

Diving and attention deficit hyperactivity disorder

Abraham L Querido¹, Robert A van Hulst²

¹ *Praktijk Querido, Larenseweg 14, Hilversum, The Netherlands*

² *Department of Experimental Intensive Care and Anaesthesiology/Hyperbaric Medicine, Academic Medical Center, Amsterdam*

Corresponding author: Abraham L Querido, Praktijk Querido, Larenseweg 14, Hilversum, The Netherlands
bram@praktijkquerido.nl

Key words

ADHD; Medications; Fitness to dive; Diving medicine; Recreational diving; Side effects; Review article

Abstract

(Querido AL, van Hulst RA. Diving and attention deficit hyperactivity disorder. *Diving and Hyperbaric Medicine*. 2019 March 31;49(1):41–47. doi: 10.28920/dhm49.1.41-47. PMID: 30856666.)

Attention deficit hyperactivity disorder (ADHD) is a psychiatric condition that affects attention, concentration, impulse control and awareness. Not only these symptoms, but also the medications used to treat ADHD (psychostimulants) pose a risk to both the diver and his or her buddy. This article presents guidelines for recreational diving in combination with ADHD and psychostimulants. These guidelines are based solely on ‘expert’ opinion and were adopted at a meeting of the Dutch Association for Diving Medicine in 2017.

Introduction

Scuba diving, with millions of participants across the world, is a generally safe sport, provided reasonable limits of depth/time/frequency are observed by a reasonably fit and well-trained diver.¹ To certify that a person is fit to be taught to dive ideally implies that he/she is physically fit, medically healthy and psychologically stable. A preventative diving medical examination is aimed at detecting any medical risks and issuing an appropriate recommendation. Psychiatric issues and psychopharmacology pose a risk to both the diver and his or her buddy. Little is known about how medicines and hyperbaric or diving conditions might interact. Psychotropic medicines may increase susceptibility to nitrogen narcosis and cerebral oxygen toxicity; however, there is no experimental evidence for these claims.

The Divers Alert Network Europe, in discussing the lack of knowledge about the interaction between psychiatric disease and pharmacological agents used in its treatment, makes the general comment that “*stimulant medications used to treat attention deficit hyperactivity disorder (ADHD) show no clear risk; the greater risk is the loss of medication benefit if it is not taken in a timely fashion*”.²

The following guidelines were endorsed by the Dutch Association of Diving Medicine at its annual meeting in 2017 and formulate advice for recreational diving in people with ADHD and taking psychostimulants.³ The guidelines cannot be substantiated beyond the level of ‘expert opinion’ but are intended to support rational clinical practice.

Method

A systematic search of the literature was performed using PubMed up to November 2017. A screening literature search was used to identify all literature discussing scuba diving and any ADHD topics. Search terms included: (Ritalin[tiab] concerta [tiab] or Dexedrine [tiab] or Strattera [tiab] or methylphenidate[tiab] or “*Methylphenidate*” [Mesh] or “*Dextroamphetamine*” [Mesh] or “*Atomoxetine hydrochloride*” [Mesh] or “*Attention deficit disorder with hyperactivity*” [Mesh] or “*ADHD*” [tiab] or “*ADD*” [tiab] or (attention [tiab] and deficit [tiab]) AND (“*Diving*” [Mesh] or Diving [tiab] or SCUBA [tiab] or divers [tiab])). The search resulted in identification of 29 titles, with only one relevant research article.⁴

In addition, handbooks on diving medicine and diving medical books which discussed medical examination, psychological and psychiatric areas of attention were screened to identify additional information.^{5–9}

Applicability of the recommendations in these guidelines:

- This document relates to recreational sports diving. The recommendations given are not aimed at professional divers, including dive masters and instructors who dive recreationally.
- Under Dutch occupational law (ARBO-besluit, H6, Afd 5, Art 6.14) an instructor must be “*physically and mentally capable of recognizing and, if possible, preventing hazards*”.
- Divemasters and instructors with psychiatric issues

Table 1
Clinical manifestations of ADHD

Core symptoms	
Attention problems	Easily distracted or bored Difficulty finishing tasks Switching from one activity to another Inability to distinguish between primary and secondary elements Poor planning, organization and decision-making Only able to read for a short while; only able to concentrate if the topic is of great personal interest Difficulty listening and allowing information to sink in Getting lost in the details or being overly precise Endless procrastination Difficulty with filling in forms, understanding instructions, remembering things Indecisiveness Forgetfulness Often loses things Is chaotic Temporary overconcentration or hyperfocus
Hyperactivity	Difficulty sitting still Preoccupied Always having to go and fetch something A feeling of internal restlessness Fidgeting Not able to relax in a calm way Rapid speech
Impulsiveness	Blurts things out Interrupts others Impatience Acts without considering the consequences (spends too much money, gambles, steals, impulsive eating binges, etc.) Starts and ends relationships or jobs impulsively
Mood swings and fits of rage	Short fused Rapidly changing moods in the event of setbacks, up to five times daily

are in principle unsuitable for carrying out diving instruction, but may be deemed suitable for personal recreational sports diving activities based on the current guidelines.

- These guidelines articulate recommendations which are not set in stone. The scientific rationale has limitations and deviation from the recommendations may be justifiable in individual cases.
- The key principle is that the individual diver is primarily responsible for his/her health and safety, as well as the health and safety of his/her buddy.
- The existence of other medical contraindications should be checked for each diver, including the indication for the use of the relevant substances.

Prevalence

ADHD is one of the most common psychiatric disorders in children, with a prevalence estimated to be 4–8%.¹⁰ For a long time, ADHD was thought to be a developmental

problem that would resolve automatically with age, but recent research shows that over two-thirds of adults who had childhood ADHD still had the disorder in adulthood.¹¹ Estimates of the prevalence of ADHD in adults varies from 2.5 to 5%; a meta-analysis reported an average of 2.5%.¹²

Neurodevelopmental disorders

The fifth edition of *Diagnostic and statistical manual of mental disorders* (DSM-5), a classification system of psychiatric disorders developed under the auspices of the American Psychiatric Association,¹³ contains a new category of ‘neurodevelopmental disorders’; a group of disorders that manifest during the course of an individual’s development, often at a very young age. ADHD, amongst others, belong to this group. A diagnosis of ADHD can only be asserted if the symptoms are of such a nature that they cause severe impairment to social, educational or occupational functioning. It is also required to specify the severity level of the ADHD as either mild, moderate, or severe.

Core symptoms

The core symptoms of ADHD are attention or concentration disorders, hyperactivity or (inner) turmoil and impulsive behaviour (Table 1).¹⁴ DSM-5 classifies hyperactivity and impulsiveness as a single symptom criterion; the other symptom criterion being inattentiveness. Attention problems generally become apparent with matters that require prolonged attention and are boring, complex and/or repetitive. Hyperfocus is a specific type of attention problem – an intense form of mental concentration in which attention is focused on a single subject or a task. When someone is hyperfocused, they are oblivious to external stimuli and have little or no concept of time.

Hyperactivity in children is often expressed in a more physical way, whereas adults are usually more ‘mentally’ preoccupied and complain of inner turmoil and chaos. Impulsiveness is expressed, amongst other ways, by acting before thinking, answering a question before it has been asked in full, starting and ending things like relationships and jobs impulsively. Sensation seeking is a specific form of impulsiveness, seeking excitement and sensation because of a need for new stimuli, variation, excitement and change, as well as making risky decisions.¹⁵

Comorbidity

Management of ADHD is complex because of the chronicity and the frequent comorbidity of other psychiatric disorders. Mood and anxiety disorders and substance abuse are frequent comorbidities, but also personality, autism spectrum, eating disorders and sleep problems are all reported in association with ADHD. In three-quarters of patients, ADHD is associated with one or more psychiatric disorders.¹⁴

ADHD and epilepsy

The relationship between ADHD and epilepsy deserves special attention. Children with epilepsy are at increased risk of ADHD.^{16,17} Conversely, the relative risk of an epileptic seizure or epilepsy in children with ADHD is two to three times higher than in the general population.¹⁸ Electroencephalographic epileptic abnormalities are also seen more frequently in children with ADHD.¹⁹ There are thought to be different causes for an increased risk of epilepsy in individuals with ADHD, varying from a common genetic defect,²⁰ to a deficit of the central noradrenergic system.²¹ A complicating factor is that all commonly used antiepileptic drugs have some effect on cognitive function, impacting attention and memory. However, the mechanism explaining ADHD/epilepsy comorbidity is still unclear.

Medication

The Dutch guideline “*Richtlijn ADHD bij volwassenen*” (ADHD in adults) recommends methylphenidate and

dexamphetamine as the first-line medicinal treatment for ADHD in adults.²² Both work through blockade of dopamine and noradrenaline reuptake into neurons; furthermore, dexamphetamine causes release of the catecholamines dopamine and noradrenaline. If the effect of these two medications is insufficient, or they cause too many side effects, atomoxetine is the second-line treatment, with less potent bupropion being the third choice. There can be reasons for starting with atomoxetine first, such as parent/child preference, addiction (risk), comorbidity concerns, tics and prior negative experiences with stimulants. Atomoxetine is a non-stimulant medication that works via noradrenergic reuptake inhibition. Bupropion is registered as an antidepressant, it is a weak noradrenergic and dopaminergic reuptake inhibitor.

Modafinil is advised if other treatments have been implemented properly and appear to be ineffective. Little is known about the clinical effectiveness of modafinil as a treatment option for adults with ADHD because there have been only a limited number of adequately controlled studies.²²

Guanfacine has recently been registered in the Netherlands for treatment of ADHD in children and adolescents and, like clonidine, is an alpha-2 agonist (albeit a little more selective). Its mode of action in ADHD is still unknown, although it is hypothesized that it binds preferentially to postsynaptic alpha 2A receptors and thus stimulates the effect of noradrenaline postsynaptically.²² Guanfacine and clonidine could be trialed first in adults with ADHD who have a cardiovascular risk (e.g., hypertension) and with tic disorders (stimulants can actually exacerbate tics). The effectiveness of clonidine for ADHD is not included in the guideline for adults because of a lack of scientific evidence and its pronounced side effects.²³

SIDE EFFECTS OF ADHD MEDICATION²⁴

Stimulants (methylphenidate/dexamphetamine)

The most commonly occurring side effects are insomnia, agitation, headache, dry mouth, reduced appetite and tachycardia. Less common side effects include dizziness, anxiety, depression, drowsiness, changes in blood pressure and heartbeat and palpitations. A troublesome problem is the rebound that occurs once the medication has left the system; a temporary increase in ADHD symptoms.

Atomoxetine

The most commonly occurring side effects are headache, drowsiness, reduced appetite, abdominal pain, nausea, vomiting, increased blood pressure and tachycardia. Less frequently mood swings, insomnia, agitation, anxiety, depression and low mood, dizziness, skin rash, fatigue and listlessness have all been reported.

Bupropion

Commonly occurring side effects (10–30%) are insomnia, dry mouth, headache and gastrointestinal symptoms (such as nausea, vomiting, abdominal pain and constipation, particularly at the start of treatment). Less commonly (1–10%) insomnia, dizziness, tinnitus and blurred vision are reported. Anxiety, nervousness and excitability generally occur at the start of treatment and tend to reduce with time. There is an increased risk of seizures with higher doses (450 mg).

Selective serotonin reuptake inhibitors (SSRIs) may cause bleeding complications, though the absolute risk appears to be clinically insignificant in most patients, being clinically relevant only for 'at-risk' patients, e.g., those with thrombocytopenia or platelet disorders, those with coagulopathy and/or in the throes of an acute intracerebral haemorrhage and patients on multiple antiplatelet drugs. Though bupropion is not an SSRI, there may be a risk attached to the combination of bupropion with non-steroidal anti-inflammatory drugs or warfarin.²⁵

Modafinil

Headache is common, whilst rare side effects include gastrointestinal symptoms, dry mouth, symptoms of depression, dizziness, drowsiness, palpitations and blurred vision.

Guanfacine

The commonest side effects are somnolence, headache and fatigue. Reduced appetite, depression, anxiety, affective lability, insomnia, sedation, dizziness, lethargy, bradycardia and orthostatic hypotension have all been documented.

CARDIOVASCULAR EFFECTS

The cardiovascular effects of the use of ADHD medication in children and young adults are generally clinically insignificant.²⁶ However, a clinically relevant and continued increase in blood pressure can occur in individual cases, but extreme values are rare.²⁶ Thus, blood pressure and heart rate checks should form part of routine monitoring in all ADHD patients on medication.²⁷ Neither is there evidence of stimulants causing clinically significant electrocardiographic changes.²⁶ A USA study of over a million children and young adults between the ages of two and 24 years showed no significant increased risk of cardiovascular problems.²⁸ Two other studies also confirm that ADHD medication is not associated with an increased risk of serious cardiovascular problems.^{29,30}

It may be concluded from these various studies that the cardiovascular risks of stimulants is very limited in adults.²³

There are reports of sudden cardiac death but these do not appear to exceed the frequency of such incidents in the normal paediatric population.³¹ For safety's sake, a cardiac examination is recommended for children with a family history such as unexplained sudden death in the family before the age of 40 or death as a result of cardiac arrest during exercise and for children with preexisting cardiovascular conditions with potential cardiac symptoms such as syncope, extreme shortness of breath, or prolonged palpitations. It can be useful for the attending physician to refer children in these risk groups to a paediatrician or paediatric cardiologist.

SEIZURES

The *Summary of product characteristics* (SPC) is a specific document required within the European Commission before any medicinal or biocidal product is authorized for marketing. The SPC contains a warning that methylphenidate (and other amphetamines) "*should be used with caution in patients with epilepsy*".²³ Methylphenidate may lower the convulsive threshold in patients with a prior history of seizures, in patients with prior EEG abnormalities in the absence of seizures and rarely in patients without a history of convulsions and no EEG abnormalities. Given the likely fatal outcome of a seizure underwater, and considering the known increased risk of seizure with exposure to elevated oxygen partial pressures, this risk should be addressed in any assessment of diving risk.

The studies in which an increased frequency of seizures were found with methylphenidate suggest that this may occur particularly in patients with uncontrolled epilepsy^{32,33} and in patients with abnormal epileptic discharges in the absence of a history of epilepsy.³⁴ There are few data about seizure risk in non-epileptic children treated with stimulants. A review of the recent literature on the treatment of ADHD with methylphenidate identified nine relevant references.³⁵ When results from these nine studies are summarized, 92% of 201 participants did not experience an increase in seizure frequency. From these data one may conclude that methylphenidate is relatively safe for use in children with comorbid ADHD and epilepsy. The advice the authors give is to make a careful risk/benefit analysis when considering treatment of ADHD with methylphenidate in children with epilepsy.

In a large cohort study, the risk of seizures in patients aged from six to 17 years treated with either atomoxetine or stimulants for the first time was compared retrospectively (13,398 and 13,322 patients respectively).³⁶ The risk of seizure was not significantly different between pediatric patients taking atomoxetine compared with those taking stimulants.³⁶ Higher doses of bupropion, in fact, lower the threshold, but this medication also has few side effects in doses of up to 450 mg.

Hyperbaric conditions

Hardly anything is known about the influence of hyperbaric conditions on ADHD and its treatment. Animal experimentation has shown that the blood-brain barrier becomes more permeable to medications under hyperbaric conditions.³⁷ There are indications that alcohol and psychotropic drugs increase the risk of nitrogen narcosis^{38,39} and acute oxygen toxicity.^{40,41}

Discussion

ADHD is a condition that, if untreated, is associated with symptoms that may present a risk to scuba diving, such as attention problems, reduced awareness and impulsiveness. The argument that concentration underwater is particularly good is often presented by the diver, the parents or the diving instructor during a psychiatric evaluation to establish if the diver is fit to dive or not. However, over-concentration or hyperfocus means concentration is so intense at times that awareness of the external world is lost. Concentration is determined by stimuli from the environment and the task that has to be done at a certain moment. People with ADHD are easily distracted by stimuli from the environment, with the result that they have great difficulty staying focused. During diving this can result in ignoring important tasks such as maintaining buddy contact, monitoring depth and gas supply. Also, the need for excitement can lead to poor or risky decision-making since risk prevention is of particular importance in scuba diving. Since comorbidities are common in ADHD, this poses an additional risk to diving, whilst the effects of medications and their side effects are unpredictable and/or may worsen nitrogen narcosis.

Severity of ADHD can vary from one person to another, but there is also situational variability (home, school, work, sport). Some children and adults are capable of suppressing their 'ADHD behaviour' effectively but it is harder for many children to suppress this behaviour.⁴² If the severity of the condition (as specified in DSM-5) is mild, then ADHD does not need to present grounds for declaring the diver unfit for recreational diving.

Communication between the different areas of the brain is still far from optimal in adolescents. Rapid maturation of some regions of the brain, coupled with the slower maturation of others, explains many typical adolescent behaviours like acting impulsively, taking risks and mood swings. Executive functions including cognitive flexibility and working memory improve further during adolescence; in other words, young age is an additional risk factor. The sports diving physician could consider assessing a child with very mild symptoms, who is capable of controlling their behaviour effectively and where there are no complicating factors, as fit to dive with compressed air. When in doubt, the sports diving physician in the Netherlands is advised to seek a second opinion from a psychiatrist specialising in diving medicine.

The side effects of stimulants and atomoxetine, whilst diverse, are generally mild and well tolerated so may not in themselves be a contraindication to scuba diving. Rebound is incompatible with diving as it exacerbates ADHD symptoms. Depending on the medication used and the time it is taken, as a rule the medication will have left the system by late in the day, with a possible return of ADHD symptoms. For this reason, evening or night-time diving is not recommended. Somnolence, a frequent side effect of guanfacine, makes this agent less suited to diving with compressed air.

Medical recommendations for diving with ADHD

- Diving is allowable if symptoms are mild.
- No significant comorbidity is present.
- Individual has insight into and understanding of the condition.
- Age: The Dutch Association of Diving Medicine sets the age limit for responsible diving practice at 14 years, preferably 16 years. For divers with ADHD an age of 18 years and older is recommended, unless there are reasonable grounds for the attending physician (preferably in consultation with a psychiatrist specialising in diving medicine) to advise otherwise.
- Medication:
 - i. No significant side effects.
 - ii. Only a single psychotropic medicine: more than one psychotropic medicine will increase the risk of potentially dangerous side effects whilst diving and susceptibility to nitrogen narcosis.
 - iii. Medication and therapy compliant.
 - iv. Maximum diving depth 18–20 m: a maximum diving depth is advised to minimize the risk of DCI and the slight theoretical risk that some drugs might increase narcosis.
 - v. No combination with psychostimulants and epilepsy.
- Dizziness and paraesthesiae are side-effects that could mimic DCI. Whilst not necessarily a contraindication to use, such symptoms should be considered during an evaluation for diving.
- Diving is not advised in the event of rebound.

Who carries out the examination?

The recommendation to the Dutch Association for Diving Medicine is that, with the use of these guidelines, certified sports diving physicians should be able to arrive at a well-considered opinion on whether a diver should be deemed fit or unfit for diving with compressed air. In case of doubt or a complicated underlying condition, a psychiatrist/sports diving physician may be asked to carry out a specialist examination.

Conclusions

ADHD is a condition which, if untreated, is associated with symptoms such as attention problems, reduced awareness

and impulsiveness that present a risk to scuba diving. Mild ADHD need not preclude diving with compressed air. Impulsivity, risky behavior and mood swings are typical adolescent behaviours which pose an extra risk for children with ADHD because communication between the different areas of the brain is still far from optimal.

References

- 1 Germonpré P. Medical risks of underwater diving. *International Sport Med Journal*. 2006;7:1–15.
- 2 Divers Alert Network Europe. Medical conditions. [cited 2017 December 29]. Available from: <http://www.daneurope.org/web/guest/medical-questions>.
- 3 Querido AL, van Hulst R. Standpunt Duiken met ADHD/ADD. [Guidelines for diving with ADHD/ADD]. Dutch Association for Diving Medicine. [cited 2017 December 29]. Available from: https://www.duikgeneeskunde.nl/download/richtlijnen/Duiken_met_ADHD_NVDstandpunt_20mei2017.pdf. Dutch.
- 4 Fowler B, Adams J. Dissociation of the effects of alcohol and amphetamine on inert gas narcosis using reaction time and P300 latency. *Aviat Space Environ Med*. 1993;64:493–9. PMID: 8338494.
- 5 Parker JL. *The Sports diving medical: a guide to medical conditions relevant to scuba diving*, 2nd ed. Ashburton, Australia: JL Publications; 2002.
- 6 Brandt Corstius JJ, Dermout SM, Feenstra L, editors. *Duikgeneeskunde, theorie en praktijk*. Doetinchem: Elsevier; 2006. Dutch.
- 7 Bennett PB, Cronje FJ, Campbell E. *Assessment of diving medical fitness for scuba divers and instructors*. Flagstaff, AZ: Best Publishing Company; 2006.
- 8 Edmonds C, Bennett M, Lippmann J, Mitchell SJ. *Diving and subaquatic medicine*, 5th ed. Boca Raton, FL: CRC Press; 2015.
- 9 Nevo B, Breitstein S. *Psychological and behavioral aspects of diving*. San Pedro, CA: Best Publishing Company; 1999.
- 10 Faraone SV, Sergeant J, Gillberg C, Biederman J. The worldwide prevalence of ADHD: is it an American condition? *World Psychiatry*. 2003;2:104–13. PMID: 16946911. PMID: 1525089.
- 11 Tuithof M, Ten Have M, van Dorsselaer S, de Graaf R. Prevalence, persistency and consequences of ADHD in the Dutch adult population. *Tijdschr Psychiatr*. 2014;56:10–9. Dutch.
- 12 Simon V, Czobor P, Bálint S, Mészáros A, Bitter I. Prevalence and correlates of adult attention-deficit hyperactivity disorder: meta-analysis. *Br J Psychiatry*. 2009;194:204. doi: 10.1192/bjp.bp.107.048827. PMID: 19252145.
- 13 American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*, 5th ed. Arlington, VA: American Psychiatric Publishing; 2013.
- 14 Kooi, JJS. *ADHD bij volwassenen, diagnostiek en behandeling*, 4th edition. Amsterdam: Pearson; 2017. Dutch.
- 15 Dekkers TJ, Popma A, Agelink van Rentergem JA, Bexkens A, Huizenga HM. Risky decision making in attention deficit/hyperactivity disorder: a meta-regression analysis. *Clin Psychol Rev*. 2016; 45:1–16. doi: 10.1016/j.cpr.2016.03.001. PMID: 26978323.
- 16 Cohen R, Senecky Y, Shuper A, Inbar D, Chodick G, Shalev V, et al. Prevalence of epilepsy and attention-deficit hyperactivity (ADHD) disorder: a population-based study. *J Child Neurol*. 2013;28:120–3. doi: 10.1177/0883073812440327. PMID: 22550087.
- 17 Hesdorffer DC, Ludvigsson P, Olafsson E, Gudmundsson G, Kjartansson O, Hauser WA. ADHD as a risk factor for incident unprovoked seizures and epilepsy in children. *Arch Gen Psychiatry*. 2004;61:731–6. doi: 10.1001/archpsyc.61.7.731. PMID: 15237085.
- 18 Dumont G. *Praktische farmacotherapie bij ADHD*. Lannoo Campus; 2015. Dutch.
- 19 Richer LP, Shevell MI, Rosenblatt BR. Epileptiform abnormalities in children with attention-deficit hyperactivity disorder. *Pediatr Neurol*. 2002;26:125–9. PMID: 11897476.
- 20 Hamoda HM, Guild DJ, Gumlak S, Travers BH, Gonzalez-Heydrich J. Association between attention deficit/hyperactivity disorder and epilepsy in pediatric populations. *Expert Rev Neurother*. 2009;9:1747–54. doi: 10.1586/ern.09.128. PMID: 19951134.
- 21 Davis S, Heyman I, Goodman R. A population survey of mental health problem in children with epilepsy. *Dev Med Child Neurol*. 2003;45: 292–5. PMID: 12729141.
- 22 Huss M, Chen W, Ludolph AG. Guanfacine extended release: a new pharmacological treatment option in Europe. *Clin Drug Investig*. 2016;36:1–25. doi: 10.1007/s40261-015-0336-0. PMID: 26585576. PMID: 4706844.
- 23 Richtlijn ADHD bij volwassenen. [ADHD guidelines in adults.] Nederlandse Vereniging voor Psychiatrie [Dutch Association for Psychiatry]; 2015. [cited 2017 December 29]. Available from: <https://www.nvvp.net/website/nieuws/2015/monodisciplinaire-richtlijn-adhd-bij-volwassenen-fase-1-gepubliceerd>. Dutch.
- 24 Bijwerkingencentrum Lareb. [Centre for side effects drugs]. May 2018. Available from: <https://www.lareb.nl>. Dutch.
- 25 Na KA, Jung HY, Cho SJ, Cho SE. Can we recommend mirtazapine and bupropion for patients at risk for bleeding? A systematic review and meta-analysis. *J Affect Disord*. 2018;225:221–6. doi: 10.1016/j.jad.2017.08.002. PMID: 28841484.
- 26 Hammerness PG, Perrin JM, Shelley-Abrahamson R, Wilens TE. Cardiovascular risk of stimulant treatment in pediatric attention-deficit/hyperactivity disorder: update and clinical recommendations. *J Am Acad Child Adolesc Psychiatry*. 2011;50:978–90. doi: 10.1016/j.jaac.2011.07.018. PMID: 21961773.
- 27 Multidisciplinaire richtlijn voor diagnostiek en behandeling van ADHD bij kinderen en jeugdigen. [Multidisciplinary guideline for diagnosis and treatment of ADHD in children and adolescents]. Utrecht: Trimbos-instituut; 2005. Dutch
- 28 Cooper WO, Habel LA, Sox CM, Chan KA, Arbogast PG, Cheetham TC, et al. ADHD drugs and serious cardiovascular events in children and young adults. *N Engl J Med*. 2011;365:1896–904. doi: 10.1056/NEJMoa1110212. PMID: 22043968. PMID: 4943074.
- 29 Habel LA, Cooper WO, Sox CM, Chan KA, Fireman BH, Arbogast PG, et al. ADHD medications and risk of serious cardiovascular events in young and middle-aged adults. *JAMA*. 2011;306:2673–83. doi: 10.1001/jama.2011.1830. PMID: 22161946. PMID: 3350308.
- 30 Schelleman H, Bilker WB, Strom BL, Kimmel SE, Newcomb C, Guevara JP, et al. Cardiovascular events and death in children exposed and unexposed to ADHD agents. *Pediatrics*. 2011;127:1102–10. doi: 10.1542/peds.2010-3371. PMID: 21576311. PMID: 3387871.

- 31 Dierick M, Claes S, Nayer A de, Cosyns P, Constant E, Souery D. *Handboek Psychofarmacotherapie*. Gent, Belgium; Academia Press: 2012. Dutch.
- 32 Gucuyener K, Erdemoglu AK, Senol S, Serdaroglu A, Soysal S, Kockar AI. Use of methylphenidate for attention-deficit hyperactivity disorder in patients with epilepsy or electroencephalographic abnormalities. *J Child Neurol*. 2003;18:109–12. doi: [10.1177/08830738030180020601](https://doi.org/10.1177/08830738030180020601). PMID: [12693777](https://pubmed.ncbi.nlm.nih.gov/12693777/).
- 33 Torres AR, Whitney J, Gonzalez-Heydrich J. Attention-deficit/hyperactivity disorder in pediatric patients with epilepsy: review of pharmacological treatment. *Epilepsy Behav*. 2008;12:217–33. doi: [10.1016/j.yebeh.2007.08.001](https://doi.org/10.1016/j.yebeh.2007.08.001). PMID: [18065271](https://pubmed.ncbi.nlm.nih.gov/18065271/).
- 34 Hemmer SA, Pasternak JF, Zecker SG, Trommer BL. Stimulant therapy and seizure risk in children with ADHD. *Pediatr Neurol*. 2001;24:99–102. PMID: [11275457](https://pubmed.ncbi.nlm.nih.gov/11275457/).
- 35 Ravi M, Ickowicz A. Epilepsy, attention-deficit/hyperactivity disorder and methylphenidate: critical examination of guiding evidence. *J Can Acad Child Adolesc Psychiatry*. 2016;25:50–8. PMID: [27047557](https://pubmed.ncbi.nlm.nih.gov/27047557/). PMID: [27047557](https://pubmed.ncbi.nlm.nih.gov/27047557/). PMID: [27047557](https://pubmed.ncbi.nlm.nih.gov/27047557/).
- 36 McAfee AT, Landon J, Jones M, Bangs ME, Acharya N, Hornbuckle K, et al. A cohort study of the risk of seizures in a pediatric population treated with atomoxetine or stimulant medications. *Pharmacoepidemiology Drug Saf*. 2013;22:386–93. doi: [10.1002/pds.3390](https://doi.org/10.1002/pds.3390). PMID: [23280590](https://pubmed.ncbi.nlm.nih.gov/23280590/).
- 37 Cevik NG, Orhan N, Yilmaz CU, Arican N, Ahishali B, Kucuk M, et al. The effects of hyperbaric air and hyperbaric oxygen on blood-brain barrier integrity in rats. *Brain Res*. 2013;19:113–21. doi: [10.1016/j.brainres.2013.07.052](https://doi.org/10.1016/j.brainres.2013.07.052). PMID: [23920007](https://pubmed.ncbi.nlm.nih.gov/23920007/).
- 38 Fowler B, Hamilton K, Porlier G. Effects of ethanol and amphetamine on inert gas narcosis in humans. *Undersea Biomed Res*. 1986;13:345–54. PMID: [3775969](https://pubmed.ncbi.nlm.nih.gov/3775969/).
- 39 Clark JE. Moving in extreme environments: inert gas narcosis and underwater activities. *Extreme Phys Med*. 2015;4:1. doi: [10.1186/s13728-014-0020-7](https://doi.org/10.1186/s13728-014-0020-7). PMID: [25713701](https://pubmed.ncbi.nlm.nih.gov/25713701/). PMID: [25713701](https://pubmed.ncbi.nlm.nih.gov/25713701/). PMID: [25713701](https://pubmed.ncbi.nlm.nih.gov/25713701/).
- 40 Rump AF, Siekman U, Kalff G. Effects of hyperbaric and hyperoxic conditions on the disposition of drugs: theoretical considerations and a review of literature. *Gen Pharmacol*. 1999;32:127–33. PMID: [9888265](https://pubmed.ncbi.nlm.nih.gov/9888265/).
- 41 Manning EP. Central nervous system oxygen toxicity and hyperbaric oxygen seizures. *Aerospace Med Hum Perform*. 2016;87:477–86. doi: [10.3357/AMHP.4463.2016](https://doi.org/10.3357/AMHP.4463.2016). PMID: [27099087](https://pubmed.ncbi.nlm.nih.gov/27099087/).
- 42 Wakschlag LS, Briggs-Gowan MJ, Hill C, Danis B, Leventhal BL, Keenan K, et al. Observational assessment of preschool disruptive behavior, Part II: validity of the disruptive behavior diagnostic observation schedule (DB-DOS). *J Am Acad Child Adolesc Psychiatry*. 2008;47:632–41. doi: [10.1097/CHI.0b013e31816c5c10](https://doi.org/10.1097/CHI.0b013e31816c5c10). PMID: [18434925](https://pubmed.ncbi.nlm.nih.gov/18434925/).

Conflicts of interest and funding: nil

Submitted: 04 May 2018; final revision 24 December 2018

Accepted: 07 January 2019

Copyright: This article is the copyright of the authors who grant *Diving and Hyperbaric Medicine* a non-exclusive licence to publish the article in electronic and other forms.
