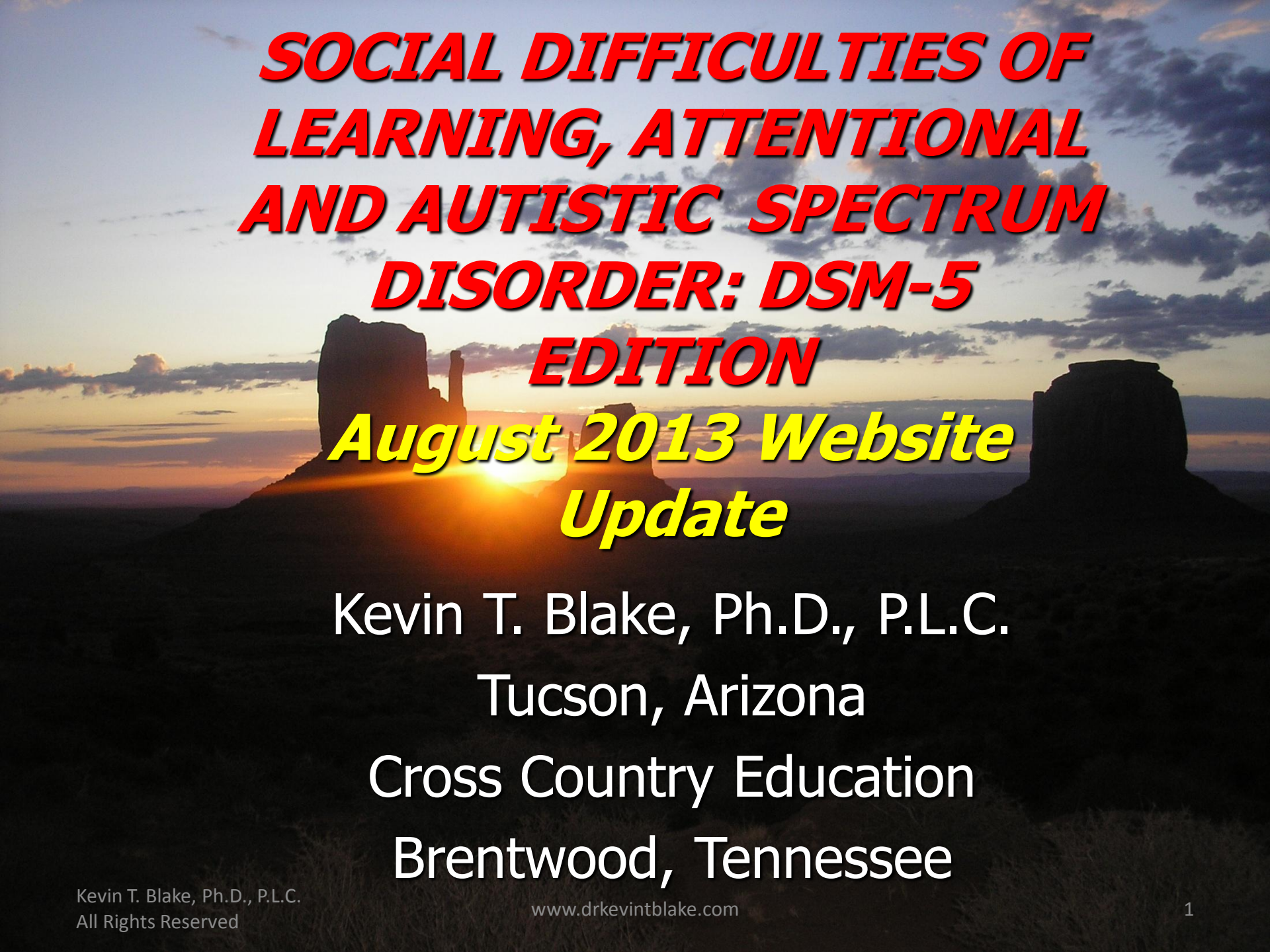

SOCIAL DIFFICULTIES OF LEARNING, ATTENTIONAL AND AUTISTIC SPECTRUM DISORDER: DSM-5 EDITION

August 2013 Website Update

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Medical Test For AD/HD?

- **July 15, 2013: FDA permits marketing of first brain wave test to help assess children and teens for ADHD**
- **"The U.S. Food and Drug Administration today allowed marketing of the first medical device based on brain function to help assess attention-deficit/hyperactivity disorder (ADHD) in children and adolescents 6 to 17 years old. When used as part of a complete medical and psychological examination, the device can help confirm an ADHD diagnosis or a clinician's decision that further diagnostic testing should focus on ADHD or other medical or behavioral conditions that produce symptoms similar to ADHD…"**

Medical Test for AD/HD?

"…The device, the Neuropsychiatric EEG-Based Assessment Aid (NEBA) System, is based on electroencephalogram (EEG) technology, which records different kinds of electrical impulses (waves) given off by neurons (nerve cells) in the brain and the number of times (frequency) the impulses are given off each second.

The NEBA System is a 15- to 20-minute non-invasive test that calculates the ratio of two standard brain wave frequencies, known as theta and beta waves. The theta/beta ratio has been shown to be higher in children and adolescents with ADHD than in children without it…"

Medical Test for AD/HD?

"…The FDA reviewed the NEBA System through the de novo classification process, a regulatory pathway for some low- to moderate-risk medical devices that are not substantially equivalent to an already legally marketed device.

In support of the de novo petition, the manufacturer submitted data including a clinical study that evaluated 275 children and adolescents ranging from 6 to 17 years old with attention or behavioral concerns. Clinicians evaluated all 275 patients using the NEBA System and using standard diagnostic protocols, including the Diagnostic and Statistical Manual of Mental Disorders IV Text Revision(DSM-IV-TR) criteria, behavioral questionnaires, behavioral and IQ testing, and physical exams to determine if the patient had ADHD…"

Medical Test for AD/HD?

"… An independent group of ADHD experts reviewed these data and arrived at a consensus diagnosis regarding whether the research subject met clinical criteria for ADHD or another condition. The study results showed that the use of the NEBA System aided clinicians in making a more accurate diagnosis of ADHD when used in conjunction with a clinical assessment for ADHD, compared with doing the clinical assessment alone."

Medical Test for AD/HD Reference

Author (July 15, 2013). FDA News Release: FDA permits marketing of first brain wave test to help assess children and teens for ADHD. Washington, DC: U.S. Department of Health and Human Services, Food and Drug Administration. From website: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm360811.htm.

Patent on "Neba System"

Patent number: US 8311622 B2

Publication date: November 15, 2012

Inventors: James D. Falk and Steven M. Snyder

Original Assignee: Neba Health LLC

Systems and methods for analyzing and assessing depression and other mood disorders using electroencephalographic (EEG) measurements. From website: https://www.google.com/patents/US8311622.

EEG as Diagnostic Marker for AD/HD

- **An 18% False positive AD/HD Diagnosis rate is too high**
- **EEG does not account for comorbidity**
- **No replication of studies have been done yet**
- **Study subject groups do not match and use very different methodologies**
- **Too much chance for conflict of interest (e.g. company stockholders, etc.)**

Reference

Loo, S.K., Makeig, S. (2012). Clinical Utility of EEG in Attention-Deficit/Hyperactivity Disorder: A Research Update. Neurotherapeutics, 9(3), 569-587. From website: http://sccn.ucsd.edu/~scott/pdf/LooMakeig_Neurotherapeutics12_share.pdf.

Meta-Analysis of EEG Theta/Beta Ratio Diagnostics with AD/HD

"Excessive TBR (Theta/Beta Ratio, sic) cannot be considered a reliable diagnostic measure of ADHD, however a substantial sub-group of ADHD patients do deviate on this measure and TBR has prognostic value in this sub-group, warranting its use as a prognostic measure rather than a diagnostic measure" (p. 374).

Arns, M, Conners, C.K., and Kraemer, H.C. (May 29, 2013). A Decade of EEG Theta/Beta Ratio Research in ADHD: A Meta-Analysis. Journal of Attention Disorders, 17(5), 374-383. From website: http://jad.sagepub.com/content/17/5/374.abstract.

Brown on EEG Theta/Beta Ratio Diagnosis of AD/HD

"…Although these measures are useful research tools, they are not sufficiently developed or normed to make them useful or valid for assessment to make or deny an ADHD diagnosis for any specific in individual…All of these measures provide only snapshots of brain functioning in brief moments of time and do not adequately capture the wide situational variability in functioning characteristic of most individuals with ADHD" (p. 4).

Reference

Brown, T.E. (2013). A New Understanding of ADHD in Children and Adults: Executive Function Impairments. New York, NY: Routledge.

Tom Brown's Letter To The FDA

"As a clinician and researcher confronted daily with the frustrations and suffering of children and adults with ADHD, I urge your agency to reconsider its approval of this device so it does not become a barrier to those who need access to diagnosis and treatment for this complex and often persistent disorder".

Brown, T.E. (July 22, 2013). An Open Letter from Dr. Brown Expressing Concern about a Recent FDA Action Related to ADHD. From website: http://www.drthomasebrown.com/an-open-letter-from-dr-brown-expressing-concern-about-a-recent-fda-action-related-to-adhd-2/.

Tom Brown on Neba System

Brown (July, 19, 2013). Said he did not believe the Neba system was useful due to its very high level of false negative "diagnoses" when used with AD/HD individuals. He said it was not helpful for ADHD diagnosis.

Brown, T.E. (July 19, 2013). Advanced Assessment and Treatment of Attention Deficit Disorders. Washington, DC: American Psychological Association Continuing Education in Psychology; webinar.

CHADD of the Neba System

"However, a recent meta-analysis which included all literature published on this measure to date – including a study from authors affiliated with NEBA – concluded that Theta/Beta ratio is not a reliable diagnostic marker for ADHD.* In a minority of ADHD patients (~25-30%), this measure is consistently found to deviate; however, such a percentage is too low to be used as a standalone diagnostic test".

Arns, M. (July 22, 2013). A comment on: FDA permits marketing of first brain wave test to help assess children and teens for ADHD. Landover, MD: CHADD Leadership Blog. From website: http://www.chaddleadershipblog.blogspot.com/2013/07/a-brain-wave-diagnostic-test-for-adhd.html.

Neurobiofeedback and AD/HD

"Thus, *the findings of the studies reviewed here do not support NF training as a firstline, stand-alone treatment for ADHD. Until NF training can demonstrate an effect that is* either superior to placebo control or equivalent to other empirically supported treatments for ADHD (i.e., psychostimulant medication, behavior therapy), it simply cannot be considered a primary treatment modality…"

Neurobiofeedback and AD/HD

"… In fact, given the expense and time/labor intensive nature of the NF, one might be hard pressed to recommend NF training over stimulant medication even if comparable effect sizes were demonstrated, unless there are clear contra-indications for medication or NF demonstrates continued long-term benefit after completion of treatment that exceeds that of medication treatment" (p. 23)

Neurobiofeedback and AD/HD

"While NF treatment is not recommended as a first-line treatment, *SCP* (Slow Cortical Potential, sic) *training appears likely to be efficacious as an adjunct treatment for a subset (~50%) of children with ADHD.* Among positive responders, SCP training appears to have specific effects on enhanced cortical regulation that is associated with improved ADHD symptomatology. Because not all children with ADHD can be expected to improve with NF training, it should be used as an adjunct treatment or as part of a multimodal treatment package that includes medication, psychosocial, and educational accommodations" (p. 23).

Reference

Loo, S.K., Makeig, S. (2012). Clinical Utility of EEG in Attention-Deficit/Hyperactivity Disorder: A Research Update. Neurotherapeutics, 9(3), 569-587. From website: http://sccn.ucsd.edu/~scott/pdf/LooMakeig_Neurotherapeutics12_share.pdf.

6 Month Follow-up of AD/HD Children's Friendships

"At Time 2, the friends of the participants with ADHD reported less positive friendship quality and more conflict with their friends than at Time 1. They were also considerably less satisfied with their friendship than 6 months prior. In contrast, the friends of comparison children reported fewer negative friendship features, more positive friendship features and a slightly greater friendship satisfaction than at Time 1. In sharp contrast with the invited friends' reports, referred children with ADHD did not report deterioration in their friendship quality over time…"

6 Month Follow-up of AD/HD Children's Friendships

"… Unlike comparison children who significantly reduced violations of game rules between Time 1 and Time 2, children with ADHD broke more game rules during the same period. In negotiating with friends, comparison children, but not children with ADHD, reduced the number of self-centered and insensitive proposals at Time 2. Controlling for Time 1 variance, violations of game rules and a self-centered, insensitive negotiation approach predicted deterioration in friendship quality for children with and without ADHD over time".

Reference

Normands, S. et al (June 6, 2013). Continuities and Changes in the Friendships of Children with and Without ADHD: A Longitudinal, Observational Study. Journal of Abnormal Child Psychology. From website: https://www.ncbi.nlm.nih.gov/m/pubmed/23740170/?i=3&from=/8362017/related.

AD/HD, Sleep & Emotional Problems

"We observed an increased sleep-dependent emotional memory bias in healthy children compared to children with ADHD and healthy adults. Frontal oscillatory EEG activity (slow oscillations, theta) during sleep correlated negatively with emotional memory performance in children with ADHD. When combining data of healthy children and adults, correlation coefficients were positive and differed from those in children with ADHD…"

AD/HD, Sleep & Emotional Problems

"… Since children displayed a higher frontal EEG activity than adults these data indicate a decline in sleep-related consolidation of emotional memory in healthy development. In addition, it is suggested that deficits in sleep-related selection between emotional and non-emotional memories in ADHD exacerbate emotional problems during daytime as they are often reported in ADHD."

Reference

Prehn-Kristensen, A., Munz, M., Molzow, I., Wilhelm, I., Wiesner, C.D., et al. (2013) Sleep Promotes Consolidation of Emotional Memory in Healthy Children but Not in Children with Attention-Deficit Hyperactivity Disorder. PLoS ONE, 8(5): e65098. doi:10.1371/journal.pone.0065098

Sleep Hygiene & AD/HD

- About 30% of typically developing children have sleep disorders
- 50 to 80% of those with AD/HD will have sleep disorders
- A recent study found no difference between the sleep hygiene of typically developing children and those with AD/HD

Bessey, M., Coulombe, J.A., and CarKum, P. (May, 2013). Sleep Hygiene in Children with ADHD: Findings and Recommendations. ADHD Report, 21(3), 1-6.

Genetics, Bipolar Disorder & AD/HD

"These data suggest that variants within *DAT1* may predispose to a subtype of BD characterized by early prodromal features that include attentional deficits" (p. 137).

Greenwood TA, Joo E-J, Shektman T, Sadovnick AD, Remick RA, Keck PE, McElroy SL, Kelsoe JR. (March, 2013). Association of Dopamine Transporter Gene Variants With Childhood ADHD Features in Bipolar Disorder. American Journal of Medical Genetics, Part B: Neurpsychitric Genetics, 162(2)B:137–145. From website: http://onlinelibrary.wiley.com/doi/10.1002/ajmg.b.32108/abstract.

Genes May Effect Atomoxetine Response in Some with AD/HD

"The results of this study suggest that DNA variants of both *SLC6A2* and *ADRA2A* in the adrenergic neurotransmitter system might alter the response to atomoxetine…" (p. 1127).

Yang, L. et al. (July, 2013). **Adrenergic neurotransmitter system transporter and receptor genes associated with atomoxetine response in attention-deficit hyperactivity disorder children. Journal of Neurotransmission, 7, 1127-1133. from website: http://link.springer.com/article/10.1007%2Fs00702-012-0955-z.**

Seizures & Atomoxetine

"These results do not support an increase in the risk of seizure with atomoxetine therapy. The risk of seizure was not significantly different between pediatric patients taking atomoxetine compared with those taking stimulants" (p. 386).

McAfee, A.T. et al. (April, 2013). A cohort study of the risk of seizures in a pediatric population treated with atomoxetine or stimulant medications. Pharmacoepidemiology and Drug Safety, 4, 386-393. From website: http://onlinelibrary.wiley.com/doi/10.1002/pds.3390/abstract.

Sluggish Cognitive Tempo & Heritability

"Our results support at the etiological level the findings of previous psychometric and longitudinal studies of ADHD, which yielded evidence of the 3 distinct—albeit correlated—problem dimensions of inattentiveness, hyperactivity-impulsivity, and sluggish cognitive tempo".

Moruzzi, S. et al. (February, 2013). A Twin Study of the Relationships among Inattention, Hyperactivity/Impulsivity and Sluggish Cognitive Tempo Problems. DOI: 10.1007/s10802-013-9725-0. From website: http://link.springer.com/article/10.1007%2Fs10802-013-9725-0.

AD/HD and Major Depressive Disorder

- **"A history of ADHD in adolescence was associated with elevated risk of MDD through early adulthood and this relationship remained significant after controlling for psychosocial impairment in adolescence and co-occurring psychiatric disorders".**
- **"Additional significant, robust predictors of MDD included female gender, a lifetime history of an anxiety disorder, and poor coping skills in mid-adolescence, as well as the onset of anxiety, oppositional defiant disorder, and substance-use disorder after mid-adolescence."**

Reference

Meinzer, M.C. et al. (June, 2013). Attention-deficit/hyperactivity disorder in adolescence predicts onset of major depressive disorder through early adulthood. Depression and Anxiety, 30(6). 546-553. From website: http://www.ncbi.nlm.nih.gov/pubmed/23424020.

AD/HD & Seizures

"The present study compared groups of clinically referred children with both ADHD-Inattentive subtype (ADHD-I) and ADHD-Combined subtype (ADHD-C) to children with ADHD-I and ADHD-C and epilepsy on neuropsychological measures of intellectual functioning, auditory attention, working memory, and sustained attention and response inhibition. Those with ADHD and epilepsy performed more poorly on measures of intellectual function (e.g., Full-Scale IQ, Verbal IQ, Performance IQ) as well as auditory attention and working memory…"

AD/HD & Seizures

“Differences across the groups were also seen on a continuous performance test. Follow-up correlational analyses showed that variables such as seizure frequency and number of antiepilepsy medications predicted cognitive dysfunction in the epilepsy groups. Overall results suggest that the neuropsychological endophenotypes in developmental ADHD versus ADHD in epilepsy differ with seizure-related variables predicting cognitive dysfunction”.

Reference

MacAllister, W.S. et al. (August, 2012). Neuropsychological Endophenotypes in ADHD With and Without Epilepsy. Applied Neuropsychology: Child, 1(2). DOI:10.1080/21622965.2012.709421. From website: http://www.tandfonline.com/doi/abs/10.1080/21622965.2012.709421#.UfmA-6w-GuI.

AD/HD, Combined Vs. Inattentive Neuropsychological Performance

"Children with ADHD-C and ADHD-PI performed significantly poorer on the mathematics calculation, written expression, fluid reasoning, and visual–motor tests compared with the controls. Inattention, but not hyperactivity or impulsivity, was found to significantly predict performance on these measures. The role of inattention on these tasks is important for understanding why children with both subtypes of ADHD experience significant academic problems even when performing in the average range on achievement tests".

Reference

Semrud-Clikeman, M. (May, 2012). The Role of Inattention on Academics, Fluid Reasoning, and Visual–Spatial Functioning in Two Subtypes of ADHD. Applied Neuropsychology: Child, 1(1), DOI:10.1080/21622965.2012.665766. From website: http://www.tandfonline.com/doi/full/10.1080/21622965.2012.665766#.UfmDz6w-GuI.

AD/HD, Working Memory & Reinforcement

"With standard reinforcement the STM (Short-Term Memory, sic.), CE (Central Executive, sic.), and WM (Working Memory, sic.) performance of children with ADHD was worse than that of controls. High reinforcement improved STM and WM performance more in children with ADHD than in controls, but was unable to normalize their performance. High reinforcement did not appear to improve the CE-related performance of children with ADHD and controls…"

AD/HD, Working Memory & Reinforcement

"Motivational deficits have a detrimental effect on both the visuospatial WM performance and the STM performance of children with ADHD. Aside from motivational deficits, both the visuospatial STM and the CE of children with ADHD are impaired, and give rise to their deficits in visuospatial WM" (p. 901).

Reference

Dovis, S. et al. (August, 2013). What Part of Working Memory is not Working in ADHD? Short-Term Memory, the Central Executive and Effects of Reinforcement. Journal of Abnormal Child Psychology, 6, 901-917. From website: http://link.springer.com/article/10.1007%2Fs10802-013-9729-9.

Adult AD/HD & Working memory Deficits

"While both groups performed significantly better during the PH (phonological, sic.) task relative to the VS (Visual-Spatial, sic.) task, adults with ADHD exhibited significant deficits across both working memory modalities. Further, the ADHD group recalled disproportionately fewer PH and VS stimuli as set-size demands increased. Overall, the CE (Central Executive, sic.) and PH storage/rehearsal processes of adults with ADHD were both significantly impaired relative to those of the healthy control adults; however, the magnitude of the CE effect size was much smaller compared to previous studies of children with the disorder. Collectively, results provide support for a lifelong trajectory of WM (Working Memory, sic.) deficits in ADHD" (p. 532)

Reference

Alderson, R. et al. (May, 2013). Working memory deficits in adults with attention-deficit/hyperactivity disorder (ADHD): An examination of central executive and storage/rehearsal processes. Journal of Abnormal Psychology, 122(2), May 2013, 532-541. doi: 10.1037/a0031742.

Boredom and AD/HD

- **People with AD/HD may be more prone to boredom due to anomalies in their orbitofrontal cortex. This would cause them not to find typical activities as rewarding as non-AD/HD people, hence the AD/HD person will attempt to find more stimulating activities. Often these can be more dangerous activities.**

Danckert, J. (July/August, 2013). Decent of the Doldrums. Scientific American Mind, 24(3), 54-59.

Specific Learning Disorder-Dyslexia is Not a Disorder of the Visual System

"Using fMRI, we demonstrate in typical readers a relationship between reading ability and activity in area V5/MT during visual motion processing and, as expected, also found lower V5/MT activity for dyslexic children compared to age-matched controls. However, when dyslexics were matched to younger controls on reading ability, no differences emerged, suggesting that weakness in V5/MT may not be causal to dyslexia…"

Specific Learning Disorder-Dyslexia is Not a Disorder of the Visual System

"…To further test for causality, dyslexics underwent a phonological-based reading intervention. Surprisingly, V5/MT activity increased along with intervention-driven reading gains, demonstrating that activity here is mobilized through reading. Our results provide strong evidence that visual magnocellular dysfunction is not causal to dyslexia but may instead be consequential to impoverished reading" (p. 180).

Reference

Olulade, O.A., Napoliello, E.M. and Eden, G.F. (June, 6 2013). Abnormal Visual Motion Processing is not a Cause of Dyslexia. Neuron, 79(1), 180-190. From website: http://www.cell.com/neuron/abstract/S0896-6273(13)00395-4.

Early Detection Dyslexia Gene

"We previously identified a putative functional risk variant, named BV677278 for its GenBank accession number, for RD in *DCDC2*. This variant consists of an intronic microdeletion and a highly polymorphic short tandem repeat (STR) within its breakpoints. We have also shown this STR to bind to an unknown nuclear protein with high specificity. Here, we replicate BV677278's association with RD, expand its association to LI, identify the BV677278-binding protein as the transcription factor ETV6, and provide compelling genetic evidence that BV677278 is a regulatory element that influences reading and language skills…"

Early Detection Dyslexia Gene

"… We also provide evidence that BV677278 interacts nonadditively with *KIAA0319*, an RD-associated gene, to adversely affect several reading and cognitive phenotypes. On the basis of these data, we propose a new name for BV677278: "READ1" or "regulatory element associated with dyslexia 1" (p. 19).

Powers, N.R. et al (June 2013). Alleles of a Polymorphic ETV6 Binding Site in *DCDC2* Confer Risk of Reading and Language Impairment. American Journal of Human Genetics, 93(1), 19-28. From website: http://www.cell.com/AJHG/abstract/S0002-9297%2813%2900221-8.

Specific Reading Comprehension Disorder

"Specifically, TD (Typical Developing Readers), sic.) showed a higher-percent signal change within right IFG (inferior frontal gyrus, sic.) for low-versus-high frequency words as compared to both S-RCD (Specific Reading Comprehension Deficits, sic.) and DYS (dyslexia, sic.) . Using psychophysiological interaction analyses, a coupling-by-reading group interaction was found in right IFG for DYS, as indicated by a widespread greater covariance between right IFG and right occipitotemporal cortex/visual word-form areas, as well as bilateral medial frontal gyrus, as compared to TD…"

Specific Reading Comprehension Disorder

"For S-RCD, the context-dependent functional interaction anomaly was most prominently seen in left IFG, which covaried to a greater extent with hippocampal, parahippocampal, and prefrontal areas than for TD for low- as compared to high-frequency words. Given the greater lexical access demands of low frequency as compared to high-frequency words, these results may suggest specific weaknesses in accessing lexical-semantic representations during word recognition. These novel findings provide foundational insights into the nature of S-RCD, and set the stage for future investigations of this common, but understudied, reading disorder" (p. 199).

Reference

Cutting, L.E. et al (2013). Not all reading disabilities are dyslexia: distinct neurobiology of specific comprehension deficits. Brain Conectivity, 3(2), 199-211. From website: http://www.ncbi.nlm.nih.gov/pubmed/23273430.

Some with ASD Outgrow Symptoms

"Optimal outcome and TD (Typical Developing children with ASD, sic.) groups' mean scores did not differ on socialization, communication, face recognition, or most language subscales, although three OO (Optimally Developing Children with ASD, sic.) individuals showed below-average scores on face recognition. Early in their development, the OO group displayed milder symptoms than the HFA group in the social domain, but had equally severe difficulties with communication and repetitive behaviors…"

Some with ASD Outgrow Symptoms

"… Although possible deficits in more subtle aspects of social interaction or cognition are not ruled out, the results substantiate the possibility of OO from autism spectrum disorders and demonstrate an overall level of functioning within normal limits for this group" (p. 195).

Fein, D. et al. (February, 2013). Optimal Outcome in Individuals with a History of Autism. Journal of Child Psychology and Psychiatry, 54(2), 195-205. From website: http://www.ncbi.nlm.nih.gov/pubmed/23320807.