ADHD in treatment seeking patients with a substance use disorder
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In the 1990's in the Netherlands there was a need for research and expertise related to the emerging idea that ADHD is not just a child and adolescent disorder, but a persisting disorder in many adult patients (Kooij et al., 1996; 1999). As a result a project was started on the development of guidance for professionals in addiction treatment centers for the diagnosis and treatment of ADHD in adult patients. After a thorough procedure of expert-panel meetings, a guideline was presented including recommendations for screening, diagnosis and treatment (medication and psychosocial interventions) and this guideline was field-tested in two addiction treatment centers. This project led to the Dutch intervention program for diagnosis and treatment of ADHD in addiction treatment centers (Van de Glind et al., 2004). Results of this project are described in chapter 3.

To increase the possibilities of an international comparison of results and to speed up data collection on the topic of ADHD and Substance Abuse, an international research network was initiated: the International Collaboration on ADHD and Substance Abuse (ICASA; www.adhdandsubstanceabuse.org). The ICASA Foundation uses scientific research to achieve the following two goals:

1) increase of the quality of diagnosis and treatment of patients suffering from both SUD and ADHD;
2) prevention of the development of SUD in children and adolescents with ADHD.

Although the goals of the network are very much practice based and directed at improvements in the lives of patients, the network decided to first establish the magnitude of the problem. In order to obtain funding for necessary future research (see chapter 9), it was crucial to show that the problem existed not only in the USA but also in many other countries. That decision led to the development of the IASP study (part 3 of this thesis). In preparing the IASP design, it was necessary to evaluate the existing scientific knowledge on the prevalence of ADHD in (treatment seeking) SUD populations. To do so, the meta-analysis and meta-regression-analysis on the prevalence of ADHD in adolescent and adult populations was performed. The results of this review are presented in chapter 4.
Abstract

The comorbidity of attention deficit hyperactivity disorder (ADHD) is frequently not well recognized in substance abuse treatment institutions in the Netherlands. As a consequence, patients with substance use disorder (SUD) and ADHD often receive suboptimal treatment. To prevent every treatment center from having to invent its own diagnostic procedure and intervention for ADHD, a national working group was established. This group developed an intervention program for the screening, diagnosis, and treatment of ADHD in patients with SUD. This article describes the development and content of this intervention program. An important part of this development was testing the intervention program in two addiction treatment centers in The Netherlands. Systematic screening of ADHD was part of the test. A self-report questionnaire was used. Subjects with positive screening results were referred for the diagnostic procedure. Nine hundred twenty-eight screenings were performed: 207 screened positive, 115 came for further diagnostics, and 65 were ultimately diagnosed with ADHD.
Introduction

Attention deficit hyperactivity disorder (ADHD) is a disorder that has become better recognized in adults during the past few years, with a reported prevalence of 1.0-2.5% in The Netherlands (Kooij et al., 2005) and 4.4% in the United States (Kessler, 2004). Adults with ADHD suffer from attention and concentration disabilities, hyperactivity or (internal) restlessness, and impulsive behavior. Many persons with ADHD also suffer from rapidly changing moods and irritability, resulting in academic and occupational underachievement and recurrent failures. Moreover, comorbidity is common among adults with ADHD. Approximately 75% of adults with this condition also manifest other disorders (Kooij, 2003, 2004). These may include learning disabilities, anxiety disorders (20-30%) or other mood disorders (20-30%), personality disorders (25%), and substance use disorders (SUDs) (15-45%) (Biederman, Faraone, & Spencer, 1993). Facial tics, autism, and behavioral disorders also often coexist with ADHD and persist in adulthood (Ferdinand & Verhulst, 1996).

Because SUD is frequently found during the treatment of ADHD, there is an expectation that it would be widely recognized and treated within addiction treatment centers. This has not been the case. This type of comorbidity is not well recognized, and expertise in treating this disorder within addiction treatment centers is lacking. There are also ethical issues, such as the reluctance to prescribe stimulants (e.g., methylphenidate [Ritalin, Novartis BV]) to patients in addiction treatment centers. This is regrettable given that positive effects of methylphenidate on the reduction of ADHD symptoms have been reported (Levin, Evans, McDowell, & Kleber, 1998; Mattes, Boswell, & Oliver, 1984; Schubiner et al., 2002; Schubiner, Tselepsis, Isaacson, Warbasse, & Musial, 1995; Spencer et al., 1995; Wilens et al., 2005).

Although an assessment and treatment program for adult ADHD was recently developed in The Netherlands (Kooij, 2003), no published intervention programs, protocols, or even case reports have been found to guide the treatment staff in addiction centers. No European data on the prevalence of substance use and ADHD comorbidity within substance abuse treatment centers have been presented. In comparison, American research shows the percentage of ADHD among substance abusers in treatment, which varies between 6.7% and 25% (Clure, Brady, Saladin, Johnson, & Rittenbury, 1999; King, 1999; Schubiner et al., 2000). Therefore, we started a project aimed at developing standardized protocols for the screening, diagnosis, and treatment of ADHD in patients with SUD. This article describes the development of the
intervention program. Some figures on screening and diagnosis are provided to illustrate the extent of the problem.

**Materials and methods**

To develop the intervention program for the screening, diagnosis, and treatment of ADHD in patients with SUD, an expert panel consisting of leading professionals and researchers in the treatment of adult ADHD and in the treatment of SUD was established. The development of the intervention program was based on three types of knowledge suggested by Sackett, Straus, Richardson, Rosenberg, and Haynes (2000): effectiveness of interventions (evidence), clinical expertise of professionals, and values of patients. To represent research evidence, an extensive literature search was performed (Kooij, Buitelaar, & van Tilburg, 1999; van de Glind, Eland, & Janssen, 2001). Clinical expertise was represented by inputs of the professionals. A representative of a patient organization participated as well.

The intervention program was tested for 10 months in two addiction treatment centers. During this test, both patients and professionals were interviewed regarding their perceptions of the program: 34 professionals (including psychiatrists, psychologists, and mental health nurses) and 12 patients were interviewed, and their reports were discussed in the expert panel.

**Results**

The intervention program consisted of screening, diagnostic, and treatment components. The intervention was meant to serve as a supplement to primary addiction treatment (Fig. 1).

*Figure 2.1.1 Steps in the screening and diagnostic procedure to diagnose ADHD*
ADHD can be reliably diagnosed in adults who currently have symptoms of ADHD and who could be asked about the history of such symptoms in childhood (Wilens, 2004). For the screening of current symptoms of ADHD, a 23-item self-report questionnaire was used, including all the 18 *DSM-IV* items on inattention, hyperactivity, and impulsivity (ADHD Rating Scale; Kooij et al., 2005). For childhood ADHD symptoms, three questions about the core symptoms of ADHD were added (as a child, I was restless; as a child, I was impulsive; as a child, I had problems with concentrating). Positive screening results were followed by a formal psychiatric diagnostic procedure, including the following:

- A semistructured psychiatric interview for ADHD and other comorbidities executed by trained and experienced treatment staff. Topics included current ADHD symptoms, impairment in work and relationships, childhood ADHD symptoms and history, family history, sensation-seeking behaviors, use of alcohol, illegal drugs, criminality, physical condition, sleeping behaviors, eating behaviors, sexuality, depression, anxiety, obsessive/compulsive behaviors, and other comorbid problems (Kooij, 2003)
- An investigator-based version of the ADHD Rating Scale to assess ADHD type and the number of current Symptoms
- A structured diagnostic interview (*DSM-IV*) with family members, preferably performed face to face or by telephone.

The inclusion criteria for an integrated treatment of ADHD, SUD, and other problems were: (a) ADHD diagnosis was based on the procedures described above; (b) abstinence from alcohol and drugs was beyond the period of withdrawal symptoms; (c) severe psychiatric comorbidity (such as anxiety and depression) was treated first; and (d) the patient gave informed consent. The expert panel decided that optimal treatment consisted of four interventions (education, medication, coaching, and peer support groups), which should be simultaneously provided with, and integrated into, the treatment of SUD.

**Education**

The education component of treatment was designed to give patients understandable information about ADHD and its symptoms, consequences, and treatment options. Different professionals throughout the treatment process provide education at standardized points during treatment (screening, start of diagnostic interview, during treatment, and end of treatment). Part of the
education is providing written materials to the patient. Most of the information is meant for the patient, but also for family members.

Pharmacotherapy
In adults as in children, pharmacotherapy is the treatment of choice in controlling the ADHD symptoms of inattention, restlessness, and impulsivity (The MTA Cooperative Group, 1999; Wilens, 2003). A positive influence of ADHD pharmacotherapy on the course of SUDs has been recorded in case reports, but it has not yet been studied in a controlled manner (Castaneda, Levy, Hardy, & Trujillo, 2000; Levin, Evans, & Kleber, 1999; Somoza et al., 2004). With the exception of one placebo-controlled study among cocaine abusers (Schubiner et al., 2002), no effectiveness studies on pharmacotherapy in adults with SUD have been found in the literature. As in children, stimulant medications methylphenidate and amphetamine are most commonly and effectively used in adults with ADHD. Longer term trials of methylphenidate support the ongoing effectiveness and tolerability of these stimulants (Wilens, Faroane, Biederman, & Gunawardene, 2003). In the future, bupropion (Zyban, Glaxo Smith Kline BV) and atomoxetine (Strattera, Eli Lilly) might be good alternatives (Wilens et al., 2005); however, the slow-release preparation of bupropion needed to adequately treat ADHD is currently not registered in The Netherlands, and long-term experience with this medication is lacking. Atomoxetine and the reliable long-acting methylphenidate preparation Concerta (Janssen-Cilag BV) were not yet available in The Netherlands at the time of the project.

Medication protocols
Short-acting methylphenidate was chosen as the first choice medication in the intervention program. The medication was induced and titrated to a stable dose over 2 weeks. During the first week, 0.5 mg/kg/day was given in four doses every 4 hours. In the second week, this was changed to four doses of 0.75 mg/kg/day. After this, an optimal dosage was established, with a maximum of 1 mg/ kg/day. The timing of medication administration was considered very important. To this end, timers were provided to the patients, and nurses were instructed to remind patients to take their medications and to regularly check their heart rhythm, blood pressure, and weight.

The second-choice medication was imipramine, given at a dose of 75-150 mg/day, which was also induced and titrated slowly to a dose that reduced symptoms. Urine checks to control for the use of illegal drugs were advised as an additional measure to assist in determining response to treatment.
**Coaching**
The coaching component of treatment was basically training in organizing skills for daily life provided in group sessions according to a protocol developed by the expert group. However, coaching and group sessions are not mandatory components of the treatment. Treatment institutions can decide about providing individual coaching sessions or combining them with group sessions.

The symptoms of ADHD cause many problems in daily-life topics, such as planning of daily activities, finances, social competence, and work. The coaching module aimed to enhance patient skills in organizing these different topics in daily life. Patients actively set goals in these topics throughout each week and reported on their improvement during the coaching group session. Coaching, together with other parts of the intervention program (education and peer support groups), helped patients learn about the consequences of ADHD on activities of daily life and how to organize those aspects to minimize problems.

**Peer support groups**
No effectiveness studies on peer support group were found. However, the professionals contacted suggested that it could have a positive effect on coping with the symptoms of ADHD and SUD. The goal of group support components was to facilitate exchange of experiences related to symptoms, use of medication, craving for drugs or alcohol, and relationships with others. In this project, a professional guided the meetings because professional exchange on medication issues and experiences was considered important. Based on the feedback received during the group sessions, the professional could directly adapt the medication to a more appropriate dosage. Moreover, an external person who would structure time and focus the topic during group sessions appeared to be an important condition for successful group sessions among patients with this disorder.

**Psychotherapy**
Limited data suggest that cognitive-behavioral therapies may be useful for adults with ADHD (Mc Dermott, 2000; Safren et al., 2005). Nonetheless, because there is no established cognitive therapy for patients with addiction plus ADHD, we did not include this in the intervention program.
Testing and evaluating the intervention program

Two large treatment centers participated in the project. "De Brijder Stichting" is located northwest of The Netherlands. The institution provides care and prevention activities for SUD. In 2003, 5,385 patients were contacted, among which 2,417 were readmissions. The other institution is "De Grift," located in the central-eastern region of The Netherlands. De Grift treated 4,538 patients in 2003, among which 2,259 were readmissions. Both institutes provide both inpatient and outpatient treatments in many locations in their regions.

During the test of the intervention program, both treatment centers introduced the screening procedure and intervention program into their outpatient locations. Patients with positive screening results were referred to the diagnostic procedure. If diagnosed with ADHD, they were then referred to inpatient treatment. In both of the institutes, one person coordinated all activities concerning the test of the intervention program.

An initial meeting to provide general information about the project to all involved professionals in each institute was organized. Next, the intake workers at the 14 intake points were given specific instructions on how to assist patients filling out the self-report questionnaire. Health care professionals were instructed to screen all new patients during the project. Answer forms were copied anonymously for research. Twelve psychologists and physicians of the institutes participated in an intensive course on the diagnosis and treatment of ADHD in adults. The treatment staff was trained in the interventions. The researcher and the coordinator handled the logistics of intake routines and organized other paperwork.

Figures
During a 10-month period, there were 1,313 admissions to the 14 sites participating in the project. Of those, 928 (70.6%) received ADHD screening according to the protocol. Of the subjects who were screened, 19.7% were women. The average age was 35.6 years. There were several reasons for not screening the remaining 385 persons (29.4%). The major reason was that several sites started implementing the protocol at different points in time. Other reasons were that there were too many admissions to screen and that some patients had problems with the Dutch language. There were only a few cases of patient refusal.
Two hundred seven of 928 screened patients scored above the threshold (22%) and were referred for additional diagnostic assessment. The instrument for screening consisted of 23 items (based on the DSM-IV criteria for ADHD) concerning ADHD symptoms in the last 6 months and three questions concerning the core symptoms of ADHD in childhood. All items could be answered in a four-point scale (0 = never or seldom; 1 = sometimes; 2 = often; 3 = very often). An item was scored positively when the patient scored 2 or 3.

The DSM-IV gives nine criteria for attention deficits and nine criteria for hyperactivity/impulsivity. The thresholds for positive screening results in this study were as follows:

- Positive scores on two or more questions regarding the core symptoms of ADHD in childhood. If this was not the case, the patient was not referred for the diagnostic procedure, regardless of the results of the 23 ADHD current status items.
- Positive scores on five items from either attention deficit items or hyperactivity/impulsivity items. This means that four items for attention deficit and four items for hyperactivity/impulsivity would not be sufficient. However, five items for attention deficit only would be enough.

The physicians and psychiatrists who performed this diagnostic procedure received training in the diagnoses and treatment of ADHD in adults. Diagnostic appointments were typically scheduled within 21 days following the screening. Sixty percent of the patients came to the same site for their diagnostic procedure, but because there was no physician or psychiatrist at every location, approximately 40% of the patients had to go to another location.

Of the 207 patients who screened positive and were referred, 115 (56%) came for further diagnostic assessment. Reasons for this high dropout are diverse. The fact that most patients had to wait for 2 weeks or more is important. Either relapse (substance abuse) or symptoms related to ADHD can contribute to this high rate of dropout. The fact that many patients had to travel for this diagnostic procedure can be part of the explanation for this dropout. Nine people filled out the forms illegibly or incorrectly, leaving 106 SUD patients whose data were included. Diagnostic testing confirmed ADHD in 65 of 106 patients (61.3%).
Evaluation

Because this evaluation was limited to the implementation of the intervention program, no systematic outcome data are available. However, quantitative information on dropout at each stage of the protocol, as well as patient and staff reactions, offers some indications of the impact of the procedure. The practical experience from this project shows that ADHD patients can be identified and that psychostimulant medications can be used safely and reliably in this higher risk patient group. Although a formal outcome evaluation was not performed, there were no indications of an increased frequency of relapse during ADHD treatment.

Quantitative evaluation

There are obvious problems with this procedure, and it is not possible at this point to estimate the actual prevalence of ADHD in this population. Nonetheless, the project was undertaken as a quantitative and as a qualitative feasibility study of a new screening and diagnostic procedure. We first review each step of the protocol from a quantitative perspective, as illustrated in Fig. 2.2.2.

Figure 2.2.2 Number of patients per step of the screening and diagnostic procedure

Time requirements

Patients spent 10 minutes, on average, filling out the screening form. Professionals used, on average, 4.4 minutes to score the form. Professionals needed 87.5 minutes, on average, to perform the diagnostic procedure.
**Dropout between steps 1 and 2**
Three hundred eighty-five new patients did not submit to ADHD screening. It seems reasonable to assume that some of the patients in this missed group would have scored a positive result on the screening. It is not reasonable to make predictions about prevalence among those not screened due to diverse reasons for screening failure.

**Dropout between steps 2 and 3**
Two hundred seven patients with positive screening results were referred for diagnostic assessment. Only 106 of the patients completed this procedure. Given that the symptoms of ADHD, combined with the symptoms of SUD, can produce lack of organization and inattention, it is possible that this group of patients may have even higher rates of ADHD, so the percentage of ADHD diagnoses among those who did show up (61.3%) could be a quite conservative estimate of true prevalence in SUD patients.

**No diagnostic testing for those who screened negative**
We did not diagnose a random sample of patients who did not screen positive for ADHD. This would have been important for the determination of the specificity and the sensitivity of the diagnostic procedure. Thus, it remains possible that our screening procedure may have missed a significant proportion of patients who actually would have met diagnostic criteria for ADHD. This is an important goal of future research.

**Qualitative evaluation**
As indicated above, we gathered qualitative data from patients (n=12) and from the treatment staff (n=35) through focus group interviews. The impressions gathered from these patients and professionals were mainly positive; ADHD screening and treatment were considered by patients and professionals alike as useful additions to the treatment of addiction.

In general, both patients and professionals supported the procedures written down in the screening and diagnostic intervention program. The professionals reported better recognition of ADHD as a result of the project. They became more aware of ADHD symptoms in their patients due to the screening of all patients during the project. ADHD was found in more patients than expected—although these initial estimates are likely quite conservative as suggested above. Professionals reported that, in most cases, the self-report questionnaire for screening was suitable. However, it was decided that the screening questionnaire had to be extended to include the same number of questions
(23) about symptoms in childhood as in adulthood. Furthermore, the instructions were improved, and staff was asked to provide more assistance to the patients during screening.

The psychiatric diagnostic procedure was experienced as being extensive and thorough. Although it was known beforehand, diagnostic comorbidity turned out to be a complicating factor in the diagnostic procedure. Overlap in symptoms complicated diagnosis, and, quite often, information from family was missing.

Although the test period was relatively short (10 months), it appeared that the professionals agreed to methylphenidate being the first-choice medication, despite possible risks to the ongoing addiction treatment, such as taking the weekend dosage all at once. Only 10.6% of the 47 professionals who filled out the questionnaire about this topic disagreed with methylphenidate as the first-choice medication.

To improve treatment, education, coaching, and peer support groups should be better specified, and participation of partners/families of patients should be stimulated. Partners and families need to receive accurate understandable information about ADHD. This information may help these family members improve medication and treatment compliance in the affected patients.

\textit{Integrating ADHD and SUD treatment}

To receive treatment, patients had to attend inpatient treatment in the participating addiction treatment centers. Only 38.5% of patients with ADHD actually came to these centers for hospitalization. Some of the patients expressed that they did not want inpatient treatment and thus refrained from participation in the project. Physicians faced with this problem decided, in many cases, to offer outpatient treatment and medication outside the project.

The evaluation showed some problems with the integration of an extensive program for a specific psychiatric disorder into an existing program for the treatment of SUD. For instance, in inpatient treatment modalities, therapeutic group interventions are commonly used. Values used within these interventions sometimes were contrary to concepts in the ADHD program. For example, intensive group therapy might be problematic for an ADHD patient due to his problems with paying attention. In the testing phase of the intervention program, professionals observed that recognition of ADHD was an important motivator to stop alcohol or drug abuse and to become abstinent-
one of the conditions for the treatment of ADHD. The interviewed patients reported relief owing to receiving the diagnosis and an explanation for lifetime failure. For 8 of 12 patients interviewed in this evaluation, this was the first time that ADHD had been diagnosed. The recognition of ADHD had significant meaning for their self-esteem. The new perspective triggered enhanced motivation for them to quit alcohol or drug abuse.

**Discussion**

ADHD appears to exist in at least 12% of our SUD treatment population and may undermine treatment outcomes in addiction centers. The nature of the relationship between ADHD and SUD is not clear. Both are chronic disorders, with possible inherited vulnerability in individuals. When ADHD is not recognized and treated, use of drugs or alcohol may occur as an attempt to reduce the ADHD symptoms (self-medication hypothesis). If ADHD is recognized and treated in early youth, risks of later SUD are shown to be reduced (Wilens et al., 2003). That the relationships between the two disorders are complicated is underlined by the observation that conduct disorder might be an intervening variable in the relationship between ADHD and SUD (Lynskey & Hall, 2001).

At the beginning of the project, not many treatment centers in The Netherlands were aware of patients having comorbid ADHD and substance dependence. Clear directions for treatment were not found; for this reason, we decided to develop an intervention program for the screening, diagnosis, and treatment of ADHD in SUD treatment centers. Development, testing, and dissemination of the program also served the greater goal of creating more awareness about ADHD in treatment centers for substance dependence. Symposia about the topic attracted many caregivers and health care professionals.

In the initial version of the intervention program, we conceptualized treatment as having several components. Pharmacotherapy, particularly methylphenidate, was considered an important part of the approach. At the time the program was developed, no controlled studies on the effects of methylphenidate on SUD patients had been published. As of this writing, there have been very few studies on ADHD medication in this group. Only one placebo-controlled study has been published (Schubiner et al., 2002). Biederman, Wilens, Mick, Spencer, and Faraone (1999) stated that successful treatment of
ADHD in childhood (even with stimulants) has a preventive effect on the risk of SUDs in adulthood. This result was replicated by Wilens et al., (2003).

The influence of ADHD screening and treatment on the prognosis of SUDs was not evaluated during this project; the mainly positive reactions of patients and professionals suggest a beneficial influence, in concordance with scientific literature. An increase in drug abuse during ADHD treatment was not observed. In general, the intervention, including the stimulant medication, was considered safe. These clinical impressions are consistent with earlier observations that ADHD treatment does not increase the risk of relapse (Schubiner et al., 2002).

**Limitations**
Because we have been aiming for pragmatic solutions in this project, more complex questions regarding effectiveness have not yet been answered. This pilot project was performed as a systematic demonstration of a recently developed type of treatment. A structured evaluation of the screening procedure to test its specificity and sensitivity will have to be performed. Without this information, it is not possible to know the true prevalence of ADHD among patients in treatment centers for SUD. Beyond the screening and diagnostic parts of the protocol, there is clear need for a randomized controlled trial of the medication, education, coaching, and group support components of the intervention.

**Conclusion**

Despite these important limitations, we found that: (1) the protocol was feasible to implement; (2) more than 20% of new patients screened positive; and (3) more than 60% of those patients who came for further diagnosis met criteria for ADHD. Thus, our initial experience has been positive, and we intend to continue efforts to provide better recognition and treatment of ADHD in this population.
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