Animal Models of Schizophrenia with a Focus on Models Targeting NMDA Receptors

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Abstract

Schizophrenia is a serious and often devastating disease, affecting approximately 1% of worldwide population. Animal models represent a suitable way for investigating serious brain diseases in preclinical research. Animal models of schizophrenia can be generally divided into several categories that include pharmacological, genetic and neurodevelopmental models. Pharmacological models are usually based on application of specific receptor ligands for neurotransmitters. Genetic models are created by genetic manipulations (mutations; often in laboratory mice). Neurodevelopmental models are induced by manipulations in early stages of life of the laboratory animal. They are manifested later in juvenile or adult age by phenotypes that are similar to schizophrenia symptoms. This review summarizes and discusses pharmacological models of schizophrenia based on application of NMDA receptor antagonists; furthermore, the study focuses on selected genetic and neurodevelopmental models.

Keywords

Schizophrenia, animal models, pharmacological models, genetic models, neurodevelopmental models, preclinical studies

Schizophrenia is a serious, complex and devastating mental disease that affects about 1% of the worldwide population (Sartorius et al., 1986). It usually manifests in late adolescence, generally earlier in men than in women (Castle et al., 1998). Many patients show deficits in areas such as social behavior (Allen et al., 2005), intellectual abilities (Amminger et al., 2000) and motor functions (Rosso et al., 2000). The symptoms of schizophrenia can be divided into positive (hallucinations, delusions, thought disorders), negative (disorder in social interactions, motivation, disorder of natural speech, anhedonia) and cognitive impairment which includes difficulties with attention, working memory, visual retrieval and intelligence (Andreasen, 1995).

Modeling human neuropsychiatric diseases such as schizophrenia is difficult partly because of the complexity of the disease but mainly because the psychological states typical for human diseases are hard to observe in animals or are not accessible at all. Therefore, researchers often focus on changes in behavior or cerebral physiology or try to derive analogies that with a certain degree of simplification reflect the clinical symptoms in patients. Currently, there is no animal model that would encompass all the features and symptoms of schizophrenia. However, a series of pharmacological neurodevelopmental and genetic models that mimic certain states of the disease and are used for developing potential antipsychotic medication have been developed (Jones et al, 2011). The most common animal models are the rodents, but primates such as capuchins (Shiigi and Casey, 1999), squirrel monkeys (Boyce et al., 1991) or vervets (Ridley et al., 1982) can also be used. The interesting fact is that some pharmacological models that used blockers of N-methyl-D-aspartate (NMDA) receptors were tested even in aquarium fish, namely in zebrafish (Danio rerio) (Seibt et al., 2011).

All animal models should have adequate validity. The validity should be phenomenological, which specifies to what extent the changes in behavior in an animal are similar to changes in a human, constructive,

which reflects the theoretical and neurobiological findings and pathology, and predictive, which show the expected pharmacological response to the treatment, that is used in clinical practice (Jones et al., 2011). In the following text a brief overview of the most common models will be provided.

Pharmacological animal models

Pharmacological models are based on acute or chronic application of substances modulating the neurotransmitter (receptor) systems. Among the most used belong e. g. the dopamine agonists such as amphetamine (Ellison et al., 1981) or apomorphine (Swerdlow and Geyer, 1993), selective agonists of serotonin receptors such as 8-OH-DPAT (Arvidsson et al., 1981), selective antagonists of serotonin receptors including also (S)-WAY 100135 (Cliffe et al., 1993), WAY- 100635 (Mathis et al., 1994) or M100907 (Schimdt et al., 1992), or antagonists of NMDA receptors such as phencyclidine (PCP) (Noda et al., 1995), ketamine (Krystal et al., 1994), MK-801 (Andino et al., 1999) and D-AP5 (Hauber and Schimdt, 1989). This paper will henceforward focus on glutamatergic animal models of schizophrenia.

Glutamatergic models

Glutamatergic hypothesis of schizophrenia posits that the endogenous dysfunction of neurotransmission mediated by NMDA receptors may contribute to the pathogenesis of schizophrenia. It is believed that low doses of PCP and ketamine selectively and non-competitively block NMDA receptors so that they bind to a site in the ion pore that is associated with these receptors (Javitt and Zukin, 1991). As mentioned before, the psychopharmacological studies in humans (Krystal et al., 1994) and behavioral studies in laboratory animals (Koek et al., 1988) suggest that the antagonists of NMDA receptors induce schizophrenia-like symptoms (Javitt and Zukin, 1991) on which the model is based. Ketamine (Swerdlow et al., 1998), PCP and MK-801 reduce the prepulse inhibition in laboratory animals (Mansbach and Geyer, 1989); furthermore, the antagonists of NMDA receptors affect also certain aspects of sensory processing (Sillito et al., 1990).

Ketamine

Ketamine is a dissociative anesthetic that was synthesized in 1962. During its administration in healthy volunteers in **subanesthetic** doses, short-term and temporary changes in behavior that are similar to positive, negative and even to cognitive symptoms of schizophrenia occur (Adler et al., 1999; Krystal et al. 1994). Ketamine also worsens the psychotic symptoms in schizophrenia patients (Lahti et al., 1995). In healthy subjects, psychotomimetic effects are significantly reduced by clozapine, the atypical antipsychotic. However, the effects are not blocked by conventional antipsychotics of older generation (Malhotra et al., 1997). In rodents, ketamine disrupts the prepulse inhibition (Swerdlow et al., 1998) and causes locomotor hyperactivity (Hetzler and Wautlet, 1985). On the contrary, one of the studies found a decrease in locomotor activity after ketamine administration in monkeys (Shiigi and Casey, 1999). Usefulness of the model with subchronic application of subanesthetic doses of ketamine was confirmed by Becker and his colleagues in their experiment. They found decreased binding of [^{3}H]L-glutamate on glutamate receptors in frontal cortex and increased binding of [^{3}H]L-spiroperidol on D2 receptor in hippocampus in brown rats that were administered with ketamine. Ketamine in low doses (10, 20, and 30 mg/kg) increases glutamate release in the prefrontal cortex (PFC), thereby it stimulates the postsynaptic non-NMDA receptors. This causes disruption of dopaminergic neurotransmission in PFC and in cognitive functions that are associated with this area. The same study found that ketamine has biphasic effect on the flow of glutamate in PFC. Low subanesthetic doses (30 mg/kg) increase the glutamate levels in PFC, whereas the anesthetic doses (200 mg/kg) reduce these levels (Moghaddam et al., 1997). In addition, the clinical studies have shown that subanesthetic doses of ketamine induce cognitive deficits in tasks that are dependent on PFC (Ghoneim et al., 1985) such as delayed verbal recall from memory

tests (Krystal et al., 1994). It is also important to mention that subanesthetic doses of ketamine induce rapid antidepressant effect which persists for a matter of days to weeks (Berman et al., 2000).

Phencyclidine

Phencyclidine is a noncompetitive antagonist of NMDA receptors which has a relatively high affinity for the D2 and 5-HT2 receptors (Kapur and Seeman, 2002). In humans, it induces a syndrome which seemingly resembles schizophrenia and which comprises both its positive and negative symptoms (Javitt and Zukin, 1991). In rodents, it primarily causes stereotyped behavior (Sams-Dodd, 1996), social withdrawal (Corbett et al., 1995), hyperactivity (Kalinichev et al., 2008) and it also disrupts prepulse inhibition (Mansbach and Geyer, 1989) and recognition memory (Egerton et al., 2005). In monkeys, the acute doses of PCP induce deficits in spatial (Boyce et al., 1991) and working memory (Baron and Wenger, 2001) and also in prepulse inhibition (Lynn and Javitt, 2001). Permanent cognitive deficit induced by sub-chronic PCP doses can be attenuated by atypical antipsychotics such as ziprasidone (a dose of 2.5 mg/kg), onlanzapine (a dose of 1.5 mg/kg) and clozapine (a dose of 5 mg/kg) (Abudl-Monim et al., 2006). The classical antipsychotics such as haloperidol (Abdul-Monim et al., 2003) and chlorpromazine have no effect on the deficit (Abdul-Monim et al., 2006).

Dizocilpine (MK-801)

Dizocilpine (MK-801) that was synthesized in 1982 is a phencyclidine-like substance. MK-801 induces hyperlocomotion and impairs cognitive functions. Unfortunately, there is only a small range of doses that can be applied in order to avoid overdosing. It then leads to neurotoxic effects (Olney et al., 1989). In rodents, subchronic exposure to high doses (≥10 mg/kg) induces cell death and neurodegeneration e.g. in olfactory bulbs, dentate gyrus and entorhinal cortex (so called Olney's lesions) (Bender et al., 2010). Likewise PCP, MK-801 also creates a spectrum of motor dysfunctions such as hyperactivity, stereotypy, cognitive deficit or ataxia (Koek et al., 1988) in various species including pigeons, rhesus monkeys and rodents.

In rats the systemic administration of MK-801 causes deterioration in various learning and memory processes, e.g. in passive place avoidance tasks (Ohno and Watanabe, 1996) or in spatial orientation tasks in radial maze (Pitkänen et al., 1995) and in water maze (Whishaw and Auer, 1989). One of the studies found that after MK-801 administration rats find the hidden platform in Morris water maze more slowly than control animals and that they exhibited increased thigmotaxis (they stay closer to the walls of the maze) (Lukoyanov and Paula-Barbosa, 2000). The results of another experiment showed that even a single dose of MK-801 (4 mg/kg) is capable of inducing changes in spatial learning in rats in Morris water maze. These changes subside within five days (Whishaw and Auer, 1989). Furthermore, it was found that the effects of systemic administration of MK-801 on spatial learning in the water maze are extremely difficult to separate from motor and sensory disorders (Ahlander et al., 1999). The results of another study show that when MK-801 is administered to naïve rats that are unfamiliar with the rules of spatial alternation task on rotating arena the working memory worsens and the efficiency of performance in this task is disrupted. However, in animals that undergo a pre-training before MK-801 administration (a dose of 0.12 mg/kg and 0.15 mg/kg) this deficit does not appear (Zemanova et al., 2013). Results of a different study showed that only the highest doses (0.2 mg/kg) of systemically administered dizocilpine induce significant deficit in active place avoidance task learning, while lower doses of MK-801 (0.1 mg/kg) do not affect performance in this task (Stuchlik et al., 2004). Another study found that even 0.15 mg/kg of MK-801 impairs spatial working memory in rodents which, when combined with other findings, suggests that NMDA receptors play a role rather in long-term storage of spatial information (White and Best, 1998). There is a number of studies that connect learning and memory with MK-801 animal model of schizophrenia. One of the studies tested the effect of MK-801 on behavioral (cognitive) flexibility in active place avoidance task and in Morris water maze tasks (MWM) in rats. It turned out that in this

schizophrenic behavior model the cognitive flexibility is impaired and that the active place avoidance task is more sensitive to this deficit (in this task the deficit was present already at the dose of 0.08 mg/kg) (Lobellova et al., 2013). Behavioral flexibility is the ability to adapt to the changes in close environment. In schizophrenia patients, this ability is often reduced which, among other things, proved the results of the patients suffering from schizophrenia in virtual decision-making tasks (Han et al., 2012). Changes in attention, behavioral flexibility and adaptation to the new conditions were also observed in animal models of schizophrenia in different experiments, e.g. after exposure to NMDA receptors in attention task (Amitai and Markou, 2010).

Mice in which an animal model of psychosis using MK-801 was induced replaced the components of behavior such as sniffing or pawing by monotonous locomotion. This fact corresponds to the positive symptoms in schizophrenia (stereotypy) and it is associated with excessive dopaminergic activity in the mesolimbic areas (Nilsson et al., 2001). The authors described the changes as overall behavioral primitivization (Nilsson et al., 2001). There is a difference is sensitivity to MK-801 between the sexes: the female rats are more sensitive to this substance probably due to the fact that MK-801 is metabolized in liver and females have lower efficiency of metabolic system (Andino et al., 1999). For the same reason, the females are more sensitive to PCP which leads to its higher concentration in plasma and brain (Nabeshima et al., 1984). It was proved that female rats show 4 to 10 times stronger behavior induced by MK-801 and up to 25 times greater serum and brain concentration of MK-801 than male rats (Andino et al., 1999).

In terms of molecular changes, one study found that MK-801 modifies the expression of NR1 splice variants and NR2 subunits of NMDA (Rujescu et al., 2006) in a similar manner that was observed in schizophrenia (Gao et al., 2000). The study also noted relatively decreased amount of GABAeric parvalbumin-positive interneurons (Rujescu et al., 2006) which is parallel to the changes that were observed in the brains of patients suffering from schizophrenia (Zhang and Reynolds, 2002). In rats, the chronic exposure to MK-801 leads to increased quantity of intracellular glutamate in hippocampus, while in the extra-hippocampal regions no change in concentration was observed (Genius et al., 2013).

It was found that the administration of 5-HT2A/2C receptor antagonists such as ritanserin and risperidone (which is also the D2 receptor antagonist) blocks the cognitive impairments induced by MK-801, while haloperidol, the D2 receptor antagonist, is not able to sufficiently correct the deficit in active place avoidance task in Carousel Maze (formerly known as Active Alothetic Place Avoidance, AAPA). This deficit is induced by MK-801 administration but it effectively blocks hyperlocomotion (Bubenikova-Valešova et al., 2008). Interestingly, after administration of risperidone and haloperidol in intact rats an impaired performance in AAPA could be observed. However, this performance impairment did not occur after ritanserin administration (Bubenikova-Valešova et al., 2008). It turned out that neuroleptics (the antipsychotic agents used for clinical purposes) antagonize behavior induced by MK-801 (Tiedtke et al., 1990) as well as PCP (Sturgeon et al., 1981). This indicates that the behavior induced by NMDA receptor antagonists can be used as complementary model of psychosis in search of new and more effective antipsychotic in schizophrenia treatment.

Neurodevelopmental animal models

Neurodevelopmental animal models are based on neurodevelopmental hypothesis of the emergence of schizophrenia. This hypothesis supposes that a disruption in prenatal or perinatal period of brain development causes dysfunctions of brain connectivity that are manifested by schizophrenia outbreak in early adulthood. This hypothesis is confirmed by e.g. studies aimed at inhibition of NMDA receptors that show that exposure to MK-801 (Harris et al., 2003) and PCP in late fetal or early postnatal period in rats increases the risk of brain

damage (Wang et al., 2001). Chronic blockade of NMDA receptors by both MK-801 (Gorter and Bruin, 1992) and PCP during this period causes cognitive deficit and impairs spatial memory in adulthood (Sircar and Rudy, 1998). The time when the inhibition of NMDA receptors increases the cell damage correlates with maximal expression of these receptors. In humans, this period corresponds to the third semester of pregnancy (Lee and Choi, 1992), in rats to the first two weeks of postnatal life (Colwell et al., 1998). Neurodegenerative changes caused by hypofunction of NMDA receptors may serve as models for pharmacotherapy of schizophrenia research (Olney and Farber, 1995).

To the neurodevelopmental models belong also the malnutrition models that address the issue of prenatal malnutrition on brain development (Llorente et al., 2007), models of viral infections (Takei et al., 1995), stress during pregnancy (Fride and Weinstock, 1988), neonatal brain lesions (Lipska and Weinberger, 1993) and other neuronal damages such as postnatal hypoxia after which changes in gene expression of NMDA receptor subunits and reduced prepulse inhibition were observed (Schmitt et al., 2007).

To create a structural model of psychosis in animals the neonatal hippocampal lesions (Lipska and Weinberger, 1993) or medial prefrontal cortex lesions (Jaskiw et al., 1990) are used. The best described neurodevelopmental animal model of psychosis was designed by Lipska and Weinberger. The model consists in performing neonatal excitotoxic ventral hippocampal lesion (Lipska and Weinberger, 1993; 1995). After amphetamine application, this lesion causes changes in behavior such as hyperlokomotion (Lipska and Weinberger, 1993). Experimental manipulations with ventral hippocampal lesions are in rats performed on the seventh postnatal day and they result in both temporary (Lipska et al., 2002b) and permanent (Lipska et al, 1993) inactivation of the ventral hippocampus. As a result of these manipulations, hyperactivity (Lipska et al., 2022b), changes in gene expression (Lillrand et al., 1996), deficits in working memory (Lipska et al., 2002b) and impaired prepulse inhibition (Daenen et al., 2003) can be observed in adult rats. It turned out that even temporary inactivation of ventral hippocampus during critical period can trigger behavioral changes similar to those that can be observed in animals with permanent excitotoxic lesions. Since the neonatal disconnection of ventral hippocampus changes the PFC development and plasticity and creates cellular changes that mimic the symptoms of schizophrenia it can represent a potential new model for studying schizophrenia (Lipska, 2004).

Selected genetic animal models

Genetic animal models of schizophrenia slowly displace pharmacological and neurodevelopmental models. The main advantage of these models is the fact that they have potentially grated construct validity (Harrison et al., 2012). There is a wide variety of genes that are, as expected, involved in the pathophysiology of schizophrenia and that can be explored. It is worth mentioning that a number of genetic manipulations aimed at variety of genes are presented as schizophrenia endophenotypes, i.e. isolatable phenotypic characteristics that are bound to a disease, frequently hereditary and often present in healthy blood relatives of these subjects (e.g. Willi et al., 2010).

One of the genes that is associated with schizophrenia is NRG1 (Neuregulin 1) located at chromosome 8p13 (in humans). 30cM region around 8p21.1-22 on the chromosome 8p is considered a locus comprising of one or more genes that are co-responsible for the onset of schizophrenia (Pulver at al., 1995). Neuregulins represent a family of growth and differentiation factors encoded by four different genes (NRG-1 to NRG-4) that are bound to ErbB family of tyrosine kinase transmembrane receptors (Papaleo et al., 2012). NRG1 modulates neuronal precursors and cell migration using radial glial cells (Schmid et al., 2003) and increases neuronal survival (Vaskovsky et al., 2000). One of the studies showed that heterozygous mice for NRG-1 receptor of ErbB4 exhibit similar abnormalities in behavior as patients suffering from schizophrenia – e.g. hyperactivity

(Gerlai et al., 2000) and that these changes can be partially reversed by clozapine (Stefansson et al., 2002). Recently, the possibility that NRG1 path may be interconnected with NMDA receptors is being considered. The connecting link between these two systems is the fact that ErbB4 receptor is bound to a postsynaptic scaffold protein PSD-95 (Huang et al., 2000) which interacts with NMDA receptors (Kornau et al., 1995).

In vitro stimulation of NRG1 was able to suppress the currents in prefrontal pyramidal neurons induced by NMDA receptors (Gu et al., 2005). Also, the activation of NMDA receptors in prefrontal cortex was significantly suppressed in patients with schizophrenia that exhibited a greater degree of Erb4 – PSD-95 signaling compared to healthy individuals. It follows that more intensive NRG1 signaling may contribute to the hypofunction of NMDA receptors (Hahn et al., 2006). An experiment investigating the short- and long-term effects of chronic blockade of NMDA receptors in the interaction between prefrontal cortex and hippocampus was carried out. 24 hours after the last injection of MK-801 the interactions of ErbB4, PSD-95 and NMDA receptors in PFC were increased. However, 12 days after the last dose these effects were not visible, indicating the reversibility of these changes. These results suggest that NRG-ErbB4 signaling may be modulated by repeated blockage of NMDA receptors and provide further evidence of interconnection of these two signaling pathways (Li et al., 2013).

Another possibility for the research is the genetic modification of the NMDA receptors themselves. The receptors are composed of a number of NR1, NR2A-D, NR3A-B subunits (Dingledine et al., 1999). An example of genetic animal model for NMDA receptor hypofunction is the NMDA receptor hypomorphic mouse that has significantly reduced the NR1 subunit (Mohn et al., 1999). These mice exhibit reduced motor activity, deficits in social interactions (Mohn et al., 1999), decreased metabolic activity in the medial prefrontal cortex and hippocampus (Duncan et al., 2002) and prepulse inhibition deficits of an acoustic startle response (Duncan et al., 2004). It was found that clozapine and haloperidol mitigate prepulse inhibition deficits in NR1 hypomorphic mice (Duncan et al., 2006a) and olanzapine reduces their locomotor hyperactivity (Duncan et al., 2006b). The significance of this model for schizophrenia is being challenged because the evidence for abnormalities in genes that cause expression of the NMDA receptor subunits has not been found yet (Nishiguchi et al., 2000). In addition, these animals showed response neither to PCP nor to MK-801 which is contrary to the conclusions that have been found in schizophrenia patients (Krystal et al., 1994). Furthermore, two lines of mouse animal model with a point mutation of glycine binding site on NR1 subunit were created: Grin1 (D481N) and Grin1 (K483Q). The second phenotype confirmed the essential role of NMDA receptor activation in neonatal survival (Kew et al., 2000). The Grin 1D481N/K483Q heterozygous mice exhibited NMDA receptor hypofunction, hyperlocomotion, stereotyped behavior and impaired performance in finding visible platform task in Morris water maze (Ballard et al., 2002). Except that, the NR2 subunit (GluRepsilon1) can also be eliminated. In these mice, NMDA receptors are malfunctioning and mice exhibit hyperlocomotion again (Miyamoto et al., 2001).

Conclusion

The aim of this study was to summarize the findings of hypoglutamatergic animal models of schizophrenia-like behavior. The main reason for this was the fact that the neurodevelopmental hypothesis of glutamate NMDA receptors hypofunction has been recently gaining interest. Currently, the non-competitive antagonists of NMDA receptors such as ketamine, phencyclidine and MK-801 are used for schizophrenia-like behavior modeling in animals. These models have a great potential even though they do not reflect all the symptoms of schizophrenia. These non-competitive antagonists bind to a site on the NMDA receptor ion channel; thereby they block and disrupt their proper functions. Chronic blockade of NMDA receptors can also be caused by application of NMDA receptor non-competitive antagonists in late fetal or early postnatal period. This results in poor brain development and onset of schizophrenia-like behavior in adult animals. In animal

models, these antagonists induce a broad spectrum of symptoms relevant to schizophrenia such as locomotor hyperactivity, stereotyped behavior, impaired recognition, and ataxia, deficits in spatial and working memory, reduced prepulse inhibition, changes in glutamate release, and also social withdrawal which is induced by low doses of MK-801. Another promising option that allows researches dealing with NMDA receptors responsibility for the onset of schizophrenia is creating genetically modified animals which exhibit similar behavioral and pharmacological changes as patients suffering from schizophrenia. The contribution of these animal models to schizophrenia research is undeniable; however, knowledge about the origin, etiology and neuropathology of the disease still remains scarce, since due to its complexity a single "ideal" and "universal" animal model that would contain all the symptoms cannot be created. Models can however mimic several important aspects and symptoms of schizophrenia. This fact is also important in finding a safer and more effective medication for the disease.

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Literature

Abdul-Monim Z., Reynolds G.P., Neill J.C. (2003). "The Atypical Antipsychotic Ziprasidone, but Not Haloperidol, Improves Phencyclidine-Induced Cognitive Deficits in a Reversal Learning Task in the Rat." Journal of Psychopharmacology (Oxford, England) 17 (1): 57–65.

Abdul-Monim Z., Reynolds G.P., Neill J.C. (2006). "The Effect of Atypical and Classical Antipsychotics on Sub-Chronic PCP-Induced Cognitive Deficits in a Reversal-Learning Paradigm." Behavioural Brain Research 169 (2): 263–73.

Adler C.M., Malhotra A.K., Elman I., Goldberg T., Egan M., Pickar D., Breier A. (1999). "Comparison of Ketamine-Induced Thought Disorder in Healthy Volunteers and Thought Disorder in Schizophrenia." The American Journal of Psychiatry 156 (10): 1646–49.

Ahlander M., Misane I., Schött P.A., Ogren S.O. (1999). "A Behavioral Analysis of the Spatial Learning Deficit Induced by the NMDA Receptor Antagonist MK-801 (dizocilpine) in the Rat." Neuropsychopharmacology: Official Publication of the American College of Neuropsychopharmacology 21 (3): 414–26.

Allen D.N., Frantom L.V., Strauss G.P., van Kammen D.P. (2005). "Differential Patterns of Premorbid Academic and Social Deterioration in Patients with Schizophrenia." Schizophrenia Research 75 (2-3): 389–97.

Amitai N., Markou A. (2010). "Disruption of Performance in the Five-Choice Serial Reaction Time Task Induced by Administration of N-Methyl-D-Aspartate Receptor Antagonists: Relevance to Cognitive Dysfunction in Schizophrenia." Biological Psychiatry 68 (1): 5–16.

Amminger G.P., Schlögelhofer M., Lehner T., Looser Ott S., Friedrich M.H., Aschauer H.N. (2000). "Premorbid Performance IQ Deficit in Schizophrenia." Acta Psychiatrica Scandinavica 102 (6): 414–22.

Andiné P., Widermark N., Axelsson R., Nyberg G., Olofsson U., Mårtensson E., Sandberg M. (1999). "Characterization of MK-801-Induced Behavior as a Putative Rat Model of Psychosis." The Journal of Pharmacology and Experimental Therapeutics 290 (3): 1393–1408.

Andreasen N.C. (1995). "Symptoms, Signs, and Diagnosis of Schizophrenia." Lancet 346 (8973): 477–81.

Arvidsson L.E., Hacksell U., Nilsson J.L., Hjorth S., Carlsson A., Lindberg P., Sanchez D., Wikstrom H. (1981). "8-Hydroxy-2-(di-N-Propylamino)tetralin, a New Centrally Acting 5-Hydroxytryptamine Receptor Agonist." Journal of Medicinal Chemistry 24 (8): 921–23.

Ballard T.M., Pauly-Evers M., Higgins G.A., Ouagazzal A.M., Mutel V., Borroni E., Kemp J.A., BluethmannH., Kew J.N. (2002). "Severe Impairment of NMDA Receptor Function in Mice Carrying Targeted Point Mutations in the Glycine Binding Site Results in Drug-Resistant Nonhabituating Hyperactivity." The Journal of Neuroscience 22 (15): 6713–23.

Baron S.P., Wenger G.R. (2001). "Effects of Drugs of Abuse on Response Accuracy and Bias under a Delayed Matching-to-Sample Procedure in Squirrel Monkeys." Behavioural Pharmacology 12 (4): 247–56.

Becker A., Peters B., Schroeder H., Mann T., Huether G., Grecksch G. (2003). "Ketamine-Induced Changes in Rat Behaviour: A Possible Animal Model of Schizophrenia." Progress in Neuro-Psychopharmacology & Biological Psychiatry 27 (4): 687–700.

Bender C., de Olmos S., Bueno A., de Olmos J., Lorenzo A. (2010). "Comparative Analyses of the Neurodegeneration Induced by the Non-Competitive NMDA-Receptor-Antagonist Drug MK801 in Mice and Rats." Neurotoxicology and Teratology 32 (5): 542–50.

Berman R.M., Cappiello A., Anand A., Oren D.A., Heninger G.R., Charney D.S., Krystal J.H. (2000). "Antidepressant Effects of Ketamine in Depressed Patients." Biological Psychiatry 47 (4): 351–54.

Bonfoco E., Krainc D., Ankarcrona M., Nicotera P., Lipton S.A (1995). "Apoptosis and Necrosis: Two Distinct Events Induced, Respectively, by Mild and Intense Insults with N-Methyl-D-Aspartate or Nitric Oxide/superoxide in Cortical Cell Cultures." Proceedings of the National Academy of Sciences of the United States of America 92 (16): 7162–66.

Boyce S., Rupniak N.M., Steventon M.J., Cook G., Iversen S.D. (1991). "Psychomotor Activity and Cognitive Disruption Attributable to NMDA, but Not Sigma, Interactions in Primates." Behavioural Brain Research 42 (2): 115–21.

Bubenikova-Valesova V., Stuchlik A., Svoboda J., Bures J, Vales K. (2008). "Risperidone and Ritanserin but Not Haloperidol Block Effect of Dizocilpine on the Active Allothetic Place Avoidance Task." Proceedings of the National Academy of Sciences of the United States of America 105 (3): 1061–66.

Castle D., Sham P., Murray R. (1998). "Differences in Distribution of Ages of Onset in Males and Females with Schizophrenia." Schizophrenia Research 33 (3): 179–83.

Cliffe I.A., Brightwell C.I., Fletcher A., Forster E.A., Mansell H.L., Reilly Y., Routledge C., White A.C. (1993). "(S)-N-Tert-Butyl-3-(4-(2-Methoxyphenyl)-Piperazin-1-Yl)-2-Phenylpropanamide [(S)-WAY-100135]: A Selective Antagonist at Presynaptic and Postsynaptic 5-HT1A Receptors." Journal of Medicinal Chemistry 36 (10): 1509–10.

Colwell C.S., Cepeda C., Crawford C., Levine M.S. (1998). "Postnatal Development of Glutamate Receptor-Mediated Responses in the Neostriatum." Developmental Neuroscience 20 (2-3): 154–63.

Corbett R., Camacho F., Woods A.T., Kerman L.L., Fishkin R.J., Brooks K., Dunn R.W. (1995). "Antipsychotic Agents Antagonize Non-Competitive N-Methyl-D-Aspartate Antagonist-Induced Behaviors." Psychopharmacology 120 (1): 67–74.

Daenen E.W., Wolterink G., Van Der Heyden J.A., Kruse C.G., Van Ree J.M. (2003). "Neonatal Lesions in the Amygdala or Ventral Hippocampus Disrupt Prepulse Inhibition of the Acoustic Startle Response; Implications for an Animal Model of Neurodevelopmental Disorders like Schizophrenia." European Neuropsychopharmacology: The Journal of the European College of Neuropsychopharmacology 13 (3): 187–97.

Dingledine R., Borges K., Bowie D., Traynelis S.F. (1999). "The Glutamate Receptor Ion Channels." Pharmacological Reviews 51 (1): 7–61.

Duncan G., Miyamoto S., Gu H., Lieberman J., Koller B., Snouwaert J. (2002). "Alterations in Regional Brain Metabolism in Genetic and Pharmacological Models of Reduced NMDA Receptor Function." Brain Research 951 (2): 166–76.

Duncan G.E., Moy S.S., Lieberman J.A., Koller B.H. (2006a). "Effects of Haloperidol, Clozapine, and Quetiapine on Sensorimotor Gating in a Genetic Model of Reduced NMDA Receptor Function." Psychopharmacology 184 (2): 190–200.

Duncan G.E., Moy S.S., Lieberman J.A., Koller B.H. (2006b). "Typical and Atypical Antipsychotic Drug Effects on Locomotor Hyperactivity and Deficits in Sensorimotor Gating in a Genetic Model of NMDA Receptor Hypofunction." Pharmacology, Biochemistry, and Behavior 85 (3): 481–91.

Duncan G.E., Moy S.S., Perez A., Eddy D.M., Zinzow W.M., Lieberman J.A., Snouwaert J.N., Koller B.H. (2004). "Deficits in Sensorimotor Gating and Tests of Social Behavior in a Genetic Model of Reduced NMDA Receptor Function." Behavioural Brain Research 153 (2): 507–19.

Egerton A., Reid L., McKerchar C.E., Morris B.J., Pratt J.A. (2005). "Impairment in Perceptual Attentional Set-Shifting Following PCP Administration: A Rodent Model of Set-Shifting Deficits in Schizophrenia." Psychopharmacology 179 (1): 77–84.

Ellison G., Nielsen E.B., LyonM. (1981). "Animal Model of Psychosis: Hallucinatory Behaviors in Monkeys during the Late Stage of Continuous Amphetamine Intoxication." Journal of Psychiatric Research 16 (1): 13–22.

Fride E., Weinstock M. (1988). "Prenatal Stress Increases Anxiety Related Behavior and Alters Cerebral Lateralization of Dopamine Activity." Life Sciences 42 (10): 1059–65.

Gao X.M., Sakai K., Roberts R.C., Conley R.R., Dean B., Tamminga C.A. (2000). "Ionotropic Glutamate Receptors and Expression of N-Methyl-D-Aspartate Receptor Subunits in Subregions of Human Hippocampus: Effects of Schizophrenia." The American Journal of Psychiatry 157 (7): 1141–49.

Genius J., Geiger J., Dölzer A.L., Benninghoff J., Giegling I., Hartmann A.M., Möller H.J., Rujescu D. (2013). "Glutamatergic Dysbalance and Oxidative Stress in in Vivo and in Vitro Models of Psychosis Based on Chronic NMDA Receptor Antagonism." PloS One 8 (7): e59395.

Gerlai R., Pisacane P., Erickson S. (2000). "Heregulin, but Not ErbB2 or ErbB3, Heterozygous Mutant Mice Exhibit Hyperactivity in Multiple Behavioral Tasks." Behavioural Brain Research 109 (2): 219–27.

Ghoneim M.M., Hinrichs J.V., Mewaldt S.P., Petersen R.C. (1985). "Ketamine: Behavioral Effects of Subanesthetic Doses." Journal of Clinical Psychopharmacology 5 (2): 70–77.

Gorter J.A., de Bruin J.P. (1992). "Chronic Neonatal MK-801 Treatment Results in an Impairment of Spatial Learning in the Adult Rat." Brain Research 580 (1-2): 12–17.

Hahn C.G., Wang H.Y., Cho D.S., Talbot K., Gur R.E., Berrettini W.H., Bakshi K., Kamins J., Borgman-Winter K.E., Siegel S.J., Gallop R.J., Arnold S.E. (2006). "Altered Neuregulin 1-erbB4 Signaling Contributes to NMDA Receptor Hypofunction in Schizophrenia." Nature Medicine 12 (7): 824–28.

Han K., Kim I.Y., Kim J.J. (2012). "Assessment of Cognitive Flexibility in Real Life Using Virtual Reality: A Comparison of Healthy Individuals and Schizophrenia Patients." Computers in Biology and Medicine 42 (8): 841–47.

Harris L.W., Sharp T., Gartlon J., Jones D.N., Harrison P.J. (2003). "Long-Term Behavioural, Molecular and Morphological Effects of Neonatal NMDA Receptor Antagonism." The European Journal of Neuroscience 18 (6): 1706–10.

Harrison P.J., Pritchett D., Stumpenhorst K., Betts J.F., Nissen W., Schweimer J., Lane T., Burnet P.W., Lamsa K.P., Sharp T., Bannerman D.M., Tunbridge E.M. (2012). "Genetic Mouse Models Relevant to Schizophrenia: Taking Stock and Looking Forward." Neuropharmacology 62 (3): 1164–67.

Hauber W., Schmidt W.J. (1989). "Effects of Intrastriatal Blockade of Glutamatergic Transmission on the Acquisition of T-Maze and Radial Maze Tasks." Journal of Neural Transmission. General Section 78 (1): 29–41.

Hetzler B.E., Wautlet B.S. (1985). "Ketamine-Induced Locomotion in Rats in an Open-Field." Pharmacology, Biochemistry, and Behavior 22 (4): 653–55.

Huang Y.Z., Won S., Ali D.W., Wang Q., Tanowitz M., Du Q.S., Pelkey K.A., Yang D.J., Xiong W.C., Salter M.W., Mei L. (2000). "Regulation of Neuregulin Signaling by PSD-95 Interacting with ErbB4 at CNS Synapses." Neuron 26 (2): 443–55.

Jablensky A. (2000). "Epidemiology of Schizophrenia: The Global Burden of Disease and Disability." European Archives of Psychiatry and Clinical Neuroscience 250 (6): 274–85.

Jaskiw G.E., Karoum F., Freed W.J., Phillips I., Kleinman J.E., Weinberger D.R. (1990). "Effect of Ibotenic Acid Lesions of the Medial Prefrontal Cortex on Amphetamine-Induced Locomotion and Regional Brain Catecholamine Concentrations in the Rat." Brain Research 534 (1-2): 263–72.

Javitt D.C., Zukin S.R. (1991). "Recent Advances in the Phencyclidine Model of Schizophrenia." The American Journal of Psychiatry 148 (10): 1301–8.

Jones C.A., Watson D.J. Fone K.C. (2011). "Animal Models of Schizophrenia." British Journal of Pharmacology 164 (4): 1162–94.

Kalinichev M., Robbins M.J., Hartfield E.M., Maycox P.R., Moore S.H., Savage K.M., Austin N.E., Jones D.N. (2008). "Comparison between Intraperitoneal and Subcutaneous Phencyclidine Administration in Sprague-Dawley Rats: A Locomotor Activity and Gene Induction Study." Progress in Neuro-Psychopharmacology & Biological Psychiatry 32 (2): 414–22.

Kapur S., Seeman P. (2002). "NMDA Receptor Antagonists Ketamine and PCP Have Direct Effects on the Dopamine D(2) and Serotonin 5-HT(2)receptors-Implications for Models of Schizophrenia." Molecular Psychiatry 7 (8): 837–44.

Kew J.N., Koester A., Moreau J.L., Jenck F., Ouagazzal A.M., Mutel V., Richards J.G., Trube G., Fischer G., Montkowski A., Hundt W., Reinscheid R.K., Pauly-Evers M., Kemp J.A., Bluethmann H. (2000). "Functional Consequences of Reduction in NMDA Receptor Glycine Affinity in Mice Carrying Targeted Point Mutations in the Glycine Binding Site." The Journal of Neuroscience: The Official Journal of the Society for Neuroscience 20 (11): 4037–49.

Koek W., Woods J.H., Winger G.D. (1988). "MK-801, a Proposed Noncompetitive Antagonist of Excitatory Amino Acid Neurotransmission, Produces Phencyclidine-like Behavioral Effects in Pigeons, Rats and Rhesus Monkeys." The Journal of Pharmacology and Experimental Therapeutics 245 (3): 969–74.

Kornau H.C., Schenker L.T., Kennedy M.B., Seeburg P.H. (1995). "Domain Interaction between NMDA Receptor Subunits and the Postsynaptic Density Protein PSD-95." Science (New York, N.Y.) 269 (5231): 1737–40.

Krystal J.H., Karper L.P., Seibyl J.P., Freeman G.K., Delaney R., Bremner J.D., Heninger G.R., Bowers Jr M.B., Charney D. S. (1994). "Subanesthetic Effects of the Noncompetitive NMDA Antagonist, Ketamine, in Humans. Psychotomimetic, Perceptual, Cognitive, and Neuroendocrine Responses." Archives of General Psychiatry 51 (3): 199–214.

Lahti A.C., Koffel B., LaPorte D., Tamminga C.A. (1995). "Subanesthetic Doses of Ketamine Stimulate Psychosis in Schizophrenia." Neuropsychopharmacology: Official Publication of the American College of Neuropsychopharmacology 13 (1): 9–19.

Lee H., Choi B.H. (1992). "Density and Distribution of Excitatory Amino Acid Receptors in the Developing Human Fetal Brain: A Quantitative Autoradiographic Study." Experimental Neurology 118 (3): 284–90.

Li H.B., Matsumoto K., Yamamoto M., Watanabe H. (1997). "NMDA but Not AMPA Receptor Antagonists Impair the Delay-Interposed Radial Maze Performance of Rats." Pharmacology, Biochemistry, and Behavior 58 (1): 249–53.

Li J.T., Feng Y., Su Y.A., Wang X.D., Si T.M. (2013). "Enhanced Interaction among ErbB4, PSD-95 and NMDAR by Chronic MK-801 Treatment Is Associated with Behavioral Abnormalities." Pharmacology Biochemistry and Behavior 108 (July): 44–53.

Lillrank S.M., Lipska B.K., Bachus S.E., Wood G.K., Weinberger D.R. (1996). "Amphetamine-Induced c-Fos mRNA Expression Is Altered in Rats with Neonatal Ventral Hippocampal Damage." Synapse (New York, N.Y.) 23 (4): 292–301.

Linn G.S., Javitt D.C. (2001). "Phencyclidine (PCP)-Induced Deficits of Prepulse Inhibition in Monkeys." Neuroreport 12 (1): 117–20.

Lipska B.K. (2004). "Using Animal Models to Test a Neurodevelopmental Hypothesis of Schizophrenia." Journal of Psychiatry & Neuroscience: JPN 29 (4): 282–86.

Lipska B.K., Aultman J.M., Verma A., Weinberger D.R., Moghaddam B. (2002a). "Neonatal Damage of the Ventral Hippocampus Impairs Working Memory in the Rat." Neuropsychopharmacology: Official Publication of the American College of Neuropsychopharmacology 27 (1): 47–54..

Lipska B.K., Halim N.D., Segal P.N., Weinberger D.R. (2002b). "Effects of Reversible Inactivation of the Neonatal Ventral Hippocampus on Behavior in the Adult Rat." The Journal of Neuroscience: The Official Journal of the Society for Neuroscience 22 (7): 2835–42.

Lipska B.K., Jaskiw G.E., Weinberger D.R. (1993). "Postpubertal Emergence of Hyperresponsiveness to Stress and to Amphetamine after Neonatal Excitotoxic Hippocampal Damage: A Potential Animal Model of Schizophrenia." Neuropsychopharmacology: Official Publication of the American College of Neuropsychopharmacology 9 (1): 67–75.

Lipska B.K., Weinberger D.R. (1993). "Delayed Effects of Neonatal Hippocampal Damage on Haloperidol-Induced Catalepsy and Apomorphine-Induced Stereotypic Behaviors in the Rat." Brain Research. Developmental Brain Research 75 (2): 213–22.

Lipska B.K., Weinberger D.R. (1995). "Genetic Variation in Vulnerability to the Behavioral Effects of Neonatal Hippocampal Damage in Rats." Proceedings of the National Academy of Sciences of the United States of America 92 (19): 8906–10.

Llorente R., Arranz L., Marco E.M., Moreno E., Puerto M., Guaza C.,De la Fuente M., Viveros M.P. (2007). "Early Maternal Deprivation and Neonatal Single Administration with a Cannabinoid Agonist Induce Long-Term Sex-Dependent Psychoimmunoendocrine Effects in Adolescent Rats." Psychoneuroendocrinology 32 (6): 636–50.

Lobellova V., Entlerova M., Svojanovska B., Hatalova H., Prokopova I., Petrasek T., Vales K., Kubik S., Fajnerova I., Stuchlik A. (2013). "Two Learning Tasks Provide Evidence for Disrupted Behavioural Flexibility in an Animal Model of Schizophrenia-like Behaviour Induced by Acute MK-801: A Dose-Response Study." Behavioural Brain Research 246 (June): 55–62.

Lu Y.M., Jia Z., Janus C., Henderson J.T., Gerlai R., Wojtowicz J.M., Roder J.C. (1997). "Mice Lacking Metabotropic Glutamate Receptor 5 Show Impaired Learning and Reduced CA1 Long-Term Potentiation (LTP) but Normal CA3 LTP." The Journal of Neuroscience: The Official Journal of the Society for Neuroscience 17 (13): 5196–5205.

Lukoyanov N.V., Paula-Barbosa M.M. (2000). "A Single High Dose of Dizocilpine Produces Long-Lasting Impairment of the Water Maze Performance in Adult Rats." Neuroscience Letters 285 (2): 139–42.

Malhotra A.K., Adler C.M., Kennison S.D., Elman I., Pickar D., Breier A. (1997). "Clozapine Blunts N-Methyl-D-Aspartate Antagonist-Induced Psychosis: A Study with Ketamine." Biological Psychiatry 42 (8): 664–68.

Mansbach R.S., Geyer M.A. (1989). "Effects of Phencyclidine and Phencyclidine Biologs on Sensorimotor Gating in the Rat." Neuropsychopharmacology: Official Publication of the American College of Neuropsychopharmacology 2 (4): 299–308.

Moghaddam B., Adams B., Verma A., Daly D. (1997). "Activation of Glutamatergic Neurotransmission by Ketamine: A Novel Step in the Pathway from NMDA Receptor Blockade to Dopaminergic and Cognitive Disruptions Associated with the Prefrontal Cortex." The Journal of Neuroscience: The Official Journal of the Society for Neuroscience 17 (8): 2921–27.

Mohn A.R., Gainetdinov R.R., Caron M.G., Koller B.H. (1999). "Mice with Reduced NMDA Receptor Expression Display Behaviors Related to Schizophrenia." Cell 98 (4): 427–36.

Nabeshima T., Yamaguchi K., Furukawa H., Kameyama T. (1984). "Role of Sex Hormones in Sex-Dependent Differences in Phencyclidine-Induced Stereotyped Behaviors in Rats." European Journal of Pharmacology 105 (3-4): 197–206.

Nilsson M., Waters S., Waters N., Carlsson A., Carlsson M.L. (2001). "A Behavioural Pattern Analysis of Hypoglutamatergic Mice--Effects of Four Different Antipsychotic Agents." Journal of Neural Transmission (Vienna, Austria: 1996) 108 (10): 1181–96.

Nishiguchi N., Shirakawa O., Ono H., Hashimoto T., Maeda K. (2000). "Novel Polymorphism in the Gene Region Encoding the Carboxyl-Terminal Intracellular Domain of the NMDA Receptor 2B Subunit: Analysis of Association with Schizophrenia." The American Journal of Psychiatry 157 (8): 1329–31.

Noda Y., Yamada K., Furukawa H., Nabeshima T. (1995). "Enhancement of Immobility in a Forced Swimming Test by Subacute or Repeated Treatment with Phencyclidine: A New Model of Schizophrenia." British Journal of Pharmacology 116 (5): 2531–37.

Ohno M., Watanabe S. (1996). "Interactive Processing between Glutamatergic and Cholinergic Systems Involved in Inhibitory Avoidance Learning of Rats." European Journal of Pharmacology 312 (2): 145–47.

Olney J.W., Farber NB. (1995). "Glutamate Receptor Dysfunction and Schizophrenia." Archives of General Psychiatry 52 (12): 998–1007.

Olney J.W., Labruyere J., Price M.T. (1989). "Pathological Changes Induced in Cerebrocortical Neurons by Phencyclidine and Related Drugs." Science (New York, N.Y.) 244 (4910): 1360–62.

Papaleo F., Lipska B.K., Weinberger D.R. (2012). "Mouse Models of Genetic Effects on Cognition: Relevance to Schizophrenia." Neuropharmacology 62 (3): 1204–20.

Pitkänen M., Sirviö J., MacDonald E., Niemi S., Ekonsalo T., Riekkinen Sr P. (1995). "The Effects of D-Cycloserine and MK-801 on the Performance of Rats in Two Spatial Learning and Memory Tasks." European Neuropsychopharmacology: The Journal of the European College of Neuropsychopharmacology 5 (4): 457–63.

Pulver A.E., Lasseter V.K., Kasch L., Wolyniec P., Nestadt G., Blouin J.L., Kimberland M., Babb R., Vourlis S., Chen H. (1995). "Schizophrenia: A Genome Scan Targets Chromosomes 3p and 8p as Potential Sites of Susceptibility Genes." American Journal of Medical Genetics 60 (3): 252–60.

Ridley R.M., Baker H.F., Owen F., Cross A.J., Crow T.J. (1982). "Behavioural and Biochemical Effects of Chronic Amphetamine Treatment in the Vervet Monkey." Psychopharmacology 78 (3): 245–51.

Rosso I.M., Bearden C.E., Hollister J.M., Gasperoni T.L., Sanchez L.E., Hadley T., Cannon T.D. (2000). "Childhood Neuromotor Dysfunction in Schizophrenia Patients and Their Unaffected Siblings: A Prospective Cohort Study." Schizophrenia Bulletin 26 (2): 367–78.

Rujescu D., Bender A., Keck M., Hartmann A.M., Ohl F., Raeder H., Giegling I., Genius J., McCarley R.W., Möller H.J., Grunze H. (2006). "A Pharmacological Model for Psychosis Based on N-Methyl-D-Aspartate Receptor Hypofunction: Molecular, Cellular, Functional and Behavioral Abnormalities." Biological Psychiatry 59 (8): 721–29.

Sams-Dodd F., Lipska B.K., Weinberger D.R. (1997). "Neonatal Lesions of the Rat Ventral Hippocampus Result in Hyperlocomotion and Deficits in Social Behaviour in Adulthood." Psychopharmacology 132 (3): 303–10.

Sartorius N., Jablensky A., Korten A., Ernberg G., Anker M., Cooper J.E., Day R. (1986). "Early Manifestations and First-Contact Incidence of Schizophrenia in Different Cultures. A Preliminary Report on the Initial Evaluation Phase of the WHO Collaborative Study on Determinants of Outcome of Severe Mental Disorders." Psychological Medicine 16 (4): 909–28.

Schmid R.S., McGrath B., Berechid B.E., Boyles B., Marchionni M., Sestan N., Anton E.S. (2003). "Neuregulin 1-erbB2 Signaling Is Required for the Establishment of Radial Glia and Their Transformation into Astrocytes in Cerebral Cortex." Proceedings of the National Academy of Sciences of the United States of America 100 (7): 4251–56.

Schmitt A., Fendt M., Zink M., Ebert U., Starke M., Berthold M., Herb A., Petroianu G., Falkai P., Henn F.A. (2007). "Altered NMDA Receptor Expression and Behavior Following Postnatal Hypoxia: Potential Relevance to Schizophrenia." Journal of Neural Transmission (Vienna, Austria: 1996) 114 (2): 239–48.

Seibt K.J., Piato A.L., da Luz Oliveira R., Capiotti K.M., Vianna M.R., Bonan C.D. (2011). "Antipsychotic Drugs Reverse MK-801-Induced Cognitive and Social Interaction Deficits in Zebrafish (Danio Rerio)." Behavioural Brain Research 224 (1): 135–39.

Shiigi Y., Casey D.E. (1999). "Behavioral Effects of Ketamine, an NMDA Glutamatergic Antagonist, in Non-Human Primates." Psychopharmacology 146 (1): 67–72.

Sillito A.M., Murphy P.C., Salt T.E., Moody C.I. (1990). "Dependence of Retinogeniculate Transmission in Cat on NMDA Receptors." Journal of Neurophysiology 63 (2): 347–55.

Sircar R., Rudy J.W. (1998). "Repeated Neonatal Phencyclidine Treatment Impairs Performance of a Spatial Task in Juvenile Rats." Annals of the New York Academy of Sciences 844 (May): 303–9.

Stefansson H., Sigurdsson E., Steinthorsdottir V., Bjornsdottir S., Sigmundsson T., Ghosh S., Brynjolfsson J., Gunnarsdottir S., Ivarrson O., Chou T.T., Hjaltason O., Birgisdottir B., Jonsson H., Gudnadottir V.G., Gudmundsdottir E., Bjornsson A., Ingvarsson B., Ingason A., Sigfusson S., Hardardottir H., Harvey R.P., Lai D., Zhou M., Brunner D., Mutel V., Gonzalo A., Lemke G., Sainz J., Johannesson G., Andresson T., Gudbjartsson D., Manolescu A., Frigge M.L., Gurney M.E., Kong A., Gulcher J.R., Petursson H., Stefansson K. (2002). "Neuregulin 1 and Susceptibility to Schizophrenia." American Journal of Human Genetics 71 (4): 877–92.

Stuchlik A., Rezacova L., Vales K., Bubenikova V., Kubik S. (2004). "Application of a Novel Active Allothetic Place Avoidance Task (AAPA) in Testing a Pharmacological Model of Psychosis in Rats: Comparison with the Morris Water Maze." Neuroscience Letters 366 (2): 162–66.

Sturgeon R.D., Fessler R.G., London S.F., Meltzer H.Y. (1981). "A Comparison of the Effects of Neuroleptics on Phencyclidine-Induced Behaviors in the Rat." European Journal of Pharmacology 76 (1): 37–53.

Swerdlow N.R., Bakshi V., Waikar M., Taaid N., Geyer M.A. (1998). "Seroquel, Clozapine and Chlorpromazine Restore Sensorimotor Gating in Ketamine-Treated Rats." Psychopharmacology 140 (1): 75–80.

Swerdlow N.R., Geyer M.A. (1993). "Clozapine and Haloperidol in an Animal Model of Sensorimotor Gating Deficits in Schizophrenia." Pharmacology, Biochemistry, and Behavior 44 (3): 741–44.

Takei N., Murray R.M., Sham P., O'Callaghan E. (1995). "Schizophrenia Risk for Women from in Utero Exposure to Influenza." The American Journal of Psychiatry 152 (1): 150–51.

Tiedtke P.I., Bischoff C., Schmidt W.J. (1990). "MK-801-Induced Stereotypy and Its Antagonism by Neuroleptic Drugs." Journal of Neural Transmission. General Section 81 (3): 173–82.

Vaskovsky A.,Lupowitz Z., Erlich S., Pinkas-Kramarski R. (2000). "ErbB-4 Activation Promotes Neurite Outgrowth in PC12 Cells." Journal of Neurochemistry 74 (3): 979–87.

Wang C., McInnis J., Ross-Sanchez M., Shinnick-Gallagher P., Wiley J.L., Johnson K.M. (2001). "Long-Term Behavioral and Neurodegenerative Effects of Perinatal Phencyclidine Administration: Implications for Schizophrenia." Neuroscience 107 (4): 535–50.

Whishaw I.Q., Auer R.N. (1989). "Immediate and Long-Lasting Effects of MK-801 on Motor Activity, Spatial Navigation in a Swimming Pool and EEG in the Rat." Psychopharmacology 98 (4): 500–507.

White A.M., Best P.J. (1998). "The Effects of MK-801 on Spatial Working Memory and within-Session Spatial Learning." Pharmacology, Biochemistry, and Behavior 59 (3): 613–17.

Willi R., Weinmann O., Winter C., Klein J., Sohr R., Schnell L., Yee B.K., Feldon J., Schwab M.E. (2010). "Constitutive Genetic Deletion of the Growth Regulator Nogo-A Induces Schizophrenia-Related Endophenotypes." The Journal of Neuroscience: The Official Journal of the Society for Neuroscience 30 (2): 556–67.

Zemanova A., Stankova A., Lobellova V., Svoboda J., Vales K., Vlcek K., Kubik S., Fajnerova I, Stuchlik A. (2013). "Visuospatial Working Memory Is Impaired in an Animal Model of Schizophrenia Induced by Acute MK-801: An Effect of Pretraining." Pharmacology, Biochemistry, and Behavior 106 (May): 117–23.

Zhang Z.J., Reynolds G.P.(2002). "A Selective Decrease in the Relative Density of Parvalbumin-Immunoreactive Neurons in the Hippocampus in Schizophrenia." Schizophrenia Research 55 (1-2): 1–10.

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