The Role of Serum Response Factor in Incentive Learning

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Background
- Serum Response Factor (Srf) is a transcription factor that regulates the activity of immediate early genes that are implicated in neural plasticity (Ramanan et al., 2005).
- Since plasticity underlies learning and memory, we investigated whether two lines of Srf mutant mice were capable of learning simple cue-reward associations (Pavlovian conditioning) and whether such cues were capable of supporting novel instrumental responding (conditioned reinforcement) (Mackintosh, 1974).
- These processes are often implicated in the control of drug-seeking and abuse.

Srf mutant mice
- Deletions of SRF were targeted using the Cre/loxP system.
- Srf was deleted in forebrain/limbic circuitry using a CamKII promoter (Srf CamKII-Mutant).
- Deletions were restricted to the CA3 and DG of the hippocampus using a Synapsin promoter (Srf Synapsin-Mutant) (Ramanan et al., 2005)

Training
- There were no genotype effects on Pavlovian discrimination acquisition
- In separate groups the CRf procedure assessed the ability of a tone paired with sucrose (CS+) to acquire incentive motivational properties, such that in test it was capable of reinforcing a novel instrumental nose-poke response

Conditioned Reinforcement Test
- Srf CamKII-Mutant mice are impaired on Conditioned Reinforcement
- During the testing phase (conducted under extinction conditions), mice were presented with two novel nose-poke recesses on either side of the magazine
- Responses to one nose-poke resulted in CS+ presentation
- Responses to the other nose-poke resulted in CS- presentation

Figure 1. Pavlovian Training (a) The percentage of time spent in the magazine during CS+ increased as (b) the percentage of time spent in the magazine during the CS- decreased in all groups. (c) Discrimination ratios [%CS mag time / (CS+ + CS-)] show comparable levels of acquisition in all groups.

Figure 2. (a) The number of total responses made to each nose-poke recess and (b) discrimination ratios [nCS+/CS−] show biased responding to the CS+ associated nose-poke in all groups except the Srf CamKII-Mutant group.

Summary
Forebrain/limbic Srf was critical for the acquisition and/or expression of conditioned incentive value. In contrast, Srf deletions restricted to CA3 and DG did not attenuate conditioned reinforcement but increased locomotor activity.

Conclusion
Collectively these results suggest that forebrain/limbic Srf is necessary for a cue to acquire conditioned incentive value and reinforce subsequent behaviour. Ongoing research seeks to elaborate upon this finding and to pursue potential implications for drug-seeking and abuse.

References

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