Immune activation impairs the acquisition and consolidation of lithium chloride-induced anticipatory nausea in a rodent model

Introduction. Up to 45% of individuals undergoing chemotherapy experience anticipatory nausea (AN). Here, cues from the hospital context become associated with the nauseating chemotherapy and returning to the hospital elicits nausea in the absence of chemotherapy. In rodents this is modeled by pairing a context with a nauseating stimulus, like lithium chloride (LiCl), which leads to conditioned disgust behaviours (e.g., gaping) upon exposure to the context alone. Current antiemetic treatments are unsatisfactory for AN. New evidence suggests that selective immune activation may treat AN.

Methods. Within the LiCl-induced AN paradigm adult male Long Evans rats were intraperitoneally (ip) injected with LiCl (127 mg/kg) or NaCl and placed into a distinct context for 30 mins on 4 conditioning days (CDs). *Experiment 1: Acquisition.* 32 rats were ip injected with LPS (cell wall component of Gram-negative bacteria, 200 μg/kg) or NaCl 90 mins before the LiCl-induced AN paradigm on each CD. *Experiment 2: Consolidation.* 48 rats were ip injected with LPS or NaCl immediately after the LiCl-induced AN paradigm on each CD. *Experiment 3: Delayed Consolidation.* 48 rats were ip injected with LPS or NaCl 24hrs after the LiCl-induced AN paradigm on each CD. *Experiments 1-3: Extinction.* CDs were followed by 4 no injection test days (TDs).

Results. LiCl induced conditioned gaping in rats on CD 4 and TD 1 across experiments (*ps*<.01). On these days, LPS administered before the LiCl-induced AN paradigm impaired AN acquisition (*ps*<.01). LPS administered immediately after the paradigm impaired AN consolidation (*ps*<.05). LPS impaired the delayed consolidation of AN when administered 24hrs later (*ps*<.05). A rapid extinction of conditioned gaping was found in LiCl treated rats in all experiments after TD 1.

Implications. LPS significantly impaired both the acquisition and consolidation of LiCl-induced AN, lending support to the role of immune activation in the treatment of AN.