International Core Journal of Engineering Volume 7 Issue 3, 2021
ISSN: 2414-1895 DOI: 10.6919/ICJE.202103_7(3).0064

The Effects of Arc Gene Mutation on LTP: Synaptic Plasticity

Evan J Wang

High School Affiliated to Renmin University of China, Beijing, 100080, China.

Abstract

Purpose: This study investigates the effects of Arc gene mutation on Arc's functions, including LTP modification and capsid forming. A mutated Arc gene will be introduced into the cell to replace the wild type Arc gene. The sequence in the Arc gene that codes for capsid forming will be tested by analogy between Arc and retrovirus. The effects of the mutation on synaptic plasticity and long-term potentiation (LTP) will be tested with experiments that associate LTP with electronic shock on rats. There are two possible results: (1) The mutation in the Arc gene will affect the formation of the Arc capsid and the intracellular transportation of the Arc mRNA leading to effects on LTP and LTD. (2) The mutation on the Arc gene will not affect plasticity LTP. Mutation of the Arc gene may interfere with the Arc-GAG interaction and thus prevent the formation of the capsid. Consequently, intercellular transportation, plasticity LTP, and LTD will be affected.

Keywords

Arc Gene; Capsids; Mutation; Synaptic Plasticity; LTP.

1. Introduction

Arc is an RNA sequence embedded in human genome. It is translated into a synaptic protein which, in cooperation with Arc RNA, facilitates the consolidation of long-term memory and synaptic plasticity (Pastuzyn [1], 2017; Erlendsson[2], 2020)

Mutations in the Arc gene might affect the formation of capsids or its function of packing the Arc mRNA. The consequence of these effects is prevention of Arc from traveling from one neuron to another, such that increased Arc expression that occurs when there is stimulation to produce LTP will be confined to the cell in which Arc expression is increased (the presynaptic neuron). Any effect that normally occurs as a consequence of Arc capsid transferring Arc mRNA to the postsynaptic neuron will not occur. This could mean changes to the cytoskeleton in the axon terminus, since Arc regulates the actin cytoskeleton. (De Guzman[3], 1998)

This experiment aims to illustrate the importance of the Arc transfer in LTP. If Arc transfer is required for LTP (or at least if LTP is reduced), it suggests that the transfer process plays an important functional role in memory.

2. Methods

2.1 Gene regulation

To control level of mutated Arc production and enable different experiments, a promoter and a regulatory sequence will be inserted before the mutated sequence. The mutated gene can be turned on and off by injecting specific type of chemical into the cell.

2.2 Designing a mutation

First, delete the whole loop sequence of the Arc gene;

ISSN: 2414-1895 DOI: 10.6919/ICJE.202103_7(3).0064

Then modify RNA sequence, deform and unstabilize the loop, making sure there's no other possible structure that can lead to NMR. Use GFP(Green Florescent Protein) or Florescent Chemical to GAG protein as mutation indicators;

After that, deliver the gene into mice embryo cells using plasmid or viral vectors;

Finally, carry out immunofluorescent assay to ensure the mutated gene has been integrated into the genome.

2.3 Qualitative experiment

Three groups of sample will be used:

Wild type nerve cells with florescence attached (Figure1 A);

Nerve cells with mutated Arc gene attached with florescence (Figure1 B);

Wild type nerve cells without florescence attached. (Figure1 C)

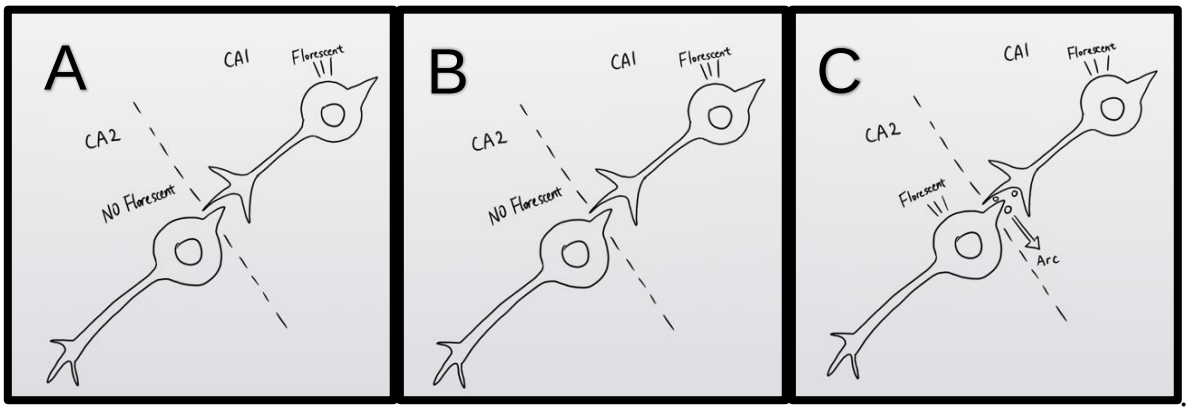

Figure1.Experimental groups used in the qualitative experiment

2.4 Quantitative experiment

First attach Stem Loop structures to another type of mRNA sequence in wild type cells;

Then apply RNA-ase to break down all the mRNA in cytoplasm so only mRNA in Arc-capsid would be left;

Finally, use qPCR to analyze the RNA in the extract of neurons, check the mRNA sequence.

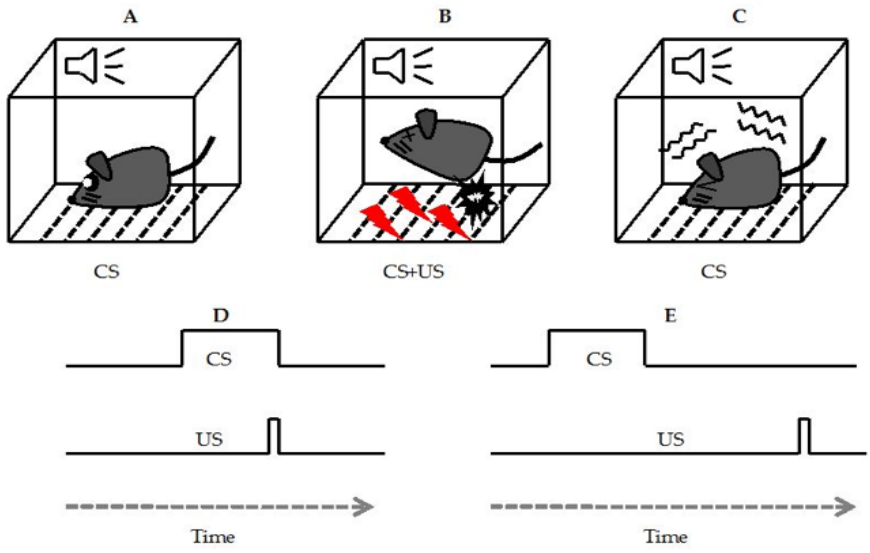

Figure 2. Fear Conditioning experiment

ISSN: 2414-1895 DOI: 10.6919/ICJE.202103_7(3).0064

2.5 Associated learning experiment, fear conditioning

Two groups of rats with similar intelligence and body weight will be used. The control group of rats has no mutation, while the experimental group has the mutated gene introduced into the genome;

The rats are given an electric shock (Figure2 B) short after the appearance of an auditory signal (Figure2 A).

The auditory signal and the electric shock can be associated and LTP can be formed in this experiment. So that the rat should freeze as it hear the sound (Figure2 C).

The degree of learning can be recorded by measuring the freezing time. (Figure2 D, Figure2 E).

3. Results

3.1 Possible result 1: The mutation in the Arc gene did not affect capsid formation nor plasticity LTP

The mutation in the Arc gene is a silent mutation. The mutated part of the gene does not code for capsids and is not involved in the function of forming plasticity LTP.

The rats in the experimental group responded to the stimuli the same way as those in the control group.

3.2 Possible result 2: The mutation in the Arc gene did not affect capsid formation but slowed down the formation of synaptic plasticity

The mutation in the Arc sequence slows the formation of LTP but does not affect capsid forming and protein attaching.

The mutated part in the sequence is involved in the formation of plasticity LTP, by affecting either the packing of Arc mRNA into the capsid or the release of Arc mRNA in the recipient cell.

The formation of LTP in rats of the experimental group took a longer time than those in the control group.

3.3 Possible result 3: The mutation in the Arc gene prevented capsid formation and blocked Arc intracellular activities and was no longer involved in the formation of plasticity LTP

The mutated part of the Arc gene is responsible for capsid formation. The mutation caused a malfunction in protein synthesis or folding, making the capsid unable to form or function properly.

Without the capsids the Arc mRNA cannot accomplish intracellular activities and will not be able to help with LTP formation nor synaptic plasticity modification.

The rats in the experimental group werel not able to form LTP as quick as those in the control group. It took a considerable extra amount of time for rats in the experimental group to build the association between shocking and visual signal.

4. Conclusions

This study investigates on the effects of mutation in the Arc gene on Arc's function, including LTP modification and synaptic plasticity. The Arc gene regulates plasticity LTP by forming capsids that is packed with Arc mRNAs. Mutation in the Arc gene couldresult in deficiencies in capsid formation and intracellular communication.

By conducting these experiments, we successfully introduced the mutation in the Arc gene and was able to control their expression through translation control. We also tested the presence of capsids by attaching GFP and analyzed the RNA in the extract of neurons.

The results suggest the relationship between mutation in the Arc gene and capsid formation and Arc intracellular activity. This study adds new body of evidence to the important role the Arc gene in the human genome plays. Future research may reveal additional functions played by the Arc gene.

ISSN: 2414-1895 DOI: 10.6919/ICJE.202103_7(3).0064

References

[1] Pastuzyn, et al, 2018, The neuronal gene arc encodes a repurposed retrotransposon Gag protein that mediates intercellular RNA transfer. Cell 172: 275–288

[2] Erlendsson et al, 2020, Structures of virus-like capsids formed by the Drosophila neuronal Arc proteins. Nat Neuroscience 23:172-175.

[3] De Guzman, 1998, Structure of the HIV-1 nucleocapsid protein bound to the SL-3 psi-RNA recognition element. Science 279:384-388.