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X-linked spermine synthase gene (SMS) defect: the first polyamine deficiency syndrome.

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We reported the first polyamine deficiency syndrome caused by a defect in spermine synthase (SMS). The defect results from a splice mutation, and is associated with the Snyder-Robinson syndrome (SRS, OMIM_309583), an X-linked mental retardation disorder. The affected males have mild-to-moderate mental retardation (MR), hypotonia, cerebellar circuitry dysfunction, facial asymmetry, thin habitus, osteoporosis, kyphoscoliosis, decreased activity of SMS, correspondingly low levels of intracellular spermine in lymphocytes and fibroblasts, and elevated spermidine/spermine ratios. The clinical features observed in SRS are consistent with cerebellar dysfunction and a defective functioning of red nucleus neurons, which, at least in rats, contain high levels of spermine. Additionally, the presence of MR reflects a role for spermine in cognitive function, possibly by spermine's ability to function as an 'intrinsic gateway' molecule for inward rectifier K +channels.