Inter-individual differences in fMRI entropy measurements in old age

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INTRODUCTION

Sources of inter-individual differences in cognitive ageing are unclear. Age-related cognitive performance differs between individuals with an identical amount of age related changes in the brain in the absence of pathology. When the brain is examined as a system with inputs and output, characterisation of signal structure provides a practical and potentially informative approach to understanding sources of individual differences in brain function. One such characterisation is to measure the signal's complexity.

Signal complexity changes with ageing and disease however the direction of that change is unclear. Vaillancourt, (2002) has postulated that the directional change of the complexity (measured using entropy) of a physiological or behavioral system with ageing or disease depends on the dimension of the intrinsic dynamic that organizes the system output. They define two systems with either a fixed point or an oscillatory attractor. An attractor is the state to which a system returns to after perturbation.

This study investigated if differences in cognitive performance are associated with differences in the entropy measure calculated from fMRI data. Here, we hypothesize that higher levels of entropy will be associated with better cognitive performance.

We employ a psychophysical task of speed of information processing that assesses the efficiency of iconic memory in the early stages of visual information processing called inspection time (IT) (Deary 2001). There are individual differences in the efficiency of information processing assessed by the inspection time procedure which are significantly correlated with individual differences in higher level mental abilities including psychometric tests of intelligence (Grudnik and Kranzler 2001).

METHODS

40 volunteers without dementia were recruited from the 1936 Aberdeen Birth Cohort (1936 ABC) and were brain imaged between the age of 68 – 70 years.

MRI data were obtained by a 1.5T scanner (NVi, General Electric Medical Systems, Milwaukee, WI, USA) using the standard head coil while performing a visual information processing task (inspection time: IT). Figure 1 describes the cue, stimuli, and backward mask for the inspection time task. fMRI data were acquired using a T2* weighted gradient echo echo-planar imaging sequence (EPI) in the axial plane with TR/TE of 2500/40 ms, matrix 64 X 64, field of view of 24cm^2, thickness of 5mm, 30 slices per volume (292 time points/volume in total).

In addition to the fMRI data, the IT performance, childhood intelligence age 11 (Moray House Test; MHT) and a fluid intelligence measure (Raven's Progressive matrices RPM) data at age about 68 years were also available for analysis. Approximate Entropy (ApEn) (an estimate of signal complexity) was measured for each voxel in the brain. A high ApEn indicates unpredictability and random variation (high complexity), whereas low ApEn indicates predictability and structure (low complexity) (Pincus 1991). Whole brain ApEn maps for each individual were generated and compared using an SPM approach. Figure 2 depicts the ApEn map of a whole brain for one of the volunteers. The associations between cognitive measures were tested on a global and regional basis.

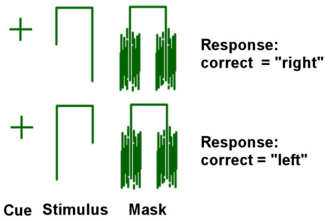

Figure 1: The cue, stimuli, and backward mask for the inspection time task.

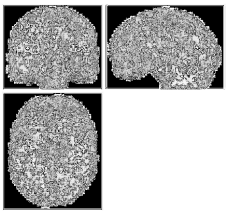

Figure 2: A whole brain ApEn map of 288 volumes with mean ApEn of 1.1991.

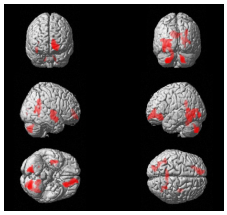

Figure 3: IT has positive correlation with entropy

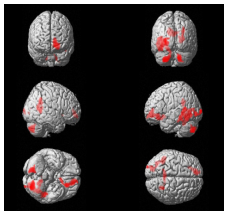

Figure 4: Relationship between IT and entropy after adjusting for MHT

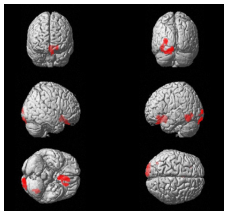

Figure 5: Relationship between IT and entropy after adjusting for RPM.

Table 1: Association of IT with entropy and adjustment for MHT and RPM (with initial threshold of p<0.005 and extent voxel of N>250)

Indicator of Cognitive Performance	Correlation with entropy	Talairach coordinate (XYZ)	Hemisphere	Region in the Brain	Cluster p value (corrected)	Extent
IT	Positive	-26 -76 -44	Left	Pyramis	0.000	360
		16 -76 -40	Right	Pyramis	0.002	293
		-38 -54 -8	Left	Sub-Gyral	0.000	1214
		-32 -68 2	Left	Middle Occipital Gyrus	0.000	436
		-10 -52 -26	Left	Fastigium	0.000	757
		38 0 -14	Right	Superior Temporal Gyrus	0.000	437
		38 -10 -6	Right	Insula	0.000	370
IT after adjusting for MHT	Positive	-26 -76 -44	Left	Pyramis	0.000	417
		16 -76 -40	Right	Pyramis	0.001	325
		26 -72 -50	Right	Inferior Semi-Lunar Lobule	0.000	1737
		-36 -56 -8	Left	Sub-Gyral	0.000	659
		-34 -68 0	Left	Middle Occipital Gyrus	0.000	394
		-44 -40 -14	Left	Sub-Gyral	0.001	351
IT after adjusting for RPM	Positive	-20 28 -12	Left	Sub-Gyral	0.000	793
		0 16 -12	Left	Inter-Hemispheric	0.000	640
		-12 38 -38	Left	Sub-Gyral	0.004	274
		-12 -100 -22	Left	Lingual Gyrus	0.000	388

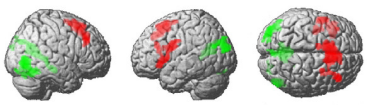

Figure 6. Relationship between BOLD activation and the inspection time task (Red denotes increase; green, decrease).

RESULTS

No global entropy associations were found between IT, MHT and RPM.

Using a regression approach and initial threshold of p<0.005, Table 1 shows the locations of the positive regional entropy association with IT corrected cluster level significance (p<0.05 N>250). Figure 3 shows the regions with significant positive associations between IT and entropy, i.e. the higher the IT (better visual information processing) the more complex fMRI signal.

When the association between IT and entropy was tested after adjusting for MHT, the positive association of IT with entropy remained significant in Figure 4.

In Figure 5, after adjusting the RPM the positive entropy association with IT remained significant.

The rationale for adjusting for intelligence test scores in the assocation between inspection time and entropy is because inspection time and intelligence have a known association, and so any association with entropy could just be due to that fact. The survival of the entropy-inspection time associations after adjusting for intelligence could suggest that it is the non-intelligence variance in inspection time that is in part leading to the association.

CONCLUSIONS

Our results show that inter-individual differences in IT may be associated with regional differences in ApEn calculated from fMRI data. Some of the locations identified appear to be independent of the other cognitive measures

The results show that high ApEn values are associated with better cognitive performance. This implies that the nature of the underlying mechanism has a constant attractor as described by Vaillancourt (Vaillancourt, 2002).

The locations found (IT) have some similarities with those found to be associated with better IT scores, in this data set by Waiter et al (Waiter et al, 2008) using a conventional fMRI approach (Figure 6). Regions in the parietal-occipital-temporal territory appear common to both analyses. This would imply that the IT performance is correlated with the fMRI signal contrast it initiates and the overall complexity of that signal. Our analysis also found associations in the cerebellum and orbital frontal region, which were not identified by the previous analysis. It may well be that those regions, do not exhibit a measureable contrast during the task but are part of an extended network used to perform it. Estimates of signal entropy at those locations may therefore be a proxy for cognitive health, or conversely decreasing entropy in these regions may be an early correlate of cognitive decline.

ACKNOWLEDGEMENTS

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REFERENCES

Deary, I.J. (2001). 'Human intelligence differences: towards a combined experimental-differential approach. Trend Cogn. Sci. vol. 5, 164 – 170.

Grudnik, J.L., Kranzler, J.H. (2001) 'Meta-analysis of the relationship between intelligence and inspection time', Intelligence vol. 29, 523 – 535.

Pincus, S.M. (1991), 'Approximate entropy as a measure of system complexity', Proceedings of the National Academy of Sciences of the United States of America, vol. 88, no. 6, pp. 2297-2301.

Vaillancourt, D.E. and Newell, K.M. (2002), 'Changing complexity in human behaviour and physiology through aging and disease', Neurobiology of Aging, vol. 23, pp 1 – 11.

Waiter, G.D., Fox, H.C., Murray, A.D., Starr, J.M., Staff, R.T., Bourne, V.J., Whalley, L.J. and Deary, I.J. (2008), 'Is retaining the youthful functional anatomy underlying speed of information processing a signature of successful cognitive ageing? An event-related fMRI study of inspection time performance', NeuroImage, vol. 41, pp. 581–595