

Morphine Effects on the Spontaneous Electroencephalogram in Polydrug Abusers: Correlations with Subjective Self-Reports

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The spontaneous electroencephalogram (EEG) was recorded after the intramuscular (IM) injection of morphine sulfate (15, 30 mg) or saline (0.9% NaCl). Correlations between changes in EEG spectral power and subjective self-reports, as measured on subscales of the Addiction Research Center Inventory (ARCI), were evaluated. Morphine increased α_1 and α_2 power and theta power, and attenuated the increase in delta power observed after placebo. Positive correlations were found between the change in α_1 , α_2 , β_1 , and β_2 power in response to 30 mg of morphine and scores

on Morphine-Benzedrine Group (MBG) subscale of the ARCI. Negative relationships were observed between changes in α_1 , and β_2 and scores on the Pentobarbital Chlorpromazine Alcohol Group (PCAG) subscale. The findings indicate that positive subjective effects of opioids, as measured by the MBG subscale, are related to increases in alpha and beta activity and are associated with reduction of opioid-induced sedation, as measured by the PCAG subscale.

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The subjective effects of opioids have been studied extensively in human volunteers (Martin 1983). Morphine produces a wide variety of effects, including analgesia, drowsiness, changes in mood, and mental clouding (Jaffe and Martin 1985). In detoxified volunteers with histories of opioid abuse, arousal is produced (Kay et al. 1969), mental clouding is less prominent, and positive effects on mood are more pronounced than in nor-

mal subjects (von Felsinger et al. 1955). Although considerable information about the actions of opioid drugs in the nervous system exists, little is known about the central mechanisms underlying their effects on mood and feeling state in human subjects.

Effects of morphine on the electroencephalogram (EEG) have been tested in several species. In rats, opioids increase the abundance of low frequencies in the EEG (Wikler 1954; Khazan and Colasanti 1971; Young et al. 1980; Young and Khazan 1984, 1986). In the dog, periods of burst-slow activity have been observed (Wikler 1952). Slowing of the EEG is observed in the cat as well (De Andrés and Caballero 1989).

Opioid-induced slowing of the EEG in human subjects was first discovered by visual observation of EEG tracings (Berger 1937; Andrews 1941, 1943; Gibbs and Maltby 1943). Slowing has been defined in several ways. Earlier studies defined slowing as a decrease in the dominant frequency of the EEG tracings (Fig. 1a) or as the appearance of bursts of slow wave activity (Fig. 1b). Later studies using more quantitative methods defined slowing as a decrease in the α frequency (Fig. 1c)

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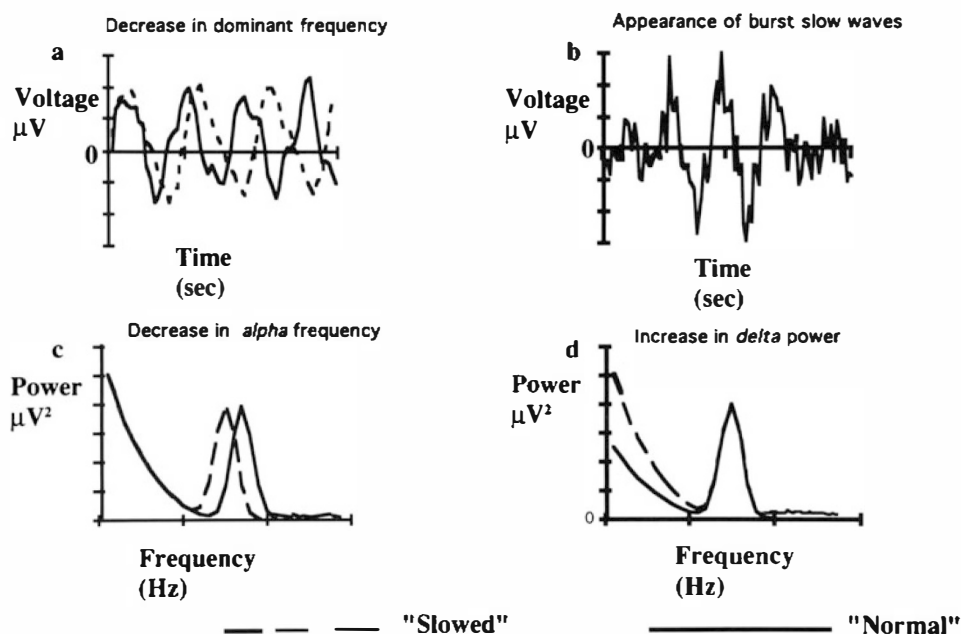


Figure 1. Definitions of EEG slowing. The four conditions presented are not mutually exclusive.

or as an increase in low frequency (*delta* and/or *theta*) power (Fig. 1d). A decrease in the dominant frequency of the EEG tracing can be due either to a decrease in *alpha* frequency, a decrease in *alpha* power relative to *delta* and/or *theta* power, or an increase in *delta* and/or *theta* power (Lukas 1991).

Effects of opioids on the EEG of human subjects with a history of opioid abuse have been reported. Both heroin and methadone decreased *alpha* frequency and increased *delta* and *theta* abundance (Fink et al. 1971; Volavka et al. 1979). Biphasic EEG effects of intravenous heroin have been reported. Increased *alpha* power and decreased *alpha* frequency were found during the first 2 to 3 minutes; after 3 to 5 minutes, a decrease in *alpha* amplitude and an increase in *theta* abundance occurred (Volavka et al. 1970). Kay et al. (1969) reported diminished amplitude of *delta* waves with an increased incidence of unusual EEG patterns such as bursts of multiple frequency waves and mixtures of *alpha* and *delta*.

Effects of opioids on the EEG vary with the drug histories of the subjects. In surgical patients, the injectable opioid anesthetics, fentanyl, sufentanil, and alfentanil, increased abundance of EEG *delta* power and decreased abundance of *alpha* and/or *beta* power (Sebel et al. 1981; Bovill et al. 1983; Smith et al. 1984; Wauquier et al. 1984; Bromm et al. 1989; Scott et al. 1991). In contrast, in normal, pain-free human subjects, a small decrease in *delta*, an increase in slow *alpha* with a decrease in relative fast *alpha*, and an increase in *beta* power occurred 1 to 2 hours after subcutaneous administration of morphine (4 and 8 mg) (Matejcek et al. 1988).

These changes were accompanied by significant increases in self-reports of drowsiness, lethargy, and mental slowness. Opioid-naive subjects gave self-reports of being dizzy, nauseous, itchy, warm, and headachy more often in response to morphine than to placebo (Beecher 1959).

Despite differences in the specific opioid drugs and doses and populations tested, increased EEG slow-wave activity (*delta* and/or *theta* abundance) has been the common response to opioids in human subjects. However, there has been no previous attempt to correlate the magnitude of EEG changes after opioid drug treatment to scores of mood and feeling state. In the present study, self-reports of mood and feeling state were correlated with the quantitative changes in the EEG produced by morphine in polydrug abusers with histories of opioid use and dependence.

MATERIALS AND METHODS

Subjects

Subjects were paid volunteers who resided on a closed research ward for the duration of the study. Nineteen subjects enrolled in the study, but data were only available for twelve. EEG data from seven of the subjects was not retained either because of equipment failure or because the subjects had subjective responses that were not characteristic of polysubstance abusers that are enrolled in studies at the Addiction Research Center (i.e., extremely weak response to 30 mg intramuscular (IM) morphine or strong response to placebo). The

Table 1. Effects of Morphine on Visual Analog Scale (VAS) Responses

VAS Question	Saline	Morphine (15 mg)	Morphine (30 mg)
How strong is the drug effect? ^{†§}	5 (7)	32 (19)	54 (18)
Does the drug have good effects? ^{†§}	4 (6)	32 (18)	59 (22)
Does the drug have bad effects?	4 (5)	7 (7)	13 (17)
How much do you like the drug? ^{†§}	4 (6)	38 (24)	59 (28)
How high do you feel? ^{†§}	4 (6)	29 (17)	57 (21)
How much do you want to take the drug again? [†]	9 (18)	51 (35)	70 (26)

Numerical columns with mean (SD).

[†] Significant main effects of treatment ($p < .0001$) by repeated-measures ANOVA.

[§] Response to 30 mg morphine significantly different from response to 15 mg morphine, $p < .05$ by Bonferroni-corrected t -test.

remaining 12 subjects were 26–39 years of age (mean = 35; SD = 4.5).

A recent history of intravenous usage of opioids was a criterion for admission. The time from the last use of opioids prior to admission to the study was 3 (4) (mean [SD]) weeks. Subjects were confirmed to be opiate-free by urine testing prior to admission and while in the study. Screening instruments included the National Institute of Mental Health (Bethesda, MD) Diagnostic Interview Schedule (Robins et al. 1981), as modified for computerized administration. Full details of the screening process are presented elsewhere (London et al. 1990). All but one subject met DSM-III (1980) criteria for opioid dependence, although none showed signs of physical dependence at the time of admission or during participation in the study. Most other diagnoses for which Axis I criteria were met related to substance abuse disorders; however, one subject met criteria for psychosexual dysfunction, one met criteria for simple phobia, and two met criteria for agoraphobia. Axis II diagnoses of borderline personality disorder (one subject) and antisocial personality disorder (three subjects) were also allowed.

All subjects gave informed consent to the procedures in the protocol, which was approved by the Institutional Review Boards of Johns Hopkins Medical Institutions and Francis Scott Key Medical Center, where the NIDA Addiction Research Center is located.

Drug Treatments

Morphine sulfate (Mallinckrodt, Paris, KY) was dissolved in 0.9% NaCl at a concentration of either 15 or 30 mg/ml as the salt. The control vehicle was 0.9% NaCl. Doses of morphine were presented in ascending order to reduce the chance of untoward effects. A saline control session was randomly inserted in the sequence. Administration was by IM injection in a volume of 1 ml. The test compounds were administered double-blind. The doses were selected from previous data showing

that 60% and 95% of detoxified, previously opioid-dependent, human subjects could correctly discriminate 15 mg and 30 mg of morphine IM as an opioid drug rather than a sedative or marijuana (Kay et al. 1967).

Test Sessions

Subjects were administered the Morphine-Benzedrine Group (MBG); Pentobarbital Chlorpromazine Alcohol Group (PCAG); and lysergic acid diethylamide (LSD) subscales of the Addiction Research Center Inventory (ARCI) (Jasinski et al. 1967; Haertzen 1974) and the Single Dose Questionnaire (SDQ) (Fraser et al. 1961; Jasinski et al. 1971). The MBG subscale consists of 16 questions, which relate primarily to positive effects on mood. The PCAG subscale primarily measures sedation and lethargy. The LSD subscale is sensitive to weird feelings, disorientation, and increased awareness of bodily sensations. The SDQ consists of questions relating to the identification and liking of drugs. Subjects also rated the strength of the treatment effect and their liking of it on six 100-mm visual line analog scales (VAS) similar to those used by others (Preston et al. 1988). The six questions from the VAS are listed in Table 1. These questionnaires were administered 45 minutes after injection of the test compound.

During the 45-minute measurement of spontaneous EEG, the subject was blindfolded and listened to a tape of white noise on which was recorded a beep tone at 1-minute intervals. At the sounding of this tone, the subject was to respond to the question "How high do you feel?" on a scale of 0 ("no effect") to 4 ("extremely"). Pupillary diameter was measured from photographs taken of the subject's eyeball at 30 minutes before injection of the test compound (before the blindfold was applied) and at 45 minutes after injection of the test compound (after the blindfold had been removed). Pulse and blood pressure were measured 60 and 30 minutes before and 10, 20, and 45 minutes after injection of the test compound.

EEG Recording

Electrodes made of Ag/AgCl (Beckman Instruments, Irvine, CA) were attached to the scalp by collodion or adhesive collars according to the international ten twenty system (Jasper 1958). All montages included leads F₃, F₄, F₇, F₈, T₃, T₄, C₃, C₄, O₁, O₂, P₃, and P₄. Some also included leads C_z, F_{pz}, F_z, P_z, O_z, T₅, T₆, F_{p1}, and F_{p2}. All leads were referenced to the left ear (A1). Eight subjects had 12-lead montages; the last four subjects had 21-lead montages. Data from only the twelve leads common to all subjects were used for analysis.

Data from eight of the subjects were recorded in analog mode using an FM tape recorder at a recording speed of 15/16 inches/second, and subsequently were digitized into a computer off-line. Data from the last four subjects were digitized directly, using a different computerized system. In all cases, the data were digitized at 200 samples/second/channel. The data were acquired for a 3-minute period before injection (baseline) and for a 45-minute period starting immediately after administration of the test compound.

Digitized EEG data were reformatted using programs written by one of the authors (RLP) for use in the EEGSYS software system (Friends Medical Science Research Center, Baltimore, MD). The data were screened by a blinded, trained technician for artifacts due to eye motion or facial motion, using the DIS program of the EEGSYS software. Such artifacts generally occurred in conjunction with the "beep" prompts. During some recording sessions, one or more leads became detached. When this occurred, data from that lead were rejected, but data from other leads were used.

An autoregressive filter (Coppola 1979) with a time constant of 200 msec. was used to remove low frequency harmonics from the remaining data. The effect of the filter was to reduce power at frequencies <0.5 Hz by at least a factor of 2, while not appreciably affecting power at frequencies >1 Hz. The data were analyzed using a 2.56-second (512-data point) epoch by fast Fourier transform. The resulting spectra were averaged over 3-minute intervals. The power spectra were summed to form banded data based on frequency (*f*) as follows: *delta* (1 ≤ *f* < 6 Hz), *theta* (6 ≤ *f* < 8.5 Hz), *alpha* (8.5 ≤ *f* < 10.5 Hz), *alpha*₂ (10.5 ≤ *f* < 12.5 Hz), *beta*₁ (12 ≤ *f* < 18.5 Hz) and *beta*₂ (21 ≤ *f* < 30 Hz). The selection of bands was based on previous results showing that these bands reduce the amount of data without sacrificing useful drug-related information (Coppola and Hermann 1987). Finally, the data were transformed to percent change from baseline. The power-weighted mean frequency within each frequency band was also calculated.

Analysis

Self-reports of mood and feeling state (on MBG, PCAG, LSD subscales of ARCI and on VAS) were tested for

significant effects of drug by a one-way repeated measures analysis of variance (ANOVA). When a significant effect of drug was found, post hoc tests using matched-pair *t*-tests with a Bonferroni correction were performed to assess significance of differences between placebo and each dose of morphine and between the two doses of morphine (three *t*-tests per variable).

Data on spectralized abundance were analyzed by a three-way ANOVA (LEAD × TIME × TREATMENT) for each spectral band using the SAS (SAS Institute, Cary, NC) procedure GLM (General Linear Models). A second set of analyses were performed in a mixed ANOVA (LEAD × TIME × TREATMENT) and regression (MBG, LSD, or PCAG score) analysis. The mixed ANOVA calculated an overall significance of the regression analysis used to determine correlations between the two types of continuous variables. The analyses treated TIME as a repeated measure and all other effects as between-subjects factors. Data used in the LEAD factor were from the 12 leads common to all subjects. The probability (*p*) values were adjusted using the Greenhouse-Geisser correction where appropriate.

Post hoc Bonferroni-corrected *t*-tests were performed using the MEANS option of the GLM procedure or the MEANS procedure from the SAS program system. Further post hoc analysis included correlation analysis between changes in power in each of the six spectral bands, analyzed during each of the three test sessions, with scores on the MBG, LSD, and PCAG subscales of the ARCI and the VAS scores obtained 45 minutes after injection of the test compound. Correlation analyses were only performed when the mixed regression ANOVA analysis showed a significant correlation effect, corrected for effects of TIME, LEAD, and TREATMENT. The dependent variable in all cases was the average spectral power; the independent variable was the score from the self-report scale.

RESULTS

There were no significant effects of morphine or placebo on heart rate or blood pressure; however, morphine caused a significant, dose-dependent decrease in pupillary diameter ($F = [11.3]$, $df = [2, 8]$, $p < .005$ for a main effect of TREATMENT). Post hoc tests showed that pupil size in each of the three drug conditions were significantly different from one another (placebo, 15 and 30 mg morphine). The results on the SDQ indicated that 12, 3, and 1 subjects identified the test compound as "blank" when given saline, 15 mg and 30 mg morphine, respectively. None of the subjects ever identified the test substance as any drug other than "dope."

Table 1 shows the effects of morphine on responses to the VAS. Scores for the five questions relating to positive effects (questions 1, 2, 4, 5, and 6) showed a gener-

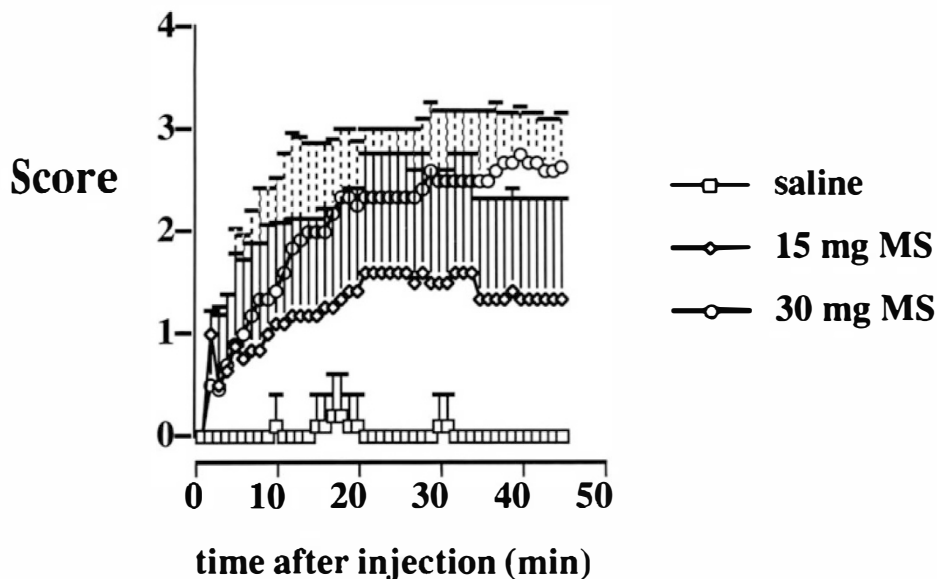


Figure 2. Effect of morphine on the verbal response to the question "How high do you feel?" A score of 0 was equivalent to the response "not at all"; increasing scores were equivalent to responses of "slight," "moderate," "high," and "extremely high." Note the dose-dependent response to morphine. Subjects were instructed to score their responses to this question every time they heard a "beep" prompt, which was recorded over white noise and presented via earphones.

ally dose-dependent increase by morphine. The responses to these questions were highly correlated with one another. Correlation coefficients ranged from 0.74 to 0.995 between any two questions in each test condition. The lowest correlations involved question 6 ("How much do you want to take the drug again?"). There was no significant change from zero in response to the question "Does the drug have bad effects?" Coefficients of ~ 0.4 were obtained for the correlation of VAS score with α_1 power after treatment with either dose of morphine; there were smaller correlation coefficients for other bands and test conditions. The correlation coefficients were not significant for any lead nor for the average of all leads but did achieve statistical significance for calculations including each lead separately in one analysis. Four subjects showed no response to 15

mg morphine; one also showed no response to 30 mg morphine.

Figures 2 and 3 show subjective self-reports of the effects of morphine. The response (prompted by the "beep") to the question "How high do you feel?" was immediate (Fig. 2). The onset of the response was faster and the magnitude was larger when the higher dose of morphine was given. The ARCI revealed an increase in the MBG score in response to morphine (Fig. 3). The overall effect of TREATMENT was statistically significant ($F = [14.7]$, $df = [2, 10]$, $p < .001$). Post hoc t -tests showed that the MBG scores after each of the two doses of morphine were significantly different from the response to placebo but not from each other. The effect of morphine on responses to the PCAG subscale was significant ($F = [6.19]$, $df = [2, 10]$, $p < .02$), but there

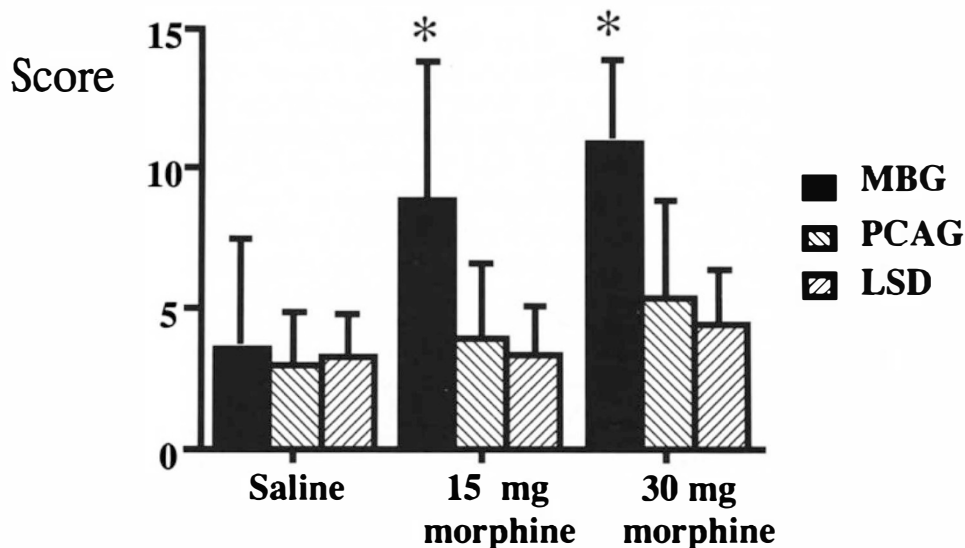


Figure 3. Effect of morphine on responses to the MBG, PCAG, and LSD subscales of the ARCI 45 minutes after the injection of the drug. Error bars indicate one standard deviation. * Significantly different from placebo ($p < .05$) by Bonferroni-corrected matched pair t -test.

Table 2. Analysis of Variance Effects of Drug Treatment, Lead, and Time on Change in EEG Spectral Power from Baseline

Band	Treatment		Time		Time × Treatment		Lead	
	F	p (F)	F	p (F)	F	p (F)	F	p (F)
Delta	2.42	0.0905	4.13	0.0288	4.52	0.0046	0.45	0.9334
Theta	6.96	0.0011	14.46	< 0.0001	4.40	< 0.0029	0.34	0.9764
Alpha ₁	39.76	< 0.0001	17.95	< 0.0001	10.94	< 0.0001	0.81	0.6335
Alpha ₂	3.21	0.0416	15.96	< 0.0001	3.03	0.0003	0.27	0.9912
Beta ₁	7.45	0.0007	12.88	< 0.0001	5.22	< 0.0001	0.99	0.7762
Beta ₂	10.24	< 0.0001	9.77	< 0.0001	5.29	< 0.0001	0.87	0.5694
df	2, 284		15, 4260		30, 4260		11, 284	

Results of Multivariate ANOVA testing whether the different drug treatment conditions (TREATMENT), leads (LEAD), or time after injection (TIME) have statistically significant effects on the percent change in spectral power during the first 45 minutes after injection of test compound. Separate ANOVA procedures were performed for each spectral power band. The *p* value shown for the effect of TIME and the interaction of TIME and TREATMENT is the Greenhouse-Geisser adjusted *p* value where appropriate.

were no significant post hoc comparisons. Morphine did not significantly affect responses on the LSD sub-scale ($F = [2.21]$, $df = [2, 10]$, $p > .1$).

Table 2 shows the results of ANOVAs testing the effects of morphine on percent change in spectral power. There were no significant effects of LEAD nor of any interaction term involving LEAD. A confirmatory factor analysis showed that, for each treatment condition and band, a single factor explained 75% to 95% of the variance across TIME and LEAD. This factor was loaded equally into all leads.

Figures 4, 5, and 6 show the time course of the percent change in spectral power over the duration of the experiment. Delta power increased in the placebo condition (Fig. 4a). The increase was reversed by both doses of morphine, and was shown by a significant main effect of TIME and a significant interaction of TIME with TREATMENT. Individual ANOVAs at each time performed by repeated-measures-contrast ANOVA showed that, at most times after injection, there was a significant effect of TREATMENT. Figure 4b shows the effects of morphine on percent change in theta power. There was a significant effect of TREATMENT as well as of TIME and a TREATMENT-with-TIME interaction. There was an increase in theta power during the first 12 and last 6 minutes of the experiment in response to 30 mg morphine. Theta power decreased slightly in response to the saline and the injections of 15 mg morphine.

Figure 5 shows the effects of morphine on alpha power, separated into two bands, low (alpha₁) and high (alpha₂). Both bands showed significant effects of TREATMENT and TIME, and a significantly TREATMENT-by-TIME interaction. These effects reflected an overall increase in alpha₁ power in response to morphine. The increase was greater after administration of morphine, particularly in response to the 30 mg dose. In this case, the increase after 24 minutes was 30% to 40% over baseline. During the first 15 minutes after injection, there was an increase in alpha₂ power that dis-

sipated more rapidly after the injection of saline than after the injection of morphine.

Figure 6 shows the results for beta power. According to repeated-measures ANOVA, both beta₁ and beta₂

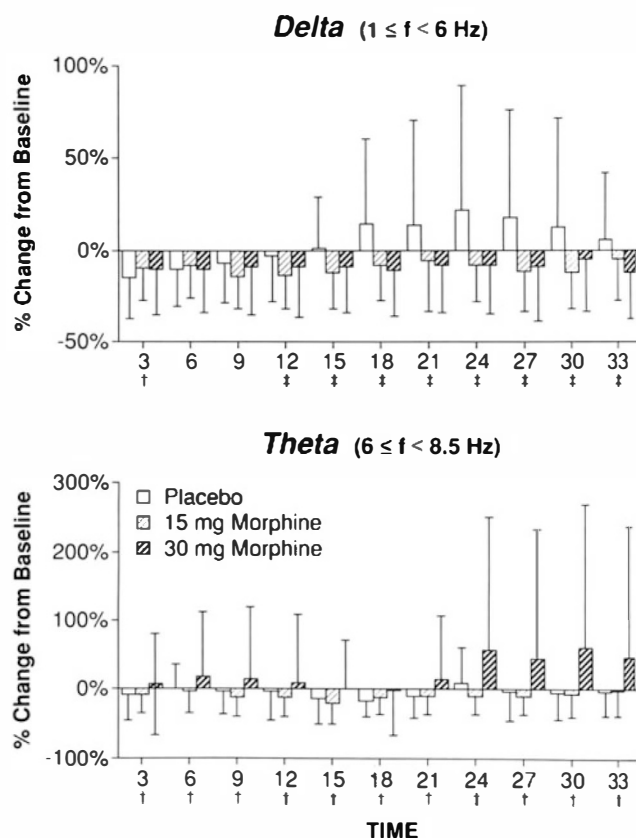


Figure 4. Effects of morphine on low-frequency spectral power. Figure shows change from baseline (pre-injection) epoch. Error bars indicate one standard deviation. † Response to 30 mg of morphine differed significantly from the response to either 15 mg morphine or placebo, $p < .05$ by Bonferroni-corrected *t*-test. ‡ Responses to 15 mg and 30 mg of morphine differed significantly from the response to placebo but not from each other, $p < .05$ by Bonferroni-corrected *t*-test.

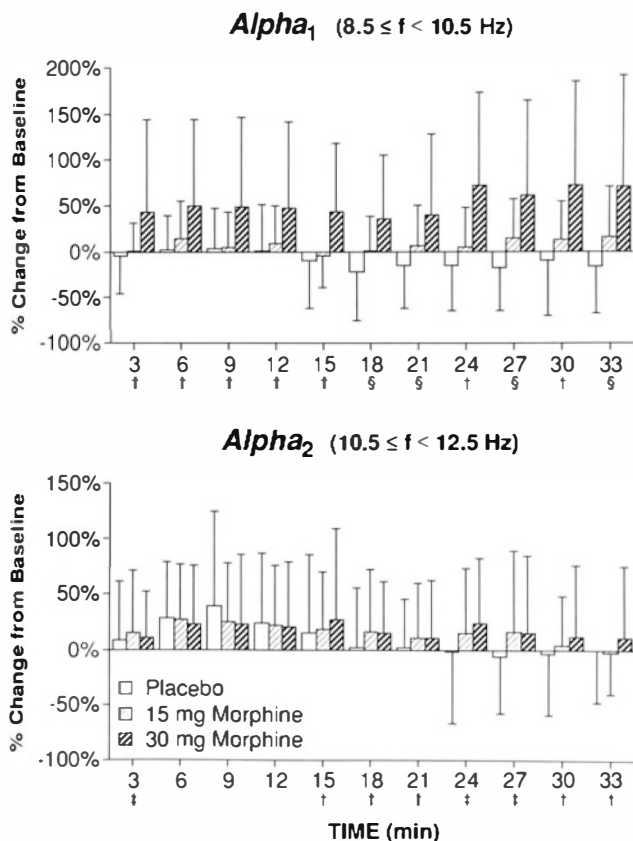


Figure 5. Effects of morphine on *alpha* frequency spectral power. Figure shows change from baseline (pre-injection) epoch. Error bars indicate one standard deviation. † Response to 30 mg of morphine differed significantly from the response to either 15 mg morphine or placebo, $p < .05$ by Bonferroni-corrected *t*-test. ‡ Response to 15 mg and 30 mg of morphine differed significantly from the response to placebo but not from each other, $p < .05$ by Bonferroni-corrected *t*-test. § Response to 15 mg and 30 mg of morphine and to placebo differed significantly from each other, $p < .05$ by Bonferroni-corrected *t*-test.

power showed significant effects of TREATMENT, TIME and a TIME-by-TREATMENT interaction. There was an increase in *beta*₁ during the first 15 minutes after injection of either placebo or morphine. The effect dissipated during the next 15 minutes; 24 minutes after the injection of 30 mg morphine *beta*₁ increased. *Beta*₂ increased during the first 15 minutes after injection and dissipated during the rest of the experiment. The duration of the increase in *beta*₂ appeared to be dose related, lasting the longest after injection of 30 mg morphine.

Table 3 shows the results of a test (by mixed ANOVA regression) for significant correlation between change in EEG spectral power from baseline and scores on the three subscales of the ARCI. The procedure tested correlation of the score on each subscale nested within TREATMENT and LEAD. Positive correlations

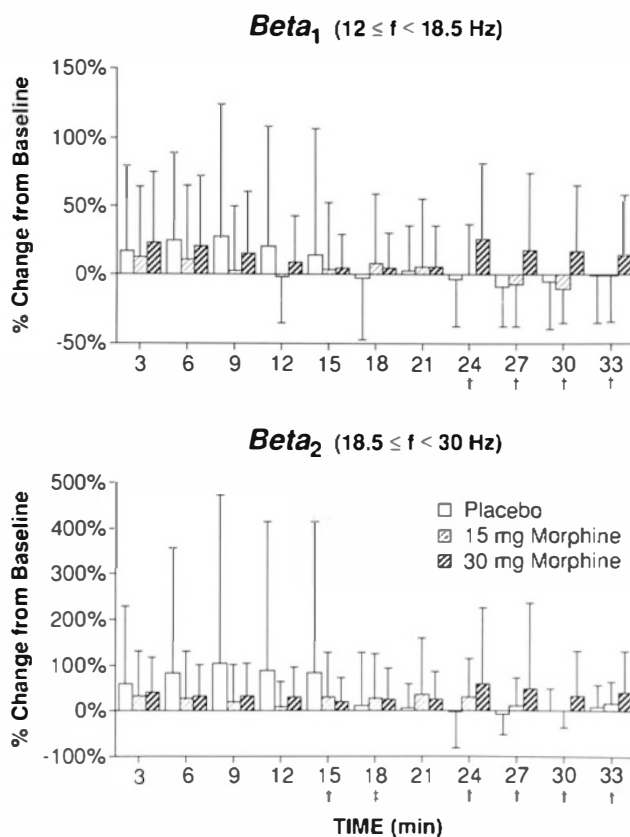


Figure 6. Effects of morphine on *beta* spectral power. Figure shows change from baseline (pre-injection) epoch. Error bars indicate one standard deviation. † Response to 30 mg of morphine differed significantly from the response to either 15 mg morphine or placebo, $p < .05$ by Bonferroni-corrected *t*-test. ‡ Response to 15 mg and 30 mg of morphine differed significantly from the response to placebo but not from each other, $p < .05$ by Bonferroni-corrected *t*-test.

were found between change in *theta*, *alpha*, and *beta* power and MBG score; negative correlations were found with PCAG and the *alpha*₁ and *beta*₂ bands. The scores on the LSD subscale showed no tendency for correlation with EEG measures. There was no correlation of changes in power in the *delta* band with any of the scores on the three subscales.

After the ANOVA, individual correlation analyses were performed. In these analyses, each factor (TREATMENT, LEAD, and TIME) were separated so that (3 × 12 × 15 =) 540 correlation analyses were performed. Without the ANOVA to provide a protecting analysis, a correction for multiple comparisons (such as that of Bonferroni) would have been necessary and a value $p < 10^{-4}$ would have been the criterion for significance. With the covering analysis, we used an uncorrected *p* value less than .05 as the criterion for significance.

Using the *alpha*₁ band and lead F₇ as an example, there were 10/15 and 12/15 times when the percent

Table 3. Significance of Covariance Between Scores on Subscales from the ARCI and Percent Change in EEG Spectral Power from Baseline

Band	MBG		LSD		PCAG	
	F	p (F)	F	p (F)	F	p (F)
Delta	0.40	0.992	0.59	0.9712	0.62	0.9578
Theta	2.07	0.0070	0.26	1.000	0.48	0.9949
Alpha ₁	4.74	< 0.0001	0.95	0.5549	3.17	< 0.0001
Alpha ₂	1.67	0.0127	1.36	0.0901	0.54	0.9864
Beta ₁	1.53	0.0325	0.75	0.8470	1.22	0.1888
Beta ₂	1.33	0.0108	0.80	0.7897	2.85	< 0.0001

The procedure tests for a significant correlation between change in EEG power in each band nested within the factors TREATMENT and LEAD but averaged over all 15 times after injection.

change in EEG power from baseline was significantly correlated ($p < .05$) with the score on the MBG and PCAG subscales, respectively, in response to 30 mg morphine. The correlations never achieved statistical significance in response to 15 mg morphine or placebo. The correlation of change in EEG power vs. score on the LSD subscale never attained statistical significance. Figure 7 shows a typical example of the scatter plots illustrating the correlation. Similar findings were obtained from all of the other eleven leads from which data were analyzed.

DISCUSSION

As slow-wave sleep is associated with an increase in *delta* power and a decrease in *alpha* power (Walter 1959), morphine-induced decreases in *delta* power and increases in *alpha* power suggest that opioids produce arousal in subjects tolerant to the sedative effects of these drugs. This view is consistent with reports that morphine produces psychomotor activation in rodents (Babbini and Davis 1972; Shuster et al. 1975; Joyce and Iversen 1979). Because *alpha*₁ and *beta*₂ power are negatively correlated with scores on the PCAG subscale and positively correlated with scores on the MBG subscale of the ARCI, reduced sedation (inferred from the PCAG score) accompanies positive affect (indicated by the MBG score) induced by morphine. These findings support and extend previous observations that morphine, like other opioids, induces insomnia in men who are not physically dependent upon opioids but have histories of opioid abuse (Kay et al. 1969).

Differences in the behavioral response to morphine, depending on the subject population, may explain some of the discrepancies observed with regard to EEG effects caused by or associated with morphine. It is well established that morphine is a sedating drug in normal subjects (Matejcek et al. 1988). Naive users also reported dizziness, nausea, and headache in response to morphine (Beecher 1959). Conversely, in experienced users,

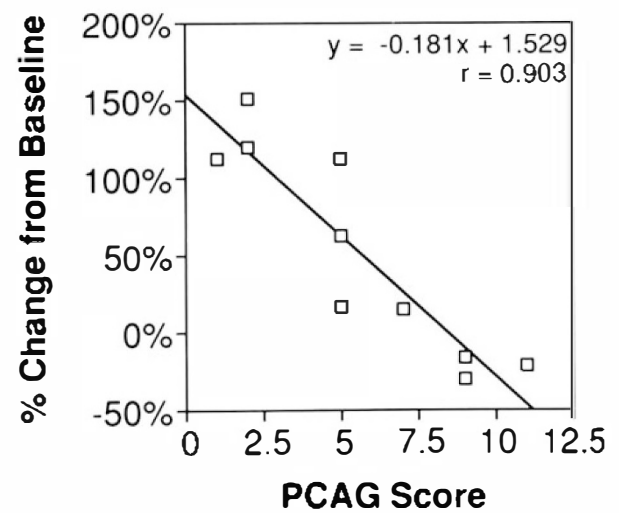
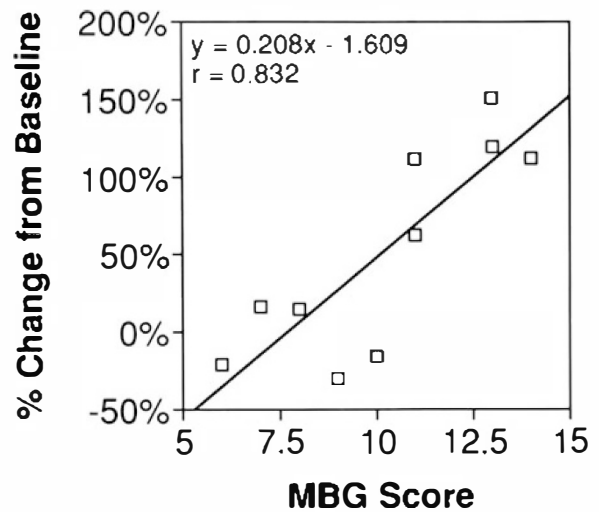


Figure 7. Correlation between change in EEG power in the *alpha*₁ band and scores on the MBG and PCAG subscales of the ARCI. MBG and PCAG were administered 45 minutes after injection. EEG data shown were measured 15 minutes after injection of 30 mg morphine; EEG data were taken from a single lead (F₇); other leads showed similar patterns.

positive effects of the drug may keep subjects interested during an experimental procedure when they otherwise would lose interest and might fall asleep.

Although EEG activity recorded from a particular lead on the scalp does not necessarily reflect cortical activity immediately below that lead, the absence of a significant effect of LEAD in this study is consistent with the finding that morphine produces an overall reduction of glucose metabolism throughout the entire cortex (London et al. 1990). These findings imply that positive effects of morphine on mood in polydrug abusers involve large cortical areas or subcortical regions rather than discrete loci in the cortex.

Positive correlations were found between the changes in α_1 , α_2 , β_1 , and β_2 power in response to 30 mg morphine and scores on the MBG subscale of the ARCI. In contrast, negative correlations were observed between changes in α_1 and β_2 and scores on the PCAG subscale. These correlations imply that positive effects of morphine, as measured by the MBG score, are related to increases in α and β activity and to a reduction in sedation, as measured on the PCAG subscale. Although these correlations are consistent with the significant increases in α power produced by morphine, statistically significant increases in β power were not observed. The lack of a consistent increase in β power in response to morphine contrasts with the effects of cocaine, which clearly increases β activity (Berger 1931; Herring et al. 1985).

Despite marked differences in the behavioral and physiological activities of drugs of abuse, an emerging literature suggests that there are commonalities in the actions of these drugs, extending beyond their assignment to pharmacological classes. These commonalities include the ability to activate neuronal systems that produce positive affective states and attribute "incentive salience" (Robinson and Berridge 1993). In physiological terms, a variety of studies performed in animals have implicated central dopaminergic systems in the common behavioral effects of abused drugs (Hubner and Koob 1993). Studies in human volunteers have indicated that a common effect of drugs of abuse in experienced drug users is a reduction of cerebral glucose metabolism (London and Morgan 1993). The presenting findings with morphine extend observations with other drugs of abuse to indicate that an increase in α power may be another common action of drugs of abuse. Aside from the present and previous observations that morphine increases α power (Lukas et al. 1982; Lukas 1991), enhancement of α power has also been observed after administration of cocaine (Berger 1931) and doses of alcohol that had positive effects on mood (Lukas et al. 1986a, 1986b; Cohen et al. 1993; Lukas 1993).

Identification of a physiological process that underlies the behavioral aspects of drug abuse would be an

important step in elucidating the addictive process. It appears that an increase in α power is related to the positive rewarding properties of morphine. Further investigation of the anatomical substrates of the drug-induced increase in α power and its role in the acute and chronic effects of drugs of abuse appears to be warranted.

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