

features of BPD in the US sample (i.e., affective instability and identity problems). Mediation analyses demonstrated that BPD features, particularly self-harm, as well as affective instability and negative relationships, mediated the relationship between sexual identity and SUDs but only for females.

Conclusions: Results suggest that development of BPD features may be one mechanism through which risk for SUDs is conferred in NHSI females. These findings highlight the potential utility of SUD interventions targeting emotion dysregulation, which is considered the core dysfunction in BPD.

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Neonatal abstinence syndrome in methadone exposed infants: Role of genetic variability



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Aims: NAS incidence & severity in infants exposed to methadone during gestation is independent of maternal methadone dose. The incidence & severity of NAS could be in part due to genetic variability of key genetic loci related to opioid response; the interleukin-1beta (IL-1B) & mu opioid receptor (OPRM1) genes. This study aimed to investigate the impact of genetic variability in IL-1B -31 or OPRM1 A118G on NAS incidence (treatment required) & severity (dose of morphine).

Methods: This pilot study collected cheek cells from 71 methadone exposed infants; 46 required treatment. Complete genetic & morphine treatment data were obtained for a subset of 26 NAS infants.

Results: There were no difference in IL-1B or OPRM1 genotypes between infants with, & without NAS (OR (p) = 1.9 (0.21) and 0.23 (0.24), respectively). There was also no impact of genetic variability at IL-1B and OPRM1 on morphine treatment (median, mg): initial morphine dose – wild-type (WT, n = 21) 0.15 and variant (Var, n = 5) 0.2 (p = 0.06) and WT (n = 24) 0.17 and Var (n = 2) 0.22 (p = 0.73), respectively; maximum morphine dose – WT (n = 21) 0.3 and Var (n = 5) 0.28 (p = 0.94) and WT (n = 24) 0.29 and Var (n = 2) 0.24 (p = 0.39), respectively; and total morphine in the first month of life – WT (n = 20) 33.8 and Var (n = 5) 34.8 (p = 0.67) and WT (n = 23) 34.8 and Var (n = 2) 25.4 (p = 0.38), respectively.

Conclusions: Despite genetic variability at these loci being reported to impact opioid response in adults, our study to date has not replicated these findings in infants. However, infant numbers in each genotype group were low. Therefore, the possibility remains for an association between genetic variability and NAS, leading to predictive tools to pre-determine NAS incidence & severity. Data collection for this project continues.

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Primary care buprenorphine detoxification vs. maintenance for prescription opioid dependence



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Aims: The favorable clinical characteristics and improved treatment outcomes for prescription opioid dependent (POD) patients, and modest severity of withdrawal symptoms with buprenorphine/naloxone (bup/nx), have led physicians to offer detoxification with bup/nx for POD patients. We sought to determine whether bup/nx stabilization followed by detoxification (DTX) or maintenance (MTN) leads to greater reduction in illicit opioid use and treatment completion among POD patients treated in primary care.

Methods: 113 patients were randomized to DTX (n = 57) or MTN (n = 56) in an 18-week study. DTX patients underwent bup/nx stabilization for 6 weeks, a 4-week taper, and were offered naltrexone. DTX patients with 2 consecutive weekly urines with opioids following taper were offered re-induction onto bup/nx. MTN patients received bup/nx stabilization and maintenance for the study duration. All patients were offered physician management and drug counseling for the study duration. Urine toxicologies were collected weekly. Mean proportion of opioid negative urines was evaluated with missing urines considered positive. Treatment completion was assessed at 18 weeks. Analyses and p -values were adjusted for baseline differences and an interim safety analysis.

Results: At baseline, patients randomized to MTN reported more days of opioid use in the past 30 days than those randomized to DTX (p = .01), otherwise treatment groups did not differ. Patients assigned to MTN had a greater mean proportion of opioid negative urines compared to DTX (.64 vs. .50; p = .001). MTN patients achieved longer maximum consecutive weeks of opioid negative urines (6.3 vs. 3.9, p = .005). MTN patients were more likely to complete treatment (66%, n = 37 vs. 10%, n = 6, p < .001) and remained in treatment longer (98 days vs. 65 days, p < .001). 30% (n = 16) of DTX patients required re-induction onto bup/nx.

Conclusions: MTN is more efficacious than DTX for POD patients treated with bup/nx in primary care.

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PlayForward: A videogame that increases drug, alcohol and sexual risk knowledge in teens



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Aims: Substance use is often initiated during adolescence. Given that most teens play videogames and that videogames can be effective health interventions, the play2PREVENT™ Lab developed a videogame, PlayForward: Elm City Stories, for overall risk reduction and HIV prevention in 11–14 year olds. We sought to determine the impact of PlayForward on drug/alcohol/sex risk-related (DAS) knowledge.

Methods: PlayForward was developed for the iPad through an iterative process that involved researchers, educators, videogame designers/developers, and community organizations. The efficacy of 6 weeks of twice-weekly PlayForward game play (2 h per session) is being evaluated against a set of time/attention control games in a randomized controlled trial. To date we have enrolled 165 teens and conducted 6-week and 3-month follow-up assessments of DAS knowledge on 93 using a 22-item instrument. In addition, we have analyzed videogame log files generated through iPad software in 41 teens randomized to PlayForward as a measure of intervention exposure using the R statistical software package.

Results: Participants were 53% male with a mean age of 12.9 years. There were no baseline differences in DAS knowledge. At 6-week follow-up the PlayForward group had higher DAS knowledge scores ($M = 15.9$, $S.D. = 4.7$) than the control group ($M = 12.5$, $S.D. = 4.6$; $p < 0.001$). These differences remained at the three-month follow-up (Intervention: $M = 15.2$, $S.D. = 5.2$; Control: $M = 12.3$, $S.D. = 4.6$; $p = 0.005$). Analysis of 603,431 events in log files revealed that the number of game levels completed during game play was positively correlated with gains in knowledge measured at 6 weeks ($r = 0.51$; $p < 0.001$). The correlation remained at the 3-month ($r = 0.50$; $p < 0.001$) follow-up.

Conclusions: Playing the videogame PlayForward is associated with increased DAS knowledge in teens. Greater exposure to the PlayForward appears to promote retention of DAS knowledge.

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Behavior problems among cocaine-exposed children: Role of physiological regulation and parenting



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Aims: We hypothesized that low baseline respiratory sinus arrhythmia (BRSA) and low RSA change in response to challenge at 13 months would mediate the relation between prenatal cocaine exposure and behavior problems at 36 months. We also hypothesized that maternal negative affect at 13 months of age would moderate the relation between RSA and behavior problems.

Methods: Participants included 216 high risk mother–infant dyads participating in an ongoing longitudinal study of prenatal cocaine exposure. Baseline RSA was calculated during an initial 3-minute video. RSA change reflects the difference between baseline RSA and average RSA during an arm restraint task. Parenting behavior was assessed from video of 10 min parent–child interaction. Child behavior problems were assessed by maternal report.

Results: Structural equation modeling (SEM) was utilized to test all hypotheses. The causal paths from PCE to the 13 month BRSA and RSA change variables were significant. Contrary to expectations, RSA change was unrelated to behavior problems while low baseline RSA at 13 months predicted low rather than high behavior problems. The indirect effect linking cocaine exposure to low behavior problems via low baseline RSA was statistically significant, providing support for mediation. High maternal negative affect moderated the association between baseline RSA and behavior problems.

Conclusions: The finding that low baseline RSA predicts lower rather than higher behavior problems was unexpected and may

be related to unique characteristics of the current sample. Because children with high baseline RSA are believed to be more actively engaged with their surroundings, such children may be more susceptible to the negative characteristics of their caregiving environment. Consequently, high BRSA children who experience high levels of maternal negative affect within high-risk environments may be particularly likely to develop behavior problems.

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Effects of HZ-166, a novel $\alpha 2$ and $\alpha 3$ subunit-containing GABA_A receptor agonist, on inflammatory pain and operant behavior in mice



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Aims: GABAergic inhibition in the spinal dorsal horn is thought to contribute significantly to nociceptive processing. The present study assessed the anti-hyperalgesic effects of the novel 8-acetylene imidazobenzodiazepine HZ-166 which demonstrates selective efficacy at $\alpha 2$ and $\alpha 3$ subunit-containing GABA_A receptors. For comparison, the effects of HZ-166 were also assessed in an assay of schedule-controlled responding.

Methods: The antihyperalgesic effects of HZ-166 were assessed in a model of inflammatory pain. Here, the yeast extract zymosan A (24 h pretreatment; 0.06 mg/0.02 ffjg) was injected subcutaneously into the plantar surface of the footpad. Mechanical sensitivity was then assessed before and 10–320 min following HZ-166 administration. In a separate group, the response rate-decreasing effects of HZ-166 were examined in an assay of schedule controlled responding. Here, mice were trained on a fixed ratio 3 schedule of liquid food presentation. Once response rates were stable, the response rate-altering effects of HZ-166 were assessed.

Results: In the model of inflammatory pain, injection of zymosan A produced an increase in sensitivity to mechanical stimulation. HZ-166 (1.0–32 mg/kg, i.p.) produced dose- and time-dependent reversal of mechanical sensitivity and peak effects were observed at 80 min. When administered as an 80 min pretreatment, HZ-166 (3.2–32 mg/kg, i.p.) did not produce significant changes in response rates in the assay of schedule controlled responding.

Conclusions: These data provide evidence suggesting that systemic administration of a $\alpha 2$ and $\alpha 3$ subunit-containing GABA_A receptor agonist produce selective antihyperalgesic effects while having minimal effects on operant responding. Together, these observations should provide a framework for studying GABA_A receptor pharmacology which in turn should help guide the development of improved therapeutic agents for the treatment of pain.

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