P-1126 - SENSITIZATION INDUCED BY HALOPERIDOL AND OLANZAPINE IS SITUATIONALLY SPECIFIC

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Rationale: Repeated administration of haloperidol and olanzapine causes a progressively enhanced disruption of conditioned avoidance responding and a progressively enhanced inhibition of phencyclidine (PCP)-induced hyperlocomotion in rats. Both actions are thought to reflect the intrinsic antipsychotic activity.
Objective: The present study examined to the extent to which antipsychotic-induced sensitization in one model (e.g. conditioned avoidance response model) can be transferred or maintained in another (e.g. PCP hyperlocomotion model).
Methods: We first induced behavioral sensitization in one model through repeated administration of haloperidol or olanzapine to male Sprague-Dawley rats, then tested its expression in another model, and finally retested its expression back in the first model.
Results: Repeated haloperidol and olanzapine induced a robust behavioral sensitization in both models. Its expression was highly situational specific as it only manifested itself in the model in which it was being induced.
Conclusions: Based on these and other findings, we propose that three behavioral mechanisms regulate antipsychotic sensitization and its *situational specificity*:
(1) Repeated antipsychotic treatment induces an unconditioned and nonassociative enhanced behavioral effect (i.e. sensitization) by progressively decreasing motivational salience of stimuli, an effect attributable to the *direct* pharmacological action of a drug;
(2) Distinct contextual cues develop an association with unconditional drug effects via a Pavlovian conditioning process, thus acquiring the ability to elicit antipsychotic-like effects. This associative learning process may potentiate the sensitized behavioral response in an expected situation;
(3) Contextual stimuli and interoceptive drug state also serve as *occasion-setters* to modulate the expression of sensitized responses.

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