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# Philip S. Holzman

1922-2004

Dr. Philip S. Holzman, a preeminent figure in the world of schizophrenia research and one of the country's leading schizophrenia researchers, died on June 1, 2004, at the age of 82. Dr. Holzman is survived by Ann Holzman, his wife of 58 years; his children Natalie Bernardoni, Carl Holzman and Paul Holzman; his son-in-law Gene Bernardoni; his daughter-in-law Mira Kopell; his grandchildren Joseph, Neena and Daniel; and his sister, Sylvia Steinbrock. Born in New York City in 1922, Dr. Philip Holzman graduated from the College of the City of New York in 1943 and later in 1952, completed a doctoral degree from the University of Kansas. After working at the Menninger Foundation and the University of Chicago, he founded the Psychology Research Laboratory at McLean Hospital in Belmont, MA, in 1977, and became an integral part of the research group at the Mailman Research Center that Seymour Kety had organized.

Dr. Holzman had an extraordinarily distinguished career that was based on his seminal observations regarding the thought disorder and the presence of abnormal smooth pursuit eye movements (SPEM) or eye tracking dysfunction (ETD) in schizophrenics and their biological first-degree relatives. Dr. Holzman's career was notable for his use of the scientific method to carefully uncover the genetic components to its pathophysiology. He was among the first to appreciate the importance of including the biological relatives of schizophrenics in his studies, so that he could begin to parse out underlying features of the pathophysiology that might be related to susceptibility genes for this disorder. Holzman and his colleagues noted that the eyes of schizophrenic subjects lag behind when following a moving target and they compensate for this by generating ballistic, rapid movements to bring the target back onto the fovea. He and his colleagues quickly ruled out a possible role for antipsychotic medication by observing that drug-free and/or drug-naïve patients also showed ETD. He went on to demonstrate, moreover, that eye tracking dysfunction, occurs in 50-80% of schizophrenics and in about 45% of their unaffected first-degree relatives. The familial tendency of ETD suggested that it might be genetic. He went on to show that concordance rates in monozygotic (MZ) and dizygotic (DZ) twins were consistent with genetic transmission, and in examining the distribution of eye tracking and schizophrenia in families, he showed that an autosomal dominant pattern of inheritance could potentially account for their transmission. Later, he pursued the pathophysiology of ETD by showing that a deficit in motion processing was one of the substrates of the smooth pursuit abnormalities. Based on these observations, Dr. Holzman suggested that this might be a trait marker or endophenotype for schizophrenia. In subsequent studies, he showed that ETD and schizophrenia may be transmitted as independent manifestations of an autosomal dominant trait.

Holzman observed that ETD occurred when a subject pursued a moving target and he postulated that impaired motion processing, rather than a general visual defect, played a role in this phenomenon. Schizophrenic subjects and their first-degree relatives were found to have raised motion discrimination deficits, which were, in turn, correlated with sluggish initiation of smooth pursuit. Based on lesion studies,

Dr. Holzman postulated that the motion sensitive areas of the parietal lobe, i.e. the medial temporal (MT) and medial superior temporal (MST) regions, and an extended network of connections that included frontal and prefrontal areas plays a role in ETD in schizophrenia.

Dr. Holzman had a broad and encompassing vision of how the activity of extended brain circuits created a framework within which genes could regulate brain-behavior units and ultimately the overall behavioral output of the brain. To shed light on this model, he moved his research in a very deliberate way toward demonstrating that the ‘schizophrenia spectrum’ is only one manifestation of a pathological process that includes ETD, mild forms of thought slippage and perhaps other co-familial traits, such as impaired spatial working memory. Holzman reasoned that such endophenotypes for schizophrenia might be more penetrant expressions of schizophrenia susceptibility genes than schizophrenia itself and might therefore improve the power of linkage studies.

There are many ways of defining Philip Holzman’s scientific life. He was the recipient of many prestigious awards and honors, such as the Lieber Prize from the National Alliance for Research on Schizophrenia and Depression (NARSAD), the Gold Medal Award for Lifetime Achievement from the American Psychological Foundation, the Stanley R. Dean Award from the American College of Psychiatrists, the William K. Warren Award from the International Congress of Schizophrenia Research, the Townsend Harris Medal of the City College of New York and most recently, he was the first recipient of the Alexander Galnick Research Investigator Award. He was a member of the Institute of Medicine of the National Academy of Sciences, the American Academy of Arts and Sciences, the Board of Trustees of the Menninger Foundation and the Scientific Advisory Committee of the Health Program of the John and Catherine T. Mac Arthur Foundation. Perhaps most notable were his contributions to NARSAD, where he was one of its scientific pillars throughout the period when the field of schizophrenia research was being formulated as a sub-discipline of clinical neuroscience. We will miss the richness and complexity of his scientific insights and the intricacies of the dialectical process he used to frame his hypotheses and scientific experiments. Mostly, we will miss his unwavering commitment to schizophrenia research and his enduring belief that the scientific method will advance our understanding of this very complex disorder.

Dr. Holzman was a beloved friend and colleague, nurturing mentor, and intrepid researcher who enriched generations of scholars. His extraordinary vision, humor, relentless enthusiasm and indomitable optimism inspired all of us who had the privilege of working with him. We will miss him terribly. It is of some consolation to know that his many contributions to the fields of psychology, psychiatry and cognitive neuroscience, including his love of teaching others, will serve as a lasting legacy to the entire scientific community.

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