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Dear **F.Kh. Azizova, G.I. Madaminova, P.Kh. Azizova, I.R. Tursunmetov, D.R. Sobirova**

Title: **MORPHOFUNCTIONAL FEATURES OF THE FORMATION OF THE TESTICULAR GENERATIVE FUNCTION IN THE FEMALE RATS' OFFSPRING WITH EXPERIMENTAL HYPOTHYROIDISM**

We pleased to inform you that your above mentioned article has been accepted for publication in **NeuroQuantology**.

Regards

Editor
NeuroQuantology

Morphofunctional Features of the Formation of the Testicular Generative Function in the Female Rats' Offspring with Experimental Hypothyroidism

F.Kh. Azizova[1*], G.I. Madaminova[2], P.Kh. Azizova[3], I.R. Tursunmetov[4], D.R. Sobirova[5]

Abstract

This article is devoted to identification the morphological and functional features of the postnatal formation of thetesticles generative function of offspring obtained under conditions of experimental hypothyroidism of pregnancy in the mother. Hypothyroidism in female rats was induced by oral administration of the antithyroid drug Mercazolil at the rate of 0.5 mg per 100 g of body weight for 21 days. After establishing a steady decrease in the concentration of free thyroid hormones (T4 and T3), females were fertilized by healthy males. Females continued to receive a maintenance dose of the drug during periods of pregnancy and lactation. The testes of the offspring were studied on the 60th day after birth using morphological, morphometric, electron microscopic and statistical research methods.

It has been established that in the offspring of female rats with experimental hypothyroidism, the generative function of the testes is inhibited, which manifests itself in the form of a decrease in the number of tubules that actively produce spermatozoa, the index of spermatogenesis, the number of spermatogenic epithelium cells, which is accompanied by a significant increase in the level of destructive changes in germ cells and endocrineLeydig glandulocytes.

Thus, maternal hypothyroidism leads to a significant disruption of the process of postnatal growth and formation of the testes in the offspring.

Key Words: Hypothyroidism in Pregnancy, Offspring, Postnatal Ontogenesis, Testes, Generative Function.

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Introduction

The problem of human reproductive health has become increasingly important in recent years and is becoming a medical and social problem. When addressing issues of birth control, two opposite situations are considered: on the one hand, a significant part of the world's population needs reliable and modern contraceptives, on the other hand, millions of married couples need medical care due to severe neuroendocrine disorders of reproductive function. The current stage in the development of biomedical science is associated with the widespread penetration of endocrinology into the problem of human reproductive health [5,6]. A close relationship between the reproductive and endocrine systems has been shown in several works [5,12]. In this regard, the relationship of the thyroid gland with the reproductive system deserves special attention. Experimental studies have confirmed that thyroid hormones, as well as thyroid-stimulating hormone, have a modulating effect on the generative and endocrine functions of the gonads [11, 17, 18, 26].

Among the dysfunctions of the thyroid gland, a special place is occupied by the so-called "maternal hypothyroidism" (hypothyroidism of pregnant women or gestational hypothyroidism), which in recent years has attracted increasing attention of researchers.

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Hypothyroidism of pregnant women, according to various data, is observed in 2-2.5% of all pregnant women and can manifest itself in subclinical or manifest forms. Since the embryo does not yet have its thyroid hormones, it uses maternal hormones for its growth and development. The relevance of the problem of hypothyroidism in pregnant women in the practice of doctors of various specialities is undeniable since, with a deficiency of thyroid hormones necessary for the normal development and functioning of almost every cell of the human body, severe changes develop in all organs and systems without exception [1,20].

An analysis of the literature showed that the main attention of researchers is paid to the study of the nervous system of offspring that were born from mothers with hypothyroidism of pregnancy. Experimental studies show that hypothyroidism during pregnancy leads to certain changes in the brain neurons of the offspring, a decrease in the proliferative activity of cells with an increase in their apoptosis [20,26].

Antenatal and early postnatal age are recognized as one of the main periods of ontogenesis, in which the foundations of health in the broad sense of the term are laid. There is no doubt that the nature of reproductive function at a young age is largely determined by the antenatal period [7,23].

At the same time, the influence of maternal hypothyroidism on the processes of pre-and postnatal development and functioning of the reproductive system of the offspring has been studied extremely insufficiently. Structural and functional mechanisms of postnatal growth and development of the reproductive system remain practically unexplained. The extreme topicality of the problem of hypothyroidism in pregnant women, the uncertainty and insufficient knowledge of its negative consequences on the reproductive system of offspring determine the high degree of relevance of further research in this direction.

The work aimed to identify the features of the morphological and functional formation of the generative function of the testicles of the offspring of female rats with experimental hypothyroidism.

Material and Methods

Hypothyroidism in female rats was induced by per os administration of the antithyroid drug Mercazolil at the rate of 0.5 mg per 100 g of body weight for 21 days (experimental group). After establishing a steady decrease in the concentration of free thyroid hormones (T4 and T3), females were fertilized by healthy males. During periods of pregnancy and lactation, females continued to receive a maintenance dose of the drug at the rate of 0.25 mg per 100 g of body weight. The control group of females received an equal volume of sterile saline.

The testicles of offspring from control and experimental females on the 60th day after birth served as the material for the study, since, according to the literature data, the period of puberty in rats begins on the 60th day [3,9].

Animals were slaughtered in compliance with the principles of humanity outlined in the directives of the European Community (86/609/EEC) and the Declaration of Helsinki and by the requirements of the rules for working with experimental animals. After slaughtering the animals, the testicles were weighed and their total weight (in mg) and their ratio to body weight (mass index) were determined.

For morphological studies, the testicles after weighing were fixed in 10% neutral formalin solution. Then the testis pieces were dehydrated in alcohols with increasing concentration, and embedded in paraffin. Sections 5-7 μm thick, stained with hematoxylin and eosin, were examined using morphological and morphometric methods. Morphometric studies included measuring the average diameter of the convoluted seminiferous tubules with the calculation of the spermatogenesis index, counting the average number of seminiferous tubule cells, Sertoli cells and endocrine glandulocytes (Leydig cells).For electron microscopy, testis pieces were fixed in 1.25% glutaraldehyde solution with additional fixation in 1% OsO4 solution in phosphate buffer (pH 7.3). After dehydration in alcohols and absolute acetone, the pieces were poured into a mixture of epon and araldite. Ultrathin sections after contrasting in uranyl acetate and lead citrate were examined using a JEM-100SX electron microscope (Japan).

Results and Discussion

It is known that the weight characteristics of the gonads are one of the leading indicators of the physiological maturity of animals [4]. With this in mind, we analyzed the total weight of the testicles and their ratio to body weight (mass index) in control and experimental rat pups. The analysis showed that in rat pups obtained from females with

experimental hypothyroidism, there was a tendency to increase both the weight of the testicles and body weight in general. In 60-day-old experimental rats, the body weight was 174.3 + 13.1 g, the weight of the testes was 1.7 + 0.04 g, the mass index of the testes was 0.97 + 0.01, while in control animals data the indicators were 168.6+12.4 g, 1.45+0.14 g and 0.86+0.01, respectively. In our opinion, a slight macroorchidism observed in experimental rat pups is primarily associated with testicular oedema, as one of the manifestations of mucous oedema in general [8,25], and there is also evidence that the increase in testicular weight in hypothyroidism is mainly due to activation of the thyroid receptor TRa 1, but the mechanism by which this occurs remains unclear [13].

Morphological studies of the testicles showed that on the 60th day after birth, on the background of relatively intact seminiferous tubules, tubules with destruction and extrusion of spermatogenic cells were detected in experimental rat pups, an increase in the area of interstitial tissue between the convoluted seminiferous tubules was noted, which may be associated with its oedema. The structure of the cells of the spermatogenic layer in individual tubules was disturbed - mislocalization of spermatocytes and spermatids was observed as a result of pronounced intercellular oedema. Against the background of oedema in some tubules, attention was drawn to a decrease in the number of spermatogenic cells, mainly spermatocytes and spermatids; pronounced signs of a delay in spermatogenesis at the level of the stages of maturation and formation were found. The number of spermatozoa in the lumen of the tubules significantly decreased, and in many tubules, they were completely absent.

These morphological changes, detected by light microscopy, were also confirmed by electron microscopy. In spermatocytes, vacuolization and lysis of individual sections of the cytoplasm, detachment of the outer nuclear membrane with the expansion of the perinuclear space were often detected. The appearance of large vacuoles containing membrane and granular structures was also observed in the cytoplasm of spermatids. Destructive changes, along with immature cells of spermatogenesis, were also subjected to mature spermatozoa. They manifested themselves as swelling and lysis of the plasmalemma, local oedema of the flagellar section of the cells.

Studies on rats and other mammals have shown that the efficiency of spermatogenesis depends on the total number of Sertoli cells, which are known to be one of the main regulatory cells in the process of spermatogenesis [16,21]. With the appearance of receptors for androgenic hormones in them, these cells actively create an appropriate microenvironment for maturing spermatogenesis cells. At the same time, the functional state of Sertoli cells, in turn, is closely related to the hormonal balance in the body, primarily thyroid hormones [26].

According to our data, Sertoli cells also underwent pronounced morphological changes. Electron microscopic studies revealed an increase in their size, some of them showed signs of functional tension. One of the characteristic features of Sertoli cells under conditions of hypothyroidism was the presence of numerous heterophagosomes at various stages of decay and lysis. In their ultrastructure, individual phagosomes resembled phagocytosed spermatogenesis cells, all of which indicated an increase in the phagocytic activity of Sertoli cells in response to increased destruction of maturing spermatogenesis cells as a result of hormonal imbalance in the body. At the same time, it is possible that as a result of a deficiency of thyroid hormones, the process of apoptosis of spermatogenic cells is enhanced, which under natural conditions acts as one of the factors regulating spermatogenesis [19,26].

It is known that Leydig cells, in addition to the general endocrine action, also have a paracrine one, since the testosterone synthesized by these cells diffuses through the basement membrane of the seminiferous convoluted tubules, thereby regulating the intensity of spermatogenesis processes [10,22, 24]. Therefore, the study of the endocrine compartment of the testes is a necessary condition to evaluate the generative function.

Studies have shown that interstitial Leydig cells decreased in number and were detected in the form of clusters of 2-3 cells, while in the control they formed clusters of 10 or more cells. Electron microscopy revealed destructive changes in most Leydig cells in the form of local lysis of the cytoplasm, swelling and vacuolization of mitochondria, and a decrease in the number and electron density of granules. As a rule, there was a reduction in the granular endoplasmic reticulum and the Golgi complex, and as a result of this, a 3-fold decrease in testosterone was noted.

All this indicates that hypothyroidism leads to a violation of not only the process of spermatogenesis but also significant changes in the production of steroid hormones in the testes. We cannot agree with the opinion of some authors that hypothyroidism in early postnatal ontogenesis can cause an increase in the process of spermatogenesis and an increase in the production of steroid hormones in the testes [14,15].

The obtained morphological data found their full confirmation in the study of the morphometric parameters of the testicles. The results of morphometry showed that in the testes of offspring of female rats with experimental hypothyroidism, there was a decrease in the number of tubules that actively produce spermatozoa by 19%. Accordingly, the index of spermatogenesis also decreased, which was 80% of the control values, the average diameter of the convoluted seminiferous tubules was only 81% of the control value.

The calculation of the average number of cells of the seminiferous tubules showed that in hypothyroidism the number of spermatogonia decreased by 43%, spermatocytes and spermatids by 19% compared to the control indicators, which led to a decrease in the total number of spermatogenic cells by 20% of the control, while the number of Sertoli cells did not differ significantly from the control values.

All this indicates that hypothyroidism in the mother during pregnancy and breastfeeding significantly disrupts the process of postnatal growth and development of the testes in their offspring.

Conclusions

1. Experimental hypothyroidism in the mother during pregnancy and breastfeeding leads to a violation of the morphofunctional formation of the male gonads of their offspring, which is confirmed by a change in both quantitative and qualitative characteristics of the sex and endocrine cells of the organ.
2. Early diagnosis and treatment of hypothyroidism in pregnant women and their children is the most important condition for the prevention of male infertility in adulthood.

References

Akhmedov Sh. S., Abdunabieva Kh. M. Hypothyroidism//Re-health journal.-2021. No. 1 (9). - P.288-291.

Bryukhin G.V., Antonov S.D. Characteristics of the viability of spermatozoa in the offspring of female rats with experimental type 1 diabetes mellitus under the action of immobilization stress//Russian Journal of Physiology named after I.M. Sechenov. - 2020. - V.106, No. 1. -P.55-65.

Dudenkova N.A., Shubina O.S. Morphological features of the structure of the testes of white rats during postnatal ontogenesis // Postgraduate doctor. - 2015. - V.72, No. 5. - P.31-40.

Laskov D.S., Bryukhin G.V., Sizonenko M.L. Features of the morphological and functional characteristics of spermatozoa in the offspring of female rats with experimental liver damage of alcoholic origin//Problems of reproduction. - 2014. - V.20, No. 2. - P.18-22.

Reproductive endocrinology: translation from English. / Kronenberg G.M., Melmed Sh., Polonsky K.S., Larsen P.R., ed. I.I. Dedova, G.A. Melnichenko. - Moscow: GEOTAR-Media, 2018. - 504 p.

Serov V.N., Prilepskaya V.N., Ovsyannikova T.V. Gynecological endocrinology. - M.: 2004. 528 p.

Sizonenko M.L. Characteristics of the spermatogenic epithelium of the testes // Morphology, 2014. No. 2, 42-45.

Tukhtaev K.R., Tillabaev M.R., Azizova F.Kh. Morphological features of spermatogenesis in experimental hypothyroidism in juvenile age / Proceedings of the Congress of the International Association of Morphologists / / Morphology, 2004. - No. 4 (126). - P.125.

Chalyapina V.G. Endocrinology of reproduction. - St. Petersburg: Science, 1991. - 192 p.

Shevlyuk N.N., Stadnikov A.A. Leydig cells of testes of vertebrates (ontogeny, ultrastructure, cytophysiology, factors and mechanisms of regulation) // Orenburg: Orgma, 2010. - 484 p.

Shelkovnikova T.V., Dogadin S. A. Modern ideas about the relationship between thyroid hormones and gonads in men // Siberian Medical Review: Clinical Medicine. - 2013. - No. 1. – P.9-14.

Shirshov V.N. The current state of the problem of male infertility: a review of the clinical guidelines of the European Association of Urologists//Clinical practice. - 2016. - No. 1. - P.39-50.

Ahmed J.S., Brown, S.D. et all. Akt1 protects against germ cell apoptosis in the postnatal mouse testis following lactational exposure to 6-N-propylthiouracil// Reproductive toxicology. Elsevier Science Ltd, New York, NY, 2011; 31(1):17-25.

Cooke P.S. Thyroid hormones and testis development: a model system for increasing testis growth and sperm production//Ann N Y Acad.Sci.-1991.-V.637.-№1.-P.122-132.

Corrales Hernandez J.J. et all. Primary hypothyroidism and human spermatogenesis//Arch.Androl.-1990.-V.25.- .-№1.-P.21-27.

Griswold M.D. 50 years of spermatogenesis: Sertoli cells and their interactions with germ cells // Biology of Reproduction, 2018, 99(1), 87–100.

Kalcioglu, M.T., Sallavaci, S., Hrncic, N., Beishenova, M., Cakar, M.D., Vlaski, L., & Ankarali, H. (2021). Prevalence of and factors affecting otitis media with effusion in children in the region from Balkans to Caspian basin; A multicentric cross-sectional study. International Journal of Pediatric Otorhinolaryngology, 143, 110647.

Botirov, A.J., Isroilov, R.I., Matkuliyev, K.H.M., SH, K.U.K., Akhundjanov, N.O., Djuraev, J.A., & Zokirova, Z.J. (2020). Clinical and morphological results of xenografts to use in

myringoplasty. The International Tinnitus Journal, 24(1), 1-6.

Khasanov, U.S. (2005). Etiology and pathogenesis of postintubation scarred stenosis of the larynx and trachea. Vestnikotorinolaringologii, (4), 56-58.

Mirazizov, K.D., Palvanov, B.B., & Khasanov, U.S. (2003). Computed tomography in diagnosis of laryngeal diseases. Vestnikotorinolaringologii, (2), 36-37.

Abdullaeva, N.N., Khasanov, U.S., & Baĭbekova, E.M. (2002). Morphological changes in airway tissues in patients with laryngeal and tracheal deformations. Vestnikotorinolaringologii, (6), 24-26.

Vokhidov, Ulugbek & Shernazarov, O. & Yakubdjanov, D. &Djuraev, J. &Sharipov, S.. (2021). Paralytic stenosis of the larynx: Patients surgical overview. International journal of health sciences. 5. 386-392. 10.53730/ijhs.v5n3.1680.

Tukhtaev, K.R., Khasanov, B.B., & FKh, A. (2003). Structural and functional interrelations of immunocompetent cells in the mammary gland of lactating rats and in the small intestine of newborn rats during suckling period. Morfologiia (SaintPetersburg, Russia), 124(6), 70-72.

Zufarov, K.A., ZSh, S., Iuldashev, M.A., & FKh, A. (2002). Age dynamics of cell populations and mast cell density in human bronchial mucosa. Morfologiia (SaintPetersburg, Russia), 121(1), 78-80.

Azizova, F.K., Bazhakova, D.B., Akhmedova, K.I., & Gaffarova, E.A. (2001). Age-dependent Structural-Functional Characteristics of the Small Intestine in Rats Born to Females With Chronic Toxic Hepatitis. Likars' kasprava, (1), 103-105.

FKh, A., Tukhfatullin, F.F., Tursunmetov, I.R., & Tukhtaev, K.R. (2001). Some aspects of the formation of the immune system organs in newborn rats born to females with chronic hepatitis. Likars' kasprava, (2), 100-103.

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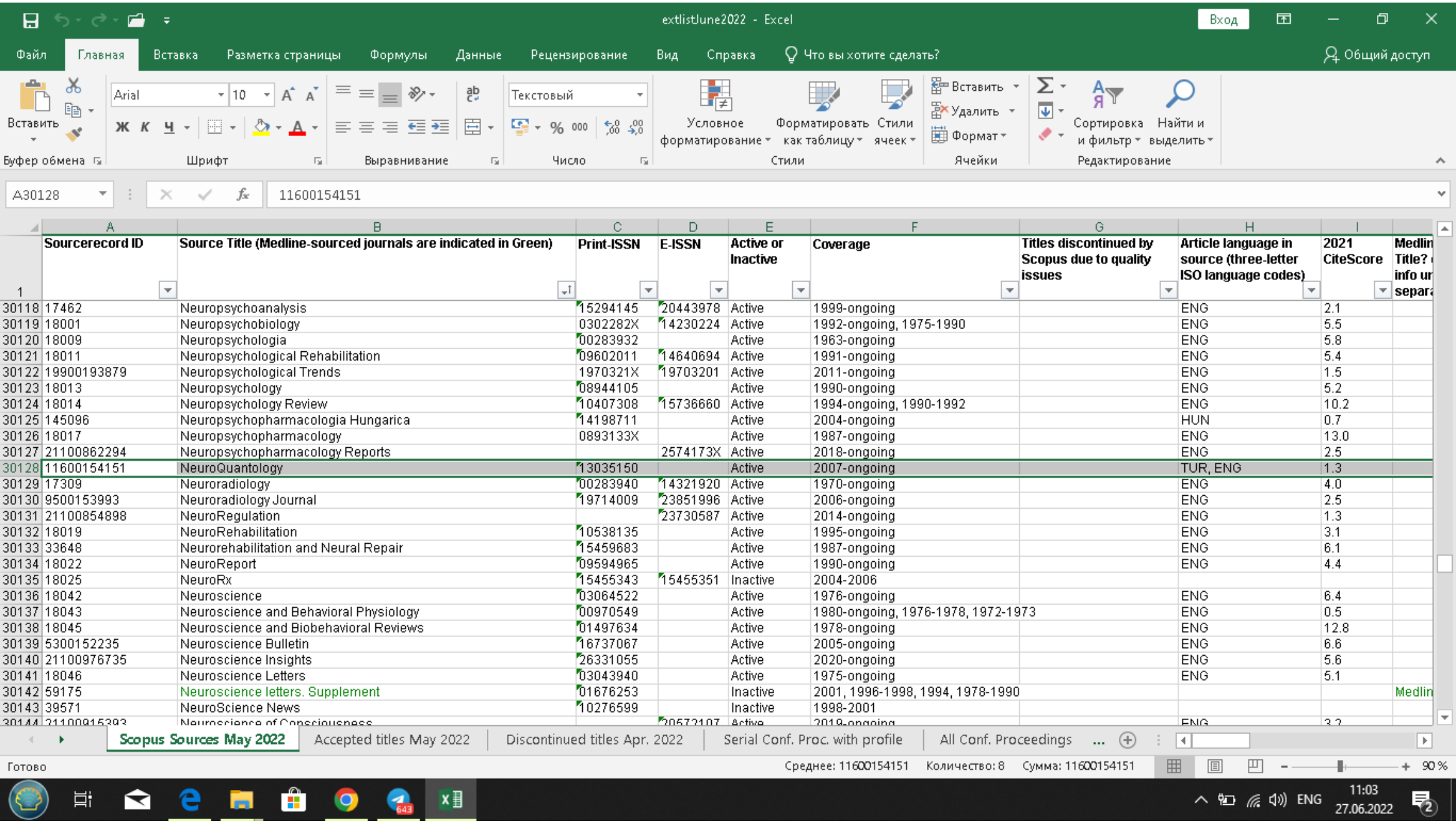

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