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Original Article

LncRNA NEAT1 promotes Alzheimer's disease by down regulating micro-27a-3p

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Abstract: Objective: Alzheimer's disease (AD) is a common neurodegenerative disease. This study was designed to investigate the roles of lncRNA NEAT1/miR-27a-3p axis in AD. Methods: Amyloid protein was used to treat SH-SY5Y cells and rats to construct AD model. RT-qPCR was used to quantify lncRNA NEAT1 and micro-27a-3p in AD model cells. Western blot was used to determine the β-amyloid-precursor-protein-cleaver-enzyme 1 (BACE1), amyloid, Tau protein and its phosphorylation, Caspase 3 protein and its lytic cell protein and amyloid precursor protein (APP). Flow cytometry was used to detect apoptosis. The cell activity was detected by CCK-8. The lncRNA NEAT1 and miR-27a-3p inhibition or over-expression vectors were constructed. The dual luciferase reporter gene and RNA pull-down assay were used to detect the targeting relationship between lncRNA NEAT1 and micro-27a-3p. The cognitive function of rats was tested by water maze. Results: After being induced by amyloid protein, lncRNA NEAT1 was up-regulated while micro-27a-3p was down-regulated in SH-SY5Y cells. Apoptosis rate was increased and cell activity was decreased. Amyloid protein, BACE1 protein, APP protein, Tau protein and its phosphorylation, Caspase 3 protein and its lytic cell protein were up-regulated. Down-regulation of lncRNA NEAT1 or up-regulation of micro-27a-3p could reduce cell apoptosis, increase cell activity, down-regulate amyloid protein, BACE1 protein, APP protein, Tau protein and its phosphorylation, and up-regulate caspase 3 protein and its lysate protein. Dual luciferase reporter gene assay and RNA pull-down experiments revealed that micro-27a-3p was the target gene of lncRNA NEAT1. Down-regulation of micro-27a-3p could offset the changes caused by LncRNA NEAT1. AD caused cognitive dysfunction in rats, which was improved by down-regulation of lncRNA NEAT1. Conclusion: lncRNA NEAT1 regulates the development of AD by down-regulating micro-27a-3p.

Keywords: Alzheimer's disease, miR-27a-3p, lncRNA NEAT1

Introduction

Alzheimer's disease (AD) is a heterogeneous disease that leads to cognitive degeneration [1]. Clinically, patients with AD are manifested as amyloid β accumulation, neurofibrils twisted into tangles, neural inflammatory and synaptic toxins, neuronal degeneration and cognitive impairment [2]. Changes in neurons are closely related to AD. Their synchronicity maintains dynamic balance in normal resting brain, but it changes in AD [3]. Genes and their encoded proteins play an important role in the development and progression of AD [4]. Changes in the coding genes of the above proteins may cause the development and progression of AD. Therefore, it is possible to understand the mechanism of AD by studying the gene regulation of neuronal cells.

In the cell process, long-chain non-coding RNA (lncRNA) can be involved in gene regulation through sponge miRNA. Nuclear enriched abundant transcript 1 (lncRNA NEAT1) is an active member of lncRNA family. Previous studies have shown that lncRNA NEAT1 is involved in regulating the development and progression of cervical cancer [5], pancreatic cancer [6], liver cancer [7], prostate cancer [8] and multiple myeloma [9]. LncRNA NEAT1 plays an indispensable role in the development and progression of AD. Ke et al. [10] have indicated that

lncRNA NEAT1 enhances the neuron damage induced by Aβ through sponging miR-107, thus promoting the development and progression of AD. Zhao et al. [11] have believed that lncRNA NEAT1 promotes the development of AD by regulating the miR-124/BACE1 axis, and it might become a new target for AD therapy. Micro-27a is located on human chromosome 19 and it is sheared to form micro-27a-3p. micro-27a-3p plays an important role in glioma, pulmonary fibrosis and other diseases [12-18]. Studies [19] have shown that miR-27a-3p is down-regulated in the cerebrospinal fluid of patients with AD and it has potential biomarker value for AD.

In this paper, amyloid protein was used to induce SH-SY5Y cells and construct AD model. During this process, the cell activity was decreased, the apoptosis was increased, lncRNA NEAT1 was up-regulated, and micro-27a-3p was down-regulated. The results of the bioinformatics tool showed that there was a pairing relationship between the two base sequences. At present, the interaction of lncRNA NEAT1 and micro-27a-3p in AD is not clear. Therefore, this study was designed to explore the relationship between the two and AD by regulating their expressions.

Methods

Amyloid (Aβ) induced AD model in SH-SY5Y cells and rats

SH-SY5Y cells were purchased from ATCC. Cells were cultured with dulbecco's modified eagle medium (Solarbio, China) containing fetal bovine serum (Hyclone, USA) and penicillin-streptomycin solution (Gibco, USA). After the cells were cultured to a good growth condition, the cells were cultured with Aβ protein (10 μM) for 24 h, and AD-related proteins BACE1, APP, Tau protein and p-Tau were detected. Lipofectamine 2000 transfection kit (invitrogen, USA) was used to transfect cell lines. NEAT1 siRNA, micro-27a-3p mimics, micro-27a-3pminitor, NC siRNA, NC mimics and NC inhibitor were purchased from GeneCopoeia. SD rats (n=30) were anesthetized by intraperitoneal injection of 1% pentobarbital sodium (40 μg/g). Microinjectors were used to insert needles vertically from the brain surface for 3 mm, and Aβ1-40 was injected into CA1 area of bilateral hippocampus at a slow and constant speed, with 10 μg (1 μL) each, and then the needles were retained for 5 min. The wounds were sutured after withdrawal. Rat model of AD (n=24) was successfully established. After successful modeling, the rats were randomly divided into control group, AD model group, AD model + NC siRNA group and AD model + NEAT1 siRNA group. In the AD model + NC siRNA group and AD model + NEAT1 siRNA group, rats were injected with NC siRNA and NEAT1 siRNA in tail vein, respectively. In each group, the rats were tested by water maze, and their cognitive function was evaluated by swimming speed, times of crossing platform, time to reach platform and swimming path distance. At the end of experiments, all rats were euthanized, and the hippocampal tissues were extracted to detect the expression of NEAT1 and miR-27a-3p. This research was ratified by the hospital ethics committee, and all animal experiments strictly complied with the ethical requirements of animal experiments.

Apoptosis

Cells were fixed with 70% ethanol ice-cold solution for 30 min. Then, the ethanol solution was removed and the cell particles were incubated in Annexin V-FITC/PI-A mixed solution. Then, FACScan flow cytometer (BeamDIAG, Changzhou, China) and CytoSYS 1.1 (BeamDIAG, Changzhou, China) were used to determine the apoptosis.

Cell activity

The 96-well plates were obtained. Three wells were selected to inoculate cells, with 3×10^3 cells in each well, and a total of 4 plates were inoculated. Cells were cultured at 37°C in 5% CO_2 incubator. One well plate was taken out after inoculation for 24 h, 48 h, 72 h and 96 h respectively. CCK-8 solution was added to wells. The culture medium was removed after continuous culture for 4 h. After shaking, the OD value of the solution at 450 nm was measured with enzyme-labeling instrument.

qPCR

Triol was used to extract total RNA from tissues and cells. The OD value at 260 nm and 280 nm was determined. All-in-One™ miRNA qRT-PCR Detection System (GeneCopoeia, China) was used for qPCR. Micro-27a-3p and lncRNA NEAT1 primers were designed and synthesized

by GeneCopoeia. The qPCR reaction system (20 μL) and program were referenced from user manual. The internal reference genes were U6 and GAPDH, which were standardized by $2^{-\Delta\Delta Ct}$. The upstream primer of LncRNA NEAT1 (5'→3') was TGG CTA GCT CAG GGC TTC AG, and the downstream primer (5'→3') was TCT CCT TGC CAA GCT TCC TTC. The upstream primer of Micro-27a-3p (5'→3') was ATG GTT CGT GGG TTC ACA GTG GCT AAG TTC CG, and the downstream primer (5'→3') was TGG TGT CGT GGA GTC G. The upstream primer of U6 (5'→3') was CTC GCT TCG GCA GCA CA, and downstream primer (5'→3') was AAC GCT TCA CGA ATT TGC GT. The upstream primer of GAPDH (5'→3') was AGA AGG CTG GGG CTC ATT TG, and the downstream primer (5'→3') was AGG GGC CAT CCA CAG TCT TC.

Western blot

RIPA lysis buffer was used to lyse cells and then the lysate was centrifuged at $1.6\times10^4\times g$ at 4°C for 20 min. The precipitate was discarded, and the supernatant was obtained to determine the protein concentration using a BCA kit (Thermo Fisher Company). SDS-PAGE electrophoresis was used to separate protein. The protein was transferred to polyvinylidene fluoride membrane (EMD millipore Company). The primary antibodies were added and cultured at 4°C overnight. Then, secondary antibody was added and cultivated at room temperature for 1 h. Finally, polyvinylidene fluoride membrane was washed with PBS, and ECL luminescent solution was used for visualization. The internal reference protein was β-actin. The antibodies were purchased from Abcam. Primary antibodies included Caspase 3 (1:5000, ab32351), cleaved Caspase 3 (1:500, ab2302), BACE1 (1:1000, ab108394), APP (1:2000, ab241592), Aβ (1:500, ab201060), Tau (1:1000, ab32057), and phosphorylation-Tau (p-Tau, 1:2000, ab92676).

Dual-luciferase reporter gene

Starbase3.0 was used to analyze the sequence information of lncRNA NEAT1 and micro-27a-3p. The pmirGLO vector was used to construct the NEAT1 wild type (containing micro-27a-3p binding site) and NEAT1 mutant type (without micro-27a-3p binding site) respectively. The above vectors were transfected into cells respectively, and the luciferase intensity was detected using a dual luciferase reporter gene detection system (Promega).

RNA pull-down experiment

Starbase3.0 was used to predict the sequence information of lncRNA NEAT1 and micro-27a-3p. NEAT1 wild-type with MS2 hairpin structure (containing predicted binding site) and NEAT1 mutant (without predicted binding site) were constructed. Magna RIPTM RNA-binding protein co-immunoprecipitation kit (Millipore) was used for co-immunoprecipitation. Subsequently, RNA purification was performed and the enrichment degree of miR-27a-3p was quantified by qPCR.

Statistics and analysis

SPSS 22.0 (IBMgon, USA) was used for data analysis. Graphpad 8.0 (USA) was used for figure generation. The differences between the two groups were compared by independent sample t test. One-way ANOVA was used to analyze the differences among groups. Afterwards, pairwise comparison was conducted by LSD-t test. All comparisons were two-sided. 95% was taken as the confidence interval and the difference was statistically significant when P value was less than 0.05.

Results

Amyloid (Aβ) induced AD model in SH-SY5Y cells

Protein Aβ was used to construct AD model in SH-SY5Y cells. The effects of AD on SH-SY5Y cells apoptosis, AD related protein (BACE1/APP/Aβ/Tau/p-Tau) and cell activity were detected. Meanwhile, the abnormal expression of lncRNA or miRNA in AD model was observed. **Figure 1** showed that after being induced by protein Aβ, cell apoptosis and Caspase 3 lysis were increased, expressions of BACE1, APP, Aβ, Tau and p-Tau were up-regulated, while cell activity was decreased in SH-SY5Y cells. In this process, lncRNA NEAT1 was increased and micro-27a-3p was decreased.

Regulatory effect of NEAT1 on Aβ-induced SH-SY5Y cells

The expression of lncRNA NEAT1 was increased in AD model, which drove us to explore the pos-

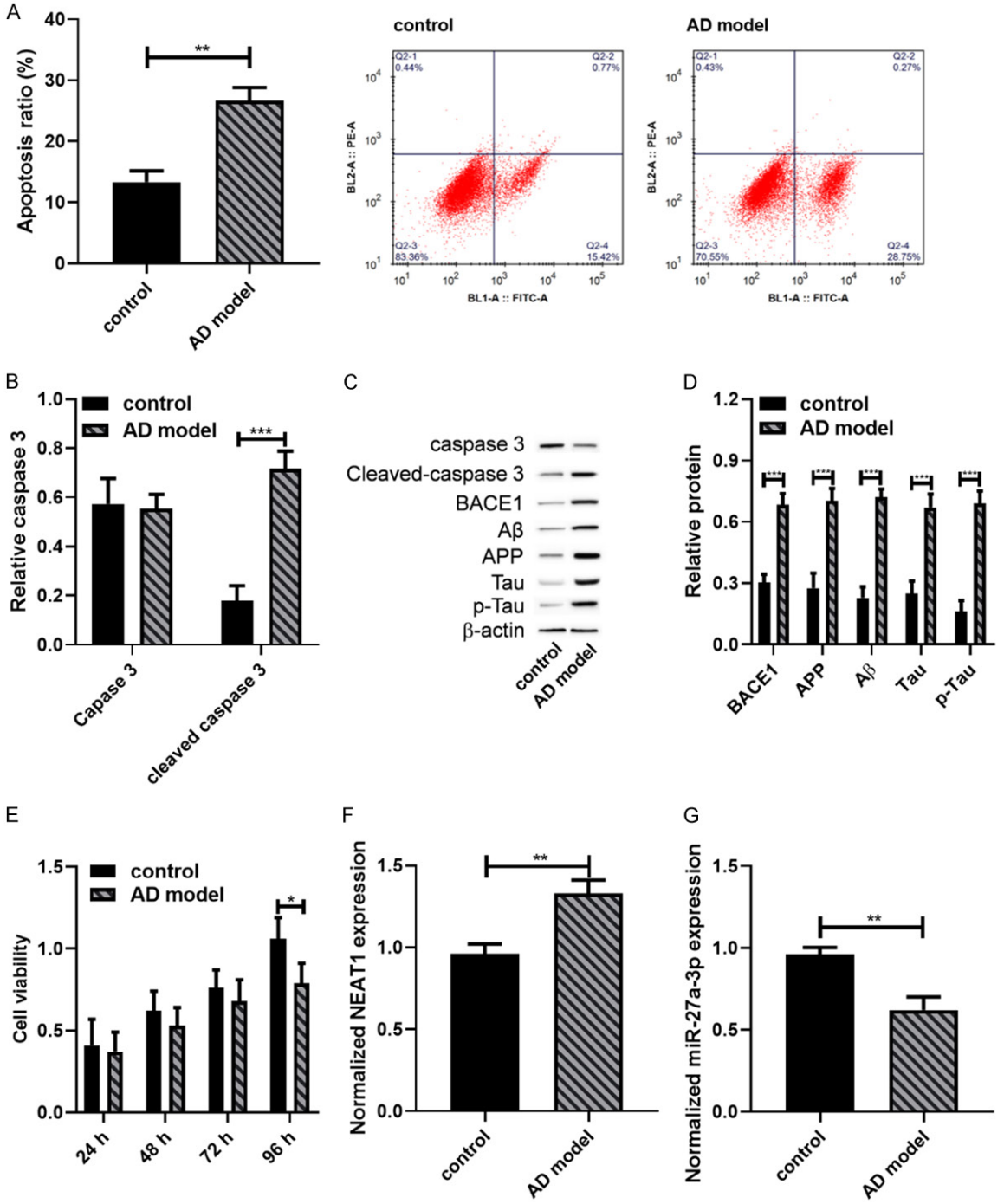

Figure 1. Amyloid was used to induce AD model in SH-SY5Y cells. A: Increased apoptosis was observed in SH-SY5Y cells after induction; B: Caspase 3 cleavage was observed in SH-SY5Y cells after induction; C: Western blot map; D: Up-regulation of AD related proteins BACE1, APP, Aβ, Tau and p-Tau was observed in SH-SY5Y cells after induction; E: Reduced cell proliferation was observed in SH-SY5Y cells after induction; F, G: Increased NEAT1 and reduced miR-27a-3p was observed in SH-SY5Y cells after induction. p-Tau, Tau protein phosphorylation. AD: Alzheimer's disease. *P<0.05, **P<0.01, ***P<0.001.

sible relationship between NEAT1 and AD. In this study, lncRNA NEAT1 was down-regulated by NEAT1 siRNA, the apoptosis was detected by flow cytometry, and the cell activity was detect-

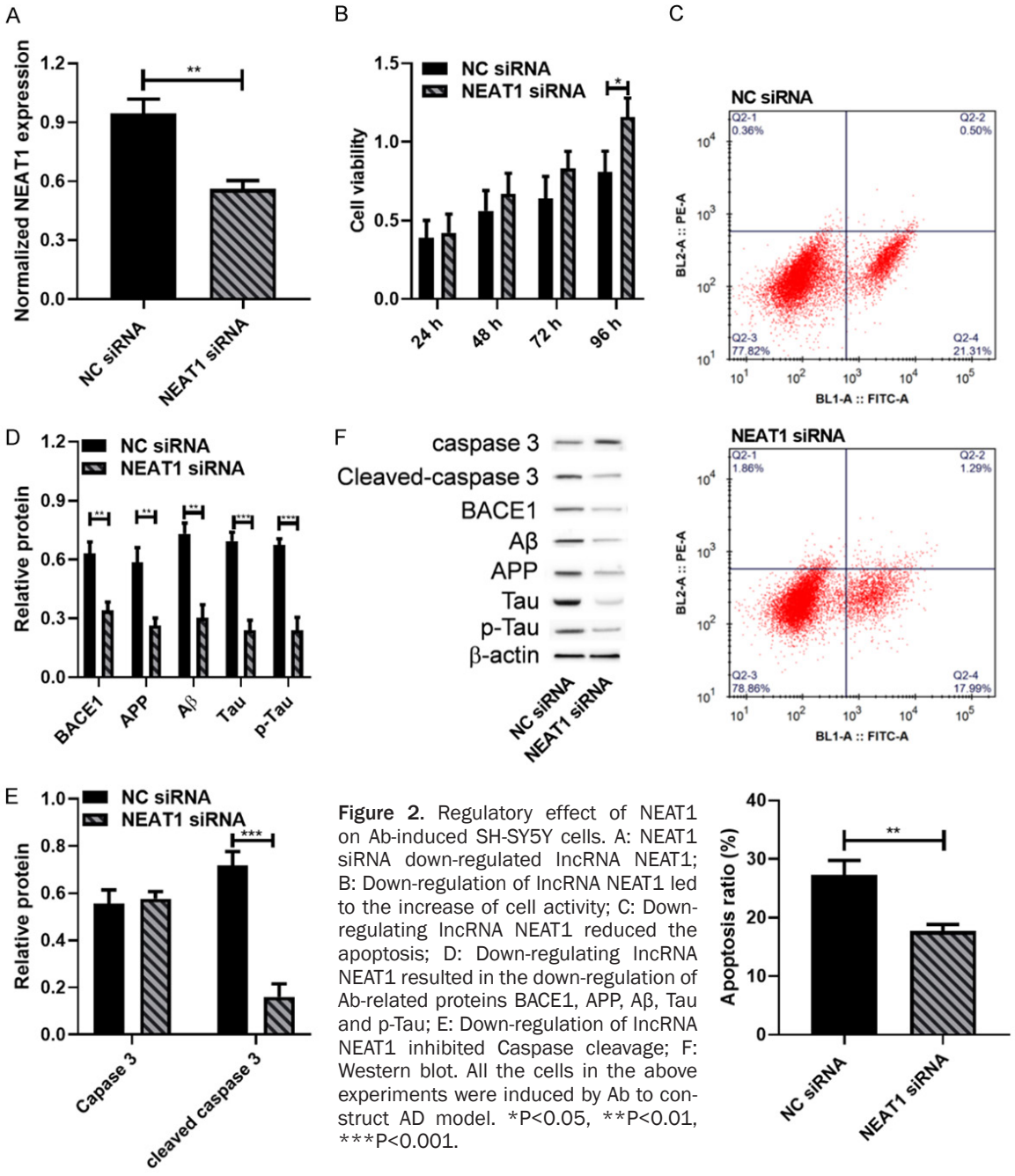

Figure 2. Regulatory effect of NEAT1 on Ab-induced SH-SY5Y cells. A: NEAT1 siRNA down-regulated lncRNA NEAT1; B: Down-regulation of lncRNA NEAT1 led to the increase of cell activity; C: Down-regulating lncRNA NEAT1 reduced the apoptosis; D: Down-regulating lncRNA NEAT1 resulted in the down-regulation of Ab-related proteins BACE1, APP, Aβ, Tau and p-Tau; E: Down-regulation of lncRNA NEAT1 inhibited Caspase cleavage; F: Western blot. All the cells in the above experiments were induced by Ab to construct AD model. *P<0.05, **P<0.01, ***P<0.001.

ed by CCK-8 kit. RNA was quantified by qPCR and protein level was detected by Western blot. **Figure 2** shows that down-regulating lncRNA NEAT1 increased the activity of AD model cells, reduced apoptosis, down-regulated AD related proteins BACE1, APP, Aβ, Tau, p-Tau, and inhibited Caspase 3 cleavage. According to the above results, it was speculated that down-regulating lncRNA NEAT1 could alleviate cell damage in AD model.

Regulatory effect of micro-27a-3p on Aβ-induced SH-SY5Y cells

Downregulation of micro-27a-3p in AD model also drove us to explore the relationship between micro-27a-3p and AD. In this study, micro-27a-3p was increased by micro-27a-3p mimics. AS shown in **Figure 3**, up-regulating micro-27a-3p increased the activity of AD model cells, reduced apoptosis, down-regulat-

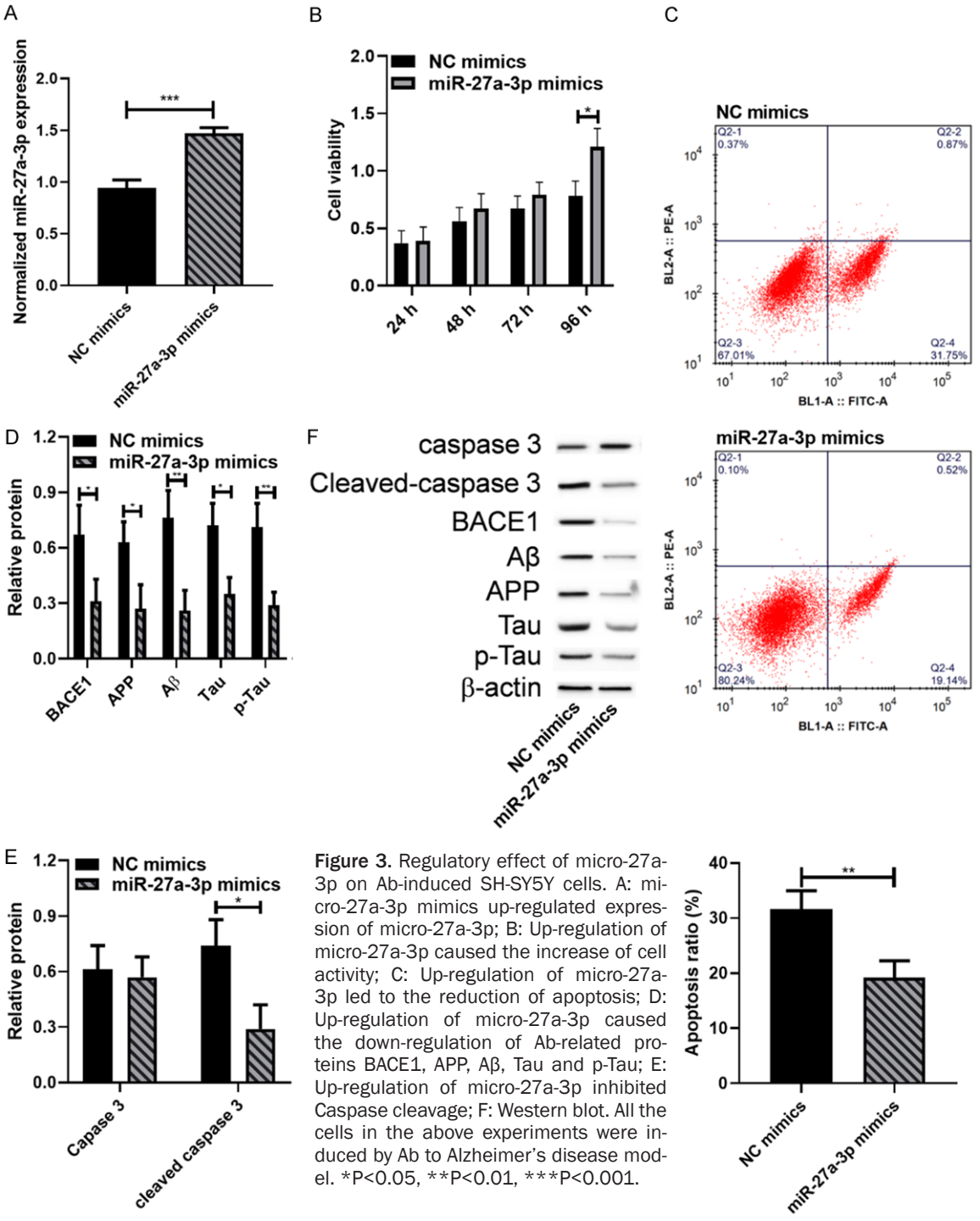

Figure 3. Regulatory effect of micro-27a-3p on Ab-induced SH-SY5Y cells. A: micro-27a-3p mimics up-regulated expression of micro-27a-3p; B: Up-regulation of micro-27a-3p caused the increase of cell activity; C: Up-regulation of micro-27a-3p led to the reduction of apoptosis; D: Up-regulation of micro-27a-3p caused the down-regulation of Ab-related proteins BACE1, APP, Aβ, Tau and p-Tau; E: Up-regulation of micro-27a-3p inhibited Caspase cleavage; F: Western blot. All the cells in the above experiments were induced by Ab to Alzheimer's disease model. *P<0.05, **P<0.01, ***P<0.001.

ed AD related proteins BACE1, APP, Aβ, Tau, p-Tau, and inhibited Caspase 3 cleavage. This was similar to down-regulation of lncRNA NEAT1. It was speculated that up-regulating micro-27a-3p could improve cell damage in AD model.

micro-27a-3p was a downstream target of lncRNA NEAT1

LncRNA could participate in gene regulation by sponging miRNA. In this study, down-regulating lncRNA NEAT1 could increase micro-27a-3p

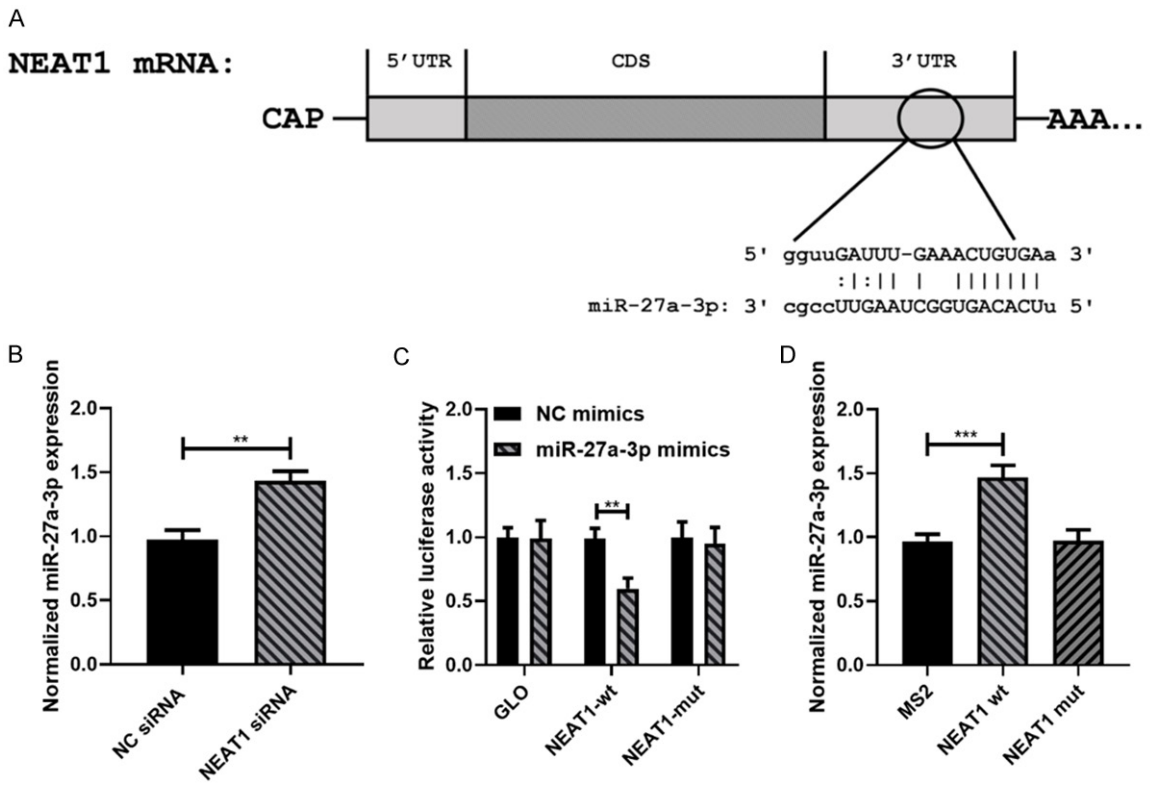

Figure 4. micro-27a-3p was a downstream target of lncRNA NEAT1. A: Starbase 3.0 was used to predict the binding site between lncRNA NEAT1 and micro-27a-3p; B: Down-regulation of NEAT1 increased micro-27a-3p expression; C: Dual luciferase report; D: RNA pull-down experiment. CAP: m7GPPPN structure. UTR: untranslated area. AAA: ploy A tail. **P<0.01, ***P<0.001.

(**Figure 4B**). Therefore, lncRNA NEAT1 may negatively regulate micro-27a-3p through sponging. Starbase3.0 predicted that the 3' untranslated region of lncRNA NEAT1 had a sequence site binding to miR-27a-3p (**Figure 4A**). According to this prediction site, NEAT1 mutant was constructed. Dual luciferase reporter gene assay and RNA pull-down experiments showed that lncRNA NEAT1 could bind to miR-27a-3p through the prediction site and negatively regulate the miRNA. The above results suggested that micro-27a-3p was the downstream target of lncRNA NEAT1 (**Figure 4C** and **4D**).

Offsetting effect between micro-27a-3p and lncRNA NEAT1

The above results revealed that micro-27a-3p was the downstream target of lncRNA NEAT1, and lncRNA NEAT1 and micro-27a-3p might participate in the regulation of AD model cells. This part revealed that lncRNA NEAT1 regulated AD model cells through miR-27a-3p. In this study, miR-27a-3p inhibitor was used to down-regulate miR-27a-3p, and NEAT1 siRNA was used to down-regulate lncRNA NEAT1. **Figure 5** showed that down-regulating lncRNA NEAT inhibited apoptosis and Caspase 3 cleavage, promoted cell activity and decreased BACE1, APP, Aβ, Tau, p-Tau. However, down-regulating micro-27a-3p could offset the above regulation. According to the results, lncRNA NEAT1 regulated AD model cells through micro-27a-3p.

The role of lncRNA NEAT1/miR-27a-3p on cognitive function

As shown in **Figure 6**, we constructed an AD rat model *in vivo*. The results showed that AD caused the up-regulation of lncRNA NEAT1 and the decrease of miR-27a-3p in hippocampus, and down-regulation of lncRNA NEAT1 in AD could increase the expression of miR-27a-3p. Then, the cognitive function of rats was evaluated in each group by water maze. The results showed that AD caused cognitive decline in rats, while down-regulating lncRNA NEAT1 could improve their cognitive function. The

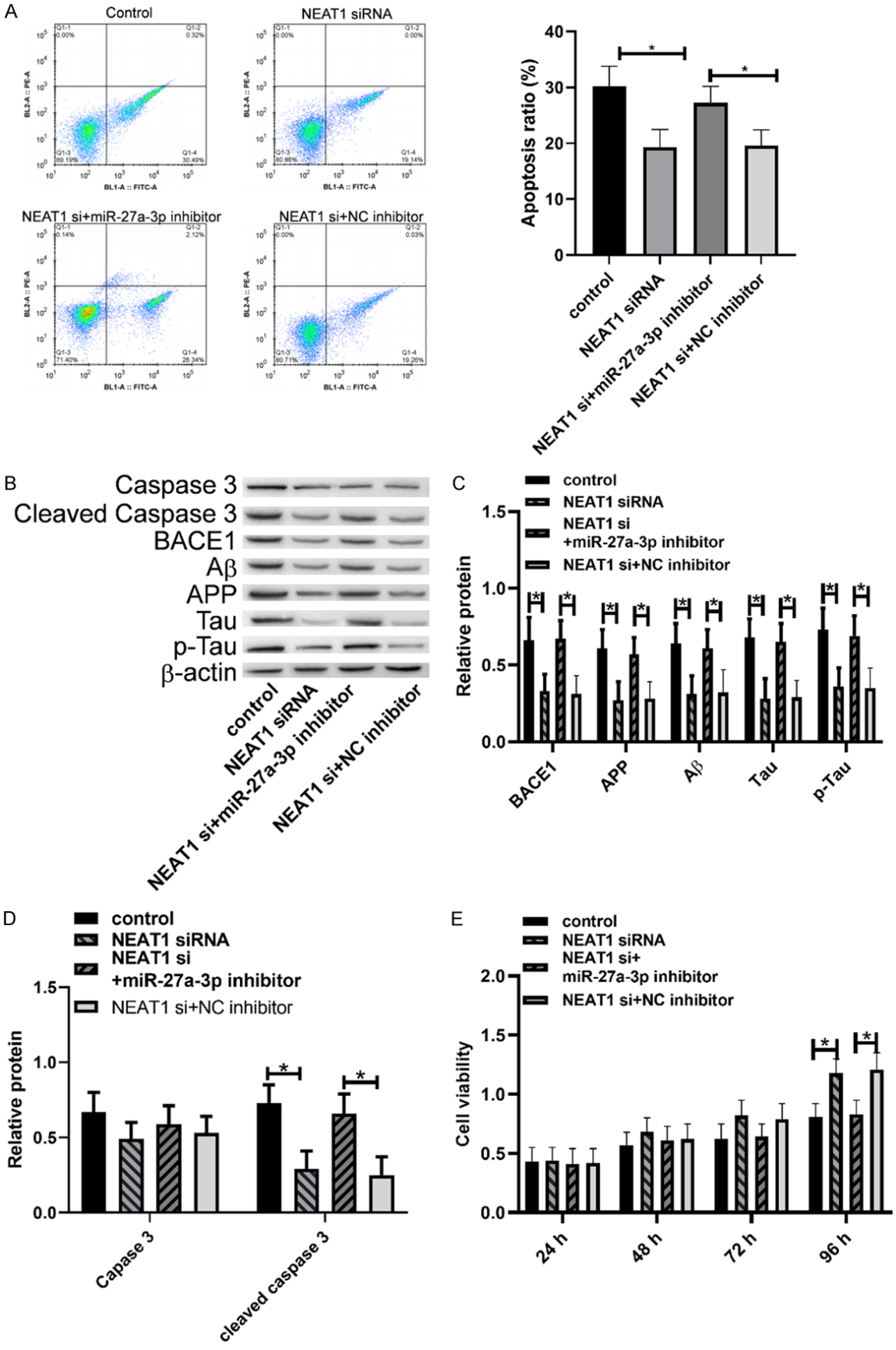
A
Control
NEAT1 siRNA
NEAT1 si+miR-27a-3p inhibitor
NEAT1 si+NC inhibitor
Apoptosis ratio (%)
control
NEAT1 siRNA
NEAT1 si+miR-27a-3p inhibitor
NEAT1 si+NC inhibitor
B
Caspase 3
Cleaved Caspase 3
BACE1
Aβ
APP
Tau
p-Tau
β-actin
C
control
NEAT1 siRNA
NEAT1 si +miR-27a-3p inhibitor
NEAT1 si+NC inhibitor
Relative protein
BACE1
APP
Aβ
Tau
p-Tau
D
control
NEAT1 siRNA
NEAT1 si +miR-27a-3p inhibitor
NEAT1 si+NC inhibitor
Relative protein
Capase 3
cleaved caspase 3
E
control
NEAT1 siRNA
NEAT1 si+ miR-27a-3p inhibitor
NEAT1 si+NC inhibitor
Cell viability
24 h
48 h
72 h
96 h

Figure 5. Offsetting effect between micro-27a-3p and lncRNA NEAT1. A: Down-regulation of micro-27a-3p offset the influence of lncRNA NEAT1 on apoptosis; B: Western blot; C: Down-regulation of micro-27a-3p offset the influence of lncRNA NEAT1 on AD-related proteins; D: Down-regulation of micro-27a-3p offset the influence of lncRNA NEAT1 on Caspase 3 cleavage; E: Down-regulation of micro-27a-3p offset the influence of lncRNA NEAT1 on cell activity.

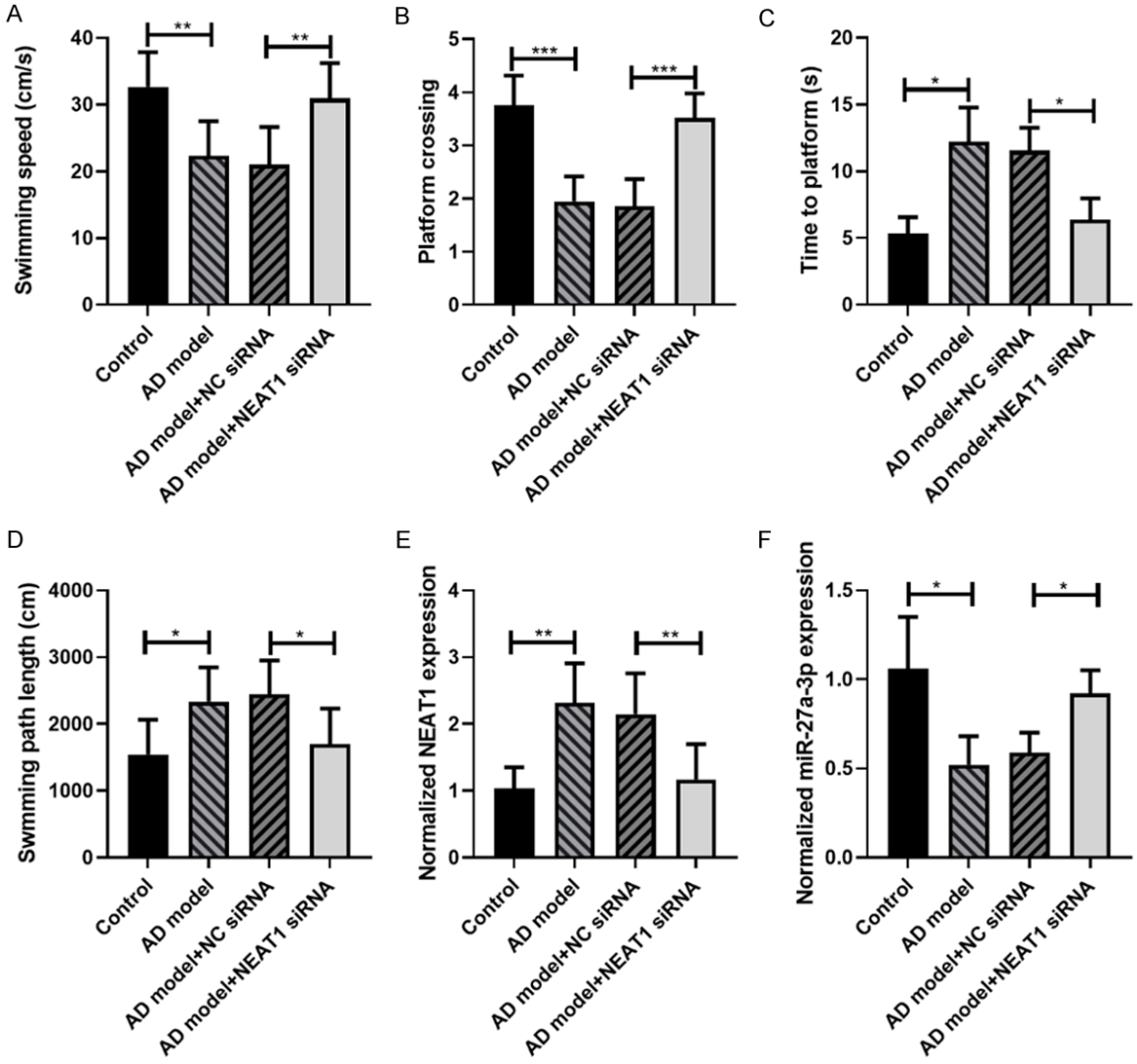

Figure 6. lncRNA NEAT1 regulated cognitive function of AD rats *in vivo* through miR-27a-3p. A: Swimming speed of rats in each group. B: The number of crossing the platform of rats in each group. C: The time to reach the platform of rats in each group. D: Swimming path distance of rats in each group. E, F: Expression of NEAT1 and miR-27a-3p in hippocampus of rats in each group. Each group consisted of 6 rats (n=6).

results indicated that lncRNA NEAT1/miR-27a-3p axis was involved in the regulation of cognitive function in rats.

Discussion

AD seriously affects patients' cognitive function and quality of life, so it is urgent to understand its molecular mechanism, so as to facilitate the development of targeted therapy. This research has uncovered that AD can induce the up-regulation of lncRNA NEAT1 and the down-regulation of miR-27a-3p *in vivo*. At the same time, AD causes cognitive dysfunction in rats, and down-regulating lncRNA NEAT1 can enhance the cognitive function of rats. The results indicate that lncRNA NEAT1 and miR-27a-3p may be related to the progression of AD.

In this study, Aβ-induced SH-SY5Y cells were used to construct AD model. After being induced by Aβ, SH-SY5Y showed up-regulated AD-related proteins (amyloid protein, BACE1 protein and APP protein), hyperphosphorylation of Tau protein, increased apoptosis, reduced cell activity and Caspase 3 lysis. Interestingly, lncRNA NEAT1 was up-regulated and micro-27a-3p was down-regulated in this process. According to the above results, it is speculated that lncRNA NEAT1 and micro-27a-3p may be related to AD induced by Aβ in SH-SY5Y cells. Therefore, the over-expression/inhibition expression vectors were constructed to regulate the expression of lncRNA NEAT1 or micro-27a-3p in Aβ-induced SH-SY5Y cells, so as to discover the role of lncRNA NEAT1 and micro-27a-3p in AD. In response to either NEAT1 downregulation or miR-27a-3p upregulation, there was an increased activity and decreased apoptosis in Aβ-induced SH-SY5Y cells, with significant reductions of cleaved Caspase 3, amyloid, BACE1, APP, Tau and phosphorylated-Tau. Amyloid protein β (Aβ), β amyloid precursor protein cleaver enzyme 1 (BACE1), Tau, amyloid precursor protein (APP), etc. are involved in the pathogenesis of AD. Upregulation of APP evoked the production of Aβ in AD. BACE1 cleaves APP embedded in cell membrane, resulting in the release of Aβ short peptide on APP. Aβ is enriched with β-pleated sheet and aggregated into bundles after other processing and modification. Finally, Aβ acts on neuronal cells, resulting in the development and progression of AD [20-23]. Tau is the promoter of axon microtubule assembly. Neurofibrillary tangles in patients with AD are related to hyperphosphorylated/highly aggregated Tau [24, 25]. Interestingly, this study also revealed that the regulation of lncRNA NEAT1 or miR-27a-3p could cause changes in the activity of apoptosis pathway mediated by Caspase 3, suggesting that lncRNA NEAT1 or miR-27a-3p could participate in the regulation of apoptosis through Caspase 3. Therefore, amyloid protein accumulation and neurofibrillary tangles caused by the interaction of the above proteins are common pathological features of patients with AD. The increase in apoptosis and decrease in proliferation of neuronal cells mean that neuronal cells are damaged, which may cause the cognitive dysfunction, thus leading to cognitive impairment in patients with AD.

However, down-regulating lncRNA NEAT1 and up-regulating micro-27a-3p could obviously offset the above changes, which seem to imply that down-regulation of lncRNA NEAT1 and up-regulation of micro-27a-3p might be used for treatment and remission of AD.

Is there a regulatory relationship between lncRNA NEAT1 and micro-27a-3p? At present, there are still controversies regarding the hypothesis that NEAT1 acts as a ceRNA. Some studies [26] have revealed the following points: 1) NEAT1 may be transported into the cytoplasm; 2) miRNAs are transported into the nucleus. Although the specific mechanism of NEAT1 as a ceRNA has not been confirmed yet, many studies [27-29] have shown that NEAT1 can directly interact with miRNA in diseases, thereby regulating related cell biological functions. Studies by Ke et al. [10] and Zhao et al. [11] have also revealed that lncRNA NEAT1 can participate in the development and progression of AD through sponging miRNA. Biological information tools were used to analyze the sequence information of lncRNA NEAT1 and micro-27a-3p in this study. The results showed that there was a pairing site binding to micro-27a-3p in the 3'UTR region of lncRNA NEAT1. According to this prediction site, the NEAT1 mutant was constructed in this paper, which was in contrast to the NEAT1 wild type. The wild type and mutant type of NEAT1 were combined with pmirGLO vector or MS2 vector respectively to observe whether micro-27a-3p could combine with NEAT1 and the enrichment degree on NEAT1. The results showed that the relative fluorescence intensity decreased when micro-27a-3p mimic was co-transfected with NEAT1 wild type. micro-27a-3p could be enriched on lncRNA NEAT1. The above results indicated that lncRNA NEAT1 could regulate micro-27a-3p through predictive sites.

In this study, the lncRNA NEA1/micro-27a-3p axis was involved in regulating amyloid-induced apoptosis and proliferation of SH-SY5Y cells, so lncRNA NEA1 and micro-27a-3p might be related to the development and progression of AD. Neural inflammation is closely related to AD, so whether lncRNA NEAT1/micro-27a-3p is related to neuronal inflammatory cytokines such as TNF-α and IL-1β will be discussed in future studies. In this study, we only discussed the regulatory effect of lncRNA NEAT1/micro-27a-

3p axis in SH-SY5Y cells. Whether this axis has similar regulatory effect in AD model animals is unknown. This doubt will also be answered in future studies. The downstream target protein or signal pathway of LncRNA NEAT1/micro-27a-3p axis, the relationship between lncRNA NEAT1, micro-27a-3p and the clinicopathological features of AD patients, as well as their application in clinical evaluation, will all be discussed in future studies.

To sum up, lncRNA NEAT1 regulates SH-SY5Y cell apoptosis and proliferation through micro-27a-3p, so it causes changes in amyloid protein, BACE1 protein, APP protein and Tau protein, thus participating in the development of AD. Down-regulation of lncRNA NEAT1 or up-regulation of micro-27a-3p may be molecular mechanisms that inhibit neuronal cell damage in AD, so the therapeutic value of both in AD needs to be further studied.

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Disclosure of conflict of interest

None.

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