Attention-Deficit/Hyperactivity Disorder: Focus upon Aberrant N-Methyl-D-Aspartate Receptors Systems

Trevor Archer and Danilo Garcia

Abstract Attention-deficit/hyperactivity disorder (ADHD) pathophysiology persists in an obscure manner with complex interactions between symptoms, staging, interventions, genes, and environments. Only on the basis of increasing incidence of the disorder, the need for understanding is greater than ever. The notion of an imbalance between central inhibitory/excitatory neurotransmitters is considered to exert an essential role. In this chapter, we first review how the default mode network functions and dysfunction in individuals diagnosed with ADHD. We also present and briefly review some of the animal models used to examine the neurobiological aspects of ADHD. There is much evidence indicating that compounds/interventions that antagonize/block glutamic acid receptors and/or block the glutamate signal during the "brain growth spurt" or in the adult animal may induce functional and biomarker deficits. Additionally, we present evidence suggesting that animals treated with glutamate blockers at the period of the "brain growth spurt" fail to perform the exploratory activity, observed invariably with control mice, that is associated with introduction to a novel environment (the test cages). Later, when the control animals show less locomotor and rearing activity, i.e., interest in the test cages, the MK-801, ketamine and ethanol treated mice showed successively greater levels of locomotion and rearing (interest), i.e., they fail to "habituate" effectively, implying a cognitive dysfunction. These disturbances of glutamate signaling during a critical period of brain development may contribute

T. Archer (✉) · D. Garcia
Department of Psychology, University of Gothenburg, Box 500,
SE 40530 Gothenburg, Sweden
e-mail: trevor.archer@psy.gu.se

T. Archer · D. Garcia
Network for Empowerment and Well-Being, University of Gothenburg,
Gothenburg, Sweden

D. Garcia
Blekinge Center of Competence, Blekinge County Council, Karlskrona, Sweden

D. Garcia
Centre for Ethics, Law and Mental Health (CELAM), University of Gothenburg,
Gothenburg, Sweden

Curr Topics Behav Neurosci (2016) 29: 295–311
DOI 10.1007/7854_2015_415
Published Online: 31 December 2015

to the ADHD pathophysiology. As a final addition, we have briefly identified new research venues in the interaction between ADHD, molecular studies, and personality research.

Keywords Hyperactivity · Attention-deficit · Glutamate antagonists · Motor activity · Deficits · Brain regions · Mice

Contents

The incidence of attention-deficit/hyperactivity disorder (ADHD) is, very likely, increasingly diagnosed, from about 5 % of all children in the USA (Kalat 2001), to 5.1 million or 8.8 % of all children in the age-group 4–17 years (CDC 2011). The incidence over developmental trajectory breaks down as follows: (i) 6.8 % of all children aged 4–10 years (1 in every 14), (ii) 11.4 % of all children aged 11–14 years (1 in every 9), and (iii) 10.2% of all children aged 16–17 years (1 in every 10), with average age at current diagnosis 6.2, with "mild" ADHD diagnosed at 7 years, "moderate" at 6.1 years and "severe" at 4.4 years 3.5 million children taking medication. Boys (12.1 %) remain as more likely to be diagnosed than girls (5.5 %) to be diagnosed. High rates of comorbidity with of oppositional defiant disorder (ODD), anxiety, and depression in children with ADHD have been reported (Anckarsäter et al. 2006; Mitchison and Njardvik 2015; Garcia et al. 2013). The primary symptoms manifested in children with ADHD include: incessant talking in the classroom, restlessness, inattention, impulsiveness, lack of concentration, and hyperactivity (Antonini et al. 2015; Barkley et al. 2002; Bussing et al. 2015; Swanson et al. 1998). In adults with ADHD, symptom profiles are defined by poor attention with excessive distractibility, over-impulsivity, i.e., thoughtless utterances/actions, restlessness/hyperactivity, chronic procrastination, difficulty initiating and completing tasks, frequently losing objects, poor organization, planning and time management, and excessive forgetfulness (Froehlich et al. 2007, 2009, 2010, 2011; Jaber et al. 2015; Lin and Gau 2015; Micoulaud-Franchi et al. 2015). Individuals presenting ADHD exhibit excessive levels of default mode network[1] activity during goal-directed tasks, which are associated with attentional disturbances and performance decrements. However, the process of downregulating the default mode network activity when preparing to switch from rest to task is

[1]A network of brain regions that are active when the individual is not focused on the outside world and the brain is at wakeful rest.

unimpaired in adults with ADHD adults and these adults also lack switch-specific deficit in right anterior insula modulation (Sidlauskaite et al. 2015). In addition, individuals presenting ADHD show difficulties in upregulating the default mode network activity when switching from task phase to rest phase (Sidlauskaite et al. 2015). Kucyi et al. (2015) showed evidence of impaired cerebellar areas of the default mode network coupling with cortical networks in adult patients with ADHD and highlights a role of cerebro–cerebellar interactions in cognitive function. ADHD is associated with significantly increased mortality rates and individuals diagnosed with ADHD during adulthood show higher mortality rates than did those diagnosed in childhood and adolescence (Dalsgaard et al. 2015).

The vast number of studies examining neurobiological aspects of ADHD attests to variety of laboratory animal models available including (i) genetically based models, (ii) neurotoxin-induced models, (iii) Neonatal NMDA-R antagonist administration models, (iv) environmentally based models, and (v) sleep disorder problems. (i) Genetically based models present strains of rats/mice with particular, measureable ADHD phenotypes with phenotypic behaviors and biomarkers such as spontaneously hypertensive (SHR) rats, Naples high-excitability (NHE) rat, rats giving poor performers in the 5-choice serial reaction time task, dopamine transporter (DAT) knock-out mice, SNAP-25-deficient mutant coloboma mice, mice expressing a human mutant thyroid hormone receptor, nicotinic receptor knock-out mice, 22q11.2 deletion syndrome (Meechan et al. 2015), and tachykinin-1 receptor knock-out mice. (ii) Neurotoxin-induced models of ADHD applying N-(2-chloroethyl)-N-ethyl-2-bromobenzylamine (DSP-4) or 6-hydroxydopamine (6-OHDA) as catecholamine neurotoxins or 5,7-dihydroxytryptamine (5,7-DHT) to induce deficits. (iii) NMDA-R antagonist administration models administer MK-801, ketamine, ethanol, polychlorinated biphenyls, or phencyclidine (PCP). (iv) Environmentally based models such as pups reared in deprived environments or isolated housing or neonatal anoxia or variations of environmental stress (Ishii and Hashimoto-Torii 2015). (v) Complex regulatory circuits involving clock genes themselves and their influence on circadian rhythms of diverse body functions and behavioral domains form an important aspect of the gene-environment interaction (Dueck et al. 2015).

As indicated by Russell (2011), one major insight provided by animal models was the consistency of findings regarding the involvement of dopaminergic, noradrenergic, and sometimes also serotonergic systems, as well as glutamateric and GABAergic pathways (see also Russell 2007). Blockade of the N-methyl-D-aspartate receptors (NMDA-Rs) during the neonatal period has been to induce long-term behavioral and neurochemical alterations that are applied as laboratory models for ADHD, schizophrenia, borderline personality disorder and depression. During development, GABA exerts a depolarizing action on immature neurons. Ende et al. (2015) studied glutamate and GABA influences in relation to impulsiveness and aggressive behavior associated with the anterior cingulate cortex in the groups of female patients presenting borderline personality disorder and ADHD, respectively. The links between glutamate and GABA levels and further borderline personality disorder (symptom severity) and ADHD aspects (hyperactivity and

inattention) were evaluated in an explorative manner. They acquired 1H MR spectra at 3T to determine the glutamate to total creatine ratios (Glu/tCr) and GABA levels from the anterior cingulate cortex in a borderline personality disorder group (n = 26), an ADHD group (n = 22), as well as a healthy control (HC) group (n = 30); all the participants were females. Both patient groups, i.e., borderline personality disorder and ADHD, presented higher scores on self-reported impulsiveness, anger, and aggression compared with the healthy controls. Anterior cingulate cortex GABA levels were significantly lower in ADHD than HC. Although measures of impulsiveness were related positively to glutamate and negatively to GABA, in the case of aggression only a negative correlation with GABA was obtained. This pattern of results may provide human in vivo evidence for the role of anterior cingulate cortex Glu/tCr and GABA in impulsiveness and aggression.

1 N-Methyl-D-Aspartate Receptors (NMDA-R) Linked ADHD Models

ADHD pathophysiology persists in an obscure manner with complex interactions between symptoms, staging, interventions, genes, and environments (Archer and Bright 2012; Archer and Kostrzewa 2012; Archer et al. 2011; Kyeong et al. 2015; Rommel et al. 2013; Schuch et al. 2015). Functional magnetic resonance imaging (fMRI) has shown that almost all test–retest reliability of resting state fMRI metrics presented significantly higher intra-class correlation coefficient in typically developing children than in with ADHD children for one or more brain regions studied (Somandepalli et al. 2015). Several physiological biomarkers besides brain neurochemical show deficits in the disorder: for example, serum levels of oxytocin in total subjects presenting ADHD were reduced significantly compared with those levels of neurotypical control individuals, and serum levels of oxytocin in drug naïve ADHD patients were significantly lower than those in medicated ADHD patients. Interestingly, there was a significant negative correlation between serum oxytocin levels and ADHD-RS total scores, as well as ADHD-RS inattentive scores in all ADHD patients Sasaki et al. 2015). The genetic factor in ADHD is undeniable (Fang et al. 2015; Salatino-Oliveira et al. 2015; Thapar and Cooper 2015; Van Rooij et al. 2015a; Pettersson et al. 2013), connected with sibling associations (Richards et al. 2015; Thissen et al. 2015; Van Rooij et al. 2015b), parents (Costa Dde et al. 2015; Grizenko et al. 2015; Van der Kolk et al. 2015), and with extremely high twin concordance (Arcos-Burgos et al. 2004; Ehli et al. 2012; Langner et al. 2013; McLoughlin et al. 2014; Garcia et al. 2014) and comorbidity (Volh et al. 2005; Garcia et al. 2013). The notion of an imbalance between central inhibitory/excitatory neurotransmitters is considered to exert an essential role in the pathophysiology of ADHD (Purkayastha et al. 2015; Sadile et al. 1996), although this is not always the case (Endres et al. 2015). For instance, in contrast to children, adult patients presenting ADHD display altered cerebral levels of GABA+ in a subcortical voxel (Bollmann et al. 2015).

Additionally, there are also increased cerebral glutamine levels in children with ADHD, but this difference is normalized among adults with ADHD (Bollmann et al. 2015). In other words, suggesting that this alteration might change through development.

There is a plethora of results showing that compounds/interventions that antagonize glutamic acid receptors and/or block the glutamate signal during the "brain growth spurt" or in the adult animal may induce functional and biomarker deficits (Davison and Dobbing 1968; Di Miceli and Gonier 2015; Fredriksson and Archer 2002, 2003; Fredriksson et al. 2004; Pozzi et al. 2011; Zimmermann et al. 2015; Zhou et al. 2011). Normal regional brain development follows an inherited, preprogrammed route that differentiates the specific structural characteristics and functional domains that are expressed in the adult human and animal (Dobbing and Sands 1970, 1979). Any interference with the course of normal brain development threatens the regional structural and functional integrity with more or less permanent consequences for the individual (Chen et al. 1999; Dobbing 1970a, b, c, 1971; Huebner et al. 2015). The period of the "brain growth spurt" starts with the final trimester of pregnancy in humans and continues until about three years after birth (Ikonomidou et al. 2001). The corresponding period in rodents is encompassed by a rapid increase in brain weight, proliferation of astroglial and oligodendrocyte cells, axonal elongation, arborization, and synaptogenesis (Byrnes et al. 2001; Davison and Dobbing 1966). Agents affecting glutamate system are implicated highly in the vulnerability of brain development since chronic prenatal exposure to an ethanol regimen throughout gestation induced suppression of the hippocampal glutamate-NMDA receptor-NOS signaling system, decreased number of hippocampal CA1 pyramidal cells, increased spontaneous locomotor activity, and impaired performance in the Morris water maze (Byrnes et al. 2001; but see also Byrnes et al. 2003, 2004). Anticonvulsant drugs can initiate neuron and oligodendroglia apoptosis, suppress neurogenesis, and inhibit normal synapse development and regional-sculpting (Turski and Ikonomidou 2012). The behavioral correlates in rodents and non-human primates consist of long-lasting cognitive impairment and motor deficits. Physiological apoptosis and that caused by other agents, a naturally occurring process of the developing brain, modulates regional progressions at cellular and circuitry levels periodically (Dikranian et al. 2001; Ishimaru et al. 1999; Olney et al. 2000).

Several studies have demonstrated marked deficits in behavioral domains in the adult animal following disruptions in glutamate signaling and GABAergic activity (Cohen Kadosh et al. 2015; Kim et al. 2015; Tzanoulinou et al. 2015; Zhang et al. 2015) in the prenatal or neonatal human and animal (Higuera-Matas et al. 2015; Jantzie et al. 2015; Keimpema et al. 2014; Kleteckova et al. 2014; Simões et al. 2015). It was shown more than twenty years ago that chronic neonatal treatment with the glutamate antagonist, MK-801 (postnatal days 8 to 19), induced marked alterations of monoamines (Gorter et al. 1992a) whereby dihydroxyphenylacetic acid (DOPAC) concentrations were elevated (greater than 40 %) in both regions (cortex and striatum) tested, while 5-hydroxyindoleacetic acid (5-HIAA) concentration was significantly elevated only in the cortex (19 %), and 3-methoxy-4-hydroxyphenylglycol (MHPG)

only in the striatum (47 %). When tested spatial learning and memory using a water maze, the neonatal MK-801-treated rats were shown to be capable of learning the spatial task as well as control rats but did so at a significantly slower rate. Their performance in a visual cue task was not affected by the neonatal treatment, suggesting that the slower spatial learning is not caused by locomotor or sensory deficits (Gorter and de Bruin 1992). The authors interpreted their findings to imply that chronic NMDA receptor blockade during the neonatal period leads to long-lasting disturbances of hippocampal function (but see also Gorter et al. 1991, 1992b). The glutamate antagonists, MK-801 (3 × 0.5 mg/kg), ketamine (1 × 50 mg/kg), and ethanol (2 × 2.5 mg/kg) were administered postnatally to mouse pups on days 10 or 11 postpartum (cf. Fredriksson and Archer 2004), and behavioral testing was performed at adult ages over and above 65 days-of-age. At testing, it was found that over 60-min periods of motor activity testing, the mice administered the glutamate antagonists showed a somewhat bizarre pattern of activity that was completely different to that shown by untreated, saline- or vehicle-treated, or sham-operated mice: The former presented markedly lower levels of motor activity than the latter during the initial period of activity testing (1st 20 min) and then successively greater levels of motor activity than the latter during the middle and final periods of activity testing (2nd and 3rd 20 min periods). Table 1 presents the motor activity, locomotion, and rearing of

Table 1 Locomotion and rearing behavior expressed as percent of control values (0.9 % saline-vehicle) over successive 20-min periods in the motor activity test cages by adult mice administered either MK-801, ketamine or ethanol, glutamate antagonists at the doses used, or diazepam, GABA agonist at the doses used. MK-801 (0.5 mg/kg, s.c.) was administered to male mouse pups on postnatal day 11 on three occasions over that day. Ketamine (1 × 50 mg/kg, s.c.) and ethanol (2 × 25 mg/kg, s.c., with a 2-h interval between injections) were administered on postnatal day 10

Neonatal treatment	20-min period	Locomotion % of control values	Rearing % of control values
MK-801	20	38	32
	40	199	247
	60	3439	8405
Ketamine	20	36	34
	40	207	225
	60	1967	3812
Diazepam	20	99	86
	40	112	101
	60	189	544
Ketamine + Diazepam	20	35	27
	40	188	261
	60	2617	7422
Ethanol	20	38	29
	40	224	239
	60	2128	4122

mice injected postnatally with either MK-801, ketamine, or ethanol expressed as a percentage of each respective vehicle control group. It will be noted that the mice administered glutamate antagonists evidenced massively greater levels of apoptosis (as measured by fluoro-jade positive staining) in several brain regions, including frontal cortex, hippocampus, cerebellum, parietal cortex, and laterodorsal thalamus, compared to controls, 24 h after administration of the drugs, MK-801, ketamine, or ethanol. The results on Table 1 indicate that these animals fail to perform the exploratory activity, observed invariably with control mice, that is associated with introduction to a novel environment (the test cages). Later, when the control animals show less locomotor and rearing activity, i.e., interest in the test cages, the MK-801-, ketamine-, and ethanol-treated mice showed successively greater levels of locomotion and rearing (interest), i.e., they fail to "habituate" effectively, implying a cognitive dysfunction. The cognitive dysfunctionality of the MK-801-, ketamine-, and ethanol-treated mice was demonstrated in both the radial arm maze and the circular swimming maze (Fredriksson and Archer 2004). Spontaneously hypertensive rats (SHRs) present several of the characteristic behavioral anomalies observed in ADHD children and adults: hyperactivity, impulsiveness and poorly sustained attention, restlessness, and comorbid drug self-administration (Grünblatt et al. 2015; Jordan et al. 2015; Womersley et al. 2015).

2 Aberrant Glutamate in Spontaneously Hypertensive (SHR) Rats

There is emerging evidence that spontaneously hypertensive (SHR) rats possess disruptions in glutamate systems or in glutamate signaling or in region (e.g., nucleus accumbens) characteristics (Russell 2003). For example, it was observed that the glutamatergic system in the prefrontal cortex of the SHR rats was hyper-functional (Miller et al. 2014). Sterley et al. (2015) have provided evidence for a disturbed glutamatergic and GABAergic transmission in the hippocampus of SHRs and that maternal separation induced effects on glutamate uptake in these rats and Wister-Kyoto and Sprague-Dawley rats as well. Furthermore, compared to control animals, SHRs displayed a lower expression of both NMDA (Grin1) and AMPA (Gria1) gene receptors in the nucleus accumbens. It has been observed also that SHRs express decreased levels of several proteins involved in energy metabolism, cytoskeletal structure, myelination, and neurotransmitter function when compared to Wistar-Kyoto rats[2] (Dimatelis et al. 2015). Liso Navarro et al. (2014) found significant correlations between brain metabolites and the behavior registered in the open field and elevated plus maze: SHR rats expressing higher levels of brain total creatine levels and glutamate levels exhibited higher levels of hyperactivity in a familiar environment, but conversely, risk-taking exploratory behavior, an

[2]The Wistar rat is an outbred albino rat.

indication of impulsivity, of the elevated plus maze's open arms correlated negatively with forebrain total N-acetylaspartate and lactate levels. It has been shown also that there is a reduction in extracellular concentrations of GABA in the hippocampus of SHR rats, in vivo, by comparison with Wistar-Kyoto and Sprague-Dawley rats (Sterley et al. 2013). The authors suggest that an underlying defect in GABA function may be the underlying cause of the dysfunction in catecholamine transmission noted in SHR and may underlie their ADHD-like behaviors (see also Mc Fie et al. 2012; Miller et al. 2012). Ye et al. (2013) observed that there were increases in presynaptic group II metabotropic glutamate receptor activity at the glutamatergic terminals at hypothalamic paraventricular nucleus sites in SHR rats. The activation of group II metabotropic glutamate receptors in the hypothalamic paraventricular nucleus inhibits sympathetic vasomotor tone through attenuation of increased glutamatergic input and neuronal hyperactivity in SHR rats, thereby affecting sympathetic outflow in hypertension and related conditions. In this context, physical exercise was shown to ameliorate the enhancement in the tonically acting glutamatergic input to the rostral ventrolateral medulla of SHR rats, thereby reducing the sympathetic hyperactivity and blood pressure (Zha et al. 2013). Following exposure to the NMDAR antagonist, MK-801, during postnatal days 5–14, to male Sprague-Dawley rat pups (Li et al. 2015), the animals were tested for object and object-in-context recognition memory during adolescence (PND 35) and adulthood (PND 63). They examined also parvalbumin-positive GABA-ergic interneurons and presynaptic markers for excitatory and inhibitory neurons, vesicular glutamate transporter-1, and vesicular GABA transporter in the hippocampus to reflect the excitatory/Inhibitory balance. They observed that rats that had received MK-801 treatment displayed deficits of recognition memory, reduction in parvalbumin-positive cell counts, and upregulation of the vesicular glutamate transporter-1/vesicular GABA transporter ratio in both adolescence and adulthood. It would appear that the changes of the vesicular glutamate transporter-1/vesicular GABA transporter ratio at the two time points exhibited distinct mechanisms. Furthermore, prenatal alcohol exposure affected cortical angiogenesis negatively both in mice and in fetal alcohol syndrome patients, implying that vascular defects contributed to alcohol-induced brain abnormalities (Jegou et al. 2012). Postnatal treatment with domoic acid, which disturbs glutamate signaling, induced deficits in latent inhibition and sensory gating through prepulse inhibition impairments (Marriott et al. 2012).

Finally, several genetic linkage and association studies point to candidate genes relating to ADHD (Franke et al. 2009). Associations between ADHD and a handful of NMDA-R gene variants [GRM1, GRM5, GRM7, and GRM8: encoding G-protein coupled receptor family] (Diana et al. 2015; Akutagava-Martins et al. 2014). Santoro et al. (2015) compared the gene expression profile of neurotransmitter receptors and regulators in the prefrontal cortex and nucleus accumbens of SHR and control Wistar rats, as well as the DNA methylation pattern of promoter region of the genes differentially expressed. They found that four genes were downregulated significantly in the prefrontal cortex of the SHRs in comparison with Wistar rats (Gad2, Chrnb4, Slc5a7, and Qrfpr) and none of those in nucleus

accumbens. Gad2 and Qrfpr showed CpG islands in their promoter region. For both of these genes, the promoter region was hypomethylated in SHR rats and may be linked to the abnormalities displayed by these animals. Since adverse life events, dysfunctional families, pregnancy and birth complications, etc, all increase risk for ADHD (Class et al. 2014; Lindström et al. 2011; Pires et al. 2013; Webb 2013), the epigenetic influences upon glutamatergic integrity seems immeasurable (Grissom and Reyes 2013; Schuch et al. 2015). van Mil et al. (2014) examined the association between DNA methylation levels at different regions and ADHD symptoms. They observed that DNA methylation levels were linked negatively with ADHD symptoms scores in the analysis of eleven brain regions.

3 Conclusions and Final Remarks

The notion of a disruption of the normal brain developmental trajectory, due an over-stimulation of GABAergic systems and/or an understimulation (antagonism) of the glutamate systems, i.e., excitatory-inhibitory imbalance, in the underlying pathophysiology of ADHD, particularly regarding motor and cognitive domains, is appealing. The pattern of behavioral deficits when tested as adult animals and "accelerated apoptosis" 24 h after administrations of the glutamate antagonists offers a useful laboratory model of the disorder. Babenko et al. (2015) have offered a plausible account that describes the complex gene–environment interactions between prenatal stress exposure, whether chemical intervention or social-behavioral, associated changes in miRNA expression and DNA methylation in placenta and brain regions together with the possible links to greater risks of schizophrenia, ADHD, autism, anxiety-, or depression-related disorders that may be expressed later in life.

Finally, ADHD is associated with an increased risk of personality disorders and deficits and specific temperament configurations: high novelty seeking and high harm avoidance (Anckarsäter et al. 2006). Individuals high in novelty seeking tend to be highly active or to direct their attention/behaviors in response to novel stimuli, potential rewards, and punishments. This is expressed as frequent exploration of new unfamiliar places or situations, quick loss of temper, impulsive decision-making, and active avoidance of monotony. High levels of harm avoidance are expressed as the tendency to avoid or cease behaviors due to intense response to aversive stimuli expressed as fear of uncertainty, shyness of strangers, quick fatigability, and pessimistic worry of future problems (Cloninger et al. 1993). This "explosive" temperament profile (high novelty seeking and high harm avoidance) does fit in the ADHD pathophysiology outlined in this chapter. What is more, molecular genetics studies have found an association between novelty seeking and the dopamine-4 receptor (Benjamin et al. 1996; Ebstein et al. 1996; Noble et al. 1998; Ono et al. 1997) and between harm avoidance and the serotonin transporter 5HTTLPR (Rybakowski et al. 2006; Samochowiec et al. 2001).

Fortunately, recent advances using person-centered interventions (i.e., well-being coaching) suggest that the expression of genes as personality traits can be changed (Cloninger 2004; Wong and Cloninger 2010; see also Fahlgren et al. 2015), In particular when the intervention focuses on the development of character traits, such as self-directedness (e.g., sense of control, self-efficacy, self-acceptance), cooperativeness (e.g., tolerance, helpfulness, empathy), and self-transcendence (e.g., spirituality, meaningfulness, ability to experience flow). Relatedly, changes in mean levels of character traits are much greater between 20 and 45 years of age than for temperament traits (Josefsson et al. 2013). Hence, upcoming studies using person-centered interventions among individuals with ADHD are most welcome.

References

Akutagava-Martins GC, Salatino-Oliveira A, Genro JP, Contini V, Polanczyk G, Zeni C, Chazan R, Kieling C, Anselmi L, Menezes AM, Grevet EH, Bau CH, Rohde LA, Hutz MH (2014) Glutamatergic copy number variants and their role in attention-deficit/hyperactivity disorder. Am J Med Genet B Neuropsychiatr Genet 165B(6):502–509. doi:10.1002/ajmg.b.32253

Anckarsäter H, Ståhlberg O, Larson T, Håkansson C, Jutblad SB, Niklasson L, Nydén A, Wentz E, Westergren S, Cloninger CR, Gillberg C, Rastam M (2006) The impact of ADHD and autism spectrum disorders on temperament, character, and personality development. Am J Psychiatry 163(7):1239–1244

Antonini TN, Becker SP, Tamm L, Epstein JN (2015) Hot and cool executive functions in children with attention-deficit/hyperactivity disorder and comorbid oppositional defiant disorder. J Int Neuropsychol Soc 21(8):584–595. doi:10.1017/S1355617715000752

Archer T, Bright P (2012) Functional and structural MRI studies on impulsiveness: attention deficit/hyperactive disorder and borderline personality disorders. In: Bright P (ed) Neuroimaging—cognitive and clinical neuroscience. InTech, London, pp 205–228. ISBN 978-953-51-0606-7

Archer T, Kostrzewa RM (2012) Physical exercise alleviates ADHD symptoms: regional deficits and development trajectory. Neurotox Res 21(2):195–209. doi:10.1007/s12640-011-9260-0

Archer T, Oscar-Berman M, Blum K (2011) Epigenetics in developmental disorder: ADHD and endophenotypes. J Genet Syndr Gene Ther 2(104). pii: 1000104

Arcos-Burgos M, Castellanos FX, Pineda D, Lopera F, Palacio JD, Palacio LG, Rapoport JL, Berg K, Bailey-Wilson JE, Muenke M (2004) Attention-deficit/hyperactivity disorder in a population isolate: linkage to loci at 4q13.2, 5q33.3, 11q22, and 17p11. Am J Hum Genet 75(6):998–1014

Babenko O, Kovalchuk I, Metz GA (2015) Stress-induced perinatal and transgenerational epigenetic programming of brain development and mental health. Neurosci Biobehav Rev 48:70–91. doi:10.1016/j.neubiorev.2014.11.013

Barkley RA, Fisher M, Smallish L, Fletcher K (2002) The persistence of attention-deficit/hyperactivity disorder into young adulthood as a function of reporting source and definition of disorder. J Abnorm Psychol 111:279–289

Benjamin J, Li L, Patterson C, Greenberg BD, Murphy DL, Hamer DH (1996) Population and familial association between the D4 dopamine receptor gene and measures of novelty seeking. Nat Genet 12:81–84

Bollmann S, Ghisleni C, Poil SS, Martin E, Ball J, Eich-Höchli D, Edden RA, Klaver P, Michels L, Brandeis D, O'Gorman RL (2015) Developmental changes in gamma-aminobutyric

acid levels in attention-deficit/hyperactivity disorder. Transl Psychiatry 5:e589. doi:10.1038/tp.2015.79

Bussing R, Meyer J, Zima BT, Mason DM, Gary FA, Garvan CW (2015) Childhood ADHD symptoms: association with parental social networks and mental health service use during adolescence. Int J Environ Res Public Health. 12(9):11893–11909. doi:10.3390/ijerph120911893

Byrnes ML, Reynolds JN, Brien JF (2001) Effect of prenatal ethanol exposure during the brain growth spurt of the guinea pig. Neurotoxicol Teratol 23(4):355–364

Byrnes ML, Reynolds JN, Brien JF (2003) Brain growth spurt-prenatal ethanol exposure and the guinea pig hippocampal glutamate signaling system. Neurotoxicol Teratol 25(3):303–310

Byrnes ML, Richardson DP, Brien JF, Reynolds JN, Dringenberg HC (2004) Spatial acquisition in the Morris water maze and hippocampal long-term potentiation in the adult guinea pig following brain growth spurt–prenatal ethanol exposure. Neurotoxicol Teratol 26(4):543–551

Centers for Disease Control and Prevention (CDC) (2011) Key findings: trends in the parent-report of health care provider-diagnosis and medication treatment for ADHD: United States, 2003–2011

Chen WA, Parnell SE, West JR (1999) Early postnatal alcohol exposure produced long-term deficits in brain weight, but not the number of neurons in the locus coeruleus. Brain Res Dev Brain Res 118(1–2):33–38

Class QA, Abel KM, Khashan AS, Rickert ME, Dalman C, Larsson H, Hultman CM, Långström N, Lichtenstein P, D'Onofrio BM (2014) Offspring psychopathology following preconception, prenatal and postnatal maternal bereavement stress. Psychol Med 44(1):71–84. doi:10.1017/S0033291713000780

Cloninger CR (2004) Feeling good: the science of well-being. Oxford University Press, New York

Cloninger CR, Svrakic DM, Przybeck TR (1993) A psychobiological model of temperament and character. Arch Gen Psychiatry 50:975–989

Cohen Kadosh K, Krause B, King AJ, Near J, Cohen Kadosh R (2015) Linking GABA and glutamate levels to cognitive skill acquisition during development. Hum Brain Mapp. doi:10.1002/hbm.22921

Costa Dde S, Rosa DV, Barros AG, Romano-Silva MA, Malloy-Diniz LF, Mattos P, de Miranda DM (2015) Telomere length is highly inherited and associated with hyperactivity-impulsivity in children with attention deficit/hyperactivity disorder. Front Mol Neurosci. 8:28. doi:10.3389/fnmol.2015.00028

Dalsgaard S, Østergaard SD, Leckman JF, Mortensen PB, Pedersen MG (2015) Mortality in children, adolescents and adults with attention deficit hyperactivity disorder: a nationwide cohort study. Lancet 385(9983):2190–2196. doi:10.1016/S0140-6736(14)61684-6

Davison AN, Dobbing J (1966) Myelination as a vulnerable period in brain development. Br Med Bull 22(1):40–44

Davison AN, Dobbing J (1968) Applied neurochemistry. Blackwell, Oxford, pp 253–316

Di Miceli M, Gronier B (2015) Psychostimulants and atomoxetine alter the electrophysiological activity of prefrontal cortex neurons, interaction with catecholamine and glutamate NMDA receptors. Psychopharmacology 232(12):2191–2205. doi:10.1007/s00213-014-3849-y

Diana MC, Santoro ML, Xavier G, Santos CM, Spindola LN, Moretti PN, Ota VK, Bressan RA, Abilio VC, Belangero SI (2015) Low expression of Gria1 and Grin1 glutamate receptors in the nucleus accumbens of spontaneously hypertensive rats (SHR). Psychiatry Res 229(3):690–694. doi:10.1016/j.psychres.2015.08.021

Dikranian K, Ishimaru MJ, Tenkova T, Labruyere J, Qin YQ, Ikonomidou C, Olney JW (2001) Apoptosis in the in vivo mammalian forebrain. Neurobiol Dis 8(3):359–379

Dimatelis JJ, Hsieh JH, Sterley TL, Marais L, Womersley JS, Vlok M, Russell VA (2015) Impaired energy metabolism and disturbed dopamine and glutamate signalling in the striatum and prefrontal cortex of the spontaneously hypertensive rat model of attention-deficit hyperactivity disorder. J Mol Neurosci 56(3):696–707. doi:10.1007/s12031-015-0491-z

Dobbing J (1970a) Undernutrition and the developing brain. The relevance of animal models to the human problem. Am J Dis Child 120(5):411–415

Dobbing J (1970b) The kinetics of growth. Lancet 2(7687):1358
Dobbing J (1970c) Undernutrition and the developing brain. The relevance of animal models to the human problem. Am J Dis Child 120(5):411–415
Dobbing J, Sands J (1970) Growth and development of the brain and spinal cord of the guinea pig. Brain Res 17(1):115–123
Dobbing J (1971) Undernutrition and the developing brain: the use of animal models ot elucidate the human problem. Psychiatr Neurol Neurochir 74(6):433–442
Dobbing J, Sands J (1979) Comparative aspects of the brain growth spurt. Early Hum Dev. 3 (1):79–83
Dueck A, Berger C, Wunsch K, Thome J, Cohrs S, Reis O, Haessler F (2015) The role of sleep problems and circadian clock genes in attention-deficithyperactivity disorder and mood disorders during childhood and adolescence: an update. J Neural Transm (15 Oct 2015)
Ebstein RP, Novick O, Umansky R, Priel B, Osher Y, Blaine D, Bennett ER, Nemanov L, Katz M, Belmaker RH (1996) Dopamine D4 receptor (D4DR) exon III polymorphism associated with the human personality trait of novelty seeking. Nat Genet 12:78–80
Ehli EA, Abdellaoui A, Hu Y, Hottenga JJ, Kattenberg M, van Beijsterveldt T, Bartels M, Althoff RR, Xiao X, Scheet P, de Geus EJ, Hudziak JJ, Boomsma DI, Davies GE (2012) De novo and inherited CNVs in MZ twin pairs selected for discordance and concordance on attention problems. Eur J Hum Genet 20(10):1037–1043. doi:10.1038/ejhg.2012.49
Ende G, Cackowski S, Van Eijk J, Sack M, Demirakca T, Kleindienst N, Bohus M, Sobanski E, Krause-Utz A, Schmahl C (2015) Impulsivity and aggression in female BPD and ADHD patients: associations with ACC glutamate and GABA concentrations. Neuropsychopharmacology. doi:10.1038/npp.2015.153
Endres D, Perlov E, Maier S, Feige B, Nickel K, Goll P, Bubl E, Lange T, Glauche V, Graf E, Ebert D, Sobanski E, Philipsen A, Tebartz van Elst L (2015) Normal neurochemistry in the prefrontal and cerebellar brain of adults with attention-deficit hyperactivity disorder. Front Behav Neurosci 9:242. doi:10.3389/fnbeh.2015.00242
Falhgren E, Nima AA, Archer T, Garcia D (2015) Person-centered osteopathic practice: patients' personality (body, mind, and soul) and health (ill-being and well-being). PeerJ 3:e1349. doi:10.7717/peerj.1349
Fang Y, Ji N, Cao Q, Su Y, Chen M, Wang Y, Yang L (2015) Variants of dopamine beta hydroxylase gene moderate atomoxetine response in children with attention-deficit/hyperactivity disorder. J Child Adolesc Psychopharmacol (8 Oct 2015)
Franke B, Neale BM, Faraone SV (2009) Genome wide association studies in ADHD. Hum Genet 126:13–50. doi:10.1007/s00439-009-0663-4
Fredriksson A, Archer T (2002) Functional alteration by NMDA antagonist: effects of L-Dopa, neuroleptic drugs and postnatal administration. Amino Acids 25:111–132
Fredriksson A, Archer T (2003) Hyperactivity following postnatal NMDA antagonist treatment: reversal by d-amphetamine. Neurotox Res 5:549–564
Fredriksson A, Archer T (2004) Neurobehavioral deficits associated with apoptotic neurodegeneration and vulnerability for ADHD. Neurotox Res 6:435–456
Fredriksson A, Archer T, Alm H, Gordh T, Eriksson P (2004) Neurofunctional deficits and potentiated apoptosis by neonatal NMDA antagonist administration. Behav Brain Res 153:367–376
Froehlich TE, Lanphear BP, Epstein JN, Barbaresi WJ, Katusic SK, Kahn RS (2007) Prevalence, recognition, and treatment of attention-deficit/hyperactivity disorder in a national sample of US children. Arch Pediatr Adolesc Med 161(9):857–864
Froehlich TE, Lanphear BP, Auinger P, Hornung R, Epstein JN, Braun J, Kahn RS (2009) Association of tobacco and lead exposures with attention-deficit/hyperactivity disorder. Pediatrics 124(6):e1054–e1063. doi:10.1542/peds.2009-0738
Froehlich TE, McGough JJ, Stein MA (2010) Progress and promise of attention-deficit hyperactivity disorder pharmacogenetics. CNS Drugs. 24(2):99–117. doi:10.2165/11530290-000000000-00000

Froehlich TE, Anixt JS, Loe IM, Chirdkiatgumchai V, Kuan L, Gilman RC (2011) Update on environmental risk factors for attention-deficit/hyperactivity disorder. Curr Psychiatry Rep 13 (5):333–344. doi:10.1007/s11920-011-0221-3

Garcia D, Anckarsäter H, Lundström S (2013) Self-directedness and cooperativeness, psychosocial dysfunction and suffering in ESSENCE. Sci World J 2013, Article ID 416981, 1–10. doi:10.1155/2013/416981

Garcia D, Stråge A, Lundström S, Radovic S, Brändström S, Råstam M, Nilsson T, Cloninger CR, Kerekes N, Anckarsäter H (2014) Responsibility and cooperativeness are constrained not determined. Front Psychol 5:308. doi:10.3389/fpsyg.2014.00308

Gorter JA, de Bruin JP (1992) Chronic neonatal MK-801 treatment results in an impairment of spatial learning in the adult rat. Brain Res 580(1–2):12–17

Gorter JA, Botterblom MH, Feenstra MG, Boer GJ (1992a) Chronic neonatal NMDA receptor blockade with MK-801 alters monoamine metabolism in the adult rat. Neurosci Lett 137 (1):97–100

Gorter JA, Veerman M, Mirmiran M (1992b) Hippocampal neuronal responsiveness to NMDA agonists and antagonists in the adult rat neonatally treated with MK-801. Brain Res 572(1–2):176–181

Gorter JA, Veerman M, Mirmiran M, Bos NP, Corner MA (1991) Spectral analysis of the electroencephalogram in neonatal rats chronically treated with the NMDA antagonist MK-801. Brain Res Dev Brain Res 64(1–2):37–41

Grissom NM, Reyes TM (2013) Gestational overgrowth and undergrowth affect neurodevelopment: similarities and differences from behavior to epigenetics. Int J Dev Neurosci 31(6):406–414. doi:10.1016/j.ijdevneu.2012.11.006

Grizenko N, Fortier MÈ, Gaudreau-Simard M, Jolicoeur C, Joober R (2015) The effect of maternal stress during pregnancy on IQ and ADHD symptomatology. J Can Acad Child Adolesc Psychiatry 24(2):92–99

Grünblatt E, Bartl J, Iuhos DI, Knezovic A, Trkulja V, Riederer P, Walitza S, Salkovic-Petrisic M (2015) Characterization of cognitive deficits in spontaneously hypertensive rats, accompanied by brain insulin receptor dysfunction. J Mol Psychiatry 3(1):6. doi:10.1186/s40303-015-0012-6

Higuera-Matas A, Ucha M, Ambrosio E (2015) Long-term consequences of perinatal and adolescent cannabinoid exposure on neural and psychological processes. Neurosci Biobehav Rev 55:119–146. doi:10.1016/j.neubiorev.2015.04.020

Huebner SM, Tran TD, Rufer ES, Crump PM, Smith SM (2015) Maternal iron deficiency worsens the associative learning deficits and hippocampal and cerebellar losses in a rat model of fetal alcohol spectrum disorders. Alcohol Clin Exp Res. doi:10.1111/acer.12876

Ikonomidou C, Bittigau P, Koch C, Genz K, Hoerster F, Felderhoff-Mueser U, Tenkova T, Dikranian K, Olney JW (2001) Neurotransmitters and apoptosis in the developing brain. Biochem Pharmacol 62(4):401–405

Ishii S, Hashimoto-Torii K (2015) Impact of prenatal environmental stress on cortical development. Front Cell Neurosci 9:207. doi:10.3389/fncel.2015.00207

Ishimaru MJ, Ikonomidou C, Tenkova TI, Der TC, Dikranian K, Sesma MA, Olney JW (1999) Distinguishing excitotoxic from apoptotic neurodegeneration in the developing rat brain. J Comp Neurol 408(4):461–476

Jaber L, Kirsh D, Diamond G, Shuper A (2015) Long-term functional outcomes in Israeli adults diagnosed in childhood with attention-deficit hyperactivity disorder. Isr Med Assoc J 17(8):481–485

Jantzie LL, Talos DM, Jackson MC, Park HK, Graham DA, Lechpammer M, Folkerth RD, Volpe JJ, Jensen FE (2015) Developmental expression of N-methyl-D-aspartate (NMDA) receptor subunits in human white and gray matter: potential mechanism of increased vulnerability in the immature brain. Cereb Cortex 25(2):482–495. doi:10.1093/cercor/bht246

Jégou S, El Ghazi F, de Lendeu PK, Marret S, Laudenbach V, Uguen A, Marcorelles P, Roy V, Laquerrière A, Gonzalez BJ (2012) Prenatal alcohol exposure affects vasculature development in the neonatal brain. Ann Neurol 72(6):952–960. doi:10.1002/ana.23699

Jordan CJ, Taylor DM, Dwoskin LP, Kantak KM (2015) Adolescent d-amphetamine treatment in a rodent model of ADHD: Pro-cognitive effects in adolescence without an impact on cocaine cue reactivity in adulthood. Behav Brain Res. pii: S0166-4328(15)30233-3doi: 10.1016/j.bbr.2015.10.017

Josefsson K, Jokela M, Cloninger CR, Hintsanen M, Salo J, Hintsa T, Pulkki-Råback L, Keltikangas-Järvinen L (2013) Maturity and Change in Personality: De-velopmental Trends of Temperament and Character in Adulthood. Dev Psychopathol 25:713–727

Kalat JW (2001) Biological psychology. Wadsworth/Thomson Learning, Belmont, CA

Keimpema E, Zheng K, Barde SS, Berghuis P, Dobszay MB, Schnell R, Mulder J, Luiten PG, Xu ZD, Runesson J, Langel Ü, Lu B, Hökfelt T, Harkany T (2014) GABAergic terminals are a source of galanin to modulate cholinergic neuron development in the neonatal forebrain. Cereb Cortex 24(12):3277–3288. doi:10.1093/cercor/bht192

Kim J, Son Y, Kim J, Lee S, Kang S, Park K, Kim SH, Kim JC, Kim J, Takayama C, Im HI, Yang M, Shin T, Moon C (2015) Developmental and degenerative modulation of GABAergic transmission in the mouse hippocampus. Int J Dev Neurosci. pii: S0736-5748(15)30048-4. doi:10.1016/j.ijdevneu.2015.08.009

Kleteckova L, Tsenov G, Kubova H, Stuchlik A, Vales K (2014) Neuroprotective effect of the 3α5β-pregnanolone glutamate treatment in the model of focal cerebral ischemia in immature rats. Neurosci Lett 564:11–15. doi:10.1016/j.neulet.2014.01.057

Kucyi A, Hove MJ, Biederman J, Van Dijk KR, Valera EM (2015) Disrupted functional connectivity of cerebellar default network areas in attention-deficit/hyperactivity disorder. Hum Brain Mapp 36(9):3373–3386. doi:10.1002/hbm.22850

Kyeong S, Park S, Cheon KA, Kim JJ, Song DH, Kim E (2015) A new approach to investigate the association between brain functional connectivity and disease characteristics of attention-deficit/hyperactivitydisorder: topological neuroimaging data analysis. PLoS One 10(9):e0137296. doi:10.1371/journal.pone.0137296

Langner I, Garbe E, Banaschewski T, Mikolajczyk RT (2013) Twin and sibling studies using health insurance data: the example of attention-deficit/hyperactivity disorder (ADHD). PLoS One 8(4):e62177. doi:10.1371/journal.pone.0062177

Li JT, Zhao YY, Wang HL, Wang XD, Su YA, Si TM (2015) Long-term effects of neonatal exposure to MK-801 on recognition memory and excitatory-inhibitory balance in rat hippocampus. Neuroscience 308:134–143. doi:10.1016/j.neuroscience.2015.09.003

Lin HY, Gau SS (2015) Atomoxetine treatment strengthens an anti-correlated relationship between functional brain networks in medication-naïve adults with attention-deficit hyperactivity disorder: a randomized double-blind placebo-controlled clinical trial. Int J Neuropsychopharmacol. pii: pyv094. doi:10.1093/ijnp/pyv094

Lindström K, Lindblad F, Hjern A (2011) Preterm birth and attention-deficit/hyperactivity disorder in schoolchildren. Pediatrics 127:858–865. doi:10.1542/peds.2010-1279

Liso Navarro AA, Sikoglu EM, Heinze CR, Rogan RC, Russell VA, King JA, Moore CM (2014) Effect of diet on brain metabolites and behavior in spontaneously hypertensive rats. Behav Brain Res 270:240–247. doi:10.1016/j.bbr.2014.05.013

Marriott AL, Ryan CL, Doucette TA (2012) Neonatal domoic acid treatment produces alterations to prepulse inhibition and latent inhibition in adult rats. Pharmacol Biochem Behav 103(2):338–344. doi:10.1016/j.pbb.2012.08.022

Mc Fie S, Sterley TL, Howells FM, Russell VA (2012) Clozapine decreases exploratory activity and increases anxiety-like behaviour in the Wistar-Kyoto rat but not the spontaneously hypertensive rat model of attention-deficit/hyperactivity disorder. Brain Res 1467:91–103. doi:10.1016/j.brainres.2012.05.047

McLoughlin G, Palmer JA, Rijsdijk F, Makeig S (2014) Genetic overlap between evoked frontocentral theta-band phase variability, reaction time variability, and attention-deficit/hyperactivity disorder symptoms in a twinstudy. Biol Psychiatry 75(3):238–247. doi:10.1016/j.biopsych.2013.07.020

Meechan DW, Maynard TM, Tucker ES, Fernandez A, Karpinski BA, Rothblat LA, LaMantia AS (2015) Modeling a model: Mouse genetics, 22q11.2 Deletion Syndrome, and disorders of cortical circuit development. Prog Neurobiol 130:1–28. doi:10.1016/j.pneurobio.2015.03.004

Micoulaud-Franchi JA, Lopez R, Vaillant F, Richieri R, El-Kaim A, Bioulac S, Philip P, Boyer L, Lancon C (2015) Perceptual abnormalities related to sensory gating deficit are core symptoms inadults with ADHD. Psychiatry Res. pii: S0165-1781(15)30319-X. doi:10.1016/j.psychres.2015.09.016

Miller EM, Pomerleau F, Huettl P, Russell VA, Gerhardt GA, Glaser PE (2012) The spontaneously hypertensive and Wistar Kyoto rat models of ADHD exhibit sub-regional differences in dopamine release and uptake in the striatum and nucleus accumbens. Neuropharmacology 63(8):1327–1334. doi:10.1016/j.neuropharm.2012.08.020

Miller EM, Pomerleau F, Huettl P, Gerhardt GA, Glaser PE (2014) Aberrant glutamate signaling in the prefrontal cortex and striatum of the spontaneously hypertensive rat model of attention-deficit/hyperactivity disorder. Psychopharmacology (Berl) 231(15):3019–3029. doi:10.1007/s00213-014-3479-4

Mitchison GM, Njardvik U (2015) Prevalence and Gender Differences of ODD, Anxiety, and Depression in a Sample of Children With ADHD. J Atten Disord. pii:1087054715608442

Noble EP, Ozkaragoz TZ, Ritchie TL, Zhang X, Belin TR, Sparkes RS (1998) D2 and D4 dopamine receptor polymorphisms and personality. Am J Med Genet 81:257–267

Ono Y, Manki H, Yoshimura K, Muramatsu T, Mizushima H, Higuchi S, Yagi G, Kanba S, Asai M (1997) Association between dopamine D4 receptor (D4DR) exon III polymorphism and novelty seeking in Japanese subjects. Am J Med Genet 74:501–503

Olney JW, Ishimaru MJ, Bittigau P, Ikonomidou C (2000) Ethanol-induced apoptotic neurodegeneration in the developing brain. Apoptosis 5(6):515–521

Pettersson E, Anckarsäter H, Gillberg C, Lichtenstein P (2013) Different neurodevelopmental symptoms have a common genetic etiology. J Child Psychol Psychiatr Allied Discip 54 (12):1356–1365

Pires T de O, de Silva CM, de Assis SG (2013) Association between family environment and attention deficit hyperactivity disorder in children—mothers' and teachers' views. BMC Psychiatr 13:215–230. doi:10.1186/1471-244X-13-215

Pozzi L, Baviera M, Sacchetti G, Calcagno E, Balducci C, Invernizzi RW, Carli M (2011) Attention deficit induced by blockade of N-methyl D-aspartate receptors in the prefrontal cortex is associated with enhanced glutamate release and cAMP response element binding protein phosphorylation: role of metabotropic glutamate receptors 2/3. Neuroscience 176:336–348. doi:10.1016/j.neuroscience.2010.11.060

Purkayastha P, Malapati A, Yogeeswari P, Sriram D (2015) A review on GABA/glutamate pathway for therapeutic intervention of ASD and ADHD. Curr Med Chem (9 Feb 2015)

Richards JS, Hartman CA, Franke B, Hoekstra PJ, Heslenfeld DJ, Oosterlaan J, Arias Vásquez A, Buitelaar JK (2015) Differential susceptibility to maternal expressed emotion in children with ADHD and their siblings? Investigating plasticity genes, prosocial and antisocial behaviour. Eur Child Adolesc Psychiatry 24(2):209–217. doi:10.1007/s00787-014-0567-2

Rommel AS, Halperin JM, Mill J, Asherson P, Kuntsi J (2013) Protection from genetic diathesis in attention-deficit/hyperactivity disorder: possible complementary roles of exercise. J Am Acad Child Adolesc Psychiatry 52(9):900–910. doi:10.1016/j.jaac.2013.05.018

Russell VA (2003) In vitro glutamate-stimulated release of dopamine from nucleus accumbens core and shell of spontaneous hypertensive rats. Metab Brain Dis 18:161–168

Russell VA (2007) Neurobiology of animal models of attention-deficit hyperactivity disorder. J Neurosci Methods 161(2):185–198

Russell VA (2011) Overview of animal models of attention deficit hyperactivity disorder (ADHD). Curr Protoc Neurosci Chapter 9:Unit9.35. doi:10.1002/0471142301.ns0935s54

Rybakowski F, Slopien A, Dmitrzak-Weglarz M, Czerski P, Rajewski A, Hauser J (2006) The 5-HT2A-1438 A/G and 5-HTTLPR polymorphisms and personality dimensions in adolescent anorexia nervosa: association study. Neuropsychobiology 53:33–39

Sadile AG, Pellicano MP, Sagvolden T, Sergeant JA (1996) NMDA and non-NMDA sensitive [L-3H]glutamate receptor binding in the brain of the Naples high- and low-excitability rats: an autoradiographic study. Behav Brain Res 78(2):163–174

Salatino-Oliveira A, Wagner F, Akutagava-Martins GC, Bruxel EM, Genro JP, Zeni C, Kieling C, Polanczyk GV, Rohde LA, Hutz MH (2015) MAP1B and NOS1 genes are associated with working memory in youths withattention-deficit/hyperactivity disorder. Eur Arch Psychiatry Clin Neurosci (2 Aug 2015)

Samochowiec J, Rybakowski F, Czerski P, Zakrzewska M, Stepien G, Pelka-Wysiecka J, Horodnicki J, Rybakowski JK, Hauser J (2001) Polymorphisms in the dopamine, serotonin, and norepinephrine transporter genes and their relationship to temperamental dimensions measured by the Temperament and Character Inventory in healthy volunteers. Neuropsychobiology 43:248–253

Santoro ML, Santos CM, Ota VK, Gadelha A, Stilhano RS, Diana MC, Silva PN, Spíndola LM, Melaragno MI, Bressan RA, Han SW, Abílio VC, Belangero SI (2015) Expression profile of neurotransmitter receptor and regulatory genes in the prefrontal cortex of spontaneously hypertensive rats: relevance to neuropsychiatric disorders. Psychiatry Res 219(3):674–679. doi:10.1016/j.psychres.2014.05.034

Sasaki T, Hashimoto K, Oda Y, Ishima T, Kurata T, Takahashi J, Kamata Y, Kimura H, Niitsu T, Komatsu H, Ishikawa M, Hasegawa T, Shiina A, Hashimoto T, Kanahara N, Shiraishi T, Iyo M (2015) Decreased levels of serum oxytocin in pediatric patients with AttentionDeficit/Hyperactivity Disorder. Psychiatry Res 228(3):746–751. doi:10.1016/j.psychres.2015.05.029

Schuch V, Utsumi DA, Costa TV, Kulikowski LD, Muszkat M (2015) Attention deficit hyperactivity disorder in the light of the epigenetic paradigm. Front Psychiatry 6:126. doi:10.3389/fpsyt.2015.00126

Sidlauskaite J, Sonuga-Barke E, Roeyers H, Wiersema JR (2015) Default mode network abnormalities during state switching in attention deficit hyperactivity disorder. Psychol Med 1–10 (12 Oct 2015)

Simões RV, Cruz-Lemini M, Bargalló N, Gratacós E, Sanz-Cortés M (2015) Brain metabolite differences in one-year-old infants born small at term and association with neurodevelopmental outcome. Am J Obstet Gynecol. 213(2):210.e1–210.e11. doi:10.1016/j.ajog.2015.04.011

Somandepalli K, Kelly C, Reiss PT, Zuo XN, Cameron Craddock R, Yan CG, Petkova E, Xavier Castellanos F, Milham MP, Di Martino A (2015) Short-term test-retest reliability of resting state fMRI metrics in children with and without attention-deficit/hyperactivity disorder. Dev Cogn Neurosci. pii: S1878-9293(15)00082-1. doi:10.1016/j.dcn.2015.08.003

Sterley TL, Howells FM, Dimatelis JJ, Russell VA (2015) Genetic predisposition and early life experience interact to determine glutamate transporter (GLT1) and solute carrier family 12 member 5 (KCC2) levels in rat hippocampus. Metab Brain Dis (14 Oct 2015)

Sterley TL, Howells FM, Russell VA (2013) Evidence for reduced tonic levels of GABA in the hippocampus of an animal model of ADHD, the spontaneously hypertensive rat. Brain Res 1541:52–60. doi:10.1016/j.brainres.2013.10.023

Swanson JM, Sergeant JA, Taylor E, Sonuga-Barke EJS, Jensen PS, Cantwell DP (1998) Attention deficit hyperactivity disorder and hyperkynetic disorder. Lancet 351:329–343

Thapar A, Cooper M (2015) Attention deficit hyperactivity disorder. Lancet. pii: S0140-6736(15)00238-X. doi: 10.1016/S0140-6736(15)00238-X

Thissen AJ, Bralten J, Rommelse NN, Arias-Vasquez A, Greven CU, Heslenfeld D, Luman M, Oosterlaan J, Hoekstra PJ, Hartman C, Franke B, Buitelaar JK (2015) The role of age in association analyses of ADHD and related neurocognitive functioning: A proof of concept for dopaminergic and serotonergic genes. Am J Med Genet B Neuropsychiatr Genet. doi:10.1002/ajmg.b.32290

Tzanoulinou S, García-Mompó C, Riccio O, Grosse J, Zanoletti O, Dedousis P, Nacher J, Sandi C (2015) Neuroligin-2 expression in the prefrontal cortex is involved in attention deficits induced by peripubertal stress. Neuropsychopharmacology. doi:10.1038/npp.2015.200

Turski CA, Ikonomidou C (2012) Neuropathological sequelae of developmental exposure to antiepileptic and anesthetic drugs. Front Neurol 3:120. eCollection 2012

van der Kolk A, Bouwmans CA, Schawo SJ, Buitelaar JK, van Agthoven M, Hakkaart-van Roijen L (2015) Association between societal costs and treatment response in children and adolescents with ADHD and their parents. A cross-sectional study in the Netherlands. Springerplus. 4:224. doi:10.1186/s40064-015-0978-7

van Mil NH, Steegers-Theunissen RP, Bouwland-Both MI, Verbiest MM, Rijlaarsdam J, Hofman A, Steegers EA, Heijmans BT, Jaddoe VW, Verhulst FC, Stolk L, Eilers PH, Uitterlinden AG, Tiemeier H (2014) DNA methylation profiles at birth and child ADHD symptoms. J Psychiatry Res 49:51–59. doi:10.1016/j.jpsychires.2013.10.017

van Rooij D, Hartman CA, van Donkelaar MM, Bralten J, von Rhein D, Hakobjan M, Franke B, Heslenfeld DJ, Oosterlaan J, Rommelse N, Buitelaar JK, Hoekstra PJ (2015a) Variation in serotonin neurotransmission genes affects neural activation during response inhibition in adolescents and young adults with ADHD and healthy controls. World J Biol Psychiatry 1–10 (Oct 1 2015)

van Rooij D, Hoekstra PJ, Bralten J, Hakobjan M, Oosterlaan J, Franke B, Rommelse N, Buitelaar JK, Hartman CA (2015b) Influence of DAT1 and COMT variants on neural activation during response inhibition in adolescents with attention-deficit/hyperactivity disorder and healthy controls. Psychol Med 45(15):3159–3170. doi: 10.1017/S0033291715001130

Volk HE, Neuman RJ, Todd RD (2005) A systematic evaluation of ADHD and comorbid psychopathology in a population-based twin sample. J Am Acad Child Adolesc Psychiatry 44 (8):768–775

Webb E (2013) Poverty, maltreatment and attention deficit hyperactivity disorder. Arch Dis Child 98:397–400. doi:10.1136/archdischild-2012-303578

Wong KM, Cloninger CR (2010) A person-centered approach to clinical practice. Focus 8 (2):199–215

Womersley JS, Kellaway LA, Stein DJ, Gerhardt GA, Russell VA (2015) Effect of cocaine on striatal dopamine clearance in a rat model of developmental stress and attention-deficit/hyperactivity disorder. Stress 1–17 (23 Sep 2015)

Ye ZY, Li DP, Pan HL (2013) Regulation of hypothalamic presympathetic neurons and sympathetic outflow by group II metabotropic glutamate receptors in spontaneously hypertensive rats. Hypertension 62(2):255–262. doi:10.1161/HYPERTENSIONAHA.113.01466

Zimmermann AM, Jene T, Wolf M, Görlich A, Gurniak CB, Sassoè-Pognetto M, Witke W, Friauf E, Rust MB (2015) Attention-deficit/hyperactivity disorder-like phenotype in a mouse model with impaired actin dynamics. Biol Psychiatry 78(2):95–106. doi:10.1016/j.biopsych.2014.03.011

Zha YP, Wang YK, Deng Y, Zhang RW, Tan X, Yuan WJ, Deng XM, Wang WZ (2013) Exercise training lowers the enhanced tonically active glutamatergic input to the rostral ventrolateral medulla in hypertensive rats. CNS Neurosci Ther. 19(4):244–251. doi:10.1111/cns.12065

Zhang K, Chammas C, Soghomonian JJ (2015) Loss of glutamic acid decarboxylase (Gad67) in striatal neurons expressing the Drdr1a dopamine receptor prevents l-DOPA-induced dyskinesia in 6-hydroxydopamine-lesioned mice. Neuroscience. 303:586–594. doi:10.1016/j.neuroscience.2015.07.032

Zhou R, Bai Y, Yang R, Zhu Y, Chi X, Li L, Chen L, Sokabe M, Chen L (2011) Abnormal synaptic plasticity in basolateral amygdala may account for hyperactivity and attention-deficit in male rat exposed perinatally to low-dose bisphenol-A. Neuropharmacology. 60(5):789–798. doi:10.1016/j.neuropharm.2011.01.031