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Facial EMG as an Index of Affective Response to Nicotine

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Abstract

Negative affect reduction has been postulated to be a key feature of cigarette smoking. In the present study, facial electromyography (EMG), heart rate (HR), and skin conductance (SCR) were used to evaluate the affective significance of acute nicotine administration and overnight withdrawal. Smokers ($n=115$) attended four 90-min laboratory assessment sessions scheduled approximately three days apart. The four sessions provided a complete crossing of two pre-laboratory deprivation conditions (12-hour deprived vs. nondeprived) with two drug conditions (nicotine vs. placebo nasal spray). During each session, smokers viewed affective slides while facial EMG, HR, and SCR were recorded. Results indicated that for women, nicotine nasal spray resulted in lower corrugator EMG activity during both smoking-deprived and nondeprived sessions, compared to placebo. However, nondeprived women also showed an increase in zygomaticus EMG when given nicotine compared to placebo spray, while smoking-deprived women demonstrated a decrease in the zygomaticus response to nicotine compared to placebo. With men, nicotine also appeared to lower corrugator during deprivation, but not nondeprivation, compared to placebo spray, though the contrast only approached significance. With zygomaticus EMG, nicotine spray decreased men's zygomaticus responding during nondeprivation but not during deprivation, compared to placebo spray. The HR results reflected the stimulatory properties of the drug rather than nicotine's affective properties, while SCR was unresponsive to our experimental manipulations. The corrugator EMG results support negative reinforcement models of smoking that postulate that acute nicotine use reduces withdrawal-driven negative affect.

Keywords

EMG; heart rate; skin conductance; nicotine; affect

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Negative affect has been found to be a contributing factor in over 50% of smoking lapses (Shiffman, Paty, Gnys, Kassel, & Hickcox, 1996) following a quit attempt and has been positively related to treatment failure and relapse across a variety of treatment modalities (Borrelli et al., 1996; Kenford et al., 2002). Despite clinical evidence for the association of affect and smoking behavior, the mechanisms linking the modulation of affect to the direct effects of nicotine have not been reliably demonstrated in human laboratory studies (see Kassel, Stroud, & Paronis, 2003, for a review). For example, smoking has been associated with self-reported anxiety reduction in some studies (Perkins & Grobe, 1992; Pomerleau & Pomerleau, 1987; Pomerleau, Turk, & Fertig, 1984), but not in others (Herbert, Foulds, & Fife-Schaw, 2001; Jarvik, Caskey, Rose, Herskovic, & Sadghpour, 1989). Smoking has also been shown to attenuate laboratory-induced negative affect in some (Gilbert, Robinson, Chamberlin, & Spielberger, 1989; Gilbert & Welser, 1989; Woodson, Buzzi, Nil, & Battig, 1986), but not all (Hatch, Bierner, & Fisher, 1983; Herbert et al., 2001; Jarvik et al., 1989; Shiffman & Jarvik, 1984), studies.

While the discrepancies in the literature suggest that the effects of smoking on mood remain unclear, a possible reason for inconsistency may lie in the sensitivity of our measures to detect subtle changes in motivation and affective processes that influence smoking behavior, such as those described by Baker and colleagues (Baker, Morse, & Sherman, 1987; Baker, Piper, McCarthy, Majeskie, & Fiore, 2004; Kenford et al., 2002). Most studies have largely relied on self-report measures following short-term deprivation (e.g., Hall, Muñoz, & Reus, 1994; Hutchison, Niaura, & Swift, 1999) or retrospective self-report following relapse (e.g., Marlatt & Gordon, 1980; Shiffman, 1982). These studies have yielded important findings regarding the relationship between smoking behavior, relapse, and negative mood. However, self-report measures require extensive cognitive processing and may not be sensitive to subtle yet important changes in affect brought about by nicotine. In addition to actual symptoms of nicotine withdrawal, self-report of negative affect during withdrawal may also be influenced by the expectancy that smoking deprivation leads to increased negative mood. Additionally, self-report is unlikely to capture the low intensity interoceptive signals that may both motivate smoking behavior at the early stages of nicotine withdrawal and be reversed by acute nicotine administration (Baker et al., 2004). Using a psychophysiological approach to study the basic biological processes associated with emotion and motivation may provide a more sensitive assessment of the affective relevance of nicotine use and withdrawal while avoiding the potential biases inherent to the measurement of cognitively-mediated self-reported affect.

Facial electromyography (EMG) offers a measurement approach that is sensitive to the subtle neurophysiological shifts found with affect. Facial EMG has been found to differentiate between affective responses (e.g., Cacioppo, Petty, Losch, & Kim, 1986; Greenwald, Cook, III, & Lang, 1989; Witvliet & Vrana, 1995) and even among negatively valenced emotions such as fear and disgust (Vrana, 1993). The most commonly measured facial muscles are the zygomaticus major and corrugator supercilii, located in the cheek (smile) and eyebrow (frown), respectively. Zygomaticus potentiation has been found to be largest in response to positively valenced affective stimuli while corrugator activation is largest in response to negatively valenced affective stimuli (Dimberg, 1990; Witvliet & Vrana, 1995). The use of facial electromyography to measure affective response may help

clarify the role of nicotine in mood modulation. Previous psychophysiological studies investigating the affective properties of nicotine have relied upon autonomic nervous system (ANS) measures such as heart rate (Perkins, Grobe, Fonte, & Breus, 1992; Tsuda, Steptoe, West, Fieldman, & Kirschbaum, 1996) or skin conductance (Edman & Schalling, 2006). While there is evidence that these ANS measures are able to differentiate among emotional states (Christie & Friedman, 2004; Levenson, 1992), these measures are susceptible to the arousing properties of affective stimuli (Lang, 1979) and nicotine (Knott, 1979). Unlike these previous studies, our study used facial EMG, a somatic nervous system measure that is more reflective of affective state (valence) than of physiological arousal (Dimberg, 1990), to complement ANS measures in an attempt to disentangle the affective and stimulatory effects of nicotine on men and women. Facial EMG should allow for a determination of the affective properties of nicotine independent of the stimulatory properties detected with ANS measures and should be free of the cognitive bias frequently associated with self-report measures of affect (Waldron, 1983).

The facial EMG approach may be particularly helpful in addressing potential gender differences that have been found with smoking cessation success. Administering nicotine has been found to be less effective in ameliorating withdrawal symptoms in men, compared to women, in some studies (Hatsukami, Skoog, Allen, & Bliss, 1995; Killen, Fortmann, Newman, & Varady, 1990; Wetter et al., 1999). Women may be more sensitive to the pharmacological properties of nicotine, as women tend to consume less nicotine (Goldberg et al., 1993; Killen et al., 1990), but report greater nicotine withdrawal symptoms (Shiffman, 1979) and increased nicotine sensitivity (Battig, Buzzi, & Nil, 1982; Silverstein, Feld, & Kozlowski, 1980) than men. One possibility is that women are more sensitive to the mood-altering properties of nicotine, as research suggests that nicotine reduces the aversiveness experienced during experimentally-induced negative moods in women to a greater extent than men, using self-report (File, Fluck, & Leahy, 2001) and psychophysiological (Robinson et al., 2007) measures. Facial EMG may be a better method than self-report for examining gender differences in affective response to nicotine, given that self-report has been found to be subject to gender differences in terms of awareness of bodily responses (Roberts & Pennebaker, 1995; Waldron, 1983).

In this study, we evaluated the effects of nasal nicotine administration and acute nicotine deprivation on affective processing, using measures of facial EMG (zygomaticus and corrugator muscle groups), ANS response (heart rate and skin conductance) and self-report measures of affect. We were particularly interested in whether facial EMG would be sensitive to the potential affective consequences of nicotine deprivation and administration. We hypothesized that nicotine deprivation, compared to nondeprivation, would lead to increased negative affect in smokers and that this deprivation-induced negative affect would be reduced by nicotine spray, compared to placebo spray, as measured by facial EMG. We also sought to determine whether there are gender differences with facial EMG in response to nicotine. We hypothesized that women, compared to men, would show greater facial EMG responding indicative of decreased negative affect when given nicotine nasal spray compared to placebo spray. Finally, we evaluated the extent to which ANS measures were concordant with facial EMG responses to nicotine. We hypothesized that the facial EMG measures would provide patterns of response more indicative of affective change to the

deprivation and nasal spray manipulations, while the ANS measures were expected to be more reflective of the arousing properties of nicotine.

METHOD

This study manipulated nicotine deprivation and acute nicotine administration using a within-subjects design while measuring facial EMG and ANS response to affective slides. Smokers attended four 90-min laboratory assessment sessions scheduled approximately three days apart. The four sessions provided a complete crossing of two pre-laboratory deprivation conditions (12-hour deprived vs. nondeprived) with two drug conditions (nicotine vs. placebo nasal spray). During each session, smokers viewed two blocks of affective slides while facial EMG, heart rate, and skin conductance was recorded. The first was a habituation block, which was used to acclimate the participant to the novel effects of the nasal spray administration and general laboratory surroundings. All participants received placebo spray before this block. The second (test) block was similar to the habituation block in terms of slide content. Smokers received either nicotine or placebo nasal spray before the test block of trials. Before involvement in the laboratory portion of the experiment, smokers reported their levels of nicotine use, acute stress, depressed affect, and body mass. The affective startle response was also measured and these results are reported in Cinciripini et al. (2006) and Robinson et al. (2007).

Participants

One hundred fifteen cigarette smokers (63 male, 52 female) were recruited using newspaper ads from the Houston metropolitan area and were paid \$125 for attending one screening and four laboratory sessions. Participants provided informed consent and the protocol was approved by the University of Texas M. D. Anderson Cancer Center's Institutional Review Board. Only smokers who were between the ages of 18 and 59, smoked 10 or more cigarettes per day, produced an expired carbon monoxide level greater than 8 ppm (or produced saliva cotinine >30 ng/ml), were fluent in English, and had no uncontrolled medical illness were included in the study. Individuals were excluded if they were taking psychotropic or narcotic medication, met criteria for a current psychiatric disorder, reported hearing loss, or were involved in current smoking cessation activity. Twenty-four additional participants met inclusionary criteria but were completely excluded from analyses due to experimental noncompliance, including use of exclusionary substances, failure to abstain from smoking on their deprivation sessions, a startle nonresponse/missing rate greater than 30%, or due to completing only a single lab session.

Procedure

Screening and Orientation—All smokers were initially screened by telephone to establish their eligibility for the study. Potential participants were administered a telephone version of the PRIME-MD (Spitzer et al., 1994), which screened for major mental disorders (depression, anxiety, somatoform, alcohol dependence and eating disorders). Participants eligible after the phone screening attended an orientation visit and completed questionnaires concerning demographic, health, mood, and smoking history, including the Fagerström Test for Nicotine Dependence (FTND; Heatherton, Kozlowski, Frecker, & Fagerström, 1991).

Laboratory Sessions

Smoking deprivation and assessment: Before the deprivation sessions, participants were instructed to refrain from smoking for 12 hours before their laboratory visit. Compliance with nicotine deprivation instructions was assessed using expired CO to confirm abstinence. Smokers were required to produce a CO level below 10 ppm or 50% of their baseline level as assessed during the orientation visit. Nonabstinent participants in the deprived condition were rescheduled¹. Smoking was unrestricted before the nondeprived sessions. In order to ensure similar conditions of nondeprivation, participants in the non-deprived condition smoked one cigarette preceding the affective slide viewing. All participants were asked to limit their intake of caffeinated beverages to no more than two cups taken before 8:00 AM on the day of the laboratory session.

Physiological measurement: After completing the questionnaires, EMG electrodes (Ag-AgCl) filled with saline gel were attached in the participant's face to the right corrugator supercilii and zygomaticus major regions using a bipolar configuration (Fridlund & Cacioppo, 1986). These EMG signals were acquired and amplified with BIOPAC Systems' (Goleta, CA) EMG100A Electromyogram Amplifier modules. A 10–500 Hz bandpass filter (Tassinari & Cacioppo, 2000) and a 60 Hz notch filter were used for EMG. Skin conductance response (SCR) amplitude was collected by placing an electrodermal response transducer on the fore and ring fingers of the participant's nondominant hand using BIOPAC Systems' GSR100C Electrodermal Response Amplifier. Phasic increase in skin conductance following slide onset was measured, with a high pass filter set at 0.05 microsiemens (μS ; Dawson, Schell, & Fillion, 2000). Heart rate (HR) was collected by placing a photoelectric pulse plethysmogram transducer on the middle finger of the participant's nondominant hand using BIOPAC Systems' PPG100C Photoplethysmogram Amplifier. The data was recorded and displayed using BIOPAC Systems' AcqKnowledge III data acquisition software (version 3.5.3) installed on a Pentium III computer. Recording resolution was 1000 Hz. Following sensor attachment, participants sat quietly for 5 minutes to allow for initial habituation to the environment.

Affective slide viewing: Forty-eight color slides were presented, twelve each from the categories of positive, neutral, negative, and cigarette. The positive, neutral, and negative slides were selected from the International Affective Picture System (IAPS; Center for the Study of Emotion and Attention, 1999)². The negative slides were selected from the negatively valenced, high arousal (interest) dimensions, the positive slides from the positively valenced, high arousal dimensions, and the neutral slides from the neutrally valenced, low arousal dimensions. The cigarette slides, consisting of smoking cues such as images of burning cigarettes and people smoking in a social context, were created for this

¹Three smokers reported smoking within 9 to 11 hr of a deprivation session. Excluding these sessions did not affect any of the analyses involving the deprivation status variable. Additionally, we conducted analyses where we excluded sessions where smokers produced CO above 10 ppm on deprived days. This more stringent definition of deprivation also did not alter the results. Thus, the decision was made by the authors to not exclude any of these sessions in the analyses.

²The following IAPS slides were used: Positive, 4220, 4652, 4658, 4659, 4660, 4670, 5621, 5629, 8030, 8370, 8490, and 8500; Neutral, 7000, 7010, 7020, 7030, 7040, 7050, 7060, 7080, 7090, 7100, 7150, and 7170; Negative, 3010, 3060, 3100, 3120, 3130, 3150, 3170, 3500, 6230, 6350, 6560, and 9410. The positive ($M = 6.54$, $SD = 0.59$) and negative pictures ($M = 6.96$, $SD = 0.30$) did not differ on arousal but did differ from neutral ($M = 2.80$, $SD = 0.39$), $p < .05$.

experiment and are validated elsewhere (Carter et al., 2006). A PC using Psychology Tools' Eprime software (Pittsburgh, PA) presented a 91.5 cm x 122 cm image of the slides using a digital projector, on a screen approximately 1.5 m from the participant. Participants were instructed to sit quietly and keep their eyes on the images during the slide viewing task. Self-reported mood and craving assessments, not instructionally linked to the slides, were presented on screen to the participants every third slide and are reported elsewhere (Robinson et al., 2007).

Two separate blocks of trials (habituation and test), each consisting of 24 slides, were presented using procedures similar to those of Cuthbert et al. (1996). Within each block, the 24 slides were arranged such that each block included 6 slides of each valence. Each slide was presented for 6 s followed by a randomly determined inter-slide interval that varied from 10 to 20 s. The order of slide presentation was counterbalanced, so that participants saw each picture equally often in the first through sixth positions within each block, and each block occurred first or second with equal frequency. Four separate slide orders, one for each session, were counterbalanced across subjects.

Nasal spray administration: Participants received two administrations of nasal spray each session, one before each of the two slide blocks. After the initial 5-min rest period, participants received placebo nasal spray followed by a 5-min absorption period. Following this absorption period, the block 1 (habituation) slides were presented and physiological recording was initiated. The habituation block was included in the design to allow the participant to become accustomed to the laboratory environment, the potential novelty effects of the startle procedure, and the aversiveness of the nasal spray. Smokers received either nicotine nasal spray (1 mg) or placebo spray (0 mg), depending on the session, five minutes before block 2 (test). Participants self-administered one spray per nostril (either 0 or 0.5 mg nicotine per spray). Participants were blind to the content of the spray. The nicotine spray is commercially available from Pharmacia & Upjohn, Inc. (Peapack, NJ) and marketed as a nicotine replacement product (Nicotrol NS). Peak arterial levels of nicotine of about 10 ng/ml occur within five minutes of a single application of the nasal spray (0.5 mg/nostril; Gourlay & Benowitz, 1997). The placebo spray was packaged identically to the nicotine spray and was also provided by Pharmacia & Upjohn. It contained piperine to simulate the nasal sensory stimulation of the nicotine spray.

Data Reduction & Analysis

The 6 s after the onset of each slide was scored in 1-s epochs for all psychophysiological channels, in order to produce mean amplitude values. SCR was scored in 1-s epochs from 2–7 s after slide onset due to the latency of the sweating response (Stern, Ray, & Quigley, 2001)³. Collapsing across these 6 epochs created a single mean for each slide. Six slides of each valence were presented in each block. Scoring was conducted offline using the AcqKnowledge software. Corrugator and zygomaticus facial EMG were scored in microvolts (μ V) after being rectified and integrated using a 20-ms time constant. HR was scored as beats per minute (BPM) and SCR was scored in microsiemens (μ S). Trials with

³We analyzed peak SCR values during the 2–7 s window, but the results were not different from those produced using mean SCR.

clear movement artifact or excessive baseline activity were marked as missing. To minimize the impact of outliers, 1% of observations were trimmed from both sides of the overall distribution for each of the psychophysiological measures (Winer, 1971)⁴. For the four psychophysiological variables, each cell of the 2 (Gender) x 2 (Nasal Spray) x 2 (Deprivation Status) x 4 (Slide type) design was composed of six observations.

The hypotheses concerning the effects of Nicotine and Nicotine Deprivation on physiological responding were evaluated using mixed models analysis (SAS Proc Mixed) on block 2 (test) values separately for each physiological variable. The hypotheses listed below were evaluated using both between- and within-subject fixed effects, with subject and session as random effects. The mixed model approach is a form of the generalized linear model (GLM) that allows for more specific estimation of the correlation structure of the residuals and that will not exclude cases with missing observations, thus allowing the use of all available data (Bageilla, Sloan, & Heitjan, 2000). Gender was modeled as a between-subjects fixed effect and Deprivation Status (12-hr nicotine deprived vs. nondeprived), Nasal Spray (nicotine vs. placebo), and Slide type (positive, neutral, negative, & cigarette) as within-subjects fixed effects. The models also contained session and trial as covariates to account for habituation to the stimuli between and within sessions. A single acoustic startle probe was presented during two thirds of the slides, occurring at a random time of 2.5 to 5 s after slide onset. The startle methodology and results are described in Cinciripini et al. (2006). To account for the effects of the probe on the physiological measures used in this study, we included the presence of a startle probe as a covariate in these analyses. All descriptions of differences between means following a significant mixed model effect were the result of comparisons of least-square means of fixed effects using SAS contrast statements. Because previous research suggests that zygomaticus EMG may increase to both highly negative and positive pictures (Lang, Greenwald, Bradley, & Hamm, 1993), we tested for a quadratic relationship between slide type valence and zygomaticus EMG

Additional analyses were performed on the models involving psychophysiological measures that included the habituation block (block 1) as a covariate. These covariate analyses were used to examine adaptation in the startle response across the two blocks, which in this case could be influenced by either nicotine spray or placebo (given in block 2) or deprivation. This approach has several methodological advantages over computing a difference score between the two blocks (Mulligan & Wiesen, 2003).

RESULTS

Participant Characteristics

Participant characteristics for this sample are tabled in Robinson et al. (2007) and are summarized here. The amount smoked by participants in this study averaged about a pack a day ($M=22.26$, $SD=10.26$) with a mean FTND score of 5.00 ($SD=2.18$). In terms of race/

⁴The distributions for corrugator EMG (skewness = 11.30, kurtosis = 135.71), zygomaticus EMG (skewness = 32.02, kurtosis = 1111.44), heart rate (skewness = 1.39, kurtosis = 6.93), and skin conductance (skewness = 6.38, kurtosis = 112.61) were greatly skewed by outliers prior to trimming. The distributions for corrugator EMG (skewness = 3.72, kurtosis = 18.81), zygomaticus EMG (skewness = 2.18, kurtosis = 9.00), heart rate (skewness = 0.27, kurtosis = -0.19), and skin conductance (skewness = 0.62, kurtosis = 9.02) were closer to normality following 1% trimming on both ends of the distributions.

ethnicity, 48.7% of the participants were African American, 41.7% were European American, and 9.6% were of non-African American minority status. Education and occupation data suggested that a significant portion of the participants came from lower socioeconomic backgrounds, with 37.4 % of the participants indicating that they were currently unemployed and not in school.

Corrugator Supercilii EMG

A significant 3-way Gender x Deprivation Status x Nasal Spray interaction was found, $F(1, 95)=8.12, p<.006$ (see Figure 1). Test of simple main effects indicated that for women, nicotine nasal spray resulted in lower corrugator activity during both smoking-deprived, $F(1, 95)=19.99, p<.0001$, and nondeprived sessions, $F(1, 95)=59.75, p<.0001$, compared to placebo. Nicotine also appeared to lower corrugator in deprived men compared to placebo spray, as the contrast approached significance ($p<.06$). However, corrugator did not vary by spray type in nondeprived men. A significant Gender x Nasal Spray interaction and main effects for gender, deprivation status, and spray were also found, but were not interpreted in light of the 3-way interaction.

A significant main effect for slide type was found, $F(3, 348)=37.47, p<.0001$, with post hocs indicating that corrugator response was larger during negative slides compared to all other types ($p's<.0001$), while neutral, positive, and cigarette slides did not differ from each other. A significant main effect for probe indicated that slide trials containing an acoustic startle probe produced larger corrugator responses ($M=6.17 \mu V, SE=0.28$) than trials without a probe ($M=6.02 \mu V, SE=0.28$), $F(1, 116)=7.22, p<.009$. None of the results were altered when block 1 (habituation) corrugator values were included as a covariate.

Zygomaticus Major EMG

A significant Gender x Deprivation Status x Nasal Spray 3-way interaction was also found for zygomaticus EMG, $F(1, 99)=94.15, p<.0001$ (see Figure 2). For smoking-nondeprived women, an increase in zygomaticus EMG was found following nicotine compared to placebo spray, $F(1, 99)=11.78, p<.001$, while smoking-deprived women demonstrated a decrease in response to nicotine compared to placebo, $F(1, 99)=40.18, p<.0001$. With men, nicotine spray decreased zygomaticus responding during nondeprivation, $F(1, 99)=111.76, p<.0001$, but not during deprivation ($p=.78$), compared to placebo spray. Significant Gender x Deprivation Status and Gender x Nasal Spray interactions, as well as deprivation status and spray main effects, were found but not interpreted in light of the significant 3-way interaction involving those terms. A main effect was found for probe, such that slides containing a startle probe produced larger zygomaticus values ($M=11.31 \mu V, SE=0.04$) compared to non-probed slides ($M=11.29 \mu V, SE=0.04$), $F(1, 116)=4.20, p<.05$. We also tested for a quadratic relationship between slide type and zygomaticus EMG but the main effect was nonsignificant. A main effect for slide type was not found. Covarying block 1 (habituation) zygomaticus EMG did not change any of the above results.

Heart Rate

We found a significant Gender x Deprivation Status x Nasal Spray 3-way interaction, $F(1, 92)=21.90, p<.0001$ (see Figure 3). Nicotine spray increased HR for deprived men, $F(1,$

92)=185.86, $p<.0001$, deprived women, $F(1, 92)=216.72$, $p<.0001$, as well as nondeprived men $F(1, 92)=27.02$, $p<.0001$, compared to placebo spray. However, spray did not affect nondeprived women. Significant Deprivation Status x Nasal Spray and Gender x Deprivation Status interactions, and main effects for deprivation status and nasal spray, were found but were not interpreted in light of the significant 3-way interaction. No main effect for slide type or startle probe were found. Including block 1 (habituation) HR did not alter these significant findings.

Skin Conductance

No significant interactions or main effects were found for SCR, with the exception of a main effect for probe, $F(1, 116)=120.10$, $p<.0001$. Trials containing startle probes producing larger SCR ($M=0.02 \mu S$, $SE=0.003$) than trials without probes ($M=0.001 \mu S$, $SE=0.003$). This finding was not altered by the inclusion of block 1 (habituation) SCR.

DISCUSSION

These results suggest that facial EMG is sensitive to the interactive effects of overnight nicotine deprivation and acute nicotine administration on the affective processing of emotionally-valenced stimuli. Significant 3-way Gender x Deprivation Status x Nasal Spray interactions were found for both the corrugator supercilii and zygomaticus major. Nicotine nasal spray reduced mean corrugator supercilii EMG responding compared to placebo nasal spray. This was true for women during nondeprived and smoking-deprived sessions and for men during deprived sessions, though the contrast only approached significance for deprived men. We failed to find an interaction between slide type and either deprivation or nasal spray, suggesting that the affective states produced by the presence or absence of onboard nicotine were sufficiently intense as to overshadow any potential affective variance introduced by the slides.

One interpretation of the overnight deprivation corrugator EMG results is that both male and female smokers experience a reduction in deprivation-driven negative affect when given nicotine spray compared to placebo spray. It is certainly possible that nicotine increases positive affect, given its ability to stimulate reward pathways in the brain (Volkow, Fowler, & Wang, 2004; Wise & Rompre, 1989). However, our pattern of results gives somewhat more weight to the argument that nicotine reduces the negative affect brought upon by deprivation, at least with our sample of older, experienced smokers. If so, these results support an important aspect of recent theories of negative reinforcement (Baker et al., 1987; Baker et al., 2004; Kenford et al., 2002), namely that acute use of nicotine provides relief from withdrawal-induced negative affect.

It is unclear whether corrugator supercilii EMG is reflective of the preconscious interoceptive cues of negative affect, which is postulated to motivate smoking (Baker et al., 2004), or simply tracks conscious cognitive appraisal of mood state. On the one hand, facial EMG of muscles such as the corrugator has been shown to be a sensitive measure of covert facial activity in response to affective stimuli that are too subtle or fleeting to be observed (Cacioppo et al., 1986), such as to brief (30 ms) backward-masked affective stimuli (Dimberg, Thunberg, & Elmehed, 2000). On the other hand, the results of self-reported

affect from this trial, reported in an earlier study (Robinson et al., 2007), indicated that the deprived smokers did differentiate between the nicotine and placebo nasal spray conditions. Although facial EMG has been found to be responsive to stimuli outside of awareness and to affective states not reflected in self-reported mood, using this particular design, we are ultimately unable to conclude whether our corrugator EMG results reflect conscious or preconscious negative affect.

Nicotine nasal spray increased zygomaticus major responding for nondeprived women. Increased zygomaticus responding is usually found in response to strongly positive or strongly negative affective states (Lang et al., 1993). If, based on the corrugator results (Figure 1), we assume that giving nondeprived women nicotine spray compared to placebo decreased negative affect processing, then this zygomaticus result is concordant with the corrugator result for women in these conditions. In contrast, for nondeprived men and deprived women, nicotine nasal spray actually decreased zygomaticus responding compared to placebo spray. These apparently contradictory zygomaticus results are possibly the result of zygomaticus EMG having been found to be a less reliable indicator of affective state compared to corrugator EMG, which is supported by our finding that only corrugator was sensitive to slide type (i.e., corrugator response was greater in the presence of negative stimuli). For example, one study found that, for men, valence and zygomaticus EMG produced almost no correlation ($r=.04$), with approximately 74% of male subjects showing no relationship, while women showed a moderate correlation ($r=.36$), with only 24% of women showing no relationship (Lang et al., 1993). Other studies found that zygomaticus EMG was responsive only to the highest rated positive pictures (Larsen, Norris, & Cacioppo, 2003), or to both highly negative and positive pictures (Lang et al., 1993), suggesting a quadratic relationship. That is, strongly aversive stimuli may cause a grimace which leads to both increased corrugator and zygomaticus activation. However, in addition to finding no linear valence main effect for slide type with the zygomaticus EMG measure, we also found no quadratic relationship between slide type and zygomaticus EMG.

Another possible reason that we failed to find consistent results with the zygomaticus major is that it overlaps or is adjacent to other muscle groups, including the zygomaticus minor, buccinator, and the masseter (Tassinari & Cacioppo, 2000). This likely makes it difficult to isolate the signal coming from the zygomaticus major from the contaminating signals of these other muscles. The corrugator supercilii is located on a region of the face with less muscle density. Additionally, the corrugator supercilii is bilaterally innervated, meaning that it is less sensitive to fine motor control, whereas the zygomaticus major is contralaterally innervated and more sensitive to fine motor control (Rinn, 1984). Thus, compared with the corrugator supercilii, the zygomaticus major may provide a less “clean” signal from which to measure affective modulation of facial EMG.

Our HR results were also sensitive to the manipulation of nicotine, as a significant 3-way Gender x Deprivation Status x Nasal Spray interaction was found for this measure. Nicotine nasal spray increased HR compared to placebo for men during deprived and nondeprived sessions and for women during deprived sessions. As HR is innervated by both the sympathetic and parasympathetic systems and is influenced by circulating hormones, it is more likely to be subject to multiple and potentially competing physiological mechanisms

(Gilbert & Welser, 1989). In this study, however, it appears that the predominant determinant on HR was the increased sympathetic activation due to the acute nicotine nasal spray dose (see e.g., Epstein & Jennings, 1986). This sympathetic effect likely overshadowed any orienting response to the affective stimuli, which typically results in HR deceleration during the viewing of arousing negative and positive images (Bradley, Lang, & Cuthbert, 1993). Thus, HR was likely reflecting the stimulatory properties of the drug rather than an affective change as demonstrated by facial EMG, indicating that the two response systems were not concordant.

No interactions were found for skin conductance, indicating that it was not sensitive to our experimental nicotine manipulations. We failed to find a main effect or interaction with slide type, which is surprising given that the craving literature has typically found increases in skin conductance to smoking stimuli compared to neutral stimuli (e.g., Carter & Tiffany, 1999; Field & Duka, 2004; Orain-Pelissolo, Grillon, Perez-Diaz, & Jouvent, 2004). Skin conductance is a measure of autonomic activity that is primarily responsive to the sympathetic nervous system (Dawson et al., 2000). Given the sympathetic effects of nicotine, we would have expected that SCR would have been responsive to the presence of nicotine nasal spray compared to placebo. However, while previous research has found that smoking increases SCR compared to baseline (Mucha, Mutz, Stephan, & Pauli, 1996), other studies have found that both smoking and sham smoking increase SCR relative to baseline (Hori et al., 1994; Morris & Gale, 1993), suggesting that the effect is not specific to nicotine. If the effect of smoking is not specific to nicotine and is instead related to the conditioned act of smoking, then administering nicotine independent of smoking should not necessarily result in SCR increases.

Another explanation for this lack of a nicotine effect is that we recorded SCR rather than skin conductance level (SCL). We decided to record SCR to capture the phasic increase in skin conductance following (2–7 s) the onset of our picture stimuli. However, in doing so, we were unable to capture the tonic level of conductivity using SCL (Dawson et al., 2000). In other words, rather than capturing absolute levels of skin conductance, we captured reactive changes in skin conductance to our picture stimuli. Thus, our skin conductance measure was unlikely to capture the overall impact of nicotine deprivation and administration on a session. The only possible nicotine effects we could have detected using SCR would have been Nasal Spray x Slide Type or Deprivation Status x Slide Type interactions, neither of which we found.

Trials containing startle probes produced larger corrugator EMG, zygomaticus EMG, and SCR compared to trials without a startle probe. The corrugator and SCR results are not surprising, given that a stimulus that elicits an involuntary startle response is by definition aversive and that the startle reflex is considered defensive in nature (Lang, Bradley, & Cuthbert, 1990). The increase, rather than decrease, in zygomaticus EMG is possibly due to the co-innervation of that muscle along with several other facial muscles.

There are several limitations to this study that suggest further research. For example, it is not clear how these results generalize to the use of cigarettes. It is possible that the zygomaticus results would have been clearer had we used cigarettes instead of spray, given the secondary

reinforcement associated with the act of smoking. There is also evidence from other research that SCR is responsive to the act of smoking rather than simply to nicotine intake. The nicotine dose administered using the nasal spray was fixed and likely did not match the amount of nicotine typically inhaled through smoking for many of our participants. Also, it is unclear how longer or shorter periods of nicotine deprivation may have an impact on the results. Future studies should manipulate nicotine dose and deprivation period to help tease apart the effects of affect from the arousing properties of the drug. Another issue is the generalizability of the emotion-eliciting slides. The lack of interactions involving slide type with nicotine spray and deprivation status suggests that the slide stimuli may not have been as affectively salient for the participants as was the presence or absence of nicotine. Future work will be needed to investigate the relationship between laboratory affective stimuli and smokers' "real world" affective experiences, to facilitate our understanding of the roles environmental emotional cues play in maintaining smoking. Finally, both the nicotine and placebo nasal sprays produce a burning or stinging sensation that lasts for several minutes following administration, responses to which we did not measure. It is possible that subjective response to the sensory properties of the nasal spray could have confounded the gender results. Replicating these results using a less aversive delivery method would help to determine what, if any, role the sensory properties of the delivery mechanism have on facial EMG during affective processing.

In summary, the corrugator EMG, zygomaticus EMG, and HR were responsive to the nicotine deprivation and acute nicotine administration manipulations. Overall, the corrugator results suggested that administering nicotine nasal spray resulted in a reduction in negative emotional processing compared to giving placebo spray. The HR data showed that overnight nicotine deprived smokers given nicotine nasal spray produced increased HR compared to those given placebo, consistent with the stimulatory properties of the drug. However, the zygomaticus EMG results were largely unexpected given the corrugator results, possibly due to the lack of specificity in affective response that has been found for zygomaticus EMG. Skin conductance was not sensitive to the nicotine manipulations, though this is likely due our measure of relative phasic skin conductance amplitude (SCR) rather than absolute tonic skin conductance (SCL). There were no consistent differences between men and women on any of these physiological measures. The corrugator EMG results support negative reinforcement models of smoking that postulate that acute nicotine use reduces withdrawal-driven negative affect.

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Figure 1.

A significant 3-way Gender x Deprivation Status x Nasal Spray interactions for corrugator EMG. Note: Dep = Deprived, NDep = Nondeprived, Nic = Nicotine Spray, Plac = Placebo Spray.

Figure 2.

A significant 3-way Gender x Deprivation Status x Nasal Spray interactions for zygomaticus EMG. Note: Dep = Deprived, NDep = Nondeprived, Nic = Nicotine Spray, Plac = Placebo Spray.

Figure 3.
A significant 3-way Gender x Deprivation Status x Nasal Spray interactions for