Prenatal Development of Temporo-Mandibular Joint: State of Art

Francesco Carini¹,³, Margherita Mazzola¹,*, Serena Nobile¹, Francesca Rappa¹, Sabrina David¹, Giuseppe Alessandro Scardina, Chiara Lo Piccolo⁴, Giovanni Zummo¹, Felicia Farina¹, Francesco Cappello¹,⁵, Provvidenza Damiani³, and Giovanni Tomasello¹,²,³,⁵

¹Department of Experimental Biomedicine and Clinical Neuroscience, Section of Human Anatomy, (BIONEC), University of Palermo, Italy
²School of Medicine and Surgery, Hypatia Course, University of Palermo, Italy
³AOUP “P. Giaccone,” School of Medicine and Surgery, University of Palermo, Italy
⁴European Oncologic Institute, Milano, Italy
⁵Euro-Mediterranean Institute of Science and Technology (IEMEST), Palermo, Italy

Abstract

The aim of this work is to analyze the state of the art of temporo-mandibular joint (TMJ) to understand the various stages of the development of the same during embryogenesis.

Various theories have been analyzed, such as the formation of apoptotic or the important role of growth factors, or the Valencia et studies in which are analyzed to numerous articular discs in various stages of development.

By the aforementioned studies show that many factors, of a different nature, are to be involved in the prenatal development of this important joint.

Keywords: TMJ, development, morphogenesis

Introduction

The jaw of mammals is a complex morphological structure formed by various morphogenetic components of different embryonic origin [1].
Temporo Mandibular Joint (TMJ) is a complex structure and its role is to connect the jaw to the skull, allowing the movement of the same and the performance of vital functions for humans: chew in adults and breastfeeding in infants [5].

Anatomically it is formed by two bones, the temporal bone and mandibular bone, including an interposed articular disc. The articular disc is inside the joint cavity, formed by the glenoid fossa of the temporal bone and mandibular condyle. Within the joint cavity we find the synovial fluid, which has lubricating function and enabling the proper functioning of the joint [2, 3, 4].

The TMJ articular disc divides the joint cavity in two region, above and under disc (5,6). It is able to adapt to the articular surfaces of the two bones that form the articulation and its role is to cooperate with the synovial fluid in order to eliminate the friction and provide resistance to loads and forces. These capacities are dependent on its thickness, which can also be less than 1 mm [7].

Morphologically, the articular disc is a fibro-cartilage structure that is divided into four bands and that we can describe as a concave lens provided with two edges (one lateral and one medial), two ends (front and rear) and two sides (upper and below) [5, 6].

Currently in the literature there are no precise models of prenatal development of the TMJ and its components [8].

Compared to other body joints such as those of the limbs, the ATM has a late embryologically development [9]. The joint cavity limb begins to develop the 8th week of pregnancy, while only around the 9th week that begins to form the joint cavity bottom of TMJ. At the 10th week begins the development of the articular disc cartilage, through the organization of fibroblasts in collagen fibers. At the 11th week it starts to form the upper joint cavity [10].

The formation of the articular cartilage of the condyle, the articular and articular cavity disc is linked to a number of transcription factors such as Runx2, Osterix, and Sox9, and at various growth factors such as fibroblast growth factor (FGF) and insulin growth factor (IGF) [11].

At the 12th week, the articular disc and the joint cavity TMJ are fully formed [5].

Neuromuscular ability to perform prenatal movements of opening and closing of the jaw is acquired around the 20th week, along with the formation and maturation of the condylar process [8]. The TMJ is fully differentiated between the 25th and the 26th week of gestation [12].

To better understand the formation of the TMJ during embryogenesis have been made various studies. Among the starting hypothesis regarding the mechanism of formation of the joint cavity, there are the theory of training apoptotic - mediated, according to which the cavity is formed as a result of apoptosis of some cells contained at the level of the future joint cavity, and the hypothesis of the slit, in which it is claimed that the joint cavity is formed through a mechanical stimulation leading to expansion of a slot [13] present at the level of the future superior articular cavity [14].
The purpose of our work is to provide an analysis of the literature comparing different studies carried out on fetal development TMJ to understand how they actually form this structure. We compared each other about 7 studies.

One of the first studies on fetal development TMJ is accomplished by Valenza et al. [15]. In this study we were compared 14 joint discs of seven human fetuses, between the 10th and 32nd week of gestation. What has been observed is that already at the 10th week is observed a biconcave lamina of connective tissue thickened due to the articular disk. At the 14th week the album is more defined, thin in the middle, but increased in thickness in the lateral and medial. At the 20th week, finally it could be observed posteriorly of elastic fibers [15].

Shibata et al. [11], in 2012, have instead made a study on the factors involved in fetal development of the condylar cartilage and TMJ. The study, done on rats and conducted with methods of immunofluorescence in situ, showed that there is a significant increase of the growth factors IGF - I at the level of the joint cavity during embryogenesis, and in particular it was noted that the growth factor IGFBP-2 appears to be related to the formation of the joint cavity [11].

Another study, conducted by Mérida-Velasco et al. [10] instead corroborates the hypothesis that the articular cavity TMJ do not develop synchronously. According to this study the lower joint cavity begins its development around the 9th week of gestation, and appears as a thin slit interposed between the articular disc and the mandibular condyle. The upper joint cavity instead begins to appear on the 11th week of gestation, between the squamous part of the temporal bone and the articular disc. At 12th weeks finally the two articular cavity are well formed and the synovial membrane begins to acquire its functionality [10].

The latter study is in contrast to those made by Sperber (16), Ögutcen-Toller [17], Burdi [18] and Van der Linden et al. [19] who argue that the lower joint cavity begins to form during the 10th week of gestation, while the upper joint cavity begins to form from the 11th week of gestation [16, 17, 18, 19].

Van der Linden et al. [19] also show how in human fetuses there is a distribution of the blood capillaries in the front and rear peripheral portions of the articular disc, while it seems to be totally absent in the central portion [19].

Matsuda et al. [13] have instead suggested the involvement of apoptosis in the formation of the joint cavity. The studies were performed using the TUNEL assay. This showed the presence of apoptotic bodies in the electron microscope during the evolutionary process TMJ in humans [13].

Interesting is the study done by Leonardi et al. [20] on the expression of heat shock protein (HSP) during the development of human fetuses. This study involved twelve joint discs of adult subjects (including 10 healthy patients and 2) and 5 fetal articular disc. They were performed immunohistochemical investigations of HSP27, a protein with cytoprotective and biosynthetic functions within chondrocytes which could also play an anti-apoptotic function. Through this study it was seen that in fetuses there is no HSP27 expression [20] and this could validate the hypothesis of the formation of the joint cavity through the apoptotic pathway.
Finally to also mention the study of Carini et al. [21] in which the fetuses were examined between 6th and 14th weeks of gestation. This study showed that the condylar blastema is the first item that appears between the sixth and eighth week, while the ninth week begins appearing temporal elements. The lower joint cavity was seen appearing around the 12th week, while the upper joint cavity between the 13th and the 14th week [21].

**CONCLUSION**

The comparison between the studies is evident that there is still no data on certain TMJ development and its components. Further studies are needed about but difficult to execute them on humans fetuses and therefore must be used as alternative models TMJ mice or cell cultures. However, this might be a problem for the understanding of human embryogenetic mechanisms as models may not be exactly human embryogenesis.

**REFERENCES**


