

Murine *in vivo* experiments were conducted on female Swiss Webster mice (10 per group). Femoral fractures were induced with a 3-point bending device and stabilized. Mice were dosed with 3 nmol/kg/d of targeted-ePTHrP, non-conjugated (free) ePTHrP, or saline. Following a 4-week study, fracture callus densities were measured using microCT. Canine *in vivo* experiments were conducted on 1-year-old male beagles. Beagles underwent a 10 mm bilateral ulnar osteotomy. Two dogs in the treatment group and Three dogs in the control group were dosed daily with either targeted-ePTHrP 0.5nmol/kg/d or saline respectively. Dogs were x-rayed weekly for the first 6 weeks and then every other week thereafter. One tailed ANOVA followed by Dunnett's post-hoc test was used to establish significance. All animal experiments were conducted as described in approved IACUC protocols. $P < 0.05$ was considered significant. RESULTS/ANTICIPATED RESULTS: RESULTS SECTION: In the murine studies we observed a marked increase in fracture callus size and a 2-fold increase in bone deposition was observed in the targeted-ePTHrP group over the saline group ($P < 0.01$). A significant doubling in bone density was also observed. Targeted-ePTHrP group fractured femurs were able to achieve their pre-fracture strength as early as 3 weeks compared to 9 weeks in the saline mice representing a 66% reduction in healing time. In the canine studies, we observe a significantly higher closure of the osteotomy gap than saline controls ($P < 0.05$). In addition, no significant differences in weight are observed in the treatment vs. saline controls. No significant difference between the control group and treatment groups was found in a histological investigation of the organs. DISCUSSION/SIGNIFICANCE OF IMPACT: DISCUSSION: Although attempts have been made in developing a systemically administered fracture therapeutic for fracture repair, i.e. teriparatide, to date, no such anabolics have been approved for this use. In these studies there is evidence that anabolic activity was occurring at the fracture site, but at a level that did not meet FDA required end-points.² It is plausible that if sufficient drug were to be delivered to a fracture site then improved fracture repair would be possible. In previous studies, we demonstrated fracture specific accumulation bone anabolics can be achieved by modifying the drug with acidic oligopeptides.³ Here, by modifying a safe, clinically proven, parathyroid hormone receptor agonist with an acidic oligopeptide we observe improved bone deposition and strength in mice. Furthermore, when administered to canine critical sized defect osteotomies, a more relevant and difficult model, we observe improved osteotomy closure. CLINICAL RELEVANCE:: The ability to accelerate bone fracture repair is a fundamental need that has not been addressed by conventional methods. By targeting bone anabolic agents to bone fractures, we can deliver sufficient concentrations of anabolic agent to the fracture site to accelerate healing, thus avoiding surgery and any ectopic bone growth associated with locally-applied bone anabolic agents.

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Frontal Alpha Asymmetry in Alcohol-Related Intimate Partner Violence

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OBJECTIVES/SPECIFIC AIMS: The current study is the first investigation of frontal alpha asymmetry in distressed violent (DV) and distressed nonviolent (DNV) partners during a placebo-controlled alcohol administration and emotion-regulation study. Because this is the first study of the pharmacological effects of alcohol on FAA, the first portion of the study was conducted to characterize alcohol

effects in DV and DNV partners during the baseline condition. The subsequent portions of the study were conducted to characterize the effects of alcohol and evocative stimuli on FAA in DV and DNV partners. We hypothesized that DV partners would demonstrate greater left frontal alpha asymmetry when intoxicated and viewing evocative partner stimuli than DNV partners. Lastly, we attempted to replicate previous research that has found associations between baseline measures of FAA and the State-Trait Anger Expression Inventory – 2 (Spielberger, 1999) subscales of Trait Anger, Anger Expression-Out, Anger Expression-In, Anger Control-Out, Anger Control-In (Hewig, Hagemann, Seifert, Naumann, & Bartussek, 2004). METHODS/STUDY POPULATION: Partners in the present study were drawn from a larger study investigating over-arousal as a mechanism between alcohol use and intimate partner violence (AA022367). Couples were recruited from the community via radio, television and newspaper advertisements, and eligibility screening occurred at the couple level. Participants included in the present analysis were 23 DV partners (12 female, 11 male), and 15 DNV partners (7 female, 9 male). The mean age of the sample was 32 (SD 4.8 years, range 23-40 years). Data from two DV partners were not included in the analyses of the FAA in the emotion-regulation tasks due to movement artifacts during the alcohol condition leaving too little data for analysis. RESULTS/ANTICIPATED RESULTS: The expected beverage by couple type interaction did not reach significance [$F(1, 36) = 3.93, p = .055$], but the between-subjects effects of couple type revealed a significant difference [$F(1, 36) = 4.425, p = .042$]. Contrary to our hypothesis, however, these results suggest that under conditions of alcohol, DV partners evidenced significantly greater relative right frontal alpha power asymmetry whereas DNV partners evidenced greater relative left frontal alpha power asymmetry. Although there was no significant between-subjects effect, there was a nearly significant interaction between beverage type and emotion regulation condition [$F = (1, 36) = 4.032, p = .052$] and a significant main effect of emotion regulation condition [$F(1, 36) = 7.579, p = .009$]. It appears that asking the participants to “not react” to their partners’ evocative stimuli caused significantly greater right frontal alpha asymmetry. Because intimate partner violence is best understood in the context of conflict between two partners, we also examined partner-reported experiences of anger as predictors of DV participant’s FAA. The model as a whole predicted 67.4% of the variance in DV partner FAA, R squared change = .674, F Change (5, 15) = 6.21, $p = .003$. Three anger experience scales were statistically significant. The partner Anger Control-Out ($B = -1.23, p = .001$) scale recorded a higher standardized beta value and accounted for 40% of the variance in this model. Anger Control-In ($B = .63, p = .022$) accounted for 14% of the variance in the model, and Anger Expression-Out scale ($B = .57, p = .024$) accounted for 13.7% of the variance in the model. DISCUSSION/SIGNIFICANCE OF IMPACT: The current study is the first pharmacological study of the effects of alcohol on frontal alpha asymmetry in distressed violent and distressed nonviolent partners. Contrary to our hypothesis, under acute alcohol intoxication during the baseline condition, DV partners exhibited significantly greater relative right FAA compared to DNV partners who exhibited significantly greater relative left FAA. Because intimate partner violence is best understood in the context of couple conflict, we examined the ability of partners’ anger experiences to predict DV and DNV partners’ FAA, and a very interesting pattern emerged among our DV participants and their partners. The anger experiences of our DV participants’ partners accounted for 67% of the variance in the FAA of our DV participants when they were intoxicated and viewing evocative stimuli.