Healthy aging attenuates task-related specialization in the human medial temporal lobe

Recent research on aging has established important links between the neurobiology of normal aging and age-related decline in episodic memory, yet the exact nature of this relationship is still unknown. Functional neuroimaging of regions such as the medial temporal lobe (MTL) have produced conflicting findings. Using functional magnetic resonance imaging (fMRI), we have recently shown that young healthy individuals show a stronger activation of the MTL during encoding of objects as compared with encoding of positions. Using the same encoding task, the present study addressed the question whether this greater MTL activation during encoding of objects varies with age. Fifty-four healthy individuals aged between 18 and 81 years underwent functional magnetic resonance imaging while they encoded and subsequently made new-old judgments on objects and positions. Region of interest (ROI) analysis of task related changes in the blood oxygen level-dependent (BOLD) signal was performed in native space after correction for gender effects and individual differences in cerebral blood flow. The hippocampus, amygdala, and parahippocampal, perirhinal, entorhinal, and temporopolar cortices of right and left hemisphere were defined as ROIs. Aging had an adverse effect on memory performance that was similar for memorizing objects or positions. In left and right MTL, relatively greater activation for object stimuli was attenuated in older individuals. Age-related attenuation in content specificity was most prominent in the recognition stage. During recognition, the larger response to objects gradually decreased with age in all ROIs apart from left temporopolar and entorhinal cortex. An age-related attenuation was also present during encoding, but only in right parahippocampus and amygdala. Our results suggest that memory-related processing in the MTL becomes gradually less sensitive to content during normal aging.
Aging, Episodic memory, Encoding, Specialization, Recognition, Neural specificity, Working memory

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**Longitudinal MRI studies of brain morphometry**

High resolution MR images acquired at multiple time points of the brain allow quantification of localized changes induced by external factors such as maturation, ageing or disease progression/recovery. High-dimensional warping of such MR images incorporates changes induced by external factors into the accompanying deformation field. Deformation fields from high dimensional warping founds tensor based morphometry (TBM), and provides unique opportunities to study human brain morphology and plasticity. In this thesis, specially adapted image processing streams utilizing several image registration techniques to characterize differences between brains, demonstrate the versatility and specificity of the employed voxel-wise morphometric methods. More specifically TBM is used to study neurodegenerative changes following severe traumatic brain injuries. Such injuries progress for months, perhaps even years postinjury. Little information is known about the spatial distribution and the clinical significance of this late atrophy. TBM revealed a large coherent cluster of significant atrophy consisting of the brain stem and cerebellar peduncles extending bilaterally through the thalamus, internal and external capsules, putamen, inferior and superior longitudinal fasciculus, corpus callosum and corona radiata. This indicates that the long-term atrophy is attributable to consequences of traumatic axonal injury.
Despite progressive atrophy, remarkable clinical improvement occurred in most patients. The other study utilized TBM and voxel based morphometry (VBM) in two separate papers concerning antipsychotic-naïve first episode schizophrenia. Volume reductions of hippocampal and caudate regions were found in patients compared to controls using VBM. Six months later, TBM revealed continued volume loss in striatum and hippocampus, despite treatment with quetiapine. The mechanisms underlying these progressive brain dynamics, specific antipsychotic compounds and clinical symptoms warrant further clarification.

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Response inhibition is associated with white matter microstructure in children
Cognitive control of thoughts, actions and emotions is important for normal behaviour and the development of such control continues throughout childhood and adolescence. Several lines of evidence suggest that response inhibition is primarily mediated by a right-lateralized network involving inferior frontal gyrus (IFG), presupplementary motor cortex (preSMA), and subthalamic nucleus. Though the brain's fibre tracts are known to develop during childhood, little is known about how fibre tract development within this network relates to developing behavioural control. Here we examined the relationship between response inhibition, as measured with the stop-signal task, and indices of regional white matter microstructure in typically-developing children. We hypothesized that better response inhibition performance would be associated with higher fractional anisotropy (FA) in fibre tracts within right IFG and preSMA after controlling for age. Mean FA and diffusivity values were extracted from right and left IFG and preSMA. As hypothesized, faster response inhibition was significantly associated with higher FA and lower perpendicular diffusivity in both the right IFG and the right preSMA, possibly reflecting faster speed of neural conduction within more densely packed or better myelinated fibre tracts. Moreover, both of these effects remained significant after controlling for age and whole brain estimates of these DTI parameters. Interestingly, right IFG and preSMA FA contributed additively to the prediction of performance variability. Observed associations may be related to variation in phase of maturation, to activity-dependent alterations in the network subserving response inhibition, or to stable individual differences in underlying neural system connectivity. (C) 2009 Elsevier Ltd. All rights reserved.
Segmentation by Large Scale Hypothesis Testing - Segmentation as Outlier Detection

We propose a novel and efficient way of performing local image segmentation. For many applications a threshold of pixel intensities is sufficient but to determine the appropriate threshold value can be difficult. In cases with large global intensity variation the threshold value has to be adapted locally. We propose a method based on large scale hypothesis testing with a consistent method for selecting an appropriate threshold for the given data. By estimating the background distribution we characterize the segment of interest as a set of outliers with a certain probability based on the estimated densities thus with what certainty the segmented object is not a part of the background. Because the method relies on local information it is very robust to changes in lighting conditions and shadowing effects. The method is applied to endoscopic images of small particles submerged in fluid captured through a microscope and we show how the method can handle transparent particles with significant glare point. The method generalizes to other problems. This is illustrated by applying the method to camera calibration images and MRI of the midsagittal plane for gray and white matter separation and segmentation of the corpus callosum. Comparing the methods corpus callosum segmentation to manual segmentation an average dice score of 0.86 is obtained over 40 images.

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From ecstasy to agony: chronic effects of MDMA use on emotional processing

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Gradient non-linearity correction relocates normalized group activation hotspot

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Long-term global and regional brain volume changes following severe traumatic brain injury: A longitudinal study with clinical correlates

Traumatic brain injury (TBI) results in neurodegenerative changes that progress for months, perhaps even years post-injury. However, there is little information on the spatial distribution and the clinical significance of this late atrophy. In 24 patients who had sustained severe TBI we acquired 3D T1-weighted MRIs about 8 weeks and 12 months post-injury. For comparison, 14 healthy controls with similar distribution of age, gender and education were scanned with a similar time interval. For each subject, longitudinal atrophy was estimated using SIENA, and atrophy occurring before the first scan time point using SIENAX. Regional distribution of atrophy was evaluated using tensor-based morphometry (TBM). At the first scan time point, brain parenchymal volume was reduced by mean 8.4% in patients as compared to controls. During the scan interval, patients exhibited continued atrophy with percent brain volume change (%BVC) ranging between −0.6% and −9.4% (mean −4.0%). %BVC correlated significantly with injury severity, functional status at both scans, and with 1-year outcome. Moreover, %BVC improved prediction of long-term functional status over and above what could be predicted using functional status at not, vert, similar 8 weeks. In patients as compared to controls, TBM (permutation test, FDR 0.05) revealed a large coherent cluster of significant atrophy in the brain stem and cerebellar peduncles extending bilaterally through the thalamus, internal and external capsules, putamen, inferior and superior longitudinal fasciculus, corpus callosum and corona radiata. This indicates that the long-term atrophy is attributable to consequences of traumatic axonal injury. Despite progressive atrophy, remarkable clinical improvement occurred in most patients.
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Long-term regional atrophy and association with clinical outcome following severe traumatic brain injury: A tensor based morphometry study

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Regional activation of the human medial temporal lobe during intentional encoding of objects and positions

The medial temporal lobe (MTL) consists of several regions thought to be involved in learning and memory. However, the degree of functional specialization among these regions remains unclear. Previous studies have demonstrated effects of both content and processing stage, but findings have been inconsistent. In particular, studies have suggested that the perirhinal cortex is more involved in object processing than spatial processing, while other regions such as the parahippocampal cortex have been implicated in spatial processing. In this study, functional magnetic resonance imaging (fMRI) optimized for the MTL region was used to probe MTL activation during intentional encoding of object identities or positions. A region of interest analysis showed that object encoding evoked stronger activation than position encoding in bilateral perirhinal cortex, temporopolar cortex, parahippocampal cortex, hippocampus and amygdala. Results also indicate an unexpected significant correlation in activation level between anterior and posterior portions in both the left parahippocampal cortex and left hippocampus. Exploratory analysis did not show any regional content effects during preparation and rehearsal stages. These results provide additional evidence for functional specialization within the MTL, but were less clear regarding the specific nature of content specificity in these regions. (C) 2009 Elsevier Inc. All rights reserved.
The effects of age on functional specialization in the human medial temporal lobe

Recent advances in the cognitive neuroscience of ageing have uncovered important links between age-related neurobiological changes and their role in cognitive and behavioural changes. However, the exact nature of this relationship is still unresolved, and studies of regions such as the medial temporal lobe (MTL) have produced conflicting findings. Here, we report the results from a functional Magnetic Resonance Imaging (fMRI) study of the effect of age on functional specialization in the MTL region during intentional encoding and recognition of objects and positions. We applied a region of interest analysis in native space and corrected for the effects of gender and individual differences in cerebral blood flow. Behavioural results demonstrated that performance on both the object and position tasks declined equally with increasing age. Our fMRI results showed that during the encoding and recognition stage, increasing age was associated with a reduction in functional specialization in a number of MTL regions. These findings are discussed in light of theories of the effects of age on functional specialization in the brain.
Verbal fluency performance is associated with white matter microstructure in a left hemisphere network in children

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Coupled Shape Modeling of the Medial Temporal Lobe
Here we investigate how regions in the Medial Temporal Lobe (MTL) in a dataset consisting of 13 different people changes using a Principal Component Analysis (PCA). The regions investigated are the Temporopolar, Parahippocampal, Entorhinal, Hippocampal, Perirhinal and Amygdalar regions. The MTL is located fairly deep in the brain where the contrast is quite low, and region-boundaries can be difficult to find, which is why a shape guiding term would be helpful for a segmentation algorithm. An expert used an interactive tool to draw binary (1 inside and 0 outside) Volumes Of Interests (VOI) for each of the 13 subjects. As the brain is symmetric, 12 VOIs has been drawn for each subject. A simultaneous multi-shape rigid registration scheme, similar to the one used in [Tsai et al., 2004] was used on the training shapes to remove linearties. As these are binary shapes, a set-difference cost function is minimized between all shapes. To represent shapes in the coupled shape model, signed distance maps (SDM) was used, [Tsai et al., 2004]. The eigen-problem was solved on the covariance matrix using svd, to find the eigenshapes and their magnitude. Seven modes of variation was extracted, representing 75% of the total variance which each represents different modes of variations. An interactive program was developed to investigate how the first seven modes changes the shapes. In figures 1 to 3 the most significant mode is seen varying with $\frac{2}{3}$ from the meanshape. Fig. 1. meanshape + $\frac{2}{3}$ Fig. 2. meanshape Fig. 3. meanshape - $\frac{2}{3}$ References [Tsai et al., 2004] Tsai, A., Wells, W., Temppany, C., Grimson, E. og Willsky, A. (2004). Mutual information in coupled multi-shape model for medical image segmentation. Elsevier Science.
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