Published in final edited form as:

Alcohol Clin Exp Res. 2010 July ; 34(7): 1127–1139. doi:10.1111/j.1530-0277.2010.01189.x.

ERP and RT delays in long-term abstinent alcoholics in processing of emotional facial expressions during gender and emotion categorization tasks

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Abstract

Background—There is considerable evidence that alcoholics differ from non-alcoholics in the processing of stimuli that have emotional content. The current study examines those differences that are present in multi-year abstinent individuals.

Methods—We compared RT, accuracy, and ERP measures in long-term abstinent alcoholics (LTAA, $n = 52$) with that in age and gender comparable non-alcoholic controls (NAC, $n = 47$). Subjects were presented with male and female faces exhibiting happy, neutral or sad facial expressions, and were instructed to identify the picture gender in one task and the emotion being expressed in a subsequent task.

Results—LTAA had slower RTs than NAC when instructed to identify emotion, while RT was comparable when identifying gender. There were no differences between groups on task accuracy. P160 latency was increased in LTAA for both tasks compared to NAC, though P160 amplitude did not differ between groups. The P160 effect was about 5 X as large as the RT effect and was statistically independent of the RT effect while the RT effect was no longer present after removing variance due to the P160 effect.

Conclusions—Our data demonstrate slower early processing of emotional facial stimuli in alcoholics that is unresolved by long-term abstinence, and is most sensitively indexed by delayed P160 latency in LTAA.

Keywords

Alcoholism; P160; Emotion; Faces; ERP

INTRODUCTION

Alcoholics process emotional information differently than non-alcoholics and other psychiatric populations. In experiments using socially-relevant stimuli that express emotion, such as speech tone (Monnot et al., 2001, Uekermann et al., 2005), written words (Clark et al., 2007) and facial expression (Philippot et al., 1999), alcoholic's have shown slower reactions and responses, mislabeling of emotions (Frigerio et al., 2002) and overrating emotional intensity (Oscar-Berman et al., 1990), especially negative emotions such as fear, anger, disgust and contempt (Townshend and Duka, 2003). It is not clear to what degree

these characteristics reflect the predisposition to problem drinking vs. a result of excessive drinking. These phenomena may contribute to the interpersonal conflict that characterizes alcoholics. Misinterpreting an emotional signal can affect an individual's motivation for approach, avoidance, and aggression, and may negatively impact the success of interpersonal interactions, which are crucial for successful recovery from alcoholism (Uekermann et al., 2007, Uekermann and Daum, 2008).

When perception of emotional facial expression (EFE) is considered, alcoholics have shown normal reaction times when identifying non-emotional facial features, such as gender, but were slower to answer questions about the emotion of these same pictures, (Foisy et al., 2007a, Maurage et al., 2009a). The labels given to happy, sad, and fearful faces were more negative in alcoholics than nonalcoholic controls (NAC), though this effect may be related to co-morbid depression, which has been associated with intensity rating deficits (Oscar-Berman et al., 1990, Townshend and Duka, 2003, Maurage et al., 2009b). Some studies have not found EFE perception differences between alcoholics and controls (Cermak et al., 1989, Oscar-Berman et al., 1990, Uekermann et al., 2005), suggesting that effects may be specific to testing paradigms or study sample characteristics. In studies of Korsakoff's syndrome, deficits in labeling anger, fear and surprise, and the memory for and intensity of these emotions (Oscar-Berman et al., 1990) have been found, and attributed to subcortical damage (Montagne et al., 2006). Alcoholics studied to date in EFE studies have been mostly recently detoxified (2–4 weeks) and/or in short to mid-term abstinence (average of about 2 months).

It is not clear whether alcoholic emotional processing effects are present before chronic alcohol consumption, reflecting a vulnerability factor, or whether they result from excessive alcohol consumption. It is also unclear whether and to what extent these effects persist in long-term abstinent alcoholics (LTAA) (> 6 months sobriety). One longitudinal study of short-term abstinent alcoholics showed no improvement in EFE decoding (Foisy et al., 2007b), consistent with Kornreich et al.'s (2001) cross-sectional study in LTAA (2 months – 9 years), but the latter study did find a normalization of EFE intensity ratings.

There have been 3 EFE ERP studies comparing alcoholics with an average of about 2 weeks of abstinence to NAC (Maurage et al., 2008a, 2008c, 2008d). EFE effects may involve perceptual (early), attentional (early to mid-latency), and/or decisional processes. Maurage et al., (2008c), using an oddball paradigm found no group effect on N100 or N170 latencies or amplitudes to EFEs of anger and disgust. Alcoholics did have later N2b and P3 components (Maurage et al., 2008a, 2008c), only the latter of which showed reduced amplitude in alcoholics. These results are consistent with general target detection task findings in alcoholics and may not be dependent on the stimuli being EFEs.

Longer RTs in emotion identification and delays in P100 latency along with lower P300 amplitudes have been found with EFEs in alcoholics with and without depression (Maurage et al., 2008a), but it is difficult to disentangle the relative contribution of alcohol vs. depression to those data. In the same sample, there was no difference between alcoholics and NAC in a gender processing task (Maurage et al., 2008b)

The frontally located P160 component is elicited by facial stimuli. The P160 is larger for facial stimuli vs. control stimuli (Herrmann et al., 2002, Ashley et al., 2004), and has been shown to be influenced by the emotion of the facial stimulus (Eimer and Holmes, 2007). The P160 is also elicited by unattended facial stimuli (Holmes et al., 2006). Two recent studies comparing men and women found P160 amplitude to be larger in women (Proverbio et al., 2006, Suyama et al., 2008) with P160 earlier in women in one of the studies (Suyama et al., 2008).

The current study examined whether middle-aged long term abstinent alcoholics (LTAA) differed from controls in identifying the gender or emotion of faces that varied in emotional content. Differences were examined using both RT and ERP measures.

MATERIALS AND METHODS

Participants

Participants (n=99) were recruited from Northern California as respondents to flyer postings, mailings, newspaper advertisements, internet postings and referrals. The LTAA group (n = 52) consisted of 24 women and 28 men, ages 35 to 58 (mean = 46.6 ($\pm$ 6.9) years) with an education level ranging from 10 to 20 years (mean = 15.5 ($\pm$ 2.1) years). LTAA met lifetime DSM-IV (American Psychiatric Association, 2000) criteria for alcohol dependence and were abstinent from alcohol and drugs (except nicotine and caffeine) for 6 months to 21 years (mean = 6.3 ($\pm$ 5.9) years). NAC consisted of 22 women and 25 men, ages 34 to 60 (mean = 45.5 ($\pm$ 6.8) years) with an education level ranging from 12 to 23 years (mean = 16.2 ($\pm$ 2.1) years). The inclusion criterion for the NAC group was a lifetime drinking average of less than 30 standard drinks per month, with no periods of drinking more than 60 drinks per month.

Exclusion criteria for both groups were: 1) positive diagnoses for schizophrenia or schizophreniform disorder, assessed using the computerized Diagnostic Interview Schedule (c-DIS) (Robins et al., 1998), 2) manic episode within the prior 12 months, 3) history of drug dependence other than nicotine or caffeine, 4) significant history of head trauma or cranial surgery, 5) history of diabetes, stroke, or hypertension that required an emergent medical intervention, or of other significant neurological disease, 6) laboratory evidence of hepatic disease, 7) clinical evidence of Wernicke-Korsakoff syndrome, and 8) current substance abuse other than caffeine or nicotine.

Participant screening was initially conducted by a phone interview assessing alcohol use/dependence, use/dependence of other drugs, medical history and mental health history. Participants that met all inclusion/exclusion criteria were to complete four sessions, scheduled on four separate days, that included clinical, neuropsychological, electrophysiological, and neuroimaging assessments. During the first session, alcohol use history was assessed using the timeline follow-back methodology of the Lifetime Drinking History questionnaire (Skinner and Sheu, 1982, Sobell et al., 1988, Sobell and Sobell, 1990). This provided alcohol use variables for both lifetime and peak use phases. The density of a family history of alcohol problems was assessed using the family history drinking questionnaire (Mann et al., 1985, Stoltenberg et al., 1998). The family history density measure was the proportion of first-degree relatives who had alcohol problems. Psychiatric diagnoses were established using the computerized diagnostic interview schedule (cDIS) (Robins et al., 1998). These results were reported in a prior publication (Di Sclafani et al., 2007). Eighty-seven percent of LTAA were found to have at least one lifetime psychiatric diagnosis (including mood, anxiety, and externalizing disorders), compared to 58% of NAC. Thirty-five percent of LTAA with at least 18 months of abstinence (so that only periods after six months of abstinence are counted) had a current psychiatric diagnosis (often treated with medication) compared to 6% of NAC. Cognitive function was assessed using the MicroCog battery (Powell et al., 1993) supplemented by a number of individual tests, and was reported in a prior publication (Fein et al., 2006). LTAA performed comparably to NAC in all domains, except for a suggestion of persistent deficits in spatial processing abilities (Table 1). We also reported persistent cortical atrophy in LTAA compared to NAC, with parietal gray matter volumes being associated with spatial processing performance in LTAA, but not NAC (Fein et al., 2009). The ERP experiment to emotional facial expressions was administered during the EEG testing session on the third day.

Approval for the study was obtained from a free-standing independent human subjects research review committee [Independent Review Consulting, Corte Madera, CA], and each person was informed of the study's procedures and goals, and signed a consent form prior to participation.

Procedure

Facial stimuli were photographs of young adults of European descent, head shot only, on a black background with facial features unobstructed by hair from the eyebrows down (Figure 1). The photos were originally used by Marinkovic & Halgren (1998) and were unfamiliar people to this study's subjects. The volunteers were instructed on how to express sad, neutral (no emotion) or happy expressions and practiced before photos were taken. The photographs used were a subset selected based on a 95% inter-rated consistency score from 25 judges for emotional expression type: happy, neutral or sad. Stimuli were presented on a computer monitor using the E-prime software system (Psychology Software Tools, Inc., Pittsburgh, PA) with a horizontal and vertical visual angle of approximately $12.4^\circ \times 15.7^\circ$. Images of emotional facial expressions were presented on a black screen for 2000 ms, or until the subject pressed a response key, with a 2000 ms ISI consisting of a completely black screen. Less than 2% of trials were missed and advanced by computer.

EEGs were recorded throughout the experiment while subjects watched faces on a computer screen and responded through a 5-key response box, using both index fingers regardless of task. Faces were not repeated in the gender and emotion blocks to prevent repeated exposure effects, i.e. each face was new and presented once only. Subjects were presented with 180 faces in three blocks of 60 trials each, there were 30 each of male and female, and 10 each of sad, neutral and happy expressions in each block. In the first block the subject was instructed to identify which faces were female and which were male by pressing the 1 or 2 button, respectively. In the second block the subject was presented again with male and female faces showing happy, neutral, or sad emotions. The subject was asked to identify the emotion by pressing a corresponding button (1, 2, or 3). Accuracy was assessed after 5 practice trials at the beginning of each block and the practice trials were repeated if the subject responded incorrectly. In the third block, the memory section, subjects were asked to identify whether the face presented was previously seen in the experiment or if it was 'entirely new' to them. A mix of new faces and old faces were presented. For all blocks, the subjects were instructed to make their response as quickly as possible after making the category judgment. The memory data is not part of this current report.

EEG Acquisition & Analysis

During the course of the study, three EEG acquisition systems were used, a 32-channel system ($n = 7$), a 40-channel system ($n = 84$) and a 64-channel system ($n = 8$). Midline electrodes were common across all systems, evidenced the maximal signal to noise ratio in the latency range of 75–200 ms, and are the subject of this report. The reference was the right ear for all recordings, and ground was 4 cm above the nasion for the 32-channel and 40-channel caps and 8 cm above the nasion for 64-channel caps. EEG data were acquired using the NuAmps (Compumedics Neuroscan, Inc., El Paso, TX) single-ended, 32/40-channel amplifier and Scan 4.2 Acquisition Software (Compumedics Neuroscan, Inc., El Paso, TX) for the 32-channel and 40-channel recordings. The NuAmps amplifier had a fixed range of $\pm 130 \mu\text{V}$ sampled with a 22-bit A/D converter where the least significant bit was $0.062 \mu\text{V}$. For the 64-channel recordings, EEG data were acquired using the SynAmps2 (Compumedics Neuroscan, Inc., El Paso, TX) amplifier and Scan 4.3 Acquisition Software (Compumedics Neuroscan, Inc., El Paso, TX). The SynAmps2 amplifier had a fixed range of $\pm 333 \mu\text{V}$ sampled with a 24-bit A/D converter where the least significant bit was $0.019 \mu\text{V}$. Electrode impedances were maintained below 10 kOhms. The sampling rate was 250

samples/sec. Data from control participants whose data were collected using the different amplifier systems (NuAmps, SynAmps2) were examined and revealed no differences associated with the different acquisition amplifiers. Vertical eye movements were recorded by electrodes above and below the left eye for later reduction of ocular artifact.

EEG recordings were processed offline using the Edit program in Scan 4.3 (Compumedics Neuroscan, Inc., El Paso, TX). Artifacts from eye movements were removed using the ocular artifact reduction algorithm (ARTCOR procedure) in Scan 4.3. Data were then band-pass filtered between 0.5Hz and 30Hz using a zero phase lag filter at 48dB/octave. Stimulus-locked epochs were created from all instances of each experimental conditions and were baseline corrected using the 100 ms pre-stimulus interval. Any epochs with out of range voltages ($\pm 75\mu\text{V}$) were rejected as artifacts and excluded from further processing. To extract the P160, epochs were averaged using the AVERAGE procedure, producing one average waveform per condition per subject. The time windows for the P160 and P300 components were determined by visual inspection of grand averaged waveforms and the maximal positive amplitude between 120–180ms and 250–550ms post-stimulus was scored as the P160 and P300.

Electrode Selection

Examination of contour plots made with NeuroScan (V 4.3.1), and reviewing 3-D color maps of midline electrodes (Figure 2) created in Sigma Plot (v 7.0) revealed maximum amplitude for the P160 and P300 signals to be along midline electrodes, with the maxima for both peaking at Fz (Figure 3). Values extracted from this site were used for the subsequent statistical analysis; it is also important to note that the results were unchanged if measured at FCz, Cz, Cpz and Pz, but were attenuated at Oz.

Neuropsychological Assessment

The neuropsychological assessment consisted of the MicroCog Assessment of Cognitive Functioning (standard version) (Powell et al., 1993) supplemented by a number of additional tests (see (Fein et al., 2006) for a listing of all tests, references, and norms). Ten domain scores were computed based on these tests (see Fein 2006), and as noted above, LTAA only evidenced impairment in the spatial processing domain, scores of which are presented in Table 1.

Statistical Analysis

All analyses were performed using SPSS (SPSS Inc., 2004). Repeated Measures ANOVA was used for the primary analysis. Group and subject gender were the between subject factors, with experimental condition and face gender as the repeated factors. For the electrophysiological data, analyses were conducted for four dependent variables (i.e. P160 and P300 amplitude and latency). To determine whether P300 latency effects were a consequence of effects on P160 latency, the latency difference between both components was analyzed. Effect sizes were computed as partial eta squared (η_p^2), which is calculated as the proportion of variance of the dependent variable independently accounted for by the variable under examination. Spearman's correlations were calculated within each group between lifetime drinking history variables, family history density of alcohol problems and the dependent variables.

RESULTS

Behavioral RT & Accuracy

LTAA had slower RTs than NAC in the identify emotion task ($F(1, 95) = 4.94, p = 0.029$) (Table 2). There was no main effect of group on RT in the identify gender task ($F(1, 95) =$

2.59, $p = 0.111$). A Mann-Whitney U test showed that this lack of difference was not due to outliers ($p = 0.161$). There were no main effects of participant gender on RT.

There was an effect of picture emotion on RT for the gender ($F(1, 95) = 9.78, p = 0.0001$) and emotion ($F(1, 95) = 54.2, p < 0.001$) tasks. Participants were fastest to happy and neutral stimuli in the gender task, the mean RTs of which were highly similar, and slowest to sad stimuli. In the emotion task, RTs to happy stimuli were more than 100 ms faster than to either neutral or sad stimuli, which were similar (Figure 4).

There were complicated and opposite effects of picture gender, and interactions of picture gender by picture emotion for the emotion and gender tasks (all p 's < 0.05). For the emotion task, RTs were faster for female faces vs. male faces for positive and negative emotions, but slower for female faces vs. male faces for neutral emotion faces ($F(1, 95) = 4.96, p = 0.028$). The results were the opposite for the gender task ($F(1, 95) = 6.2, p = 0.015$) (Figure 5).

To dissect the interactions, we divided the three picture emotions into two contrasts. The first compared RTs for emotionally valent (happy and sad) stimuli to that for neutral stimuli. The second compared RTs for happy vs. sad faces.

In the first contrast there was an effect of valence, with faster RTs to emotionally valent stimuli in the emotion task ($F(1, 95) = 24.62, p < 0.0001$), and slower RTs to emotionally valent stimuli in the gender task ($F(1, 95) = 5.93, p = 0.017$). In the gender task there were two significant interactions: picture gender $\times$ valence ($F(1, 95) = 18.21, p < 0.0001$) where RTs were faster to emotional male faces compared to neutral male faces, and faster to neutral female faces compared to emotional female faces. The second interaction was picture gender $\times$ participant gender ($F(1, 95) = 6.695, p = 0.011$) with all participants responding faster to male pictures, but with the effect larger in females. In the emotion condition there was a significant interaction of picture gender $\times$ valence ($F(1, 95) = 46.89, p < 0.0001$), with participants being faster to emotional female pictures vs. emotional male pictures.

In the second comparison (happy vs. sad), participants were faster to happy faces for both tasks (emotion task: $F(1, 95) = 98.31, p < 0.0001$; gender task: ($F(1, 95) = 16.02, p < 0.0001$)). When neutral faces were excluded, picture gender had a significant effect for both happy and sad faces with faster responses to pictures of females (emotion task: $F(1, 95) = 41.99, p < 0.0001$; gender task: ($F(1, 95) = 16.59, p < 0.0001$)).

Behavioral Accuracy

There was no effect of group (LTAA vs. NAC) or participant gender on accuracy, with an overall accuracy rate of 93% (Table 3). Accuracy results were similar to RT results, with picture emotion leading to more accurate responses for happy and neutral compared to sad stimuli, for both tasks. There was an effect of picture emotion in the identify emotion task, with accuracy declining from happy to neutral to sad faces. Participants were more accurate to female vs. male faces in the emotion condition, and more accurate to male vs. female faces in the gender condition, similar to the RT results.

Identify Emotion, Identify Gender, P160 Latency and Amplitude

There was a main effect of group on P160 latency (Figure 6)-it was delayed in the LTAA compared to NAC, collapsed across tasks ($F(1, 94) = 20.58, p < 0.001$) (Figure 7). P160 amplitude did not differ between LTAA and NAC. There was a noticeable peak at P300 (Figure 2), and the latency difference (P300–P160) was examined. ANOVA results were not significant, indicating that any P300 latency effects were a direct consequence of P160 latency effects (Table 4).

Emotion Identification Task – P160 Latency and Amplitude

In the emotion identification task, P160 latency was delayed in LTAA compared to NAC ($F(1, 94) = 25.02, p < 0.001$). The P160 amplitude did not differ between the groups. There was a main effect of participant gender on P160 latency, with males having longer latencies than females ($F(1, 94) = 5.12, p < 0.026$). There were no main effects of emotion on P160 latency or amplitude, nor were there any significant interaction effects.

Gender Identification Task-P160 Latency and Amplitude

In the gender identification task, P160 latency was delayed in LTAA compared to NAC ($F(1, 94) = 21.74, p < 0.001$) (Figure 6), similar to the emotion task (Figure 7). As in the emotion task, there was a main effect of participant gender, with males having longer latencies than females ($F(1, 94) = 6.96, p < 0.01$). There was a significant picture emotion $\times$ participant gender interaction on P160 latency ($F(1, 94) = 3.38, p = 0.038$), with females having longest P160 latencies to neutral faces, while males had longest P160 latencies to negative faces. There were no other P160 latency effects. There were no significant main or interaction effects for P160 amplitude.

P300 Amplitude

There was no group effect on P300 amplitude for the gender or emotion task. There were no effects of picture emotion on P300 amplitude, nor any interaction effects.

Association Between P160 latency, Reaction Time and Alcohol use Variables

Spearman correlations were performed between P160 latency and RT for each group and were not significant (LTAA ($R = 0.075, p = 0.599$), NAC ($R = 0.149, p = 0.319$)). There were no significant correlations between any drinking history or family history variables and P160 or RT within either group. Analysis of variance showed that group accounted for 21.2% of the variance of P160, but only 4.5% of the variance of RT. Using analysis of covariance, removing the variance due to the RT delay, there remained a highly significant group effect on P160 latency ($F(1,98) = 23.0, p < 0.0001$, Effect Size = 19.6%). In contrast, removing the variance due to the P160 latency delay, the group difference on RT no longer remained ($F(1,98) = 2.6, p = 0.114$, Effect Size = 2.6%). These associations between the RT and P160 latency findings were present in both males and females.

DISCUSSION

Our primary finding is that LTAA compared to NAC have delayed RTs and delayed early ERP component latencies to EFE stimuli. Alcoholics in early abstinence, when evaluating EFE, have been shown to mislabel emotions, overrate their intensity, and respond more slowly (as in the current study, evident in both RTs and ERPs (Maurage et al., 2008a, 2008b, 2008c)). Our results show that the slowing in alcoholics is present after multi-year abstinence. Analysis of covariance indicates that the P160 latency delay is independent of the observed RT delay and of much larger magnitude (about 5 times as large). In addition, in the gender identification task, there were no RT group differences while P160 latency effects were of comparable size to those in the identify emotion task, providing additional evidence that the P160 latency effect is dissociable from the RT delays observed.

We also did not support the hypothesis that differences between alcoholics and controls are larger for negative emotional stimuli than neutral or positive emotional stimuli. We found comparable differences between groups for happy, neutral, and sad emotional stimuli. The cross-sectional nature of our study precludes us from making statements about normalization of emotional stimulus processing in alcoholics with long-term abstinence. We only observe those deficits that are present in long-term abstinence.

Accuracy of Emotion Identification

A mixed cross-sectional and longitudinal study of EFE processing found no improvement in decoding of happiness, anger, sadness and disgust over 3 months of abstinence (Foisy et al., 2007a), where the poorer the EFE recognition at the beginning of abstinence, the less likely abstinence would be maintained. In the current study, emotion identification accuracy did not differ between groups. The high (93%) accuracy rates across conditions may indicate a ceiling effect. Incorporating distracters, decreasing target discriminability and/or increasing stimulus presentation rates may unmask such effects in future studies. Studies that include a wider variety of emotional stimuli (happiness, sadness, anger, fear, contempt, surprise, disgust, shame) and more than one level of stimulus intensity (30%, 70%) have shown such effects in alcoholics (Kornreich et al., 2001, Frigerio et al., 2002, Foisy et al., 2007a). But other studies have not found group differences in performance between alcoholics and NAC (Maurage et al., 2007a, 2008a, 2008c).

Reaction Time, Picture Emotion, Picture Gender, Other Visual Features

The effect of picture emotion on RT was consistent with earlier findings using the same stimuli (i.e., with RTs fastest to happy when compared to neutral and sad stimuli (Marinkovic and Halgren, 1998)).

Encoding, Decoding, Processing, Motor Response

The delayed RT in LTAA could reflect a visuo-spatial encoding, decoding, and/or processing group difference that varies by task. It is known that eyes, mouth, and forehead are used in detecting emotions, and it is possible that when asked to identify emotion, alcoholics search face-referenced visuo-spatial information differently than NAC, and that this effect is markedly reduced when processing gender information. Perhaps alcoholics pay more and longer attention to cues in the identify emotion condition. One could investigate this hypothesis using eye tracking. Also filming participants would allow the measurement of emotional facial reactions to images which may also differentiate the groups if alcoholics are more reactive to emotional stimuli (Ekman, personal communication, August 5, 2009). It is most parsimonious to explain the current effect as an emotion effect rather than a visual spatial frequency effect. Maurage et al. (2008b) have shown that the emotion processing demand influences RT, delaying RTs to emotion identification vs. gender, age and race identification tasks. In support of the effect being specific to emotion identification, other groups have used degraded stimuli as control stimuli and still found EFE effects (Eimer and Holmes, 2007). We note that although ERPs have a higher sensitivity to group differences than do RT or task accuracy, these behavioral measures are more sensitive to task effects that do not differ between alcoholics and controls.

P160 Waveforms Amplitude and Latency

The scalp topography and waveforms in the current study are similar both to earlier findings that used the same face stimuli (Marinkovic and Halgren, 1998), and to other studies that used comparable stimuli (Herrmann et al., 2002, Eimer and Holmes, 2002, Gan et al., 2009). Studies have found significant amplitude differences in the P160 for fearful facial expressions only when comparing neutral and fearful expressions (Holmes et al., 2006), while another also found a significant amplitude increase for fearful but not for happy vs. neutral stimuli (Ashley et al., 2004). These results are not inconsistent with our findings, but their direct evaluation would require presentation of fearful and other high intensity emotional facial stimuli.

The frontally prominent positive peak around 160ms also was consistent with Eimer & Holmes (2002 Eimer & Holmes (2007), but not Maurage et al.(2008a, 2008c), who used

morphed facial stimuli and a different (oddball task) paradigm, finding P1 amplitude at T6 and minimal for Oz, partly consistent with our results. The finding that P160 latency was later in men compared to women follows along the lines of similar studies in relation to gender differences in ERP's elicited by faces (Proverbio et al., 2006, Suyama et al., 2008), though these studies found increased amplitude in women, which we did not replicate.

The literature is equivocal about the effect of alcoholism on early ERP latencies to EFE. Maurage et al. did not find an effect of alcoholism on the P1, N100 or N170 latency to faces displaying anger or disgust, but did find longer latencies of these waves in a study of anger and sadness (Maurage et al.). An earlier study by the same group found increased latencies of P1 and N170 in alcoholics (Maurage et al., 2007b). All the participants above were short-term abstinent alcoholics (2–3 weeks abstinent).

We did not find a main effect of group or emotion on P160 amplitude, consistent with Maurage et al. (2007b, 2008a, 2008c). There has been one report of an interaction effect of electrode site and group on P1 amplitude to EFE, with higher amplitude P1 in temporal region for NAC but not for alcoholics (Maurage et al., 2007b).

LTAA latency delay mechanisms

The LTAA population is complex. LTAA vs. NAC effects could reflect phenomena that predispose individuals to severe alcoholism, the effects of severe alcoholism, the effects of long-term abstinence, or phenomena that facilitate individuals' ability to attain long-term abstinence. Given that the P1 and N170 latency effects are present in other studies of treatment naïve and short-term abstinent alcoholics (Maurage et al., 2007b, 2008a, 2008d) it is likely that the latency findings are an effect of severe alcohol abuse that persists into long-term abstinence.

Neural Circuits Alcoholism, Faces and Emotion

The ERP latency effect was maximal frontally, consistent with a frontal cortex locus for the persistent EFE effects in LTAA. One theory is that certain areas of the prefrontal cortex perform cognitive control processes that down regulate amygdala activity and other systems (structures) in encoding emotionally salient stimuli (Anderson and Phelps, 2001, Adolphs, 2002). Marinkovic et al. (In Press) proposes that LTAA compensate for subcortical damage via the prefrontal cortex. In LTAA, Marinkovic et al. (In Press) find that amygdala activity, measured with fMRI, was inversely correlated with lateral prefrontal activation to faces, interpreted as a compensatory effect. A frontal lobe hypothesis has been proposed to explain the social cognitive impairments in alcoholism as resulting from the vulnerability of the prefrontal cortex to the neurotoxic effects of alcohol (Oscar-Berman et al., 1990, Uekermann and Daum, 2008).

There are four major limitations of this study. First, stimuli were presented for two relatively low arousal emotions. It is possible that higher arousal emotions such as anger, surprise and fear might have triggered stronger and more varied ERP effects (Marinkovic and Halgren, 1998, Balconi and Pozzoli, 2003). Second, the gender task was always presented first, and task and order are confounded. Third, in the ERP analysis, we focused primarily on the midline P160 component. Other peaks and laterality effects can be elicited by facial stimuli, (Marinkovic and Halgren, 1998) and will be the focus of another paper. Fourth, as mentioned above, our conclusions are limited by the groups studied. Without further samples we cannot distinguish between the contributions of the predisposition to alcoholism, the effects of chronic alcoholism, and the effects of long-term abstinence to our results.

In summary, this study examined EFE processing in LTAA vs. age and gender comparable NAC. It shows P160 latency delays during gender identification and emotion identification

tasks, and RT delays during the emotion identification task only. The RT delays were not independent of the P160 delays. In contrast, the P160 delays were, for the most part, independent of the RT results, with large effects remaining after removing shared variance with RT. Moreover, the P160 latency effects were over 5 times the size of the RT effects. The current data show that slower processing of EFE stimuli in alcoholics is present after at least 6 years of abstinence. RT and accuracy task effects were present, but did not differ between alcoholics and controls. The finding of a latency delay in alcoholics indicates inefficiency in early face processing in alcoholics. Behavioral differences across tasks likely result from down-stream processing differences between tasks due to task saliency and attention. Differences between groups in these effects might be elicited by more intense and varied EFE stimuli or more difficult task conditions (e.g., using degraded stimuli). We are following up on these results in experiments with individuals dependent on alcohol only or alcohol and drugs using more intense and varied EFE stimuli.

Acknowledgments

This work was supported by National Institutes for Health, NIH Grants #1R21AA017311, #1R01AA016944 and #2R01AA013659.

Authors appreciate and note the contributions of Hugh Chung and Danielle Luciano for subject testing and data analysis.

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FIGURE 1.

Examples of female and male happy, neutral, and sad emotional facial expressions. In the emotion identification task participants were instructed to classify each facial expression as 'happy,' 'neutral,' or 'upset' with a button press. In the gender task the response choices were to identify each picture as 'male' or 'female'.

FIGURE 2.

Color maps used to identify time course of maximal amplitude in the midline electrodes, showing intensity in μV , coded by color, by time in ms across electrodes anterior to posterior.

FIGURE 3.

The averaged waveform from LTAA, emotion task, sad picture emotion, with head contour plots that illustrate the scalp distribution of the P160. A P300 peak was present and is representative of other conditions.

FIGURE 4.
Mean RT of both groups for the emotion and gender tasks by facial expression.

FIGURE 5.

The mean RT and SD of both groups for the emotion and gender identification tasks broken down by picture sex and picture emotion.

FIGURE 6.

Grand averages of EEG waveforms comparing P160 in LTAA to NAC in emotion and gender identification tasks. Note the increased latencies for alcoholics.

FIGURE 7.

Mean latencies and standard errors for P160 in emotion and gender identification tasks. Note the significant interaction of group (LTAA, NAC) by picture emotion between tasks ($F(2, 98) = 8.27, p = 0.001$).

Table 1

Sample Demographics and Neuropsychological Scoring

Demographic Variables	LTAA		Controls		Effect Size (%)		
	Male (n=28)	Female (n=24)	Male (n=25)	Female (n=22)	Group	Sex	Group × Sex
Age (Years)	44.9 ± 6.9	48.4 ± 6.4	43.4 ± 6.3	48.0 ± 6.7	0.6	8.9**	0.2
Family Drinking Density ¹	0.40 ± 0.26	0.44 ± 0.30	0.14 ± 0.22	0.17 ± 0.21	23.9***	0.4	<0.1
Years Education	15.5 ± 2.0	15.5 ± 2.4	16.3 ± 2.2	16.1 ± 1.9	2.6	0.1	0.1
Alcohol Use Variables							
Duration of Active Drinking (months)	260 ± 90	280 ± 110	230 ± 130	290 ± 130	0.1	2.8	1.0
Average Lifetime Drinking Dose (std. drinks/month)	180 ± 150	130 ± 80	7 ± 8	7 ± 8	41.0 ²	1.1	1.1 ²
Lifetime Alcohol Use (std. drinks)	54,000 ± 59,000	40,000 ± 38,000	1,800 ± 2,200	2,000 ± 2,300	28.3 ²	0.6	0.7 ²
Duration of Peak Drinking (months)	61 ± 58	92 ± 82	70 ± 81	104 ± 105	0.8 ²	3.4	0.1 ²
Average Peak Drinking Dose (std. drinks/month)	340 ± 250	270 ± 200	15 ± 14	17 ± 23	42.8 ²	0.6	0.6 ²
Peak Alcohol Use (std. drinks)	26,000 ± 44,000	25,000 ± 29,000	900 ± 1,100	1,000 ± 1,500	17.3 ²	<0.1	<0.1 ²
Abstinence Duration (Months)	75 ± 73	75 ± 68	N/A	N/A	N/A	<0.1	N/A
Neuropsychological domains (Z-scores)							
Abstraction/Cognitive Flexibility	0.00 ± 0.64	0.40 ± 0.43	0.19 ± 0.56	0.37 ± 0.56	0.5	6.5**	1.1
Attention	-0.15 ± 0.58	0.10 ± 0.39	0.05 ± 0.59	0.18 ± 0.52	1.8	3.3	0.4
Auditory Working Memory	-0.07 ± 0.71	-0.029 ± 1.15	0.14 ± 0.87	-0.20 ± 1.27	0.6	2.0	0.1
Immediate Memory	0.48 ± 0.63	0.60 ± 0.40	0.54 ± 0.57	0.71 ± 0.46	0.6	1.9	0.1
Delayed Memory	0.01 ± 0.85	0.27 ± 0.72	0.06 ± 0.81	0.45 ± 0.98	0.5	3.7	0.2
Psychomotor	-0.31 ± 0.59	0.13 ± 0.81	-0.21 ± 0.98	0.02 ± 0.90	0.0	4.1*	0.4
Reaction Time	0.30 ± 0.43	0.24 ± 0.42	0.32 ± 0.43	0.27 ± 0.51	0.1	0.3	0.0
Spatial Processing	0.14 ± 0.53	0.14 ± 0.50	0.42 ± 0.56	0.29 ± 0.50	4.0*	0.4	0.4
Verbal	0.97 ± 0.48	1.20 ± 0.50	0.87 ± 0.74	1.13 ± 0.55	0.6	4.3*	0.0
Average Domain Z-score	0.16 ± 0.36	0.32 ± 0.34	0.26 ± 0.46	0.36 ± 0.52	0.8	2.3	0.2
Global Clinical Impairment Score (GCIS)	0.56 ± 1.00	0.30 ± 0.64	0.62 ± 1.05	0.52 ± 1.04	0.8	1.2	0.1

¹ Family drinking density is the proportion of first-degree relatives who were problem drinkers; statistical comparisons (and estimates of effect size for family drinking density were performed after normalizing the proportions via the arcsine transformation.

² Statistical comparisons between groups are not valid since the inclusion criteria were associated with this variable.

Effect is significant:

* $p \leq 0.05$,
 ** $p \leq 0.01$,
 *** $p \leq 0.001$.

TABLE 2

mean, $\pm$ standard deviation in ms for all conditions and ANOVA results for LTAA vs NAC by task. There were no 3-way or 4-way T.

LTAA				Controls				Effect Sizes (% of Variance)					PG* SG
Female (n=24)		Male (n=28)		Female (n=22)		Male (n=25)		Group	Subject Gender (SG)	Picture Emotion (PE)	Picture Gender (PG)	PG* PE	
Female Faces	Male Faces	Female Faces	Male Faces	Female Faces	Male Faces	Female Faces	Male Faces						
161 ± 130	671 ± 182	734 ± 161	713 ± 161	686 ± 155	650 ± 112	685 ± 120	680 ± 145	-	-	-	-	-	-
160 ± 99	678 ± 191	712 ± 132	773 ± 186	660 ± 115	662 ± 135	679 ± 143	684 ± 125	-	-	-	-	-	-
145 ± 108	683 ± 184	765 ± 164	764 ± 182	742 ± 151	651 ± 126	710 ± 130	680 ± 127	-	-	-	-	-	-
117 ± 112	677 ± 182	737 ± 152	750 ± 176	696 ± 140	654 ± 124	691 ± 131	681 ± 132	2.7	1.4	17.2***	6.1*	18.3***	7.1**
n													
170 ± 137	870 ± 140	756 ± 153	814 ± 174	720 ± 127	776 ± 124	733 ± 142	802 ± 167	-	-	-	-	-	-
160 ± 180	892 ± 177	947 ± 163	909 ± 188	855 ± 150	830 ± 141	897 ± 155	843 ± 180	-	-	-	-	-	-
129 ± 132	921 ± 140	903 ± 147	910 ± 185	818 ± 122	813 ± 138	873 ± 163	928 ± 185	-	-	-	-	-	-
186 ± 150	894 ± 139	867 ± 154	878 ± 182	798 ± 133	806 ± 134	834 ± 153	858 ± 177	4.9*	0.3	54.2***	5.0*	43.7***	0.5

TABLE 3

ous to Table two, but for accuracy instead of RT. For accuracy, the emotion identification task showed a 3-way interaction of picture gender × emotion × subject gender that accounted for 8.3% of variance ($p \leq 0.05$).

Stimulus	LTAA				Controls				Effect Sizes (% of Variance)					
	Female (n=24)		Male (n=28)		Female (n=22)		Male (n=25)		Group	Subject Gender (SG)	Picture Emotion (PE)	Picture Gender (PG)	PE* PG	
	Female Faces	Male Faces	Female Faces	Male Faces	Female Faces	Male Faces	Female Faces	Male Faces						
Identification														
Accuracy	9.04 ± 1.08	9.83 ± 0.38	9.46 ± 0.51	9.75 ± 0.52	9.32 ± 0.65	9.68 ± 0.48	9.36 ± 0.81	9.92 ± 0.28	-	-	-	-	-	
Accuracy	9.92 ± 0.28	9.83 ± 0.48	9.75 ± 0.59	9.57 ± 0.57	9.50 ± 0.60	9.68 ± 0.65	9.72 ± 0.54	9.60 ± 0.71	-	-	-	-	-	
Accuracy	8.71 ± 0.81	9.79 ± 0.51	8.46 ± 1.11	9.71 ± 0.54	8.36 ± 1.36	9.82 ± 0.50	8.4 ± 0.96	9.64 ± 0.57	-	-	-	-	-	
Mean	9.22 ± 0.72	9.82 ± 0.46	9.22 ± 0.74	9.66 ± 0.54	9.06 ± 0.87	9.73 ± 0.54	9.16 ± 0.77	9.72 ± 0.52	1.2	0.0	45.3***	46.3***	43.3***	
Identification														
Accuracy	9.92 ± 0.28	9.33 ± 1.05	9.82 ± 0.48	9.75 ± 0.52	9.91 ± 0.29	9.50 ± 1.14	9.88 ± 0.33	9.60 ± 0.65	-	-	-	-	-	
Accuracy	9.25 ± 1.29	9.38 ± 1.31	9.25 ± 0.89	8.82 ± 1.42	9.23 ± 0.81	9.73 ± 0.55	9.28 ± 1.10	9.40 ± 1.12	-	-	-	-	-	
Accuracy	8.75 ± 1.51	8.50 ± 1.29	9.18 ± 1.06	8.75 ± 1.18	9.14 ± 1.08	8.91 ± 1.66	8.64 ± 1.11	8.28 ± 1.70	-	-	-	-	-	
Mean	9.31 ± 1.02	9.07 ± 1.22	9.42 ± 0.81	9.11 ± 1.04	9.43 ± 0.73	9.38 ± 1.12	9.27 ± 0.85	9.09 ± 1.16	0.3	0.4	38.0***	9.7**	9.9*	

gnificant:

TABLE 4

Mean P160 latency and amplitude by group for electrode Fz by task, and stimulus emotion. Grand averages, task, stimuli and ANOVA results.

Variables	LTAA		Controls		Effect Sizes (% of Variance)				
	Female (n= 24)	Male (n= 28)	Female (n= 22)	Male (n= 25)	Group (G)	Subject Gender (SG)	Picture Emotion (PE)	PE* SG	SG* G
Gender Task									
Happy Faces									
Amplitude (μV)	10.05 $\pm$ 3.59	10.61 $\pm$ 4.19	11.16 $\pm$ 4.14	11.35 $\pm$ 3.84	-	-	-	-	-
Latency (ms)	149.50 $\pm$ 18.53	161.14 $\pm$ 17.68	135.64 $\pm$ 14.86	142.40 $\pm$ 18.37	-	-	-	-	-
Neutral Faces									
Amplitude (μV)	10.40 $\pm$ 4.03	10.16 $\pm$ 3.65	10.42 $\pm$ 3.87	11.05 $\pm$ 3.91	-	-	-	-	-
Latency (ms)	152 $\pm$ 20.50	161.57 $\pm$ 16.49	138 $\pm$ 14.80	141.28 $\pm$ 14.59	-	-	-	-	-
Sad Faces									
Amplitude (μV)	10.1 $\pm$ 4.43	9.52 $\pm$ 4.22	10.40 $\pm$ 3.86	11.92 $\pm$ 3.95	-	-	-	-	-
Latency (ms)	150.50 $\pm$ 21.58	161.71 $\pm$ 16.45	136.36 $\pm$ 16.19	147.68 $\pm$ 24.57	-	-	-	-	-
Overall Means									
Amplitude (μV)	10.18 $\pm$ 4.02	10.10 $\pm$ 4.02	10.66 $\pm$ 3.96	11.44 $\pm$ 3.9	1.7	0.2	1.4	0.2	2.0
Latency (ms)	150.67 $\pm$ 20.20	161.47 $\pm$ 16.87	136.67 $\pm$ 15.28	143.79 $\pm$ 19.18	18.6***	6.8**	3.3	6.7*	1.6
Emotion Task									
Happy Faces									
Amplitude (μV)	9.67 $\pm$ 4.90	10.19 $\pm$ 3.86	10.50 $\pm$ 3.98	10.95 $\pm$ 4.50	-	-	-	-	-
Latency (ms)	149.83 $\pm$ 20.19	162.71 $\pm$ 20.89	134.91 $\pm$ 15.23	144.32 $\pm$ 23.55	-	-	-	-	-
Neutral Faces									
Amplitude (μV)	9.77 $\pm$ 4.52	9.73 $\pm$ 3.93	10.17 $\pm$ 4.12	9.99 $\pm$ 3.51	-	-	-	-	-
Latency (ms)	154 $\pm$ 23.68	163.43 $\pm$ 20.88	135.64 $\pm$ 17.50	141.12 $\pm$ 16.15	-	-	-	-	-
Sad Faces									
Amplitude (μV)	9.35 $\pm$ 4.75	9.75 $\pm$ 4.19	10.57 $\pm$ 3.68	12.08 $\pm$ 4.78	-	-	-	-	-
Latency (ms)	153.50 $\pm$ 23.97	162 $\pm$ 18.62	137.64 $\pm$ 16.78	141.76 $\pm$ 16.97	-	-	-	-	-
Overall Means									
Amplitude (μV)	9.60 $\pm$ 4.72	9.89 $\pm$ 3.99	10.41 $\pm$ 3.93	11.01 $\pm$ 4.26	1.7	0.4	2.8	2.6	4.6
									0.0

Variables	LTAA		Controls		Effect Sizes (% of Variance)					
	Female (n= 24)	Male (n= 28)	Female (n= 22)	Male (n= 25)	Group (G)	Subject Gender (SG)	Picture Emotion (PE)	PE* SG	PE* G	SG* G
Latency (ms)	152.44 ± 22.61	162.71 ± 20.13	136.06 ± 16.50	142.40 ± 18.89	20.8***	5.1 *	0.3	2.5	2.8	0.3

Effect is significant:

* p≤0.05

** p≤0.01

*** p≤0.001