



Recent Advances

AUTISM

SPECTRUM DISORDERS

Edited by Michael Fitzgerald

Autism Spectrum Disorder

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Preface

This book starts with a new sub category of Autism Criminal Autistic Psychopathy and school shootings. It focuses on a number of interventions, including speech and language pathology, speech and language assessment instruments, occupational therapy, improving functional language development in autism with natural gestures, communication boards etc as well as helping people with autism using the pictorial support, training of concepts of significant others, theory of mind, social concepts and a conceptual model for empowering families of children with autism cross culturally.

It also examines the issue of hyperandrogenism and evidence-based treatments of autism. In terms of assessment, it focuses on psychological and biological assessment including neurotransmitters systems, structural and functional brain imaging, coping strategies of parents, examines the intertwining of language impairment, specific language impairment and ASD, as well as implicit and spontaneous Theory of Mind reading in ASD.

In terms of aetiology, it focuses on genetic factors, epigenetics, synaptic vesicles, toxicity during neurodevelopment, immune system and sex differences.

It also examines the link between social cognitive anatomical and neurophysiologic biomarkers and candidate genes.

This book will be relevant to all mental health professionals because autism occurs in all the different areas of psychiatry and professionals who will find it helpful will be psychiatrists, psychologists, social workers, nurses, teachers and all those working with persons with Autism including parents who nowadays are interested in knowing more and more, at a detailed level about their children or adults with autism.

Autism and School Shootings — Overlap of Autism (Asperger's Syndrome) and General Psychopathy

Michael Fitzgerald

Additional information is available at the end of the chapter

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1. Introduction

The vast majority of persons with Autism Spectrum Disorders are highly moral but can show aggression of a non-lethal severity. Nevertheless there are a small number of persons with Autism or Asperger's Syndrome who do show lethal violence. I have described these as Criminal Autistic Psychopathy [(Fitzgerald 2010)]. The rate of these problems in special hospitals and prisons is almost twice the general population prevalence of Autism and Asperger's Syndrome. Originally, these conditions were called Autistic Psychopathy by Hans Asperger 1938 and 1944. [9] I am suggesting that we bring back the diagnosis of Autistic Psychopathy for those persons with Autism and Asperger's Syndrome who engage in criminal activities with the new diagnosis Criminal Autistic Psychopathy. These persons have the dual features of Autism and Psychopathy. The seriousness of this condition is often missed with the sole diagnosis of Autism or Asperger's Syndrome. There are overlapping features but also differences from General Psychopathy as described in these examples of school killers in the literature.

In relation to the school shooting at Sandyhook School, Solomon (214) noted that from his conversation with Peter Lanza that his son Adam who shot 26 people at his school showed poor eye contact, problems with social relationships, preservation of sameness, narrow interests, poor communication skills and sensory issues. These are the classic features of Asperger's Syndrome DSM IV or the sub group of Asperger's Syndrome called Criminal Autistic Psychopathy [11].

2. Social relationship problems

Father [16] p.38) described him as showing "social awkwardness" and one of his psychiatrists Robert King [16] p.39) noted that he declined "to shake hands" when he met him. Adam was extremely controlling and dominating and had very little capacity for social reciprocity. He became very withdrawn and isolated as he grew up. Father said [16] p.40) that his son "was not open to therapy" and "did not want to talk about problems". Poor concentration is central to Asperger's Syndrome and Criminal Autistic Psychopathy. He showed problems in that area. He had major empathy deficits in relation to other people. According to [16] when his mother "asked Adam whether he would feel sad if anything happened to her, he replied "no". He found it much easier to communicate online. It's online that the true state of affairs of people with dangerous thoughts and fantasies particularly those with Asperger's Syndrome, Criminal Autistic Psychopathy sub type can be noticed. He felt hostile to people particularly females. On his computer he wrote "why females are inherently selfish" [16] misogyny is very common in these conditions. Father [16] states that "Adam would have killed me in a heartbeat, if he'd had the chance". He shot his mother "four times". [16].

In relation to social relationships the State Attorney [16] stated that he "was more likely to be victimised than to act in violence against another". This is usually what happens to people with Asperger's Syndrome. He once asked his father "why do you need friends?" [16].

2.1. Preservation of sameness

[16] describes him as showing "sclerotic orderliness". He found changing classes during the school day very stressful. His psychiatrist King also noted that "if mother walks in front of him in the kitchen, he would insist she re-do it" [16]. He had evidence of OCD and according to [16] "washed his hands excessively".

2.2. Narrow interests

He would spend hours playing with lego with his brother [16] and indeed "invented his own board games". [16]. He wrote violent stories. [16]. He was "fascinated with guns and with the second world war, and showed an interest in joining the military". [16]. He became pre-occupied with "mass murder". [16] and "left a photograph of himself with a gun to his head". [16]. He created his own private autistic world. He loved hi-tech matters and "was a member of his school hi-tech club". [16]. Mother tried to fit in with his special interests for example taking him to the shooting range. She did her best. His interest in violence was best seen in his essays and online.

2.3. Non-verbal behaviour

He showed poor eye contact and the psychiatrist Robert King described him as "pale, gaunt, awkward, young, adolescent standing rigidly with downcast gaze". [16].

2.4. Sensory issues and motor issues

He suffered from sensory overload, which of course made school much more difficult for him. [16] noted that he "showed hyper-sensitivity to physical touch that tags had to be removed from his clothing and "sometimes he smelled things that weren't there". I don't agree with this as he had hyper-sensitivity to smell and could smell things that the average person would be unable to do so. In relation to visual hyper-sensitivity "colour graphics" upset him. [16]. He probably also had clumsiness with a "stiff lumbering gait" [16]. His father stated that he had an "awkward walk" [16] pointed out that he was "intolerant of his mother brushing by his chair and objected to her new high heels, high heel boots, because they were "too loud". This was according to psychiatrist King.

2.5. Verbal communication

King [16] also noted that he "had relatively little spontaneous speech but he responded in a flat tone with little inflection and almost mechanical prosody". And when King asked about his three wishes he replied "that whatever was granting the wishes would not exist".

2.6. Anxiety and depression

He suffered from anxiety and depression and was prescribed Lexopro an anti-depressant but got side effects and stopped it. Father described him as suffering from "uncomfortable anxiety" [16]. He had negative thinking, low self-esteem and mother noticed that "he was exhausted and lethargic all day" and had a "sense of hopelessness". [16]. He was tearful and his mother described his "escalating misery". [16].

2.7. School

He was a bright boy nevertheless school was experienced as a challenge for him both socially and academically which led to some home schooling. He was an autodidact. There was evidence of symptoms of Attention Deficit Disorder in terms of poor concentration. He showed poor school progress and his mother reported that he was in despair "when faced with some course work in German" [16]. Nevertheless he set himself very high standards.

3. Eric Harris: Columbine

Eric had Criminal Autistic Psychopathy with a Narcissistic Personality and Depression.

3.1. Early years

He was a highly intelligent child. He loved fishing with his father and loved the quietness of the mountains and lake. He was very visual and had a keen appreciation of landscape and appreciated the effect of light on water and in particular loved "water". [5]. [5] describes a neighbour's comment on Eric that he was "nice, polite, preppy, and a dork". [5] noted that "his

hand was always shooting up in a class and he always had the right answer". Page 9. He was highly intelligent and of course in the long term this increased his dangerousness. He was also described as being "painfully shy". [5]. He had surgery for "pectus excavatum, an abnormally sunken sternum". [5]. This was a narcissistic wound for him as a child. Eric was "gifted analytically, excellent at maths, a technology expert and into "gadgets, computers, video games". [5]. Here again we see some overlap between General Psychopathy and Criminal Autistic Psychopathy. Cullen notes that a Little League Team mate described Eric as the "shyest out of everybody" and was restricted in what he said. His coach [5] noted that "he didn't want to miss (a ball). He didn't want to fail" and therefore he was very slow to swing a bat. This again shows his narcissistic vulnerability and his fear of missing which he found humiliating. In a way according to [5] Eric "scripted Columbine, as a made for TV murder". [5]. This is further evidence of his narcissism and in fantasy he re-enacted the pleasure of the massacre endlessly in the long period leading up to it. In his own mind he was the superior one, the man who was awesome and frightened the world.

[5] noted that "Eric wanted to be remembered". He certainly left his mark on the sands of time. He wanted to be feared and wanted to be in a position where nobody ever looked down on him again.

3.2. Narcissism

The FBI analyst who examined his motives suggested that Harris was a classical psychopath and had a "messianic level superiority complex and hoped to illustrate his massive superiority to the world". Immelmann (2009) described Eric as possessing a "malignant narcissism... a Pathological Narcissistic Personality Disorder with borderline and anti-social features, also with some paranoid traits and unconstrained aggression". Eric wrote according to [5] that "my belief is that if I say something, it goes. I am the law. If you don't like it, you die". [5] summarised Fuseliers opinion that "Eric had a preposterously grand superiority complex, a revulsion for authority, an excruciating need for control". This was largely inherent in Eric with huge innate factors and again we see the overlap with Criminal Autistic Psychopathy. Eric also stated "I feel like God and I am higher than almost anyone in the fucking world in terms of universal intelligence". [5]. This was not psychosis but it is close to psychosis.

Eric also said that "Zeus and I also get angry easily and punish people in unusual ways". [5]. In a way Zeus was one of the superior Gods. After Eric was arrested for the breaking into the car he switched from being an "observer to enforcer". [5]. This was a critical life event and even though he was the perpetrator he understood it himself as that he was the victim and how dare they arrest him and put him in handcuffs. This speeded up his sense of injustice, his hatred of humanity and simply accelerated his wish to do the massacre. Of course he was on that path before he was arrested. Eric "fancied himself as a non-conformist, but he craved approval and fumed over the neighbour's disrespect". [5]. Eric was hypersensitive to any rejection or criticism and [5] noted that Eric had "a long list of betrayals, an actual "shit list" on his computer of despicable young girls". He talked a lot about people who "knifed... him in the back". Most of this was more imaginary than real. Nevertheless it was psychologically very real to him.

3.3. Attitude to other people

Eric stated on one occasion "I hate almost everyone" and ah yes "I wanna rip his head off and eat it" in a "flat voice". [5]. After a fishing trip he talked about going back to "shithead society populated by automatons too dense to comprehend what was out there". [5]. Eric also wrote "if you have a problem with my thoughts, come and tell me and I'll kill you" [5]. Another one of his rants was "I hate". [5]. According to [5] p.216 Eric's "only internal struggle concerned which stupid bastards was more deserving of his wrath". He saw himself as an avenging God. Before the massacre of course he was a petty criminal. [5]) noted that Eric "savoured the idea (of) heroic opportunities to obliterate alien hoards. His dreams were riddled with gunfire and explosions" and "he was always dazzled by fire". Eric made "death threats" to another student. [5] p.88. Eric wrote on his website that he wanted to "mow down" the people of his area and that "I don't care if I live or die in the shootout..."all I want to do is kill and injure as many of you pricks as I can". [5] p.216. [5] p. 219 notes that Eric "described going to some random downtown area....and blowing up and shooting up everything he could. He assured us he would feel no remorse, no sorrow, no shame. He would make them pay". This shows an incredibly deep hatred of the human race and he did not have a traumatic childhood. Again we are dealing with a personality and with problems largely coming from inside him.

In 1998 he wrote in a notebook "I hate the fucking world" and that "I am not respected". [5]. This was a largely paranoid thought and not based on reality. Eric also stated that "human beings were pathetic fuckheads too dense to perceive their lifeless existence...automatons" and people were "assembly-line robots". In a way Eric wanted to destroy humanity in the world. In addition Eric "had a grander vision. All his writing alluded to a wider slaughter; killing everything, destroying the human race" and he also wrote "kill them all. Well if you have not figured it out yet, I'd say "kill mankind". [5].

3.4. Eric's description of himself and description of him by others

Cullen (2009) states that girls found him "cute" and that "he'd always hated his appearance". Eric also could be charming and told a great deal of lies. He did not suffer from guilt for his actions. [5] noted that his Principal in college Frank de Angelis noted that Harris was "the type of kid who, when he was in front of adults, he'd tell you what you wanted to hear". Cullen also noted that a classmate had "the impression... (that Eric) wanted to be an outcast. He was also described as "moody and aggressive". P. 140. He suffered from depression. Eric was "egotistical, empathy-free". [5]. When Eric was asked to describe himself in filling out a questionnaire which focused on distrust etc., he described himself as agreeing with some of the following descriptions: jealous "anxiety, suspiciousness, temper, obsessive thoughts, mood swings, disorganised thoughts, homicidal thoughts" [5]. When mental health professionals assessed him he seethed "as he scrawled out his answers" and he considered "the nerve of these low lifes judging him" and how he "hated fools telling him what to do." [5]. In addition, Eric was "a dreamer" of "a world where the rest of us had been removed". [5]. [5] described Harris as a "cold-blooded, predatory psychopath". Fusilier [5] noted that Eric showed "cold rational calculation-(was) charming, callous, cunning, manipulative, comically grandiose, egocentric, with appalling failures of empathy". He had the capacity when he wanted to to fool people

and deceive people and was a superb liar and he was also a sensation seeker and novelty seeker. Therapy for persons with psychopathy often makes them better at psychopathy and improves their destructive social skills. He was in therapy but only pretended to engage himself from it. He was "unemotional" and was extremely dominating and controlling. [5].

He was well able to manage adults and to tell adults what they wanted to know and what they wanted to hear. His parents described him earlier as "getting angry all the time.at almost anything he didn't like" and he would "punch a wall" [5].

3.5. Interests

Eric wrote (Cullen 2009) that "guns! boy, I loved playing guns". He was also superb at violent video games. He used to sketch "medieval armour and sub-machine guns" and would draw "victims (who) were frequently on fire and freshly decapitated" as well as he showed a great interest in the Nazis and their activities. [5], p.81. Another great interest was in "explosives". [5]. He loved to make home made bombs. Other interests included "Nietzsche, Freud, Hitler" and he used to say "Sich Heil" or "Heil Hitler". He was obsessed with massacres and mayhem on television.

3.6. Relationship with girls and other adults

Eric was a boy who "smoked, drank, dated" (page 6 [5] and he would walk up to "hotties in the Mall". "He won them over with quick wit, dazzling dimples and a disarming smile". [5]. Nothing could be further from Asperger's Syndrome than this. This was his genuine evidence of an element of General Psychopathy.

3.7. Control and domination

[5] stated that when "somebody needed to take control. Eric was your man. He was like a robot under pressure". The local Pizza Store where he worked had a particularly good opinion of his capabilities and put him "in charge when he left". [5]. He had excellent management skills and found it very easy to manage his co-killer Dylan Klebold.

3.8. Conclusion

In writing there was often contradictions and Eric's writing wasn't always logical. Eric had excellent social know how compared to Dylan. Dylan and Eric had major empathy deficits and were both hostile and somewhat paranoid people. Both suffered from depression. They became a most dangerous murderous couple. Eric was the active one the leader and Dylan was the follower the passive one. They played out their killing in fantasy many times before they carried it out. The warning signs were mainly in their writings and on their website. Nevertheless they both had contact with the police. Clearly if teachers read the kind of essays that they write and their pre-occupations from now on they should take these writings very seriously and take action on them.

4. Dylan Klebold

4.1. Childhood

Dylan was described by his parents as an "introverted and has grown up isolated" and is "often angry or sullen and his behaviours seemed disrespectful to and intolerant of others". [5]. Dylan [5] was "born brilliant" and went to school "a year early" and was sent to a gifted child programme because he was "a maths prodigy". Everybody said he was extremely shy. He was extremely sensitive to criticism and could have meltdowns that could take quite a while for him to recover from. He had very vulnerable self-esteem and criticism would easily lead to a meltdown.

4.2. Social relationships

[5] points out that Dylan Klebold was "meek, self-conscious and shy. He could barely speak in front of a stranger, especially a girl. He'd follow quietly after Eric (co-mass killer) on the Mall conquests attempting to appear invisible". Eric flattered "girls" with compliments; "Dylan passed them chips, cookies to let them know he liked them. Dylan's friends said he had never been on a date; he may never have asked a girl out". Not surprising Dylan wrote in 1997 "I feel so lonely without a friend". [5]. Dylan was a loner, which caused him pain and "felt cut off from humanity". [5] Dylan described himself as someone who had "no girl (friends)/not even platonic, no other friends, nobody accepting him, doing badly in sports, looking ugly and acting shy, getting bad grades, having no friends in life". [5]. Dylan did at times regard other humans as "zombies" and wrote about himself "I am God compared to some of these un-existable brainless zombies". [5]. This was projection and shows that he had some grandiosity as well which is often hidden behind low self-esteem.

He was very naive and tended to be caught if he did anything wrong. This is typical of persons with Autism. He was caught when he broke into a car and stole stuff with his friend Eric Harris (co-mass killer). According to [5] "Dylan Klebold was not a man of action. He was conscripted by a boy who was". Persons with Asperger's Syndrome are very easily led. They are often led into serious crime by other people particularly persons with psychopathy like Eric Harris. He shared talents with Eric Harris including great mathematical ability, technological expertise and in particular Dylan was excellent at "analysing, inventing, deconstructing". [5]. Dylan would hammer at "ideas relentlessly". [5]. Dylan wanted to become a specialist in computing technology and there was no doubt he would have achieved that if he hadn't met Eric Harris.

4.3. Interests

Dylan was very interested in "classical philosophers and renaissance literature". [5]. Dylan was into polarities and felt himself to be split in his mind. One of the polarities that fascinated him was "good and bad". This was a major focus for him [5]. [5] that "Dr Fuselier from the FBI stated that "both boys fantasised about murder, but Dylan focused on a single attack".

4.4. Sense of self

[5] points out that Dylan did believe in God but that he would "cry out, cursing God for making him a modern Job, demanding an explanation for the divine brutality of his faithful servant. It's hardly surprising he considered suicide as a way out. Dylan wrote that "God had chosen him" as someone "in search of answers, never finding them, yet in hopelessness understands things. He seeks knowledge of the unthinkable, of the undefinable, of the unknown. He explores everything/using his mind, the most powerful tool known to him". [5].

4.5. Depression

Dylan had fantasies about relationships with a girl which were very powerful. He suffered from depression which is very typical with Autism indeed he wrote "good God I hate my life, I want to die really bad right now". [5]. He also had preservation of sameness and was very much a routine driven boy.

4.6. Naivety

When Dylan hacked into the school computer he was caught and reprimanded. [5] wrote that when Dylan was "caught scratching obscenities into a freshman's locker, he was called before the school Dean and went ballistic. He cussed the Dean and bounced off the walls" and acted bizzarely.

4.7. Home movies

Dylan had acting potential which was really one area where he was superior to Eric Harris his leader. It is well known (Fitzgerald 2014) that many great actors had Autism or Asperger's Syndrome. [5] noted that on film Dylan "unleashed his anger and he was that crazy man disintegrating in front of the camera. His eyes bulged out". It was also noticed that in life generally he was not very capable and was not given complex tasks to do.

Overall he had no ability to plan an operation on his own like the massacre and was simply led in a very naive way by a person with psychopathy Eric Harris.

5. Virginia tech shootings

Cho Seung-Hui the mass killer at Virginia Tech also had a diagnosis of Autism. He was a shy, withdrawn child who had problems with social know how and social cop on. He hated hugging as a child and was very violent. He was clingy to his mother. He showed poor communication and often gave one word answers to questions. He great aunt [2] stated that "when others called his name he just answered yes or no but never showed any feelings or emotions. We started to worry he was autistic". Later he was formally diagnosed with Autism. He was bullied within the educational system.

A Professor Lucinda Roy complained to the campus police about him and she also gave him "individual lessons" and said to him: "You seem so lonely"- "Do you have any friends?". "I am

lonely". Cho replied. "I don't have any friends". A student at Virginia Tech Karen Grewal [17] noted that "he was so quiet, it was almost as if he wasn't there and was invisible. He must have been worried that he'd would be found out".

[3] noted that there were "college girls who reported him to the police for stalking and got him carted off to a mental hospital after he sent them shy love messages full of meaning". Cho [3] also wrote "by a name, I know not how to tell who I am". This is typical of the identity diffusion of autism. He was unable to get a girlfriend and "he had to make up with a fantasy girlfriend". [3]. He was a loner as a child. [2] notes that a fellow student noted he was "obsessed with violence and with serious personal problems". He admired the Columbine killers. Professor Nikki Giovanni one of his teachers at Virginia Tech was concerned about his writing i.e. "your bra is torn and I am looking at your flesh". [3]. He'd never speak but he frightened everyone. According to [17] "he insisted on wearing sunglasses and pulling his baseball cap low on his forehead" and that neighbours "described him as a surly youth who did not communicate and ignored them in the street". He was a major mathematical talent like many with Autism. [9]. Professor Louis Schlesinger a Professor of Forensic Psychology states that "mass killers tend to be aggrieved, hurt, clinically depressed, socially isolated and above all paranoid". (Begley 2007).

In the psychiatric hospital in 2007 a psychiatrist noted his "affect is flat and mood is depressed". (Begley 2007).

6. Conclusion

School shootings and mass killings are not uncommonly committed by persons with neuro-developmental disorders i.e. Criminal Autistic Psychopathy/Asperger's Syndrome with often a good deal of warning based on writings on the internet and elsewhere.

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References

- [1] Asperger H. (1944-1991) Die "Autistischen Psychopathen". i.m Kindesalter, Archives fur Psychiatrie und Nervenkrankheiten 117, 67-136. Translated in U. Frith (ed) Autism and Asperger's Syndrome, Cambridge University Press 39-92.

- [2] Baxter S. 2007 Cold Childhood of Cho. Sunday Times April 22nd p.27
- [3] Baxter S. 2007 American Psycho. Sunday Times Review April 22nd p. 1-2
- [4] Cullen Davi Eric's Big Lie (<http://columbine-online.com/journals/columbine-eric-harris-big-lie.htm>)columbineonline
- [5] Cullen D. 2009 Columbine. Oldst publishing; Devon U.K.
- [6] Dylan showed classical Asperger's Syndrome ICD 10 that is Criminal Autistic Psychopathy sub-type (Fitzgerald 2010).
- [7] FBI The Depressive and the Psychopath: The FBI analysis of the killer's motives. (<http://www.slate.com/id/20992031>).Slate April 20th 2004
- [8] Fitzgerald M (2005) Malignant alienation or Asperger's Syndrome. The Journal of Psychiatric Practice, 29, 5, 193.
- [9] Fitzgerald M. James I. 2007 The Mind ofthe Mathematician. John Hopkins University Press: Baltimore
- [10] Fitzgerald (2014 In Press) The Mind of the Artistic. Nova Science: New York.
- [11] Fitzgerald (2010) Young Violent and Dangerous to Know. Nova Science: New York.
- [12] http://en.wikipedia.org/wiki/columbine_high_school_massacre.
- [13] Immelman, Aubrey August (2004) Eric Harris: personality profile. (<http://www.csbsju.edu/usbb/Criminalp20filing/Columbine-eric-harris-profile.html>).
- [14] Lyons V. Fitzgerald M. (2009) Asperger & Kanner, the two pioneers of Autism. Journal of Autism and Developmental Disorders 37, 2022-2023.
- [15] Patrick C. J. (2006) Handbook of Psychopathy. Gilford Press: New York.
- [16] Solomon .A 2014. The reckoning March 17th The New Yorker 36-45.
- [17] Sherwell P. Shipman T. 2007. He'd never speak, but he frightened everyone. Sunday Independent. April 2nd 2002.

Neurotransmitter Systems in Autism Spectrum Disorder

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1. Introduction

Neurotransmitters, which connect neurons with each other, have key roles in normal development of brain, memory, motor activity and behavior regulation [1]. Based on these knowledge, neurotransmitter system dysfunction thought to be the cause of Autism Spectrum Disorder (ASD), by affecting neuronal cell migration, differentiation and synaptogenesis and eventually developmental processes of the brain [2, 3]. In pathophysiology of ASD many neurotransmitter systems has been investigated and dysfunction of these systems has been shown to be responsible. In the literature, neurotransmitters that are most commonly associated with the pathogenesis of ASD are, GABAergic, glutamatergic and serotonergic systems [4].

2. GABA

In order to maintain function and homeostasis of Central Nervous System (CNS) the balance between excitation and inhibition of neurons is very important. Main inhibitory neurotransmitter in the brain is gamma amino butyric acid (GABA) [5]. GABA is synthesized from glutamate by the enzyme glutamic acid decarboxylase (GAD) [6]. This enzyme has two isoforms known as GAD67 and GAD65, these are encoded by GAD1 and GAD2 gene. These enzymes different from each other in terms of the intracellular localization, expression, and enzymatic activity [7]. After GABA synthesized, it is taken to the vesicle by vesicular GABA transporter (VGATs) [8]. GABA is released to synaptic space under influence of Action Potential (AP) and binds to the GABA_A and GABA_C ionotropic receptors or metabotropic GABA_B receptors [9]. The activity of GABA that is released to the synaptic space is ended by GABA transporters which are located at cell membrane (GAT) [10]. Finally GABA that

is taken to the inside cell furtherly degrades by the transaminase or succinate semialdehyde dehydrogenase enzymes [9].

GABA has a key role in the regulation of early developmental stages of cell migration, neuronal differentiation and stages of maturation [11]. Besides, formation of GABAergic system has a critical role in migration of GABAergic neurons and formation of glutamergic system mediated excitatory processes that regulate cortical inhibitory system [12]. Therefore, it is not surprising that especially in ASD and in many neurodevelopmental disorders GABAergic system is the main responsible [13, 14]. In addition, the high prevalence of epilepsy in patients with autism have made it worth to investigate GABA neurotransmitter system in individuals who has ASD [15].

Neurochemical abnormality that postulated to be associated with pathophysiology of ASD is the reduction in the expression of GAD65 and GAD67 which cause suppression of GABAergic inhibition [16]. Fatemi and his colleagues [17], in the cerebellum and parietal cortex of patients has shown significantly decrease in two isoforms of the rate-limiting enzyme which are responsible for the conversion of glutamate to GABA. Detection of low platelet GABA levels in children with ASD [18] and postmortem studies that illustrated significant reduction in GABA_A and GABA_B receptor subunit in various brain regions [19, 20] support the widespread dysfunction of GABAergic system in patients with ASD. Reduced production or signaling of GABA cause hyperexcitability state and leads to cognitive dysfunction [21]. Deletional mutations of genes encoded by chromosome 15q11-q13 which is some of the GABAA receptor subtype unites (GABRB3, GABRA5 and GABRG3) might be cause of reduction in GABAergic transmission, and these mutations have been suggested to be a risk factor ASD [14]. Also, many of the candidate genes associated with ASD are expressed in interneurons [22]. Antiepileptic agents, especially benzodiazepines has been used in ASD and epilepsy coexisted patients and they have shown to improve socialization and communication skills, though, in some cases, they lead to increased anxiety and aggression, because of this, the information mentioned above is not clear yet [23,24]. Lemonier and Ben-Ari [25] suggested that the inhibition of Na / K / Cl transporter (NKCC1) lead intracellular increased Cl levels, so the GABAergic transmission will change depolarization to the hyperpolarization and in five ASD cases they get positive results after the treatment with NKCC1 inhibitor bumetanide. Then they carried out double blind randomized controlled clinical trial of bumetanide for treatment of ASD for 3 months of period in 54 patients, the results has shown to provide a significant improvement of ASD symptoms [26]. In utero exposure to valproate in mice model, has caused disappearance of swith between GABA excitation / inhibition and this problem has shown to lead the development of chronic chlorine deficits and autistic-like behavior [27]. Ion channels mutated mouse model which led to the reduced GABAergic transmission, and the corelation between ASD symptoms and reduced GABAergic transmission level and with benzodiazepine treatment autistic-like behavior to has shown to decrease [28].

As a result of animal model publications and studies conducted in patients with ASD has confirmed the hypothesis of "decreased GABAergic transmission in ASD patients". In future studies, to develop a new therapeutic agents, and to even prevent the disease focus should be directed on the GABA neurotransmitter system.

3. Glutamate

Glutamate is essential excitatory neurotransmitter of the central nervous system. It is synthesized from glutamine via glutaminase enzyme. There are two types which are ionotropic and metabotropic receptors. Metabotropic receptors (mGluR) are coupled with G protein and within the cell according to signaling pathways they divided 3 into subtypes: Group I (mGluR1 and mGluR5), group II (mGluR2 and mGluR3), Group III (mGluR4 and mGluR6-8). Group I works through activation of phospholipase C whereas Group II and Group III works through decreasing cyclic AMP level [29]. Ionotropic receptors which are coupled with ion-channel, have 3 sub-types: N-methyl-D-aspartate (NMDA), α -amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid (AMPA) and kainate receptors. Kainate receptors located presynaptically at the hippocampus, stimulation of them reduce glutamatergic transmission [30]. Induction of AMPA receptors, these are associated with learning and memory, lead to the long-term potentiation (LTP) and long-term depression of (LTD) [31]. High levels of glutamate leading to overstimulation of NMDA receptors and cause a high amount of calcium influx, which is main responsible for excitotoxicity lead to the neuronal damage. Therefore, optimization of the level of glutamate in the synaptic cleft is critical. To protect post-synaptic neurons from excitotoxic effect the neuronal glutamate transporters which reside at the presynaptic membrane take back glutamate into cell from synaptic cleft. In final stage, glutamate is destroyed with GAD [1]. Balance between excitation / inhibition is crucial for synaptogenesis and plasticity, especially in first 3 years of life [32]. Blockade of NMDA receptors in the prenatal period initiates apoptosis in neurons [1].

From this point, glutamate plays a central role in shaping the architecture of the brain. Cell migration, maturation and developmental stages, such as synaptogenesis and neuroplasticity is accomplished with the optimum glutamate transmission level [33, 34]. At the same time it is directly associated with cognitive processes such as memory and learning [35].

Glutamate receptors associated with ASD are highly expressed in the hippocampus and cerebellum [36]. For these reasons, the role of glutamatergic system in patients with ASD has been substantially investigated, two opposite hypotheses regarding the role of this system have been proposed [37]. First hypothesis of ASD has been proposed hypoglutamatergic state [38, 39, 40], the second postulated the depletion of GABAergic inhibition / excitation rate which eventually lead to the hyperglutamatergic state [41, 42, 43]. Consistent with the hypothesis suggested that ASD is hypoglutamatergic disorder, in 1998 Carlsson has postulated decrease in glutamate signaling lead to activation of receptors at the cortical GABA interneurons and this state cause significant depression in excitatory glutamate circuit [38, 44].

Other supportive evidence is hypoglutamatergic state in mouse models caused similar presentation to ASD including inability to change behavior paradigm, limitation in habits and behavior [45] In a postmortem study patients with ASD has shown significant decrease in AMPA type 2 and 3 in cerebellum tissue [40].

Another hypothesis that might be surrogate to explain ASD is hypoglutamatergic state and associated cortical tissue hyperexcitability in specific cortical areas. Some studies has demon-