

Young adult APOE-e4 carriers show different patterns of neural activity during a subsequent memory task

Evans SL¹, Dowell NG², Tabet N², King SL¹, Hutton S¹, Rusted JM¹



¹ School of Psychology, University of Sussex, Brighton BN1 9QG, UK

² Brighton and Sussex Medical School, Brighton BN1 9RR, UK



Introduction

- The APOE e4 allele is a well-established genetic risk factor for sporadic Alzheimer's disease (AD).
- e4 carriers (e4+) have a 4-fold increased risk of developing AD relative to non-e4 carriers (e4-).
- e4+ also affects healthy ageing: e4+ show greater declines in cognitive performance with age (Caselli et al., 2009).
- Studies have also looked for brain activation differences in e4+, at young adulthood.
- Functional imaging (fMRI) studies have shown that young adult e4+ activate their medial temporal lobe (MTL) more strongly. The MTL supports memory formation. e4+ show greater MTL activity, during both memory tasks and other tasks which shouldn't activate the MTL at all (Trachtenberg et al., 2012; Rusted et al., 2013).
- Could young adult e4+ be 'working' their brains harder, which leads to problems later in life?
- Could this mean they are exerting greater cognitive 'effort' (although performance tends to be similar)?

Aims

- To show MTL overactivity in young adult e4+ during a memory task.
- To measure pupil diameter as an index of 'cognitive effort'.

Methods and task

- Task completed in brain scanner (fMRI, 1.5T) while eyetracker measured pupil diameter.
- 'Acquisition' phase: 100 words presented serially; (1 sec/word); make button press to profession words (8/100).
- Surprise 'recall' phase (35 min delay): 100 'old' words plus 80 'new' words; button press for old/new decision.
- Contrast brain activation patterns at acquisition for words subsequently remembered/forgotten.

Participants

- 26 e4- and 28 e4+ recruited (age 18-28)
- All participants performed with high accuracy at acquisition (95%).
- Exclude participants who scored <50% on 'old words' (7 e4+, 7 e4-)

Group	Age (years)	Gender
e4- (n=26)	20.9 ± 1.90	14F/12M
e4+ (n=28)	20.9 ± 2.59	19F/9M
t-statistic	0.44, ns	

Table 1. Volunteer characteristics

Results

- Recall performance: no genotype differences (see Table 2).
- fMRI: Compare brain activity to words later remembered (R) vs. forgotten (F).
- Activation in all participants in temporal lobe (adjacent to MTL, see Fig. 1a).
- Only e4+ showed greater activity to remembered words within MTL (Fig. 1b)

Group	'Old' p.c.	'New' p.c.
e4-	61 ± 10	75 ± 12
e4+	60 ± 11	76 ± 11

Table 2. Performance during recall phase (% correct)

Fig. 1a. Greater activity in middle temporal lobe to remembered items

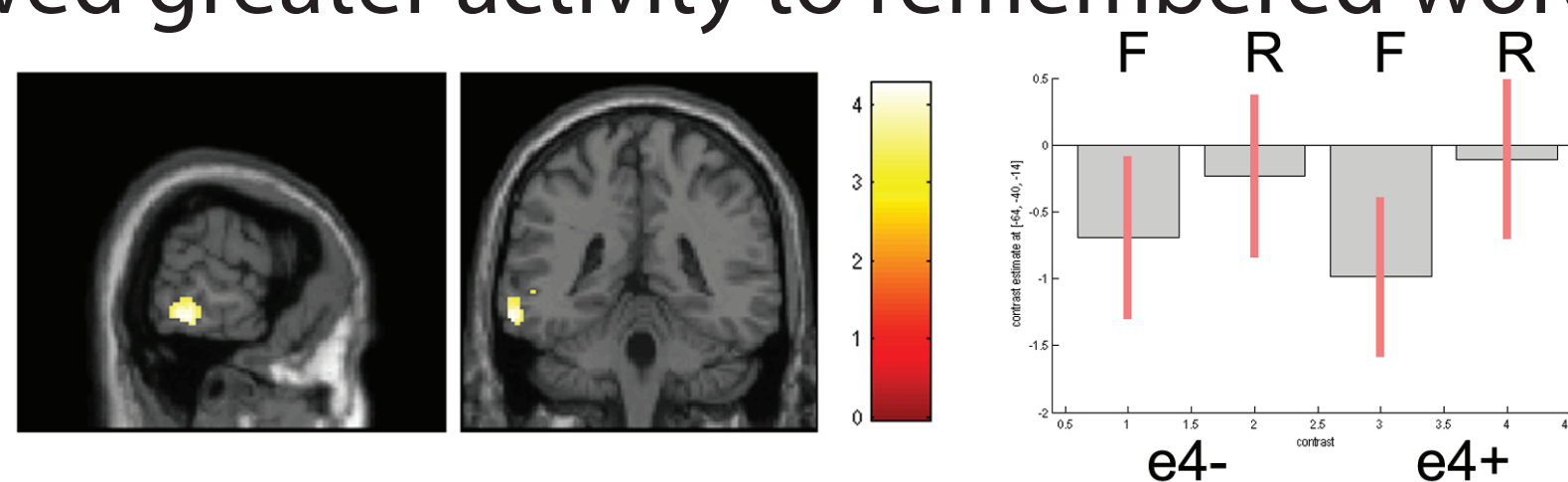
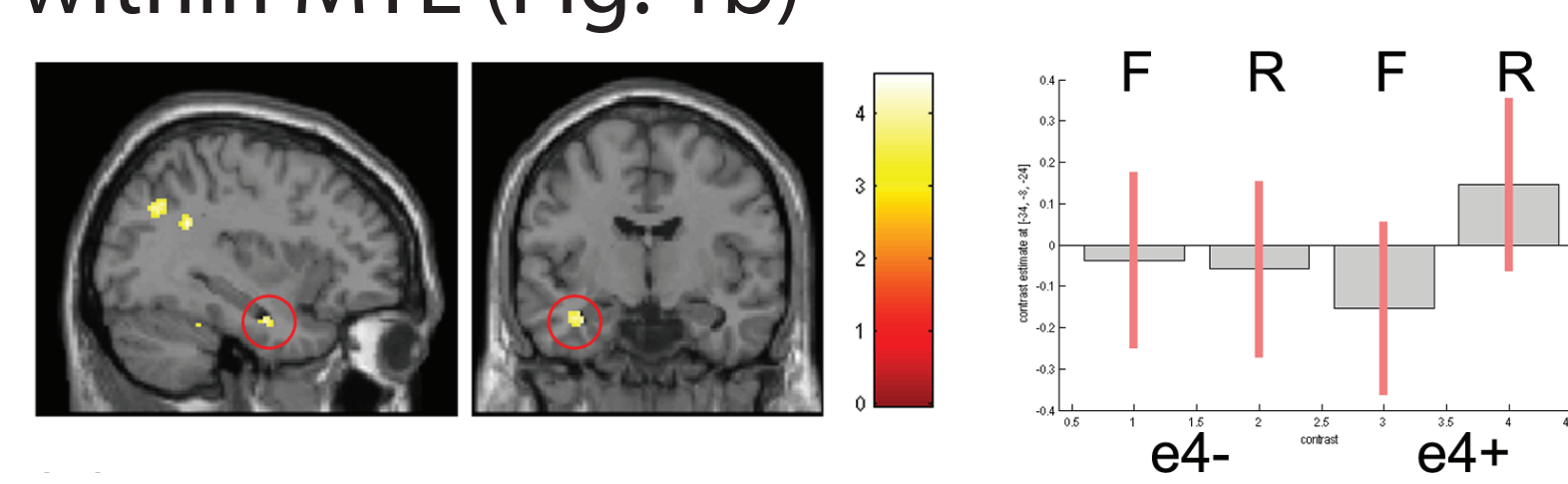


Fig. 1b. Greater hippocampal activity to remembered items in e4+



- Pupillometry: e4+ fail to show the normal increase in pupil diameter to remembered words.
- How does this relate to brain activity? Examine correlation patterns between pupillometry and fMRI data.
- Common patterns between e4+ and e4- in visual areas (Fig. 2a), differential patterns in parietal lobe (Fig. 2b)

Fig. 2a. Pupil diameter correlates with brain activity in visual cortex, in all participants

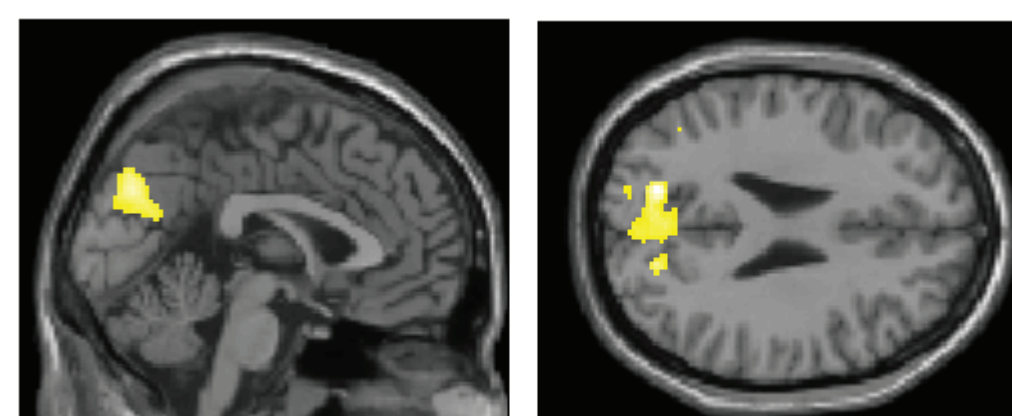
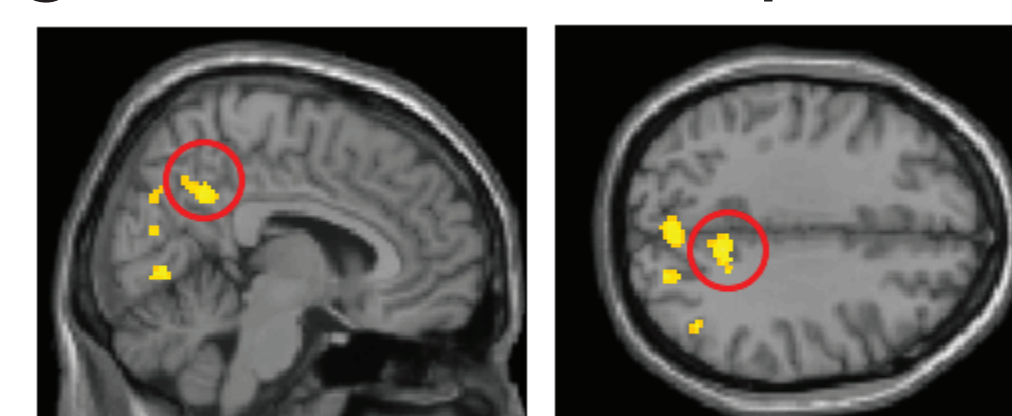


Fig. 2b. e4- show a negative correlation between brain activity and pupil diameter in parietal lobe (precuneus)



Discussion

- In line with previous findings, e4+ showed greater MTL activity to remembered items in a memory task.
- Pupillometry measures showed an unusual pattern in e4+ with no link between cognitive effort and recall.
- In e4+, enhanced MTL activity was observed, but e4+ did not show the normal pattern of downregulation in precuneus (usually indicating deactivation of the default mode network).
- This activation pattern is reminiscent of that seen in the early stages of MCI, thought to reflect inefficient cognitive processing, and predictive of subsequent cognitive decline.