is that many of these tasks have instructions that are too difficult for very young children to understand. In recent years, several new tests have been developed to be more appropriate to

pre-schoolers, including the NEPSY: A Developmental Neuropsychological Assessment (Korkman, Kirk, & Kemp, 1998), Test of Everyday Attention for Children (Manly, Robertson, Anderson, & Nimmo-Smith, 1999), and the Das-Naglieri Cognitive Assessment System (CAS, Naglieri & Das, 1997). The present study will consult these instruments to develop tests that are appropriate to measure inhibition, working memory, planning/strategy use, sustained attention, and self-monitoring/set shifting in Taiwan.

Based on reports that the IA subtype has a “daydreamy” or “sluggish” presentation (McBurnett et al., 2001), this group is predicted to perform less well than other groups on tasks requiring sustained attention. In contrast the HI subtype is expected to perform poorly on tasks requiring inhibition. Furthermore, based on Barkley’s (1996) theory, this group is also predicted to perform poorly on working memory, planning/strategy use, and self-monitoring/set shifting. The Combined subtype is predicted to experience difficulty on all tasks, but the level of their performance may not differ from the other subtypes.

研究目的

In summary, the specific aims of the present study are as follows:

1. Compare the executive function of ADHD subtypes (Inattentive, Hyperactive-Impulsive, Combined).
2. Develop tests of executive function that are appropriate to Taiwan’s culture, and obtain normative data for comparison with the ADHD groups.

研究方法

Participants

Subjects will be 60 children meeting diagnostic criteria for Attention-Deficit/Hyperactivity Disorder (ADHD), equally distributed among the Inattentive (IA), Hyperactive-Impulsive (HI), and Combined (C) subtypes. The groups will not be matched on age because of the observed phenomenon that the HI subtype tend to be younger at time of assessment compared to the IA subtype; selecting only subjects who are matched on age may miss actual differences in executive function between groups.

Because the three ADHD groups may potentially have different age ranges, three groups of control subjects will be recruited, each matched to a respective ADHD group. Exclusionary criteria for all subjects include: 1) history of neurological disorder such as epilepsy, tumor, or brain injury; 2) history of psychiatric disorders such as Obsessive-Compulsive Disorder, Tourette’s Disorder, Pervasive Developmental Disorders, Mental Retardation, and current major depressive episode. Children with comorbidity of Oppositional-Defiant Disorder and Learning Disability will not be excluded from the ADHD groups because studies show that the comorbidity of these disorders with ADHD is high, 22% for Learning Disability (August & Garfinkel, 1989), 54-67% for Oppositional-Defiant Disorder (Barkley, 1998). To exclude these children may result in a

specific population of ADHD where results cannot be generalized to the general ADHD population. Instead, comorbid diagnosis will be recorded, and statistical analyses will be conducted with and without exclusion of these subjects to see if comorbidity makes a difference in findings. Exclusionary criteria for the control groups include subjects meeting five criteria for inattention or hyperactivity/impulsivity, because field trial data indicated that these borderline cases might have ADHD (Lahey et al., 1994). Inclusionary criteria for the all subjects include: 1) age 4-12, and 2) intelligence quotient between 70 and 130 as estimated from the Wechsler Intelligence Scale for Children – Third Edition, Chinese Version (WISC-3; 陳榮華，1997).

Subjects taking medication will be requested to be off medication for at least 24 hours before testing. Diagnostic category will be obtained from psychiatrists referring the ADHD subjects and ascertained using the Composite International Diagnostic Interview (CIDI; WHO, 1998). The CIDI will be administered by trained graduate students of clinical psychology. Written consent will be obtained from children subjects' parents and oral assent will be obtained from children subjects before proceeding with testing of children subjects.

Measures

Tests measuring inhibition, working memory, planning/strategy use, sustained attention, and self-monitoring/set shifting will be developed after reviewing published instruments, including tests already developed in Taiwan. Newly developed tests will be piloted on developmentally normal children before the experimental data are collected.

結果與討論

During the first year of this study, we have reviewed available instruments and developed tests appropriate to Taiwan's language and culture. The following is our battery to examine the five targeted areas of executive function:

The CPT developed by 張如穎 (one of the co-investigators during the second year of this study) has two subtests: Inhibition and Executive Function. The Inhibition subtest may be an excellent measure of motor inhibition. This task requires subjects to respond to all targets but not to the "dog." Targets are all pictured, which makes this task attractive and appropriate for use with young, pre-literate children. Subjects establish an automatized response tendency, which must be inhibited upon seeing the "dog." The spirit of this test is similar to the Go-No Go, which is a common clinical instrument used to test inhibition. The advantage of this newly developed Inhibition over the Go-No Go is that accuracy and reaction time can be objectively quantified. The traditional Go-No Go requires subjective judgment of error production, and reaction time cannot be collected. The Executive Function subtest is a measure of sustained attention. On this task, subjects are to respond "dog" when they see "pig," respond "pig" when they see "dog," and respond "bull" when they see "bull." The spirit of this task is similar to NEPSY's Auditory Attention and Response Set (Korkman et al., 1998), which is one of the core subtests in NEPSY's

Attention/Executive Function domain score. Subjects are required to keep these three rules in mind and focus on the computer screen as targets flash through. Good performance is dependent on the subject's ability to sustain attention on this task. The NEPSY Auditory Attention and Response Set subtest is purposely excluded because inter-rater reliability is judged to be less than optimal even after four hours of training. Given the subjectivity involved in scoring, it was decided to use the CPT Executive Function subtest, as accuracy and response time can be objectively measured.

Several subtests from NEPSY are included in the current battery, including Visual Attention, Design Fluency, and Tower (Korkman et al., 1998). The Visual Attention subtest is a visual search task. Its scores incorporate accuracy, commission error, and time. Good performance is dependent on subject's ability to conduct visual search and focus on the task. It is included in this battery as a measure of Sustained Attention. The Design Fluency subtest requires subjects to produce as many unique designs as possible in one minute. The number of unique designs produced, which is the only NEPSY score, will be used as a measure of Self-Monitoring/Response Shifting because good performance is dependent on the subject's ability to constantly monitor his/her own responses and shift mental set to come up with new designs. We will also look at two other scores developed specifically for this study: Perseveration and Strategy scores. The Perseveration score is the number of repeated, or non-unique, designs produced. Perseverations reflect an inability to inhibit a previously generated response and will be a part of the Inhibition domain. The Strategy score is defined as number of designs that relates to be immediate previous design by 1) being a mirror image, 2) being in a rotated form, or 3) adding or subtracting one line. Such responses reflect a systematic strategy to produce unique designs, and will contribute to the Planning/Strategy Use domain. The Tower subtest requires subjects to configure three balls into a designated position on three towers in a limited number of moves. Accurate performance on the more difficult items requires subjects to move away from the goal state first, in order to reach the goal state. Thus this problem-solving task requires planning, and will contribute to the Planning/Strategy Use domain.

There are already working memory measures that are appropriate for use in Taiwan, and these will be used in this study. 曾世杰's 工作記憶測驗(民88)is an auditory working memory test. It requires subjects to repeat, in correct sequence, items among a set that meet a pre-specified criteria. This task requires working memory because subject cannot just rehearse the heard sequence; s/he must select items that meet the pre-specified criteria and state only these items, in their correct sequence. We will compare performance on this subtest with the Digit Span subtest of the Wechsler Intelligence Test for Children, Third Edition. The second part of the Digit Span has more working memory components than the first, because it requires mental manipulation of auditory stimuli in addition to pure rehearsal of heard stimuli. We will also use 洪儷瑜's 記憶廣度 subtest, which is a part of

her 漢字視知覺測驗（民 88）. Targets for this test are Greek alphabets, which are presented in subsequently lengthier strings. Subjects must identify targets from foils. This is a good visual working memory task because most Taiwanese students are unfamiliar with Greek alphabets and thus can only process them non-linguistically.

Another published test we will be using is the Children's Color Trails Test (CCTT; Llorente, Williams, Satz, & D'Elia, 2003). This test was based on the Trialsmaking Test, but the original Trialmaking Test requires familiarity with English alphabets, which has been problematic to use in non-English speaking countries. The CCTT requires subjects to execute an automatized set (i.e., connect numbers) but shifting between two different colors (Part 2). Thus the time score from Part 2 of the CCTT will be used in this study as a measure of Self-Monitoring/Response Shifting.

Two tests have been developed by our group to meet our needs for tests of Planning/Strategy Use and Self-Monitoring/Response Shifting. The first of these, Coding, is based on a subtest from the CAS (Naglieri & Das, 1997). There are three items for this test, all requiring subjects to complete a page of codes based on the model on the top of the page. Written codes are patterns of circles (e.g., right circle, left circle, two circles) to minimize the need for good motor coordination, which may be difficult for pre-school children. The first item has random target codes and serves as a baseline against which to evaluate the latter two items. The second item has organized target codes, with the same target code appearing in each column. The third item also has organized target codes, with the same target code appearing in diagonal positions on the page. An efficient approach would be to complete one target code before moving on to the next. The difference score between items two and three from item one (baseline) will be use as an index of Planning/Strategy Use. The second test that we developed is based on a subtest from the Test of Everyday Attention for Children (TEACh; Manly et al., 1999). This test requires subjects to count, and upon meeting a specific cue, to change the direction of counting. This test requires subjects to monitor their own execution of a mental set (counting), and upon meeting a cue, to shift mental sets to another manipulation of the same set (count backwards). Thus its accuracy score will contribute to the Self Monitoring/Set Shifting domain.

We are currently piloting these tests on 30 children recruited from 台北市大安區銘傳國小. Once pilot data have been completed, we will exclude those tests that are inappropriate to or insensitive to abilities present in the 4-12 year age range. We expect pilot data will be collected through July. Two of the graduate research assistants have gone through training for administering the CIDI. Anticipated schedule for the coming year is as follows:

	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sept	Oct	Nov	Dec
2004	Test development & CIDI training					Pilot stage		Finalize battery	Collect ADHD & control data			

2005	Collect ADHD & control data	Data analysis	

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