Attention Deficit Hyperactivity Disorder – an overview

Dr Christine GALEA, Dr Christopher SCIBERRAS, Dr Marthese GALEA

ABSTRACT

Attention Deficit Hyperactivity Disorder (ADHD) is a neurobehavioural disorder found more commonly, but not exclusively, in school-age children. The hallmarks of the condition are inattention and hyperactivity/ impulsivity, which often go together. Although the term ADHD was coined relatively recently, ADHD has in fact been described as early as 1902. This review article will go through the most important historical aspects of the condition, and will also give an account of what is known about the aetiology of ADHD. The diagnostic criteria issued by the American Psychiatric Association in DSM-5, have been last updated in May 2013. This article will highlight the differences between DSM-5 and the previous version, DSM-IV-TR, and will also touch upon the latest developments in electroencephalographybased investigations and imaging studies for ADHD. Although the condition cannot be cured, symptoms can be managed using various modalities such as behaviour intervention strategies and medication, such that the individual affected by ADHD can have the least possible disruption to social and academic functioning.

ABBREVIATIONS

ADHD – Attention Deficit Hyperactivity Disorder DSM-5 – Diagnostic and Statistical Manual of Mental Disorders, 5th Edition

CDC – Centers for Disease Control and Prevention (US) FDA – Food and Drug Administration

INTRODUCTION

Attention Deficit Hyperactivity Disorder (ADHD) is characterized by inattention, hyperactivity and impulsivity. It is a common and widely studied neurobehavioural disorder in school age children (Desmond, 2011). Some leading figures in the ADHD field have questioned whether ADHD, as it is being diagnosed today, actually does exist or whether it has become convenient to merely attribute behavioural

difficulties to ADHD, resulting in overdiagnosis and inappropriate treatment of children.

HISTORY

The recognition of ADHD as a neurobehavioural disorder goes back over one hundred years, although the term ADHD was only coined in 1987. In 1902, Sir George Frederick Still (1868-1941) published a paper in *The Lancet* entitled, 'Some abnormal psychical conditions in children: the Goulstonian lectures'. He described 43 children who he had come across in his practice, who displayed behavioural features that could today be attributed to ADHD, such as poor attention, difficulty with self-regulation, emotional lability, disinhibited behaviour and normal cognitive functioning. Still chose to call this constellation of features, 'Disorders of Moral Control'.

In 1917, the Romanian psychiatrist and neurologist, Constantin von Economo (1876-1931) described the encephalitis epidemic that was rampant between 1915 and 1926 mainly in Europe and North America. This atypical form of encephalitis was known as encephalitis lethargica or Von Economo disease. Adult survivors often developed a parkinsonian-like post-encephalitic phase, sometimes after a latent period of several years, while children tended to develop behavioural difficulties, including overactivity, impulsivity and poor coordination (Arnold, 1995; Wender, 1995). This was called minimal brain dysfunction-like behaviour. Von Economo also described the histology and showed that encephalitis lethargica mainly affected the dopamine-rich areas of the brain, often with autoantibodies against human basal ganglia antigens. Nowadays, it is widely known and accepted that the dopamine pathway is affected in ADHD sufferers (Dawei et al., 2006).

In 1923, Franklin G. Ebaugh, an American physician, published a paper in the *American Journal of Diseases of Children* entitled 'Neuropsychiatric sequelae of acute epidemic encephalitis in children'. Ebaugh was the

first to realise that ADHD could be the result of brain injury in children who had no prior behavioural issues (Spencer, 2007).

In 1937, Charles Bradley (1902-1979), a Rhode Island paediatrician, made an unexpected discovery when he realised that children who had behavioural difficulties and poor academic performance, showed a marked improvement when given benzedrine, a stimulant. At the time, Bradley was carrying out diagnostic procedures called pneumoencephalographies, where most of the patient's cerebrospinal fluid (CSF) was drained to be replaced by air or helium, thereby obtaining a clearer X-ray image of the brain. Benzedrine was administered so as to increase CSF production and reduce the severe headaches that were so common after this procedure. In 1936, benzedrine was FDA-approved as treatment for ADHD symptoms (CDC, 2014).

EPIDEMIOLOGY AND AETIOLOGY

The American Psychiatric Association reports that 5% of children have ADHD (APA, DSM-5, 2013). However, the CDC data obtained from the National Survey of Children's Health which has been carried out every 4 years from 2003, quotes a much higher figure of around 11% of children aged 4-17 years. The diagnosis is on the increase, 5% per year increase over the period 2003–2011. It is more common in boys (13.2% in boys, 5.6% in girls), with an average age at diagnosis of 7 years (CDC, 2013). Approximately half of all children with ADHD go on to have symptoms in adulthood. The National Resource Centre on AD/HD (2014), quotes a prevalence rate of ADHD in adults in the United States, of 4.4%.

It is widely accepted that ADHD is a neurobiologic disorder primarily affecting the dopamine and noradrenaline pathways in the brain (Medscape Pediatrics, n.d.), with a strong genetic influence (Ross, 2012). There is a 50% concordance in first degree relatives. Several other factors have been attributed to the aetiology of ADHD, especially antenatal complications, prematurity and low birth weight, as well as tobacco smoking and alcohol consumption by the mother during pregnancy. Postnatal injury to the prefrontal areas of the brain has also been implicated (CDC, 2014). It is thought that azo dyes, a type of synthetic food colouring, may have an impact on ADHD behaviours, probably by causing zinc deficiency and, thereby, interfering with the processes that eliminate mercury from the body (Dufault, 2009). To this effect, in July 2008, the European Union ruled that as of July 2010, apart from the relevant E number for the particular azo dye, the product must clearly display the phrase 'may have an adverse effect on activity and attention in children' (McBurney, 2011). Studies show no cause-effect relationship between sucrose ingestion and ADHD (Benton, 2008). However, an important point of consideration is that the sugar that is found ubiquitously in processed foods, particularly sweets and sugary drinks, is not sucrose but high fructose corn syrup (HFCS), and therefore, one can only conclude that a high-sucrose diet, not a high-sugar diet, does not cause ADHD. HFCS is often contaminated with mercury while it is produced, and further studies are needed to determine whether ingestion of HFCS is associated with ADHD (Dufault, 2009).

Exposure to heavy metals from the diet, particularly in the prenatal period and in the first few years of life, has an impact on ADHD. High body lead levels have long been known to cause neurobehavioral problems. Mercury exists in two main forms - the inorganic form that is found mainly in soil and water, and the organomercurials. The earliest evidence that mercury is toxic to humans dates from the 1950s-1960s when mercury-containing industrial effluent from acetaldehyde production, was discharged into Minimata Bay, Japan. The result was that people who consumed fish and seafood caught from the bay in question, developed neurological and developmental disorders. Methylmercury is an organic type of mercury that is concentrated in the aquatic food chain. Current FDA recommendations for pregnant women are to eat no more than two portions (12 ounces or 340g) of fish or seafood per week, and to choose fish that is relatively low in mercury, such as salmon, shrimp, pollock, canned light tuna and catfish. Due to their high mercury levels, shark, swordfish, king mackerel and tilefish should be avoided in pregnancy, so as to reduce exposure of the foetus to the heavy metal (FDA, 2004).

Ethylmercury is another type of organic mercury, which however, appears to be less toxic to humans because it is metabolized and excreted differently to methylmercury. The main way in which humans are exposed to ethylmercury is through thiomersal, a preservative used first in the 1930s in biological products and some vaccines, but is now being phased out (FDA, 2014). Thiomersal is still used in some multi-dose vials of inactivated influenza vaccine, but these are not imported in Malta and Gozo. As a result, all vaccines that are administered to children and pregnant women locally, are thiomersal-free or have a trace amount of thiomersal (<1microgram of mercury per dose).

An interesting study that looked at the effects of mercury (from seafood) and lead (from gunshot pellets in birds and animals that are hunted for food) in Arctic Canada, showed that prenatal methylmercury exposure was linked to ADHD symptoms later in childhood, and that even a low lead level in childhood, is associated with ADHD (Boucher et al., 2012).

DIAGNOSIS

The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), was issued by the American Psychiatric Association on 18th May 2013 (APA, DSM-5, 2013). This replaced the previous DSM-IV-TR version. Table 1 highlights the changes in DSM-5 as compared to the previous edition. DSM uses the term ADHD, which is then subclassified into three presentations. The World Health Organization's (WHO)

International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10), in use since 1992, uses the term Hyperkinetic Disorder (HKD), with ADHD listed as a subcategory. ICD-10 will be superseded by ICD-11 in 2017. The DSM-5 criteria cater for adolescents and adults who have ADHD symptoms, which were not necessarily present in early childhood.

The diagnosis of ADHD is made by obtaining a detailed history from the parents, caregivers and teachers, and from the adolescent or adult patient. Behaviour rating scales, of which there are several available, are the main tools used to diagnose ADHD. Conners Rating scale, perhaps the most well known and widely used system, was devised by Carmen Keith Conners, a clinical psychologist who set up the ADHD program at Duke University, USA. This behaviour rating scale is currently in its third edition, Conners 3[™], to reflect

 Table 1: ADHD diagnostic criteria, main differences between DSM-IV-TR and DSM-5

DSM-IV-TR (2000)	DSM-5 (2013)
Criteria now obsolete	Criteria currently in use
ADHD listed under Disruptive Behavior Disorders	ADHD listed under Neurodevelopmental Disorders
9 inattentive & 9 hyperactive	e-impulsive behaviours listed
	examples given of behaviours expected in older child/ adolescent
6 symptoms needed	to make a diagnosis
	only 5 symptoms needed to make a diagnosis in >17 years & adults
symptoms which are not in-keeping with child's d	evelopmental level, present for 6 months or longer
symptoms must be present and cause impairment by 7 years of age	symptoms must be present, but not necessarily cause impairment, by 12 years of age
symptoms cause some impairment in at least 2 settings	several symptoms present in two or more settings
'clinically significant impairment in social, academic or occupational functioning'	'clear evidence that the symptoms interfere with, or reduce the quality of, social, academic, or occupational functioning'
3 subtypes:	3 presentations:
Predominantly Inattentive Type	Predominantly Inattentive Presentation
Predominantly Hyperactive-Impulsive Type	Predominantly Hyperactive-Impulsive Presentation
Combined Type	Combined Presentation
	Can change from one to the other
If symptoms no longer fulfill diagnosti	ic criteria, specify in 'Partial Remission'
	ADHD diagnosis made as mild, moderate or severe
ADHD cannot be diagnosed with Autistic Spectrum Disorder	Recognizes that ADHD can coexist with Autistic Spectrum Disorder

Imaging studies, including single-photon emission computed tomography (SPECT), positron emission tomography (PET), and functional magnetic resonance imaging (fMRI), have shown that there is about a 3 year delay in brain maturation and some differences in brain activity in children with ADHD when compared to controls (Watson, 2013). SPECT, a costly procedure, which uses an injectable radioactive substance to measure blood flow and brain activity, is not yet FDA-approved for ADHD diagnosis. In July 2013, FDA approved the first brain imaging test for ADHD diagnosis in patients of 6-17 years of age. This Neuropsychiatric EEG-Based Assessment Aid (NEBA) System is a 15 minute EEGbased test which measures the theta-beta ratio of brain waves emitted (FDA, 2013). This ratio is known to be higher in individuals with ADHD as compared to controls. The procedure, pioneered by Howard Merry, has come under criticism because of the way FDA approved the test based only on Merry's study of 275 individuals, and also because of the cost involved to carry out this test (Brauser, 2014). NEBA is not a stand-alone diagnostic test for ADHD, but should be used in conjunction with the standard behaviour rating scales and fulfilment of DSM-5 criteria. It remains to be seen whether NEBA is useful in distinguishing ADHD from bipolar disorder in adolescents, a distinction that can be very difficult to make accurately.

It is imperative that a diagnosis of ADHD is made accurately by stringent use of the DSM 5 criteria. Otherwise, we run the risk of overdiagnosing and overtreating patients. Some leading figures in the ADHD field have questioned whether ADHD really does exist. To cite one example, reference is made to an opinion piece that was published on *Time* on 14th March 2014 by Dr Richard Saul, a fellow with the American Academy of Paediatrics and an associate fellow of the American Academy of Neurology. 'I've come to believe based on decades of treating patients that ADHD — as currently defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM) and as understood in the public imagination — does not exist' (Saul, 2014).

MANAGEMENT

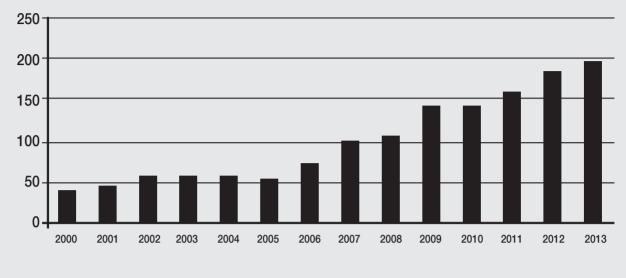
Apart from the use of medications, the management of ADHD involves behavioural intervention strategies and educating the family on how to deal with the condition. It also has implications on schooling - some children with ADHD may benefit from the help of a Learning Support Assistant.

The Feingold[®] diet is an elimination diet that is free from dyes, artificial flavours, sweeteners and preservatives, and can be used both as a diagnostic tool to determine whether any dietary factors are negatively affecting ADHD behaviours, as well as a treatment modality for ADHD. Using a double-blind randomised controlled trial, Rucklidge et al., (2014), showed that a micronutrient supplement consisting of various vitamins and minerals may have some efficacy in managing adults with ADHD.

Drugs are FDA-approved from 6 years of age, and once started, it is recommended to stop the treatment for a couple of weeks, usually in the summer, so as to determine whether the patient still requires medication or not. Other factors to keep in mind are adverse drug effects, drug interactions, co-morbid conditions and parent and child-preferences.

The two main groups of drugs for ADHD treatment are the stimulants and non-stimulants. The drugs that are available locally are the stimulants Ritalin[®] and Concerta[®] (both methylphenidate) and the non-stimulant Strattera[®] (atomoxetine).

Methylphenidate is a dopamine-reuptake inhibitor, and so increases extracellular dopamine in the striatium. Ritalin® is an immediate-release form with a duration of action of 3-4 hours (SPC Ritalin®, 2013), whereas Concerta[®], which is intermediate-release with a duration of action of up to 12 hours (SPC Concerta[®], 2014), has the advantage of once daily dosing. The dose is increased in a stepwise fashion over a 4 week period. Around 75% of patients respond to treatment, while the remainder either show no improvement or have side effects which necessitate stopping the drug. The most common side effects are reduced appetite, transient weight loss, irritability and sleep disturbance. In January 2009, the European Medicines Agency (EMEA) issued some recommendations on the safe use of methylphenidate (EMEA, 2009). Because of the cardiovascular and cerebrovascular risks, all patients should have their blood pressure and heart rate measured before starting treatment, and every 3 months while on medication. Prior to starting methylphenidate, one should ask about Figure 1: Number of patients started on Ritalin® in Malta over the period 2000-2013



Approvals for Ritalin®

a family history of cardiovascular disorders, and in those patients with a positive family or personal history or an abnormal cardiovascular examination, an ECG and cardiology consultation would be warranted. The patient's height and weight should be measured, and one must look out for the development of psychiatric disorders.

The use of methylphenidate locally has shown a 4 fold increase since the year 2000, as shown in Figure 1.

Strattera[®] is a selective noradrenaline reuptake inhibitor, with a duration of action of 12 hours. It is usually given as a single daily dose in the morning, and the capsule has to be swallowed whole. The most common side effects are sleep disturbances, fatigue, nervousness, dry mouth and stomach upset. Suicidal ideation (0.4% in Strattera-treated group as compared to 0% in the placebo group); severe liver injury, including hepatic failure, which was only picked up in post-marketing surveillance of the drug; and sudden deaths in children who had an underlying structural cardiac abnormality, have been reported (SPC Strattera, 2013).

Acknowledgements

Mr Victor Pace, Directorate of Public Health, for providing the authors with the data required to draw up Figure 1.

ASSOCIATED IMPAIRMENTS

People who suffer from ADHD, may also have associated impairments. The most common problems are difficulty in peer-relationships and an increased risk of injuries. An associated learning disorder is found in approximately half of 6-11 year olds with ADHD. Data from the CDC National Health Interview Survey (2008) shows that in the US over the period 2004-2006, 5% of children aged 6-17 years had ADHD without a learning disability, 5% had a learning disability without ADHD, and 4% had both conditions. Oppositional Defiant Disorder and Conduct Disorder are less common.

The ADHD Family Support Group Malta is a non-governmental organization which holds monthly meetings for families of ADHD-sufferers as well as the public in general.

CONCLUSION

Over the past years, ADHD has been studied closely and much research has been carried out, particularly to elucidate the aetiology of the condition, to make a more accurate and timely diagnosis, and for effective treatments to be made available. However, much still remains to be known.

Reference

- American Psychiatric Association, 2013. Diagnostic and Statistical Manual of Mental Disorders, Fifth edition: DSM-5. [pdf] Vancouver: American Psychiatric Association. Available at: http://www.DSM5.org [Accessed 19 April 2014].
- American Psychiatric Association, 2013. DSM-5 Attention Deficit/Hyperactivity Disorder Fact Sheet. [pdf] Vancouver: American Psychiatric Association. Available at: http://www.dsm5.org/Documents/ADHD%20Fact%20Sheet.pdf> [Accessed 19 April 2014].
- Armstrong, T., 1996. ADD: Does It Really Exist? [online] Available at: <http:// education.jhu.edu/PD/newhorizons/Exceptional%20Learners/ADD%20 ADHD/Articles/ADD%20Does%20it%20Exist/> [Accessed 19 April 2014].
- Arnold, L.E. and Jensen, P.S., 1995. Attention Deficit Disorders. In: H.I. Kaplan and B.J. Sadock, eds. 1995. Comprehensive Textbook of Psychiatry, vol 2. 6th edition. Baltimore, Maryland. Williams & Wilkins.
- Benton, D., 2008. Sucrose and Behavioral Problems. Critical Reviews in Food Science and Nutrition, 48(5), pp.385-401.
- Boucher, O., et al., 2012. Prenatal Methylmercury, Postnatal Lead Exposure, and Evidence of Attention Deficit/Hyperactivity Disorder among Inuit Children in Arctic Quebec. Environmental Health Perspectives, 120(10), pp.1456-1461.
- Brauser, D., 2014. Mixed Reaction to FDA Approval of ADHD Brain-Wave Test. Medscape, [online] Available at: http://www.medscape.com/viewarticle/809079 [Accessed 21 April 2014].
- Centers for Disease Control and Prevention, 2014. Attention Deficit / Hyperactivity Disorder (ADHD). [pdf] Atlanta: CDC. Available at: http://www.cdc.gov/ncbdd/adhd/facts.html [Accessed 20 April 2014].
- Conners, C. K., 2013. Conners 3rd Edition TM. Multi-Health Systems. [online] Available at: <http://www.mhs.com/product.aspx?gr=edu&id=overview&p rod=conners3> [Accessed 19 April 2014].
- Cunningham, N.R. and Jensen, P., 2011. Attention-Deficit/Hyperactivity Disorder. In: R.M. Kliegman et al., eds. 2011. Nelson Textbook of Pediatrics. 19th edition. Philadelphia: Elsevier Saunders. Ch.30.
- Dawei, L., et al., 2006. Meta-analysis shows significant association between dopamine system genes and attention deficit hyperactivity disorder (ADHD). *Human Molecular Genetics*, [online] Available at: http://hmg.oxfordjournals.org/content/15/14/2276.long [Accessed 28th October 2014].
- Dufault, R., et al., 2009. Mercury exposure, nutritional deficiencies and metabolic disruptions may affect learning in children. *Behavioral and Brain Functions*, [online] Available at: http://www.behavioralandbrainfunctions.com/ content/5/1/44> [Accessed 30 June 2014].
- Eli Lilly and Company (Ireland) Limited, 2013. Summary of Product Characteristics, Strattera[®]. [pdf] Dublin: Eli Lilly and Company (Ireland) Limited. Available at: http://www.medicines.org.uk/emc/medicine/14482/SPC/Strattera+1 Omg, +18mg, +25mg, +40mg, +60mg, +80mg+or+100mg+hard+capsul es./> [Accessed 25 April 2014].
- European Medicines Agency, 2009. European Medicines Agency makes recommendations for safer use of Ritalin and other methylphenidate-containing medicines in the EU. Press release, 22 January 2009.
- FDA, U.S. Food and Drug Administration, 2004. What You Need to Know About Mercury in Fish and Shellfish (Brochure). [pdf] Silver Spring, Maryland: FDA. Available at: http://www.fda.gov/food/resourcesforyou/consumers/ ucm110591.htm [Accessed 30 June 2014].
- FDA, U.S. Food and Drug Administration, 2013. FDA permits marketing of first brain wave test to help assess children and teens with ADHD. Press release, 15 July 2013.
- FDA, U.S. Food and Drug Administration, 2014. Thimerosal in Vaccines. [pdf] Silver Spring, Maryland: FDA. Available at: http://www.fda.gov/biologicsbloodvaccines/safetyvauilability/vaccinesafety/ucm096228 [Accessed 21 April 2014].
- Feingold® Association of the United States, 2013. [online] Available at: http://www.feingold.org/what.php> [Accessed 30 June 2014].
- Janssen-Cilag Ltd., 2014. Summary of Product Characteristics, Concerta[®]. [pdf] High Wycombe, Bucks: Janssen-Cilag Ltd. Available at:
- <https://www.medicines.org.uk/emc/medicine/8382/SPC/ Concerta+XL+18+mg+-+36+mg+prolonged+release+tablets/> [Accessed 25 April 2014].
- Kelly, A.M., Margulies, D.S. and Castellanos, F.X., 2007. Recent advances in structural and functional brain imaging studies of attention-deficit/ hyperactivity disorder. *Current Psychiatry Reports*, [e-journal and in print] 9(5). Abstract only. Available through: PubMed.gov website http://www.ncbi.nlm.nih.gov/pubmed/17915080 [Accessed 15 April 2014].

- Lawton, G., 2014. A Musing Pediatrician. My Own Private A.D.H.D. Conspiracy Theory. Medscape [online] Available at: <htp://boards.medscape.com/forum s/?128@@.2a5c1c0flcomment=1> [Accessed 19 April 2014].
- McBurney, M., 2011. ADHD, Medication risks, and Labeling of Azo Dyes. [online] Available at: <http://www.dsm.com/campaigns/talkingnutrition/en_US/ talkingnutrition-dsm-com/2011/12/20111213azo-dyes.html> [Accessed 19 April 2014].
- Medscape Pediatrics, n.d. Part 1. ADHD: Recent Advances in Diagnosis and Treatment. [online] Available at: <http://www.medscape.org/viewarticle/443113> [Accessed 20 April 2014].
- National Resource Center on AD/HD: A Program of CHADD, 2014. ADHD Data and Statistics. Lanham, Maryland: National Resource Centre on AD/HD.
- Novartis Pharmaceuticals UK Ltd, 2013. Summary of Product Characteristics, Ritalin[®]. [pdf] Surrey: Novartis Pharmaceuticals UK Ltd. Available at: ">http://www.medicines.org.uk/emc/medicine/1316/SPC/ritalin/> [Accessed 25 April 2014].
- Pastor, P.N. and Reuben, C.A., 2008. Diagnosed Attention Deficit Hyperactivity Disorder and Learning Disability: United States, 2004-2006. Washington: National Center for Health Statistics. Vital and Health Statistics.
- Porter, E., 2012. Conners Scale for Assessing ADHD. [online] Available at: ">http://www.healthline.com/health/adhd/conners-scale#1>"/></adhdine@ndowada/"/></adhdine@ndowada/"/>
- Ross, R.G., 2012. Advances in the Genetics of ADHD. The American Journal of Psychiatry, [online] Available at: <http://www.ajp.psychiatryonline.org/article. aspx?articleid=483676> [Accessed 22 April 2014].
- Rucklidge, J., et al., 2014. Vitamin-mineral treatment of attention-deficit hyperactivity disorder in adults: double-blind randomised placebo-controlled trial. *The British Journal of Psychiatry*, [online]. Abstract only. Available at: http://bjp.rcpsych.org/content/204/4/306.abstract [Accessed 30 June 2014].
- Saul, R., 2014. Doctor: ADHD Does Not Exist. Time. [online] Available at: http://time.com/25370/doctor-adhd-does-not-exist/ [Accessed 19 April 2014].
- Spencer, T.J., Biederman, J. and Mick, E., 2007. Attention-Deficit/Hyperactivity Disorder: Diagnosis, Lifespan, Comorbidities, and Neurobiology. *Journal of Pediatric Psychology* 32(6) pp.631-642.
- Watson, S., 2013. Worth 1,000 Words: What a Brain Scan Reveals About ADHD. [online] Available at: <http://www.healthline.com/health-slideshow/brainscans-adhd#promoSlide> [Accessed 22 April 2014].
- Wender, P.H., 1995. Attention Deficit Hyperactivity Disorder in Adults. New York: Oxford University Press. pp.80-81.
- Wender, P.H., Wolf, L.E. and Wasserstein J., 2001. Adults with ADHD: an Overview. Annals of the New York Academy of Sciences, 931, pp.1-16.

Dr Christine GALEA

MD, MRCPCH

Resident Specialist, Department of Paediatrics, Mater Dei Hospital

Email: christine.a.galea@gov.mt

Dr Christopher SCIBERRAS

MD, MRCPCH, MRCP(UK), MSc.Comm. Paeds (Warwick), DCH (Dublin), Cert. Dev. Paeds. (London) Consultant Paediatrician, Community Paediatrics and Disability Services, Department of Paediatrics, Mater Dei Hospital

Dr Marthese GALEA

MD, MRCPCH Resident Specialist, Department of Paediatrics, Mater Dei Hospital