ADULT ADHD AND SUBSTANCES

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Abstract:
In recent literature there has been an increasing interest in discussing the diagnosis, evolution, therapeutic approach in ADHD patients, because of the innovation regarding this pathology. ADHD symptoms are rather chronic over the life of the individual, the disorder persisting in the adult life. Frequently the symptoms are complicated by the development of comorbidities, some of them being the substance-use disorders. Several topics have been discussed. Some of them explain the way these disorders appear, how they are temporally connected. Other mechanisms involved refer to the necessity of autocorrecting ADHD symptoms by the use of different substances (automedication). Another important issue is the possible influence of the stimulant medication in generating addictive problems, an important element that has been debated.

Keywords: adult patients ADHD, comorbidities, psychoactive substances use, specific treatment

There has been an increasing interest in the description of ADHD and other comorbid disorders. Sometimes symptoms suggest that there is an overlap between pathologies. One of the frequent associations is the one between ADHD and substance use disorders (SUD).

Different areas of interest approached have been: the way the two types of pathologies are connected temporally, how can they be dealt with, which is the best therapeutic strategy.

When is the moment in life that they become apparent? It is known that ADHD symptomatology is usually visible the moment the child goes to school, different deficits being seen by parents but also by teachers. It is considered that 50% of individuals remain symptomatic in adulthood, the hyperactivity usually being diminished, with an inner sense of restlessness (1).

Substance use disorders start usually in adolescence and the period of young adulthood. It is considered that substance use disorders (SUD) affect approximately 30% of US adults. (2,3). Smoking is the one that leads the way towards alcohol and illicit drug use. Adolescence is the period the child faces challenges. He is more independent, he enters a broader collectivity. The adolescent goes to parties, wants to have many friends, to impress, starts dating. Substances are seen like a tool to become more disinhibited.

There has been a discussion about ADHD as a risk factor for substance use disorders (SUD). Considering the fact that from a developmental perspective ADHD is manifested earlier than SUD, many researchers tried to find a correlation between the two pathologies. ADHD is considered a vulnerability factor for developing SUD later in life, having in mind the presence of impulsivity, risky behaviors, characteristics of ADHD patients (4).

Wilens found that one quarter to one half of adolescents and adults with SUD have ADHD. The methods of evaluation included structured diagnostic interviews. In a study in 1998 he found 15-25% ADHD in alcohol and drug users (5). If one refers to the type of substances used, it can be found that the drug abusers show greater ADHD pathology compared to the alcohol abusers (6).

The association of these disorders has to be taken into consideration also because it has been shown that ADHD combined with SUD increases the risk for the development of other psychiatric disorders. If we are to consider the onset of the SUD, we can find several elements that are worth mentioning. The onset is usually in adolescence, when the individuals are exposed to an apparent freedom. Usually, smoking is the one that leads the way to alcohol and then illicit drugs. As a characteristic, the onset of the substance use is earlier in ADHD individuals.

If we pay attention to the pattern of the substance use, we usually notice that the substance pathology developed is usually more severe. The occasional use rapidly leads to dependence installation, a more accelerated process when we are confronted with ADHD individuals (7).

Familial elements

The relationship between substance use disorders (SUD) and ADHD has been evaluated also in terms of the familial burden regarding the two pathologies. Different studies evaluated the risk of the two disorders present in the case of the family members of the subjects diagnosed with ADHD and SUD.

The correlation between the two pathologies has been noticed many years ago, when there have been noticed elevated rates of alcoholism in the parents of children and adolescents with ADHD (8).

There are studies that showed the presence of substance related pathology in the case of patients that present SUD. Usually, the presence of substance use disorders can associate aggressive and antisocial behavior (9). Other related elements are cognitive and behavioral traits such as attention deficit, impulsivity, hyperactivity, elements that correlate to ADHD spectrum (10).

A recent study showed that the risk for ADHD is elevated in the individuals with substance-use disorders relative to controls (11). So, we can conclude that the predisposition towards developing ADHD or SUD is...
Prenatal exposure to different substances has been also incriminated in the development of postnatal complications that can lead to neuropsychiatric anomalies. Some of them can lead to attentional and hyperactivity problems. One example is the case of children diagnosed with fetal alcohol syndrome that show these types of symptoms.

**Functionality**

An important aspect that has caught the attention of different researchers has been the fact that the importance of the attention towards this pathology stays in the longitudinal impact of the symptomatology, having in mind the fact that symptoms remain clinically significant in 50% of the individuals. This means that the disease is rather chronic and that it has an impact on the development of the patient.

The individual develops from childhood to adulthood, gathering different abilities at every stage in his life. The incapacity of adapting to every stage of his life can lead to dysfunctionality. Sometimes deficits are subclinical and can go unnoticed by the members of the family.

The first contact with the psychiatrist is usually in childhood, when symptoms are noticed by teachers, when the child first goes to school and has different tasks: to stay in place for a longer period of time, to concentrate to several tasks, to get along with other children.

At this level, different comorbidities can be apparent: conduct disorder, learning disorders, oppositional defying disorder.

This is a period in the individual life that is important for future directions, as it is a developing period, when different skills should be acquired and influence other choices in life.

In adolescence, the educational process continues, but the individual has to face a lot of other challenges. He faces an apparent freedom, participates to different social events, parties where he has access to substances like cigarettes, alcohol, drugs. The adolescent starts dating, is exposed to different risky behaviors, starts driving. Sometimes substances are consumed like an automedication to suppress anxiety, depression, to make social interaction more easy, or in the case of ADHD patients, to camouflage symptoms. The way the individual overcomes this transition to adulthood is definitory for assessing the abilities necessary for adult responsibilities, the choice of a job and the capacity of maintaining a family.

The adolescence is usually the period when children diagnosed with ADHD lost contact with psychiatric services, as the disorder was not considered in the adult pathology.

In adults, when challenges are more complex, the ADHD symptomatology has an impact on the familial environment, the social one, the way the individual handles work responsibilities, the acquisition of friends and the possibility of maintaining them. The symptoms suffer some modifications, in the sense that hyperactivity diminishes, sometimes being expressed as a feeling of inner restlessness. The attentional problems persist. The individuals have a short attention span for details, the organizing capacity is rather low, it is hard for them to complete different tasks. The rapport with others is rather difficult: they cannot work efficiently in a team, frequent conflicts appear. Familial problems are rather the rule: they are alone, in a problematic relationship or divorced.

As adults, the inclination towards risk becomes even more obvious. This dimension is evaluated by the functionality scales, an example being the Weiss scale for functionality (WFIRS)(12).

Risky behaviors appear by increased problems relied to driving vehicles, frequent fines, driver license suspension, accidents. In this category appear the inclination towards aggression, physical or verbal, low frustration tolerance, leading to fighting and frequent other conflicts. The substance-use is frequent, either alcohol or illicit drugs, leading to dependence, that is apparent more easier and more complicated in ADHD individuals (13).

Any diagnosis today has to be sustained by a standardized evaluation with specific scales. In the case of ADHD pathology, they are the following:

- screening tools
  - ASRS (the Adult Self Report Scale)
  - the Barkley scale (Barkley’s Adult ADHD symptoms checklist)
- diagnostic interviews
  - DIVA (The Diagnostic Interview for ADHD in Adults)
  - Connors (CAADID – The Conners Adult ADHD Diagnostic Interview)

A detailed evaluation of functionality can be made by WFIRS (Weiss Functional Impairment Rating Scale)

The presence of comorbidities has to be also evaluated, especially the ones that appear with an increased frequency in the case of ADHD patients. UKAAN recommends the evaluation of disorders like bipolar disorder, depression, anxiety, obsessive-compulsive disorder, schizophrenia, personality disorders, substance use disorders, and disorders of the childhood like tics, autism, learning disorders.... Standardized scales can be used, like: SCID, MINI, HAMD, HAMA. MADRS, YMRS, PANSS (14).

Neuropsychological evaluation can be of help:
- the intelligence quotient (Wechsler Adult Intelligence Scale),
- attention evaluation by specific tests,
- impulsivity evaluation (the Stroop test)
- other cognitive tests

One of the most used scales is DIVA (The Diagnostic Interview for ADHD in Adults), by Kooji and Franken, a clinical structured interview, a very accessible scale, used also in a clinical setting, but also in research. There are available scales translated in several languages. It assesses childhood and adult present symptomatology, based on DSM IV items.

Lately the impact of ADHD symptomatology on functionality has been of a special interest. The best way to evaluate this dimension is the WFIRS scale (Weiss Functional Impairment Rating Scale). It consists of 68 items from several domains:

- A. Home
- B. Work
- C. School
- D. Life skills
- E. Life concept
- F. Social
The influence of ADHD treatment in generating SUD.

An important aspect to be discussed is the influence of ADHD treatment on the possibility of later developing a SUD. ADHD treatment is a a pharmacological one (first line treatment) but also a psychological one (CBT, occupational therapy, psycho-education). The pharmacological treatment consists of stimulant medication (methylphenidate, amphetamine) or non-stimulant medication (atomoxetine, bupropion, venlafaxine, clonidine). The specialist choses the best therapeutic option, taking into consideration the comorbidities. In Europe methylphenidate is the first therapeutic option, followed by dexamphetamine and atomoxetine. In case of abuse potential, atomoxetine is the first indication (a non-stimulant substance) followed by other possibilities, like bupropion, venlafaxine, etc. (15,16,17).

The stimulant medication

The stimulant treatment in ADHD is the most used and therefore the most studied. This kind of medication has been extensively used in children, but in recent years it has been also used in adults. It has been proven to be effective, well tolerated and safe to be used. Inattention, hyperactivity and impulsivity is reduced, but the influence is also on long term disabilities, like low self-esteem, cognition and the overall functionality in society or in family, improving relationships.

There have been conducted a series of studies that were meant to establish the efficacy but also the tolerability of the stimulant medication. The use of stimulants was considered controversial in adults, having in mind the abuse concerns. Studies used either MTH (methylphenidate), or AMPH-based medications (amphetamine).

The response to stimulants in children and adolescents has been considered „robust”, of „approximately 70 %” (18,19,20). On the contrary, in adults, the response has been considered variable, „equivocal”, „ranging from 25% to 88%” (21). This variable response has been caused by different factors like: diagnostic criteria, different doses, comorbidities, that are rather frequent in adults, different methods of response evaluation.

In relation to dosing, it has been found that higher doses show better efficacy. For example, Spencer et al. showed that 40mg of d-MPH XR resulted in a larger response that 20mg. (22, 23)

The strategy is similar to that used in children. Treatment can be initiated with either immediate release (IR) or extended release (ER) preparations at a low dose. The doses are then titrated up observing the potential side effects. Typically, in adults MPH is used in a dose of 30mg, three or four times a day and AMPH in a dose of 15 to 20mg three to four times a day.

If we look towards potential side effects, we can find symptoms like anorexia, irritability, nausea, impaired sleep, weight loss, dysphoria (24). A preoccupation lies in the effects on the cardiovascular system, such as increased heart rate, increased blood pressure. The cardiovascular effects are one of the concerns in relation to stimulants used in the adults population (25).

Another concern regarding stimulants in adults is the abuse potential, that makes their use in the substance-use pathology controversial.

Methylphenidate was one of the first medications used in adult ADHD. At first, the studies conducted to assess the efficacy of MTH showed equivocal responses that were later shown to be caused by some „methodological procedures” like diagnostic criteria and low dosing of the medication (26). Criteria used were different from ADHD DSM criteria, based mainly on symptoms that were rather close to personality disorders like anxiety, explosive temper, stress intolerance, not so specific to ADHD.

Later, in another study (pilot MGH methylphenidate study), that was randomized, double-blind placebo-controlled, doses used were similar to pediatric doses (1mg/kg/day), almost double doses compared to earlier studies. Diagnostic criteria were DSM based. The results were considered robust, 50% better than other previous results (27).

A larger study (NIMH MGH methylphenidate study) was meant to assess the efficacy and safety of MPH treatment in adults, by studying a larger sample of adults (146 subjects). The diagnosis was clinical and confirmed by structured diagnostic interview. Patients with other unstable psychiatric conditions were excluded (psychosis, suicidality, bipolar disorder). The maximum dose used was 1,3 mg/kg. The mean daily doses were 82mg MPH (1,1 mg/kg). The response to treatment was considered robust. Effects were on inattentive but also on hyperactive/impulsive symptoms. No significant side effects were found. Some of the side effects reported were appetite suppression, weight loss, a mild Qtc prolongation, increased pulse rate (28).

Other researchers studied the efficacy of long acting versus short-acting MTH (MGH osmotic-release oral system methylphenidate study – OROS) in adults with ADHD (29). Results were positive.

Later research showed that there is stereoselectivity in MPH receptor. The d-methylphenidate is the active form. This is how the form dexamethylphenidate appeared (Focalin and then Focalin XR)(30).

Amphetamine is another stimulant medication used in ADHD treatment. The compounds used are amphetamine (AMPH), dexamphetamine (d-AMPH), lisdexamphetamine (LDX), mixed amphetamine salts (MAS), MAS-XR (mixed amphetamine salts extended release).

For example, in one study compounds used in ADHD treatment were the mixed amphetamine salts –
Adderall: dextroamphetamine sulfate, dextro-, levoamphetamine sulfate, dextro-, levoamphetamine aspartate, dextroamphetamine saccharate. The pilot study that used amphetamine lasted 7 weeks, was placebo controlled, double-blind (31). The average dose of the medication was 54 mg a day, in two doses. The results were significant, ADHD symptoms being improved (42% decrease on the ADHD Rating Scale).

The initial attempts to establish the efficacy and tolerability of mixed amphetamine salts have been replicated on a larger scale, on a larger group and using different methods of evaluating symptomatology (32). The efficacy of MAS XR (extended release mixed amphetamine salts) has been used and the effects were assessed using CAARS-S-S-ADHD (Conner’s Adult ADHD rating scale). Results were favorable.

The initial studies that evaluated the efficacy and tolerability of amphetamine in ADHD have been replicated on larger scale and the results have been positive. The results of studies that assessed the effects of stimulants in ADHD are relevant especially on short term. Long-term results are not frequently found. Some researchers managed to follow individuals and proved the effectiveness of stimulants on long term.

Non-stimulant medication

Treatment with non-stimulant medication has been also studied in adults. There were used several substances from categories like: antidepressants, alpha agonists, aminoacids, wake promoting agents and other experimental agents (33).

The first medication approved for adults was atomoxetine (ATMX). It has been proven to be effective on ADHD symptoms in adults, improving 30% of symptoms (34).

The appropriate dosing means starting with a minimal dose and gradually increasing it to a maximum of 1,2 or 1,4 mg/kg/day or 100mg/day.

ATMX is considered more appropriate when ADHD presents comorbidities with anxiety, mood disorders or tics.

Another important aspect is the lack of abuse potential, present in stimulants, that makes it particularly useful in substance-use disorders. Wilens studied it in alcoholics, with good results (35). The absence of pharmacological interactions with drugs like marijuana is another advantage (36).

The side effects are represented by dry mouth, constipation, insomnia, decreased appetite, insomnia.

Bupropion is also a non-stimulant medication used in ADHD. Studies that used bupropion has showed it to be moderately effective, reducing symptoms in 52% of subjects (37).

It is particularly considered useful in patients with comorbidities like depression, anxiety, substance-use. A disadvantage is the risk for seizures.

Other substances used are MAOI antidepressants (selegiline), alpha agonists, modafinil, nicotinic agents or aminoacids (38).

It is known that the most problematic psychiatric comorbidity is substance-use pathology, the presence of which usually orients the clinician towards a non-stimulant medication, with a low risk of addiction. There are also other issues like the somatic pathology, cardiovascular events, that restrains the use of some of the medication, with a special somatic monitoring. Guidelines for prescribing the medication have been elaborated (e.g. NICE guidelines) (39).

The risk of the development of a substance use disorder in relation to the ADHD treatment

There have been many debates concerning this issue. The most important reason for this concern is the addictive potential of the stimulant medication.

When assessing the implications of ADHD treatment in relation to the abuse potential we have to have in mind first the potential for abuse potential of this type of medication (especially the stimulants) and second, the effects on ADHD individuals.

Initial studies have been made on animal models that evaluated effects of MPH and AMPH. For example, low doses of MPH early in life reduced sensitivity to the rewarding properties of cocaine (40). Exposure later in life was shown to increase self-administration of cocaine later in life (41). The mechanisms involved are thought to be related to dopaminergic function.

When research was done on human population stimulant sensitization has been found in case of AMP but also MPH use. It has also been demonstrated an increased metabolism in the frontal, parietal and occipital cortices and hippocampus (42).

There were several studies that assessed the problem of stimulant treatment. One of the first ones showed that individuals were more likely to smoke cigarettes and have problems with cocaine (43). Others, on the contrary, that the medication is protective (44). A meta-analysis that included studies that followed ADHD longitudinally have concluded that stimulant treatment early in life has a protective function against SUD (45).

Stimulant medication has been studied to assess the abuse potential. This has been made by determining the capacity to determine reinforcing effects, the capacity to be discriminated and the capacity to produce subjective effects (45).

Both amphetamine and methylphenidate produce significant changes in subjective effects when healthy subjects were used (46). However, in the case of ADHD individuals the subjective effects failed to appear (47). The conclusion is that in spite of the abuse potential of stimulant medication, this is much lower in the case of individuals with ADHD pathology.

The nonstimulant medication (atomoxetine and modafinil) didn’t show a significant abuse potential (48).

The more common problem is the use of these substances in the case of individuals not diagnosed with ADHD. It has been shown to be found in the case of college students that use it to increase their performance or to stay up more late at parties. In these cases, we can talk about abuse.

In the case of ADHD individuals, the neurobiological differences make them rather protected towards abuse or dependence.

Management of ADHD comorbid with substance use disorders

In the case of substance use disorders, it is considered that they have to be solved before ADHD specific treatment. Firstly, the presence of SUD can interfere with ADHD evaluation. Moreover, there are
different risks and impairments associated with different substances. Concomitant substances can lead to potential side effects or interactions that can interfere with treatment.

If we are considering treating the SUD comorbid with ADHD, we have to take into consideration the clinical implications of SUD. Sometimes patients need inpatient treatment, if the disorder is severe enough and has a long-lasting history.

First of all, it is known that ADHD patients that do not receive any kind of treatment have a double risk of developing SUD compared to the general population.

In conclusion, many studies have been conducted that have evaluated patients longitudinally. Some of the conclusions have shown that some of these concerns are not founded. Wilsens conducted a meta-analysis in 2003 the prognosis of ADHD individuals in regard to developing SUD in relation to ADHD treatment. The conclusion has been that treatment lowers the risk for developing SUD in ADHD patients, almost like in the general population. So, we can say that stimulant treatment doesn’t produce substance pathology, but on the contrary, it reduces the risk for developing one, a risk that is increased in the case of ADHD patients, caused by the inclination towards risky behaviors (49,50)

Cigarette smoking

There were discussions referring to the relationship between ADHD and cigarette smoking. First of all, smoking is the behavior that leads to the developing of other substances use, either alcohol, or illicit drugs. It has been noticed that ADHD patients start cigarette smoking at a younger age than controls. The highest rate of smoking has been found in the case of patients that present different other comorbidities, such as conduct disorders, mood or anxiety disorders (51,52)

Antisocial activity

Another topic is the frequent association of ADHD and SUD with aggression and antisocial activity. It has been found that it is a frequent reduction of aggression and antisocial activity in the case of ADHD patients that receive treatment.

Comorbidities – influence on substance use disorders (SUD)

Whenever we evaluate and treat an ADHD individual we must have in mind the presence of comorbidities, that are as mentioned rather frequent. Usually, if we refer to anxiety, mood disorders, they have to be treated first as they can interfere with diagnosing ADHD symptoms and their approach (53,54). Comorbidities complicate the clinical presentation and it is found that they increase the risk for developing SUD.

The presence of different comorbidities is not only likely to increase the risk for substance-use disorders, but it also causes a clear aggravation of symptomatology, from a less severe substance use to a more severe one. Usually the occasional use rapidly shifts to a regular one and then to dependence (55,56)

Psychotherapeutic treatment

Other interventions imply psychotherapeutic treatment, some of them consisting in behavioral and cognitive techniques. Other interventions include the self-help groups, like AA.

Substances like automedication in ADHD patients

One of the theories that explain the onset of a substance use is the one that incriminates automedication. Individuals that present symptoms of depression, anxiety, even aggressive symptoms try to resolve them by using alcohol and drugs, leading to a further dependence (57)

An explanation of the mechanism of the SUD in ADHD patients is also the possibility of attenuating disturbing symptoms by the different effects of substances - restlessness, distractibility, reduced capacity of concentration. Having in mind that ADHD symptoms are rather chronic and lifelong, the impact on functionality usually leads to demoralization, low self-esteem. This leads to a frequent association of a SUD in adolescence (58)

- nicotine – improves attention and executive function
- marijuana – calming effects, reduces hyperactivity
- stimulant drugs – increase the concentration

If we are to consider the types of substances used, we can find characteristics. A study conducted by Biederman showed that ADHD individuals prefer rather drugs, over alcohol (59), moreover, even if we would expect that the stimulant drugs would be the most used by ADHD individuals, it has been found that marijuana is in fact the most popular substance.

Intervention in ADHD and substance use disorders

An appropriate intervention needs a correct evaluation of both pathologies followed by a multimodal treatment for the two disorders and other possible problems.

Treatment includes:
- pharmacotherapy,
- a psycho-therapeutic intervention (CBT, support)

A useful approach in these pathologies are the prevention strategies. For instance, an ADHD patient is best suited for jobs like sales agent, broker, athlete, lawyer, or work in other domains like emergency, press, publicity, television, where the ADHD individual can speculate and use the ADHD features – the interest for novelty, innovation, restlessness, etc.

What are the perspectives for these individuals?
Some of them are negative: rejection from family and friends, frequent conflicts at work, with colleagues or at home, failure in establishing and maintaining relationships, reduced performance in education, getting fired from work.

But there are also some positive perspectives that include better performance by getting treatment, better functionality, tolerance to stressful factors.

Conclusions

ADHD is a disorder present lifelong that frequently associates substance use. This includes the use of alcohol, drugs, smoking.

Substance use is partially explained by the risky behaviors that are frequent in the case of ADHD individuals. Other possible mechanisms include the use as an automedication, to diminish some of the ADHD symptoms, like restlessness, distractibility, lack of sleep or to improve performance.

Even if there is a well-known addictive potential of some of the substances used in the treatment of ADHD, it has been demonstrated that treatment doesn't increase, but on the contrary, it decreases the development of SUD.

The intervention implies a multimodal approach – pharmacologic, psychotherapeutic, prophylactic, that
addresses both pathologies – ADHD and substance use disorders.

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