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Letter to the Editor

SOMATOMEDIN (INSULIN-LIKE GROWTH FACTOR) IS IMPORTANT FOR DEVELOPMENT, MATURATION, AND BRAIN FUNCTION

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INTRODUCTION

The name somatomedin (SM) is composed of *somato*, meaning "factor with a target inside the body", and *medina*, the intermediary of the somatotropic hormone. SM is a molecule present in the serum and an intermediary of somatotropin which acts on tissues and first appeared in the scientific literature in 1972 (1). Growth hormone (GH) does not directly affect tissues; instead, it acts through SM, which is synthesized in the liver and released into the bloodstream (2). Since these factors, in addition to causing tissue growth, are mitogenic, they have been called insulin-like growth factors (IGFs) (3).

Somatomedin (SM) is a molecule present in the serum that acts in cooperation with growth hormone (GH). SM, also called insulin-like growth factor (IGF) (4), is synthesized by the liver, circulates in the bloodstream, and acts on tissues as a mitogen. In the serum, there are two SMs that act as transporters that bind to its receptor on the target cell, producing an effect on somatostatins. SM is composed of IGFs-1 and 2, SM-A, and multiplication-stimulating factor (MSF), which mediate the GH on skeletal tissues. Experiments have shown that in hyposectomized rats, GH alone does not act as a mitogen. Instead, it becomes active in combination with SM. IGFs-1 and 2 have a chemical formula similar to insulin and biological effects on the growth of children. SM is a mediator of GH and promotes cell differentiation and multiplication in both muscle and cartilage.

DISCUSSION

SM is a small GH-dependent peptide that is composed of insulin-like growth factors (IGFs)-1 and 2, SMs-A and C, and multiplication-stimulating factor (MSF), that mediates the GH on skeletal tissues (5). Two SMs are present in the serum, and they have a high molecular weight (150 and 60 Kd) (6). The complex of these two transporter proteins, and their effect on the biological activity of somatostatins, creates a complicated physiological control that includes the delivery of SM to its receptor which is located on the target cell.

In experiments, it was seen that cartilage mucopolysaccharides can be stimulated with the addition of serum in hyposectomized rats that were pretreated with GH (7). Treatment with GH alone does not cause tissue stimulation (8); Rather, the stimulating factor results from SMs-A and C (9). IGF-1 and IGF-2 have a formula which is similar to insulin and they are composed of A domains homologous to the A chain of insulin, B domains homologous to the B chain, C

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domains homologous to the C chain of proinsulin and D domains extending from the C terminals of A Chains (10). SM-C is identified as IGF-1 because they have the same amino acid chain.

SM is associated with protein macromolecules and can be extracted from human plasma where it circulates. Its molecular structure is similar to that of insulin and SM plays a key role in the growth of children (11). SM is a mediator of GH and promotes cell differentiation and multiplication in both muscle and cartilage (12). Therefore, SM plays a role in the activity of chondrocytes by promoting the synthesis of cartilage and osteoblasts (13). In GH-deficient individuals such as children, plasma concentrations of SM are low. SM secretion is inhibited by cortisol, and this could explain its negative effects on body structure (14). SM is produced by various tissues and organs, including the liver, under the stimulus of GH or the somatotropic hormone produced by the pituitary gland (15). Even after childhood, SM continues to affect the tissues into adulthood (16). IGF-1 levels in the blood begin to increase in childhood, until reaching a maximum peak level around 40 years of age and then gradually decreasing after that age (17). SM has anabolic activity and is a cellular growth factor, although the dynamic effects on cells have not yet been clarified.

IGF-1 is a powerful hormone produced by liver cells and chondrocytes that regulates cartilage synthesis. After generation, IGF-1 is released into the circulation, where it binds to the transport proteins IGF-binding proteins (IGF-BP), which increases its plasma half-life (18). IGF-1 (also known as SM) is a hormone that is molecularly similar to insulin and plays a very important role in the growth processes of children, maintaining its effects even into adulthood (19). GH has been found in human brain tissue and IGF-2 has also been detected in cerebrospinal fluid (CSF). The mammalian brain expresses the SM receptors IGF-1R and IGF-2R (20). GH is generated in human brain tissue and carries out its biological action in collaboration with IGF-1. These hormones mentioned above are very important for brain function and development and increase the ratio between neurons and glia (21). For children with impaired brain development, treatments with human GH (hGH) improve growth recovery and intelligence quotient (22). Therefore, GHs and SMs are very important in the development, maturation, and function of the brain in childhood.

The genetic deficiency of SM results in functional brain damage with reduced capacity of its receptors and can cause growth delays (23). Inflammatory processes influence the hypothalamic-GH-IGF-1 axis, causing resistance to GH and a decrease in IGF-1 (24). The binding of IGF to its receptor activates a biochemical cascade that includes phosphatidylinositol 3-kinase (PI3K), mTOR and MAPK involved in cell growth and differentiation, producing biological effects which are also shared by insulin signaling pathways (25)

Both IGF-1 and IGF-2 act on the IGF-1R which is ubiquitous in all tissues (26). It has been reported that the chemical structure of IGF-1R is similar to that of the insulin receptor (27). The extracellular region of IGF-1R is composed of alpha and beta subunits which act as a ligand and the intracellular part of the receptor consists of the tyrosine kinase domain with the beta subunit. After the IGF-1R receptor binds the binding protein, it undergoes structural rearrangement. IGF-1 binding to IGF-1R occurs at two separate sites: one with high affinity and one with low affinity (28). Transgenic mice lacking the IGF-2 gene show dysfunction in embryonic growth and have approximately 70% less body weight at birth (29). This demonstrates the importance of IGF in pre- and post-natal body development.

CONCLUSIONS

SM is important for the growth of tissues, as well as brain function and development in children. GHs and SMs are very important in the development, maturation, and function of the brain in childhood. Treatments with hGH improve cerebral growth and cognition, and genetic deficiency of SM causes functional brain damage with reduced receptor capacity and possible delays in growth. Further studies are needed to clarify the real effects of SM on the brain. In addition, research is currently targeting IGF-1 and IGF-2 since these two molecules are also involved in other diseases.

Conflict of interest

The authors declare that they have no conflict of interest.

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