Intrinsic functional connectivity between the retrosplenial cortex and the hippocampus: links to episodic memory and dopamine D2 receptor density

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Background:
The default mode network (DMN) involves interacting cortical areas including posterior cingulate (PC), precuneus and retrosplenial (Rsp) cortices, and subcortical areas including the hippocampus (HC). Resting-state (RS) functional connectivity (FC) between HC and cortical areas of the DMN, particularly the posterior parietal areas, has been shown to predict episodic memory (EM) recollection. However, RS studies investigating the link between posterior parietal DMN-HC FC and offline EM yielded inconsistent results. One possible explanation for the conflicting results can be due to the fact that posterior DMN has a complex structure, including precuneus (Brodmann Area [BA] 31), PC (BA 23), and Rsp (BA 29 & 30), with morphological and connectivity differences. Thus, it is important to tease apart FC between HC and different posterior parietal DMN areas. Previously, pharmacological studies showed that dopamine modulates FCs within the DMN. However, it is unclear whether individual differences of FC between DMN subsystems can be explained in terms of striatal dopamine.

Methods:
We studied 181 healthy adults (age range 64-68) who underwent comprehensive assessment of EM (word recall, number-word recall, and object-position recall), along with fMRI during RS. Also, DAD2 receptor availability was assessed with PET using 11C-raclopride. Applying independent component analysis, we identified 39 RS networks including HC, Rsp, and posterior DMN (mainly including PC and precuneus) and studied FC of HC and Rsp and posterior DMN, respectively. Associations between FC with EM and striatal DA D2 were also investigated.

Results:
HC was more connected to Rsp than other posterior DMN areas (t=5.06, p<0.001). Second, the degree of HC-Rsp FC predicted EM performance (r=0.17, p=0.02). Third, FC between HC and a specific part of the Rsp was modulated by striatal dopamine (r=0.30, p=0.00005). Mediation analysis indicated that Rsp serves as a key node within DMN to increase its functional integrity by mediating the relation between the HC and other cortical DMN areas.

Conclusions:
Our finding highlights the importance of Rsp within the DMN and its interaction with HC, which has implication for EM. We also reveal a potential dopaminergic neurobiological basis for inter-individual differences in FC between DMN subsystems.