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Attention Deficit Hyperactivity Disorder in the Elderly
Yaşlılarda Dikkat Eksikliği ve Hiperaktivite Bozukluğu

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Abstract
Attention deficit hyperactivity disorder (ADHD) is a neuropsychiatric syndrome which is hereditarily inherited, affected by environmental factors, and most commonly seen in childhood. It is a disorder that can continue in adulthood and is seen even in the geriatric population. ADHD, which may manifest itself with different symptoms in the geriatric population and the diagnosis of which is often overlooked, may sometimes present itself with dementia or depressive symptoms. Its prevalence is thought to be 3-4% in the elderly population. However, the diagnostic criteria of the ADHD in elderly population are not yet available and the diagnosis is made based on the criteria found in the DSM-5 (Diagnostic and Statistical Manual of Mental Health Disorders, 5th edition). Although some imaging and neurophysiological methods are utilized, there is no specific finding or image for ADHD. Defects in gray matter lesions in frontal and prefrontal areas can be demonstrated by magnetic resonance imaging (MRI). Some researchers think that functional MRI will provide more promising results in the future. Although the pathophysiology of ADHD has not yet been fully elucidated, clinical features are observed in a wide spectrum ranging from sleep disorders to dementia in the geriatric population. Therefore, ADHD should be examined in detail in the elderly population and new diagnostic criteria should be developed for the disorder by new studies. Because it is thought that the frequency of ADHD in the current literature is much less than that in real life.
Keywords: Attention deficit hyperactivity disorder, elderly, diagnosis

Öz
Dikkat eksikliği hiperaktivite bozukluğu (DEHB), kalıtsal olarak geçebilen, çevresel faktörlerden etkilenen, çocukluk çağının en yaygın görülen nöropsikiyatrik sendromu olup, yetişkin çağda da devam edebilen ve hatta geriatrik popülasyonda görülebilen bir bozukluktur. Geriatrik popülasyonda kendini farklı semptomlarla gösterebilen, tanısı genelde göz ardı edilen DEHB, kimi zaman kendini demans ya da depresyon belirtileri ile de gösterebilmektedir. Yaşlı popülasyonda prevalansın %3-4 oranında olduğu düşünülmektedir. Henüz yaşlılara özgül DEHB tanı ölçütleri mevcut olmamakla birlikte DSM-5'de bulunan ölçütlerden-yararlanılarak tanı konulmaktadır. Görüntüleme ve nörofizyolojik yöntemlerden yararlanılsa da DEHB'ye yönelik özgül bir bulgu ya da görüntü yoktur. Frontal ve prefrontal alanlarda, gri cevher lezyonlarında bozukluklar manyetik rezonans görüntüleme (MRI) ile gösterilebilmektedir. DEHB patofizyolojisi tam olarak aydınlatılamamış olsa da geriatrik popülasyonda uyku bozukluklarından demansa kadar uzanan geniş bir spektrumda klinik özellikler gözlenmektedir. Dolayısıyla yaşlı bireylerde DEHB ayrıntılı bir şekilde incelenmeli ve yeni çalışmalarla hastalığa özgül tanı ölçütleri geliştirilmelidir çünkü mevcut literatürde belirtilen DEHB sıklığının gerçek yaşamdakinden çok daha az olduğu düşünülmektedir.
Anahtar sözcükler: Dikkat eksikliği hiperaktivite bozukluğu, yaşlılık, tanı

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ATTENTION deficit hyperactivity disorder (ADHD) is a syndrome accompanied by attention deficit and/or hyperactivity, which adversely effects the functionality and daily living activities of an individual (Springer 2018). ADHD effects a patient throughout his/her life and shows its initial symptoms in childhood. Although the disorder can be seen also in females, it rather effects males and the symptoms are more noticeable in males (Golden et al. 2016, Springer 2018). There are 3 important clusters of symptoms that help the diagnosis: attention deficit, hyperactivity, and impulsivity. With these symptoms, the life and functionality of individuals are effected negatively. Although it is generally thought to be only a childhood disorder, the fact that the symptoms persist with age and even some of them are seen in old people increases the importance of ADHD with time and shows that it is also an old age disorder (APA 2000, Michielsen et al. 2012). However, the exact diagnosis of ADHD in the elderly population still remains unclear. Although there are patients diagnosed during childhood, there are many problems such as misdiagnosis in childhood, overlooked diagnosis in the elderly population, and the presence of underlying ADHD despite the diagnosis of mild cognitive disorder (Springer 2018).

In this review, it is pointed out that ADHD is an important disease which should not be missed. The difficulty of making a diagnosis in the elderly population is mentioned. The pathophysiology, prevalence, diagnosis, treatment and prognosis of ADHD were investigated in detail.

Pathogenesis

The pathogenesis of the disorder cannot be explained by a single mechanism. Genetic, psychosocial, neurochemical, neurophysiological and environmental factors play an important role in the formation of ADHD. Genetic predisposition is one of the most important factors in the development of ADHD. Studies conducted on families showed that the risk increased 4-6 folds in people having relatives with ADHD. In twin studies, ADHD was seen at a rate of 30-40 % in a twin if the other twin had ADHD. These data emphasize the genetic aspect of the disorder (Faraone 2000, Kooij et al. 2019). Especially two dopamine-related genes come into prominence in neurogenetic studies. The first is the DAT1 gene, which is a membrane protein that controls dopamine reuptake and is also involved in the pathophysiology of bipolar disorder. The second gene is the DRD4 gene, which is a receptor protein that inhibits the adenylate cyclase. Among all the genes found, the DDR4 gene currently has the highest risk of disorder. But it should be noted that a single gene is not responsible for the disorder (Yener 2017, Springer 2018). In another study (Gizer et al. 2009), It was shown that other disorder - related genes might be DRD5, 5HTT, HTR1B, and SNAP25. Genetic studies on the adrenergic pathway, serotonin pathway, and noradrenalin pathway are still in progress.

Considering the psychosocial and environmental factors involved in the emergence of the disorder, factors such as low birth weight, alcohol or drug use during the pregnancy, diagnosis of hypertension and use of valproic acid in pregnancy, perinatal stress, psychiatric disorder in parents, stay in the orphanage, which can lead to emotional neglect in the childhood, low social status, and domestic violence pave the way for the disorder (Tannock 1998, Stefanatos and Baron 2017, Kooij et al. 2019).

One of the factors involved in disease pathogenesis is changes in the endocrine system (Marthel et al. 2009, Roberts and Martel 2013). Exposure to high testosterone

levels in the prenatal period has been shown to increase the risk of ADHD in boys and girls at an early stage (Liu ve Wang 2002, Roberts and Martel 2013). Testosterone increases dopamine and vesicular monoamine transporter mRNA expression in substantia nigra. Thus, it changes the dopamine response in the nigrostriatal pathway. It has been claimed that testosterone may cause dysfunction in this pathway in children with ADHD. (Romanos et al. 2010, Purves-Tyson et al. 2014, Kozlowska et al. 2019).

There are also inflammatory changes in the pathophysiology of ADHD (Mittleman et al. 1997). In a study (Kozlowska et al. 2019) conducted in children, measurable levels of IL-2, IL-5, IL-10 and TNF-B were determined in CSF. Children with ADHD had high levels of IL-6 and IL-10 (Donfrancesko et al. 2016). Oades et al. (2010) had found significant correlation between ADHD symptom severity and proinflammatory cytokines.

As the individual maturates, executive functions, goal-directed behaviors, impulse control, and planning skills develop, and these behaviors are controlled by the structural and functional regions of the brain such as the prefrontal cortex, frontal lobe, basal ganglia, and parietotemporal region (Sowell et al. 2004, Luna et al. 2010). Definitions such as "delayed normal brain development" or "minimal brain disorder" have been proposed for ADHD with the clarification of the neuroanatomic structure and functions. Neurochemical and neurobiological aspects of the disorder are also clarified with the developing technology (Ellison et al. 2008, Nakao et al. 2011).

Neuroimaging and neurophysiology

Patients with ADHD were started to be investigated with methods such as Positron Emission Tomography (PET) and Magnetic Resonance Imaging (MRI) with the development of neuroimaging systems. One meta-analyse (Ellison et al. 2008) related to the brain morphology revealed a decrease in the gray matter in basal ganglia. One of these meta-analyses included 7 studies and compared the brain structures of 114 ADHD patients and 143 healthy individuals. As a result of the comparison, it was determined that the gray matter was decreased in the right putamen and globus pallidus of the patients with ADHD (Ellison et al. 2008). Studies with children, adolesean and adults showed significant impairment in right globus pallidus, right putamen, and caudate of both lobes. (Nakao et al. 2011, Frodl and Skokauskas 2012). Hoogman et al. (2011) showed that individuals with ADHD had less accumbenbs, amygdala, caudate, hippocampal, putamen and brain volume. No significant difference was found between the two groups in the volume covered by pallidum. Shaw et al. (2007) showed that cortical maturation of children with ADHD was slower. ADHD developed after physical trauma in 15 of the 76 children who had no history of ADHD (Casey et al. 2007, Ellison et al. 2008). In other studies, decreases were determined in the thicknesses of the frontal lobe, parietotemporal region, basal ganglia, cerebellum, and corpus callosum (Ellison et al. 2008, Nakao et al. 2011, Shaw et al. 2017). In another study (Castellanos et al. 2002), it was observed that the structural defect in the basal ganglia of individuals with ADHD was improved with increasing age and the use of psychostimulant.

Functional disorders in the brain, as well as structural impairment, have been investigated along with the development of advanced neuroimaging methods such as Functional MRI, PET, and Single Photon Emission Computed Tomography (SPECT). Particularly the functional MRI has been gaining importance increasingly in recent years. Func-

tional MRI is a measurement technique based on the oxygen use of the brain and includes 2 different measurement methods. The first of these is the event-related design and it takes images that occur following the stimulation of the brain. In a task-based study, different results were obtained and the resting state rs-fMRI studies were started in individuals with ADHD when inconsistent results were encountered (Rosazza and Minati 2011, Sokunbi et al. 2013). More consistent results were obtained in rs-fMRI studies compared to task-based imaging studies. Functional MRI has shown not only structural defects but also functional reductions in dorsolateral and inferior frontal region, frontostriatal connections, anterior singular region, cerebellum, and temporoparietal region in individuals with ADHD when compared to the control group and these are the regions where inhibitor behaviors and clinical features such as attention and planning play an active role in the development of ADHD (Schneider et al. 2006, Cubillo and Rubia 2010, Cubillo et al. 2012). In individuals with ADHD, there were abnormal findings in the connections including the medial prefrontal cortex named as default mode network (DMN), posterior cingulate cortex, precuneus and medial, lateral, and inferior-parietal regions (Fassbender et al. 2009). It was shown that there was a reduction in the connections between bilateral ventrolateral prefrontal cortex, superior parietal lobe, anterior cingulate cortex, and cerebellum in adults with ADHD (Wolf et al. 2009). It was determined that there was an increase in connections in the left dorsal cingulate cortex, right prefrontal regions, and left cuneus.

In addition to the imaging modalities, electroencefalography (EEG) is another method used in neurology and demonstrates the neurophysiological aspect of the disorder. In a meta-analysis of 9 studies (Snyder and Hall 2006), there was an increase in the tetra wave, a decrease in the beta wave and an increase in the tetra/beta wave ratio of 1498 individuals diagnosed with ADHD. Another result in this meta-analysis is the fact that the tetra/beta ratio in the EEG changed as the symptoms changed with age in individuals with ADHD. While several studies have shown that this rate may increase also in other disorders, this meta-analysis emphasizes the need for further studies to provide standardization for ADHD. Neuroimaging studies are usually on adults and children, and there is not enough information for the elderly.

Epidemiology

Although awareness of ADHD in adulthood has increased compared to previous years, sufficient awareness and the sufficient number of studies on ADHD in the elderly population are still not available (Wetzel and Burke 2008, Simon et al. 2009, Brod et al. 2012). In a comprehensive meta-analysis conducted in childhood and in adults, the prevalence of ADHD was found to be between 5.9% and 7.1%. In the past years, ADHD has been thought to be only a childhood disorder, while studies have shown that ADHD continues in adulthood at a rate of 40%. The frequency of ADHD decreases with the increasing age. The prevalence of ADHD in the elderly population is estimated to be 3-4% (Michielsen et al. 2012, Kooij et al. 2016). In another study (Michielsen et al. 2012) remarkable results were obtained in a study of 231 patients over 65 years of age in the Netherlands. The first of these results is the fact that the prevalence of symptomatic ADHD was found as 4.2%. The second result, however, shows that there are more ADHD symptoms in relatively younger individuals (60-70 years) when compared to older ones (71-94 years). Authors interpreted this in a way that there might be a reduc-

tion in the symptoms with increasing. There is a very limited number of studies that investigate the prevalence of ADHD in the elderly population. In a study (Guldberg and Johansson 2009) conducted in Sweden including a total of 2500 elderly individuals between the ages of 65-80, the Wender Utah Rating Scale (WURS), which included 25 questions, was implemented to each participant. Of the participants, 64% filled the scale and 36 points and above was accepted as ADHD. With this result, the frequency of ADHD was found as 3.3% between the ages of 65-80. Elderly individuals diagnosed with Alzheimer's disorder, mild cognitive disorder, bipolar disorder, depression, or personality disorder may either be diagnosed with ADHD or have ADHD symptoms since childhood. Although this issue has not yet been fully described in the literature, it is mentioned in some data that ADHD may be one of the causes of early-onset dementia (Faraone et al. 2006, Guldberg and Johansson 2009). In a study conducted on students between 7-15 years of age in our country, the frequency of ADHD was found to be 6.2% (Senol et al. 2018). However, there is no study evaluating the frequency of ADHD in the elderly population.

Diagnosis and clinical features

Although the definition of this disorder was made as the hyperkinetic impulse disorder in the 1900s, in 1902 Sir George defined it for the first time with the name of "abnormal psychological states in some children", implying the attention deficit hyperactivity disorder (Springer 2018). This definition is the starting point of ADHD (Lange et al. 2010). It was considered as the hyperkinetic reaction of childhood in DSM-II (APA 1968). Then it was divided into 2 groups as according to the presence of attention deficit and hyperactivity disorder in DSM-III and was defined as the attention deficit and hyperactivity disorder with DSM-III-R (APA 1978, 1987). It appeared under the title of attention deficit and disruptive behavior disorders in DSM-IV-TR, and took part under the title of neurodevelopmental disorders in DSM-5 (APA 2000 2013). ADHD was described in detail in the latest DSM-5 guideline. In the guideline, the criteria related to attention deficit and hyperactivity/impulsivity were mentioned and these symptoms are as follows (APA 2013).

1. Attention deficit

   The person

   a. may make mistakes in his/her work life, school or courses due to attention deficit much more than normal people,
   b. has difficulties in finishing a task or subject in his/her social and business life and in maintaining his/her concentration until he/she finishes a work or a task,
   c. seems as if he/she does not pay attention or is not interested while he/she is spoken to,
   d. starts the tasks given in school life and work life as soon as possible, but he/she has difficulty in finishing them,
   e. has difficulties in planning and managing them for a suitable time when there is more than one job and task,
   f. avoids jobs and tasks that force his/her mind and require careful thinking,
   g. loses things continuously in his/her life, both in his/her work and in his/her daily life,

h. suddenly starts to think non-related things and becomes distracted because of things around him/her while talking to the other person or dealing with a task,
i. often forgets the tasks and activities that he/she has to do during the day or planned earlier.

2. Hyperactivity/Impulsivity

The person

a. has difficulty in standing or sitting in the same position with his/her hand and foot are in constant motion,
b. has difficulty in sitting and stands up in the work life or school,
c. feels unpeaceful and inappropriately starts to walk and move and tries to climb somewhere,
d. has difficulty in playing on his/her own inside the house, remains calm at a corner and has difficulty in standing on his/her own feet,
e. has an unpreventable impulse for motion and tries to act constantly,
f. talks a lot in his/her family, work and social life and people around him/her complain about this,
g. tries to reply to any question asked in the class out of his/her turn, does not care about others' turn and interferes the speeches of people.
h. has difficulty in awaiting his/her turn where others are waiting in a line,
i. interferes with the speech of the other party and begins to talk unless he/she finishes the speech or meddle in others' jobs even if it is not his/her job.

According to these criteria, the ADHD symptoms are addressed in two groups and 9 symptoms are included in each of the attention deficit and hyperactivity/impulsivity symptom groups. The presence of 6 or more symptoms in at least one of these two groups and the persistence of symptoms for 6 months are necessary for the diagnosis of ADHD. When there are 6 or more attention deficit but 5 or less hyperactivity/impulsivity symptoms, the diagnosis is made as ADHD-AD, where attention deficit becomes prominent, and when there are 6 or more hyperactivity/impulsivity but 5 or less attention deficit symptoms, the diagnosis is made as ADHD-HA, where hyperactivity/impulsivity becomes prominent. The diagnosis is combined type in the presence of 6 or more symptoms from both symptom groups (APA 2013, Yener 2017). Some changes were made with the publication of the DSM-5 in May 2013. The first of these changes was the inclusion of the ADHD into the neurodevelopmental disorders category which includes also disorders in brain development. That the DSM-5 reduced the relevant age limit as the age of 7 and below was another change, while some findings should have been at least at the age of 12 and below. While 6 criteria were enough for those at the age of 17 and over and the elderly population, it is mentioned that 5 criteria were enough for the diagnosis in the DSM-5 (APA 2013).

There are also some scanning methods in the literature and adult ADHD self-report measure (ASRS) has the highest specificity among these. There are also different scales, some of which are Wender Utah Rating Scale, Diagnostic Interview for ADHD (DIVA-5), and ADHD Child Evaluation Semi Structured Diagnostic Interview (ACE+) (APA 2013, Kooij et al. 2019).

When making the ADHD diagnosis, it is necessary to adapt the criteria and symptoms according to the age of the individual. Although there are criteria, it is very difficult to diagnose ADHD in the elderly population. It would be appropriate that the diagnosis

is made by a psychiatrist or an ADHD specialist. First of all, the individual's comprehensive clinical history, family history, the presence of preterm stress, psychiatric evaluation, detailed background and symptoms of the individual in daily life, and behavioral symptoms and duration of these symptoms should be examined. Not only that, information should be obtained from the social environment, family and friends of the individual. A comprehensive history obtained from the parents and teachers of a child or detailed information obtained from the wife, partner, family, and caregiver of an elderly individual can be helpful. Then a diagnosis can be made according to the ADHD criteria in the DSM-5 (Guldberg and Johansson 2009, APA 2013, Yener 2017, Springer 2018). It should be kept in mind that the prevalence of ADHD increases in children with premature birth history, mood disorders, children or adults with behavior disorders, those with ADHD in their families, epilepsy patients, those with a neurodevelopmental disorder (such as autism), learning disability, criminal history or brain damage, and those with substance use disorder (Spirnger 2018).

ADHD in the elderly population

There can be some changes in the symptoms of the disorder with increasing age. Sometimes, the symptoms in elderly individuals can be mistakenly perceived as a part of dementia (Brod et al. 2012). ADHD can manifest itself also as social isolation, loneliness, an increase in depressive symptoms, unhappiness, cyclothymic characteristics, personality disorders, bipolar disorder, anxiety, and change in cognitive functions (Michielsen et al. 2013, Surman and Goodman 2017, Kooij et al. 2019). Another issue that needs to be emphasized is that there can be also sleep disorders in elderly individuals with ADHD. The diagnosis of ADHD should be kept in mind in patients presenting with difficulty in falling asleep and waking up in the morning, insomnia, and breathing problems associated with sleep. Women who were not diagnosed with ADHD in childhood but were diagnosed with ADHD in advanced age were found to feel lonely. In addition, it was revealed that the elderly people included in the study thought that they were different from their peers in their youth and they made more efforts to appear normal to other people. Interestingly, in some of the elderly individuals, ADHD can manifest itself as more creative characteristic in the work and social life. Although it is not often, some women with ADHD see themselves as oppressed (Henry and Hill 2011). In another study (Wetzel and Burke 2008), it was found that some of the elderly individuals diagnosed with ADHD had a childhood history where he/she misbehaved and caused problems. In some studies, it was reported that Lewy body dementia was more common in elderly individuals with ADHD compared to Alzheimer's dementia. Researchers have suggested that this may be due to a decrease in norepinephrine and dopamine in both disorders (Golimstok et al. 2011, Fischer et al. 2012). Attention deficit is a situation that increases with age, and some cases such as Lewy body dementia, cerebrovascular disorders, ischemic stroke, traumatic brain injury, delirium, and Alzheimer's disorder should be excluded in order to diagnose the ADHD. This makes the diagnosis more difficult. However, a detailed anamnesis and background of the patient should be obtained, which is very hard to do, in order to make the diagnosis. Records erased over time, difficulty in reaching family members, school records are other factors that make the diagnosis difficult (Fischer et al. 2012). Due to the misdiagnosis of ADHD in the elderly population,

unfortunately, many elderly individuals experience the problems caused by ADHD during their lives (Springer 2018).

There is no specific blood test or imaging method for the diagnosis of ADHD. Functional MRI is becoming increasingly important for ADHD with the developing technology. There are different imaging techniques in this method which is based on the measurement of the amount of oxygen in the blood reaching the brain tissue. Especially in resting state functional MRI, the neuronal networks of the brain that are active in resting can be examined and this method can be used in ADHD as well as other neurological disturbances such as Alzheimer's and epilepsy (Rosazza and Minati 2011). Significant differences detected by the resting state functional MRI measurement particularly in the frontal, striatal and cerebellar regions attract attention in individuals with ADHD compared to healthy individuals (Sokunbi et al. 2013). Attention deficit hyperactivity disorder in adults 2018). But it should be kept in mind that specific imaging studies in elderly individuals diagnosed with ADHD are not at a sufficient level yet (Sokunbi et al. 2013). Neglect, abuse, drug addiction, mental retardation, learning disorder, bipolar disorder, and bad and complex family structure should also be considered in the differential diagnosis of ADHD (Wetzel and Burke 2008, APA 2013).

Treatment

The treatment requires a multidisciplinary approach and various treatment modalities are available, including drug therapy, dietary changes, behavior control, cognitive therapies, game therapy, vitamin support, and various oils. The effects of ADHD symptoms on social life, family and occupational life should be questioned before starting the treatment (Springer 2018, Kooij et al. 2019). Since children cannot express their behavior very clearly, while therapies involving game therapy or behavioral changes are effective, there is currently no adequate data and studies to suggest that the cognitive therapy should be the initial therapy for adults (Springer 2018). It was stated that drug use increased due to ADHD in individuals over 50 years of age between 2000 and 2012 (Ormhøj et al. 2018). It was revealed that there was one comorbid disorder in 23%, and two comorbid disorders in 14% of the patients with ADHD (Fayyad et al. 2017, Kooij et al. 2019). This stands out as a different subject to be questioned.

Amphetamine group drugs or stimulant agents are the first options in pharmacotherapy. These are methylphenidate, dexamphetamine, and side effects have been reported as insomnia, decreased appetite, increased heart rate, increased blood pressure, and very rarely as sudden cardiac death (Kooij et al. 2019). Methylphenidate provides an improvement in 70% of individuals with ADHD. It was determined that methylphenidate inhibited striatal dopamine transporters and increased dopamine in the striatal region and catecholamine levels in the frontal region (Krause 2008). In a meta-analysis (Fusar et al. 2012), an increase was seen in the dopamine transporter levels of the brain with the long-term use of methylphenidate and a decrease was determined in the dopamine transporter levels in patients who did not receive treatment. This might be because the use of long-term methylphenidate caused plasticity in the brain and altered the level of neurotransmitters. While some studies recommended dexamphetamine as the first option, amphetamines were found to be more effective (Faraone and Glatt 2010). Methylphenidate or dexamphetamine is recommended in the newly published 2019 European consensus report as the first choice and it is stated that there is no significant

difference between them (Kooij et al. 2019). Real-life studies have shown that individuals who use these drugs have fewer traffic accidents, commit fewer crimes, decrease in depression and suicide frequency, and mortality rates, but these studies are not randomized and double-blind studies (Chen et al. 2014, Chang et al. 2014, Chang et al. 2016, Kooij et al. 2019).

Another drug that has been shown to be beneficial in treatment is atomoxetine and its efficacy starts in 1-2 weeks after first use. Atomoxetine selectively inhibits the reuptake of noradrenaline. In cases where the stimulant agents cannot be administered, the long-release form of guanfacine, which is an alpha-2 adrenergic agonist, can be used and this may be added to the stimulant treatment in some cases. Therefore, it may be effective in both combined and mono treatment, but there is not enough study about its efficacy in the adult group (Butterfield et al. 2016, Kooij et al. 2019). Clonidine may also be influential through the alpha blockade and may be used in addition to monotherapy or psychostimulants between the ages of 6-17 (Kollins et al. 2011, Jain et al. 2011, Kooij et al. 2019). Differently from these drugs, some studies suggest that reboxetine may be used as an alternative to atomoxetine (Riahi et al. 2010, Ghanizadeh 2015). There is not enough data on the use of tricyclic antidepressants and it is not recommended to use it alone (Kooij et al. 2019). The use of a selective serotonin reuptake inhibitor (SSRI) alone is also not recommended (Kooij et al. 2019). Treatment for ADHD may change in some cases. For example, disorders such as depression and substance use associated with ADHD may lead to some changes in the treatment. Bupropion may be a good choice in ADHD accompanied by depression (Maneeton et al. 2011). SSRIs may be a good choice besides psychostimulants in ADHD accompanied by anxiety, or mood stabilizers can be used if there is the comorbidity of bipolar disorder. In addition to these treatments, the addition of psychotherapy, behavior control therapy, and ADHD coaching to the pharmacological treatment may increase the chance of success (Kooij et al. 2019).

The first step in the treatment of ADHD in elderly individuals is to give a detailed education about the disease to the individual and his / her family. The environmental and psychological factors that affect the disease should be explained and information about the problems that may be encountered in the following years should be given. It should be explained that the treatment of the disease first involves recognizing the disease and learning to live with it. The information sholuld be given to not only the individual himself, but also his relatives, and those who live with him at home (Kooji 2016). Care should be taken with respect to the comorbidities accompanying ADHD in the elderly. In the elderly population, as in adults, the first choice drugs are stimulants. Stimulants are highly potent and have fewer side effects than other drugs. The second and third choice drugs for ADHD are atomoxetine and bupropion (Bolea et al. 2012, Seixas et al 2012, Kooji et al 2016). Elderly people usually need lower drug doses. (Chang et al. 2015).

Methylphenidate is the most preferred drug among stimulants (Kooji et al. 2016, Kooji et al. 2019)There are some issues that need to be considered in the elderly. A low dose of the drug should be started and then titrated. Side effects should be observed carefully. It should be noted that the cardiovascular side effects of stimulant drugs are dose-dependent (Kendall et al. 2008, Chang et al. 2015). Methylphenidate; should not be preferred when ADHD is accompanied by disorders such as epilepsy, arrhythmia, glaucoma, hyperthyroidism, hypertension, anxiety. If it should be used, firstly, comorbid diseases should be treated and then treatment should be started (Kooji et al. 2004, Kooji

et al. 2016). When methylphenidate is not effective, dexamphetamine may be used. The side effects of dexamphetamine may initially be palpitation and irritability, and have been shown to pass over time. It shows similarities with methylphenidate in terms of contraindications (Kendall et al. 2008, Kooji et al. 2016).Another group of drugs in ADHD is atomoxetine. Atomoxetine may be used in patients with side effects or with insufficient response to stimulant agents. Side effects of atomoxetine include dry mouth, insomnia, fatigue, nausea (Adler et al. 2009, Kooji et al. 2016). There are conflicting data on bupropion and can be used only in patients with no response from all other drugs (Kooji et al. 2019).

In addition to drugs, non-drug therapies such as cognitive behavior therapy, participation in support groups are also important (Kooji et al. 2019).

Conclusion

ADHD is a psychiatric disorder that is becoming increasingly important, which starts from childhood and continues until advanced ages. The presence of the disorder in the geriatric population is an important problem, and the lack of valid and reliable diagnostic methods for this age group makes the problem more complicated. The presence of comorbidities in this population creates difficulties in selecting appropriate treatment. There are not enough studies to specific the elderly population yet. The presence of depression, insomnia, sleep disturbance, substance abuse, and crime in the old age may be a part of the ADHD, but this diagnosis can be overlooked because of inadequate diagnosis made by clinicians and inadequate objective criteria. The current criteria are often used for the the diagnosis ADHD in children and young adults, and it may not be the right approach to make a diagnosis in the elderly population based on these criteria. Hence, information about the ADHD in the elderly population was shared in this review and it was shown that the current literature was not sufficient yet in this subject. There is a need for studies on the ADHD specific diagnostic methods and treatment options in the elderly population.

References

Adler L, Wilens T, Zhang S, Durell T, Walker D, Schuh L (2009). Retrospective safety analysis of atomoxetine in adult ADHD patients with or without comorbid alcohol abuse and dependence. Am J Addict, 18:393-401.

APA (1968) Diagnostic and Statistical Manual of Mental Health Disorders, 2th edition (DSM-II). Washington DC, American Psychiatric Association.

APA (1978) Diagnostic and Statistical Manual of Mental Health Disorders, 3th edition (DSM-III). Washington DC, American Psychiatric Association.

APA (1987) Diagnostic and Statistical Manual of Mental Health Disorders, 3th edition (DSM-III-R). Washington DC, American Psychiatric Association.

APA (2000) Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV-TR). Washington DC, American Psychiatric Association.

APA (2013) Diagnostic and Statistical Manual of Mental disorders, 5th edition (DSM-5). Washington DC, American Psychiatric Association.

Bolea-Alamanac B, Nutt DJ, Adamou M, Asherson P, Bazire S, Coghill D et al. (2014) Evidence-based guidelines for the pharmacological management of attention deficit hyperactivity disorder: update on recommendations from the British Association for Psychopharmacology. J Psychopharmacol, 28:179–203.

Brod M, Schmitt E, Goodwin M, Hodgkins P, Niebler G (2012) ADHD burden of illness in older adults: a life course perspective. Qual Life Res, 21:795-799.

Butterfield ME, Saal J, Young B, Young JL (2016) Supplementary guanfacine hydrochloride as a treatment of attention deficit hyperactivity disorder in adults: a double blind, placebo-controlled study. Psychiatry Res, 236:136-141.

Casey B, Epstein JN, Buhle J, Liston C, Davidson MC,Tonev ST et al. (2007) Frontostriatal connectivity and its role in cognitive control in parent-child dyads with ADHD. AM J Psychiatry, 164:1729-1736.

Castellanos FX, Lee PP, Sharp W, Jeffrie NO, Greenstein DK, Clasen SL et al. (2002) Developmental trajectories of brain volume abnormalities in children and adolescents with attention-deficit/hyperactivity disorder. JAMA, 288:1740-1748.

Chang F, O'Hare AM, Miao Y, Steinman MA (2015) Use of renally inappropriate medications in older veterans: a national study. J Am Geriatr Soc, 63:2290-2297.

Chang Z, D'Onofrio BM, Quinn PD, Lichtenstein P, Larsson H (2016) Medication for attention-deficit/hyperactivity disorder and risk for depression: a nationwide longitudinal cohort study. Biol Psychiatry, 80:916-922.

Chang Z, Lichtenstein P, D'onofrio BM, Sjölander A, Larsson H (2014) Serious transport accidents in adults with attention-deficit/hyperactivity disorder and the effect of medication: a population-based study. JAMA Psychiatry, 71:319-325.

Chen Q, Sjölander A, Runeson B, D'onofrio BM, Lichtenstein P, Larsson H (2014) Drug treatment for attention-deficit/hyperactivity disorder and suicidal behaviour: register based study. BMJ, 348: g3769.

Cubillo A, Halari R, Smith A, Giampietro V, Taylor E, Rubia K (2012) Fronto-cortical and fronto-subcortical brain abnormalities in children and adults with ADHD: a review and evidence for fronto-striatal dysfunctions in adults with ADHD followed up from childhood during motivation and attention. Cortex, 48:194-215.

Cubillo A, Rubia K (2010) Structural and functional brain imaging in adult attention-deficit/hyperactivity disorder. Expert Rev Neurother, 10:603-620.

Donfrancesco R, Nativio P, Di Benedetto A, Villa MP, Andriola E, Melegari MG et al. (2016) Anti-Yo antibodies in children with ADHD: first results about serum cytokines. J Atten Disord, 1087054716643387.

Ellison WI, Ellison WZ, Bullmore E (2008) Structural brain change in attention deficit hyperactivity disorder identified by meta-analysis. BMC Psychiatry, 8:51.

Faraone SV (2000) Genetics of childhood disorders: XX. ADHD, part 4: is ADHD genetically heterogeneous? J Am Acad Child Psychiatry, 39:1455-1457.

Faraone SV, Biederman J, Mick E (2006) The age-dependent decline of attention deficit hyperactivity disorder: a meta-analysis of follow-up studies. Psychol Med, 36:159-165.

Faraone SV, Glatt SJ (2010) A comparison of the efficacy of medications for adult attention-deficit/hyperactivity disorder using meta-analysis of effect sizes. J Clin Psychiatry, 71:754-763.

Fassbender C, Zhang H, Buzy WM, Cortes RC, Mizuiri D, Beckett L et al. (2009) A lack of default network suppression is linked to increased distractibility in ADHD. Brain Res, 1273:114-128.

Fayyad J, Sampson NA, Hwang I, Adamowski T, Gaxiola S, Al-Hamzawi A et al. (2017) The descriptive epidemiology of DSM-IV adult ADHD in the world health organization world mental health surveys. Atten Defic Hyperact Disord, 9:47-65.

Fischer BL, Gunter HG, Steinhafel CH, Howell T (2012) The identification and assessment of late-life ADHD in memory clinics. J Atten Disord, 16:333-338.

Frodl T, Skokauskas, N (2012) Meta - analysis of structural MRI studies in children and adults with attention deficit hyperactivity disorder indicates treatment effects. Acta Psychiatr Scand, 125(2):114-126.

Fusar-Poli P, Rubia K, Rossi G, Sartori G, Balottin U (2012) Striatal dopamine transporter alterations in ADHD: pathophysiology or adaptation to psychostimulants? A meta-analysis. Am J Psychiatry, 169:264-272.

Ghanizadeh A (2015) A systematic review of reboxetine for treating patients with attention deficit hyperactivity disorder. Nord J Psychiatry, 69:241-248.

Gizer IR, Ficks C, Waldman ID (2009) Candidate gene studies of ADHD: a meta-analytic review. Hum Genet, 126:51-90.

Golimstok A, Rojas J, Romano M, Zurru M, Doctorovich D, Cristiano E (2011) Previous adult attention - deficit and hyperactivity disorder symptoms and risk of dementia with Lewy bodies: a case–control study. Eur J Neurol, 18:78-84.

Guldberg KT, Johansson B (2009) Old people reporting childhood AD/HD symptoms: Retrospectively self-rated AD/HD symptoms in a population-based Swedish sample aged 65–80. Nord J Psychiatry, 63:375-382.

Henry E, Hill JS (2011) Experiences of older adult women diagnosed with attention deficit hyperactivity disorder. J Women Aging, 23:246-262.

Hoogman M, Bralten J, Hibar PD, Mennes M, Zwiers MP, Schweren L et al. (2011) Subcortical brain volume differences in participants with attention deficit hyperactivity disorder in children and adults: a cross-sectional mega-analysis. Lancet Psychiatry, 4:310-319.

Jain R, Segal S, Kollins SH, Khayrallah M (2011) Clonidine extended-release tablets for pediatric patients with attention-deficit/hyperactivity disorder. J Am Acad Child Psychiatry, 50:171-179.

Kendall T, Taylor E, Perez A, (2008) Diagnosis and management of attention-deficit/hyperactivity disorder in children, young people, and adults: summary of NICE guidance. BMJ, 337:a1239.

Kollins SH, Jain R, Brams M, Segal S, Findling RL, Wigal SB et al. (2011) Clonidine extended-release tablets as add-on therapy to psychostimulants in children and adolescents with ADHD. Pediatrics, 127:1406-1413.

Kooij JJS, Bijlenga D, Salerno L, Jaeschke R, Bitter I, Balázs J et al. (2019) Updated European Consensus Statement on diagnosis and treatment of adult ADHD. Eur Psychiatry, 56:14-34.

Kooij JJS, Burger H, Boonstra A, Van Der Linden D, Kalma LE, Buitelaar JK (2004) Efficacy and safety of methylphenidate in 45 adults with attention-deficit/hyperactivity disorder. A randomized placebo-controlled double-blind cross-over trial. Psychol Med, 34:973–982.

Kooij JJS, Michielsen M, Kruithof H, Bijlenga D (2016) ADHD in old age: a review of the literature and proposal for assessment and treatment. Expert Rev Neurother, 16:1371-1381.

Kozłowska A, Wojtacha P, Równiak M, Kolenkiewicz M, Huang A (2019) ADHD pathogenesis in the immune, endocrine and nervous systems of juvenile and maturating SHR and WKY rats. Psychopharmacology (Berl), 236:2937-2958.

Krause J (2008) SPECT and PET of the dopamine transporter in attention-deficit/hyperactivity disorder. Expert Rev Neurother, 8:611-625.

Lange KW, Reichl S, Lange KM, Tucha L, Tucha O (2010) The history of attention deficit hyperactivity disorder. Atten Defic Hyperact Disord, 2:241-255.

Liu Y,Wang Y (2002) Cognitive functions of children with attention deficit/ hyperactivity disorder. Zhonghua Yi Xue Za Zhi 82:389–392.

Luna B, Padmanabhan A, O'Hearn K (2010) What has fMRI told us about the development of cognitive control through adolescence? Brain Cogn, 72:101-113.

Maneeton N, Maneeton B, Srisurapanont M, Martin SD (2011) Bupropion for adults with attention - deficit hyperactivity disorder: Meta - analysis of randomized, placebo-controlled trials. Psychiatry Clin Neurosci, 65:611-617.

Martel MM, Klump K, Nigg JT, Breedlove SM, Sisk CL (2009). Potential hormonal mechanisms of attention-deficit/hyperactivity disorder and major depressive disorder: a new perspective. Horm Behav, 55:465-479.

Michielsen M, Comijs HC, Semeijn EJ, Beekman AT, Deeg DJ, Kooij JJS (2013) The comorbidity of anxiety and depressive symptoms in older adults with attention-deficit/hyperactivity disorder: a longitudinal study. J Affect Disord, 148:220-227.

Michielsen M, Semeijn E, Comijs HC, Van de Ven P, Beekman AT, Deeg DJH et al. (2012) Prevalence of attention-deficit hyperactivity disorder in older adults in The Netherlands. Br J Psychiatry, 201:298-305.

Mittleman BB, Castellanos FX, Jacobsen LK, Rapoport JL, Swedo, SE, Shearer GM (1997) Cerebrospinal fluid cytokines in pediatric neuropsychiatric disease. J Immunol, 159:2994 -2999.

Nakao T, Radua J, Rubia K, Mataix-Cols D (2011) Gray matter volume abnormalities in ADHD: voxel-based meta-analysis exploring the effects of age and stimulant medication. Am J Psychiatry, 168:1154-1163.

Oades RD, Dauvermann MR, Schimmelmann BG, Schwarz MJ, Myint AM (2010) Attention-deficit hyperactivity disorder (ADHD) and glial integrity: S100B, cytokines and kynurenine metabolism-effects of medication. Behav Brain Funct, 6:29.

Ormhøj SS, Pottegård A, Gasse C, Rasmussen L (2018) Use of attention - deficit/hyperactivity disorder medication among older adults in Denmark. Br J Clin Pharmacol, 84:1505-1513.

Purves-Tyson TD, Owens SJ, Double KL, Desai R, Handelsman DJ, Weickert CS (2014) Testosterone induces molecular changes in dopamine signaling pathway molecules in the adolescent male rat nigrostriatal pathway. PLoS One, 9:e91151.

Riahi F, Tehrani DM, Shahrivar Z, Alaghband RJ (2010) Efficacy of reboxetine in adults with attention - deficit/hyperactivity disorder: A randomized, placebo - controlled clinical trial. Psychopharm Clin, 25:570-576.

Roberts BA, Martel MM (2013) Prenatal testosterone and preschool disruptive behavior disorders. Pers Individ Diff, 55:962–966.

Romanos M,Weise D, Schliesser M, Schecklmann M, Löffler J,Warnke A et al. (2010) Structural abnormality of the substantia nigra in children with attention-deficit hyperactivity disorder. J Psychiatry Neurosci, 35:55–58.

Rosazza C, Minati L (2011) Resting-state brain networks: literature review and clinical applications. Neurol Sci, 32:773-785.

Schneider M, Retz W, Coogan A, Thome J, Rösler M (2006) Anatomical and functional brain imaging in adult attention-deficit/hyperactivity disorder (ADHD) a neurological view. Eur Arch Psychiatry Clin Neurosci, 256:32-41.

Seixas M, Weiss M, Muller U (2012) Systematic review of national and international guidelines on attention- deficit hyperactivity disorder. J Psychopharmacol, 26:753–765.

Senol V, Unalan D, Akca RP, Basturk M (2018) Prevalence of attention-deficit/hyperactivity and other disruptive behaviour disorder symptoms among primary school-age children in Kayseri, Turkey. J Int Med Res, 46:122-134.

Shaw P, Eckstrand K, Sharp W, Blumenthal J, Lerch J, Greenstein D et al. (2017) Attention-deficit/hyperactivity disorder is characterized by a delay in cortical maturation. Proc Natl Acad Sci U S A, 4:19649-19654.

Simon V, Czobor P, Bálint S, Mészáros A, Bitter I (2009) Prevalence and correlates of adult attention-deficit hyperactivity disorder: meta-analysis. Br J Psychiatry, 194:204-211.

Snyder SM, Hall JR (2006) A meta-analysis of quantitative EEG power associated with attention-deficit hyperactivity disorder. J Clin Neurophysiol, 23:441-456.

Sokunbi MO, Fung W, Sawlani V, Choppin S, Linden DE, Thome J (2013) Resting state fMRI entropy probes complexity of brain activity in adults with ADHD. Psychiatry Res, 214:341-348.

Sowell ER, Thompson PM, Toga AW (2004) Mapping changes in the human cortex throughout the span of life. Neurol Sci, 10:372-392.

Springer R (2018) ADHD: The lifespan and effects from adolescence through adulthood (Dissertation). Murray, Murray State University.

Stefanatos GA, Baron IS (2017) Attention-deficit/hyperactivity disorder: A neuropsychological perspective towards DSM-V. Neuropsychol Rev, 17:5-38.

Surman CB, Goodman DW (2017) Is ADHD a valid diagnosis in older adults? Atten Defic Hyperact Disord, 9:161-168.

Tannock R (1998) Attention deficit hyperactivity disorder: advances in cognitive, neurobiological, and genetic research. J Child Psychol Psychiatry, 39:65-99.

Wetzel M, Burke W (2008) Addressing attention-deficit/hyperactivity disorder in later adulthood. Clin Geriatr, 16:33-39.

Wolf RC, Plichta MM, Sambataro F, Fallgatter AJ, Jacob C, Lesch KP et al. (2009) Regional brain activation changes and abnormal functional connectivity of the ventrolateral prefrontal cortex during working memory processing in adults with attention - deficit/hyperactivity disorder. Hum Brain Mapp, 30:2252-2266.

Yener S (2017) Dikkat eksikliği-hiperaktivite bozukluğu yaraticiliği tetikler mi? Psikolojik iklimin aracı rolü. Sinop Üniversitesi Sosyal Bilimler Dergisi, 1:115-148.

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