

Behavioral Phenotypes in Dysmorphic Syndromes

Syndromes with congenital anomalies usually are diagnosed by their physical features or a particular combination of features that are observed on clinical grounds. Recently, objective means of defining and measuring behavior such as specific patterns of speech and language, types of attention deficits, particular social impairments, and other behavioral disturbances such as self-injury, skin scratching, and lip biting have been developed. These even have been quantified. Thus, it now becomes possible to define the specific behavior phenotypes in a number of syndromes. For instance, mimicking is common in Down syndrome. A discrepancy between performance and verbal skill also is typical of Turner syndrome. Impaired speech and language development often is found in Klinefelter syndrome. Learning and language difficulties, impaired social relations, and crimes against property often are found in individuals with the XYY syndrome. In the fragile X mental retardation syndrome, visuo-spatial skills are impaired such that there is difficulty in climbing stairs and problem solving for sequential events. Autistic and ritualistic disturbances also are frequent. In tuberous sclerosis, autism, hyperactivity, and hypsarrhythmic salaam attacks are seen. In Williams syndrome, superior vocal skills are observed, resulting in "cocktail party" chatter. Patients with this syndrome also have hyperacusis. In Prader-Willi syndrome, hypotonia, hyperphagia, and tantrums are typical; and in Angelman syndrome, a happy disposition with paroxysmal laughter and a jerky ataxic gait usually are seen. In Rett syndrome, loss of mental abilities together with hand-wringing are seen. In Sotos

syndrome, hyperactivity, clumsiness, and poorly articulated speech are observed. The authors urge better description of behavior in future clinical reports.

Turk J, Hill P. *Clin Dysmorphol* 1995;4:105-115.

Editor's comment: *It is clear that defining the behavior seen in syndromes will help to make specific diagnoses. The opportunity to record movement and behavior using video cameras now exists. Just as with physical features, it is sometimes hard to describe accurately types of movements and various facial expressions. Recording and studying behavior will be important for the future in order to delineate the mechanisms involved in a particular disorder.*

Because of the lack of specificity and quantification in the past, it was often hard to describe the behavioral characteristics found in a specific syndrome. Abnormal respiration is another type of behavior, and is characteristic in the Joeebert syndrome. Our ability to define behavioral characteristics will increase with time. I expect there will be many "behavior" syndromes with normal physical features—after all, half the human genes have to do with the brain.

In addition, the authors have very thoroughly reviewed the historical and behavioral perspectives of various syndromes. Geneticists, pediatric endocrinologists, psychologists, and nurses dealing with syndromes should benefit significantly by reading the complete article.

Judith G. Hall, MD

Autoantibodies to the Extracellular Domain of the Calcium Sensing Receptor in Patients With Acquired Hypoparathyroidism

The autoimmune pathogenesis of acquired hypoparathyroidism has been difficult to document with certainty. Earlier studies reported the presence in sera from patients with acquired hypoparathyroidism of antibodies to parathyroid tissue identified by indirect immunofluorescence. Antibodies have also been observed that inhibit the secretion of parathyroid hormone, or that are cytotoxic to parathyroid cells, but such studies have been difficult to replicate. The present investigators hypothesized that patients with this disorder may have antibodies to the G protein-associated calcium sensing receptor, which is expressed on the cell membrane of parathyroid cells.

In preliminary studies, antibodies to extracts of human parathyroid glands were detected by immunoblot analysis in only 5 of 25 (20%) patients with acquired hypoparathyroidism. Since the antigen appeared to be of the same size as the calcium sensing receptor (120 to 140 kd), further studies utilizing the membrane calcium sensing receptor expressed in transfected cells were undertaken. In 8 of 25 (32%) patients (which included all those previously positive by immunoblot

analysis of human parathyroid tissue), antibodies to this receptor were detected by immunoblot. When the calcium sensing receptor was differentially expressed as its extracellular domain and as its transmembrane-intracellular domain, 14 of 25 (56%) patients demonstrated antibodies to the extracellular portion of the receptor and none to the transmembrane-intracellular domain. Patients with both idiopathic acquired hypoparathyroidism as well as those with type I autoimmune polyglandular syndrome demonstrated antibodies to this segment of the calcium sensing receptor. In none of 50 patients with a variety of other autoimmune diseases or in normal controls were antibodies to this antigen detected.

The authors concluded that many patients with acquired hypoparathyroidism have antibodies to the extracellular portion of the calcium sensing receptor. They speculate that some patients in whom these antibodies were not detected may have had the disease for prolonged periods, leading to loss of the autoantigen needed for stimulation.

Li Y, et al. *J Clin Invest* 1996;97:910-914.