Neural tube defect etiology

Ongoing research in the etiology of neural tube defects is increasingly being directed towards the molecular mechanisms at work in the formation of these complex lesions.

Partington et al. undertook to review the family history of patients in a large myelomeningocele/spina bifida clinic in an effort to identify genetic trends in these families, particularly as they relate to current research efforts and laboratory models. Surveys were received from 363 patients (35.5% of the clinic population) and analyzed. The myelomeningocele recurrence rate was 4.3%. Seven sets of twins were identified and all were discordant for their spinal lesions. A family history of spina was found to be evenly distributed between maternal and paternal relatives, rather than tending to follow through the maternal side. Epilepsy was more commonly found on the maternal side of the family, most likely reflecting the postulated causal relationship between maternal anticonvulsant use and the occurrence of spina bifida, although also possibly supporting the concept that a genetic predisposition for maternal epilepsy may also be associated with a higher frequency of birth defects among children of epileptics, independent of anticonvulsant use. Patients with spina bifida in the setting of Waardenburg syndrome and fragile X syndrome were also identified and will be discussed [1].

The association between single nucleotide polymorphisms of the VANGL1 gene and NTDs in a Han population of Northern China was principally studied. Missense single nucleotide polymorphisms (rs4839469 c.346G > A p.Ala116Thr and rs34059106 c.1040A > C p.Glu347Ala) of the VANGL1 gene were analyzed by polymerase chain reaction (PCR) and sequencing methods in 135 NTD cases and 135 normal controls. Genotype and allele frequency distribution was calculated, and the spatial structure of the protein was predicted. The results showed that the VANGL1 gene sequence at the rs4839469 locus exhibited Ala116Thr and Ala116Pro polymorphisms, and allele and genotype distributions were significantly different ($p = 0.036$ and 0.010) between the case and control group. Genotype GC was newly discovered, and its odds ratio value versus GG genotype was 10.241; the α helix fragment of the Ala116Pro mutant was significantly shortened compared with wild type. The rs34059106 site showed alleles of A and did not display C alleles in the two groups. Therefore, the rs4839469 allele of VANGL1 was obviously associated with NTDs. And genotype GC increased the risk of NTDs, changes in the three-dimensional protein structure may have impacted its biological functions, and the rs34059106 polymorphism had no significant correlation with NTDs [2]

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Partington MD, McLone DG. Hereditary factors in the etiology of neural tube defects. Results of a survey. Pediatr Neurosurg. 1995;23(6):311-6. PubMed PMID: 8744000.
2)
Cai C, Shi O, Wang B, Chang B, Yang R, Wang Y, Wang F, Shen C. Association between VANGL1 Gene Polymorphisms and Neural Tube Defects. Neuropediatrics. 2014 Jan 9. [Epub ahead of print] PubMed PMID: 24407469.