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Specifically for the RCT S64197 "SIESTA: Sleep IntervEntion as Symptom Treatment for ADHD - Blended CBT sleep intervention to improve sleep, ADHD symptoms and related problems in adolescents with ADHD"
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S64197 "SIESTA: Sleep IntervEntion as Symptom Treatment - Blended CBT sleep intervention to improve sleep, ADHD symptoms and related problems in adolescents with ADHD"

Introduction

Up to 72% of adolescents with ADHD experience sleep problems.[1] A systematic review by Lunsford-Avery and colleagues (2016) and a meta-analysis done by our research group show that adolescents with ADHD have a more disrupted sleep and experience more sleep problems compared to their typically developing peers.[2,3] This is particularly concerning, because disrupted sleep is related to worsened clinical, neurocognitive, and functional outcomes in adolescents with ADHD and leads to increased ADHD symptom impairment.[4] Therefore, more information on the effectiveness of sleep interventions specifically for adolescents with ADHD would be beneficial and may inform treatment guidelines for ADHD, as these often note problems in sleep in ADHD but lack evidence supporting specific intervention guidelines for ADHD.[5,6] Although it is still unclear which factors underly worsened sleep and sleep problems in adolescents with ADHD, inadequate sleep hygiene practices are likely to be an important factor.[7] Sleep hygiene entails various modifiable factors and behaviors that influence sleep (i.e. sleep practices, physiological factors like caffeine and alcohol use, sleep environment) and thus is an important intervention target to improve disrupted sleep.

Up to now, there is no evidence-based cognitive behavioral treatment (CBT) aimed at improving sleep specifically for adolescents with ADHD. A proof of principle is available in children with ADHD,[8-12] in typically developing adolescents,[13,14] and in adults with ADHD and sleep problems.[15] However, treatments for adolescents with ADHD have received little attention so far. This might be due to the difficulty of providing treatment for adolescents in general and adolescents with ADHD in particular. For children with ADHD parent-mediated interventions have been proven to be effective. However, they generally do not work for adolescents due to a growing need for autonomy.[16] Furthermore, adolescents with ADHD are known to have motivational difficulties, which are seen by enhanced treatment drop-out and non-compliance to treatment.[17] Moreover, they have severe problems with planning and organization in daily life,[18] and resisting immediate temptations.[19] These difficulties are likely to affect their sleep; due to organizational difficulties they do not manage to get enough sleep, or may not be able to resist immediate temptations such as mobile phones or social media. Given the specificity of this developmental phase in ADHD, interventions may need to be adapted both towards the developmental phase and the disorder. Therefore, experts in the field of sleep, psychopathology and functional disabilities recommend that sleep disorders should be treated together with functional disabilities such as ADHD symptoms, as they are interactively and bidirectionally related to each other.[20,21]

Recently, one small scale pilot study has been published that shows that the existing CBT based Transdiagnostic Sleep and Circadian Intervention for Youth [TranS-C][22] resulted in improvements in sleep, mental health symptoms, and daily life executive functioning in 14 adolescents with ADHD.[23] However, the parents of the participants were all highly educated and participants themselves were very motivated, which is likely not to be a representation of all adolescents with ADHD.[23] Thus, there still is a clear need for a sleep treatment specifically developed for adolescents with ADHD, tailored to their specific difficulties with motivation and

planning and organization. Therefore, our lab developed a CBT intervention that integrates sleep training with motivational interviewing, and planning/organizational skills with the aim of improving sleep problems in adolescents with ADHD.[24,25] The acronym is SIESTA [Sleep IntervEntion as Sympom Treatment for ADHD]. To tailor the intervention optimally towards the needs of adolescents with ADHD and enhance feasibility of the assessment and study protocol of our RCT, we piloted our SIESTA intervention and the study protocol in eight adolescents with ADHD and sleep problems.[26] Fine-tuning of the intervention and study protocol was based on the outcomes of the pilot study and feedback from adolescents with ADHD and parents from focus groups.

The objective of this study is to test the effectiveness of SIESTA in combination with treatment as usual (TAU) for ADHD symptomatology compared to TAU only in a randomized controlled trial. SIESTA is expected to improve sleep architecture measured both objectively and subjectively; specified as total sleep time (TST), sleep onset latency (SOL), sleep efficiency (SE), and number of awakenings (NoA), sleep problems and sleep hygiene practices (primary outcomes). Regarding secondary outcomes SIESTA is expected to improve ADHD symptoms, comorbid symptoms and functional outcomes. Both primary and secondary outcomes are expected to show greater improvement in the SIESTA group, both on the short (post-test) and middle long term (approximately three months follow-up), than in the TAU only group.

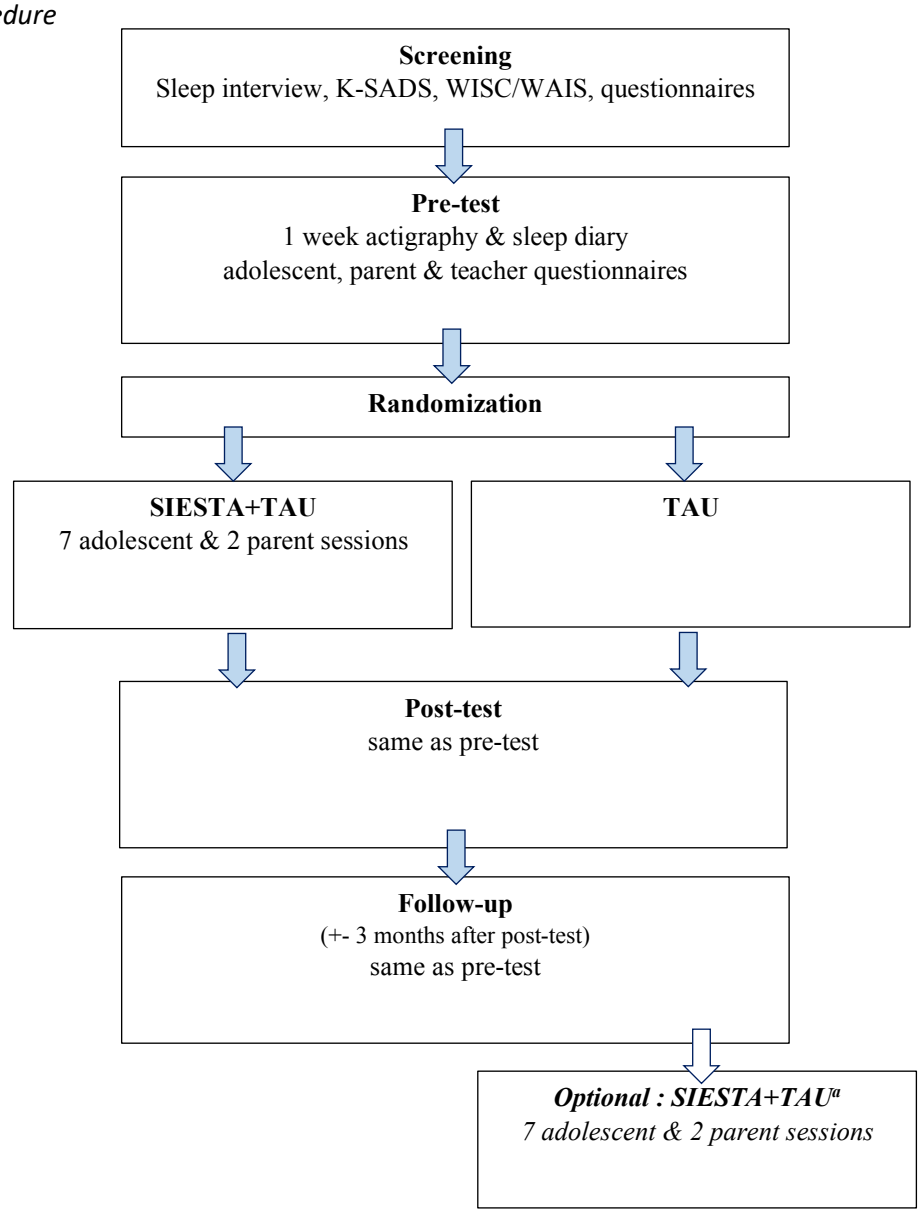
Methods and analysis

Study design

A randomized, controlled, investigator blinded monocenter trial is used to test whether SIESTA in combination with TAU results in greater improvement in sleep than TAU only in adolescents with ADHD. This trial was pre-registered at ClinicalTrials.gov (Identifier: NCT04723719; all items from the World Health Organization Trial Registration Data Set are further elaborated on in this registration) and we adhered to the SPIRIT recommendations when drafting this protocol (see Supplement 1).[27] This study consists of five waves of recruitment, always following the same procedure (see Figure 1); January-March 2021, September-October 2021, January-March 2022, September-October 2022, and January-March 2023. We aimed to be outreaching and provide treatments close to where the adolescents live, therefore our therapists travel to different locations in Flanders (Leuven, Antwerp, Hasselt, Brussels, Gent, and Roeselare). These different locations in rural and urban areas are chosen to remove barriers for accessibility and to be able to include a diverse sample.

Figure 1

Study procedure



Note. K-SADS = Kiddie Schedule for Affective Disorders and Schizophrenia for school aged children (6-18 years) Present and Lifetime version based on the DSM-5;[28] WISC = Wechsler Intelligence Scale for Children, fifth edition;[29] WAIS = Wechsler Adult Intelligence Scale, fourth edition;[30] SIESTA = Sleep IntervEntion as Symptom Treatment for ADHD; TAU = treatment as usual.

[a] Those randomized to TAU can voluntary choose to receive SIESTA after the last follow-up. These treatments after the last follow-up are not part of the study protocol anymore.

Participants

Inclusion and exclusion criteria can be found in Table 1.

Table 1

Inclusion and exclusion criteria

Inclusion	Exclusion
• 13 - 17 years old • Attending secondary education • ADHD diagnosis[a] • Sleep problems[b]: (⩾ 3 days/week and lasting ⩾ 3 months) ○ Sleep onset > 20 min ○ and/or wake up time after sleep onset > 30 min ○ and/or < 7h sleep ○ and at least one inadequate sleep hygiene practice ○ and distress reported by adolescent and/or parent • IQ ≥ 80[c] • Stable use of ADHD medication (4 weeks before screening)	• Comorbid disorders: ○ Conduct disorder[a] ○ ASD[d] ○ Depressive disorder with suicide risk or active suicidality[a] • Sleep disorders[b]: ○ Narcolepsy ○ Sleep breathing disorder ○ Restless leg syndrome • Substance abuse[e] (except nicotine), however substance use is not an exclusion criterion • Physical or medical problems (and medication) causing sleep problems • Medication for sleep, anxiety or depression • Melatonin use (2 week washout of melatonin before participation) • Acute crisis situation at home • CBT sleep intervention participation (< 6 months ago)

Note. [a] Verified by the semi structured interview K-SADS-PL DSM-5 with the parents;[28]
[b] Determined in an extensive sleep interview based on the DSM-5 and ICSD-3 criteria with parents and adolescents;[20,31]
[c] Verified by the subtests Vocabulary and Matrix reasoning from the Wechsler Intelligence Scale for Children for adolescents aged 13 to 16 years old or the Wechsler Adult Intelligent Scale for adolescents aged 17 years old;[29,30]
[d] As indicated by the parents;
[e] Verified by the subscale 'Disorders in the use of substances and behavioral addictions' of the Measurements in the Addictions for Triage and Evaluations - youth (MATE-Y).[32]

Patient and public involvement

The intervention, study design, and research questions were developed with adolescents with ADHD in mind as the researchers have extensive (clinical) experience with ADHD. To fine-tune and adapt SIESTA and the study design to the needs and perceptions of adolescents with ADHD and their parents, a pilot study (N=8) preceded the RCT.[33] Adolescents with ADHD and sleep problems and their parents who received the pilot version of SIESTA gave feedback on the intervention and addressed points of improvement in focus groups. Focus groups were conducted separately with adolescents and parents. Regarding the intervention, feedback was given on the duration, complexity, feasibility, suitability, relevance and representation of ADHD in the materials used in treatment. Regarding the study design and assessment protocol, feedback was given on the (amount of) questionnaires, usability and feasibility of the sleep diary, and actigraphy.

Randomization and blinding

Participants are randomly assigned to either the treatment (SIESTA+TAU) or control (TAU) group with a 1:1 allocation stratified by ADHD medication use (yes/no) and location (Leuven, Antwerp, Hasselt, Brussels, Gent, Roeselare) using permuted blocks of random sizes.[34,35] We randomize per location to ensure practical feasibility for our therapists of the KU Leuven (i.e. there is a maximum amount of adolescents that can be treated per location). Randomization is done by an

independent researcher who is not involved in the study in any way. Due to the nature of the psychological treatment neither participants nor clinicians can be blinded to allocation. Researchers who are responsible for the practical side of the study (LK, FM), are not blinded to allocation, however, the principal investigator (SVDO) and the other researchers DB, BB and MD are blinded throughout the study.

Intervention and comparison

SIESTA is based on a CBT sleep intervention for typically developing adolescents and a CBT intervention focused on motivational planning for adolescents with ADHD, both developed by (amongst others) the project applicants.[36,37] The training follows a structured workbook for the adolescent which can be used during sessions and at home.[24] The instructions for the therapist are described in a therapist manual.[25] SIESTA consists of seven individual sessions with the adolescents, and two parental sessions. An overview of the content of the sessions can be found in Table 2. This RCT uses as control condition TAU for ADHD symptomatology. In Flanders TAU for ADHD primarily consists of medication with stimulants.

Table 2

Overview of the Adolescent and Parent Sessions of SIESTA

Session 1	Psychoeducation on sleep in adolescents with ADHD. Focus on goal setting and adolescent motivation.
Session 2	In-depth psychoeducation on sleep hygiene (sleep practices, physiological factors like caffeine and alcohol use, sleep environment). Adolescent sleep behavior research: What does the adolescent already know and what more information is needed?
Session 3	Adjustments to align better with healthy sleep practices. Discussing trying out an alarm and relaxation exercises.
Parent session 1	Psychoeducation on sleep in adolescents with ADHD. Discussing and creating realistic expectations of parents towards the intervention and their adolescent.
Session 4	Aimed at drawing up a functional and topographical analysis of the sleep problem and specify the goals of *session 1* based on that. An individualized sleep plan is made to target their sleep problem.
Session 5	An extra plan can be added to the sleep plan: this can focus on rumination, planning and organization, circadian rhythm and motivation.
Session 6	The sleep plan is finalized. Making sure it is adapted towards the adolescent.
Parent session 2	Finding a balance between controlling and letting go of the sleep of the adolescent. Positive communication about the sleep of the adolescent.
Session 7	Relapse prevention.

Outcome measures

Primary outcomes

Objective sleep architecture: TST, SOL, SE, and NoA. Sleep is registered with wrist actigraphy (Motionwatch, CamNtech Ltd) as objective measurement. Participants wear an actigraph for five school nights and two weekend nights, as based on previous research,[38] this is sufficient to be able to compute reliable sleep architecture estimates. Actigraphy has been reliably used in adolescents with sleep problems and has been shown to be sensitive to treatment effects.[13,38,39] Participants use the event marker button on the actigraph to indicate lights out and getup times.[40] If they forget to press the button, those time points are extracted from the sleep diary data. Using this data, TST (time asleep between sleep onset and sleep offset), SOL (time from lights out to sleep onset), and SE (percentage of time spent asleep TST while in bed TiB), and NoA (number of times awake after sleep onset and before sleep offset) are calculated.

Subjective sleep architecture. Sleep is registered with a sleep diary as subjective measurement. The adolescents fill out the sleep diary for five school nights and two weekend nights, keeping track of lights out, sleep onset, sleep offset and getup via an ecological momentary assessment app m-Path.[41] TST, SOL, SE, and NoA are calculated analogous to the actigraph data.

Sleep problems. Sleep problems are measured using two self-report and one parent-reported questionnaire. The following two subscales of the School Sleep Habits Survey are used: Sleepiness and sleep/wake problem behaviors.[42] This is a validated self-report questionnaire with acceptable internal consistency (sleepiness; α = .70; sleep/wake problem behaviors; α = .75).[43] To measure sleep deprivation, the Chronic Sleep Reduction Questionnaire is used (CSRQ).[44] This self-report questionnaire is validated, and has good internal consistency (α = .85 in clinical and α = .87 in control sample).[45] Children Sleep Habits Questionnaire (CSHQ) is used to gain insight in parents' perception of their children's sleep.[46] This is a validated, parent-report questionnaire with acceptable internal consistency (α = .78 in clinical and α = .68 in control sample) and acceptable test-retest reliability (.62 - .79).[46]

Sleep hygiene. Sleep hygiene is measured with the revised Adolescent Sleep Hygiene Scale (ASHSr).[47] This is a validated self-report questionnaire with adequate to good internal consistency (total scale *α* = .84 and subscales *α* = .60 - .81).[47]

Secondary outcomes

ADHD symptoms. Inattention and hyperactivity-impulsivity subscales of the Disruptive Behavior Disorder Rating Scale (DBDRS) are used to measure ADHD symptoms.[48] This parent-reported questionnaire is validated, and the internal consistency of the scales in a Flemish sample is good for inattention and hyperactivity-impulsivity.[48]

Comorbidities. Symptoms of multiple comorbidities are measured using self-, parent- and teacher-report questionnaires. The ODD subscale of the parent-reported DBDRS is used.[48] To evaluate symptoms of anxiety, the SCARED-R is administered.[49] The SCARED-R is a validated, self-report questionnaire with good psychometric properties.[50] The self-reported Child Depression Inventory 2 (CDI-2) is administered to assess depressive symptoms.[51] Again, this is a validated questionnaire with good internal consistency (α = .88).[51]

Functional outcomes. Parent-adolescent conflict is measured using the Conflict Behavior Questionnaire (CBQ).[52] This is a validated, parent-report questionnaire with acceptable to good internal consistency (appraisal of parent; α = .73; appraisal of dyad; α = .89).[53] To evaluate adolescents' educational achievement, parents complete the Homework Problems Checklist (HPC)[54] and teachers the Classroom Performance Scale (CPS).[55] Both questionnaires are validated and have an excellent internal consistency (HPC: α ranging from .90 to .92; CPS: academic competence; α = .98; interpersonal competence; α = .91).

Additionally, exploratory at baseline two questionnaires are assessed as potential moderators; the self-rated Quick Delay Questionnaire (QDQ [58]) and the parent/guardian views on neuropsychological (dys)functioning of their adolescents (the Cognition And Motivation in Everyday Life; CAMEL [59]).

Sample size estimates

A recent study in typically developing adolescents with sleep problems found large effects (β= 0.91) at post-test of a CBT sleep treatment as compared to waitlist controls on their primary sleep related outcome measure (objectively measured) and a medium effect size for reduction of ADHD symptoms[13,14]. Based on this research, moderate to large effect sizes can be expected for SIESTA in combination with TAU for ADHD on sleep outcomes as compared to TAU for ADHD only. Therefore, using G*power we calculated with this large effect size a power of .8 and an alpha of .5 for our desired sample size. There are at least 40 participants per condition needed for analyzing the data implementing a linear mixed effects model. However, to anticipate for possible drop-out or lack of response on assessment (although expected to be minimal due to inclusion of motivational interviewing and the pilot study) and as the effect size of the ADHD outcome is medium and not large

[d=.55] an additional 15% will be recruited. Resulting in a total of 92 participants, with 46 participants per condition.

Data management

Each participant will receive a unique code that allows to link the data of a participant over time, as well as to link all data of adolescents, parents, teachers and clinicians. After each assessment, the pseudonymized data are uploaded immediately from the researchers computers to secure network shared drives, whereas paper data is in locked archive cabinets. After all waves have been completed and all data has been linked, the dataset containing the names and codes is deleted. It is assured that data are stored securely. During the study, data is stored on secure network drives in the KU Leuven datacenter. The secure network drives are hosted by central ICTS services and managed by the IT service. More information on data management can be found in our Data Management Plan 'Blended CBT sleep intervention to improve sleep, ADHD symptoms and related problems in adolescents with ADHD - FWO DMP title' on http://DMPonline.kuleuven.be (this also includes further information regarding access to data and dissemination policy).

Where is the treatment provided?

The treatment will be provided within the KU Leuven Association at different locations (e.g. ADHD-clinic of the KU Leuven Academic Hospital, PraxisP, FARESA – Hasselt, FARESA – Brussels, ZitStil – Antwerp, Konekt – Gent and Huis in de Stad – Roeselare). There are written agreements stating that psychologists from SIESTA provide the training at these locations. In case of a COVID-19 outbreak or if preferred, the treatment is provided online via Mynexuzhealth (or via the platform of PraxisP, backup Skype for Business).

Data are gathered by questionnaires, diagnostic interviews and actigraphs. Every data gathering can take place online. Informants are parent(s)/guardian(s), teachers and adolescents. Some of the questionnaires and interviews might have already been completed during a diagnostic trajectory at the ADHD clinic. Patient files are consulted to gather that information, but where data are lacking all questionnaires have to be completed.

For the screening, all informants will fill out the questionnaires in Qualtrics and the researchers will be available either in person or via phone in case any questions arise. Additionally, the sleepinterview and K-SADS can be administered face-to-face or via Mynexuzhealth (or via the platform of PraxisP, backup Skype for Business). For pretest, posttest and follow-up, all questionnaires will again be filled out via Qualtrics. The questionnaires for the teachers will be send as a Qualtrics link via e-mail by the parent(s)/guardian(s), ensuring anonymity for the teacher towards the researchers.

The interviews are carried out and scored by researchers who were trained to use these instruments and in this methodology. Completion of all the applicable questionnaires takes an individual participant, parent/guardian or teacher maximum one hour at each time point.

Participant recruitment

Participants with ADHD and sleep problems are recruited through the ADHD clinic of the UZ Leuven (Child and adolescent psychiatry services UZ Leuven), PraxisP (the academic clinical centre of the Faculty of Psychology and Educational Sciences, KU Leuven) and the network of the advisory committee (ZitStil, VvGT, Ligant, CARs, Sig vzw, BASS). For the RCT, 92 to 100 adolescents and their parent(s)/guardian(s) will participate in the study. Only minors are recruited for the study (going to school and aged 13-17).

At the start of a diagnostic trajectory of the ADHD clinic, parent(s)/guardian(s)/guardians of the child are asked whether they could be contacted in the future for participation in clinical studies and information will be given about the current study.

Further, participants can specifically apply for the purpose of this study to the ADHD clinic. There are different possibilities to contact the researchers when participants are interested; e-mail addresses,

phone numbers and QR code (to website).
GDPR will be applied as the adolescents receive an explanation conform their development level prior to their participation in the study and the participants parent(s)/guardian(s) must always give permission to participate in the study. Adolescents are asked assent to participate in the study, and if they do not agree, they cannot participate. Even with the assent of the adolescent, consent from the parent or guardian for participation is still required. Parent(s)/guardian(s) will sign an informed consent document. In the informed consent form, permission to participate, consult the patient files and collect data are asked. Both the informed consent and assent will be discussed in detail with the participants in understandable language. Adolescents and their parent(s)/guardians(s) are told that they can follow this treatment at no cost and that they receive a reasonable compensation.

Ethics & procedure
The information participants, parent(s)/guardian(s) and teachers provide may contain sensitive data and this will be taken into account at every moment during the study. Participants will be assured that all efforts will be done to protect the confidentiality: participants' names will be coded and the code will be destroyed directly after the last wave of data collection. Actual names will be matched with a code in a password protected excel file. Any identifying information such as email addresses, phoneumbers, birthday,… will be kept in an excel file which will in itself be password protected. Only the researchers directly involved in performing the research will have access to this file. The data will be stored on a password protected shared network drive on the KU Leuven server. The password will only be given to the researchers. For every participant there will be multiple informants (parent(s)/guardian(s), teacher and the participant himself), but information given by another informant concerning the same participant will not be shared with the other informants.

The informed consent (parent(s)/guardian(s)/guardians) /assent (adolescent) will be send to the participants before the first meeting and they are required to sign it and send it back via email. In case of questions, the researchers are available via the phone and any uncertainties can be discussed during the first meeting. During the first meeting it is assessed whether the adolescent meets inclusion criteria for the study. In this session the K-SADS (parent(s)/guardian(s)) and the sleep interview (adolescent and parent separately) are conducted, either face-to-face or via Mynexuzhealth (or via the platform of PraxisP, backup Skype for Business). Then, the HSDQ and the subscale "Disorders in the use of substances and behavior addictions" of the MATE-Yand the SCARED are administered via Qualtrics. Next 2 subtests of the WISC/WAIS (vocabulary and matrix reasoning) are administered. Further, the adolescent is explained about the wrist actigraphy and sleep logs that need to be recorded in the next week. To remind them to fill out the sleep diary from the previous night, messages will be send when they arrive from school or other activities. Phone numbers of the participants will be stored in a separate password protected excel document on our secure network drive with only the participant number as reference. Using phone numbers exclusively requested for this study, reminders to fill out the sleep diary will be sent. In the phones, which are password protected, no names will be stored, only the participant numbers. When there is a COVID-19 outbreak, an appointment is made so that a courier service can bring the actigraphs to the adolescents. Before and after use, they will be disinfected. Another appointment will be made for one week later when either the researchers or the courier service will collect the actigraph at the home of the adolescent. The reason for not letting the adolescents send back the actigraph is that they are a very specific population. They have great problems with planning and organization. Thus, to prevent that the actigraphs are not send back or get lost, they will be picked up. Within one week after collection of the actigraph the psychologist of the study informs the adolescents and his/her parent(s)/guardian(s) whether he/she meets inclusion criteria for the study.
After the screening, feedback in the form of a summary of the obtained data will be given to involved clinicians. This data will concern relevant information for the clinician giving the treatment, namely a summary of the sleep- and K-SADS interview and the results of the questionnaires (HSDQ, and MATE-Y).

When the adolescent meets inclusion criteria, the adolescent has to fill out the pretest questionnaires in Qualtrics. Parent(s)/guardian(s) of the adolescent are also asked to answer questionnaires in Qualtrics; also, they are asked to mail the link of the questionnaire (CPS) in Qualtrics to the teachers of the adolescent for their evaluation of the adolescent. Moreover the teacher will be asked how many lesson times per week he/she has contact with the participant. The names of the teachers will not be known by the researchers.
After the pretest is conducted, appointments for the treatment are made. However, participants are informed that those appointments can either happen as planned or that the treatment will take place 6 months later, due to the condition their child was assigned to. To avoid the possibility of a systematic bias in the assignment of participants to both groups (SIESTA treatment and treatment as usual (TAU) versus TAU only), randomization happens. We will use a stratified permuted block randomization based on medication use (yes/no) in blocks of 2 participants whereby an independent researcher performs the randomization. After the last treatment session, both the adolescent who followed the treatment and the paired adolescent from the TAU-group, are contacted by the researchers and provided with the actigraphs. The daily sleep logs are again filled out in Qualtrics. Within one week after the last treatment session a posttest session is planned in which the adolescent and parent(s)/guardian(s) are asked to fill out the questionnaires in Qualtrics. Filling out the questionnaires should not take longer than 1 hour for any informant. The actigraphs will again be picked up by a researcher or the courier service. The same procedure is applied during the follow-up measure after 3 months, including the actigraph/daily logs and the questionnaires. After follow-up, the treatment is provided to the adolescent in the TAU-group from that block.
In case of serious adverse events or a crisis situation, e.g. suicidality, during any phase of the study, (previously involved) clinicians will be contacted by the researchers. Also, if necessary at any time of the study, additional psychological aid can be given.

On top of the free training, adolescents receive a financial reward for participating in this study. In total 50 euros can be earned. As filling out the sleep diary is most likely to be forgotten, we reward participants for each day they fill it out. To keep participants motivated throughout the entire study this amount is divided over three time points, the pretest, posttest and follow-up.
Pre-test: 1.40 euros per day

- If they can participate, there is a maximum of 10 euros to be earned
- If they cannot participate, we give an extra 15 euros for completing the questionnaires (maximum 25 euros)

Post test: 1.40 euros per day (they can earn a maximum of 10 euros)
Follow-up: 4.30 euros per day (they can earn a maximum of 30 euros)
The reason that we give more of the maximum amount of 50 euros during the follow-up is to motivate the young people with ADHD even more to participate in the entire study.

Safety

Recording of adverse events: The participant will be asked to report any adverse event related to the study-specific intervention to the study team. These reported events will be documented by the Investigator in the source documents.
The following minimum information should be recorded for each AR:

- AE description
- start and stop date of the AR
- severity
- seriousness
- causality assessment to the study interventions
- outcome

Reporting to the Ethics Committee
The sponsor will assess whether any relevant safety information that becomes available during the study should be reported ad hoc to the EC.

The sponsor has the obligation to, once a year throughout the clinical trial (or on request), submit a progress report to the EC containing an overview of all SARs occurred during the reporting period and taking into account all new available safety information received during the reporting period.

During the first two sessions of the intervention, participants can freely report any adverse event related to the study-specific intervention to their therapist. From the third session on the following question will be posed: “Has anything happened last week that was a danger to you? Like suicidal thoughts, risk-seeking for example bingedrinking, or anything like that.”. We argue that posing this question best starts during the third session as during the first two sessions the main focus is on forming a relationship and building trust. However, asking this type of question is not a risk factor to elicit suicidal thoughts or behavior even in at-risk adolescents. Research shows that talking about suicide and idealization, reduces suicide and improves mental health (e.g. Dazzi et al., 2014).

Confidentiality

In accordance with the Belgian law of 22 August 2002 on patient rights and the General Data Protection Regulation (or GDPR) (EU) 2016/679 of 27 April 2016 on the protection of individuals with regard to the processing of personal data and on the free movement of that data will respect participants privacy.

All information collected during this study will be pseudonymized. In the case of pseudonymisation, the key to these codes will only be accessible to the researchers. The key to pseudonymizing the data is deleted after all waves of the study. Only the coded data will be used in all documentation, reports or publications (in medical journals or congresses) about the study. Confidentiality of the data is therefore always guaranteed. The data controller is KU Leuven. The KU Leuven research team will have access to the personal data relevant to UZ Leuven's research (including questionnaire material, intelligence research, clinical psychological interviews). Limited information from the sleep interview, K-SADS and the results from the questionnaires HSDQ and MATE-Y collected at the first appointment (relevant for the intervention) will be fed back to the study psychologist involved. Furthermore, in the case of Serious Adverse Events (Serious Adverse Events) or a crisis situation, for example suicidality, (already involved) health professionals can be contacted by the researchers.

KU Leuven representatives, auditors, the Medical Ethics Committee and the competent authorities have direct access to your files to check the procedures of the study and / or the data, without violating confidentiality. This is only possible within the limits allowed by the relevant laws. By signing the consent form (parent(s)/guardian(s)/guardians) and the assent form (adolescents), after prior explanation, participants agree to this access.

Participants have the right to make a complaint about how their information is treated, with the KU Leuven and Belgian supervisory authority responsible for enforcing data protection legislation.

Statistical analysis

The analyses are based on an intent-to-treat approach, whereby participants are analyzed as a function of the condition to which they had been assigned. A longitudinal linear mixed effects model will be applied, with the variance components error correlation structure among the repeated measures over pre-test, post-test, and follow-up. The model contains a random intercept varying over participants, a fixed effect of time (pre-test, post-test and follow-up), a random slope for time varying over participants, a fixed effect of condition (1 = SIESTA+TAU; 0 = TAU), and an interaction effect between time and condition. We will correct for multiple testing in the multilevel analyses. Additionally, the potential impact of COVID-19 restrictions is taken into account by including wave as a level in the multilevel analyses. Effect sizes (ESs) are computed by calculating the difference in change scores for SIESTA+TAU as compared to TAU only between post-treatment/follow-up and pre-test and dividing this amount by the pooled standard deviation of the change scores for SIESTA+TAU and TAU only. Confidence intervals for ESs are computed using procedures delineated by Odgaard and Fowler (2010).[56] Although participants are instructed to be off sleep medication and to not change their ADHD medication, they may not comply. Therefore, this is thoroughly assessed both at

post-test and follow-up. This allows for potential sensitivity analyses in the sleep medication free sample, and those that did not change ADHD medication.

Ethics and dissemination

Ethical considerations

The study application was submitted to the Ethical Committee Research UZ/KU Leuven. The study activities and informed consent forms have been approved. The study will be conducted according to ethical principles based on the Helsinki Declaration, good clinical practice (GCP), national regulatory mandatory instructions and this protocol. GDPR General Data Protection Regulation (or GDPR) ((EU) 2016/679 of 27 April 2016; https://eur-lex.europa.eu/eli/reg/2016/679/oj) will be applied as the adolescents and their parents are informed about the study and the informed assent and consent form are presented in understandable language before participation. Adolescents are asked assent to participate in the study (Supplement 2). Additionally, consent from the parent is required for participation (Supplement 3).

Safety considerations

Once a year throughout the clinical trial, a progress report is submitted to the Ethical Committee Research UZ/KU Leuven containing an overview of all serious adverse events (as defined by the Ethical Committee Research UZ/KU Leuven)[57] occurred during the reporting period and taking into account all new available safety information received during the reporting period. Adverse events will be recorded and systematically assessed during the sessions of the treatment. If adverse advents are reported, these will be documented in a separate document by the therapists who provide the treatment and reported to the Ethical Committee Research UZ/KU Leuven, both directly after the report and annually in a summary. The following minimum information is recorded for each adverse event: 1) description, 2) start and stop, 3) severity and seriousness, 4) causality assessment to the study treatment, 5) outcome.

Dissemination plan

Implementation is a major part of this project. To this end an advisory board is involved from the start of the project; they meet twice yearly in the first and last year, and yearly in the second and third year of the project and on demand. This board consists of important societal representatives of mental health care in Flanders i.e. the advisory board consists of representatives of private practices, the Flemish Behavior Therapy Association, the ADHD reference network Flanders, the Specialized sleep center UZ Leuven, the Patient organization ADHD ZitStil, Sig vzw (educational organization rehabilitation centers), the Belgian Association for Sleep research and Sleep medicine, and the European ADHD Guidelines group. Also, the project partners are involved in governmental organizations relating to mental health care policy (e.g. members of the Hoge Gezondheidsraad ADHD; expert advisory board to the minister of health in Belgium; members of the European ADHD Guidelines Group). Both the project applicants and the advisory board will join forces across four lines of (mental) health care for optimal implementation when SIESTA is proven effective; line 1) governmental organizations and mental health care policy makers/non-discriminatory transfer to the EU, line 2) mental health care organizations, specialized sleep centers, and a network of sleep experts in Flanders, line 3) clinicians and other professionals working with adolescents with ADHD and/or individuals with sleep problems, and line 4) patient organizations, adolescents with ADHD and their parents. These combined efforts will lead to an optimal implementation of the following products and knowledge acquired by this project if proved effective: a workbook and therapist manual of SIESTA, a training module for clinicians wanting to provide SIESTA, and a website containing all information and training materials regarding SIESTA for adolescents, parents, clinicians, mental health organizations and governmental organizations. Additionally, results of the study will be communicated to other researchers via publications in academic journals and presentations at conferences.

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References

1. Langberg JM, Molitor SJ, Oddo LE, et al. Prevalence, patterns, and predictors of sleep problems and daytime sleepiness in young adolescents with ADHD. *J Atten Disord* 2017;24:509-523. doi:10.1177/1087054717690810
2. Lunsford-Avery JR, Krystal AD, Kollins SH. Sleep disturbances in adolescents with ADHD: A systematic review and framework for future research. *Clin Psychol Rev* 2016;50:159–174. doi:10.1016/j.cpr.2016.10.004
3. Marten F, Keuppens L, Baeyens D, et al. Sleep problems in adolescents with and without ADHD: A systematic review and meta-analysis. [Manuscript in preparation] *X* n.d.;x:x-x.
4. Becker SP, Epstein JN, Tamm L, et al. Shortened sleep duration causes sleepiness, inattention, and oppositionality in adolescents with attention-deficit/hyperactivity disorder: Findings from a crossover sleep restriction/extension study. *J Am Acad Child Adolesc Psychiatry* 2019;58:433-442. doi:10.1016/j.jaac.2018.09.439
5. Zorgpad ADHD. Slaapproblemen [Internet]. Gent: Federale overheidsdienst Volksgezondheid, veiligheid van de voedselketen en leefmilieu (BE); [reviewed 2022; cited 2022 Dec 20]. Available from: https://www.adhd-traject.be/nl/pagina/slaapproblemen
6. GGZ Standaarden. 5.12 Behandelingen bij comorbiditeit 5.12.1 Behandeling ADHD en slaapproblemen [Internet]. Utrecht: Akwa GGZ (NL); [reviewed 2019 Feb 04; cited 2022 Dec 20]. Available from: https://www.ggzstandaarden.nl/zorgstandaarden/adhd/behandeling-en-begeleiding/behandelingen-bij-comorbiditeit/behandeling-adhd-en-slaapproblemen
7. Martin CA, Hiscock H, Rinehart N, et al. Associations between sleep hygiene and sleep problems in adolescents with ADHD: A cross-sectional study. *J Atten Disord,* 2020;24:545-554. doi:10.1177/1087054718762513
8. Keshavarzi Z, Bajoghli H, Mohamadi MR, et al. In a randomized case–control trial with 10-years olds suffering from attention deficit/hyperactivity disorder (ADHD) sleep and psychological functioning improved during a 12-week sleep-training program. *World J Biol Psychiatry* 2014,15:609–619. doi:10.3109/15622975.2014.922698
9. Corkum P, Lingley-Pottie P, Davidson F, et al. Better Nights/Better Days-Distance Intervention for Insomnia in School-Aged Children With/Without ADHD: A Randomized Controlled Trial. *J Pediatr Psychol* 2016;41:701–713. doi:10.1093/jpepsy/jsw031
10. Hiscock H, Mulraney M, Heussler H, et al. Impact of a behavioral intervention, delivered by pediatricians or psychologists, on sleep problems in children with ADHD: a cluster-randomized, translational trial. *J Child Psychol Psychiatry* 2019;60:1230-1241. doi:10.1111/jcpp.13083
11. Hiscock H, Sciberras E, Mensah F, et al. Impact of a behavioural sleep intervention on symptoms and sleep in children with attention deficit hyperactivity disorder, and parental mental health: Randomised controlled trial. *BMJ* 2015;350:1–14. doi:10.1136/bmj.h68
12. Sciberras E, Mulraney M, Mensah F, et al. Sustained impact of a sleep intervention and moderators of treatment outcome for children with ADHD: a randomised controlled trial. *Psychol Med* 2020;50:210-219. doi:10.1017/S0033291718004063
13. de Bruin EJ, Bögels SM, Oort FJ, et al. Efficacy of Cognitive Behavioral Therapy for Insomnia in Adolescents: A Randomized Controlled Trial with Internet Therapy, Group Therapy and A Waiting List Condition. *Sleep* 2015;38:1913–1926. doi:10.5665/sleep.5240
14. de Bruin EJ, Bögels SM, Oort FJ, et al. Improvements of adolescent psychopathology after insomnia treatment: results from a randomized controlled trial over 1 year. *J Child Psychol Psychiatry and Allied Disciplines* 2018;59:509–522. doi:10.1111/jcpp.12834
15. Jernelöv S, Larsson Y, Llenas M, et al. Effects and clinical feasibility of a behavioral treatment for sleep problems in adult attention deficit hyperactivity disorder (ADHD): a pragmatic within-group pilot evaluation. *BMC Psychiatry* 2019;19:226. doi:10.1186/s12888-019-2216-2

16. Evans SW, Van der Oord S, Rogers EE. Academic Functioning and Interventions for Adolescents with ADHD. In: Becker SP, eds. ADHD in Adolescents: Development, Assessment, and Treatment. The Guilford Press 2020:148-169
17. Johnson E, Mellor D, Brann P. Differences in dropout between diagnoses in child and adolescent mental health services. *Clin Child Psychol Psychiatry* 2008;13:515-530. doi:10.1177/1359104508096767
18. Boyer BE, Geurts HM, Van der Oord S. Planning skills of adolescents with ADHD. *J Atten Disord* 2018;22:46-57. doi:10.1177/1087054714538658
19. Dekkers TJ, de Water E, Scheres A. Impulsive and risky decision-making in adolescents with attention-deficit/hyperactivity disorder (ADHD): The need for a developmental perspective. *Curr Opin Psychol* 2022;44:330-336. doi:10.1016/j.copsyc.2021.11.002
20. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*. 5th edn. text revision. Washington DC: American Psychiatric Association, 2013.
21. Becker SP, Langberg JM, Byars KC. Advancing a Biopsychosocial and Contextual Model of Sleep in Adolescence: A Review and Introduction to the Special Issue. *J Youth Adolesc* 2015;44:239–270. doi:10.1007/s10964-014-0248-y
22. Harvey AG. A transdiagnostic intervention for youth sleep and circadian problems. *Cogn Behav Pract* 2016;23:341–355. doi:10.1016/j.cbpra.2015.06.001
23. Becker SP, Duraccio KM, Sidol CA, et al. Impact of a Behavioral Sleep Intervention in Adolescents With ADHD: Feasibility, Acceptability, and Preliminary Effectiveness From a Pilot Open Trial. *J Atten Disord* 2021;10870547211056965. doi:10.1177/10870547211056965
24. Beerts E, Boyer B, Kuin M, et al. SIESTA Sleep IntervEntion as Symptom Treatment for ADHD: Een flexibel behandelprotocol voor slaapproblemen bij jongeren met ADHD – Werkboek voor jongeren. X; n.d.
25. Beerts E, Boyer B, Kuin M, et al. SIESTA Sleep IntervEntion as Symptom Treatment for ADHD: Een flexibel behandelprotocol voor slaapproblemen bij jongeren met ADHD – Trainershandleiding. X; n.d.
26. Keuppens L, Marten F, Baeyens D, et al. A pilot study of a cognitive-behavioral sleep intervention specifically for adolescents with ADHD and sleep problems: A qualitative and quantitative evaluation. [Manuscript in preparation]. *X* n.d.;x:x
27. Chan AW, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. *Ann Intern Med* 2013;158:200-207.
28. Kaufman J, Birmaher B, Axelson D, et al. The KSADS-PL DSM-5. Kennedy Krieger Institute. Baltimore, MD; 2016.
29. Wechsler D. Wechsler Intelligence Scale for Children (5th ed.). Bloomington, MN: Pearson 2014.
30. Wechsler D. Wechsler Adult Intelligence Scale--Fourth Edition (WAIS-IV) [Database record]. PsycTESTS 2008.
31. American Academy of Sleep Medicine. *International classification of sleep disorders.* 3rd edn. Darien, IL: American Academy of Sleep Medicine, 2014.
32. Schippers GM, Broekman TG. MATE-Y 2.1a. Handleiding en protocol voor de MATE-Jeugd. Nederlandse bewerking: Schippers GM, Broekman TG. Bêta Boeken; 2013.
33. Keuppens L, Marten F, Baeyens D, et al. A pilot study of a cognitive-behavioral sleep intervention specifically for adolescents with ADHD and sleep problems: A qualitative and quantitative evaluation. Poster presented at ABCT 56th Annual Convention; 2022 November 18-20; New York, NY.
34. Broglio K. Randomization in clinical trials: permuted blocks and stratification. *Jama* 2018;319:2223-2224. doi:10.1001/jama.2018.6360
35. Kernan WN, Viscoli CM, Makuch RW, et al. Stratified randomization for clinical trials. *J Clin Epidemiol* 1999;52:19-26. doi:10.1016/S0895-4356(98)00138-3
36. Kuin M, Boyer BE. Super Slaap Plan. Werkboek Slaaptraining voor jongeren op basis van CGT en motiverende gespreksvoering. Bohn Stafleu van Loghum 2019.

37. Kuin M, Boyer BE, Van der Oord S. Zelf Plannen werkboek. Lannoo 2013.
38. Acebo C, Sadeh A, Seifer R, et al. Estimating sleep patterns with activity monitoring in children and adolescents: how many nights are necessary for reliable measures? *Sleep* 1999;22:95-103. doi:10.1093/sleep/22.1.95
39. Ancoli-Israel S, Cole R, Alessi C, Chambers M, Moorcroft W, Pollak CP. The role of actigraphy in the study of sleep and circadian rhythms. Sleep. 2003;26:342-392. doi:10.1093/sleep/26.3.342
40. CamNtech. The MotionWatch and MotionWare User Guide: Issue 1.2.26a [Internet]. Cambridgeshire; CamNtech Ltd (UK); 2019 [updated 2019; cited 2022 Dec 20]. Available from https://www.camntech.com/Products/MotionWatch/The%20MotionWatch%20User%20Guide%201_2_26a.pdf.
41. Mestdagh M, Verdonck S. m-Path (Version 2.5.7) [app]. Google Play Store 2019.
42. Wolfson AR, Carskadon MA, Acebo C, et al. Evidence for the validity of a sleep habits survey of adolescents Evidence for the Validity of a Sleep Habits Survey for Adolescents. *Sleep* 2003;26:9–12. doi:10.1093/sleep/26.2.213
43. Wolfson AR, Carskadon MA. Sleep schedules and daytime functioning in adolescents. *Child dev* 1998;69:875-887. doi:10.1111/j.1467-8624.1998.tb06149.x
44. Meijer AM. Chronic sleep reduction, functioning at school and school achievement in preadolescents. *J Sleep Res* 2008;17:395-405. doi:10.1111/j.1365-2869.2008.00677.x
45. Dewald-Kaufmann JF, Bruin EJ, Smits M, et al. Chronic sleep reduction in adolescents—clinical cut-off scores for the Chronic Sleep Reduction Questionnaire (CSRQ). *J Sleep Res* 2018;27:e12653. doi:10.1111/jsr.12653
46. Owens JA, Spirito A, McGuinn M. The Children's Sleep Habits Questionnaire (CSHQ): psychometric properties of a survey instrument for school-aged children. *Sleep-New York-* 2000;23:1043-1052.
47. Storfer-Isser, A., Lebourgeois, M. K., Harsh, J., Tompsett, C. J., & Redline, S. (2013). Psychometric properties of the Adolescent Sleep Hygiene Scale. *Journal of Sleep Research, 22*(6), 707–716. https://doi.org/10.1111/jsr.12059
48. Oosterlaan J, Baeyens D, Scheres A, et al. *VVGK6-16. Vragenlijst voor Gedragsproblemen bij kinderen 6-16 jaar. Handleiding.* Harcourt Publishers, 2008.
49. Muris P, Bodden D, Hale W, et al. *SCARED-NL. Vragenlijst over angst en bang-zijn bij kinderen en adolescenten. Handleiding bij de gereviseerde Nederlandse versie van de Screen for Child Anxiety Related Emotional Disorders.* Boom test uitgevers, 2007.
50. Hale WW, Crocetti E, Raaijmakers QAW, et al. A meta-analysis of the cross-cultural psychometric properties of the Screen for Child Anxiety Related Emotional Disorders (SCARED). *J Child Psychol Psychiatry* 2011;52:80–90. doi:10.1111/j.1469-7610.2010.02285.x
51. Kovacs M. *CDI-2: Screeningsvragenlijst voor depressie bij kinderen en jongeren, Nederlandse bewerking.* Hogrefe, 2016.
52. Prinz RJ, Foster S, Kent RN, et al. Multivariate assessment of conflict in distressed and nondistressed mother-adolescent dyads. *J Appl Behav Anal* 1979;12:691–700. doi:10.1901/jaba.1979.12-691
53. Khan NR, Malik JA, Kamal A. Discrepancies in Parents-Adolescents Conflicts across Gender: A Step Forward in Validation of Conflict Behavior Questionnaire-44. *Univers J Psychol* 2015;3:34-40. doi:10.13189/ujp.2015.030202
54. Anesko KM, Schoiock G, Ramirez R, et al. The Homework Problem Checklist: Assessing children's homework difficulties. *Behav Assess* 1987;9:179-185
55. Brady CE, Evans SW, Berlin KS, et al. Evaluating school impairment with adolescents using the Classroom Performance Survey. *School Psych Rev* 2012;41:429-446. doi:10.1080/02796015.2012.12087498
56. Odgaard EC, Fowler RL. Confidence intervals for effect sizes: Compliance and clinical significance. *J Consult Clin Psychol* 2010;78:287-297. doi:10.1037/a0019294

57. Ethical Committee Research UZ/KU Leuven. Ernstige Ongewenste Voorvallen (Serious Adverse Events). *UZ Leuven* 2020, January 24; access date 2022 May 30. https://www.uzleuven.be/nl/ethische-commissie-onderzoek/goedgekeurde-studie-ec-onderzoek-aanvullen/ongewenste-voorvallen-en-protocol-violationdeviation-bij-ec-onderzoek/ernstige-ongewenste-voorvallen-serious-adverse-events
58. Clare S, Helps S.,Sonuga-Barke E. The Quick Delay Questionnaire: A Measure of Delay Aversion and Discounting in Adults. *ADHD Atten Def Hyper Dis 2*-2010*;* 2.1: 43-48.
59. Van Liefferinge D, Sonuga-Barke E, Van Broeck N, Van Der Oord S, Lemiere J, & Danckaerts M. A rating measure of ADHD-related neuropsychological impairment in children and adolescents: Data from the Cognition and Motivation in Everyday Life (CAMEL) Scale from population and clinical samples. *Child Neuropsychol* 2016*;* 1-19.