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MICROGLIA PHAGOCYTIC ACTIVITY IN RATS WITH DIFFERENT MODELS OF ALZHEIMER'S DISEASE

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Neuroinflammation is a key feature of Alzheimer's disease (AD), a progressive neurodegenerative disorder. Microglia, the resident immune cells of the central nervous system, are involved in the AD pathogenesis and are principal players of neuroinflammation. Enhanced phagocytic activity is one of the main features of microglial cells mediated neuroinflammation. Correct reproduction of neuroinflammation in animal models is one of the main methodological approaches for studying AD pathogenesis and pathophysiology. The aim of the study was to conduct a comparative assessment of the microglia phagocytic activity of in rats with AD induced by intrahippocampal injection of amyloid β (Aβ) 1–40 and Aβ25-35.

Methods. Male Wistar rats were used in the study. Intact and sham-operated animals were used as controls. The development of the disease was confirmed by the assessment of cognitive impairment in the Barnes maze behavioral test, as well as by the level of dopaminergic neurons (DN) loss. The microglia phagocytic activity, as well as oxidative metabolism and the expression of phenotypic markers CD86 and CD206 were determined by flow cytometry.

Results. In animals with Aβ1-40-induced AD, significant impairment of cognitive activity and DA loss were registered, microglia was characterized by an increase in the proportion of phagocytic cells with up-regulated endocytic activity along with increased oxidative metabolism and overexpression of CD86 and CD206. In animals with Aβ25–35-induced AD, moderate impairment of cognitive activity was observed, microglia was characterized only by an increase in the number of phagocytizing cells without changes in endocytic activity, oxidative metabolism, and expression of phenotypic markers of phagocyte polarized activation.

Conclusion. Thus, in animals with Aβ1-40-induced AD, the proinflammatory metabolic profile of microglia, which is characteristic for neuroinflammation in the clinical course of the disease, is more adequately reproduced.

Key words: Alzheimer's disease; microglia; phagocytosis; inflammation.

Alzheimer's disease (AD) is the leading progressive neurodegenerative disorder associated with memory loss and disability, which affects millions of people worldwide. It ranks seventh among the leading causes of death in people aged ≥ 65 [1–3]. AD is characterized by the accumulation of extracellular senile plaques of abnormally folded amyloid β (Aβ) and intracellular deposits of tau protein, causing the neurons loss and cognitive impairment [4]. Neuroinflammation, involving the microglia proinflammatory activation, reactive astrogliosis, the expression of proinflammatory cytokines, and the release of reactive oxygen and nitrogen species, is considered one of the key mechanisms of the AD pathogenesis, which underlies the initiation and progression of neurodegeneration [5, 6]. The main effectors of neuroinflammation are microglial cells — specialized resident macrophages in the central nervous system (CNS), which respond to tissue damage and the presence of pathogens by removing cellular debris, misfolded protein aggregates, damaged

neurons as well as foreign inviders through the process of phagocytosis [7].

Microglia is activated in response to Aβ deposition and are thought to play a dual role in the AD pathophysiology. On the one hand, it participates in phagocytosis and clearance of Aβ, and on the other hand, it can release pro-inflammatory mediators that can increase neuronal damage and promote disease progression [8]. Resting microglia has a small cell body and very thin, highly ramified processes, and maintains an anti-inflammatory state with low expression of pro-inflammatory mediators and low phagocytic activity [9, 10]. Recognition of Aβ causes a change in the microglia morphology with the acquisition of a rounded cell shape with almost completely absent processes (dendrites), and stimulates phagocytic activity for amyloid clearance. Microglial cells express several phagocytic receptors involved in Aβ clearance: scavenger receptors (SR-AI/II), CD36, RAGE (receptor for advanced glycosylation end products), Fc receptors, TLRs (toll-like receptors) [11]. Removal of Aβ from the extracellular space by phagocytosis is thought to limit its accumulation. AD occurs when the formation of Aβ exceeds its removal by microglia [12].

The exact mechanisms underlying impaired microglial phagocytosis of Aβ remain a subject of active research and debates. Recent data indicate that the AD development is associated with phagocytic dysfunction of microglia [10, 13]. It is noted that the presence of large heterogeneous intracellular inclusions indicates that increased engulfment, but inefficient phagolysosomal degradation of the phagocytosed material may be associated with aging of microglia and, as a result, with ineffective Aβ clearance [12]. A decrease of phagocytic activity in the brain of AD patients is also associated with genetic defects of microglial, as well as astroglial cells [14].

On the other hand, there are also data on the increased microglia phagocytic activity, which correlates with cognitive impairment both in AD patients and in animals with a model of this disease [15]. Recent studies have shown that in AD there is an increase in microglial phagocytosis simultaneously with an increase in the level of production of reactive oxygen species (ROS) by these cells, which is known to lead to increased inflammation and neuron damage [16].

However, all authors agree that the microglia phagocytic activity plays a decisive role in the pathogenesis of neuroinflammation in AD and requires more thorough research.

One of the methodological approaches used to study the AD pathogenesis and search for new therapeutic targets are interventional models based on intracerebral administration of Aβ [17]. In this study, two most commonly used AD animal models based on intrahippocampal Aβ administration: the Aβ1-40-induced model and the Aβ25-35-induced were compared. Senile plaques in AD patients are usually composed of Aβ1-42 and Aβ1-40. The AD animal model based on intrahippocampal administration of Aβ1-40 is a classic interventional model of this disease and is accompanied by the development of progressive neuroinflammation. However, although Aβ1-40 is the form of amyloid most prone to aggregation [18], the ability to cause cognitive impairment is inherent not only to Aβ1–40, but also to some fragments, in particular the undecapeptide Aβ25–35. This fragment, located at the C-terminus of the molecule, is the functional domain of Aβ, required for both neurotrophic and neurotoxic effects. Taking this into account, Aβ25-35 is often chosen as AD model for in-depth study of the effects of Aβ-mediated neurotoxicity. More pronounced cognitive disorders in experimental animals are observed when aggregated Aβ25–35 is administered [19]. According to literature data, intrahippocampal administration of Aβ25-35 causes the development of neuroinflammation with increased synthesis of neurotoxic reactive oxygen and nitrogen species by microglial cells. Data on the phagocytic activity of microglia, which is assigned a significant role in the process of neurodegeneration, in these two AD models are absent in the literature.

The aim of the study was to conduct a comparative assessment of the phagocytic activity of microglia in rats with AD induced by intrahippocampal administration of Aβ1-40 and Aβ25-35.

Materials and Methods

Animals and study design. 14-month-old male Wistar rats (300–500 g) bred in the vivarium of the Educational and Scientific Center “Institute of Biology and Medicine” of Taras Shevchenko Kyiv National University were used in the experiment. Animals were kept under standard conditions with access to water and food ad libitum. The animal maintenance protocol was approved by the University’s Bioethics Committee in accordance with the Animal Protection Act. All animal studies were conducted in accordance with the norms established by the Law of Ukraine No. 3447-

IV "On the Protection of Animals from Cruelty", as well as in accordance with the standards of the Convention on Bioethics of the Council of Europe "European Convention for the Protection of Vertebrate Animals Used in Experimental and Other Scientific Research goals" (1997), general ethical principles of work with experimental animals approved by the First National Congress on Bioethics of Ukraine (September 2001) and other international agreements and national legislation in this field. Before the experiment, the animals were randomly divided into 4 groups: I ($n = 10$) — intact animals kept in standard vivarium conditions and not subjected to any manipulations; II ($n = 10$) — sham-operated (placebo) rats; III ($n = 10$) — rats with Aβ1-40 induced AD; IV ($n = 10$) — rats with Aβ25-35 induced AD. Randomization was performed using the "RAND ()" function in Microsoft Excel.

Surgery and Aβ1-40 and Aβ25-35 AD induction were performed as described by Mudò et al., 2019 and Schimidt et al., 2019 correspondingly [20, 21]. Rats were anesthetized with a mixture of ketamine (75 mg/kg, Sigma, USA) and 2% xylazine (100 µl/rat, Alfasan International B.V., The Netherlands) intraperitoneally in the volume of 1 ml. After this, animals were placed in a stereotaxic apparatus (SEJ-4, Ukraine), and were scalped from the point of intersection of the sagittal suture with the bregma (zero point): 2 mm distally, 2 mm laterally, and 3.5 mm deep, and a burr hole was made with an injection needle directly into the hippocampus. Next, animals received unilateral intra-hippocampal injections of Aβ1-42 or Aβ25-35. The suspension volume was 10 µl per animal, infusion was carried out for 5 minutes at a rate of 0.5 µl/min (every 15 s). After administration of Aβ, the tip of the microinjector remained in the brain tissue for 4 min. After that, the microinjector was removed, and the soft tissues of the head were sutured. The sham group was intra-hippocampal-injected with 10 µl of sterile ddH2O.

Degeneration of hippocampal dopamineric neurons (DN) was assessed using immunohistochemical staining (IHC) with antibodies to tyrosine hydroxylase (TH) [22]. The intensity of TH-positive staining was assessed on a semi-quantitative scale using quantitation methods (as described by Quantitative Scoring Methods [http://www.ihcworld.com/ihc_scoring.htm]), taking into account the number of positive (stained) cells and staining intensity (Table 1). The results were calculated by multiplying the percentage of positive cells (P) by the intensity (I) and presented as a quick estimate (Q): $Q = P \times I$.

Spatial learning and memory of rats were assessed via navigational ability in Barnes maze [23]. The aim of the test is to assess the ability to learn and remember the location of the escape box by placing visual tips on the walls surrounding the apparatus. The Barnes maze is a round table with 16 holes. On the walls of the room, as peripheral visual cues, black marks were placed (a triangle on one wall and two parallel stripes on the other) for better orientation of the experimental animals. A box (ESCAPE BOX) was attached to one of the holes in the table, into which a standard animal filler was poured. The rest of the holes remained closed. The test consisted of 4 days of training (4trial/day on day 1, 2, 3 and 4 of the experiment), and in each trial, rats were given 180 s to find the ESCAPE BOX. On day 5, rats were placed in the maze's center and explored for 90 s for assessing initial (pre-surgery) short-term memory, and on day 9 — for assessing initial (pre-surgery) long-term memory. Post-surgery short- and long-term memory was assessed on day 23 and 27 after the intrahippocampal Aβ injection correspondingly. Test endpoints (in seconds): 1) the time required for the animal to find the entrance to the ESCAPE BOX (spatial learning and spatial memory — related to the function of the hippocampus); 2) the time spent near the entrance to closed hole (cognitive flexibility — related to the function of the frontal cortex of the brain).

The concentration of the soluble form of beta-amyloid and Tau-protein in the homogenates of the hippocampus of rats with AD was determined by ELISA (Cloud-Clone Corp Co., Ltd. Houston, TX, USA) according to the manufacturer's recommendations.

Table 1

Semi-quantitative scale for assessing the intensity of TH-positive staining by quantification methods

Score	0	1	2	3	4
Percentage of positive cells (P)	<10%	10–25%	25–50%	50–75%	>75%
Staining intensity	no	weak	moderate	high	–

To prevent proteolytic degradation of beta-amyloid in the homogenate, a complex of protease and phosphatase inhibitors was used.

Microglia cells isolation. Microglia cells were isolated using a Percoll density gradient as described previously [24]. Purity of isolated microglia cell fraction was assessed by flow cytometry using FITC-conjugated mouse anti-rat CD11b (BD Pharmingen™) and phycoerythrin (PE) mouse anti-rat CD45 (BD Pharmingen™). The percentage of CD11b + CD45+ cells was 88.9 ± 3.7. Cell viability was estimated by Trypan blue exclusion test. The percentage of viable cells was ≥93.

Microglia cell function assessment. Phagocytic activity, oxidative metabolism and phenotypic marker expression level were determined by flow cytometry as described previously [18]. Briefly, ROS generation was assessed using 2′7′-dichlorodihydrofluorescein diacetate (H2DCFDA, Invitrogen). Reactivity reserve of the oxidative metabolism was assessed by the modulation coefficient (MC). MC was estimated after the treatment of microglial cells with phorbol 12-myristate 13-acetate (PMA) (protein kinase C activator) [25] *in vitro* and was calculated using formula: $MC = ((S - B)/B) \times 100$, where S — level of ROS generated after treatment with PMA *in vitro*; B — ROS value of untreated cells (basal value). Phagocytic activity was studied with the use of FITC-labeled heat-inactivated *Staphylococcus aureus* Cowan I bacteria (collection of the Department of Microbiology and Immunology of the ESC "Institute of Biology and Medicine" of Taras Shevchenko National University of Kyiv) as an object of phagocytosis. The results were recorded as the percentage of cells emitting fluorescence (phagocytosis percentage, PhP) and as the phagocytosis index (PhI) — the mean fluorescence per cell, which is proportional to the number of phagocytosed bacteria. Phycoerythrin (PE)-labeled anti-CD206, and Alexa Fluor anti-CD86 antibodies (Becton Dickinson, Farmingen, USA) were used for phagocyte phenotyping. Samples were analyzed on a FACS Calibur flow cytometer (BD Biosciences, San Jose, CA, USA). Data were analyzed using CELLQuest software (BD; Franklin Lakes, NJ, USA).

Statistical analysis. All data are presented as mean ± SD, and Statistica.12 applied for statistical analysis. Data were tested using the Kolmogorov–Smirnov test for a normal distribution before other statistical tests. Statistical differences were calculated using ANOVA with post-hoc Tukey's multiple-comparison test. Differences were considered significant at $P < 0.05$.

Results and Discussion

According to the results of our research, intrahippocampal administration of Aβ1-40 and Aβ25-35 was not accompanied by statistically significant changes in the weight of animals and their eating behavior (data are not presented), cognitive impairment was more pronounced in rats with Aβ 1-40-induced AD (Table 2).

In the Aβ1–40 AD group, the time period to search for the "ESCAPE BOX" 1 day after the end of training, which characterizes short-term spatial memory, was on average 3 times longer, while in the group with Aβ25–35-induced model — 2 times as compared to intact and sham-operated animals. When assessing long-term spatial memory, impairments were observed only in rats with the Aβ1-40-induced model: 5 days after the training, the search time for "ESCAPE BOX" in these animals was increased by 50% compared to intact and sham-operated animals.

To check short-term and long-term cognitive flexibility, the duration of the animal's stay at the entrance to the closed hole was determined 24 hours and 5 days after training. In rats with Aβ1–40-induced AD, the values of this indicator exceeded those in both control groups, which indicates the uncertainty of the animal regarding the correctness of the selected entry option. In rats with Aβ25–35-induced AD only impairment of long-term cognitive flexibility was found. Indicators of short-term cognitive flexibility in this model were similar to animals without the disease (intact and sham-operated groups).

Additional criteria for the AD development were the number of TH-positive neurons in the hippocampus, as well as the concentration of Aβ and Tau protein in the hippocampus homogenate. TH is a marker of DN. In rats, the number of TH-positive neurons is significantly reduced with age. AD in human is also characterized by a decrease in the number of these neurons [26, 27]. Significant loss of DNs was found in rats with the Aβ1–40-induced model, whereas only moderate loss of these neurons was observed in animals with Aβ25-35-induced AD.

A threefold higher concentration of Aβ was observed in the homogenate of the hippocampus of rats with both Aβ1-40- and Aβ25-35-induced AD. A 3-3.5 times increased concentration of Tau protein was also registered in both

Table 2

Criteria for the development of AD induced by intrahippocampal injections of Aβ1-40 and Aβ25-35 in rats

Criterium	Intact animals, $n = 10$	Sham-operated, $n = 10$	Aβ1-40 indused AD, $n = 10$	Aβ25-35 indused AD, $n = 10$
Spatial memory				
Short-term post-surgery (the time required for the animal to find the entrance to the ESCAPE BOX 24 h after the training, c)	5.7 ± 1.3	4.5 ± 1.1	$17.0 \pm 7.2^{1, 2}$	$11.4 \pm 4.3^{1, 2, 3}$
Long-term post-surgery (the time required for the animal to find the entrance to the ESCAPE BOX 5 days after the training, c)	9.9 ± 4.3	11.2 ± 7.4	15.2 ± 3.3^{2}	10.3 ± 3.7^{3}
Cognitive flexibility				
Short-term post-surgery (the time spent near the entrance to closed hole 24 h after the training, c)	18.0 ± 2.2	21.8 ± 6.7	$26.8 \pm 12.2^{1, 2}$	17.4 ± 1.9^{3}
Long-term post-surgery (the time spent near the entrance to closed hole 5 days after the training, c)	16.3 ± 2.3	24.0 ± 6.3	$28.3 \pm 7.8^{1, 2}$	$28.4 \pm 5.4^{1, 2}$
The number of TH-positive neurins in the hippocampus (% of intact animals/% of sham-operated animals)	100	116.7	$38.9^{1, 2}$/ $33.3^{1, 2}$	$88.92,3/76.2^{1, 2, 3}$
Concentration of Aβ in the homogenate of hippocampus, pg/μg protein	18.8 ± 8.1	21.3 ± 15.2	$62.2 \pm 18.3^{1, 2}$	$66.5 \pm 21.0^{1, 2}$
Concentration of Tau-protein in the homogenate of hippocampus, pg/ml	22.0 ± 9.1	38.8 ± 10.6	$86.9 \pm 32.1^{1, 2}$	$92.5 \pm 28.5^{1, 2}$

Notes: 1 — $P < 0.05$ as compared to intact animals; 2 — $P < 0.05$ as compared to sham-operated animals; $P < 0.05$ as compared to animals with Aβ1-40-induced AD

groups. Accumulation of Aβ and Tau protein in the hippocampus indicates that microglia are unable to clear these substances in both models, which, nevertheless, was associated with varying degrees of neurodegeneration and the development of cognitive impairments characteristic for the disease [28].

The study of microglia phagocytic activity showed an increase in the proportion of phagocytic cells in animals with both AD models by an average of 2 times compared to control animals. At the same time, the endocytic activity of microglial cells was increased (more than 5 times) as compared to the intact control and by 2 times in comparison with sham-operated rats only in animals with Aβ1–40-induced AD. In animals with Aβ25–35-induced AD, this indicator did not differ from controls (Fig. 1). As we reported previously [29, 30], sham surgery significantly affects microglia metabolism even in the far terms after the placebo neurosurgical manipulations, indicating the necessity the use of placebo control groups in the experiments concerning neurodegenerative disease modelling in order to evade the influence of these effects on the analysis of study results

According to the literature data, a comprehensive analysis of the transcriptome and metabolome of immune cells of the CNS in neurodegenerative conditions revealed Disease-Associated Microglia (DAM), a subpopulation of microglia that concentrates in areas of neurodegeneration and is characterized by unique phenotypic and functional properties, one of which is significantly increased phagocytic activity [31].

Another functional feature of DAM, in addition to enhanced phagocytic activity, is increased antigen-presenting ability associated with up-regulated expression of histocompatibility molecules and costimulatory molecules CD80/86 [32]. According to the results of our research, in animals with Aβ1–

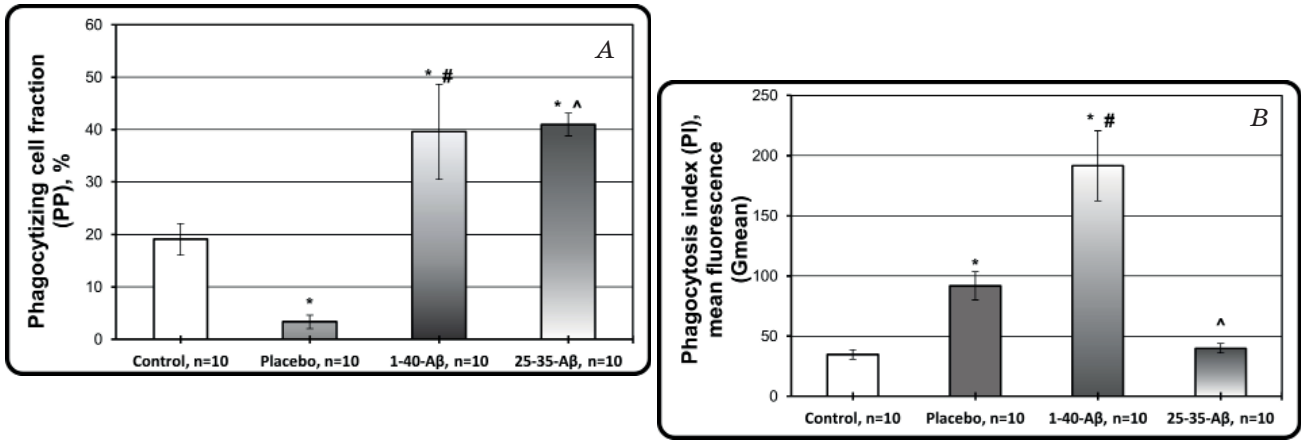

Fig. 1. **Phagocytic activity of microglial cells in rats with AD induced by injections of Aβ 1-40 and Aβ 25-35**
Phagocytizing cell fraction, PP (*A*) and phagocytosis index, PhI (*B*). Data are presented as Mean ± SD. Statistical differences are calculated using ANOVA with Tukey's post-hoc test. * and # indicate significant ($P < 0.05$) differences as compared to the values in intact and sham-operated animals correspondingly, ^ — $P \leq 0.05$ compared with the rats with AD induced by injections of Aβ1-40.

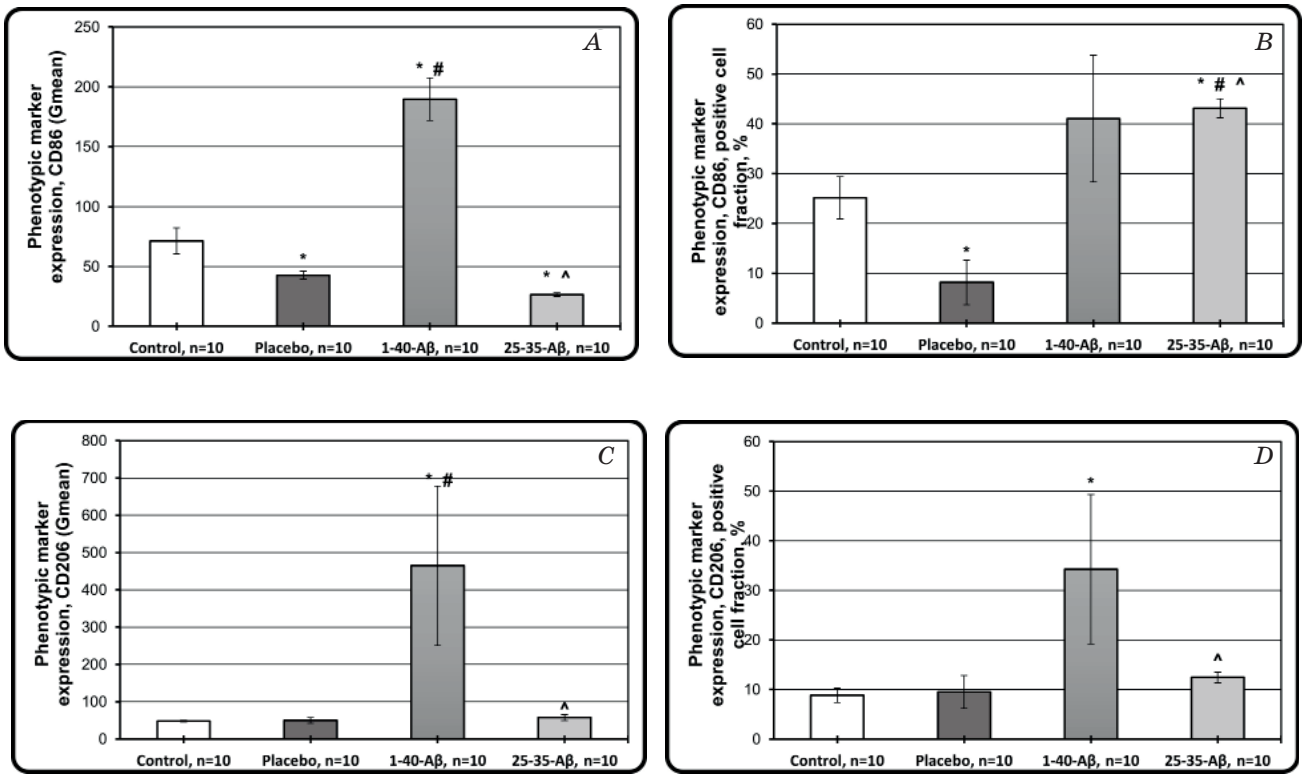

Fig. 2. **Membrane expression of CD86 — pro-inflammatory phenotype marker (*A*, *B*) and CD206, anti-inflammatory phenotype marker (*C*, *D*) in rats with AD induced by injections of Aβ 1-40 and Aβ 25-35**
Data are presented as Mean ± SD. Statistical differences are calculated using ANOVA with Tukey's post-hoc test. * and # indicate significant ($P \leq 0.05$) differences as compared to the values in intact and sham-operated animals correspondingly, ^ — $P \leq 0.05$ compared with the rats with AD induced by injections of Aβ 1-40.

40-induced AD, the number of CD86+ cells was 1.6 times higher, and the level of expression of this marker was 2.5 times higher compared to control animals (Fig. 2). In animals with Aβ25–35-induced AD, the number of CD86+ cells was also significantly higher than in controls. However, the expression level of this marker was significantly lower than the control values.

One of the phenotypic markers of DAM, which is detected in brain preparations of AD patients, is the overexpression of the mannose receptor CD206 [33]. The role of the mannose receptor in the pathogenesis of taupathies, including AD, remains unclear. Contrary to the fact that increased expression of CD206 is considered a marker of alternative (anti-inflammatory) metabolic polarization of macrophages [34], it has a special role in the assessment of polarized activation of microglia. It is known that mannose-binding lectins, including mannose receptors, are able to bind to Aβ, which causes a pro-inflammatory metabolic shift of cells of the immune system, including microglia [35, 36]. In animals with Aβ1–40-induced AD, the quantitative indicators of CD206+ cells were 3.5 times higher, and the expression level was 5 times higher as compared to the groups of control animals. In animals with Aβ25–35-induced AD, the expression indicators of this marker did not differ from those in animals in the control groups.

The concomitant increase in CD86+/CD206+ expression of animals with Aβ 1–40-induced AD may indicate an intermediate nature of microglial polarized activation, showing a mixed proinflammatory and anti-inflammatory phenotype (M1/M2) typical for DAM. In AD, microglia of intermediate polarization are involved in chronic inflammation and neurodegeneration. These microglial cells are thought to both contribute to the formation of toxic Aβ oligomers and are responsible for the clearance of Aβ plaques.

An important component of neuroinflammation is increased oxidative metabolism of microglia. As mentioned above, recent studies have shown that in AD, increased microglial phagocytosis is associated with an increase in the synthesis of ROS [37]. The development of AD, according to the results of our research, was accompanied by a significant increase in microglia oxidative metabolism (by 5 times as compared to the control) in animals with Aβ1–40-induced model (Fig. 3). In addition, treatment of cell samples from this group with PMA *in vitro* caused sharp drop of ROS level. Negative MC value –60,7 (which mirrors the residual cell ability to perform given metabolic reaction under stress) indicates extremely high activation of oxidative metabolism or cell metabolic exhaustion caused by persistent inflammation [38].

Unlike this, in animals with Aβ25–35-induced AD, the level of ROS generation was not significantly different from groups of control animals.

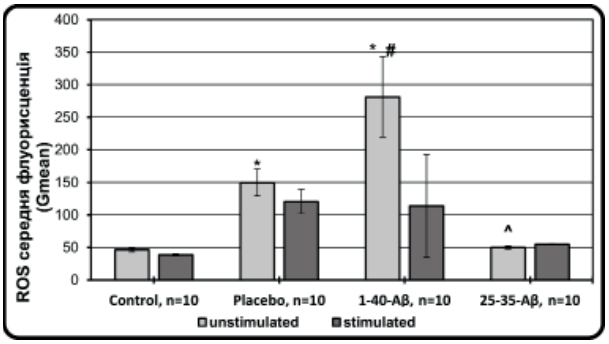

Fig. 3. **Oxidative metabolism of microglial cells in rats with AD induced by injections of Aβ1-40 and Aβ25-35**

Data are presented as Mean ± SD. Statistical differences are calculated using ANOVA with Tukey's post-hoc test. * and # indicate significant ($P < 0.05$) differences as compared to the values in intact and sham-operated animals correspondingly, ^ — $P < 0.05$ compared with the rats with AD induced by injections of Aβ1-40.

Conclusions

Comparative assessment of the microglia phagocytic activity in animals with different AD models revealed an increase in this indicator in animals with Aβ1-40-induced AD. Enhanced microglia phagocytic activity in these animals was associated with the presence of other phenotypic and functional characteristics typical for co-called DAM — the subpopulation of microglial cells that concentrates in foci of neurodegeneration in AD patients, as well as with distinct cognitive impairments. The functional profile of microglial cells in rats with Aβ25-35-induced AD indicates their moderate proinflammatory activation associated with moderate cognitive impairment. The obtained data suggest that full-length Aβ is a more powerful trigger of neuroinflammation, and the AD model induced by this Aβ is more appropriate for studying the role of neuroinflammation in the disease pathogenesis and pathophysiology.

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Conflicts of Interest

Authors declare no conflict of interest.

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ФАГОЦИТАРНА АКТИВНІСТЬ МІКРОГЛІЇ У ЩУРІВ З РІЗНИМИ МОДЕЛЯМИ ХВОРОБИ АЛЬЦГЕЙМЕРА

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Нейрозапалення є ключовою ознакою хвороби Альцгеймера (ХА), нейродегенеративного розладу, що прогресує. Мікроглія, резидентні імунні клітини центральної нервової системи, беруть участь у патогенезі ХА і є основними ефекторами нейрозапалення. Посилена фагоцитарна активність є однією з головних особливостей мікрогліальних клітин, що опосередковують нейрозапалення. Коректне відтворення нейрозапалення на тваринних моделях є одним із основних методичних підходів до вивчення патогенезу та патофізіології ХА. Метою дослідження було провести порівняльну оцінку фагоцитарної активності мікроглії у щурів з ХА, індукованою інтрагіпокампальним уведенням амілоїду β (Аβ) 1-40 та Аβ25-35.

Методи. У дослідженні використовували самців щурів лінії Wistar. Як контроль використовували інтактних і хиброоперованих тварин. Розвиток захворювання підверджували оцінкою когнітивних порушень у поведінковому тесті лабіринт Барнса, а також за рівнем загибелі дофамінергічних нейронів (ДН). Фагоцитарну активність мікроглії, а також оксидативний метаболізм та експресію фенотипових маркерів CD80 і CD206 визначали методом проточної цитометрії.

Результати. У тварин з Аβ1-40-індукованою ХА зареєстровано значне порушення когнітивної активності та втрату ДН, мікроглія характеризувалася збільшенням частки фагоцитувальних клітин із підвищеною ендоцитарною активністю, посиленням окисного метаболізму та надекспресією CD86 та CD206. У тварин з Аβ25-35-індукованою ХА спостерігалося помірне порушення когнітивної діяльності, мікроглія характеризувалася лише збільшенням кількості фагоцитувальних клітин без змін ендоцитної активності, окисного метаболізму та експресії фенотипових маркерів поляризованої активації фагоцитів.

Висновки. Таким чином, у тварин з Аβ1-40-індукованою ХА більш адекватно відтворюється прозапальний метаболічний профіль мікроглії, характерний для нейрозапалення в клінічному перебігу захворювання.

Ключові слова: хвороба Альцгеймера; мікроглія; фагоцитоз; запалення.