INTRODUCTION
The brain-derived neurotrophic factor (BDNF) receptor Tyrosine kinase B (TrkB) has been implicated in neuronal growth, survival and plasticity. Conventional gene knock-out strategies are not well suited for the in-vivo analysis of the functions of neurotrophins in the postnatal or adult nervous system, since nearly all neurotrophin and Trk null mice die perinatally.

We report a strategy which combines the specificity of gene targeting and the temporal control, reversibility and rapidly-acting properties offered by a pharmacological approach using TrkB<sup>F616A</sup> knockin mice (Chen et al., 2005). We examined the roles of TrkB in the acquisition and expression of learned incentive value, using conditioned reinforcement (CRF) procedures.

GENERATION OF TrkB<sup>F616A</sup> MICE
At the location corresponding to TrkB616, all Trk proteins have a phenylalanine (F). Substitution with alanine (A) renders the mutant Trk receptor susceptible to inhibition by 1-naphthylmethyl protein phosphatase 1 (1NMPP1), a small-molecular derivative of the kinase inhibitor PP1. Thus, the TrkB receptor can be transiently inactivated by IP injection of 1NMPP1, and its function restored by ending 1NMPP1 administration (washout in 3+ days).

1NMPP1 INJECTION PROTOCOL
In separate groups of mice, the TrkB receptor was inactivated during either Pavlovian training (when associating a tone with food could endow the tone with learned incentive value), CRF testing (when the acquired value of the tone could be expressed by its ability to reinforce new learning of an instrumental response), both phases, or neither phase.

BEHAVIOURAL PROTOCOL
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.

PAVLOVIAN TRAINING RESULTS
Inactivation of TrkB receptor had no effect on the acquisition of a simple conditioned response (entry into the food magazine).

CRF TEST RESULTS
Normal activity of TrkB receptor was critical for the acquisition, but not expression, of conditioned incentive value (failure to reinforce novel nose-poke response).

SUMMARY
All mice showed comparable levels of discrimination acquisition during the Pavlovian training phase (Figure 4a).

Control mice injected with DMSO during the training and test phases (group Control-Control) biased their responding at test to the nose-poke associated with presentations of CS+ suggesting that the cue had acquired conditioned reinforcing properties.

Mice injected with 1NMPP1 during the training phase alone (group Impaired-Control) or during both training and test phases (group Impaired-Impaired) failed in test to bias performance for the conditioned reinforcer.

Interestingly, injecting 1NMPP1 during the test phase only (group Control-Impaired) did not impair the ability of mice to attribute affective value to the reward paired cue as indexed by a clear preference for the CS+ associated nose-poke at test.

CONCLUSION
Collectively these results suggest that TrkB receptors are required for the acquisition, but not expression, of conditioned incentive value and are consistent with the involvement of these receptors in the acquisition of amygdala-dependent behaviour (Rattiner et al., 2004).

REFERENCES


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