

Role of piriform cortex afferent projections in relapse to fentanyl seeking after food choice-induced voluntary abstinence

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Background: We previously showed a role of piriform cortex (Pir) in relapse to fentanyl seeking after food choice-induced voluntary abstinence, a procedure that mimics abstinence due to availability of alternative non-drug rewards. Here, we used retrograde tracing to determine projection-specific activation of Pir afferent projections during fentanyl relapse by using Fos plus the retrograde tracer cholera toxin B (injected into Pir).

Methods: We trained male and female rats to self-administer palatable food pellets for 6 days (6-h/day) and fentanyl (2.5 microgram/kg/infusion, i.v.) for 12 days (6-h/day). We assessed relapse to fentanyl seeking after 14 voluntary abstinence days, achieved through a discrete choice procedure between fentanyl and palatable food (20 trials/day).

Results: Relapse to fentanyl seeking was associated with increased Fos expression in neurons in anterior insular (AI) and prelimbic (PL) cortex that project to Pir but not Pir-projecting cortical neurons in adjacent areas or Pir-projecting thalamic neurons. Preliminary anterograde tracing in AI or PL confirmed these AI → Pir and PL → Pir projections.

Conclusions: Results demonstrate a correlational role of AI → Pir and PL → Pir projections in relapse to fentanyl seeking after food choice-induced abstinence. In future experiments, we will determine the causal role of these projections in relapse to fentanyl seeking after food choice-induced abstinence.

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