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Dopaminergic hypothesis in neuroleptic malignant syndrome

Introduction: The research question is whether a new dopaminergic hypothesis can be given studying the clinical representations of Neuroleptic Malignant Syndrome when Schizophrenia and Affective disorders are studied separately.

Aim: To study and analyses the clinical manifestations of NMS to have a new look in Dopaminergic hypothesis with a new clinical criterion of NMS (AVS-CUV Criterion).

Methods: Twenty Schizophrenics and thirty affected disorder cases that developed NMS are studied between 1990 and 2001 prospectively. Modified criteria of Keck were used for diagnosis of NMS. Only patients who developed fever, altered sensorium, extrapyramidal and autonomic symptoms are included in Standard statistical analysis of the data which included factor analysis correction data and discriminate analysis were performed.

Results: Mean age of onset in schizophrenia was 32 years (18-58 years) and in affective disorders was 43 years (15-73 years). NMS developed within 9 hours of starting therapy and lasted for a mean duration of 23 days. In the affective disorder group, NMS developed over a period of 17 hours and lasted for a mean duration of 11 days. Fever occurred in all the cases and earlier in schizophrenia (11.9 hours) compared to affective disorders (16.8 hours). The altered sensorium occurred within 9.6 hours in schizophrenia and 25.69 hours in affective disorder. The rigidity occurred in 38.6 hours in Schizophrenia and 84.9 hours in affective disorder. Rigidity followed fever and altered sensorium in both conditions. Autonomic symptoms occurred within 48 hours in schizophrenia and 107 hours in affective disorder. The correlation analysis showed a significant correlation between NMS onset with fever and altered sensorium.Cluster analysis indicated autonomic and extrapyramidal symptoms cause for the evolution of NMS.The factor analysis of the parameter responsible for NMS in schizophrenics are extrapyramidal symptoms 0.913, autonomic symptoms 0.858, altered sensorium 0.497, whereas in

affective disorders, extrapyramidal symptoms 0.931, autonomous symptoms 0.955, fever 0.200, altered sensorium 0.181. Four patients died in the schizophrenic group. Our discriminate analysis clearly showed the importance of the parameters with the associated probability of discrimination: autonomic symptoms (0.9), extrapyramidal symptoms (0.7), altered sensorium (0.6) and fever (0.3). The misclassification rate in case of Schizophrenia is 15% and affective disorder is around 7%. AVS-CUV Criterion can be used confidently in NMS.AVS-CUV Criterion – clinically definite fever, altered sensorium, extrapyramidal symptoms and autonomic symptoms and signs. Clinically probable -extrapyramidal symptoms and autonomic symptoms. Clinically possible- altered sensorium with autonomic symptoms or extrapyramidal symptoms.

Discussion: Grace suggested the dopamine was secreted tonically from the cerebral cortex and physically from the basal ganglia. In our clinical study, we have proved in Schizophrenia, NMS takes a very short time to evolve and longer time to resolve whereas in Affective disorder, it takes longer time to evolve and shorter time to resolve.PET studies in neuroleptics naïve studies in chronic schizophrenia showed hypometabolism in cerebral cortex and basal ganglia whereas in affective disorder (Mania), study clearly showed sparing of the cortex.

Conclusions: We propose that cortex has predominantly TONIC (D1) receptors and basal ganglia have PHASIC (D2) receptors. This might plausibly explain the clinical presentations of evolution and resolution of NMS: 1) TONIC release of dopamine in the cortex is predominantly D1 receptors and the PHASIC release from basal ganglia is predominantly D2 receptors. 2) A new AVS-CUV criterion has been added to the world literature.

Biography

Avathvadi Venkatesan Srinivasan, driven by his quest for excellence joined Madras Medical College (MMC) and received MD (General Medicine) in 1978. Later he pursued and received DM in Neurology from his alma mater. His thirst for research, skills and the latest development in Neurology made him find his way to the National Institute of Neurology and Neurosurgery, his pioneering research work on Neuroleptic Malignant Syndrome got him bestowed with the PhD degree in 2002. It made him the first ever recipient in Neurology from the Tamil Nadu Dr. M.G.R. Medical University, since its inception in 1988. His path breaking research (6 papers) in Phantom limbs, Stroke etc., with Padma Bhusan Dr. V S Ramachandran, Director, Center of Brain and Cognition, University of San Diego remain acclamatory to his undisputed authority in Behavioral Neurology and Movement disorders. He authored more than 100 scientific papers; dozens of his other work have found places in reputed medical journals and has published 12 chapters. His research papers presented, won acclaims in 60 National conferences and in 25 International conferences held in UK, USA, Japan, Australia, China, Europe and other countries. He is the only one from India to collaborate with Dr. V S Ramachandran, who is the first recipient of Padma Bhusan for his contribution to Neurosciences.

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