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# A comparison of efficacy between cognitive behavioral therapy (CBT) and CBT combined with medication in adults with attention-deficit/hyperactivity disorder (ADHD)

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ABSTRACT

The study aimed to explore whether cognitive behavioral therapy (CBT) combined with medication is superior to CBT alone in core symptoms, emotional symptoms, self-esteem as well as social and cognitive functions of adult attention-deficit/hyperactivity disorder (ADHD) patients. Samples from a previous RCT study and outpatient participants were all included. A total of 124 patients received 12 weeks of manualized CBT sessions, either with ($n$ = 57) or without ($n$ = 67) medication. Efficacy variables were evaluated at baseline and each week. Mixed linear models (MLM) were used to compare differences between the two groups in all of the above domains. Within-group comparisons showed that both groups had robust improvements in core ADHD symptoms, emotional symptoms and social functional outcomes. The CBT + M group presented more domains of improvement in executive functions than the CBT group. However, comparisons between groups didn't indicate the superiority of CBT + M in core symptoms, emotional symptoms and self-esteem. Instead, the CBT group showed a greater improvement in the physical domain of the WHOQOL-BREF than the CBT + M group. This study further indicated that CBT is an effective treatment for adults with ADHD. A combination of CBT and medication presented broader improvements in executive functions, but not in clinical symptoms, than CBT alone.

## 1. Introduction

ADHD is a childhood-onset neurodevelopmental disorder characterized by inappropriate levels of inattention, hyperactivity and impulsivity (Fischer, 2012), with a prevalence rate of 3–5% in childhood (Polanczyk et al., 2015). The prevalence of ADHD in adults across twenty countries was recently estimated at 2.8%, ranging from 0.6% to 7.3% (Fayyad et al., 2017). Adults with ADHD have been associated with a high risk of personality disorders (Matthies and Philipsen, 2016) and significant impairments in academic (Kuriyan et al., 2013; Voigt et al., 2017), health (Brevik et al., 2017; Spencer et al., 2014), occupational (Hechtman et al., 2016; Kirino et al., 2015), and social (Das et al., 2012) domains.

According to the National Institute for Health and Care Excellence (NICE) guidelines (UK, 2018), pharmacological and psychological treatments are both recommended interventions for adults with ADHD (Faltinsen et al., 2018). Pharmacotherapies, both stimulants and non-stimulants, are effective on core ADHD symptoms, anxiety and depression symptoms, social functions (Mattos et al., 2013) and executive functions (Fuermaier et al., 2017; Ni et al., 2013) with long-term benefits (Fredriksen and Peleikis, 2016). Methylphenidate (MPH) was shown to be a dopamine (DA) and norepinephrine (noradrenaline, NA) reuptake inhibitor, progressively increasing the synaptic and extrasynaptic concentrations of these two neurotransmitters (Zimmer, 2017). Atomoxetine was thought to mainly act at promiscuous presynaptic norepinephrine transporters (NETs) that clear both NA and DA in the prefrontal regions (Bymaster et al., 2002). Functional imaging studies have generally suggested that positive responses to atomoxetine might reflect acute actions on the executive functions mediated by the prefrontal cortex (Cubillo et al., 2014a, b).

*Abbreviations:* ADHD, attention-deficit/hyperactivity disorder; BRIEF-A, Behavior Rating Inventory of Executive Function–Adult version; CBT, cognitive behavioral therapy; CBT + M, CBT and medication; dlPFC, dorsolateral prefrontal lobe; MPH, Methylphenidate; MTA, Multimodal Treatment Study; ODD, oppositional defiant disorder; ADHD, rating scale(ADHD-RS); SAS, Self-Rating Anxiety Scale; SDS, Self-Rating Depression Scale; SES, Self-Esteem Scale; WHOQOL-BREF, World Health Organization Quality of Life-Brief version

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However, pharmacotherapies have also had significant limitations since they have often been associated with adverse effects and high dropout rates (Cunill et al., 2016; Dibbets et al., 2010; Meijer et al., 2009; Nair and Moss, 2009), potential addictive problems (Robbins, 2000; Takahashi et al., 2011), partial treatment responses and persistent residual symptoms (Contini et al., 2013; Safren et al., 2010b; Steele et al., 2006; Yang et al., 2012)

Cognitive-behavioral therapy (CBT) has been regarded as one of the most effective psychological treatments for ADHD (Vidal-Estrada et al., 2012). Dysfunctional attitudes and negative emotions (Beck, 1993, 2016), or simultaneously influenced by an unknown third variable (Burns and Spangler, 2000), were regarded as major mediators and moderators in change of CBT progress. It has been proposed that cognitive distortion are markers of mental disorders and that the therapeutic correction of these cognitive distortions has been the cornerstone of CBT theory and practice. CBT focuses on the coherence of self-identity and stability of interpersonal relations (Dobson, 2013). CBT has helped patients to identify automated thinking, to clarify cognitive errors, to generate adaptive thinking with specific questioning techniques, to form better behavioral models using behavioral activation skills, to redirect emotions and actions and ultimately to achieve symptom improvement (Beck, 1993, 1997). Additionally, strong associations, specificity, consistency, experimental manipulations, and gradients, as well as coherence, are also important mediators in psychotherapy (Kazdin, 2009). CBT has been proven effective for ADHD's core symptoms, social functions and comorbid symptoms such as anxiety and depression (Safren et al., 2005) and has also presented long-term (up to 2 years) efficacy (Stevenson et al., 2002; Virta et al., 2010). CBT conducted in groups and with individuals have both been validated for treatment of adults with ADHD (Bramham et al., 2009; Dittner et al., 2018).

It was thought that different mechanisms of action underlie pharmacotherapy and psychotherapy. Adult ADHD patients had a wide range of brain dysfunctions, including damage in the default mode network (Hoekzema et al., 2014), emotional network (McCarthy et al., 2013), cognitive control network (Lin and Gau, 2015), and prefrontal regions, which participate in the regulation of attention, inhibition/cognitive control, motivation, and emotion (Arnsten and Rubia, 2012). Previous studies have indicated that although pharmacotherapies and CBT might share some common neural pathways in treating ADHD, there existed differences in their modes of action. Pharmacotherapies particularly affect the brain function of the limbic system by increasing neurotransmitter concentrations in the synaptic cleft and ultimately affect the functional area of the prefrontal lobe (bottom-up effect). Psychotherapy directly affects the behavior-related brain activity associated with the prefrontal lobes and then affects the release of synaptic transmitters in the limbic system (top-down effect) (Quidé et al., 2012). Experimental studies based on animal models have shown an increase in dopamine concentrations in the brain after drug treatment (Shimizu et al., 2019), and the neuropharmacology of MPH assessed via PET and MRI proved that the medication normalized brain activation patterns as well as functional connectivity (Schweren et al., 2013; Spencer et al., 2010). Psychotherapy has focused on treatments for patients to reconstruct adaptive thinking and remodel behavioral habits. CBT mobilizes patients' subjective efforts to regulate cognitive, emotional and behavioral responses, which are primarily mediated by the dorsolateral prefrontal lobe (dlPFC). Psychotherapy allowed all information to be transmitted to the emotionally relevant areas (hypothalamus, anterior cingulate gyrus, basal ganglia, and amygdala (Beauregard, 2006) after integration and evaluation in the dlPFC, which then regulated the release of neurotransmitters, thus regulating the psychological processes of motivation, decision-making and emotions, ultimately achieving therapeutic effects in terms of emotions and behaviors (Huang et al., 2014). Thus, we hypothesized that a combination of psychotherapy and pharmacotherapy would have “bottom-up effect” and “top-down effect” at the same time, resulting in superior efficacy.

In the clinic, a combination of psychotherapy and pharmacotherapy has also been recommended. The Multimodal Treatment Study (MTA) in childhood indicated that patients with a combination of medication and behavioral therapy showed significantly greater improvements in ADHD and oppositional defiant disorder (ODD) symptoms than those with behavioral therapy alone (The MTA Cooperative Group, 2004), with no differences among the groups in a 3-year (Swanson et al., 2008) and 6- to 8-year follow-up (Molina et al., 2009). In adults with ADHD, previous studies have found that adding a psychosocial intervention improved the effects of pharmacological treatment (Emilsson et al., 2011; Safren et al., 2005, 2010a; Young et al., 2015). When comparing the effects between CBT and medication (CBT + M) vs. CBT alone for patients with ADHD, few studies exist. Weiss et al. (2012) found that the use of medication (dextroamphetamine) proved to have equivalent outcomes compared with CBT alone. Philipsen et al. (2015) showed that psychotherapy combined with methylphenidate had more efficacy than psychotherapy combined with placebo at a one-year follow-up. Cherkasova et al. (2017) demonstrated that psychological interventions resulted in better outcomes of core symptoms when combined with medication than when combined with placebo. However, neither of the above two studies explored differences between groups in anxiety and depression symptoms or social function between the groups. In conclusion, both CBT alone and a combination treatment were proven to be effective on ADHD core symptoms, whereas the effect comparison between CBT + M and CBT alone remains uncertain, both on core symptoms and accompanying symptoms.

In our previous study (Huang et al., 2017), we found a significant improvements in both a CBT-alone group and a CBT-with-booster-sessions group compared with waiting-list control group on ADHD-RS, executive functions and impulsivity. In previous studies, including ours, patients under stable medication were always mixed with medication-naive patients at baseline. Whether a combination of a medication and CBT would improve clinical outcomes compared with CBT alone remains uncertain. Therefore, we aimed to compare the effects of CBT alone versus CBT combined with medication (CBT + M) on ADHD core symptoms, anxiety and depression symptoms and social functional outcomes. Based on previous studies, we hypothesized that CBT combined with medication would result in greater improvements in all outcomes than CBT alone.

## 2. Methods

### 2.1. Participants

The participants were outpatients willing to receive CBT at Peking University Sixth Hospital between September 2013 and April 2018. The inclusion criteria were as follows. 1. Outpatients from Peking University Sixth Hospital who received a diagnosis of adult ADHD through Conner's Adult ADHD Diagnostic Interview (Epstein and Kollins, 2006; Qian et al., 2010) based on the DSM-IV (Segal, 2010). 2. Patients in CBT - alone group were drug naive, and those in CBT + M group had been stable on medications (adjustments in drug dosage in previous two months was below 10% for the treatment of ADHD (Safren et al., 2005)). The key exclusion criteria included the following: 1. had organic mental disorders, acute episode of bipolar disorder that required current medication, major depression disorder with high suicide risk, clinically severe panic disorder or psychotic disorders that required medication, or pervasive developmental disorders; 2. had prior or present participation in other psychological therapies that might influence outcomes; 3. had an IQ less than 90, which might influence the outcomes of the cognitive tests (Schroeder, 2014); 4. had unstable physical conditions, such as active hepatitis and angina pectoris, that required medical treatment prior to ADHD treatment; 5. attended less than 7 sessions of CBT (Chen et al., 2006); and 6. had serious side effects of medication.

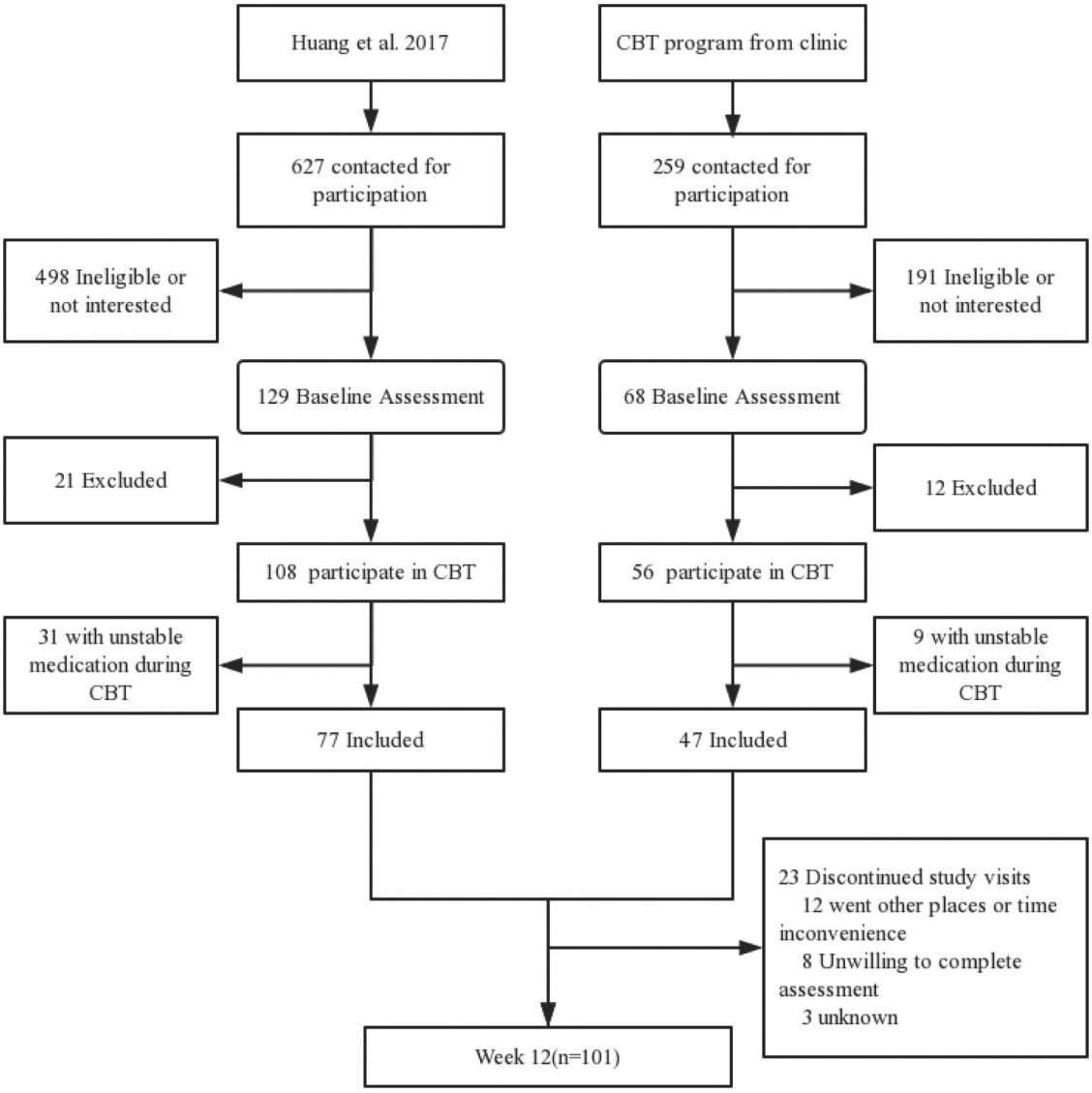


**Fig. 1.** Patients flow. Note: CBT = Cognitive Behavioral Therapy.

A total of 197 people participated in the baseline assessment. One hundred sixty-four people whose residence, schedule, and general psychological state could appropriately volunteer to participate in CBT. All enrolled patients met the above inclusion criteria and exclusion criteria. Eventually, 124 patients completed more than 7 sessions of CBT. Among the 124 patients, 57 received CBT + M treatment, and 67 received CBT treatment only (see Fig. 1). In the CBT + M group, 40 (70.18%) people were medicated with methylphenidate hydrochloride controlled-release tablets (Concerta®), with an average dose of 27.45 ± 9.97 mg. A total of 17 (29.82%) people were medicated with atomoxetine hydrochloride (Strattera®), with an average dose of 46.35 ± 20.09 mg. A total of 77 participants were selected from Huang's RCT study published in 2018 (Huang et al., 2017) (50 drug naive, 21 with Concerta® and 6 with Strattera®), and 47 participants attended the CBT program in the clinic between 2017 and 2018 (17 drug naive, 19 with Concerta® and 11 with Strattera®). The patients' demographic and clinical characteristics were listed in Table 1. There were no statistically significant differences in demographic features or baseline clinical measurements between the two groups.

### 2.2. Medication

Before enrolling, each patient's medication was titrated in the outpatient clinic until stable, during which period the appropriate drug type and dosage were determined based on the patient's ADHD symptoms and side effects. Throughout the 12 weeks of the sessions, the patients were asked to remain on the stable dose of medication. Weekly medication compliance and side effects, such as behavior, sleep, interest, appetite, emotion and autonomic nervous system responses, such as dizziness and tachycardia, were recorded by the study team. The participants were transferred to psychiatric clinics if any unbearable side effects occurred. Dose changes in the medication were described by psychiatrists and recorded by the study team. At any time, participants with serious side effects were to terminate the trial and be treated in the clinic (i.e., headache, insomnia, elevated blood pressure, increased heart rate, stomach pain, nausea, vomiting, loss of appetite, lethargy, etc.). No subjects withdrew from the study due to drug side effects in this study.

### 2.3. Cognitive behavioral therapy

The 12 weeks of group CBT was based on a published and validated manual (Safren et al., 2005, 2010a). This manual was translated into a Chinese version and was proven suitable for Chinese patients (Huang et al., 2015, 2017). The CBT program was conducted in groups, with 8 to 12 patients in each group. The CBT program consisted of 12 sessions

**Table 1**
Demographic and clinical characteristics of the two groups.

| Characteristic | | ADHD CBT group ($n$ = 67) | CBT + M group ($n$ = 57) | $\chi 2$/t value | $p$ value |
|---|---|---|---|---|---|
| Age,year(Mean ± SD) | | 27.10 ± 4.81 | 26.81 ± 5.40 | 0.32 | 0.75 |
| Male (%) | | 36(53.73%) | 31(68.89%) | 0.01 | 0.94 |
| Education, year(Mean ± SD) | | 16.68 ± 2.18 | 15.92 ± 2.76 | 1.71 | 0.09 |
| Total IQ(Mean ± SD) | | 120.28 ± 8.89 | 121.67 ± 8.92 | −0.86 | 0.39 |
| ADHD subtype (%) | | | | | |
| Predominantly inattentive | | 54(80.60%) | 46(80.70%) | 0 | 0.99 |
| Combined | | 13(19.40%) | 11(19.30%) | 0 | 0.99 |
| Current comorbid Axis I disorders (%) | | 32(47.76%) | 29(50.88%) | 0.1 | 0.73 |
| Bipolar disorder in remission | | 2(2.99%) | 4(7.02%) | 1.09 | 0.30 |
| Depressive/Dysthymic disorder | | 20(29.85%) | 19(33.33%) | 0.17 | 0.68 |
| Obsessive compulsive disorder | | 1(1.49%) | 3(5.26%) | 1.40 | 0.24 |
| Anxiety disorders | | 10(14.93%) | 2(3.51%) | 3.38 | 0.07 |
| Somatic disorder | | 0 | 1(1.75%) | 0.01 | 0.94 |
| Stress related disorders | | 1(1.49%) | 0 | 1.24 | 0.27 |
| Eating disorders | | 2(3.00%) | 1(1.75%) | 0.2 | 0.66 |
| Current comorbid Axis II disorders (%) | | 27(40.30%) | 26(45.61%) | 0.36 | 0.55 |
| Cluster A | | 4(5.97%) | 5(8.77%) | 0.06 | 0.8 |
| Cluster B | | 2(2.99%) | 5(8.77%) | 1 | 0.32 |
| Cluster C | | 25(37.31%) | 23(40.35%) | 0.12 | 0.73 |
| others | | 4(5.97%) | 9(15.79%) | 2.2 | 0.14 |
| ADHD RS | Total score | 27.5 ± 8.05 | 27.41 ± 6.73 | 0.06 | 0.95 |
| | Inattention subscale | 17.33 ± 4.01 | 17.59 ± 4.07 | −0.35 | 0.73 |
| | Impulsiveness-Hyperactivity subscale | 10.12 ± 5.4 | 9.57 ± 4.98 | 0.58 | 0.56 |
| SAS(Mean ± SD) | | 40.61 ± 8.33 | 38.95 ± 7.70 | 1.14 | 0.26 |
| SDS(Mean ± SD) | | 42.83 ± 8.78 | 42.12 ± 8.44 | 0.46 | 0.65 |
| SES(Mean ± SD) | | 26.01 ± 4.80 | 25.80 ± 4.82 | 0.24 | 0.81 |
| WHO | Physical domain | 47.09 ± 14.30 | 45.13 ± 14.62 | 0.75 | 0.45 |
| (Mean ± SD) | Psychological domain | 45.35 ± 12.36 | 44.74 ± 14.66 | 0.25 | 0.8 |
| Social domain | | 49.39 ± 18.78 | 49.70 ± 18.46 | −0.09 | 0.93 |
| Environmental domain | | 54.9 ± 11.00 | 53.99 ± 15.00 | 0.382 | 0.703 |
| Brief-A | Inhibit | 15.56 ± 2.50 | 16.04 ± 2.88 | −0.71 | 0.48 |
| (Mean ± SD) | shift | 12.39 ± 2.23 | 11.89 ± 2.81 | 0.79 | 0.43 |
| Emotional control | | 19.31 ± 4.08 | 17.67 ± 4.43 | 1.52 | 0.13 |
| Self-Monitor | | 10.78 ± 2.29 | 10.56 ± 2.65 | 0.36 | 0.72 |
| Initiate | | 17.56 ± 3.17 | 18.37 ± 2.72 | −1.07 | 0.29 |
| Working memory | | 18.36 ± 2.58 | 18.85 ± 2.30 | −0.78 | 0.44 |
| Plan/Organise | | 20.39 ± 3.78 | 22.41 ± 4.06 | −2.03 | 0.05 |
| Task monitor | | 12.97 ± 2.29 | 13.96 ± 2.01 | −1.79 | 0.08 |
| Organization of Materials | | 15.31 ± 3.92 | 18.22 ± 3.26 | −3.14 | < 0.01 |
| Behavioral Regulation Index (BRI) | | 58.03 ± 8.65 | 56.15 ± 9.68 | 0.81 | 0.42 |
| Metacognition Index (MI) | | 84.79 ± 11.44 | 91.81 ± 11.54 | −2.4 | 0.02 |
| GEC | | 142.71 ± 16.56 | 147.96 ± 17.52 | −1.27 | 0.23 |

Note. SCID-II Cluster A: Paranoid Personality Disorder, Schizoid Personality Disorder, Schizotypal Personality Disorder; SCID-II Cluster B: Antisocial personality disorder, borderline personality disorder, Schizophrenic personality disorder, Narcissistic personality disorder; SCID-II Cluster C: Avoidance personality disorder, Dependent personality disorder, Obsessive-Compulsive Personality Disorder; SCID-II Other: Personality Change Due to Another Medical Condition, Other Specified Personality Disorder, Unspecified Personality Disorder. ADHD-RS: ADHD-Rating Scale. SAS: Self-Rating Anxiety Scale. SDS: Self-Rating Depression Scale. SES: Self-Esteem Scale. WHOQOL-BREF:World Health Organization Quality of Life-Brief Version.Brief-A: Behavior Rating Inventory of Executive Function-Adult Version.

constituting six modules, including organization and planning, reducing distractibility, adaptive thinking, dealing with procrastination, building helpful relationships and reviews. The main structures and contents were as follows.

1 Behavioral strategies. Seven sessions were designed to form regular habits and time management, such as scheduling, prioritizing, attention measurement and methods of organizing a workspace. Behavioral strategies also included the application of self-reinforcing techniques in task management practices and the decomposition of complex tasks into manageable parts.
2 Cognitive strategies. Five sessions were included. An important goal of these sessions was to foster generalization and maintenance of adaptive thinking. Behavioral and cognitive changes were assimilated into all the activities of daily life in a way that they became habitual and automatic.

The CBT program was conducted in groups, with 8 to 12 patients in each group. Each session lasted for 2 h, which started with a review of each participant's reflections over the past week's home exercise and continued with the presentation of the new topic and corresponding strategies, followed by exercises to strengthen new skills. As the manual was used for individuals in previous studies, we added some strategies for group CBT in practice. The development of new skills and strategies was fostered via intensive practice during the session and during the home exercises, which followed each session, as well as by group support and positive reinforcement from the therapist and group members.

### *2.4. Therapists training and treatment adherence/competence*

All group CBT sessions were led by two trained psychiatrist therapists who had received systematic training of CBT through a 2-year continuous workshop sponsored by the Chinese Psychological Association. Written and audio records of each therapy session were maintained, and the therapists were supervised by a senior psychiatrist and a psychotherapist on a weekly basis. The therapists' abilities were assessed by an independent evaluator based on notes and recordings

(Waltz et al., 1993). The Cognitive Therapy Rating Scale (CTRS; https://www.beckinstitute.org) (Creed et al., 2016) was used to evaluate therapists' competence, with a scale from 0 to 6, which assessed treatment skills (agenda, feedback, understanding, interpersonal interaction, collaboration, pacing and efficient use of time), CBT treatment skills (guided discovery, focusing on key cognition or behaviors, strategy of change, application of CBT technology, homework) and other aspects of the actual treatment process. The higher the total score, the better the therapist regarding the treatment delivery. A total score of ≥40 was considered to be excellent in treatment ability (Shaw et al., 1999). The treatment records of 10% of the three therapists were randomly selected for statistical analysis. The results showed that the scores of the 3 main therapists were high (52.30 ± 1.83, 50.60 ± 1.14 and 51.50 ± 1.90), and there was no significant difference among them ($F = 1.273$, $p = 0.315$), representing a relatively good and consistent quality of treatment.

### 2.5. Assessment of treatment response

#### 2.5.1. ADHD-rating scale (ADHD-RS)

The ADHD-RS is a self-report 18-item scale corresponding to the DSM-IV symptoms of ADHD (Pappas, 2006). Items are rated from 0 to 3 based on symptom frequency. There are two subscales: the Inattention subscale and the Impulsiveness-Hyperactivity subscale. Higher scores reflect more severe symptoms. The primary outcomes were the ADHD-RS score changes from baseline to week 12. The ADHD-RS was rated weekly by patients during the 12 weeks of CBT. The internal consistency and construct validity of ADHD-RS have been established (Rösler et al., 2006).

#### 2.5.2. Self-Rating Anxiety Scale (SAS) and Self-Rating Depression Scale (SDS)

The SAS and SDS are both 20-item self-report scales (Zung, 1967). Items are rated on a scale from 1 (not at all) to 4 (most of the time). Higher total scores indicate more severe symptoms. Those with an overall SAS score of less than 50 are normal; scores of 50–60 indicate mild anxiety, scores of 61–70 indicate moderate anxiety, and score of 70 or more indicate severe anxiety. The SDS standard score has a cutoff value of 53 points and scores of 53–62 indicate mild depression, scores of 63–72 indicate moderate depression, and a score of 73 points represents severe depression.

#### 2.5.3. Self-Esteem Scale (SES)

It is a 10-item self-report scale (Rosenberg, 1965; Wang et al., 1999). The total score is calculated from 1 to 4 based on agreement with a self-description. A higher score reflects higher self-esteem.

#### 2.5.4. Behavior Rating Inventory of Executive Function-Adult version (BRIEF-A)

The BRIEF-A is a 75-item self-report scale that captures views of an adult's executive functions (EFs) or self-regulation in the patient's everyday environment (Du et al., 2010; Roth et al., 2013). Participants were asked 75 questions about their behavioral status during the past 6 months, with responses scored from 1 (never) to 3 (often). The results included a composite index score, the Global Executive Composite (GEC), and two subindex scores, the Behavioral Regulation Index (BRI) and Metacognition Index (MI), based on nine subscales. Higher scores indicate more severe impairment in EF.

#### 2.5.5. World Health Organization Quality of Life-Brief version (WHOQOL-BREF)

It is a 26-item self-report scale (Hao and Fanc, 2000; Power et al., 1998). Items are rated from 1 to 5 based on the degree of satisfaction. It produces scores in four domains related to quality of life: physical health, psychological, social relationships, and environment. Higher scores suggest better quality of life.

### 2.6. Statistical analysis

SPSS Version 23 (IBM; Chicago, IL) was used for all analyses. The multiple imputation (imputation 5 times) was conducted in the original data set to address missing data (Sainani, 2015). CBT and CBT + M groups were compared on baseline characteristics using t tests and Mann-Whitney U tests for continuous variables and chi-square tests for categorical variables. Repeated measures analyses of variance (ANOVA) were conducted to determine the variance between groups before and after treatment. Analyses estimating the effects of the two treatments on changes in core symptoms and emotional and functional outcome scores over time were conducted with mixed linear models (MLM), specifying the 12 assessment points as a repeated measure and treatment (CBT vs. CBT + M) as a fixed effect. The random component of the mixed model included a random intercept term for subject identifier to take account of between-subject variability and the correlation between the repeated measures. We tested Assessment point × Treatment interactions, but none were found to be statistically significant; therefore, they were excluded from the model. Additional MLMs were run to examine possible moderating effects of sex, age, estimated IQ, years of education, comorbidity, and session attendance on outcomes by testing the significance of the additional random component in the mixed model.

If an interaction term was nonsignificant at the $p$ value of 0.05, the potential moderator was removed from the model and no longer considered in the analyses.

### 2.7. Efficacy index

We defined response to treatment as a 25% decrease in the ADHD-RS score and remission as a 40% drop in the ADHD-RS-Inv score. ADHD symptomes reduction rate = (total score of ADHD-RS before treatment - total score of ADHD-RS after treatment) / total score of ADHD-RS before treatment × 100%.

## 3. Results

### 3.1. Baseline characteristics

There were no significant differences between the CBT and the CBT + M groups in the demographic background data (see Table 1). For the BRIEF-A, the CBT + M group had higher scores in plan/organize ($t = -2.032$, $p = 0.047$), organization of materials ($t = -3.136$, $p = 0.003$) and Metacognition Index (MI) ($t = -2.402$, $p = 0.019$) than the CBT group.

### 3.2. Primary outcomes

Both groups showed significant improvements in the ADHD-RS total score and inattention subscale and impulsiveness-hyperactivity subscale scores ($p < 0.01$). A decreasing trend was presented as the treatment time progressed, and the overall scores of the CBT group were higher than those of the CBT + M treatment group (Fig. 2), with no significant difference between groups.

No significant differences were found between the two groups in ADHD-RS scores. In total, 59.70% of the patients improved, and 40.30% of the patients achieved remission in the CBT group. For the CBT + M group, 56.14% ($\chi2 = 0.16$, $p = 0.689$) of the patients improved, and 38.60% ($\chi2 = 0.037$, $p = 0.847$) of patients achieved remission, with no differences between the two groups (see Table 2). Additionally, we analyzed patients taking methylphenidate and those with atomoxetine as two subgroups and found no differences among the groups (data not shown).

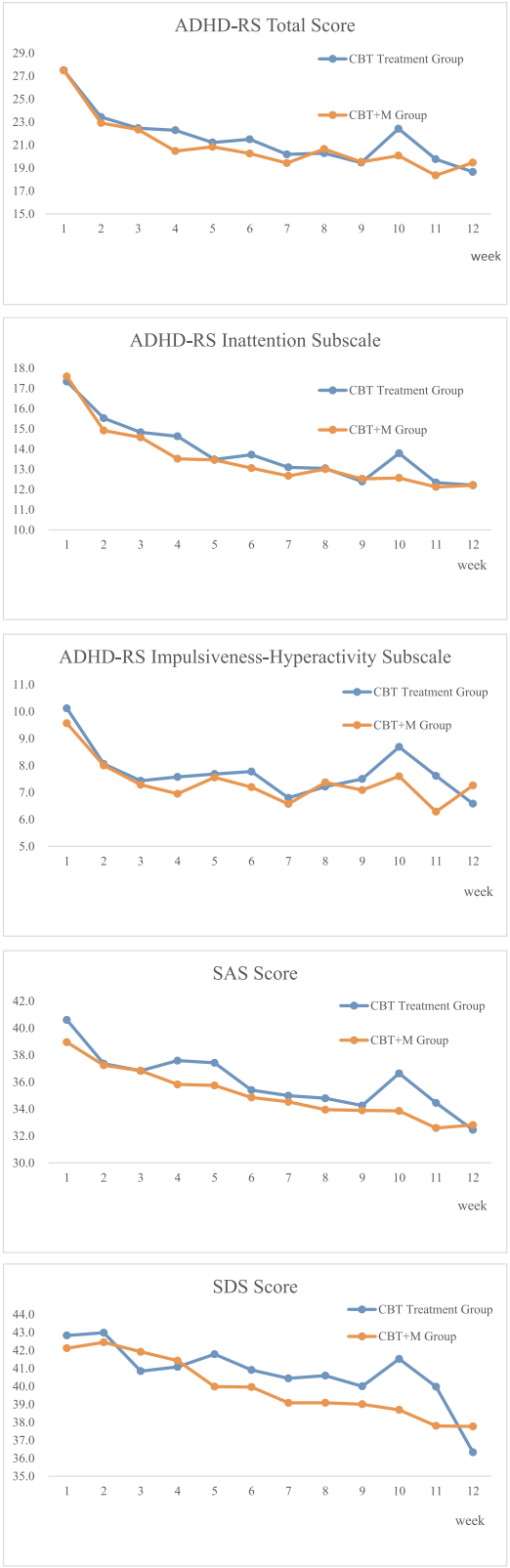


**Fig. 2.** CBT versus CBT + medication. Note: CBT = Cognitive Behavioral Therapy. CBT + M = Cognitive Behavioral Therapy combined with Medication. SAS: Self-Rating Anxiety Scale. SDS: Self-Rating Depression Scale. A decreasing trend was presented during the treatment time progress, and the overall scores of the CBT treatment group were higher than those of the CBT + M treatment group. No significant difference between groups.

### 3.3. Secondary outcomes

Both groups showed significant improvements in the SAS, SDS and SES scores ($p < 0.01$). There was a significant improvement in SES scores in both groups (see Table 3).

For the WHOQOL-BREF, the CBT group showed a significant improvement in all domains, while the CBT + M group only improved in the psychological domain ($F = 12.80$, $p < 0.01$, $\eta2 = 0.18$) and environmental domain ($F = 11.73$, $p < 0.01$, $\eta2 = 0.17$). The patients in the CBT group showed a greater improvement in the physical domain of WHOQOL-BREF ($b = 8.62$; 95% confidence interval [CI] = [3.63, 13.62], $t$ (117.989) = 4.46, $p < 0.01$, $d = 0.09$) than the patients in the CBT + M group. No significant differences were found between the two groups in the SAS, SDS, SES, BIS and other domains of the WHOQOL-BREF.

For the BRIEF-A, both groups showed significant increases in the Metacognition Index (MI) ($F = 6.99$, $p = 0.01$, $\eta2 = 0.17$ and $F = 15.36$, $p < 0.01$, $\eta2 = 0.37$) and Global Executive Composite (GEC) ($F = 5.13$, $p = 0.03$, $\eta2 = 0.13$ & $F = 11.19$, $p < 0.01$, $\eta2 = 0.30$). The CBT + M group showed a significant increase in shift ($F = 4.28$, $p = 0.05$, $\eta2 = 0.14$), self-monitor ($F = 8.84$, $p < 0.01$, $\eta2 = 0.25$), initiate ($F = 4.92$, $p = 0.04$, $\eta2 = 0.16$), working memory ($F = 9.42$, $p < 0.01$, $\eta2 = 0.27$), plan/organize ($F = 12.73$, $p < 0.01$, $\eta2 = 0.33$), task monitor ($F = 10.07$, $p < 0.01$, $\eta2 = 0.28$) and organization of materials ($F = 16.44$, $p < 0.01$, $\eta2 = 0.39$). However, the CBT group only showed a significant increase in initiate ($F = 6.01$, $p = 0.02$, $\eta2 = 0.15$), working memory ($F = 9.24$, $p < 0.01$, $\eta2 = 0.21$) and organization of materials ($F = 8.92$, $p < 0.01$, $\eta2 = 0.20$). No significant differences in efficacy in BRIEF-A were found between the two groups (see Tables 2 and 3).

## 4. Discussion

We found that our CBT treatment, both with and without medication, resulted in significant improvements relative to baseline in ADHD symptoms and emotional outcomes. Contrary to our hypothesis, we found an equivalent improvement in core symptoms and emotional symptoms between the CBT group and the CBT + M group. The CBT + M group showed singnificant improvements in self-monitor, plan/organize and task monitor domains of the BRIEF-A but not in the CBT group, suggesting that CBT combined with medication had more profound effects on executive functions.

### 4.1. Primary outcomes

Our results on core ADHD symptoms were consistent with previous findings that CBT resulted in improved ADHD symptoms. CBT could be the treatment modality with the most long-term empirical support for the treatment of ADHD in adults. Previously, meta-analytic reviews have found that CBT is effective with moderate-to-large effect size (ES) estimates on inattention and total ADHD symptoms (Young et al., 2016) as well as hyperactivity/impulsivity symptoms (López-Pinar et al., 2018).

Previous controlled studies focused more on patients with stable medication and demonstrated an additional significant treatment effect of CBT (Mongia and Hechtman, 2012). Safren et al. (2005) found that CBT could be a synergistic treatment in medicated people with consistent improvements in core symptoms both after 12 weeks of treatment and after 12 months of follow-up (Safren et al., 2010a). Furthermore, Bramham et al. (2009) and Emilsson et al. (2011) confirmed the similar conclusion that CBT plus medication resulted in greater ADHD symptoms and self-esteem improvements and a stronger self-efficacy than "treatment as usual" (patients treated with medication?).

Our study was one of a few studies to compare CBT + M vs CBT treatment alone. This study could not prove the superiority of the combination of medication and therapy over CBT therapy only, which

**Table 2**
Statistics for the mixed linear models revealing differential treatment effects of CBT versus CBT + M.

| | | Mixed linear model | | | | | CBT group ($n$ = 67) | CBT+$M$ group ($n$ = 57) |
|---|---|---|---|---|---|---|---|---|
| | | β | 95%CI | 95%CI | $p$ | Cohen's d | | |
| ADHD RS | Total score | 0.67 | −1.07 | 2.40 | 0.45 | 0.14 | 18.63 ± 8.19 | 19.46 ± 7.40 |
| | Inattention subscale | 0.38 | −0.67 | 1.43 | 0.47 | 0.13 | 12.22 ± 4.82 | 12.20 ± 4.40 |
| | Impulsiveness-Hyperactivity subscale | 0.43 | −0.68 | 1.54 | 0.44 | 0.14 | 6.58 ± 4.66 | 7.26 ± 4.84 |
| SAS | | 0.73 | −1.2 | 2.64 | 0.45 | 0.14 | 32.45 ± 8.83 | 32.81 ± 8.12 |
| SDS | | 0.79 | −1.37 | 2.95 | 0.47 | 0.13 | 36.33 ± 9.19 | 37.77 ± 10.80 |
| SES | | 0.54 | −0.96 | 2.03 | 0.48 | < 0.01 | 28.43 ± 4.91 | 27.78 ± 5.14 |
| WHO | Physical domain | 8.62 | 3.63 | 13.62 | < 0.-01 | 0.01 | 57.79 ± 13.97 | 48.02 ± 18.61 |
| | Psychological domain | 1.58 | −3.94 | 7.10 | 0.57 | < 0.01 | 54.47 ± 15.80 | 52.53 ± 18.82 |
| | Social domain | 5.95 | −0.18 | 12.08 | 0.06 | 0.03 | 58.85 ± 21.45 | 53.09 ± 19.80 |
| | Environmental domain | −1.29 | −6.20 | 3.62 | 0.60 | < 0.01 | 60.08 ± 14.78 | 60.73 ± 18.29 |
| Brief-A | Inhibit | −0.47 | −2.08 | 1.15 | 0.57 | 0.01 | 14.88 ± 2.89 | 15.50 ± 3.70 |
| | shift | 0.52 | −0.75 | 1.79 | 0.42 | 0.01 | 11.53 ± 2.20 | 10.80 ± 3.22 |
| | Emotional control | 1.77 | −0.63 | 4.18 | 0.15 | 0.04 | 18.67 ± 5.06 | 15.86 ± 5.64 |
| | Self-Monitor | 1.00 | −0.16 | 2.15 | 0.09 | 0.05 | 10.37 ± 2.74 | 9.26 ± 2.43 |
| | Initiate | −0.16 | −1.98 | 1.66 | 0.86 | < 0.01 | 16.07 ± 3.43 | 16.63 ± 4.26 |
| | Working memory | 0.17 | −1.09 | 1.43 | 0.79 | < 0.01 | 17.05 ± 2.70 | 17.13 ± 2.81 |
| | Plan/Organise | −0.16 | −2.21 | 1.89 | 0.88 | < 0.01 | 18.85 ± 3.96 | 19.64 ± 4.17 |
| | Task monitor | 0.19 | −1.03 | 1.41 | 0.75 | < 0.01 | 12.37 ± 2.47 | 12.41 ± 2.21 |
| | Organisation of Materials | −0.00 | −1.55 | 1.54 | 1.00 | < 0.01 | 13.83 ± 3.85 | 15.58 ± 3.10 |
| | Behavioral Regulation Index (BRI) | 3.03 | −2.34 | 8.40 | 0.26 | 0.02 | 55.44 ± 10.01 | 51.43 ± 13.12 |
| | Metacognition Index (MI) | −0.73 | −7.40 | 5.95 | 0.83 | < 0.01 | 78.20 ± 12.42 | 81.42 ± 13.91 |
| | GEC | 2.85 | −8.29 | 13.98 | 0.61 | < 0.01 | 133.64 ± 20.27 | 132.84 ± 25.02 |

Note. ADHD-RS: ADHD-Rating Scale. SAS: Self-Rating Anxiety Scale. SDS: Self-Rating Depression Scale. SES: Self-Esteem Scale. WHOQOL-BREF:World Health Organization Quality of Life-Brief Version.Brief-A: Behavior Rating Inventory of Executive Function-Adult Version.

**Table 3**
Improvement of ADHD-RS, SAS, SDS, SES, WHOQOL-BREF and Brief-A for the two groups between baseline and week 12 after Multiple Imputation and adjusted for baseline measurement.

| | | CBT group ($n$ = 67) | | | CBT + M group ($n$ = 57) | | |
|---|---|---|---|---|---|---|---|
| | | F | $p$ | η2 | F | $p$ | η2 |
| ADHD-RS | Total score | 14.57 | < 0.01 | 0.19 | 16.03 | < 0.01 | 0.23 |
| | Inattention subscale | 15.38 | < 0.01 | 0.20 | 14.49 | < 0.01 | 0.21 |
| | Impulsiveness-Hyperactivity subscale | 6.54 | < 0.01 | 0.10 | 5.42 | < 0.01 | 0.09 |
| SAS | | 11.58 | < 0.01 | 0.16 | 8.11 | < 0.01 | 0.13 |
| SDS | | 4.41 | < 0.01 | 0.06 | 3.60 | < 0.01 | 0.06 |
| SES | | 16.36 | < 0.01 | 0.20 | 11.96 | < 0.01 | 0.17 |
| WHO | Physical domain | 43.09 | < 0.01 | 0.40 | 1.66 | 0.20 | 0.03 |
| | Psychological domain | 20.67 | < 0.01 | 0.24 | 12.80 | < 0.01 | 0.18 |
| | Social domain | 15.40 | < 0.01 | 0.19 | 2.26 | 0.14 | 0.04 |
| | Environmental domain | 9.62 | < 0.01 | 0.13 | 11.73 | < 0.01 | 0.17 |
| Brief-A | Inhibit | 1.80 | 0.19 | 0.05 | 0.43 | 0.52 | 0.02 |
| | shift | 3.13 | 0.08 | 0.08 | 4.28 | 0.05 | 0.14 |
| | Emotional control | 0.70 | 0.41 | 0.02 | 3.24 | 0.08 | 0.11 |
| | Self-Monitor | 0.82 | 0.37 | 0.02 | 8.84 | < 0.01 | 0.25 |
| | Initiate | 6.01 | 0.02 | 0.15 | 4.92 | 0.04 | 0.16 |
| | Working memory | 9.24 | < 0.01 | 0.21 | 9.42 | < 0.01 | 0.27 |
| | Plan/Organise | 3.21 | 0.08 | 0.08 | 12.73 | < 0.01 | 0.33 |
| | Task monitor | 1.37 | 0.25 | 0.04 | 10.07 | < 0.01 | 0.28 |
| | Organisation of Materials | 8.92 | < 0.01 | 0.20 | 16.44 | < 0.01 | 0.39 |
| | Behavioral Regulation Index (BRI) | 2.17 | 0.15 | 0.06 | 4.04 | 0.06 | 0.13 |
| | Metacognition Index (MI) | 6.99 | 0.01 | 0.17 | 15.36 | < 0.01 | 0.37 |
| | GEC | 5.13 | 0.03 | 0.13 | 11.19 | < 0.01 | 0.30 |

Note. ADHD-RS: ADHD-Rating Scale. SAS: Self-Rating Anxiety Scale. SDS: Self-Rating Depression Scale. SES: Self-Esteem Scale. WHOQOL-BREF:World Health Organization Quality of Life-Brief Version.Brief-A: Behavior Rating Inventory of Executive Function-Adult Version.

was opposite to a similar study in childhood (Jensen et al., 2001; Murray et al., 2008; The MTA Cooperative Group, 1999). Researches in children with ADHD found that combination of medication was superior to behavioral therapy alone in self-reported and parent-reported core symptoms, emotional symptoms and clinical satisfaction. However, the psychotherapy in the MTA study focused more on behavioral interventions, not so much on cognitive domains. And the differences in age-based clinical efficacy may also indicate differences in the mechanisms of medication and CBT, and patient motivation, treatment adherence, and family and social support might also play a role. In regard to adulthood, our results replicated Weiss's study in 2012 (Weiss et al., 2012) but was contrary to Philipsen's study in 2015 (Philipsen et al., 2015) and Cherkasova's study in 2016 (Cherkasova et al., 2017). Inconsistent conclusions may have been a consequence of the following. First, the study designs were different. In Philipsen's research, differences were explored between patients under MPH and those with individual psychotherapy. In Cherkasova's research, group CBT was conducted, and amphetamine was chosen for the medication group. In our study, we included adults with ADHD who still had symptoms of ADHD after taking stable medication (methylphenidate or atomoxetine). We can see from Cherkasova's research that there was a large decrease in the ADHD-RS score after stable

medication (from 31.20 ± 7.10 to 21.74 ± 8.81), even lower than that of the CBT group at the end of treatment, resulting in a superior efficacy on core symptoms when compared with CBT treatment alone. It would be assumed that the effect of medication in the trial has a greater proportion, resulting in a more significant efficacy in the CBT + M treatment group. Overall, we speculated that medication is indeed effective for the core symptoms and accompanying symptoms of ADHD, and the combined CBT was effective for those who had not obtained significant improvement in symptoms. Second, different dimensions were assesed. Philipsen et al. (2015) estimated both core symptoms as well as emotional symptoms, and Cherkasova et al. (2017) estimated core symptoms and anger expression as well as functional outcomes. In addition to the above dimensions, our study added an executive function assessment questionnaire (BRIEF-A) to obtain a more thorough analysis of cognitive function in addition to the core symptoms, emotional symptoms, and social function symptoms. Additionally, the differences among previous findings might have been due to the patient's baseline symptom severity and other factors influencing outcomes of CBT, such as treatment adherence, treatment motivation and readiness to change, which should be explored in future studies.

### 4.2. Secondary outcomes

#### 4.2.1. SAS, SDS and SES

CBT was more effective on anxiety and depression symptoms as well as self-esteem in adults with ADHD than other psychotherapy approaches (Jensen et al., 2016). Previous studies showed significantly decreased symptoms of anxiety and depression (Hirvikoski et al., 2011; Jensen et al., 2016; Virta et al., 2010). A systematic review (Arnold et al., 2015) determined that patients with ADHD and comorbidities, such as anxiety, were most responsive to combination treatments. We found that CBT and CBT + M were both effective in adults with ADHD for emotional symptoms, consistent with our previous findings (Huang et al., 2017). However, no significant differences were found between CBT and CBT + M in terms of their effects on depression and anxiety symptoms. Our data did not directly explain why CBT + M did not produce superior outcomes in these areas. However, we found that SAS and SDS were in the normal range for both groups before treatment (SAS score < 50 and SDS score < 53). Although there was a significant improvement after treatment, the advantages of the combination therapy were not significantly reflected, and a ceiling effect might have affected the comparison between the groups, consistent with previous studies (Philipsen et al., 2015). The SES score was related to both ADHD symptoms and emotional status (Garofalo et al., 2016). Similarly, there were no significant differences in SES scores between the two groups.

#### 4.2.2. World Health Organization Quality of Life-Brief version (WHOQOL-BREF)

The CBT group had an improvement in the physical domain of the WHOQOL-BREF, similar to previous studies (Weiss et al., 2012; Young et al., 2015). However, we found no such significant improvement in the CBT + M group. The physical domain consists of pain and discomfort, energy and fatigue, sleep and rest, dependence on medication, mobility, activities of daily living and working capacity. We speculate that the insignificant change in the CBT + M group may be related to the decline in satisfaction caused by medication use since increased heart rate and blood pressure and reduced appetite and sleep are common side effects (Coghill et al., 2013; Mick et al., 2013), which may have an impact on life quality (Michelson et al., 2003) and treatment compliance (Fredriksen et al., 2014).

#### 4.2.3. Behavior Rating Inventory of Executive Function-Adult version (BRIEF-A)

For the BRIEF-A, we found significant improvements in both groups. In accord with our study, Stevenson et al. (2002) reported that a cognitive remediation program improved the ability to plan and organize, and Bramham et al. (2009) showed that meta-cognitive therapy could improve the ability to manage time. Similar findings could also be seen in previous studies by our team (Huang et al., 2017), both on the BRIEF-A questionnaire and on Stockings of Cambridge (SOC) thinking time in Cambridge Neuropsychological Testing Automated Battery (CANTAB) (Robbins et al., 1994). This study found that the CBT + M group performed better on more subscales than the CBT treatment group, indicating that a combination of medicine and CBT presented more benefits in executive functions. Previous studies showed that adults with ADHD demonstrated poorer executive function (EF) and medication (MPH and atomoxetine) was associated with improved EF performance, both in the BRIEF-A and other executive evaluation tests (De Bruyckere et al., 2016; Goto et al., 2017; Huss et al., 2017). Based on our previous hypothesis, a combination therapy might synthesize the “top-down” mechanism of CBT and the “bottom-up” mechanism of medication, resulting in altering more domains of executive functions.

Another considerable point is the assessment of executive functions. The BRIEF-A is a self-reported questionnaire, and more objective neuropsychological assessments are necessary in future studies. Schoenberg et al. (2014) used ERPs to objectively evaluate cognitive neurological function after MBCT treatment and found that the ERP amplitude increased during the Go-NoGo task performance after treatment. Gu et al. (2018) conducted a neuropsychological test on a network of 28 ADHD college students before and after MCBT treatment, finding that patients’ executive function significantly improved after treatment. Therefore, more evaluation tools should be included to compare the executive function levels before and after treatment.

### 4.3. Limitations

First, patients participating in this trial had relatively high IQ and education levels, which were not representative of the entire adult ADHD population. It was suspected that high IQ was a protective factor for executive function (Milioni et al., 2017). Studies have shown that IQ is closely related to the prognosis of ADHD (Paloyelis et al., 2010), both in pharmacotherapy (Buitelaar et al., 1995; Johnston et al., 2015) and psychotherapy (van den Hoofdakker et al., 2010).Long term following up researches should be conducted in the future for this high IQ sample.

Secondly this study was a secondary analysis of previous databases rather than a RCT study. The patient's own traits and characteristics might have affected the choice of treatment options, which might influence outcomes. Although there were no significant differences in clinical features between the two groups at baseline, it was difficult to determine whether the stable medicated group had more serious clinical symptoms and impaired social function and led to a weaker response to CBT treatment. Supplemental information of the clinical characteristics of individuals are needed to differentially identify the outcomes of remission and treatment failure for both CBT and medication interventions and provide a more precise and individualized treatment plan for clinical treatment.

Another shortcoming of study design was the lack of placebo administration in the CBT treatment group. Placebo effect could not be excluded in CBT + M group comparing wit CBT alone group. Additionally, in the CBT + M group, patients undertaking either of MPH and ATX would be another confounding factor, which could be controlled in future studies. Lacking waiting list control group might cause considerable difficulties with attributing causality to the CBT intervention, and therefore, many of the findings are inconclusive. Therefore, we may add the waiting list control group as a control in the future.

Lastly, we only focused on changes over the 12-week program and did not follow up the long-term efficacy. Many studies have confirmed the long-term efficacy of CBT, and further follow-up studies are needed to investigate maintenance and gains.

## 5. Conclusion

In our study, we found that 12 weeks of group CBT was effective for adults with ADHD in core ADHD symptoms, anxiety and depression symptoms, daily life EF and social functions, suggesting that CBT is a cross-cultural therapy for adult ADHD, whether administered with medications or not. This is the first study in China to demonstrate that CBT can be effective in adults with ADHD with or without medicine, with no significant differences between groups in core ADHD symptoms and anxiety and depression. CBT combined with medication may be more effective in EF than CBT alone, whereas CBT only may be more effective in life quality. Further studies are needed to develop a predictive model of efficacy to identify the characteristics of persons who respond well to specific treatment methods to determine individualized treatment plans based on individual characteristics to improve clinical efficacy as well as overall prognosis. In the future, it may be necessary to have a deeper understanding of the treatment priorities of different age groups to provide more accurate treatment services according to different treatment needs in school age patients and those in adulthood.

## Declaration of Competing Interest

None.

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## References

Arnold, L.E., Hodgkins, P., Caci, H., Kahle, J., Young, S., 2015. Effect of treatment modality on long-term outcomes in attention-deficit/hyperactivity disorder: a systematic review. PLoS ONE 10, e0116407. https://doi.org/10.1371/journal.pone.0116407.

Arnsten, A.F.T., Rubia, K., 2012. Neurobiological circuits regulating attention, cognitive control, motivation, and emotion: disruptions in neurodevelopmental psychiatric disorders. J. Am. Acad. Child Adolesc. Psychiat. 51, 356–367. https://doi.org/10.1016/j.jaac.2012.01.008.

Beauregard, M., Lévesque, J., 2006. Functional magnetic resonance imaging investigation of the effects of neurofeedback training on the neural bases of selective attention and response inhibition in children with attention-deficit/hyperactivity disorder. Appl. Psychophysiol. Biofeedback. 31, 3–20. https://doi.org/10.1007/s10484-006-9001-y.

Beck, A.T., 1993. Cognitive therapy: past, present, and future. J. Consult. Clin. Psychol. 61, 194–198. https://doi.org/10.1037//0022-006x.61.2.194.

Beck, A.T., 1997. The past and future of cognitive therapy. J. Psychother. Pract. Res. 6, 276–284.

Beck, A.T., 2016. Cognitive Therapy: Nature and Relation to Behavior Therapy – Republished Article. Behav. Ther. 47 (6), 776–784. https://doi.org/10.1016/j.beth.2016.11.003.

Bramham, J., Young, S., Bickerdike, A., Spain, D., McCartan, D., Xenitidis, K., 2009. Evaluation of group cognitive behavioral therapy for adults with ADHD. J. Atten. Disord. 12, 434–441. https://doi.org/10.1177/1087054708314596.

Brevik, E.J., Lundervold, A.J., Halmøy, A., Posserud, M.B., Instanes, J.T., Bjorvatn, B., Haavik, J., 2017. Prevalence and clinical correlates of insomnia in adults with attention-deficit hyperactivity disorder. Acta Psychiatr. Scand. 136, 220–227. https://doi.org/10.1111/acps.12756.

Buitelaar, J.K., van der Gaag, R.J., Swaab-Barnkvhld, H., Kuipkr, M.A., 1995. Prediction of clinical response to methylphenidate in children with attention-deficit hyperactivity disorder. J. Am. Acad. Child Adolesc. Psychiatry 34, 1025–1032. https://doi.org/10.1097/00004583-199508000-00012.

Burns, D.D., Spangler, D.L., 2000. Does psychotherapy homework lead to improvements in depression in cognitive-behavioral therapy or does improvement lead to increased homework compliance? J Consult. Clin. Psychol. 68, 46–56. https://doi.org/10.1037/0022-006x.68.1.46.

Bymaster, F.P., Katner, J.S., Nelson, D.L., Hemrick-Luecke, S.K., Threlkeld, P.G., Heiligenstein, J.H., Morin, S.M., Gehlert, D.R., Perry, K.W., 2002. Atomoxetine increases extracellular levels of norepinephrine and dopamine in prefrontal cortex of rat: a potential mechanism for efficacy in attention deficit/hyperactivity disorder. Neuropsychopharmacology 27, 699–711. https://doi.org/10.1016/s0893-133x(02)00346-9.

Chen, T.-H., Lu, R.-B., Chang, A.-J., Chu, D.-M., Chou, K.-R., 2006. The evaluation of cognitive–behavioral group therapy on patient depression and self-esteem. Arch. Psychiatr. Nurs. 20, 3–11. https://doi.org/10.1016/j.apnu.2005.08.005.

Cherkasova, M.V., French, L.R., Syer, C.A., Cousins, L., Galina, H., Ahmadi-Kashani, Y., Hechtman, L., 2017. Efficacy of cognitive behavioral therapy with and without medication for adults with ADHD. J. Atten. Disord. https://doi.org/10.1177/1087054716671197.

Coghill, D., Banaschewski, T., Zuddas, A., Pelaz, A., Gagliano, A., Doepfner, M., 2013. Long-acting methylphenidate formulations in the treatment of attention-deficit/hyperactivity disorder: a systematic review of head-to-head studies. BMC Psychiatry 13, 237. https://doi.org/10.1186/1471-244x-13-237.

Contini, V., Rovaris, D.L., Victor, M.M., Grevet, E.H., Rohde, L.A., Bau, C.H.D., 2013. Pharmacogenetics of response to methylphenidate in adult patients with attention-deficit/hyperactivity disorder (ADHD): a systematic review. Eur. Neuropsychopharmacol. 23, 555–560. https://doi.org/10.1016/j.euroneuro.2012.05.006.

Creed, T.A., Wolk, C.B., Feinberg, B., Evans, A.C., Beck, A.T., 2016. Beyond the label: relationship between community therapists' self-report of a cognitive behavioral therapy orientation and observed skills. Adm. Policy Ment. Health Ment. Health Serv. Res. 43, 36–43. https://doi.org/10.1007/s10488-014-0618-5.

Cubillo, A., Smith, A.B., Barrett, N., Giampietro, V., Brammer, M., Simmons, A., Rubia, K., 2014a. Drug-specific laterality effects on frontal lobe activation of atomoxetine and methylphenidate in attention deficit hyperactivity disorder boys during working memory. Psychol. Med. 44, 633–646. https://doi.org/10.1017/s0033291713000676.

Cubillo, A., Smith, A.B., Barrett, N., Giampietro, V., Brammer, M.J., Simmons, A., Rubia, K., 2014b. Shared and drug-specific effects of atomoxetine and methylphenidate on inhibitory brain dysfunction in medication-naive ADHD boys. Cereb. Cortex 24, 174–185. https://doi.org/10.1093/cercor/bhs296.

Cunill, R., Castells, X., Tobias, A., Capellà, D., 2016. Efficacy, safety and variability in pharmacotherapy for adults with attention deficit hyperactivity disorder: a meta-analysis and meta-regression in over 9000 patients. Psychopharmacology (Berl.) 233, 187–197. https://doi.org/10.1007/s00213-015-4099-3.

Das, D., Cherbuin, N., Butterworth, P., Anstey, K.J., Easteal, S., 2012. A population-based study of attention deficit/hyperactivity disorder symptoms and associated impairment in middle-aged adults. PLoS ONE 7, e31500. https://doi.org/10.1371/journal.pone.0031500.

De Bruyckere, K., Bushe, C., Bartel, C., Berggren, L., Kan, C.C., Dittmann, R.W., 2016. Relationships between functional outcomes and symptomatic improvement in atomoxetine-treated adult patients with attention-deficit/hyperactivity disorder: post hoc analysis of an integrated database. CNS Drugs 30, 541–558. https://doi.org/10.1007/s40263-016-0346-3.

Dibbets, P., Evers, E.A.T., Hurks, P.P.M., Bakker, K., Jolles, J., 2010. Differential brain activation patterns in adult attention-deficit hyperactivity disorder (ADHD) associated with task switching. Neuropsychology 24, 413–423. https://doi.org/10.1037/a0018997.

Dittner, A.J., Hodsoll, J., Rimes, K.A., Russell, A.J., Chalder, T., 2018. Cognitive-behavioural therapy for adult attention-deficit hyperactivity disorder: a proof of concept randomised controlled trial. Acta Psychiatr. Scand. 137, 125–137. https://doi.org/10.1111/acps.12836.

Dobson, Keith, S., 2013. The science of cbt: toward a metacognitive model of change? Behav. Ther. 44 (2), 224–227. https://doi.org/10.1016/j.beth.2009.08.003.

Du, Q., Qian, Y., Wang, Y., 2010. Reliability and validity of the behavior rating inventory of executive function-adult version self-report form in China. Chin. Mental Health J. 24, 625–628 (In Chinese).

Emilsson, B., Gudjonsson, G., Sigurdsson, J.F., Baldursson, G., Einarsson, E., Olafsdottir, H., Young, S., 2011. Cognitive behaviour therapy in medication-treated adults with ADHD and persistent symptoms: a randomized controlled trial. BMC Psychiatry 11, 116. https://doi.org/10.1186/1471-244x-11-116.

Epstein, J.N., Kollins, S.H., 2006. Psychometric properties of an adult ADHD diagnostic interview. J. Atten. Disord. 9, 504–514. https://doi.org/10.1177/1087054705283575.

Faltinsen, E., Zwi, M., Castells, X., Gluud, C., Simonsen, E., Storebø, O.J., 2018. Updated 2018 NICE guideline on pharmacological treatments for people with ADHD: a critical look. BMJ Evid. Based Med. 24, 99–102. https://doi.org/10.1136/bmjebm-2018-111110.

Fayyad, J., Sampson, N.A., Hwang, I., Adamowski, T., Aguilar-Gaxiola, S., Al-Hamzawi, A., Andrade, L.H.S.G., Borges, G., de Girolamo, G., Florescu, S., Gureje, O., Haro, J.M., Hu, C., Karam, E.G., Lee, S., Navarro-Mateu, F., O'Neill, S., Pennell, B.-E., Piazza, M., Posada-Villa, J., Ten Have, M., Torres, Y., Xavier, M., Zaslavsky, A.M., Kessler, R.C., 2017. The descriptive epidemiology of DSM-IV adult ADHD in the world health organization world mental health surveys. Atten. Deficit Hyperact. Disord. 9, 47–65. https://doi.org/10.1007/s12402-016-0208-3.

Fischer, B.A., 2012. A review of American psychiatry through its diagnoses: the history and development of the diagnostic and statistical manual of mental disorders. J. Nerv. Ment. Dis. 200, 1022–1030. https://doi.org/10.1097/nmd.0b013e318275cf19.

Fredriksen, M., Dahl, A.A., Martinsen, E.W., Klungsøyr, O., Haavik, J., Peleikis, D.E., 2014. Effectiveness of one-year pharmacological treatment of adult attention-deficit/hyperactivity disorder (ADHD): an open-label prospective study of time in treatment, dose, side-effects and comorbidity. Eur. Neuropsychopharmacol. 24, 1873–1884. https://doi.org/10.1016/j.euroneuro.2014.09.013.

Fredriksen, M., Peleikis, D.E., 2016. Long-term pharmacotherapy of adults with attention deficit hyperactivity disorder: a literature review and clinical study. Basic Clin. Pharmacol. Toxicol. 118, 23–31. https://doi.org/10.1111/bcpt.12477.

Fuermaier, A.B.M., Tucha, L., Koerts, J., Weisbrod, M., Lange, K.W., Aschenbrenner, S., Tucha, O., 2017. Effects of methylphenidate on memory functions of adults with ADHD. Appl. Neuropsychol. Adult 24, 199–211. https://doi.org/10.1080/23279095.

2015.1124108.
Garofalo, C., Holden, C.J., Zeigler-Hill, V., Velotti, P., 2016. Understanding the connection between self-esteem and aggression: the mediating role of emotion dysregulation. Aggress. Behav. 42, 3–15.
Goto, T., Hirata, Y., Takita, Y., Trzepacz, P.T., Allen, A.J., Song, D.-H., Gau, S.S.-F., Ichikawa, H., Takahashi, M., 2017. Efficacy and safety of atomoxetine hydrochloride in Asian adults with ADHD. J. Atten. Disord. 21, 100–109. https://doi.org/10.1177/1087054713510352.
Gu, Y., Xu, G., Zhu, Y., 2018. A randomized controlled trial of mindfulness-based cognitive therapy for college students with ADHD. J. Atten. Disord. 22, 388–399. https://doi.org/10.1177/1087054716686183.
Hao, Y., Fanc, J., 2000. The introduce and usage of WHOQOL instrument in Chinese. Mod. Rehabil. 4, 1127–1129 (In Chinese).
Hechtman, L., Swanson, J.M., Sibley, M.H., Stehli, A., Owens, E.B., Mitchell, J.T., Arnold, L.E., Molina, B.S., Hinshaw, S.P., Jensen, P.S., Abikoff, H.B., Algorta, G.P., Howard, A.L., Hoza, B., Etcovitch, J., Houssais, S., Lakes, K.D., Nichols, J.Q., 2016. Functional adult outcomes 16 years after childhood diagnosis of attention-deficit/hyperactivity disorder: MTA results. J. Am. Acad. Child Adolesc. Psychiatry 55, 945–952. e942. https://doi.org/10.1016/j.jaac.2016.07.774.
Hirvikoski, T., Waaler, E., Alfredsson, J., Pihlgren, C., Holmström, A., Johnson, A., Rück, J., Wiwe, C., Bothén, P., Nordström, A.-L., 2011. Reduced ADHD symptoms in adults with ADHD after structured skills training group: results from a randomized controlled trial. Behav. Res. Ther. 49, 175–185. https://doi.org/10.1016/j.brat.2011.01.001.
Hoekzema, E., Carmona, S., Ramos-Quiroga, J.A., Fernández, V.R., Bosch, R., Soliva, J.C., Rovira, M., Bulbena, A., Tobeña, A., Casas, M., Vilarroya, O., 2014. An independent components and functional connectivity analysis of resting state fMRI data points to neural network dysregulation in adult ADHD. Hum. Brain Mapp. 35, 1261–1272. https://doi.org/10.1002/hbm.22250.
Huang, F., Qian, Q., Wang, Y., 2015. Cognitive behavioral therapy for adults with attention-deficit hyperactivity disorder: study protocol for a randomized controlled trial. Trials 16, 161. https://doi.org/10.1186/s13063-015-0686-1.
Huang, F., Tang, Y.L., Zhao, M., Wang, Y., Pan, M., Wang, Y., Qian, Q., 2017. Cognitive-behavioral therapy for adult ADHD: a randomized clinical trial in China. J. Atten. Disord. 23, 1035–1046. https://doi.org/10.1177/1087054717725874.
Huang, X., Huang, P., Li, D., Zhang, Y., Wang, T., Mu, J., Li, Q., Xie, P., 2014. Early brain changes associated with psychotherapy in major depressive disorder revealed by resting-state fMRI: evidence for the top-down regulation theory. Int. J. Psychophysiol. 94, 437–444. https://doi.org/10.1016/j.ijpsycho.2014.10.011.
Huss, M., Duhan, P., Gandhi, P., Chen, C.-W., Spannhuth, C., Kumar, V., 2017. Methylphenidate dose optimization for ADHD treatment: review of safety, efficacy, and clinical necessity. Neuropsychiatr. Dis. Treat. 13, 1741–1751. https://doi.org/10.2147/NDT.S130444.
Jensen, C.M., Amdisen, B.L., Jørgensen, K.J., Arnfred, S.M.H., 2016. Cognitive behavioural therapy for ADHD in adults: systematic review and meta-analyses. Atten. Deficit. Hyperact. Disord. 8, 3–11. https://doi.org/10.1007/s12402-016-0188-3.
Jensen, P.S., Hinshaw, S.P., Kraemer, H.C., Lenora, N., Newcorn, J.H., Abikoff, H.B., March, J.S., Arnold, L.E., Cantwell, D.P., Conners, C.K., Elliott, G.R., Greenhill, L.L., Hechtman, L., Hoza, B., Pelham, W.E., Severe, J.B., Swanson, J.M., Wells, K.C., Wigal, T., Vitiello, B., 2001. ADHD comorbidity findings from the MTA study: comparing comorbid subgroups. J. Am. Acad. Child. Adolesc. Psychiatry 40, 147–158. https://doi.org/10.1097/00004583-200102000-00009.
Johnston, B.A., Coghill, D., Matthews, K., Steele, J.D., 2015. Predicting methylphenidate response in attention deficit hyperactivity disorder: a preliminary study. J. Psychopharmacol. 29, 24–30. https://doi.org/10.1177/0269881114548438.
Kazdin, Alan, E., 2009. Understanding how and why psychotherapy leads to change. Psychotherapy Res. 19 (4–5), 418–428. https://doi.org/10.1080/10503300802448899.
Kirino, E., Imagawa, H., Goto, T., Montgomery, W., 2015. Sociodemographics, comorbidities, healthcare utilization and work productivity in Japanese patients with adult ADHD. PLoS ONE 10, e0132233. https://doi.org/10.1371/journal.pone.0132233.
Kuriyan, A.B., Pelham, W.E., Molina, B.S.G., Waschbusch, D.A., Gnagy, E.M., Sibley, M.H., Babinski, D.E., Walther, C., Cheong, J., Yu, J., Kent, K.M., 2013. Young adult educational and vocational outcomes of children diagnosed with ADHD. J. Abnorm. Child Psychol. 41, 27–41. https://doi.org/10.1007/s10802-012-9658-z.
Lin, H.-Y., Gau, S.S.-F., 2015. Atomoxetine treatment strengthens an anti-correlated relationship between functional brain networks in medication-naive adults with attention-deficit hyperactivity disorder: a randomized double-blind placebo-controlled clinical trial. Int. J. Neuropsychopharmacol. 19. pyv094. https://doi.org/10.1093/ijnp/pyv094.
López-Pinar, C., Martínez-Sanchís, S., Carbonell-Vayá, E., Fenollar-Cortés, J., Sánchez-Meca, J., 2018. Long-term efficacy of psychosocial treatments for adults with attention-deficit/hyperactivity disorder: a meta-analytic review. Front. Psychol. 9, 638. https://doi.org/10.3389/fpsyg.2018.00638.
Matthies, S., Philipsen, A., 2016. Comorbidity of personality disorders and adult attention deficit hyperactivity disorder (ADHD)—review of recent findings. Curr. Psychiatry Rep. 18, 33. https://doi.org/10.1007/s11920-016-0675-4.
Mattos, P., Louzã, M.R., Palmini, A.L.F., Oliveira, I.R.D., Rocha, F.L., 2013. A multicenter, open-label trial to evaluate the quality of life in adults with ADHD treated with long-acting methylphenidate (OROS MPH). J. Atten. Disord. 17, 444–448. https://doi.org/10.1177/1087054711434772.
McCarthy, H., Skokauskas, N., Mulligan, A., Donohoe, G., Mullins, D., Kelly, J., Johnson, K., Fagan, A., Gill, M., Meaney, J., Frodl, T., 2013. Attention network hypoconnectivity with default and affective network hyperconnectivity in adults diagnosed with attention-deficit/hyperactivity disorder in childhood. JAMA Psychiatry 70, 1329–1337. https://doi.org/10.1001/jamapsychiatry.2013.2174.
Meijer, W.M., Faber, A., den Ban, E., Tobi, H., 2009. Current issues around the pharmacotherapy of ADHD in children and adults. Pharm. World Sci. 31, 509–516. https://doi.org/10.1007/s11096-009-9302-3.
Michelson, D., Adler, L., Spencer, T., Reimherr, F.W., West, S.A., Allen, A.J., Kelsey, D., Wernicke, J., Dietrich, A., Milton, D., 2003. Atomoxetine in adults with ADHD: two randomized, placebo-controlled studies. Biol. Psychiatry 53, 112–120. https://doi.org/10.1016/s0006-3223(02)01671-2.
Mick, E., McManus, D.D., Goldberg, R.J., 2013. Meta-analysis of increased heart rate and blood pressure associated with CNS stimulant treatment of ADHD in adults. Eur. Neuropsychopharmacol. 23, 534–541. https://doi.org/10.1016/j.euroneuro.2012.06.011.
Milioni, A.L.V., Chaim, T.M., Cavallet, M., de Oliveira, N.M., Annes, M., dos Santos, B., Louzã, M., da Silva, M.A., Miguel, C.S., Serpa, M.H., Zanetti, M.V., Busatto, G., Cunha, P.J., 2017. High IQ may "mask" the diagnosis of ADHD by compensating for deficits in executive functions in treatment-naïve adults with ADHD. J. Atten. Disord. 21, 455–464. https://doi.org/10.1177/1087054714554933.
Molina, B.S.G., Hinshaw, S.P., Swanson, J.M., Arnold, L.E., Vitiello, B., Jensen, P.S., Epstein, J.N., Hoza, B., Hechtman, L., Abikoff, H.B., Elliott, G.R., Greenhill, L.L., Newcorn, J.H., Wells, K.C., Wigal, T., Gibbons, R.D., Hur, K., Houck, P.R., 2009. The MTA at 8 years: prospective follow-up of children treated for combined-type ADHD in a multisite study. J. Am. Acad. Child Adolesc. Psychiatry 48, 484–500. https://doi.org/10.1097/chi.0b013e31819c23d0.
Mongia, M., Hechtman, L., 2012. Cognitive behavior therapy for adults with attention-deficit/hyperactivity disorder: a review of recent randomized controlled trials. Curr. Psychiatry Rep. 14, 561–567. https://doi.org/10.1007/s11920-012-0303-x.
Murray, D.W., Arnold, L.E., Swanson, J., Wells, K., Burns, K., Jensen, P., Hechtman, L., Paykina, N., Legato, L., Strauss, T., 2008. A clinical review of outcomes of the multimodal treatment study of children with attention-deficit/hyperactivity disorder (MTA). Curr. Psychiatry Rep. 10, 424–431. https://doi.org/10.1007/s11920-008-0068-4.
Nair, R., Moss, S.B., 2009. Management of attention-deficit hyperactivity disorder in adults: focus on methylphenidate hydrochloride. Neuropsychiatr. Dis. Treat. 5, 421–432. https://doi.org/10.2147/ndt.s4101.
Ni, H.-C., Shang, C.-Y., Gau, S.S.-F., Lin, Y.-J., Huang, H.-C., Yang, L.-K., 2013. A head-to-head randomized clinical trial of methylphenidate and atomoxetine treatment for executive function in adults with attention-deficit hyperactivity disorder. Int. J. Neuropsychopharmacol. 16, 1959–1973. https://doi.org/10.1017/s1461145713000357.
Paloyelis, Y., Rijsdijk, F., Wood, A.C., Asherson, P., Kuntsi, J., 2010. The genetic association between ADHD symptoms and reading difficulties: the role of inattentiveness and IQ. J. Abnorm. Child Psychol. 38, 1083–1095. https://doi.org/10.1007/s10802-010-9429-7.
Pappas, D., 2006. ADHD rating scale-IV: checklists, norms, and clinical interpretation. J. Psychoeduc. Assess. 24, 172–178. https://doi.org/10.1177/0734282905285792.
Philipsen, A., Jans, T., Graf, E., Matthies, S., Borel, P., Colla, M., Gentschow, L., Langner, D., Jacob, C., Groß-Lesch, S., Sobanski, E., Alm, B., Schumacher-Stien, M., Roesler, M., Retz, W., Retz-Junginger, P., Kis, B., Abdel-Hamid, M., Heinrich, V., Huss, M., Kornmann, C., Bürger, A., Perlov, E., Ihorst, G., Schlander, M., Berger, M., Tebartz van Elst, L., 2015. Effects of group psychotherapy, individual counseling, methylphenidate, and placebo in the treatment of adult attention-deficit/hyperactivity disorder. JAMA Psychiatry 72, 1199–1210. https://doi.org/10.1001/jamapsychiatry.2015.2146.
Polanczyk, G.V., Salum, G.A., Sugaya, L.S., Caye, A., Rohde, L.A., 2015. Annual research review: a meta-analysis of the worldwide prevalence of mental disorders in children and adolescents. J. Child Psychol. Psychiatry 56, 345–365. https://doi.org/10.1111/jcpp.12381.
Power, M., Kuyken, W., Orley, J., Herrman, H., Schofield, H., Murphy, B., The WHOQOL Group, 1998. The world health organization quality of life assessment (WHOQOL): development and general psychometric properties. Social Sci. Med. 46, 1569–1585. https://doi.org/10.1016/S0277-9536(98)00009-4.
Qian, Q., Li, Y., Wang, Y., Zhang, Y., 2010. An exploratory clinical study of attention deficit hyperactivity disorder in young adulthood. Chin. J. Nerv. Ment. Dis. 36, 75–79.
Quidé, Y., Witteveen, A.B., El-Hage, W., Veltman, D.J., Olff, M., 2012. Differences between effects of psychological versus pharmacological treatments on functional and morphological brain alterations in anxiety disorders and major depressive disorder: a systematic review. Neurosci. Biobehav. Rev. 36, 626–644. https://doi.org/10.1016/j.neubiorev.2011.09.004.
Robbins, T.W., James, M., Owen, A.M., Sahakian, B.J., Mcinnes, L., Rabbitt, P., 1994. Cambridge neuropsychological test automated battery (CANTAB): a factor analytic study of a large sample of normal elderly volunteers. Dementia Geriatric Cognit. Disord. 5, 266–281.
Robbins, T.W., 2000. Chemical neuromodulation of frontal-executive functions in humans and other animals. Exp. Brain Res. 133, 130–138. https://doi.org/10.1007/s002210000407.
Rosenberg, M., 1965. Society and the Adolescent Self-Image. Princeton University Press, Princeton, NJ. https://doi.org/10.2307/2575639.
Rösler, M., Retz, W., Thome, J., Schneider, M., Stieglitz, R.D., Falkai, P., 2006. Psychopathological rating scales for diagnostic use in adults with attention-deficit/hyperactivity disorder (ADHD). Eur. Arch. Psychiatry Clin. Neurosci. 256, i3–i11. https://doi.org/10.1007/s00406-006-1001-7.
Roth, R.M., Lance, C.E., Isquith, P.K., Fischer, A.S., Giancola, P.R., 2013. Confirmatory factor analysis of the behavior rating inventory of executive function-adult version in healthy adults and application to attention-deficit/hyperactivity disorder. Arch. Clin. Neuropsychol. 28, 425–434. https://doi.org/10.1093/arclin/act031.

Safren, S.A., Otto, M.W., Sprich, S., Winett, C.L., Wilens, T.E., Biederman, J., 2005. Cognitive-behavioral therapy for ADHD in medication-treated adults with continued symptoms. Behav. Res. Ther. 43, 831–842. https://doi.org/10.1016/j.brat.2004.07.001.

Safren, S.A., Sprich, S., Mimiaga, M.J., Surman, C., Knouse, L., Groves, M., Otto, M.W., 2010a. Cognitive behavioral therapy vs relaxation with educational support for medication-treated adults with ADHD and persistent symptoms. JAMA 304, 875–880. https://doi.org/10.1001/jama.2010.1192.

Safren, S.A., Sprich, S.E., Cooper-Vince, C., Knouse, L.E., Lerner, J.A., 2010b. Life impairments in adults with medication-treated ADHD. J. Atten. Disord. 13, 524–531. https://doi.org/10.1177/1087054709332460.

Sainani, K.L., 2015. Dealing with missing data. PM&R 7, 990–994. https://doi.org/10.1016/j.pmrj.2015.07.011.

Schoenberg, P.L.A., Hepark, S., Kan, C.C., Barendregt, H.P., Buitelaar, J.K., Speckens, A.E.M., 2014. Effects of mindfulness-based cognitive therapy on neurophysiological correlates of performance monitoring in adult attention-deficit/hyperactivity disorder. Clin. Neurophysiol. 125, 1407–1416. https://doi.org/10.1016/j.clinph.2013.11.031.

Schroeder, P.J., 2014. The effects of age on processing and storage in working memory span tasks and reading comprehension. Exp. Aging Res. 40, 308–331. https://doi.org/10.1080/0361073x.2014.896666.

Segal, D.L., 2010. Diagnostic and statistical manual of mental disorders (DSM-IV-TR). In: Weiner, I.B., Craighead, W.E. (Eds.), The Corsini Encyclopedia of Psychology and Behavioral Science, 4th ed. John Wiley and Sons, Inc, Hoboken, NJ, pp. 495–497.

Shaw, B.F., Elkin, I., Yamaguchi, J., Olmsted, M., Vallis, T.M., Dobson, K.S., Lowery, A., Sotsky, S.M., Watkins, J.T., Imber, S.D., 1999. Therapist competence ratings in relation to clinical outcome in cognitive therapy of depression. J. Consult. Clin. Psychol. 67, 837–846. https://doi.org/10.1037//0022-006x.67.6.837.

Shimizu, R., Horiguchi, N., Yano, K., Sakuramoto, M, Kanegawa, N., Shinohara, S., Ohnishi, S., 2019. Pharmacokinetic-Pharmacodynamic modeling of brain dopamine levels based on dopamine transporter occupancy after administration of methylphenidate in rats. J. Pharmacol. Exp. Ther 369, 78–87. https://doi.org/10.1124/jpet.118.252262.

Schweren, L.J., de Zeeuw, P., Durston, S., 2013. MR imaging of the effects of methylphenidate on brain structure and function in attention-deficit/hyperactivity disorder. Eur. Neuropsychopharmacol. 23, 1151–1164. https://doi.org/10.1016/j.euroneuro.2012.10.014.

Spencer, T.J., Bonab, A.A., Dougherty, D.D., Martin, J., McDonnell, T., Fischman, A.J., 2010. A PET study examining pharmacokinetics and dopamine transporter occupancy of two long-acting formulations of methylphenidate in adults. Int. J. Mol. Med. 25 https://doi.org/261-5.10.3892/ijmm_00000339.

Spencer, T.J., Faraone, S.V., Tarko, L., McDermott, K., Biederman, J., 2014. Attention-deficit/hyperactivity disorder and adverse health outcomes in adults. J. Nerv. Ment. Dis. 202, 725–731. https://doi.org/10.1097/nmd.0000000000000191.

Steele, M., Jensen, P.S., Quinn, D.M.P., 2006. Remission versus response as the goal of therapy in ADHD: a new standard for the field? Clin. Ther. 28, 1892–1908. https://doi.org/10.1016/j.clinthera.2006.11.006.

Stevenson, C.S., Whitmont, S., Bornholt, L., Livesey, D., Stevenson, R.J., 2002. A cognitive remediation programme for adults with attention deficit hyperactivity disorder. Aust. N. Z. J. Psychiatry 36, 610–616. https://doi.org/10.1046/j.1440-1614.2002.01052.x.

Swanson, J., Arnold, L.E., Kraemer, H., Hechtman, L., Molina, B., Hinshaw, S., Vitiello, B., Jensen, P., Steinhoff, K., Lerner, M., Greenhill, L., Abikoff, H., Wells, K., Epstein, J., Elliott, G., Newcorn, J., Hoza, B., Wigal, T., 2008. Evidence, interpretation, and qualification from multiple reports of long-term outcomes in the multimodal treatment study of children with ADHD (MTA). J. Atten. Disord. 12, 4–14. https://doi.org/10.1177/1087054708319345.

Takahashi, M., Takita, Y., Goto, T., Ichikawa, H., Saito, K., Matsumoto, H., Tanaka, Y., 2011. An open-label, dose-titration tolerability study of atomoxetine hydrochloride in Japanese adults with attention-deficit/hyperactivity disorder. Psychiatry Clin. Neurosci. 65, 55–63. https://doi.org/10.1111/j.1440-1819.2010.02159.x.

The MTA Cooperative Group, 1999. A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. Multimodal treatment study of children with ADHD. Arch. Gen. Psychiatr. 56, 1073–1086. https://doi.org/10.1001/archpsyc.56.12.1073.

The MTA Cooperative Group, 2004. National institute of mental health multimodal treatment study of ADHD follow-up: 24-month outcomes of treatment strategies for attention-deficit/hyperactivity disorder. Pediatrics 113, 754–761. https://doi.org/10.1542/peds.113.4.754.

van den Hoofdakker, B.J., Nauta, M.H., Veen-Mulders, L.V.d., Sytema, S., Emmelkamp, P.M.G., Minderaa, R.B., Hoekstra, P.J., 2010. Behavioral parent training as an adjunct to routine care in children with attention-deficit/hyperactivity disorder: moderators of treatment response. J. Pediatr. Psychol. 35, 317–326. https://doi.org/10.1093/jpepsy/jsp060.

Vidal-Estrada, R., Bosch-Munso, R., Nogueira-Morais, M., Casas-Brugue, M., Ramos-Quiroga, J.A., 2012. Psychological treatment of attention deficit hyperactivity disorder in adults: a systematic review. Actas Espa. Psiquiatr. 40, 147–154.

Virta, M., Salakari, A., Antila, M., Chydenius, E., Partinen, M., Kaski, M., Vataja, R., Kalska, H., Iivanainen, M., 2010. Short cognitive behavioral therapy and cognitive training for adults with ADHD - a randomized controlled pilot study. Neuropsychiatr. Dis. Treat. 6, 443–453. https://doi.org/10.2147/ndt.s11743.

Voigt, R.G., Katusic, S.K., Colligan, R.C., Killian, J.M., Weaver, A.L., Barbaresi, W.J., 2017. Academic achievement in adults with a history of childhood attention-deficit/hyperactivity disorder: a population-based prospective study. J. Dev. Behav. Pediatr. 38, 1–11. https://doi.org/10.1097/dbp.0000000000000358.

Waltz, J., Addis, M.E., Koerner, K., Jacobson, N.S., 1993. Testing the integrity of a psychotherapy protocol: assessment of adherence and competence. J. Consult. Clin. Psychol. 61, 620–630. https://doi.org/10.1037//0022-006x.61.4.620.

Wang, X., Wang, X., Hong, M., 1999. The Mental Health Scale Revised Edition. Chinese Mental Health Journal, Beijing (In Chinese).

Weiss, M., Murray, C., Wasdell, M., Greenfield, B., Giles, L., Hechtman, L., 2012. A randomized controlled trial of CBT therapy for adults with ADHD with and without medication. BMC Psychiatry 12, 30. https://doi.org/10.1186/1471-244x-12-30.

Yang, P.-C., Lung, F.-W., Chiou, S.-S., Yen, C.-F., Fuh, J.-L., 2012. Quality of life of methylphenidate treatment-responsive adolescents with attention-deficit/hyperactivity disorder. Kaohsiung J. Med. Sci. 28, 279–284. https://doi.org/10.1016/j.kjms.2011.10.013.

Young, S., Khondoker, M., Emilsson, B., Sigurdsson, J.F., Philipp-Wiegmann, F., Baldursson, G., Olafsdottir, H., Gudjonsson, G., 2015. Cognitive–behavioural therapy in medication-treated adults with attention-deficit/hyperactivity disorder and comorbid psychopathology: a randomized controlled trial using multi-level analysis. Psychol. Med. 45, 2793–2804. https://doi.org/10.1017/s0033291715000756.

Young, Z., Moghaddam, N., Tickle, A., 2016. The efficacy of cognitive behavioral therapy for adults with ADHD: a systematic review and meta-analysis of randomized controlled trials. J. Atten. Disord. https://doi.org/10.1177/1087054716664413.

Zimmer, Luc, 2017. Contribution of clinical neuroimaging to the understanding of the pharmacology of methylphenidate. Trends Pharmacol. Sci. 38 (7), 608–620 https://doi: 10.1016/j.tips.2017.04.001.

Zung, W.W.K., 1967. Factors influencing the self-rating depression scale. Arch. Gen. Psychiatr. 16, 543–547. https://doi.org/10.1001/archpsyc.1967.01730230027003.