

Unitized representation of paired objects in area 35 of the macaque perirhinal cortex

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INTRODUCTION

The **perirhinal cortex (PRh)** is a critical area for development for long-term stimulus-stimulus associative memory. It contains two distinct divisions - Area 35 and Area 36.

Previous methods for localization of the electrodes in the inferior temporal cortex hence lacked precision in targeting A35, hence targeting single unit activity in A35 has never been done before.

This study aims to utilise a novel MRI and histological approach to identify if A35 neurons could play a role in abstracting a unitized representation from multiple behaviorally-related visual objects through long-term memory. As shown in Fig 1.

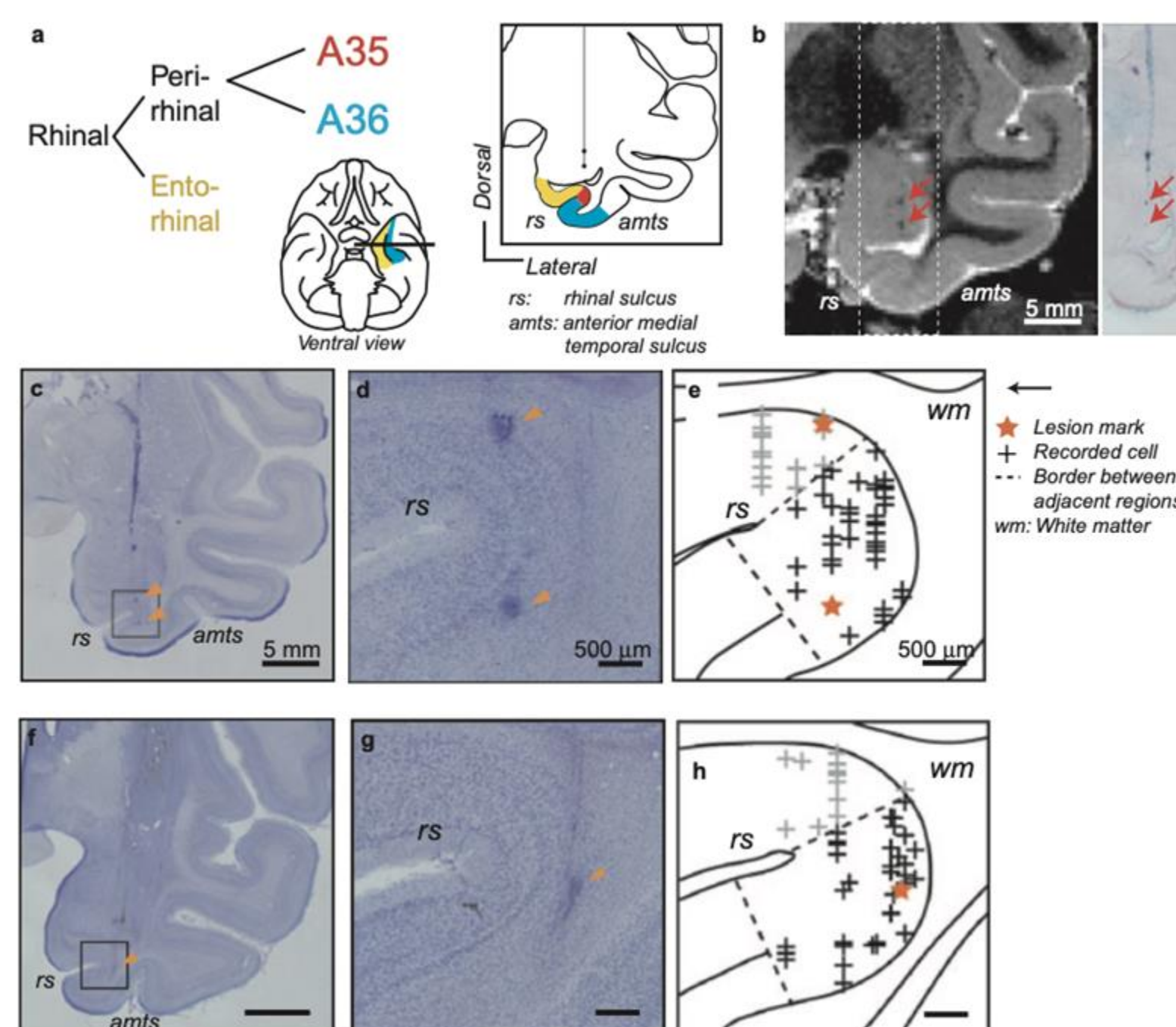


Figure 1. Targeting A35 using diagrammatic representation (a), MRI (b), Nissl-stained section containing electrolytic lesions (arrowheads) (c-d), (f-g) and their corresponding reconstructed recording sites in the coronal plane (e), (f).

MATERIALS AND METHODS

Subjects and surgery: MR-compatible head holder and chamber was implanted into the skulls of two adult monkeys for microelectrode recording

Pair-association (PA) task. 16 descriptors with geometrically distinct patterns were sorted into eight pairs. Two monkeys were trained to memorise them through repeated trials before microelectrode recording. As shown in **Figure 2**.

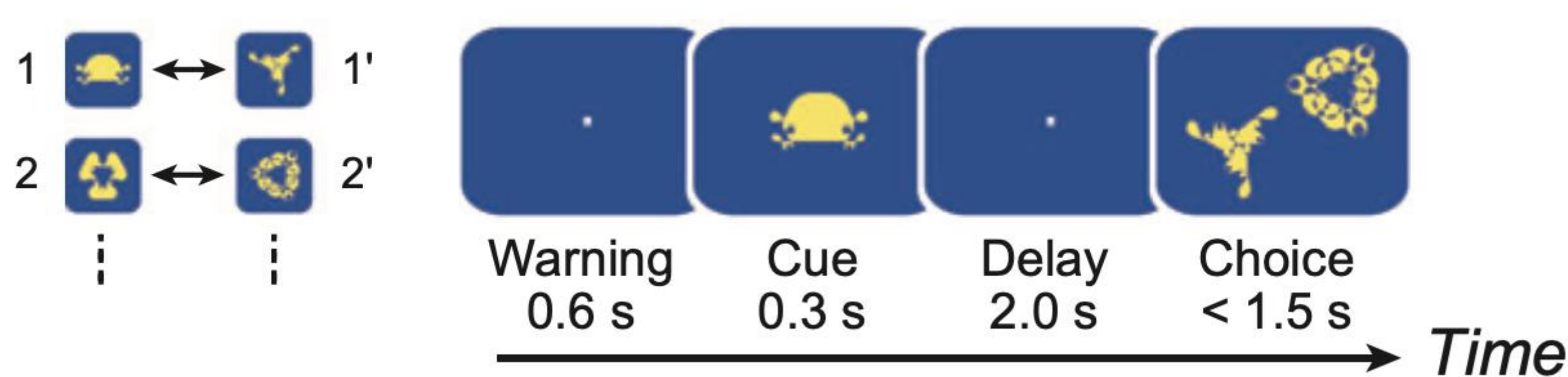


Fig. 2. Pair Association task. In each trial a cue stimulus was presented, after which two choice stimuli, i.e. the paired associate of the cue stimulus (target) and a stimulus from a different pair (distractor), were sequentially presented with a delay of 2 s

Targeting A35: Approach 1 involved placing MRI-detectable markers above the fundus of the rhinal sulcus and using MRI to determine the coordinates of A35. Approach 2 involved passing a current through the microelectrodes, creating electrolytic lesions to identify the microelectrode position. The MRI images were then correlated with the coronal sections on histology.

Data collected regarding A35 response to “Primary Pair” and “Other Pairs” was analysed.

“Cue response” is firing rate during the period extending from 70 to 370 ms after cue onset. The firing rate during the last 1 s of the delay interval was measured as the delay activity.

Receiver operating characteristic (ROC) analysis was then conducted to estimate their ability to discriminate within the primary pair.

Pair-coding index (PCI) calculation. Essentially, if a single neuron in a population showed a pattern of stimulus selectivity that was independent of the stimulus pairs, the mean value of the PCI for the neuronal population should approach 0.

Area under ROC curve (AUC) was then computed to measure the separation of responses to the two stimuli.

A36 data from 3 other monkeys were then analysed and compared to A35 neuron activity.

RESULTS

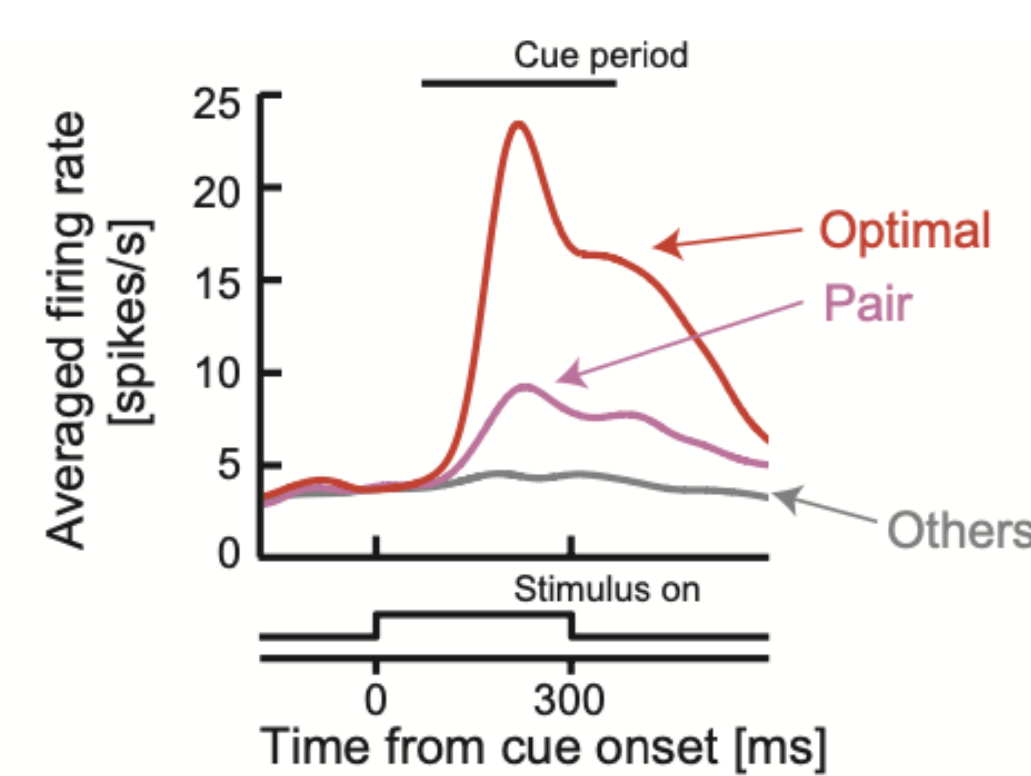


Fig. 4 Electrical activity of specific neurons are elevated for both the cue stimulus and its paired associate

Specific neurons exhibit an elevated response to both stimuli, but an increase of much greater proportion is observed when the cue stimulus is presented compared to its paired associate as shown in **Figure 4**.

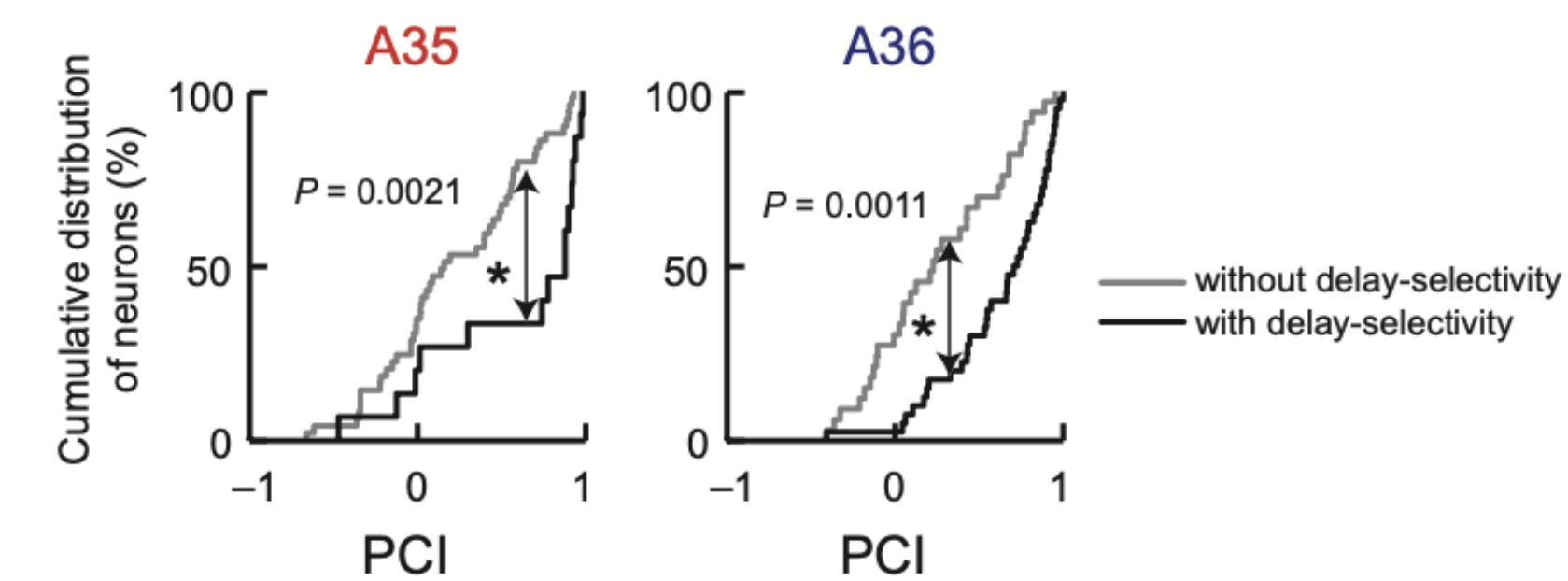


Fig. 5 Cumulative plot of PCI values in the cue-selective neurons showing delay selectivity and those without delay selectivity.

In both A35 and A36 at a population level, neurons with delay selectivity have a higher PCI than those without, as shown in **Figure 5**.

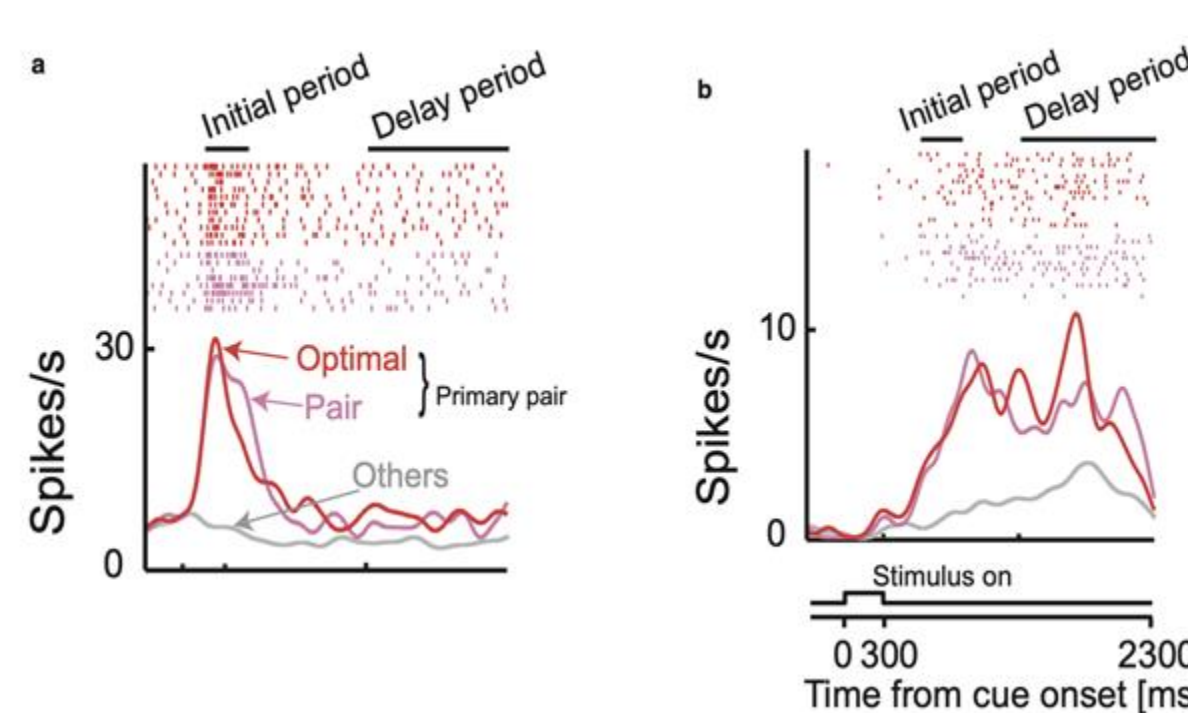


Fig. 6a, 6b. Stimulus-selective responses elicited by paired associates in two representative A35 neurons.

Figure 6a shows a selected A35 neuron that was stimulated at the start and exhibited consistent elevated activity in the delay period.

Figure 6b shows another selected A35 neuron firing late but also exhibiting elevated activity in delay period. Hence, analysis of specific neurons in A35 consistently demonstrate elevated activity during the delay period

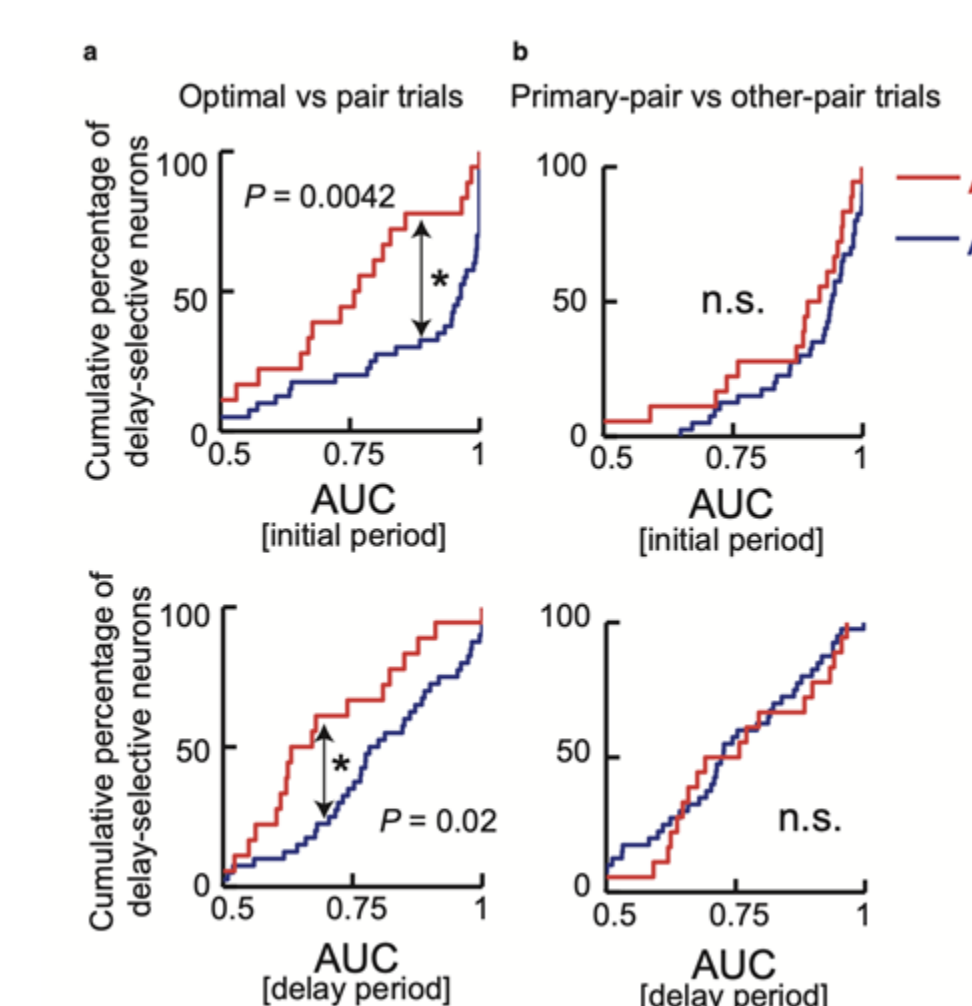


Fig. 7a and 7b compares the Area Under Curve (AUC) between A35 and A36.

In **Figure 7a**, A36 shows a right shift indicating that a higher proportion of A36 neurons exhibit discriminatory activity between the stimulus and the pair.

Figure 7b demonstrates how A35 and A36 are equally good at discriminating between the correct pair (primary pair) and other pairs. Hence both are important for paired association and forming long term memory

DISCUSSION

This study used a novel, two-track approach of MRI-guided in vivo localization with histological validation (fig. 1), thereby overcoming technical challenges posed by its narrow structure.

This study showed that delay-selective neurons in A35 exhibited unitized responses, treating paired stimuli as a single cohesive item (Fig. 4). On the other hand, A36 neurons discriminated between the items within a pair (Fig. 7a). Nevertheless, both areas still maintained their selectivity across the different pairs (Fig. 7b).

This could possibly indicate a form of **hierarchical organization** within the macaque perirhinal cortex, whereby A35 supports abstract and unified memory representations while A36 processes the more detailed associations, as shown in Fig. 8.

CONCLUSION AND FUTURE WORKS

In conclusion, delay-selective neurons in A35 represent paired stimuli as a single unitized item rather than two associated items like in A36.

In the future, conducting further lesion studies with more technological advancements may reveal further functional differentiation between A35 and A36 in the perirhinal cortex.