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E17 Opioid Action

(300) Premature infant brain function: are opioid effects evident in the short term?

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Opioids, while commonly used in the Neonatal Intensive Care Unit (NICU) for sedation and analgesia during mechanical ventilation, may not be effective for procedural pain. Potential neurologic and sleep disruption after opioid exposure during development is of concern. The immediate effect of opioid therapy has not been fully explored with regard to brain function in early life. The aim of this small n naturalistic study was to describe changes in brain wave signal variability by extracting raw EEG signal from a limited channel amplitude integrated EEG (aEEG) recording and examining differences in spectral density distribution before and after standard morphine administration. Eight infants (2 male) with median postmenstrual age (PMA) 29.4 weeks, underwent a single recording of aEEG, during standard NICU care that included up to two doses of intravenous morphine for analgesia or sedation, 2 infants were status post surgery. Signal processing with fast Fourier transformation (FFT) prepared the data for spectral density analysis. Nine morphine doses provided data at each of two time points (T1= 15 minutes prior, T2 = 30 minutes after). Multivariate repeated measures ANOVA were conducted to test for morphine effect, age effect (PMA <30 weeks) and possible interaction. Morphine effects between time points were not significantly different for measures of 90% spectral edge frequency (SEF90) or high frequency normalized spectral bands alpha (7-13 Hz) or beta (<13 Hz), whereas the age group effect was highly significant: SEF90 ($F=42.125$ $p<.0001$), Alpha ($F=104.639$, $p<.0001$), Beta ($F=11.349$, $p<.012$), an interaction effect was shown for Alpha ($F=5.991$, $p=.044$). The exploration of spectral densities may improve understanding of brain function frequency shifts within the spectrum after clinically administered opioids in early premature infants. Support for this study includes: NINR F31- NR011365, T32-NR007106 & NLM 2T15LM007442-11 American Nurses Foundation, Integra Neuroscience Nursing Foundation, Sigma Theta Tau, Psi Chapter at Large.

(301) Examining the effects of pain on morphine self-administration following a spinal contusion injury

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Morphine is one of the most effective treatments for pain after spinal cord injury (SCI), but clinicians are concerned about addiction when prescribing this drug. Experimental evidence suggests that the presence of pain lowers the potential for addiction. Indeed, we have shown that morphine self-administration is lowered after SCI, but we do not know whether pain is driving this effect. We conducted two experiments to test this. First, we examined morphine self-administration in the acute phase of injury. Rats were given a sham, mild, moderate, or severe contusion injury. They were placed into self-administration chambers for 7-days (beginning 24-hours after injury). Irrespective of injury severity, all subjects displayed the same pattern of morphine administration: animals given access to a higher concentration of morphine (3.0 mg/lever press) administered more than those given access to a moderate dose (1.5 mg). This dose-dependent effect suggests that the subjects were not simply administering the drug for analgesia. Self-administration was then assessed in the chronic phase of injury, when SCI animals begin to develop neuropathic pain. Rats were placed into self-administration chambers for 7 days beginning 14- or 28-days following injury. In contrast to the acute phase of injury, we found contused animals administered the full amount of morphine available to them each session (even at the moderate, 1.5mg, dose), at a rate commensurate with sham controls and an amount that far exceeded that needed for analgesia. Together, these results suggest the addictive potential of morphine is altered in the acute, but not the chronic phase of injury. This is in contrast to what has been reported using other models of neuropathic pain. Neuropathic pain does not appear to reduce the addictive potential of morphine in an SCI model.

E19 Noninvasive Brain Imaging

(302) Gray matter density in the primary somatosensory cortex explains individual differences in the intensity of delayed onset muscle soreness

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Imaging studies have shown that, within the primary somatosensory cortex (SI), increased gray matter density (GM) is associated with lower pain thresholds, (i.e. increased pain sensitivity), in healthy volunteers. However, reports in the literature also suggest GM decreases in SI is associated with persistent pain, while GM increases in SI is associated with pain habituation. To investigate this relationship, we examined the baseline relationship between SI-GM and lumbar pressure pain thresholds in 15 (mean age 22 ± 2.4 years, 67% female) healthy individuals before completing a single session of unfamiliar eccentric exercise to the lumbar extensor muscles, and SI-GM with the intensity of delayed onset muscle soreness (DOMS) felt at 48 hours. Specifically, we correlated pressure pain thresholds to SI-GM and conducted a linear regression with 48-hour pain intensity as the dependent variable. Due to limited sample size, we choose step-wise regression to avoid creating an oversaturated model, while still trying to statistically control for potential co-founding factors. We considered age, sex, fear of pain, baseline pressure pain threshold, total cortical GM, and left SI-GM for inclusion into the step-wise regression. We used a liberal criterion of 0.1 to be entered and 0.2 to remain in the model. At baseline the mean ($\pm$SD) pressure pain threshold was 19.23 ($\pm$8.4) lbs and was negatively correlated with SI-GM ($r=-0.37$, $p \leq 0.09$). At 48 hours, the mean ($\pm$SD) pain intensity was 15.13 ($\pm$12.54) mm on a 100mm line. Our final regression model included only SI-GM, (standardized $\beta=-0.67$, $t=-3.26$, $p \leq 0.01$), which accounted for 41% of the variance in DOMS pain intensity at 48 hours ($F1,13=10.65$, $p \leq 0.01$). Our results support the position that more SI-GM is associated with lower pressure pain threshold (higher pain sensitivity), but that following a standardized muscular injury, more SI-GM in associated with less pain experienced.

(303) Sustained thermal pain modulates spontaneous sensorimotor rhythms

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Resting human brain could generate spontaneous rhythmic activity in areas of visual, somatosensory and motor areas. Previous studies have shown that excitation in these areas in response to external stimuli will counter-modulate the spontaneous rhythmic brain activity. In the current study, we investigated the effects of sustained thermal pain on the cortical activity by measuring 64-channel scalp EEG on healthy subjects. During the experiment, each subject experienced a sustained painful stimulus using a thermode placed on their dorsal side of the left wrist. The temperature of the thermode was kept at 46°C for 30 seconds during the stimulus-on condition. The temperature was then reduced to 32°C for 60 seconds during the stimulus-off condition. Each trial was repeated 6 times. Independent component analysis (ICA) was performed. One independent component with sensorimotor alpha rhythm was found to be negatively correlated with the stimulation state with correlation coefficient equals to -0.6. Source localization based on this component yielded cortical activation at the sensorimotor area which corresponds to the site of stimulation i.e. left wrist. Frequency analysis was subsequently performed. In the temporal aspect, we found that the alpha activity at the contralateral sensorimotor electrodes was suppressed during the painful stimulation in comparison to no stimulation condition ($p< 0.05$). The alpha power at the contralateral area was also found to be statistically smaller than the alpha power of ipsilateral brain region during the painful thermal stimulation ($p< 0.05$). In summary, we found that the spontaneous sensorimotor alpha rhythm was suppressed on the contralateral side of the sensorimotor region during sustained painful thermal stimulation. Although the current finding is based on the study of healthy subjects with sustained pain from external stimuli, it may also help to broaden our understanding of cortical response in patient population who suffer from chronic pain.