Pediatric Neurology Part I: Chapter 13. Microcephaly (Handbook of Clinical Neurology)

Sandrine Passemard, Angela M. Kaindl, Alain Verloes

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True microcephaly (head circumference ≤–3SD), either primary (present at birth) or secondary (of postnatal onset) results from an imbalance between progenitor cell production and cell death that lead to a reduced number of neuronal and glial cells within the brain, resulting in reduced brain growth. Primary non-syndromal microcephalies are recessive disorders resulting from abnormal control of mitotic spindle and cell cycle kinetics in progenitor cells. Microcephaly is also a frequent sign of defects in DNA double- and/or single-strand break repair and in nucleotide excision repair, in which it often is associated with general growth impairment. In these etiologies, cognitive functions are reasonably well preserved despite severe reduction in brain volume. Neuronal migration defects are often associated with secondary microcephaly, as are anomalies of telencephalic cleavage. Secondary microcephalies are often associated with increased neuronal death, and can be associated with metabolic disorders such as serine deficiency or thiamine pyrophosphate transporter deficiency. Microcephaly can be associated with hundreds of syndromal congenital anomalies, including many chromosomal disorders. Genetic etiologies of developmental microcephalies are reviewed.

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