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Gene variant leads to better memory via increased brain activation

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Carriers of the so-called KIBRA T allele have better memories than those who don't have this gene variant. This means we can reject the theory that the brain of a non-bearer compensates for this. This is shown by researchers from Umea University in The *Journal of Neuroscience*.

In this study, KIBRA was first examined in relation to the memory performance of a group of 2,230 subjects. Just as in previous studies, carriers of the KIBRA T allele performed better than non-carriers. Then the brain activity of 83 subjects was studied with the help of fMRI. In contrast with the earlier study, higher activation of the hippocampus was observed in T carriers than in non-carriers.

Thanks to the large number of subjects in the study, the effect could also be studied in a group in which T carriers performed better (83 individuals) and in a subgroup in which the memory performance was equal between T carriers and non-carriers (63). This is especially important as differences in memory performance are regarded to be of significance in how to interpret differences in brain activation. However, in both cases, T carriers had increased hippocampus activation, which means that the effect of KIBRA on brain activation as such is not dependent on the difference in memory performance but is of importance for memory performance.

The conclusion must be that there is no support for the previous theory regarding compensatory mechanisms in non-carriers of the T allele. Instead the new findings indicate that the KIBRA gene plays a role in

memory by improving the hippocampus function in carriers of the T allele.

In a study published in *Science* in 2006 the entire genome was screened (in a so-called Genome-wide association study) for genetic variations of importance to episodic memory (Papassotiropoulos et al., 2006). Individuals who carried the T allele (CT or TT genotype) in a common C/T polymorphism in the KIBRA gene had better episodic memory than non-carriers of the T allele (CC genotype). In the same study, brain activity was examined during a memory task in 30 subjects with the help of a magnetic camera (fMRI). It was found that non-carriers of the T allele had greater activation of the hippocampus, an area in the brain that is important for episodic memory, than did T carriers.

Since the groups had the same memory performance, the results were explained as indicating that non-carriers needed to compensate for their poorer memory function with increased activation of the hippocampus in order to reach the same level of performance as T carriers. Increased activation in the hippocampus is strongly associated with positive aspects of the memory function, and with other genes related to memory the opposite has been observed: increased hippocampus activation in carriers of a gene variant that is associated with better memory (e.g. Hariri et al., 2003). In those cases a reasonable explanation has been that the gene is important for memory via a favorable effect on the hippocampus function.

Improved memory performance in carriers of the KIBRA T allele has been verified in several subsequent studies (e.g. Bates et. al., 2009, Preuschhof et al., 2010), but since the 2006 *Science* article, this is the first to study KIBRA in relation to brain activation.

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