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## ORIGINAL ARTICLE

# Quality of life of methylphenidate treatment-responsive adolescents with attention-deficit/hyperactivity disorder

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**Abstract** Quality of life (QOL) in methylphenidate treatment-responsive adolescents with attention deficit/hyperactivity disorder (ADHD) was assessed. Patients were 12- to 18-year-old adolescents with ADHD (total  $n = 45$ ) who had been on methylphenidate treatment for at least 3 months and were clinically judged to be improved. The self-completed Taiwanese Quality of Life Questionnaire for Adolescents (TQOLQA) was used, and the resulting measures were compared between adolescents with ADHD and: (1) community adolescents ( $n = 2316$ ); (2) treatment-responsive adolescents with a chronic medical condition (i.e., adolescents with leukemia in its first and complete continuous remission for at least 3 years after chemotherapy) ( $n = 39$ ). Patients' cognitive profile and their daily executive functioning were also obtained for analysis. The QOL of the treated adolescents with ADHD was reported to be worse than that of both the community healthy adolescents and the adolescent leukemia survivors in the self-reported TQOLQA domain of "psychological well-being". Treated adolescents with ADHD still had impaired executive skills in natural, everyday environments, and the scores for daily executive abilities could predict the QOL measures. Factors besides pharmacotherapy should be explored to further improve the QOL of medication-treated adolescents with ADHD. Copyright © 2012, Elsevier Taiwan LLC. All rights reserved.

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## Introduction

Attention-deficit hyperactivity disorder (ADHD) is the most common neuropsychiatric disorder of children, affecting approximately 5% of the school-age population [1]. It is characterized by developmentally inappropriate deficits in attentional performance, impulsivity, and motor restlessness or hyperactivity starting in early childhood [2]. It has been reported that hyperactivity tends to decline in adolescence and that improvements occur in attention span and impulse control [3]. However, there are increased demands in adolescence for autonomy and independence, hence symptoms may also worsen and cause progressive functional impairment, including school dysfunction, problems with peer interaction, family conflict, poor occupational performance, injuries, antisocial behavior, traffic violations, and accidents [1]. Recent prospective longitudinal studies indicate that up to 50% of individuals with ADHD continue to experience impairment from some symptoms of the disorder, if not the full syndrome, in adolescence and early adulthood [4].

Quality of life (QOL) is a multidimensional concept that encompasses psychological, physical, and social well-being. QOL instruments may be particularly relevant to research on the treatment of ADHD because this disorder has a range of psychosocial outcomes that are not captured by clinical symptoms alone [5]. Definition of children's health-related QOL has been based on function or disabilities, or in terms of a match between aspirations and experience [6]. Since children and adolescents do not share adult views about the cause, etiology and treatment of illness, and they may also adopt a different time perspective regarding the course of a disease, we have to take their age and development into account. Research from developed and developing countries has demonstrated that parents reported the health-related QOL of clinic-based samples of ADHD children to be poorer than that of the control population [7–9]. In one recent systematic review of the medication effect on the QOL in ADHD [7], 25 published papers using seven different QOL measures were identified. Most ( $n = 20$ ) of these studies focused on children and adolescents, and most investigated a single molecule, atomoxetine ( $n = 15$ ), with relatively few studies investigating methylphenidate ( $n = 5$ ), amphetamines ( $n = 4$ ) and manifaxine ( $n = 1$ ). These studies support a positive short-term effect of medication on the QOL of children, adolescents and adults with ADHD that mirrors, to some extent, the effects of these medications on ADHD symptoms, although with smaller effect sizes. However, the available data are currently rather limited in scope. For example, almost all studies used parent- rather than child-reported measures. There clearly needs to be more studies regarding self-reported QOL in those with ADHD.

The present study used the self-reported Taiwanese Quality of Life Questionnaire for Adolescents (TQOLQA) to assess the quality of life of methylphenidate-treated Taiwanese adolescents with ADHD. TQOLQA is a questionnaire that covers the important domains for adolescents, fitting the personal (physical and mental), interpersonal (family function, intimate friends, and social networks), external (income and housing), and global (macro environment)

spheres [10]. In addition, the adolescent's performance in daily executive skills after methylphenidate treatment was assessed using a parent-reported questionnaire to analyze its predictive powers in relation to adolescent QOL outcome.

## Materials and methods

### Patients

The ADHD patients were 12- to 18-year-old adolescents recruited from the outpatient service of the department of psychiatry of a university-affiliated hospital in Taiwan. To enter the study, adolescents were required to meet the following criteria: (1) diagnosis of ADHD on the basis of the *Diagnostic and statistical manual of mental disorders*, 4<sup>th</sup> edition (DSM-IV-TR) criteria; (2) continuous methylphenidate treatment for at least 3 months and improvement reported subjectively by the adolescent himself or herself; (3) improvement as rated by the treating physician using the Clinical Global Impressions-Improvement (CGI-I) scale targeting the core symptoms of ADHD listed in DSM-IV criteria; (4) the adolescent was living with his or her family, and was not in foster care or an institution; and (5) the adolescent was tested to have a full-scale intelligence quotient above 70 by the Wechsler Intelligence Scale for Children-III [11]. The diagnosis of ADHD was made through the application of multiple data sources including: (1) clinician interview; (2) clinical observation of the patient's behavior; (3) history provided by the parents and results obtained from the Chinese-language version of the Swanson, Nolan and Pelham IV scales (SNAP-IV Teacher and Parent Rating Scale, parent version) [12]. The scales completed by the parents or teachers, or both, were obtained repeatedly in the clinical services, though with different time intervals among the ADHD cases, and they contributed to the final decision of the clinician-rated CGI-I. Adolescents with a comorbid diagnosis of autism spectrum disorder were excluded from the study.

Of the 192 adolescents treated in our clinic during the 6-month recruitment period (January to June 2009), 53 were eligible for study entry. Questionnaires were delivered to these 53 adolescents and their parents, to be completed at home. We had specifically asked the parents not to help with or inspect the adolescent's reports on the questionnaires. Forty-five families (84%) mailed back their questionnaires; hence, the final study cohort included 45 adolescents with ADHD (36 males and 9 females with an average age of 14 years 10 months  $\pm$  2 years 7 months). Clinical information for each adolescent was extracted from hospital records and included both disease-related variables (e.g., ADHD subtype, age at diagnosis, intelligence quotients, comorbidity pattern) and treatment-related variables (e.g., age at starting medication, duration of pharmacological treatment, daily medication dosage).

In order to compare QOL between hospital and community samples, as well as adolescents with chronic medical versus psychiatric conditions, two groups of controls were enlisted. The first group consisted of adolescents in the community, and was drawn from the data bank of the validation study of the Taiwanese Quality

of Life Questionnaire for Adolescents. This first group of 2316 control adolescents was reported to be free of any acute or chronic illness, and was sex-matched in ratio to our case group (1910 boys, 415 girls, with an average age of 12 years 2 months  $\pm$  10 months). The second control group was a group of adolescents with a chronic medical condition (leukemia in its first and complete continuous remission for at least 3 years after chemotherapy). Adolescents with a pre-existing psychiatric disorder before receiving the diagnosis of leukemia were excluded. This second group of 39 control adolescents consisted of 26 boys and 13 girls with an average age of 14 years 5 months  $\pm$  2 years 5 months.

This study was approved by the Institutional Review Board. Informed consent was obtained from the participants' parents following the guidelines of the Institutional Committee on Clinical Investigation.

## Measures

We used the Taiwanese Quality of Life Questionnaire for Adolescents (TQOLQA), and the Behavior Rating Inventory of Executive Function (BRIEF), a behavioral rating measure.

TQOLQA is a revised version of the Quality of Life Questionnaire for Adolescents developed in China on the basis of the QOL project of the World Health Organization. The initial 90-item questionnaire was shortened to 38 items by means of principal component analyses so that a sufficiently short instrument could be used in clinical settings [10]. The TQOLQA assesses seven factors: family, residential environment, personal competence, social relationships, physical appearance, psychological well-being, and discomfort/pain. The questionnaire used a five-point Likert scale rating and enquired as to the respondent's experiences over the preceding 2 weeks. Higher QOLOA scores reflected a better QOL.

BRIEF is a behavioral rating measure that was specifically designed to assess everyday executive skills in natural, everyday environments, including the home and school of the children and adolescents [13,14]. The BRIEF is composed of two major index scales and a composite of the two: the behavioral regulation index (BRI), the meta-cognition index (MI), and the global executive composite (GEC). Each of the two major index scales is further composed of subscales. The BRI is composed of the scales inhibit, shift, and emotional control, and the MI comprises the scales initiate, working memory, plan/organize, organization of materials, and monitor. This scale has been standardized in the Chinese language with valid psychometric data [15], and we obtained this Chinese-language version from the publisher. Parents of adolescents with ADHD were asked to complete the BRIEF at the time of study entry. T-scores were used as the measure in statistical analysis. These scores are linear transformations of the raw scale scores, and higher T-scores indicate a greater degree of executive dysfunction. A T-score at or above 65 was considered to fall within the clinical range.

## Analysis

Data from self-reported TQOLQA were compared between the ADHD group and the two groups of control adolescents

separately, using independent *t* tests. Effect sizes were calculated as the means of the control sample minus the means of the ADHD sample divided by the standard deviation of the control sample [16]. The effect size of 0.2 is considered small, 0.5 is moderate, and 0.8 is large [17].

Patients' cognitive profiles and abilities in daily executive functioning were analyzed by correlational and regression analysis to determine their predictive power in relation to the measures of QOL.

## Results

### Patient characteristics

Of the ADHD adolescents, 80% were boys and the average age of initial ADHD diagnosis was 10 years 10 months, while the average current age was 14 years 10 months. ADHD adolescents were of normal intelligence with mean full-scale intelligence quotients of  $100.76 \pm 10.15$  (range 85–123). However, their performance of daily executive skills as reported by their parents in the BRIEF was in the impaired range, with average *t* scores for the BRI of  $65.39 \pm 11.57$  (range 44–92), average *t* scores for the MI of  $66.37 \pm 9.74$  (range 47–93), and average *t* scores for the GEC of  $67.37 \pm 10.18$  (range 47–94).

In all, 8.9% of the ADHD adolescents had comorbid oppositional defiant disorder, 13.3% had comorbid mood or anxiety disorders, and 17.8% had academic problems. Only 46.7% of the adolescents were free of any comorbid psychiatric disorders. Detailed clinical data for the ADHD group is presented in Table 1.

### Self-reported TQOLQA

Group comparisons of adolescents' self-reports on the TQOLQA showed that the ADHD adolescents' QOL was significantly poorer than that of the community controls in the domains of "Psychological well-being" ( $p = 0.001$ ) and "Pain/discomfort" ( $p = 0.001$ ). In addition, data showed ADHD adolescents' QOL to be significantly poorer than that of the adolescent leukemia survivors in the domains of "Psychological well-being" ( $p < 0.05$ ) and "Personal Competence" ( $p < 0.05$ ). A detailed presentation of the comparison of TQOLQA between the ADHD adolescents and the control groups is presented in Table 2.

### Predictors of QOL

Analysis revealed that the domain of "Psychological well-being" in the TQOLQA of ADHD adolescents was correlated with the three composite scores of the BRIEF as completed by their parents ( $r$  ranged from  $-0.38$  to  $-0.78$ ). Regression analysis was further performed to investigate how the impairment in daily executive skills might predict QOL measurements. In summary, performance of daily executive functions as reflected in the BRI, MI and GEC could predict the "Psychological well-being" score in the TQOLQA (all  $p < 0.01$ ). Poor daily executive skills as reported by the parents led to poor self-reported measures on QOL. The results of the regression analysis are presented in Table 3.

**Table 1** Demographic and clinical characteristics of the children with medication-treated attention deficit/hyperactivity disorder (ADHD) ( $n = 45$ ).

Characteristics	
Sex	
Male	36 (80.0)
Female	9 (20.0)
Current diagnosis	
ADHD, primary inattentive	26 (58.0)
ADHD, combined	19 (42.0)
Current age (yr)	14.82 $\pm$ 2.62
Age at diagnosis (yr)	10.80 $\pm$ 3.16
Regular medication prescribed since	
Grade 1–2	14 (31.1%)
Grade 3–4	7 (15.6%)
Grade 5–6 or after	24 (53.3%)
Comorbidity	
Oppositional defiant disorder	4 (8.9%)
Mood disorder/anxiety disorder	6 (13.3%)
Tourette/tic	4 (8.9%)
Developmental language disorder	4 (8.9%)
Academic problems	8 (17.8%)
No psychiatric comorbidity	21 (46.7%)
Verbal intelligence quotient	101.76 $\pm$ 10.97
Performance intelligence quotient	100.86 $\pm$ 10.72
Full intelligence quotient	100.76 $\pm$ 10.15
BRIEF ( <i>t</i> score) <sup>a</sup>	
Behavioral regulation index (BRI)	65.27 $\pm$ 11.67
Metacognition index (MI)	66.44 $\pm$ 9.84
Global executive composite (GEC)	67.38 $\pm$ 10.30
Medication	
Average dose	
Methylphenidate only ( $n = 43$ )	48.3 mg/day <sup>b</sup>
Methylphenidate plus antidepressant ( $n = 2$ )	54 mg/day <sup>b</sup>

Data are presented as  $n$  (%) or mean  $\pm$  SD.

<sup>a</sup> BRIEF = Behavior Rating Inventory of Executive Function; *t* scores at or above 65 were considered to fall within the clinical range.

<sup>b</sup> Average daily dose in Concerta equivalents.

## Discussion

This was a preliminary study to assess QOL in methylphenidate-responsive adolescents with ADHD in a developing Asian country. As reported, there were significant impairments in psychosocial domains of self-reported QOL measures, as compared with community controls and treated adolescents with chronic and severe medical disorders.

The disease model of medicine has long assumed that the elimination of the symptoms of disease is in itself identical to functional remission; hence reports on treatment outcome for psychiatric disorder (including ADHD) traditionally have focused on symptom-relief efficacy and

medication safety. Among many indicators, the “CGI-scale” and “time to stay on medication in the sense of self-selection for treatment discontinuation” were two frequently used outcome measures in psychopharmacology research [18]. Given that treatment responsiveness as assessed by these two indices was a condition for entry into our study, the finding that methylphenidate-responsive adolescents still have poor QOL is a further reminder that symptoms and functioning are overlapping, but not identical, constructs in ADHD. As medicine has moved from a “life-preserving” to a “health-promoting” science, QOL has become one of the important outcome measures in both clinical research and routine patient care [19]; this is especially so for psychiatric treatment programs such as that for ADHD, since psychopathology tends to persist [20].

Danckaerts and colleagues have performed a systematic review of 36 studies of QOL in children and young people with ADHD [21]. This review showed that ADHD has a robust negative impact on QOL across a broad range of psychosocial, achievement and self-evaluation domains, as reported by the parents of children with ADHD. Our finding adds support to these QOL studies in individuals with ADHD and further supports the idea that the negative impact of ADHD is a cross-cultural phenomenon.

Our comparative findings between treated adolescents with ADHD and adolescent leukemia survivors deserve further discussion. While leukemia therapies are highly effective, recent longitudinal follow-up studies have shown excesses of both mortality and morbidity in leukemia survivors. These morbidities include early death, second neoplasm, organ dysfunction, impaired growth and development, decreased fertility and impaired intellectual function [22,23]. And these late morbidities have had a negative impact on adolescents’ health-related QOL, as reported in developed Western countries [24], as well as in Taiwan [25]. The fact that medication-treated ADHD adolescents who were clinically judged to be improved should have a QOL significantly poorer than the adolescent leukemia survivors in several domains further reminds us that ADHD is a serious condition.

The finding that many patients considered to have responded to treatment do not achieve good health leaves room for improvement in the management of ADHD. One of our interesting results is that adolescent performance of daily executive functioning as measured by the BRIEF is a factor predicting QOL; this may provide an anchor point for intervention planning. The current models of ADHD include dysfunction in executive processes as one important pathway for understanding this heterogeneous disorder [26–28]. A recent meta-analytic review suggests that executive dysfunctions in ADHD have most often been observed in measures of response inhibition, vigilance, working memory, and planning [29], and that these all may affect the actual functional status of the daily executive skills of the individual adolescent. The actual concordance and association between performance-based measures of executive function (e.g., various neuropsychological tests performed in the laboratory) and ratings of executive function processes by parents (e.g., BRIEF) have been demonstrated in a previous study [30]. Our results implied that by enhancing daily executive skills through well-designed psychological interventions, an improvement in

**Table 2** Taiwanese Quality of Life Questionnaire (TQOLQA) for adolescents: results when administered in adolescents with attention-deficit/hyperactivity disorder (ADHD) and two control groups.

	Control 1 <sup>a</sup> n = 2325	Control 2 <sup>b</sup> n = 39	Treated ADHD n = 45	Effect size, control 1 versus ADHD	Effect size, control 2 versus ADHD
Age (months)	170.25 ± 9.65	173.43 ± 29.64	177.86 ± 31.43		
Sex M/F	1910/415	26/13	36/9		
Family	64.18 ± 20.33	71.87 ± 22.69	63.70 ± 20.17	0.0	0.4
Residential environment	61.29 ± 18.16	62.42 ± 24.85	63.25 ± 18.79	-0.1	0.0
Personal competence	55.79 ± 17.00	63.65 ± 22.07	53.57 ± 18.27	0.1	0.5*
Social relationship	59.26 ± 17.94	61.03 ± 21.83	63.18 ± 21.40	-0.2	-0.1
Physical appearance	69.39 ± 17.15	73.24 ± 16.5	64.31 ± 25.75	0.3	0.5
Psychological well-being	74.90 ± 16.06	76.28 ± 19.25	66.57 ± 20.52	0.5**	0.5*
Pain/discomfort	77.48 ± 15.31	72.65 ± 18.23	66.73 ± 20.56	0.7**	0.3

\**p* < 0.05; \*\**p* < 0.01 (all levels of significance drawn from independent samples *t* test).

<sup>a</sup> Control 1 = community adolescents.

<sup>b</sup> Control 2 = adolescent leukemia survivors.

QOL might be possible. Current studies on QOL have focused almost exclusively on one treatment modality (pharmacological), so systematic surveys of the impact of psychotherapy on QOL, on their own or in multimodal combinations with medication, will be an approach worthy of further pursuit.

Our study results should be viewed in the light of the study’s limitations. First, our sample size was small and we provided the experience of only one treatment center in Taiwan; the study was not national or population-based in

scope. A single institution does not have a sufficient number of patients to control for the numerous patient-specific and therapy-specific variables involved. Multi-institutional collaboration for detailed analysis in the future would be needed. Second, it has been reported that there are several levels of factors associated with a child’s QOL, which include not only the psychopathology of the child, but also family/school/social networks. Parents’ views may be influenced by the development of other children (such as the subjects’ siblings), their own conceptualization of the illness, and their own mental health [20]. In the study reported here we did not explore factors such as family composition, family socio-economic status, family social contacts, school environment, teachers’ expectations and perceived social support in their association with adolescent QOL. These may all be modulating factors in the final QOL of the treated adolescent. However, these are issues we are not able to address with currently available data. Third, since both improved physician-rated CGI and ADHD symptom improvement were required conditions for entry into the study and QOL was our focus in terms of outcome measures, we collected data only from the adolescents’ perspective. Nevertheless, children and parents do not necessarily share similar views about the impact of illness, and the correlation between the child’s self-report and the proxy report is not necessarily consistent [31,32]. Although self-reporting on QOL is assumed to be the primary method of collecting subjective information about well-being, measuring concomitant self-reported QOL and proxy (parental) reports with one instrument would probably be considered more appropriate.

In conclusion, our findings provide support that methylphenidate-treated ADHD adolescents still have multiple problems in broader health outcomes as represented by the concept of QOL. This study may serve as a cross-cultural validation of ADHD as a common concern for adolescents and families worldwide. It has been proposed that the main goal of healthcare is to improve patients’ perceptions of their health and the extent to which health problems interfere with their QOL [33].

**Table 3** Daily executive skills and cognitive function predicting quality of life index in adolescents with attention-deficit/hyperactivity disorder (ADHD).

	Self-report TQOLQA Psychological well-being
	Parameter estimate <i>p</i> (95% CI)
BRIEF	
BRI	-0.68 (-1.18, -0.19) <i>p</i> = 0.008
MI	-1.10 (-1.65, -0.56) <i>p</i> < 0.001
GEC	-0.98 (-1.51, -0.44) <i>p</i> = 0.001
Wechsler IQ	
VIQ	0.42 (-0.19, 1.02) <i>p</i> = 0.172
PIQ	0.35 (-0.28, 0.97) <i>p</i> = 0.264
FIQ	0.46 (-0.17, 1.10) <i>p</i> = 0.148

CI, confidence interval; TQOLQA = Taiwanese Quality Of Life Questionnaire For Adolescents; BRI = behavior regulation index; BRIEF = Behavior Rating Inventory of Executive Function; FIQ = full-scale intelligence quotient; GEC = global executive composite; MI = metacognition index; PIQ, performance intelligence quotient; VIQ = verbal intelligence quotient.

Therefore there is clearly a need for optimization of current treatment regimens to help adolescents with ADHD.

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