Case Report

BIOMEDICAL Journal of Scientific & Technical Research

ISSN: 2574 -1241

DOI: 10.26717/BJSTR.2022.43.006865

Pediatric Anti-Glyr Antibody-Associated Progressive Encephalomyelitis with Rigidity and Myoclonus: A Case Report and Literature Review

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ARTICLE INFO

Received: April 05, 2022

Published: April 11, 2022

Citation: Kaifan Meng, Wendong Zuo, Fei Liu. Pediatric Anti-Glyr Antibody-Associated Progressive Encephalomyelitis with Rigidity and Myoclonus: A Case Report and Literature Review. Biomed J Sci & Tech Res 43(2)-2022. BJSTR. MS.ID.006865.

Keywords: Progressive Encephalomyelitis with Tonic and Myoclonus; Pathogenesis; Clinical Manifestations; Diagnosis

ABSTRACT

Progressive encephalomyelitis with rigidity and myoclonus (PERM), a rare neurological disorder, is part of the spectrum of Stiff-Person Syndromes (SPS). SPS is a group of diseases characterized by symmetrical rigidity and muscle stiffness, especially in the axial and proximal limb muscles [1]. PERM is primarily characterized by stiffness syndrome and inflammatory cerebrospinal fluid. Clonus, brainstem symptoms, long tract signs (signs of damage to the vertebral tracts), cognitive impairment, and seizures are also observed rarely. The incidence of PERM is low and is rare in children. The clinical features and laboratory examinations of a child with anti-GlyR antibody-related progressive encephalomyelitis (PERM) with tonic and myoclonus are summarized in order to improve the understanding of pediatric neurologists.

Abbreviations: PERM: Progressive Encephalomyelitis with Rigidity and Myoclonus; SPS: Stiff-Person Syndromes; VMA: Vanillylmandelic Acid; CNS: Central Nervous System; GABA: Gamma-Aminobutyric Acid; GAD: Glutamic Acid Decarboxylase; CPK: Elevated Creatine Phosphokinase; NMS; Neuroleptic Malignant Syndrome

Introduction

Progressive encephalomyelitis with rigidity and myoclonus (PERM), a rare neurological condition, is a disease of the stiff-person syndrome (SPS). SPS is a group of diseases characterized by symmetrical rigidity and muscle stiffness, especially in the axial and proximal limb muscles. Convulsions, brainstem symptoms, long tract signs (signs of damage to the vertebral tracts), cognitive impairment, and rare seizures [2,3] are also reported. No systematic studies and long-term follow-up data have been reported on PERM yet. The differential diagnosis and treatment of the disease are reviewed, hoping to help the clinical understanding of the disease.

Case Report Results

1. One boy (4-year and 6-months old) was admitted to the hospital on January 19, 2021, mainly due to "6 months of dyskinesia". Acute onset, chronic fluctuating course, mainly 4 courses were observed. The first course of the disease revealed that more than 7 months ago (2020.6.9, 3 years and 11 months), the patient had vomiting for 3 days, was walking unsteady, manifested as soft legs, persistent right strabismus of both eyes, the disappearance of left forehead lines, closed eyes, and weakness in the nose. The labial folds became shallow and

increased with sleep. He was treated with gamma globulin (2g/kg), methylprednisolone (15 mg/kg. d), and sequential oral prednisone acetate to immune peripheral facial paralysis. The symptoms disappeared after 4 days of treatment. More than 6 months ago (July 2020), slight right lower extremity claudication appeared again, which disappeared on its own after 1 week. The second course of the disease: >5 months ago (2020.8.1), claudication of the right lower extremity occurred again, and the limbs trembled once during sleep, accompanied by crying, and sometimes with tongue biting, 5–6 times/day, no seizures were reported during waking. After being on continued gamma globulin, methylprednisolone, and prednisone for 1 week, the patient improved. After 2 weeks of treatment, he walked smoothly, and the symptoms of limb shaking and tongue biting disappeared during sleep. In the third course of the disease, > 4 months ago (2020.9.20), the limbs trembled again in sleep, and the tongue was bitten occasionally, and no diagnosis and treatment was given. Before 3 months (2020.10.1), in addition to limb shaking during sleep, right squinting and diplopia had appeared in both eyes during sleep more than once and lasted they lasted ~30 min. The 4th course of PERM: one month ago (2020.12.26, oral prednisone was stopped for 1 week), the walking instability, diplopia, and the symptoms of limb shaking showed aggravation, and the attack occurred after being shocked by the stimulation during the day, and the limb shaking continued every time. The time of limb shaking was longer than before, about 3 min, once every few days, (12.26–12.29) after giving gamma globulin 2g/kg, the seizures became more frequent, easily induced by startle stimulation, several times/day, the longest lasted 3 min in an awake state. The symptoms of diplopia and binocular strabismus disappeared 3 days prior to admission.

2. Physical examination on admission: It showed a head circumference of 49 cm, weight 21.5 kg, height 110 cm, no abnormality in the heart, lungs, and abdomen. Nervous system physical examination revealed a general condition, cranial nerve (-). There was a normal motor system with muscle strength, muscle tone, muscle volume, but because of fear "ca not sit, stand, walk". Sensory system (-), reflexes: The left knee-tendon reflex was active, and the pathological signs were negative. The meningeal irritation sign (-), autonomic nerve (-) were recorded.

3. Auxiliary examination: Cerebrospinal fluid (3 times): 8–13 nucleated cells/mm^3, normal sugar, protein, and chloride. Immunology: blood antinuclear antibody spectrum, Anti-anti-neutrophil cytoplasmic antibodies (ANCAs), blood myasthenia gravis antibody spectrum. Blood peripheral nerve antibody spectrum: negative. Blood, cerebrospinal fluid autoimmune encephalitis antibody spectrum (including Mog, GAD): negative. T, B lymphocyte subsets revealed normalcy. ESR: 17 mm/h, blood idiopathic myositis antibody spectrum: anti-Ro-52 antibody IgG (+++), anti-SS-A antibody (+). Immunoglobulin, complement: normal. Blood anticardiolipin antibodies: normal. Armor: Normal. TPOAb: 37.08 IU/mL (0–34), TgAb 136.80 IU/mL (0–115). Infection screening: Negative, T-SPOT result: negative, cerebrospinal fluid: HSV, EBV. Mycobacterium tuberculosis, *Mycoplasma pneumoniae* DNA: negative. Metabolic examination: blood biochemistry, lactate, blood ammonia, homocysteine, β-hydroxybutyric acid were all normal. Hematuria metabolism: Normal. The toxic test was negative. Tumor-related parameters of blood AFP, β-HCG, NSE, CA19–9 were normal. Urine vanillylmandelic acid (VMA) was negative.

4. Other tests: In proband whole-genome + parental whole-exome sequencing, no clear pathogenic variant was observed. In electromyography (Aug. 2020), no abnormality was found in bilateral ulnar, median, tibial and common peroneal nerves. Video EEG revealed non-epileptic events, sudden limb shaking was manifested once, leaning back, facial force, 2 times of body rigidity, continuous limb shaking, a large number of EMG artifacts on ventilation EEG, and no consistent seizure pattern was noticed. After admission, clonazepam dose was gradually increased to 0.12 mg/kg/d. After 1 week, the anti-GlyR antibody in the blood-cerebrospinal fluid was 1:100. According to the clinical symptoms and auxiliary examinations, the patients were diagnosed with anti-GlyR antibody-related rigidity and myocardium. Convulsive progressive encephalomyelitis (PERM). Afterward, he was given methylprednisolone (20 mg/kg. d) shock, gamma globulin (2g/kg), rituximab (375 mg/m^2), once a week with four times, and sequential oral prednisone acetate treatment. The child's walking has improved significantly compared with the previous follow-up, and the frequency and duration of excessive startle response and muscle rigidity episodes have significantly been reduced.

Discussion

PERM diagnosis is very challenging for several reasons. First described by Whitely et al. In 1976, it was relatively rare [4]. Diagnosis is primarily clinical, as (in most cases) imaging studies show no signs. Increased signal intensity in the cervical spinal cord and lower brainstem in T2 MRI sequences were reported in only two cases [5]. EMG and antibodies in serum and cerebrospinal fluid could help confirm the diagnosis. The initial clinical presentation can be very uncertain and rare, as in this case. The common differential diagnoses of SPS/PERM syndrome are rigid man syndrome, paraneoplastic SPS, and neuroleptic malignant syndrome (NMS) [6]. In this case report, we can add spinal myoclonus to the list

and possibly scoliosis. Overall, initial lower back pain and stiffness may have been a prerequisite for PERM syndrome symptoms. Lumbar fusion was performed on indications for scoliosis. But it does not affect SPS. In addition, the patient subsequently developed recurrent episodes of lower extremity myoclonus. These were associated with a history of spinal fusion and were incorrectly diagnosed as spinal myoclonus.

Our patient's myoclonic seizures (neuroleptic malignant syndrome, NMS) experienced in 2014 were associated with hyperthermia. Xu et al. reported that PERM could mimic NMS because of significant overlap in their symptoms. In this setting, muscle stiffness, fever, autonomic nervous system dysfunction, and altered mental status (both entities are common) can be considered favorable for NMS. However, extensive myoclonus, especially its history of relapsing patterns, and even inadequate evidence for the use of antipsychotics should alert clinicians to strengthen the diagnosis. Elevated creatine phosphokinase (CPK) levels have been reported in NMS at least four times the upper limit. Elevated CPK has been less described in the context of PERM. The literature is not particularly rich on this topic though we identified three reported cases with normal CPK values [2], while five elevated CPK values were described between 408 IU/L and 4779 IU/L [7,8].

Besides the clinical manifestations, antibodies can play a decisive role in the diagnosis of SPS. Initially, both SPS and PERM syndromes were associated with Glutamic Acid Decarboxylase (GAD) antibodies. A 60–80% correlation between GAD antibody positivity and SPS is suggested in recent literature [9]. Schmidt et al. showed that GAD-positive antibodies are present in PERM cases only. Antibodies to GlyR, found in association with PERM cases in 2008, were found absent in most SPS cases. GlyR antibody testing was not available at our institution at the time of treatment. We believe that GAD antibodies can lead to decreased brain GABA [10], which is consistent with the development of epileptic seizures. Four-channel EMG studies have revealed inhibitory deficits and hyperexcitability of brainstem reflexes mediated by dysfunctional inhibitory Gamma-Aminobutyric Acid (GABA) and glycine neurons. A post-hoc analysis of PERM cases revealed brainstem inflammation. Brainstem involvement can be used to differentiate SPS from PERM [11]. It remains debatable whether PERM belongs to the SPS spectrum and is considered an SPS-plus version of the main syndrome pain. The initial clinical presentation did indeed show significant symptom overlap. However, the fluctuating course of severe relapse in this patient supports the diagnosis of PERM.

The presence of GAD antibodies is not specific to PERM syndrome [12,13] alone and is associated with other diseases such as diabetes, schizophrenia or bipolar disorder, Parkinson's disease, cerebellar disease, and neurological disorders. Patients with type 1 diabetes usually show GAD65 antibody titers just <20, whereas patients with autoimmune diseases of the nervous system have serum antibody values >20, often even >100. The GAD65 antibody level increased to 95 units/mL in our case. However, it was related to the clinical features and its evolution, and left no doubts about our final diagnosis. Treatment recommendations for PERM patients include the use of immunomodulatory corticosteroids, immunoglobulin IV, plasma exchange, or cyclophosphamide [14]. Intrathecal Baclofen has also been used successfully [15] though the prognosis after treatment can fluctuate. There is limited literature on the long-term clinical course of PERM. Studies suggest that PERM remains latent for several years and suddenly decompensates due to infection. Chronic courses and acute exacerbations have been reported in up to 18% of PERM cases.

Relapses have been reported from a few weeks after disease onset to nine years7,8. In most cases, as in the present, relapse showed association with corticosteroid discontinuation. Typically, the dose of corticosteroids is increased upon relapse5. However, in the absence of a satisfactory response, more aggressive immunosuppressive therapy, such as cyclosporine, azathioprine, and rituximab may be required [2]. Other immunotherapies, namely plasma exchange and cyclophosphamide[16] have also been described in relapse. Long-term treatment with oral corticosteroids ranging from 8 to 20 mg/day is described in combination with azathioprine 50 mg/day to 150 mg/day [17,18]. Studies also reported combinations of oral corticosteroids with diazepam or clonazepam and intrathecal baclofen [14]. In the current situation, almost 10 years have passed from the onset of symptoms to the discovery of the correct diagnosis. Reports of delayed diagnosis of PERM are rare. One case of PERM had a 6-month delay in diagnosis and a good response to immunoglobulin therapy.

The literature review showed three case reports of delayed diagnosis of SPS, with a delay ranging from four months to three years. The first patient responded well to combination therapy with diazepam, baclofen, dexamethasone, azathioprine, and plasmapheresis, and remained moderately rigid without spasticity at 5-month follow-up. The second patient was given immunoglobulin and responded well with a 2-month follow-up. The third patient received IV diazepam and reported no recurrence at the six-month follow-up. Overall, PERM syndrome is a rare disorder and has a difficult diagnosis, as highlighted in this case report. Once the diagnosis is established, proper treatment should be followed that may help save lives. It is recommended to maintain long-term oral corticosteroid therapy to prevent a recurrence. Further, regardless of delayed diagnosis, favorable responses may be obtained with appropriate treatment in autoimmune Central Nervous System (CNS) disorders such as PERM [19]. However, this report documents only one situation and more data are required to generalize any conclusions.

The ligand or voltage-gated ion channels can be affected by mutations or autoimmune attacks, leading to channelopathy. Many CNS diseases, such as limbic encephalitis and some forms of epilepsy, are associated with specific serum autoantibodies against ion channels or related proteins (Irani and Lang, 2008). In 2008, the glycine receptor (GlyR) was first identified as a possible target of autoantibodies in patients with PERM (Hutchinson et al., 2008). GlyR, a member of the ligand-gated ion channel superfamily [20,21], includes N-methyl-d-aspartate (NMDA) receptors and nicotinic acetylcholine receptors. GlyR is present throughout the brain but most abundantly in the spinal cord and brainstem. It is also a target of the alkaloid strychnine, which causes generalized muscle spasms and cramps, muscle stiffness and tightness, agitation, increased consciousness and responsiveness, induced seizures, myoclonus, respiratory failure, and sometimes death. The symptoms of PERM include muscle spasms, cramps, myoclonus, stimulus-induced startle, and respiratory failure.

Carvajal-González et al. reported the presence of anti-glycine receptor (anti-GlyR) antibodies in a relatively large cohort of PERM patients and described the clinical and other characteristics of these patients. Using cellular analysis, the authors strongly supported that GlyR antibodies are the causative agent of PERM. The main clinical implication of this report is to demonstrate that PERM is a treatable autoimmune disease. There is a significant overlap of symptoms between PERM, Rigid-Man Syndrome (RMS), and neuromuscular rigidity. Also, antibodies against the GAD and voltage-gated potassium channel complexes were detected in both PERM and stiff-man syndrome. In the current study, Carvajal-González et al. Fifty-two patients with GlyR antibodies were prospectively identified, of whom 33 had PERM, 2 had rigid-man syndrome or Stiff-Person Syndrome (SPS), and 5 had limbic encephalitis or epileptic encephalopathy. Patients with PERM were initially identified by the presence of GlyR antibodies, but the final classification was based on criteria defined in Meinck and Thomson and Espay and Chen, where PERM was defined based on brainstem involvement, in addition to rigid man syndrome, symptoms of typical axial or limb stiffness.

Notably, many patients developed autonomic disturbances, and respiratory failure might have contributed to two of the four hospital deaths throughout the study. Another clinically important observation is the association of thymoma and lymphoma with PERM, as an SPS is often associated with breast and lung cancer. The role of amphiphiles and gephyrin autoantibodies previously found in SPS remains to be characterized in PERM. How do pathogenic immunoglobulins such as anti-GlyR antibodies enter the brain? Antibodies generally have limited ability to cross the Blood-Brain Barrier (BBB). However, the evidence that pathogenic autoantibodies can enter the CNS (Martinez-Martinez et al.). The underlying mechanism of the antibodies normally crossing the BBB remains unclear, though the permeability of the BBB is increased by a factor of 10 following a local inflammatory response (Cutler et al.). Some CNS autoimmune channelopathies occur only after the disruption in the integrity of the BBB and after the entry of an increasing number of antibodies and/or lymphocytes into brain (Martinez-Martinez et al.). Based on the ratio of GlyR antibodies to total immunoglobulins in serum and cerebrospinal fluid, Carvajal-González et al. reported that GlyR antibodies were synthesized intrathecally in three of six patients for whom matched serum and CSF samples were available.

However, this does not occur in all patients, so we have to assume that numerous antibodies enter the brain. Most of the patients in the study benefited significantly from immunotherapy. This suggests that autoantibodies cause only limited neuronal cell death, but directly affect GlyR function. Carvajal-González et al. used *in vitro* studies to analyze the mechanism of GlyR autoantibody effectors and showed that GlyR antibodies can degrade their targets through antigen regulation. Moreover, since a large proportion of GlyR antibodies belong to the IgG1 and IgG3 isotypes, they also actively complement GlyR-expressing cells *in vitro*. The extent to which these mechanisms contribute to *in vivo* pathology may depend on the density with which GlyRs aggregate through their anchoring protein gephyrin. At the neuromuscular junction, the expression of such ankyrins has been shown to strongly influence the antigenic regulation of ion channels by autoantibodies *in vivo* (Martinez-Martinez et al.). It is useful to establish active immunization with GlyR, or passive transfer animal models using patient-derived monoclonal GlyR antibodies to evaluate pathogenic mechanisms and to test symptomatic or immunosuppressive therapies or complement inhibitors.

Because few patients do not respond to ongoing immunosuppressive therapy, plasma cell-targeted therapy may play a role in the treatment of PERM in rapidly reducing autoantibody production (Gomez et al.). Also, studies of another antibody-mediated neurological disorder, myasthenia gravis, may offer valuable insights (Souroujon et al.). Additionally, electrophysiological methods may be useful to address the question of whether GlyR antibodies have any direct effect on their targets. Such effects may include competitive or allosteric impairment of ligand binding or impairment of ion channel function independent of ligand binding. In either case, once glycine is released from the nerve endings, this results in the reduction in chloride influx, which reduces neuronal inhibition. This would lead to PERM being defined as GlyR channelopathy, the autoimmune counterpart of hereditary polycerebral palsy caused by mutations in GlyR (OMIM

138491). Notably, there are other chloride channel diseases, namely myotonia congenita Thomson and Becker types, due to mutations in chloride voltage-gated channel 1(CLCN1), the gene encoding the voltage-dependent CLC-1 chloride channel in skeletal muscle.

These mutations reduce chloride channel function, leading to hyperexcitability, delayed relaxation, and stiffness of muscle fibers. The physiological role of chloride current reduction in excitatory tissue: The Nernst equilibrium potential of chloride ions is about –70 mV, which is the same or very close to the resting potential of neurons. Thus, when the chloride channel is opened, the membrane potential does not change much, but any depolarizing input is strongly inhibited because the charge carried by the sodium ions entering the neuron is shunted by the chloride conductance. Overall, impaired function of voltage-dependent chloride channel mutations in muscle, or damage to ligand-gated chloride channels in the brainstem and spinal cord causes hyperexcitability, resulting in myotonia or encephalomyelitis and PERM rigidity.

Summary and Conclusion

The clinicians are advised that many brain diseases or their subgroups can be caused by autoantibodies. Findings in this case report also extend to psychiatry, where many syndromes appear to involve subgroups involving autoantibodies. Besides, the possibility of paraneoplastic origin should be investigated in autoantibody-positive patients. Because the antibody "attack" in the brain does not necessarily involve neuronal damage, the symptoms may disappear after immunotherapy. However, continued immunosuppression may be provided as long as antibody production continues (Table 1).

Table 1.

Total cellular score (a/mm^3)	Karyocyte (a/mm^3)	Mononuclear	Multinucleate	Protein (g/L)	Suger (mmol/L)	Oxide (mmol/L)	RIQI Date
25	9	NA	NA	0.25	3.61	123.1	10/06/2020
25	8	8	0	0.2	4.28	131.8	08/09/2020
562	13	13	0	Normol	Normol	Normol	01/01/2021

Acknowledgement

Thanks for all the contributors.

Conflict of Interest

The authors declare that there is no conflict of interest.

References

1. Meinck HM, Thompson PD (2002) Stiff man syndrome and related conditions. Movement Disorders 17(5): 853-866.
2. Hutchinson M, Waters P, McHugh J, Gorman G, O'Riordan S, et al. (2008) Progressive encephalomyelitis rigidity and myoclonus: A novel glycine receptor antibody. Neurology 71(16): 1291-1292.
3. Mas N, Saiz A, Leite MI, Waters P, Baron M, et al. (2011) Antiglycine-receptor encephalomyelitis with rigidity. Journal of Neurology Neurosurgery and Psychiatry 82(12): 1399-1401.
4. Martinez-Martinez P, Losen M, Duimel H, Frederik P, Spaans F, et al. (2007) Overexpression of rapsyn in rat muscle increases acetylcholine receptor levels in chronic experimental autoimmune myasthenia gravis. American Journal of Pathology 170(2): 644-657.
5. Martinez-Martinez P, Molenaar PC, Losen M, Hoffmann C, Stevens J, et al. (2015) Auto-immune disorders as a possible cause of neuropsychiatric syndromes. Tijdschrift voor psychiatrie 57(3): 183-191.
6. Meinck HM, Balint B (2018)From stiff man syndrome to stiff person spectrum disorders. Nervenarzt 89(2): 207-218.
7. Gomez AM, Willcox N, Molenaar PC, Buurman W, Martinez-Martinez P, et al. (2012) Targeting plasma cells with proteasome inhibitors: possible roles in treating myasthenia gravis? Ann N Y Acad Sci 1274: 48-59.
8. Gomez AM, Willcox N, Vrolix K, Hummel J, Nogales-Gadea G, et al. (2014) Proteasome Inhibition with Bortezomib Depletes Plasma Cells and Specific Autoantibody Production in Primary Thymic Cell Cultures from Early-Onset Myasthenia Gravis Patients. Journal of Immunology 193(3): 1055-1063.
9. Souroujon MC, Brenner T, Fuchs S (2010) Development of novel therapies for MG: Studies in animal models. Autoimmunity 43(5-6): 446-460.
10. Liu S, Ren W, Qu MH, Xue H, Ji T, et al. (2009) Contribution of Na-K-2Cl Cotransporter to Gamma-Amino Butyric Acid (GABAA) Receptor-Mediated Membrane Depolarization in Guinea Pig Myenteric Neurons. Gastroenterology 136(5): A98-A98.
11. Iizuka T, Tominaga N, Kaneko J (2013) Clinical spectrum of anti-glycine receptor antibody-associated disease. Rinsho shinkeigaku 53(11): 1063-1066.
12. Graus F, Saiz A, Dalmau J (2020) GAD antibodies in neurological disorders - insights and challenges. Nature Reviews Neurology 16(7): 353-365.
13. Lee JW, Sim S J, Cho S M, Lee J (2005) Characterization of a self-assembled monolayer of thiol on a gold surface and the fabrication of a biosensor chip based on surface plasmon resonance for detecting anti-GAD antibody. Biosensors & Bioelectronics 20(7): 1422-1427.
14. Carvajal-Gonzalez A, Leite MI, Waters P, Woodhall M, Coutinho E, et al. (2014) Glycine receptor antibodies in PERM and related syndromes: characteristics clinical features and outcomes. Brain 137: 2178-2192.
15. Carvajal-Gonzalez A, Leite MI, Waters P, Woodhall M, Coutinho E, et al. (2014) Glycine receptor antibodies in PERM and related syndromes: characteristics clinical features and outcomes. Brain 137: 2178.
16. Espay AJ, Chen R (2006) Rigidity and spasms from autoimmune encephalomyelopathies: Stiff-Person syndrome. Muscle & Nerve 34(6): 677-690.

17. Linington C, Mathey E, Derfuss T, Rasband M, Storch M, et al. (2007) Neurofascin-specific autoantibodies mediate axonal injury in inflammatory demyelinating diseases of the central nervous system. Clinical Immunology 123: S146-S146.

18. Linington C, Mathey E, Derfuss T, Rasband M, Storch M, et al. (2007) Neu rofascin-specific autoantibodies mediate axonal injury in inflammatory demyelinating diseases of the central nervous system. Clinical Immunology 123: S129-S130.

19. Falcioni ML, Nasuti C, Bergamini C, Fato R, Lenaz G, et al. (2010) The Primary Role of Glutathione Against Nuclear Dna Damage of Striatum Induced by Permethrin In Rats. Neuroscience 168(1): 2-10.

20. Tipps ME, Lawshe JE, Ellington AD, Mihic SJ (2010) Identification of Novel Specific Allosteric Modulators of the Glycine Receptor Using Phage Display. Journal of Biological Chemistry 285(30): 22838-22843.

21. Welsh BT, Goldstein BE, Mihic SJ (2009) Single-Channel Analysis of Ethanol Enhancement of Glycine Receptor Function. Journal of Pharmacology and Experimental Therapeutics 330(1): 198-205.

ISSN: 2574-1241

DOI: 10.26717/BJSTR.2022.43.006865

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