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Review

The Effect of Muscle IGF-1 on Murine Craniofacial Growth in the Presence of Decreased Masticatory Load: A Comprehensive Review

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Abstract

Insulin-like growth factor 1 (IGF-1) is a key mediator protein of the growth hormone/IGF-1 axis and plays a central role in muscular and skeletal cellular growth and development. However, its specific role in craniofacial growth under conditions of masticatory loading has not yet been precisely established. The objective of this review was to determine the role of IGF-1 in craniofacial growth in murine models exposed to reduced masticatory loads. In this literature review, the following electronic databases were used: PubMed, Google Scholar, Scopus, and Web of Science. A total of 131 articles were identified, of which 19 met the selection criteria for qualitative evaluation. The included studies comprised transgenic overexpression models, murine knockout models, and experimental designs assessing the impact of reduced masticatory load on the craniofacial region. The analyzed evidence supports that IGF-1 plays a fundamental role in the modulation of craniofacial growth at both the bone and muscle levels, particularly under conditions of reduced masticatory load in animal models. Experimental findings indicate that the absence or deficiency of IGF-1 is associated with growth delay, morphological alterations, and decreased muscle mass, whereas its overexpression contributes to hypertrophy and tissue adaptation. Nevertheless, these findings should be interpreted with caution due to important limitations, including methodological heterogeneity among studies, the diversity of experimental models employed, and the absence of clinical research that would enable direct extrapolation of these results to clinical practice.

Keywords: IGF-1; Craniofacial, Growth; Murine; Mastication.

1. Introduction

The craniofacial region is one of the most frequently affected regions in children with genetic abnormalities.[1] Since the craniofacial region is that part of the body that is directly visible, any abnormalities affecting this region have a major effect on the individual's well-being in terms of physical and psychological aspects.[2] Children who develop craniofacial abnormalities can have a large skull and can also require orthodontic treatment, along with tooth crowding. Furthermore, along with crowding, since the cranium and face are disproportionate in growth, the eruption of the teeth can be disrupted along with having short stature overall.

Insulin-like growth factor 1 (IGF-1) is a critical protein that participates in cell development and growth. The impact of growth hormones on different body tissues is primarily regulated by IGF-1.[3] The anterior pituitary gland is the main site for the production of growth hormone (GH), after which it reaches the liver for the production of IGF-1 via the bloodstream. IGF-1 has a huge array of impact on almost every cell of the body, for example tissues of skeletal muscles, nerve tissues, bone, liver, kidney, bone, skin, bone marrow, and lungs.[4] While the liver is responsible for secreting about 75% of the circulating IGF-1,[5] some target tissues can produce and express IGF-1 locally through autocrine and paracrine roles.[6] These tissues include muscle, cartilage, bone, kidneys, and brain. Along with the insulin-like effects of IGF-1, it also controls cellular DNA synthesis, growth, and development, particularly in nerve cells.[7] Moreover, IGF-1 has a crucial role in promoting cell proliferation and preventing cell death (apoptosis).

IGF-1 plays a major role in the development of bones and muscles. In mice, when this IGF-1 factor is removed, this leads to severe retardation in the growth of the bones and muscles.[8] Therefore, it emphasizes the importance of this factor for craniofacial development. The primary source responsible for IGF-1 synthesis has been identified as the liver; however, local production also suffices for tissue growth.[9] In one study, when there was a cessation of liver IGF-1, no apparent changes were noted in the post-natal size of the muscles or body in general.[10] Furthermore, in a study on mice, excessive expression of IGF-1 led to an increase in the mass of the muscles.[11] In contrast to this finding, when the deletion of IGF-1 was found, it led to a reduction in the mass and function of the muscles in mice (Figure 1).[12]

Liu et al. in 1993 showed that animals that do not express the IGF-1 receptor led grave stunned growth and did not survive after birth.[13] McAlarney et al. in 2001 showed another IGF-1 knockout animal study in which craniofacial growth was impaired by 43-64%, especially in the neural and naso-maxillary complex.[14]

Given the impact of IGF-1 on craniofacial growth, this review aimed to determine the role of IGF-1 in craniofacial growth in murine models under reduced masticatory loads.

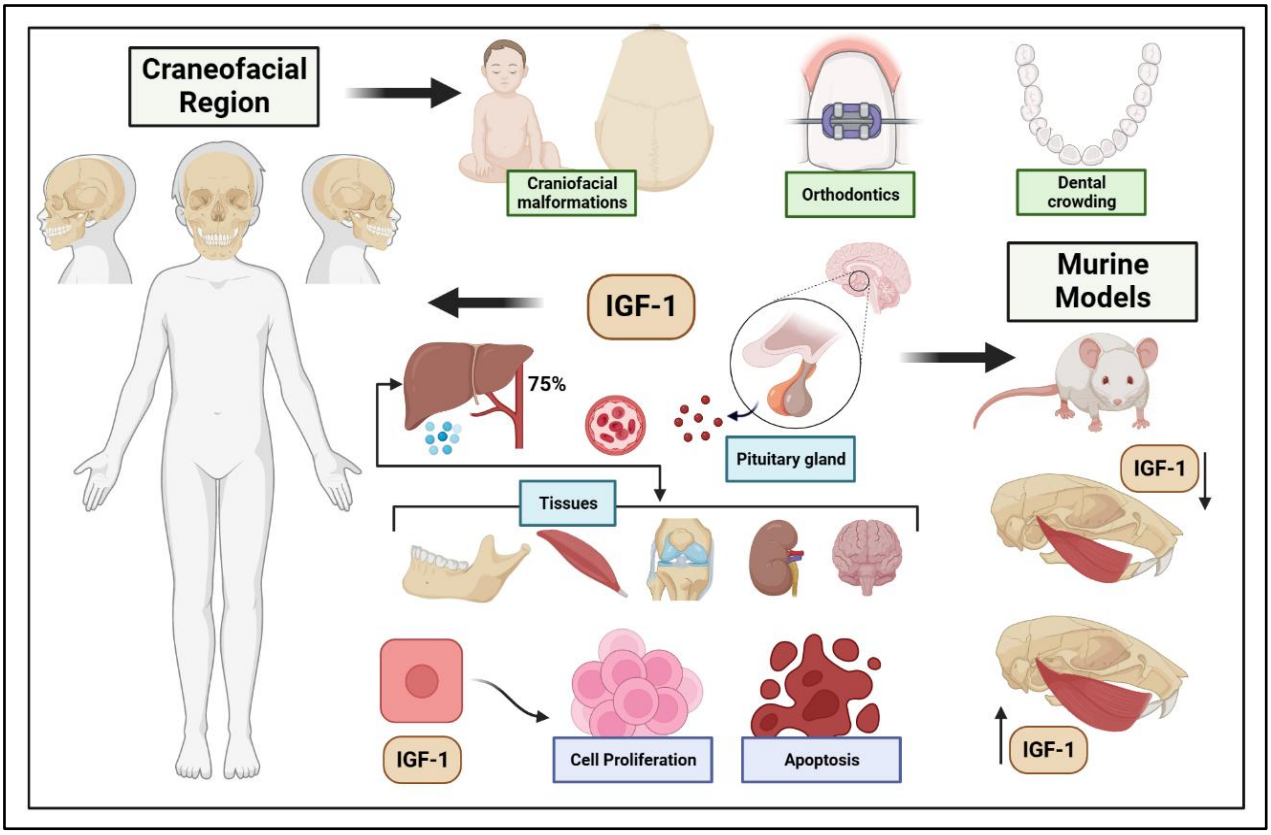

Figure 1. Effect of IGF-1 in the development of the craniofacial region in humans and murine models. IGF-1: Insulin-like growth factor 1. Created with www.biorender.com (accessed on 24 March 2023).

2. Materials and Methods

In this literature review, we used the following electronic databases as search engines: PubMed, Google Scholar, Scopus, and Web of Science. The following terms were used to search articles related to the topic of this review: "IGF-1", "Craniofacial," "Murine," and "Masticatory Load". These terms were combined using the Boolean operator "AND" across the different databases. The articles reviewed for this study ranged from 1983 to 2022, with the purpose of identifying the historical development of the topic, while placing primary emphasis on the evidence generated during the last decade. The articles that were found then underwent a second set of searches as per the inclusion and exclusion criteria of this study. Two independent researchers were responsible for reviewing the articles searched. The articles that did not meet the inclusion criteria for this research were excluded.

The criteria for inclusion were as follows:

- Clinical trials.
- Observational studies.
- Research that focused on the IGF-1 effect on craniofacial development.
- Research carried out in the English language.

The studies that belonged to one of the following criteria were excluded:

- Review articles.

- Editorials.
- Short communications.
- Research carried out in languages other than English.

In addition to studies that directly analyze and assess the role of IGF-1 in craniofacial growth in murine models, investigations with a systemic or muscular focus were also included when their results provided relevant indirect mechanisms (for example, the impact of IGF-1 on muscle mass influencing craniofacial development). This methodological decision aimed to avoid omitting complementary scientific evidence that could broaden and deepen the understanding of the topic.

The data that was collected from the articles were arranged in the topics of "year of publication," "type of study," and "outcomes of the studies." If any conflict was encountered among the principal investigators, another investigator was consulted to resolve the disputes.

3. Results and Discussion

3. 1. Outcomes of Literature Search

Based on the preliminary literature search, about 131 articles were identified. Analysis of title, abstract, and duplicate studies was done, and 112 studies were removed on the basis of the eligibility criteria of this study. A total of 19 research studies were selected for this literature review. It is worth noting that, although the primary aim of this review was to explore and analyze the role of IGF-1 in craniofacial growth, several studies of a systemic or muscular nature were also included. This inclusion was based on the fact that such studies offer indirect yet relevant findings, particularly concerning the relationship between IGF-1, muscle hypertrophy, and bone adaptation, which have implications for craniofacial development. Nonetheless, the central focus of the manuscript remains on craniofacial growth deficiency and the evidence derived from murine models.

Friedlander et al. in their study demonstrated when IGF-1 was given as a treatment for one year to elevate the levels of IGF-1 to normal, this did not result in alteration in the body composition, blood parameters, nor any improvement in bone density.[15] When recombinant IGF-1 was used for the treatment of patients who have amyotrophic lateral sclerosis (ALS), it was found that IGF-1 resulted in an improvement in the quality of life and slowed the progression of patients who have ALS without any important medical adverse effects.[16] Borasio et al., in their study, used recombinant IGF-1 in patients suffering from ALS and concluded that it can be safely used in these patients and is well tolerated.[17] In a study on mice, transverse growth of the skull influenced by masticatory muscle function was studied. They reported that mastication had a significant impact on the development of the skull in the transverse dimensions.[18] The effect of GH in acromegaly patients was studied, and it was found that enlargement of the mandible was caused by an increase in levels of this hormone.[19] In an in-vivo study, evidence was provided that higher IGF-1 levels were responsible for the skeletal muscle hypertrophy in growth stages only.[20] When IGF-1 was deleted in mice, it was found that it resulted in impairment of growth along with a disturbance in glucose homeostasis.[12] Regarding the production of IGF-1 in mice, it was found that the majority of the IGF-1 was produced in the liver.[5] Table 1 presents the summary of the findings of all the articles that were included in this study.

Table 1. Overview of research that was included in this review.

Study No.	Author/Year	Outcomes	References
1	Ewton et al., 1994	Inconsistencies were found between our findings about the IGFs and other researchers' studies regarding the impact of other mitogens.	21
2	Friedlander AL et al., 2001	Treatment with IGF-1 for one year at a satisfactory dosage to elevate circulating IGF-1 to young normal values is not an effective means to alter body composition.	15
3	Lai EC et al., 1997	Recombinant human IGF-1 slowed the process of functional impairment in ALS	16
4	Borasio GD et al., 1998	RhIGF-1 appeared to be safe and well-tolerated.	17
5	Katsaros C et al., 2002	Increased masticatory function led to greater transverse skull dimensions	18
6	Cantu G et al., 1997	With IGHD, different craniofacial skeletal parts have varying potentials regarding retardation of growth.	22
7	Takakura M et al., 1998	Increased mandibular growth	19
8	Shavlakadze T et al., 2010	Only in conditions of growth does increased IGF-1 have a hypertrophic influence on skeletal muscle.	20
9	Barton ER et al., 2002	Effective muscle regeneration therapy for secondary symptoms brought on by the principal decline in dystrophin	23
10	Liu J-P et al., 1993	IGF-1 has a role in mouse embryonic development	13
11	Vassilakos G et al., 2019	In male mice, the elimination of muscle IGF-1 causes decreased growth and gradual disturbance in glucose balance.	12
12	Musarò A et al., 2001	Localized mIgf-1 transgenic expression raises potential clinical approaches to address muscle weakness brought on by aging or illness.	11
13	Barton-Davis ER et al., 1999	By activating satellite cells and elevating protein synthesis in differentiated myofibres, IGF-1 promoted muscular growth.	24
14	Schwander JC et al., 1983	In rats, the primary site for the production of IGF-1 is the liver.	5
15	Adams GR et al., 1998	Skeletal muscle growth is caused by IGF, which directly stimulates protein synthesis and satellite cell proliferation.	25
16	Sjögren K et al., 1999	Despite the hepatocytes' complete lack of IGF-1 synthesis, post-natal body growth is not affected.	10
17	McAlarney	IGF knockout mice had a generalized decrease in	14

	ME et al., 2001	craniofacial size.	
18	Luca L et al., 2003	An increase in protrusive muscle tonus is favorable in mandibular hypoplasia.	26
19	Enomoto A et al., 2010	Mastication affects mandibular morphology and mandibular condyle growth	27

Abbreviations: IGF-1 Insulin-like Growth Factor 1; ALS Amyotrophic Lateral Sclerosis; RhIGF-1 Recombinant Human IGF-1 IGHD Isolated Growth Hormone Deficiency; mIGF-1 Muscle Insulin-like Growth Factor

3. 2. IGF-1 Research Using Animal Models Related to Muscle

According to the literature, IGF-1 has demonstrated a crucial role in coordinating muscle growth, repair, and regeneration, as well as increasing muscular mass and strength, as presented in Figure 2.

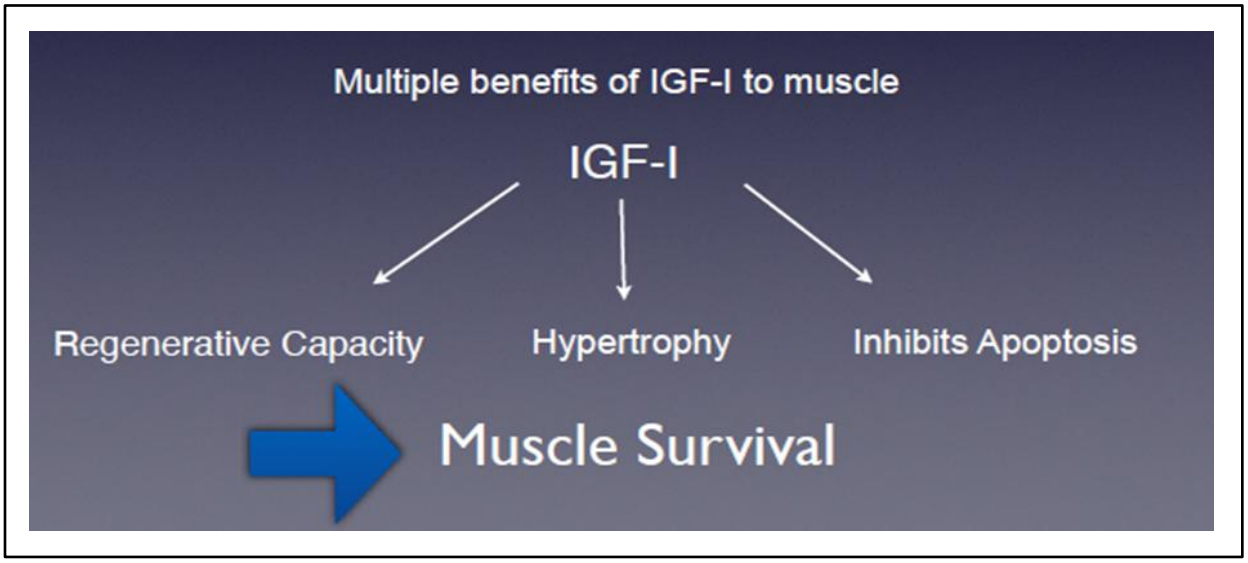

Figure 2. Functions of IGF-1 in skeletal muscles.

In animals, several methods have been used to establish that IGF-1 promotes skeletal muscle growth, including recombinant protein infusion and overexpression of the IGF-1 gene.[24, 25] IGF-1 boosts muscle mass and strength in two ways. First, IGF-1 stimulates protein synthesis and muscle hypertrophy by acting directly on muscle fibers. It also encourages active satellite cells (a stem cell-like population that lives close to muscle fibers and is a source for replenishing (muscle nuclear content) to fuse existing muscle fibers, assisting in the repair of damaged sections of the fibers and accelerating muscle growth, as presented in Figure 3.[21]

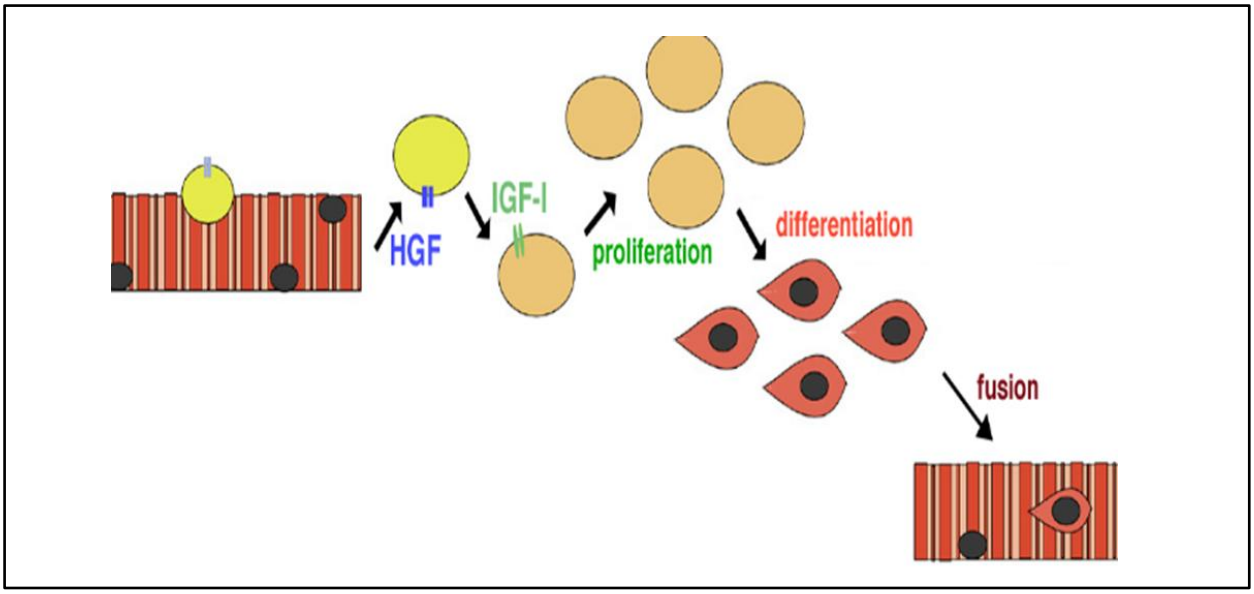

Figure 3. Activation of satellite cells.

Due to IGF-1's potential to govern both the growth and repair processes of muscle and other tissues, it has been the subject of extensive research to characterize its role in this process and the regulation of IGF-1 transcription. It has the potential to be an effective treatment option in both aging and muscle illness because it can help with tissue repair and maintenance. One study examined the effect of increased skeletal muscle mass via IGF-1 transgene on craniofacial development in growing mice.[20] The facial skeleton showed increased midfacial and total mandibular absolute length as well as increased transverse condylar and gonial width. This study suggests that an increase in muscular mass and strength in the craniofacial complex may alter the rate and final morphology of bone growth. Endochondral ossification processes seem to be more responsive where muscle attachments are present. Furthermore, this gives additional support to the idea that bone is adaptable to soft tissue changes.

3. 3. IGF-1 Research on the Effects of Reduced Masticatory Load in Animal Models

GH and IGF-1 collaborate to form what is known as the GH/IGF-1 axis, as presented in Figure 4.

Numerous studies in animal models have examined the association between mastication function and craniofacial development.

In 2003, Luca et al. compared the effects of liquid, normal, and elastic diets on mandibular morphogenesis in young rats and found that an elastic diet increased mandibular ramus length, while a liquid diet increased corpus length.[26] The researchers concluded that enhanced tonus of the protrusive muscles in mandibular underdevelopment and increased tonus of the masticatory muscles in skeletal open bite could be advantageous. Such findings are consistent with a study by Enomoto and colleagues, using microcomputed tomography, which showed increases in condylar width, mandibular length, and ramus height in young mice.[27] The study by George S. Abed et al. in 2007 supported the idea that the function of mastication is a significant factor in craniofacial developmental trajectory and that its consequences are controlled by the relative growth potential

of distinct craniofacial elements.[28] In the softer food category, all vertical measurements, as well as the majority of mandibular (67%) and transverse (67%) measurements, exhibited absolute growth deficits.

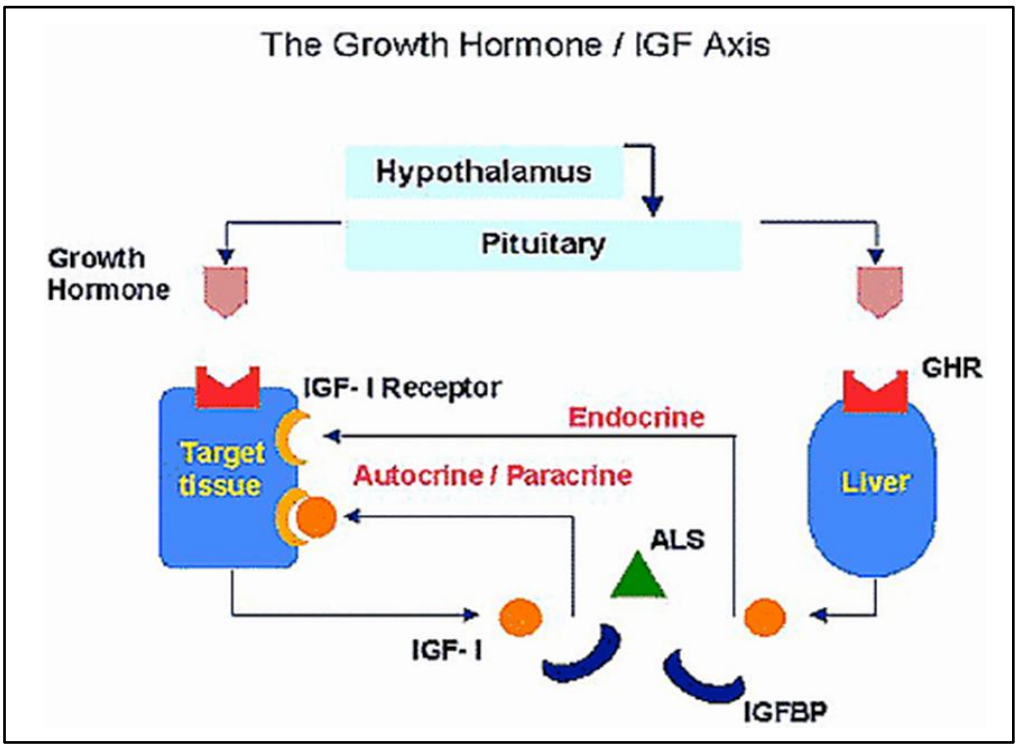

Figure 4. Growth hormone IGF-1 axis.

In 2002, Katsoras C et al. discovered an intriguing link between masticatory muscle activity and transverse skull measurements in developing rats.[18] The soft food individual's dental arch was shown to be narrower in the third molar region, perhaps due to a decrease in the development of the midpalatal suture and/or less occlusal stress. This could be because the first and second molars were occluded at the start of the trial, but the third molars had not been. Furthermore, the soft diet group had thinner premaxilla and frontal bones at the most lateral section of the temporal crest, which are locations of masticatory attachment to muscles.

3. 4. IGF-1 Therapy

Multiple trials have been conducted to evaluate the beneficial effects of systemic administration of recombinant IGF-1 in patients who potentially benefit from increased strength, as presented in Figure 5. Candidates for IGF-1 therapy include aged individuals, individuals with deficient levels of GH, patients short for gestational age (SGA), patients with muscle wasting in acquired immunodeficiency syndrome and cancer, professional athletes with acute injuries and those who suffer from muscle atrophy and weakness due to amyotrophic lateral sclerosis and muscular dystrophies. Since IGF-1 is a powerful growth hormone that exists and affects numerous tissues of the body and may be carcinogenic, researchers have used it in small doses.

As a result, the potential of IGF-1 to give any advantages to skeletal muscle is hampered by both the small amount of protein delivered and the limited transport of IGF-1 to the muscle via the bloodstream.[15-17]

Figure 5. Different types of IGF-1.

3.5. Craniofacial Effects of GH and IGF-1

Because GH, along with IGF-1 are so intimately related, an understanding of the craniofacial effects of GH should first be examined, as presented in Figure 6.

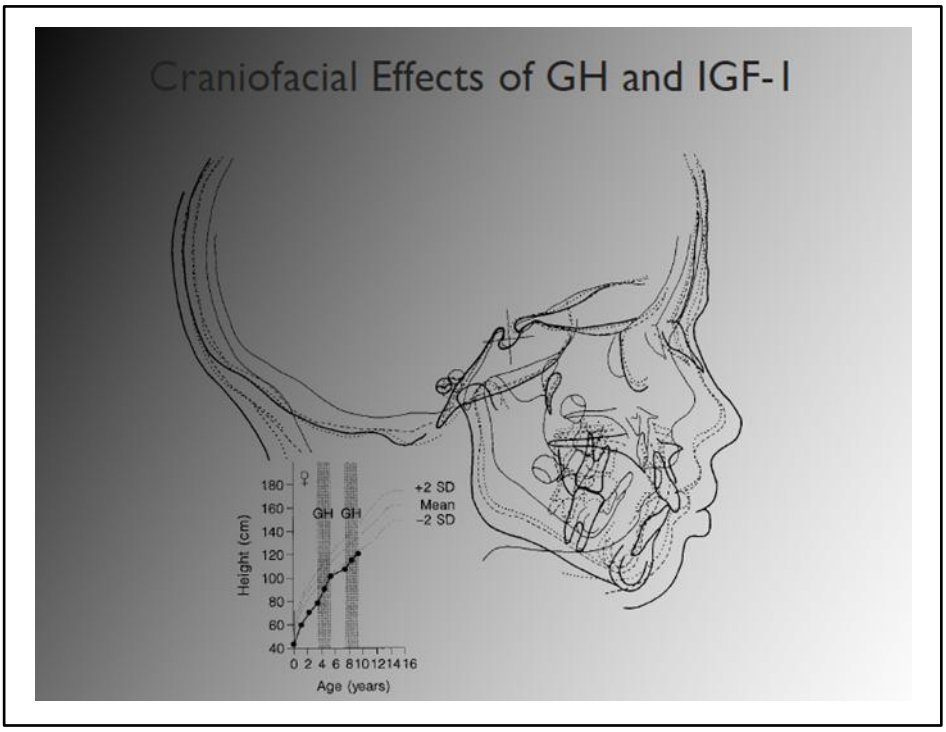

Figure 6. The effect of Insulin-like growth factor-1 and growth hormone on the craniofacial region.

Historically, patients with excessive circulating GH (acromegaly/gigantism) show distinctive craniofacial features, including: [19]

- Marked prominence of supraorbital ridges.
- Vertical maxillary deficiency with retrusion.
- Laryngeal hypertrophy.
- Macroglossia.

- Prognathic mandible.
- Class 3 dental occlusion.
- Negative overjet.
- Enlarged sella turcica (double floor).
- Negative ANB.
- Positive arch length discrepancy (spaced teeth).

SGA children have normal levels of GH in circulation but have insufficient uptake of GH into the tissue and, therefore, are limited in stature. Studies indicate that these SGA children have delayed growth not only of the skeleton but also of the craniofacial complex. [29] In addition to the anterior cranial base, mandible, and maxilla being smaller, the SGA children had high mandibular plane angles and wide cranial base angles. This suggests that insufficient growth occurs throughout the entire body, including the craniofacial complex. When these SGA children are supplemented with GH therapy, however, positive effects on height and skeletal age occur. [22] Craniofacially, GH therapy had the greatest impact on the anterior cranial base and mandibular dimension. Furthermore, significant "catch-up" growth is seen with younger patients (longer GH duration), displaying the fastest catch-up growth and suggesting the sensitivity of the mandible and craniofacial complex to systemic endocrine modifications.

Systemic circulating IGF-1 may have similar craniofacial effects as its cousin GH. Obese children, despite low levels of circulating GH, have normal to higher levels of circulating IGF-1. [30] Reports indicate that obese children had reduced anterior facial height and increased mandibular length with prognathic jaws, three standard deviations above the normal weighted children. This shows that craniofacial development is more reliant on circulatory IGF-1 than on locally generated IGF-1, albeit this remains unknown.

3.6. Isolating Muscle-Specific IGF-1 Phenotype

For a long time, it has been assumed that the amount of muscle and bone mass is related. [31] Other investigations afterward have discovered more corroborating proof that the degrees of muscle and bone composition are connected [32], and the consequent relationship between causes is known as the "muscle-bone unit". [33]

Attempts to enhance muscle growth and strength in the laboratory required strenuous activity, which introduced confounding variables. (e.g., increased bone blood flow and osteogenic factor changes like GH). [34] In order to control those confounding variables, a transgene construct that results in elevated growth of skeletal muscle and endurance would be optimal. The IGF-1 transgene construct is a good model for this.

As reported earlier, circulating IGF-1 affects almost all cells in the human body. This also means that IGF-1 is not selective as to which cell it affects. The benefits of increased IGF-1 to muscle include regenerative capacity, hypertrophy, and prevention of apoptosis, which increases muscle survival. [35] Because of its proliferative effects on cells, IGF-1 can affect appropriate tissues (muscle) and non-appropriate tissues (cancer cells). By limiting the activity of supplementary IGF-1 to the tissue of origin, we can evaluate its autocrine and paracrine involvement in skeletal muscle throughout the animal's lifetime while excluding endocrine

effects on other tissues. Research has already indicated that adult mice with an IGF-1 transgene show protection against the natural reduction of muscle tissue and regenerative capacity to injury. [24] With this construct, it is possible to test the response of bone growth to increased craniofacial muscle mass. Thus, the direct effect of IGF-1 on muscle and bone is independent.

3.7. Future Perspectives

The evidence regarding the role of IGF-1 in craniofacial growth, particularly in murine models with reduced masticatory load, has identified this factor as a key modulator of cell proliferation, tissue differentiation, and muscle–bone interaction. However, the persistence of knowledge gaps opens opportunities for future research.

First, it is necessary to design longitudinal studies in animal models to clarify the dose–response association of IGF-1 and its relevance in critical craniofacial regions, such as the condyle, mandibular symphysis, and cranial base. These investigations would allow for the determination of the level of skeletal plasticity induced by IGF-1 across different stages of development.

Second, it is essential to strengthen the clinical translation of the findings generated. Although preclinical studies demonstrate a positive impact of IGF-1 overexpression on bone and muscle growth, its therapeutic implementation remains limited. The design of future clinical trials should explore its use as an adjuvant therapy in patients with mandibular hypoplasia, craniofacial growth deficiencies associated with GH deficiency, or in cases of sarcopenia secondary to systemic diseases.

Additionally, it is crucial to consider the safety and potential oncological risk of IGF-1, due to its proliferative and anti-apoptotic nature. Future research should focus on developing administration protocols with appropriate safety standards, regulated dosages, and targeted delivery systems to the specific tissue, thereby minimizing undesirable systemic effects.

Finally, the incorporation of new molecular biology tools and genetic editing techniques will provide the opportunity to explore more specific pathways to regulate IGF-1 signaling, enhancing its therapeutic application within the framework of personalized medicine.

These future perspectives support a multidisciplinary approach that integrates molecular biology, orthodontics, orthopedics, and regenerative medicine, with the goal of harnessing the potential of IGF-1 to correct craniofacial growth disorders and improve the overall well-being of patients.

4. Conclusion

The analyzed evidence supports that IGF-1 plays a fundamental role in modulating craniofacial growth at both the bone and muscle levels, particularly under reduced masticatory load in animal models. Experimental results demonstrate that the absence or deficiency of IGF-1 is associated with growth delay, morphological alterations, and decreased muscle mass, whereas its overexpression contributes to hypertrophy and tissue adaptation. Nevertheless, these findings should be interpreted with caution, considering important limitations that include methodological

heterogeneity among studies, the diversity of models employed, and the lack of clinical research that would allow for the extrapolation of the results to clinical practice.

Within this same framework, IGF-1 is envisioned as a promising tool in the understanding and therapeutic management of craniofacial disorders related to growth deficiencies. In a clinical setting, regulation of IGF-1 signaling could contribute to the management of mandibular hypoplasia, maxillofacial growth delay associated with growth hormone deficiency, and skeletal adaptations related to muscle disorders under conditions of functional impairment. However, it will be essential to design longitudinal studies and clinical trials to assess its efficacy, safety, and applicability in clinical practice. Additionally, the incorporation of IGF-1 in combination with orthodontic, orthopedic, and regenerative therapies could open new therapeutic possibilities to enhance functional and aesthetic outcomes in pediatric and young adult populations. This field of research requires a multidisciplinary approach to translate experimental advances into clinical contexts, thereby ensuring a tangible and safe benefit for patients.

Abbreviation	Full Form
IGF-1	Insulin-like growth factor 1
GH	Growth hormone
ALS	Amyotrophic lateral sclerosis
SGA	Short for gestational age

Declarations:

Supplementary Materials: Not applicable.

Author Contributions: Conceptualization, S.-A, A.-L, D.-E, A.-A, E.U.S.-T and S.M.L.-M.; formal analysis, S.-A, A.-L, D.-E, A.-A, E.U.S.-T and S.M.L.-M.; investigation, S.-A, A.-L, D.-E, A.-A, E.U.S.-T and S.M.L.-M.; resources, S.-A, A.-L, D.-E and A.-A.; data curation, S.-A, A.-L, D.-E and A.-A.; writing—original draft preparation, S.-A, A.-L, D.-E, A.-A, E.U.S.-T and S.M.L.-M.; writing—review and editing, S.-A, A.-L, D.-E, A.-A, E.U.S.-T and S.M.L.-M.; visualization, S.-A, A.-L, D.-E, A.-A, E.U.S.-T and S.M.L.-M.; supervision S.-A, A.-L, D.-E, A.-A, E.U.S.-T and S.M.L.-M.; project administration, S.-A, A.-L, D.-E and A.-A.; All authors have read and agreed to the published version of the manuscript.

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References

1. Yoon AJ, Pham BN, Dipple KM. Genetic Screening in Patients with Craniofacial Malformations. J Pediatr Genet. 2016;5(4):220-224. doi: 10.1055/s-0036-1592423.
2. Singh VP, Moss TP. Psychological impact of visible differences in patients with congenital craniofacial anomalies. Prog Orthod. 2015;16:5. doi: 10.1186/s40510-015-0078-9.
3. Bailes J, Soloviev M. Insulin-Like Growth Factor-1 (IGF-1) and Its Monitoring in Medical Diagnostic and in Sports. Biomolecules. 2021;11(2):217. doi: 10.3390/biom11020217.
4. Hellström A, Ley D, Hansen-Pupp I, Hallberg B, Löfqvist C, van Marter L, et al. Insulin-like growth factor 1 has multisystem effects on foetal and preterm infant development. Acta Paediatr. 2016;105(6):576-86. doi: 10.1111/apa.13350.
5. Schwander JC, Hauri C, Zapf J, Froesch ER. Synthesis and secretion of insulin-like growth factor and its binding protein by the perfused rat liver: dependence on growth hormone status. Endocrinology. 1983;113(1):297–305.
6. Wang Y, Bikle DD, Chang W. Autocrine and Paracrine Actions of IGF-I Signaling in Skeletal Development. Bone Res. 2013;1(3):249-59. doi: 10.4248/BR201303003.
7. Al-Samerria S, Radovick S. The Role of Insulin-like Growth Factor-1 (IGF-1) in the Control of Neuroendocrine Regulation of Growth. Cells. 2021;10(10):2664. doi: 10.3390/cells10102664.
8. Vassilakos G, Lei H, Yang Y, Puglise J, Matheny M, Durzynska J, et al. Deletion of muscle IGF-I transiently impairs growth and progressively disrupts glucose homeostasis in male mice. FASEB J. 2019;33(1):181-194. doi: 10.1096/fj.201800459R.
9. Laron Z. Insulin-like growth factor 1 (IGF-1): a growth hormone. Mol Pathol. 2001;54(5):311-6. doi: 10.1136/mp.54.5.311.
10. Sjögren K, Liu JL, Blad K, Skrtic S, Vidal O, Wallenius V, et al. Liver-derived insulin-like growth factor I (IGF-I) is the principal source of IGF-I in blood but is not required for postnatal body growth in mice. Proc Natl Acad Sci U S A. 1999;96(12):7088-92. doi: 10.1073/pnas.96.12.7088.
11. Musarò A, McCullagh K, Paul A, Houghton L, Dobrowolny G, Molinaro M, et al. Localized Igf-1 transgene expression sustains hypertrophy and regeneration in senescent skeletal muscle. Nat Genet. 2001;27(2):195–200.
12. Vassilakos G, Lei H, Yang Y, Puglise J, Matheny M, Durzynska J, et al. Deletion of muscle IGF-I transiently impairs growth and progressively disrupts glucose homeostasis in male mice. FASEB J Off Publ Fed Am Soc Exp Biol. 2019;33(1):181–94.
13. Liu JP, Baker J, Perkins AS, Robertson EJ, Efstratiadis A. Mice carrying null mutations of the genes encoding insulin-like growth factor I (Igf-1) and type 1 IGF receptor (Igf1r). Cell. 1993;75(1):59-72.

14. McAlarney ME, Rizos M, Rocca EG, Nicolay OF, Efstratiadis S. The quantitative and qualitative analysis of the craniofacial skeleton of mice lacking the IGF-I gene. Clin Orthod Res. 2001;4(4):206–19.

15. Friedlander AL, Butterfield GE, Moynihan S, Grillo J, Pollack M, Holloway L, et al. One year of insulin-like growth factor I treatment does not affect bone density, body composition, or psychological measures in postmenopausal women. J Clin Endocrinol Metab. 2001;86(4):1496–503.

16. Lai EC, Felice KJ, Festoff BW, Gawel MJ, Gelinas DF, Kratz R, et al. Effect of recombinant human insulin-like growth factor-I on progression of ALS. A placebo-controlled study. The North America ALS/IGF-I Study Group. Neurology. 1997;49(6):1621–30.

17. Borasio GD, Robberecht W, Leigh PN, Emile J, Guiloff RJ, Jerusalem F, et al. A placebo-controlled trial of insulin-like growth factor-I in amyotrophic lateral sclerosis. European ALS/IGF-I Study Group. Neurology. 1998;51(2):583–6.

18. Katsaros C, Berg R, Kiliaridis S. Influence of masticatory muscle function on transverse skull dimensions in the growing rat. J Orofac Orthop = Fortschritte der Kieferorthopadie Organ/official J Dtsch Gesellschaft fur Kieferorthopadie. 2002;63(1):5–13.

19. Takakura M, Kuroda T. Morphologic analysis of dentofacial structure in patients with acromegaly. Int J Adult Orthodon Orthognath Surg. 1998;13(4):277–88.

20. Shavlakadze T, Chai J, Maley K, Cozens G, Grounds G, Winn N, et al. A growth stimulus is needed for IGF-1 to induce skeletal muscle hypertrophy in vivo. J Cell Sci. 2010;123(Pt 6):960–71.

21. Ewton DZ, Roof SL, Magri KA, McWade FJ, Florini JR. IGF-II is more active than IGF-I in stimulating L6A1 myogenesis: greater mitogenic actions of IGF-I delay differentiation. J Cell Physiol. 1994;161(2):277–84.

22. Cantu G, Buschang PH, Gonzalez JL. Differential growth and maturation in idiopathic growth-hormone-deficient children. Eur J Orthod. 1997;19(2):131–9.

23. Barton ER, Morris L, Musaro A, Rosenthal N, Sweeney HL. Muscle-specific expression of insulin-like growth factor I counters muscle decline in mdx mice. J Cell Biol. 2002;157(1):137–48.

24. Barton-Davis ER, Shoturma DI, Sweeney HL. Contribution of satellite cells to IGF-I induced hypertrophy of skeletal muscle. Acta Physiol Scand. 1999;167(4):301–5.

25. Adams GR, McCue SA. Localized infusion of IGF-I results in skeletal muscle hypertrophy in rats. J Appl Physiol. 1998;84(5):1716–22.

26. Luca L, Roberto D, Francesca SM, Francesca P. Consistency of diet and its effects on mandibular morphogenesis in the young rat. Prog Orthod. 2003;4:3-7. doi: 10.1034/j.1600-9975.2002.02033.x.

27. Enomoto A, Watahiki J, Yamaguchi T, Irie T, Tachikawa T, Maki K. Effects of mastication on mandibular growth evaluated by microcomputed tomography. Eur J

Orthod. 2010;32(1):66–70.

28. Abed GS, Buschang PH, Taylor R, Hinton RJ. Maturational and functional related differences in rat craniofacial growth. Arch Oral Biol. 2007;52(11):1018–25.
29. Van Erum R, Mulier G, Carels C, de Zegher F. Craniofacial growth and dental maturation in short children born small for gestational age: effect of growth hormone treatment. Own observations and review of the literature. Horm Res. 1998;50(3):141–6.
30. Ohrn K, Al-Kahlili B, Huggare J, Forsberg C-M, Marcus C, Dahllöf G. Craniofacial morphology in obese adolescents. Acta Odontol Scand. 2002;60(4):193–7.
31. Doyle F, Brown J, Lachance C. Relation between bone mass and muscle weight. Lancet (London, England). 1970;1(7643):391–3.
32. Andreoli A, Monteleone M, Van Loan M, Promenzio L, Tarantino U, De Lorenzo A. Effects of different sports on bone density and muscle mass in highly trained athletes. Med Sci Sports Exerc. 2001;33(4):507–11.
33. Rauch F, Bailey DA, Baxter-Jones A, Mirwald R, Faulkner R. The "muscle-bone unit" during the pubertal growth spurt. Bone. 2004;34(5):771–5.
34. Krzysztofik M, Wilk M, Wojdała G, Gołaś A. Maximizing Muscle Hypertrophy: A Systematic Review of Advanced Resistance Training Techniques and Methods. Int J Environ Res Public Health. 2019 Dec 4;16(24):4897. doi: 10.3390/ijerph16244897.
35. Ahmad SS, Ahmad K, Lee EJ, Lee YH, Choi I. Implications of Insulin-Like Growth Factor-1 in Skeletal Muscle and Various Diseases. Cells. 2020;9(8):1773. doi: 10.3390/cells9081773.