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The Mechanism of RNA-Dependent Intergenerational Inheritance and Factors Affecting Its Transition to Transgenerational Inheritance

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Abstract: Previous studies have shown that adult mice exposed to environmental enrichment (EE) conditions significantly increase hippocampal long-term potentiation (LTP) levels and cognitive function in their offspring. This effect is attributed to changes in the RNA composition of the father's sperm. However, this effect is only present in the F1 generation of EE-trained mice and disappears in the F2 generation, which has not been thoroughly investigated. This study focuses on the F2 generation of EE-trained mice, using RNA-seq, control experiments, and embryo injection techniques to verify the presence of latent genetic traits in the F2 generation and explore the cross-generational genetic effects of EE training on offspring synaptic plasticity and cognitive abilities, as well as their mechanisms. Additionally, this research is significant for understanding memory inheritance and treating neurodegenerative diseases.

Keywords: Environment Enrichment, Synaptic Plasticity, Intergenerational Inheritance, Transgenerational Inheritance, Memory genetics.

1. Background

1.1. Previous studies

Previous studies have shown that exercise combined with cognitive training helps enhance synaptic plasticity, learning, and memory, and reduces the risk of various complex diseases, including Alzheimer's disease. Additionally, there is evidence that exposure to environmental stimuli can transmit information to the next generation through non-genetic mechanisms[1-3]. When an individual is exposed to harmful environmental stimuli, cells adapt to protect the offspring from similar conditions[4], which also affects reproductive cells[5]and alters the biological processes in the descendants[5,6]. Evidence also suggests that exposure of juvenile mice to environmental enrichment (EE) can enhance hippocampal synaptic plasticity in their offspring[7]. However, there is no evidence that similar phenomena occur in adult mice. Researchers such as Benito, demonstrated that exposing adult mice to EE significantly increased the hippocampal long-term potentiation (LTP) levels and cognitive function in their offspring. This phenotype is associated with changes in the RNA composition of the father's sperm, with microRNAs (miR) 212/132 identified as a contributing factor. However, the study did not thoroughly investigate why the F2 generation did not exhibit similar phenomena to the F1 generation or the underlying mechanisms. Therefore, this research will

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introduce methods to determine whether the F2 generation of mice trained with EE exhibits recessive inheritance and which specific sperm RNA plays a primary regulatory role. In other words, this study aims to explore whether the enhancement of LTP levels and cognitive function in the offspring of EE-trained mice is transgenerationally inherited and to understand the mechanisms behind this phenomenon. The study will compare different experimental tools, setups, and results to develop a viable experiment to address the primary research questions.

1.2. Environment Enrichment (EE) and Home Cage (HC)

Environment Enrichment (EE) primarily refers to improving and optimizing the housing environment of mice to enhance their cognitive functions, particularly memory. This training method is based on the profound impact of the environment on animal behavior and learning abilities. It aims to promote brain development and memory formation in mice by providing a more varied, stimulating, and enriched environment. EE can be implemented through housing environment optimization, such as using sufficiently large cages, providing ample bedding materials, and adding enrichment items like various toys and hiding places.

Home Cage (HC) is a confined or semi-confined space for mice, designed to simulate their natural nesting environment. It provides food, water, shelter, and adequate space for activity. HC is commonly used as a control group or baseline environment to assess the effects of different experimental conditions on mouse behavior, physiology, and cognitive functions.

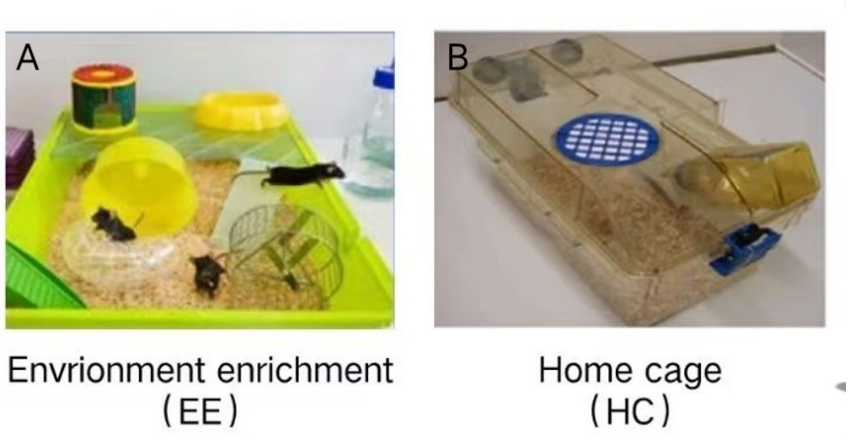

Figure 1: (A) EE environment. (B) home cage environment [8]

1.3. Intergengerational inheritance and transgengerational inheritance

Intergenerational inheritance typically refers to the process by which genetic information (mainly DNA sequences) is passed directly from parent to offspring. This is one of the fundamental principles in biology, ensuring the continuity and stability of an organism's traits and characteristics. Transgenerational inheritance, on the other hand, refers to the transmission of certain genetic information or epigenetic marks (such as DNA methylation and histone modifications) not only from parents to offspring but also potentially to subsequent generations, spanning multiple generations. This mode of inheritance involves not only the transmission of DNA sequences but also the transmission of epigenetic modifications.

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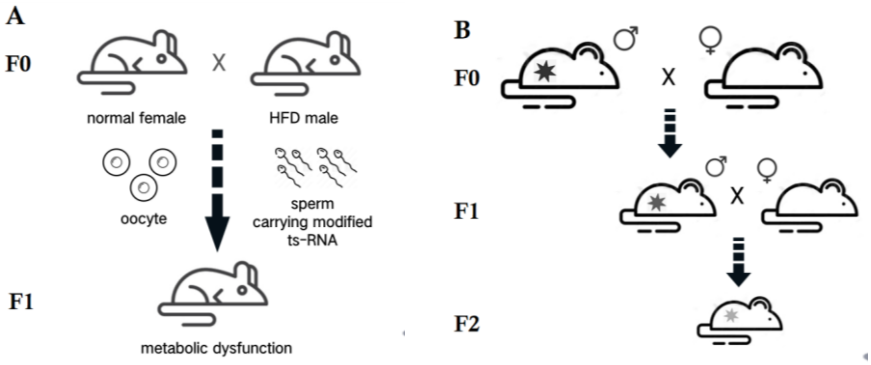

Figure 2: (A) the diagram of intergenerational inheritance. (B) the diagram of transgenerational inheritance [9]

2. Literature review

2.1. Eva Benito's studies: the main studies examined in this proposal

In the study by Benito et al., they demonstrated through control trials that EE training in mice increases hippocampal synaptic plasticity transgenerationally. RNA sequencing and PubMed searches revealed that this transgenerational enhancement of LTP is mediated by sperm RNA. Subsequent embryo injection experiments confirmed that EE training in adult males enhances hippocampal synaptic plasticity in their offspring, with this effect mediated by sperm RNA (miR212/132). They then investigated whether LTP enhancement was accompanied by improved cognitive abilities, finding a mild but significant increase in cognitive function. To explore whether the mechanisms underlying cognitive improvement are consistent with those of LTP enhancement, they conducted further embryo injection experiments and discovered that the mechanisms for synaptic plasticity and memory enhancement in the F0 and F1 generations mediated by EE might differ.

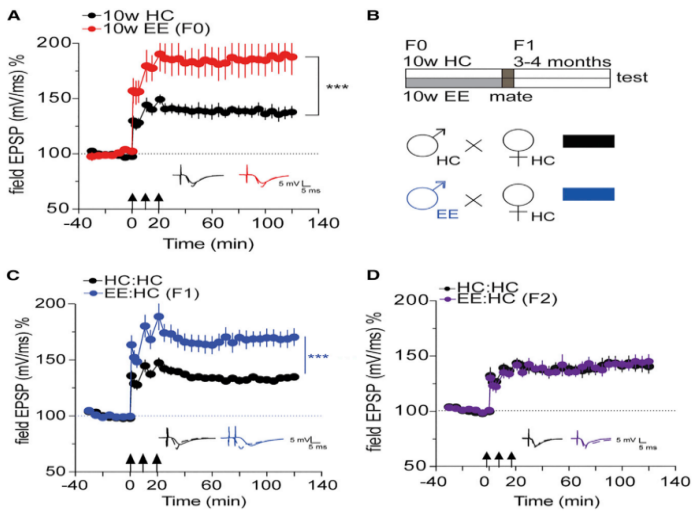

Figure 3: Intergenerational Inheritance of Enhanced LTP through EE. Compared to the HC group, (A) the LTP levels in the EE group mice are elevated. (B) Mice underwent 10 weeks of EE training and were then mated; their offspring were tested 3-4 months after birth. Compared to the HC group, (C) LTP levels are elevated in the F1 generation of the EE group mice. (D) LTP levels were not enhanced in the F2 generation[8]

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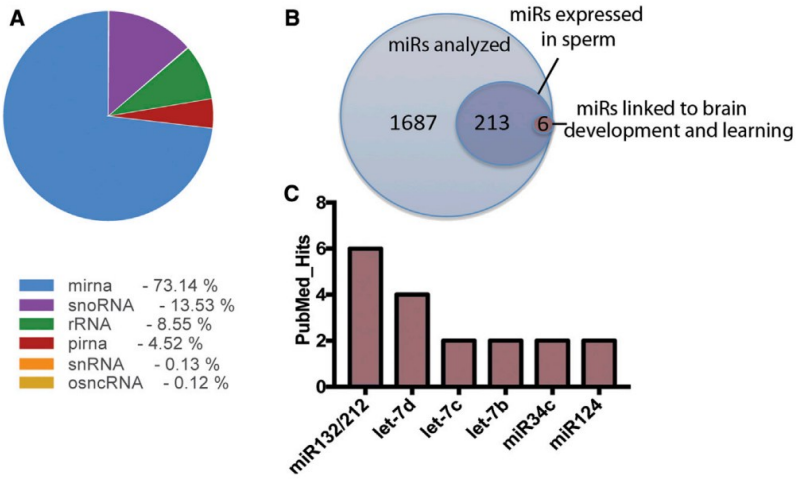

Figure 4: Candidate miRs may be related to the transgenerational transmission of enhanced LTP following EE training. (A) Shows the distribution of small RNA species in sperm from the original WT mice. (B) Out of 1886 analyzed miRs, 219 are expressed in sperm. PubMed searches for miRs related to brain function and development, synaptic plasticity, and learning and memory identified 6 candidate miRs. (C) These six miRs are ranked according to their respective click counts, with miR132/212 being the highest [8]

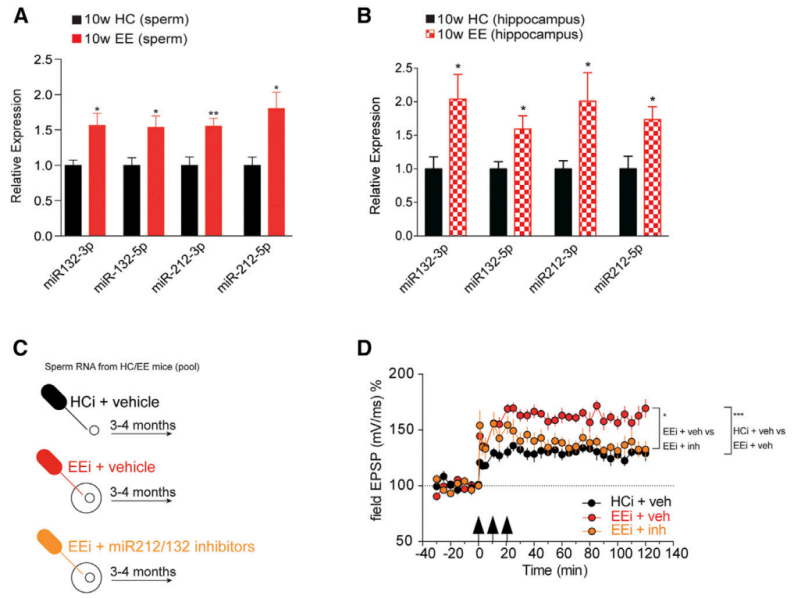

Figure 5: MiR212/132 levels are increased in the brains and sperm of EE-trained male mice, and they contribute to the transgenerational inheritance of enhanced LTP levels. (A) and (B) show that miR212/132 levels are elevated in the hippocampus and sperm of mice after 10 weeks of EE training. (C) Embryo injection scheme: the control group received HC mouse sperm RNA + interference RNA; the experimental groups received either EE mouse sperm RNA + interference RNA or EE mouse sperm RNA + miR212/132 inhibitors. (D) The experimental group injected with EE mouse sperm RNA showed elevated LTP levels, while the group injected with miR212/132 inhibitors exhibited a significant reduction in LTP levels, similar to the control group[8]

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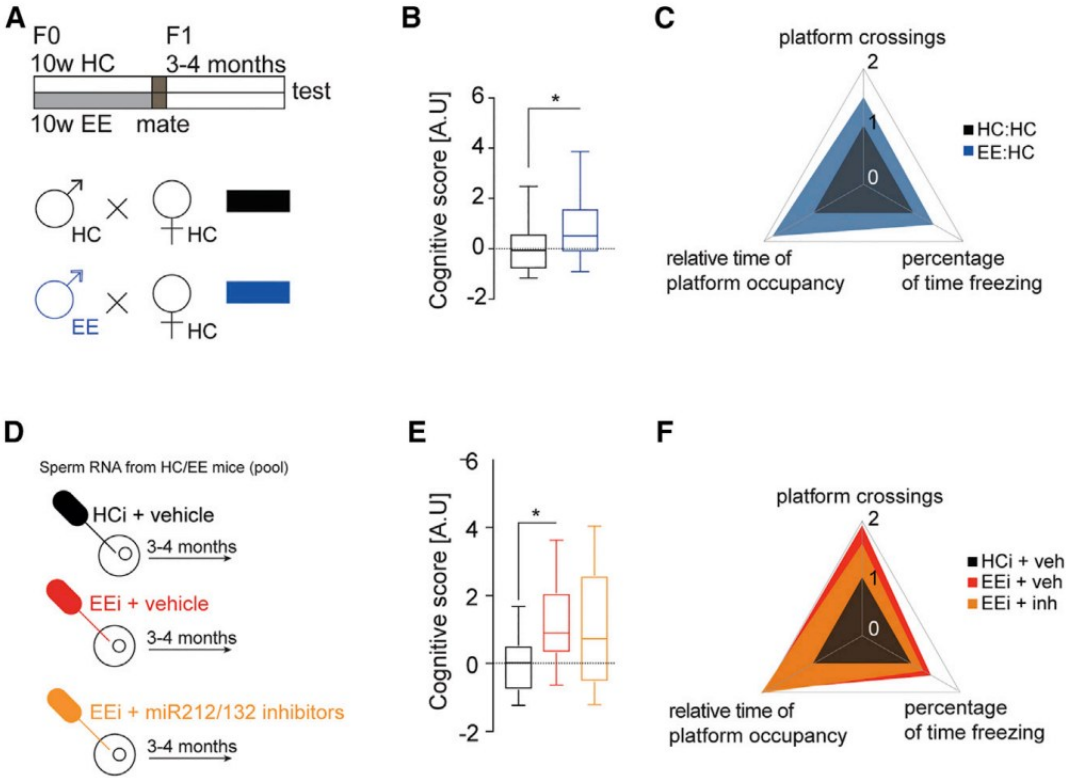

Figure 6: The offspring of EE-trained mice exhibit a mild but significant cognitive advantage. (A) Breeding scheme. (B) and (C) show enhanced cognitive abilities in the offspring of EE-trained mice. (D) The embryo injection scheme is the same as in Figure 5. (E) and (F) indicate that cognitive abilities are similar between the groups injected with EE mouse RNA and those injected with miR212/132 inhibitors[8]

2.2. Innovation and contributions to ongoing conversations in the field

Since the impact of adult EE training on synaptic function in the next generation has not been tested, this study focuses on exploring the RNA-dependent transgenerational inheritance of enhanced synaptic plasticity following environmental enrichment. Multiple experiments demonstrated that EE training significantly improved synaptic plasticity and cognitive function in the offspring of trained adult mice, primarily associated with paternal sperm RNA, with miR212/132 being a key factor in this process.

These findings provide a new mechanism for intergenerational inheritance and highlight the special role of miRs 132/212, as well as supporting the benefits of preconception exercise on offspring. Additionally, this research offers new insights and potential biomarkers for understanding and treating human neurological disorders.

However, this study did not thoroughly investigate whether the enhanced synaptic plasticity and cognitive abilities in the offspring of EE-trained mice are restricted to the F1 generation, with no observable effects in the F2 generation. Therefore, we focus on this aspect to explore whether the enhanced LTP levels and cognitive functions in the F2 generation of EE-trained mice represent a form of latent inheritance. Our goal is to determine whether these traits are transmitted across generations and to understand the underlying mechanisms of this phenomenon.

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3. Methods

3.1. RNA Seq and spatial CUT&Tag-RNA-seq

RNA-Seq is a method for determining RNA expression levels using high-throughput sequencing technology. It involves the following main steps:

First, RNA samples are extracted from cells, tissues, or organisms using appropriate methods (such as Trizol reagent) to obtain total RNA. Purification steps are then performed to remove DNA, proteins, and other impurities, ensuring the purity and integrity of the RNA.

Next, library construction is carried out, including steps such as mRNA enrichment, RNA fragmentation, reverse transcription, end repair and adapter ligation, and PCR amplification.

Finally, high-throughput sequencing is performed by placing the constructed sequencing library onto a high-throughput sequencing platform (such as the Illumina HiSeq series) for sequencing.

Spatial CUT&Tag-RNA-seq is a combined sequencing technique that integrates spatial transcriptomics and epigenomics to simultaneously detect paired transcriptomic and epigenetic regulatory information on tissue sections. The main steps include:

First, tissue section preparation is performed, followed by some preprocessing of the sections.

Next, library construction and sequencing are carried out, which involve section staining and imaging, section permeabilization, incubation, tagging, in situ reverse transcription, spatial barcode (barcode) ligation, DNA recovery, and library amplification.

Finally, high-throughput sequencing is conducted.

In this study, RNA-Seq technology is used to detect changes in RNA expression levels, and then Spatial CUT&Tag-RNA-seq technology is used to identify and locate specific locations in the hippocampus between EE mice (F0, F1, F2 generation) and HC mice with the same RNA distribution but significant differences in expression levels. The expression levels of RNA at these specific sites are then measured. This will provide deeper insights into the effects of EE training on RNA expression levels in the hippocampus of mice and its transgenerational effects.

3.2. LTP recordings and behavioral testing experiments

Previous studies have demonstrated that EE training enhances synaptic plasticity and cognitive function in mice. Synaptic plasticity is closely related to LTP levels, and behavioral tests are important tools for assessing cognitive function and learning and memory abilities in mice.

LTP levels in mice can be measured using the LTP Recording method.

Acute hippocampal slices are prepared from 3-4 month-old mice using isoflurane anesthesia, decapita tion, brain extraction, and hippocampus dissection, followed by 400μm thick transverse slices. These slices are incubated in oxygen-saturated cold artificial cerebrospinal fluid at 32°C in an interface chamber with high oxygen. After 3 hours of recovery, a monopolar platinum-iridium electrode is placed in the CA1 region for electrophysiological recordings. The slope of the field excitatory postsynaptic potential (fEPSP) is recorded using a differential AC amplifier and A/D converter, and real-time monitoring is performed with custom software. Test stimulation intensity is set to evoke a maximum 40% slope of the fEPSP. Following baseline recordings, LTP is induced using strong stimulation (100 biphasic pulses at 100Hz, with 10-minute intervals, repeated three times). fEPSP changes are recorded at various time points post-induction for up to 2 hours, with the experimenter blinded to the conditions.

Behavioral testing typically involves fear conditioning (FC) and the Morris water maze (MWM) experiments.

Mice are housed singly one week prior to testing. For FC training, mice are adapted in an FC chamber for 3 minutes, followed by a 2-second, 0.5mA shock, then left in the chamber for 10 seconds

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before returning to their original cage. Twenty-four hours later, mice are reintroduced to the conditioning chamber and their freezing behavior (≥2 seconds of immobility) is recorded for 3 minutes. This FC paradigm is a mild training procedure aimed at detecting memory enhancement.

In the MWM experiment, mice are trained for 1 minute per day for 4 consecutive days in a circular water pool to find a submerged platform; if not found, they are guided to the platform and allowed to stay for 15 seconds. Escape latency is automatically recorded by a camera. In the probe test, the platform is removed, and the percentage of time spent by the mice in the specific area (where the platform was located) is recorded. The experimenter is blinded to the experimental conditions.

3.3. Embryo injection experiment

Embryo injection involves injecting specific substances (such as exogenous genes, DNA fragments, proteins, etc.) into the cells, embryos, or blastocyst cavities of animals, plants, or microorganisms using a fine needle made from a glass capillary tube under high magnification microscopy. In this study, fertilized eggs are first collected. Then, using a 40X air objective lens and differential interference contrast (DIC) optics under an inverted microscope, RNA is injected into the cytoplasm of the zygotic stage fertilized eggs using a glass micropipette with a sharp tip. The injected fertilized eggs are then transferred into the oviducts of pseudopregnant NMRI females. The offspring produced from these injections are allowed to grow in a standard cage until they reach 3 months of age, at which point Long-Term Potentiation (LTP) levels and behavioral tests are conducted[10,11].

4. Experiment design

4.1. Animal groups

The animals are housed under standard HC or EE conditions and kept on a 12-hour light/12-hour dark cycle. All experiments, including mating, use adult mice, specifically those aged 3-4 months.

EE Mice: Mice are housed in large cages with 4-5 individuals per cage and provided with toys (including tunnels, shelters, and various objects of different shapes, with 8 toys per cage) and running wheels (2 per cage). Two toys are replaced with new ones daily, while the remaining toys are returned to the cage. Cages are cleaned weekly. Mice are placed in the EE environment at 10 weeks of age and maintained there for 10 weeks.

HC Mice: Similarly, these mice are housed in large cages with 4-5 individuals per cage but are not provided with objects or running wheels, though they follow the same cleaning schedule.

Breeding Scheme for Generational Analysis: Male mice at 10 weeks of age underwent 10 weeks of EE training as described above. HC and EE male mice were then bred with female mice that had remained in HC throughout this period. After mating, the males were immediately removed from the cages to prevent any contact with the offspring and to avoid influencing their rearing. Offspring from these pairings were housed in standard HC conditions and subjected to subsequent experiments at 3-4 months of age.

F2 generation fertilized oocytes: Set at 0.5 ng/mL, 5 mM (pH 7.4) in 250 mL 0.1mM EDTA, according to a previously published report (Gapp et al., 2014). 3 to 4 week-old C57BL/6JRj females superovulate with pregnant male serum gonadotropin (7.5 U, middle) and human chorionic gonadotropin (7.5 U, middle) and mate with C57BL/6JRj males. The donor females were killed with cervical dislocation on the day of blockage, and the fertilized oocytes were collected.

In Experiment 1, mice were divided into four groups: HC mice, EE mice, F1 offspring from EE mice, and F2 offspring from EE mice. RNA sequencing (RNA-Seq) was used to detect and analyze changes in the expression levels of relevant RNAs in the hippocampus.

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In Experiment 2, mice were divided into two groups: F2 offspring from HC mice and F2 offspring from EE mice. A comparative experiment was conducted to verify whether synaptic plasticity and cognitive ability enhancements observed after EE training are present in a transgenerational manner.

In Experiment 3, mice were divided into two groups: F1 offspring from HC mice and F1 offspring from EE mice. RNA-Seq technology was used to measure the expression levels of the selected RNAs in their sperm and hippocampus.

In Experiment 4, mice were divided into three groups: fertilized egg cells from F1 and F2 offspring of EE mice (two groups) and fertilized egg cells from F1 and F2 offspring of HC mice. Embryo injection experiments were performed to test whether the selected RNAs could enhance LTP levels and cognitive abilities in the F2 offspring of EE mice.

4.2. Experiment 1: identify RNAs whose expression levels decrease progressively with each generation

Experimental Procedure: Obtain the four groups of mice mentioned above, with the HC mice group serving as the control. Slice the brains of the four groups of mice, then use RNA sequencing (Figure7) to detect RNA expression levels. Compare the results across the four groups. Employ Spatial CUT&Tag-RNA-seq technology (Figure8) to localize the positions in the hippocampus where RNA distribution is similar among EE mice (F0, F1, F2 generations) but different from HC mice, and measure the RNA expression levels at these locations.

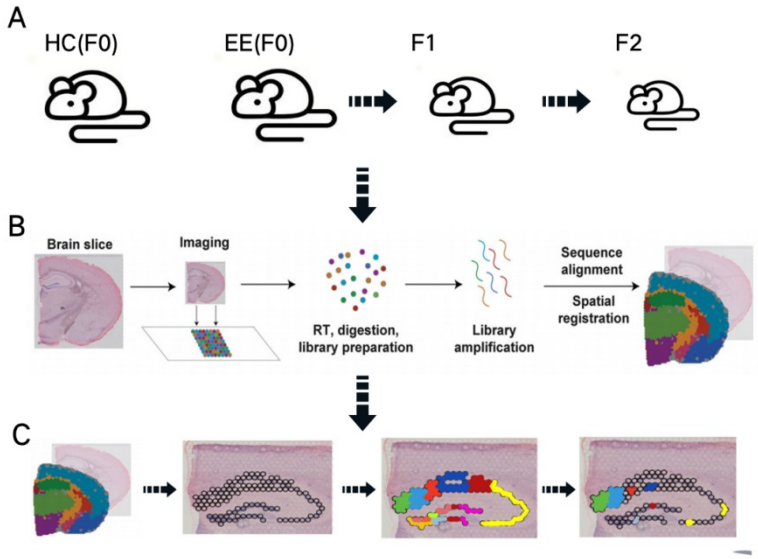

Figure 7: Experimental 1 workflow diagram.(A)Grouping of mice.(B)RNA-Seq experimental workflow diagram[10].(C)Spatial CUT&Tag-RNA-seq results schematic[10]

Data Processing: Compare the RNA expression data between EE mice (F0 generation) and HC mice to identify RNAs with differing expression levels, with the difference denoted as D1. Similarly, compare the RNA expression data between EE mice (F1 and F2 generations) and HC mice to identify RNAs with varying expression levels, denoted as D2 and D3. Analyze D1, D2, and D3 to determine their relative magnitudes and select RNAs that meet the condition "D1 > D2 > D3," indicating a progressive decrease in expression levels across generations. These RNAs are then designated as candidate RNAs.

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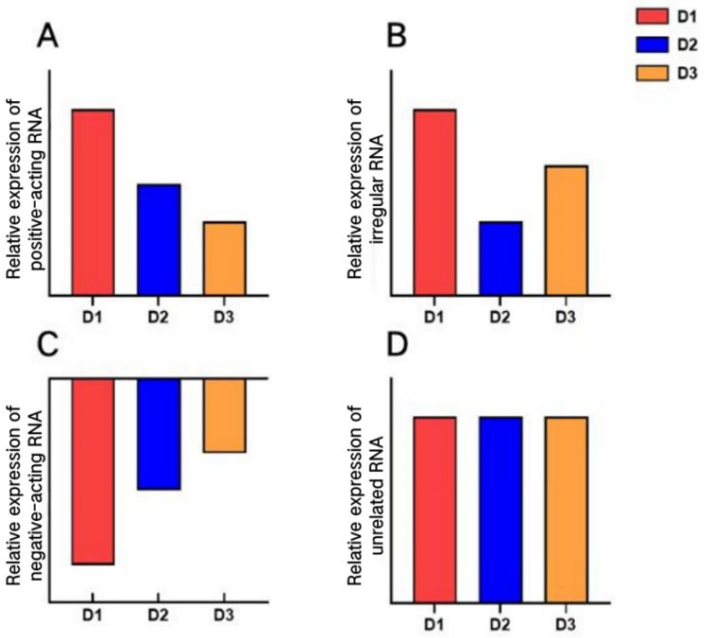

Figure 8: Changes in RNA expression levels in the offspring of EE-trained mice

(A) D1 > D2 > D3, indicating a gradual decrease in expression levels with increasing generations.
(B) D1 > D3 > D2, indicating irregular changes in expression levels with increasing generations.
(C) D1 < D2 < D3, indicating a gradual increase in expression levels with increasing generations.
(D) D1 = D2 = D3, indicating no significant change in expression levels with increasing generations.

4.3. Experiment 2: demonstrate that Enriched Environment (EE) training not only directly enhances cognitive ability and synaptic plasticity in mice but also that this effect can be inherited in a diminished form by their offspring

Experimental Procedure: In this experiment, EE male mice and HC male mice are crossbred to produce the F2 generation. Both F2 generation EE and HC mice undergo two weeks of EE training. Post-training, the mice are evaluated for LTP levels and behavior, and the results are compared. Subsequently, RNA sequencing (RNA Seq) is conducted on the trained F2 generation EE and HC mice, and the data from both groups are compared.

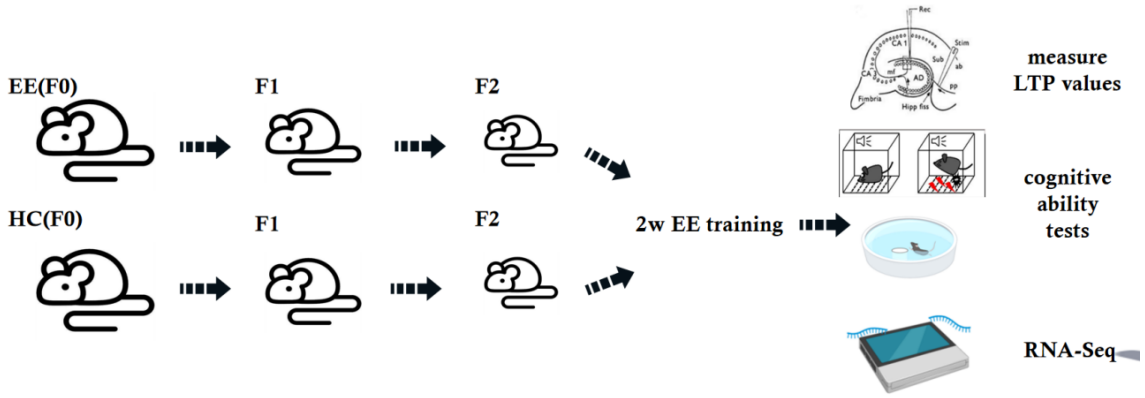

Figure 9: Experimental 2 workflow diagram

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Predicted Results:

If the offspring of EE mice (F2 generation) exhibit significantly enhanced LTP levels and cognitive abilities compared to the HC mice, it would demonstrate that EE training can lead to similar traits in the F2 generation with minimal EE stimulation, indicating that the enhanced synaptic plasticity and cognitive abilities observed after EE training do indeed exhibit transgenerational inheritance, albeit progressively weaker in each successive generation.

By comparing the differences in RNA expression levels between F2 generation mice from the EE and HC groups, potential RNA molecules that mediate the enhanced synaptic plasticity and cognitive abilities in the F2 generation can be identified.

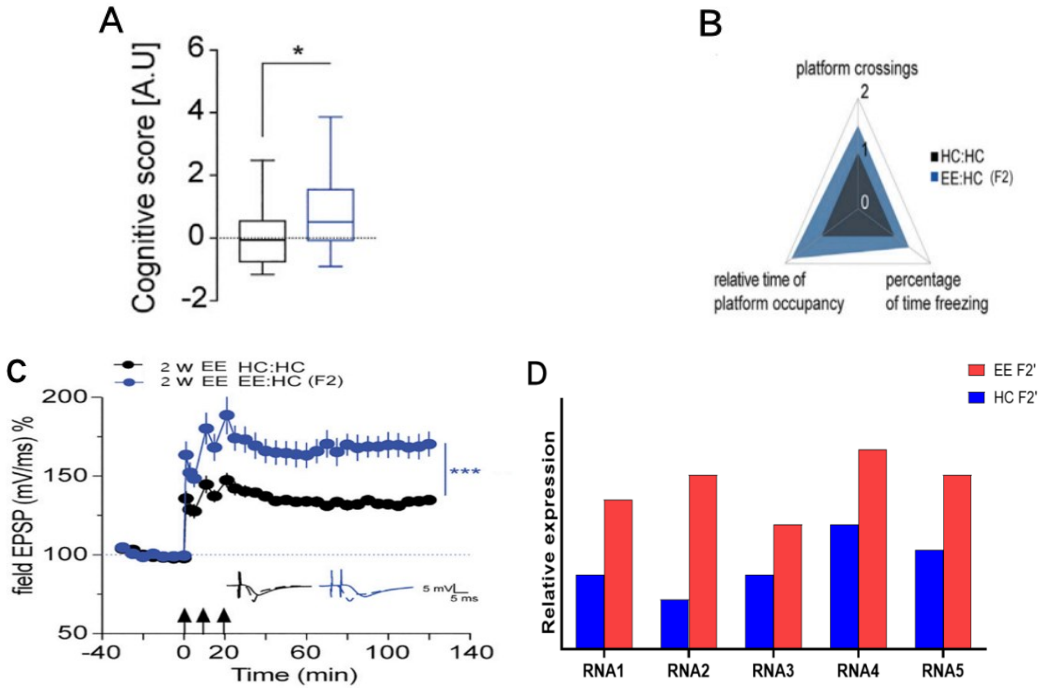

Figure 10: The enhancement of synaptic plasticity and cognitive ability following EE training exhibits transgenerational inheritance

(A) Compared to HC mice (F2 generation), The cognitive scores of the EE mice offspring (F2 generation) are significantly higher.

(B) This illustrates the magnitude of change in each individual parameter contributing to the cognitive scores.

(C) The LTP levels in the EE mice offspring (F2 generation) are increased compared to the HC mice (F2 generation).

(D) The RNA selected from Experiment 2, which is associated with the candidate RNAs from Experiment 1, shows a decrease in genetic expression with increasing generations and mediates the enhancement of synaptic plasticity and cognitive abilities after EE training. Five randomly selected RNA expressions are examined.

4.4. Experiment 3: verify whether the RNA in the F2 generation is inherited from the F1 generation

Experimental Procedure: Obtain EE male mice and HC male mice, crossbreed them to produce the F1 generation, and then use RNA-Seq technology to assess the expression levels of the five selected RNAs in the sperm and hippocampus of the F1 generation.

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Predicted Results: If the expression levels of the five RNAs are upregulated in the sperm and hippocampus of the EE mice, it would indicate that the RNAs in the F2 generation are indeed inherited from the F1 generation.

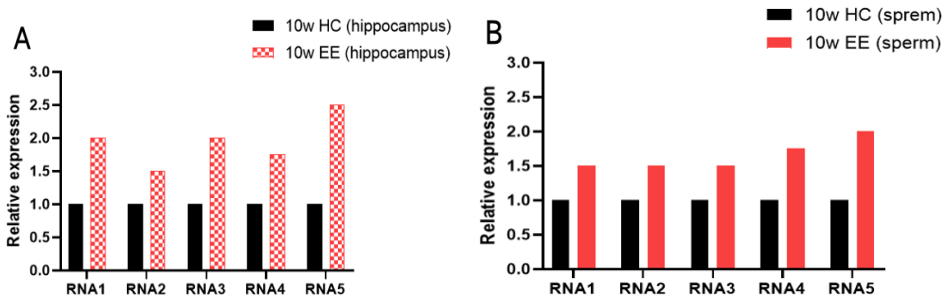

Figure 11: Increased expression levels of the five RNAs in sperm and hippocampus

(A) RNA-Seq of sperm from EE male mice (F1 generation) shows upregulation of the five RNAs compared to HC male mice.

(B) RNA-Seq of the hippocampus from EE male mice (F1 generation) also indicates upregulation of the five RNAs.

4.5. Experiment 4: validate the effect of selected RNAs on enhancing synaptic plasticity and cognitive function

Experimental Procedure: In this experiment, we will crossbreed EE and HC male mice while strictly controlling all experimental conditions. The experiment is divided into three main steps, each with specific treatment groups:

Group 1: Crossbreed EE male mice and process the F2 generation embryos to allow development. For these F2 embryos, we will inject only interference RNA to eliminate other potential confounding factors.

Group 2: Crossbreed EE male mice as well. After extracting the F2 embryos, we will inject each of the five different RNAs identified in the previous experiments. These RNAs will be injected sequentially, not mixed, into the F2 embryos to assess the independent effects of each RNA.

Group 3: Apply the same procedure to HC male mice. The F2 embryos from these mice will be injected with the five different RNAs, similar to Group 2. This group serves as a control to compare the effects of RNA injection on embryos from different types of mice.

After culturing the embryos to individuals, we will assess changes in their LTP levels and cognitive abilities, and compare the results across the three groups.

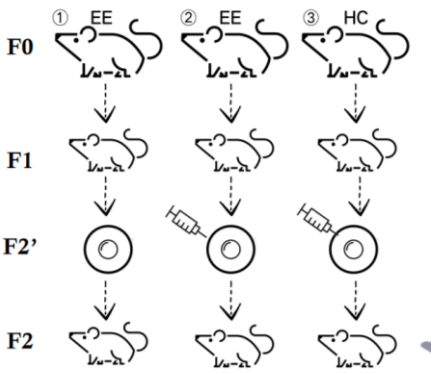

Figure 12: Experimental 4 workflow diagram

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Predicted Results:

By comparing the changes in LTP levels and cognitive abilities across Group 1, Group 2, and Group 3, if mice in Group 2 show enhanced LTP levels and cognitive abilities compared to those in Group 1 and Group 3, it would further confirm that synaptic plasticity and cognitive enhancement observed after EE training have transgenerational inheritance, albeit diminishing over generations. This effect would be mediated by sperm RNAs.

A comparison between Group 2 and Group 3 would allow us to conclude that the RNAs in Group 2 function similarly to RNA activators. Their presence enhances LTP levels and cognitive abilities in the F2 generation of EE mice, while HC mice, which have never undergone EE training, do not exhibit the same traits even when injected with these RNAs.ilities, and compare the results across the three group.

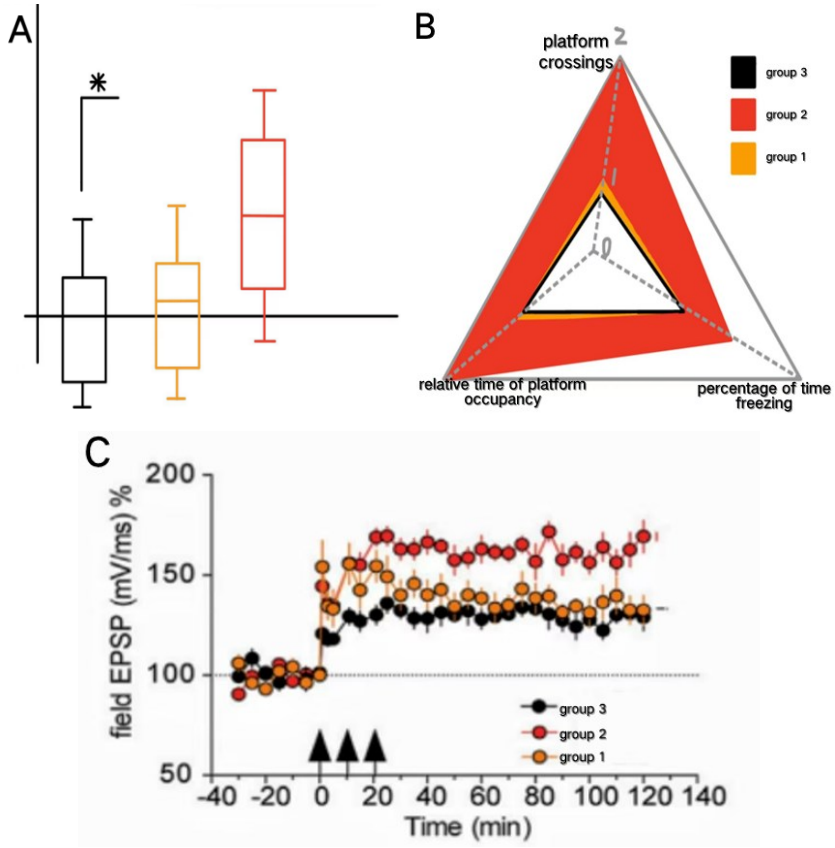

Figure 13: Five RNAs involved in the transgenerational inheritance of enhanced synaptic plasticity and cognitive abilities after EE training. Compared to Group 1 and Group 3, the F2 generation in Group 2 has higher cognitive scores (A)(B) and enhanced LTP levels (C)

4.6. Outline

Research Question: Is the enhancement of LTP levels and cognitive function in the offspring of mice that have undergone EE training considered transgenerational inheritance?

Hypothesis:

Transgenerational effect seems to weaken with each successive generation and may be mediated by sperm RNA.

Only a small amount of this trait was inherited by the F2 generation, either in its overt form or latently. However, the inherited amount was insufficient for the trait to be expressed.

Experimental Plan:

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The experiment will be divided into four main parts. To visually demonstrate the changes in RNA expression levels and distribution involved in the genetic process when EE training induces enhancement in LTP levels and cognitive function, we will use RNA sequencing technology multiple times throughout the study.

I. Experiment 1: Utilize RNA sequencing to measure RNA expression levels and distribution in HC mice (F0) and EE mice (F0, F1, F2). Identify RNAs whose expression levels gradually decrease with successive generations.

II. Experiment 2: Apply a small amount of EE stimulation to the F2 generation of HC and EE mice using a controlled variable approach. Measure and compare changes in LTP levels and cognitive function. Simultaneously, use RNA sequencing to detect RNA expression changes in these two groups of mice to identify RNAs whose expression significantly increases following EE training.

III. Experiment 3: Use RNA sequencing to measure the expression levels of the selected RNAs in the sperm and hippocampus of HC (F1) and EE (F1) mice to verify whether the RNA identified in EE mice (F2) is inherited from F1.

IV. Experiment 4: Based on the findings from the first two experiments, select RNAs that both decrease in expression with increasing generations and mediate the enhancement of synaptic plasticity and cognitive abilities following EE training. Perform embryo injection experiments to verify whether the selected RNAs can induce similar traits in EE-trained mice (F2) as observed in F1 mice when injected in small amounts.

5. Discussion

5.1. Contributions

The significance of studying memory genetics lies in uncovering how memory and learning abilities are transmitted through genetic mechanisms. Research in this area can help us understand several key points:

How memory genetics interacts with environmental factors.

How genes influence brain structure and function.

The identification of genetic variations associated with memory.

The explanation of individual differences in memory abilities and learning efficiency.

The contribution of memory genetics to understanding and developing treatment strategies for neurodegenerative diseases, such as Alzheimer's disease.

The insights into the changes in memory and learning abilities throughout the evolutionary process.

5.2. Limitations

First, there is a strong reliance on the experimental procedure: In Experiment 1, we used RNA Seq technology to detect and select RNAs whose expression levels decrease progressively with increasing generations. However, if we fail to successfully identify these RNAs, it would indicate that transgenerational inheritance of this phenomenon might not exist, potentially hindering subsequent experiments.

Second, the impact of inhibitory factors and other influences: In the process of memory regulation, there may be factors negatively correlated with memory modulation in addition to positive factors. This study only examined the effects of positive factors and did not delve into the role of these negative factors. Furthermore, the selected factors may include some that are not directly related to memory regulation, such as intermediate products.

Finally, the specific molecular mechanisms by which these factors affect the transgenerational inheritance of enhanced synaptic plasticity and cognitive abilities have not been thoroughly investigated. The overall experiment has not yet explored how specific factors regulate synaptic

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plasticity to enhance cognitive abilities and the mechanisms of these factors in transgenerational inheritance. In particular, the specific pathways and molecular basis of these factors in enhancing synaptic plasticity and cognitive abilities, as well as their genetic transmission, remain unclear.

6. Conclusions

Enriched environment (EE) training can directly enhance mice's cognitive abilities and synaptic plasticity, and this effect is heritable but weakens with each generation.

Through the above experiments, researchers can identify key RNA molecules that affect synaptic plasticity and cognitive abilities.

After EE training, comparing the two groups of mice reveals a small amount of genetic inheritance.The selected RNA is similar to substances like RNA activators. Their addition can only enhance the LTP levels and cognitive abilities of the offspring of the EE mice.

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