INTRODUCTION

Alcohol-withdrawal syndrome is characterized by signs of overactivity of the sympathetic nervous system. An increased release of noradrenalin (NA) is associated with certain symptoms of withdrawal, such as tremulousness, paroxysmal sweats, increased diastolic and systolic blood pressures, and increased heart rate (Linnoila et al., 1987). Increased neurotransmission levels of NA may subsequently also change the postsynaptic $\alpha_2$-adrenergic receptor function.

The growth hormone (GH) response to the $\alpha_2$-adrenoceptor agonist clonidine (CLON) has been used to assess central postsynaptic $\alpha_2$-adrenoceptor function in various psychiatric disorders, including alcoholism. The challenge test (CLON/GH) was thus used by Matussek et al. (1984) to assess $\alpha_2$-adrenoceptor sensitivity after alcohol consumption in heavy social drinkers. GH responses to CLON were blunted on the day after the last intake of alcohol. Nutt et al. (1988) reported blunted GH responses to CLON in alcohol-dependent men investigated 1–3 days after the end of alcohol intake. This finding was confirmed by Balldin et al. (1992b) in a study with repeated CLON/GH tests during the first week of alcohol withdrawal (see also Berggren et al., 1999; Fahlke et al., 1999). Glue et al. (1989) reported blunted GH responses in alcoholics who had been abstinent for 5 weeks. Müller et al. (1989) found no significant differences in GH responses to CLON between controls and patients in late alcohol withdrawal or the abstinence phase.

Matussek et al. (1980) were the first to report reduced GH responses to CLON in endogenous depression. Several groups have confirmed this finding (Checkley et al., 1981, 1984; Charney et al., 1982; Siever and Uhde, 1984; Anseau et al., 1988; Valdivieso et al., 1996; but see also Gann et al., 1995a). Mitchell et al. (1988) and Balldin et al. (1992a) found that the GH response to CLON was reduced after recovery from an episode of endogenous depression, suggesting that a ‘blunted GH response’ is a persistent feature that may be a trait marker for depression. Coote et al. (1998) found that GH response to CLON was blunted before electroconvulsive therapy and remained so after treatment. Blunted GH response to CLON has also been reported in patients with panic disorders (Uhde et al., 1986; Charney and Heninger, 1986; Nutt, 1989; Curtis et al., 1989; Tancer et al., 1993; Coplan et al., 1995; but see also Schittecatte et al., 1988; Gann et al., 1995b). Taken together, most of the studies suggest blunted GH response to CLON. Thus $\alpha_2$-adrenoceptor function, as reflected by GH response to CLON, appears to be subsensitive in...
both depression, panic disorder, and in alcohol withdrawal.

An interesting question is therefore whether \( \alpha_2 \)-adrenoceptor subsensitivity may predispose to the psychopathology frequently observed in alcohol withdrawal. The aim of the present study was to ascertain whether there is a relationship between GH response to CLON and symptoms of depression and anxiety in the early alcohol-withdrawal period.

Hoehe et al. (1988) have shown that a higher CLON dose is more likely to differentiate GH responders from non-responders in healthy individuals. To investigate whether this is also the case in alcohol dependence two different dosages of CLON were used in the present study.

**METHODS**

**Patients**

Patients admitted to a psychiatric hospital for treatment of alcohol-withdrawal symptoms were considered for the study. The inclusion criteria were: (1) fulfillment of the DSM-IV criteria of the American Psychiatric Association (1994) for alcohol dependence (303.9); (2) intake of alcohol in amounts exceeding 80 g of pure ethanol daily for at least 5 days prior to admission; (3) no interruption of alcohol intake earlier than 24 h before start of the study; (4) the DSM-IV criteria for the non-delirium-withdrawal syndrome (291.8). The exclusion criteria were somatic or psychiatric disorders or symptoms not associated with alcohol dependence or withdrawal. Thirty patients (2 women and 28 men), who fulfilled the above criteria, were included in the study. Background data for these patients are given in Table 1.

CLON/GH tests, assessments of withdrawal psychopathology, blood sampling for determinations of liver function, and blood glucose levels were made on days 1 and 7 after the end of alcohol intake. In addition, urine analyses for determination of narcotic drugs, including benzodiazepines, were performed before all challenge tests.

**Challenge tests**

CLON/GH tests were performed between 08:00 and 09:00 after an overnight fast (from 24:00). Clonidine hydrochloride (Catapres\textsuperscript{®}) was given in two dosages [1.5 \( \mu \text{g/kg} \) body wt, i.v. (CLON\textsubscript{1.5}, \( n = 17 \)) and 2.0 \( \mu \text{g/kg} \) body wt, i.v. (CLON\textsubscript{2.0}, \( n = 13 \)). The two dosages of CLON were selected because they are commonly used and neither of them is known to have serious effects on blood pressure (see Müller et al., 1989; Tulen et al., 1992).

The patients were placed in a supine position and a cannula was inserted into a brachial vein. A blood sample was drawn for analyses of GH, glucose, and liver parameters immediately before CLON administration (at time 0). CLON (150 \( \mu \text{g/ml} \) dissolved in 10 ml of 0.9% w/v NaCl) was administered slowly i.v. over 10 min. Blood samples for GH determinations were collected at 30, 45, and 60 min after the start of the CLON injection. The blood was centrifuged and serum kept at \(-20^\circ\text{C}\) until assayed. GH was determined by a double-antibody radioimmunoassay method as described earlier (Balldin et al., 1982). All values for serum GH concentrations are given as mU/l; 1 mU/l corresponds to 0.5 ng/ml.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CLON\textsubscript{1.5}</th>
<th>CLON\textsubscript{2.0}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>44 ± 7 (33–57)</td>
<td>48 ± 11 (26–65)</td>
</tr>
<tr>
<td>Duration of alcohol misuse (years)</td>
<td>11 ± 9 (2–30)</td>
<td>13 ± 9 (2–30)</td>
</tr>
<tr>
<td>Length of time of alcohol misuse prior to admission (days)</td>
<td>34 ± 84 (5–360)</td>
<td>47 ± 64 (5–180)</td>
</tr>
<tr>
<td>Mean estimated daily consumption prior to admission (g of pure alcohol)</td>
<td>247 ± 94 (105–480)</td>
<td>209 ± 64 (80–356)</td>
</tr>
</tbody>
</table>

Table 1. Background data for 30 patients with alcohol dependence
The baseline serum GH concentration was defined as the value at time 0. A low baseline GH concentration is important, since GH inhibits its own secretion and baseline levels which are too high may reduce the drug-induced hormonal responses. GH concentrations above 10 mU/l were therefore regarded as too high as suggested by Hohe et al. (1988) and results of the corresponding loading tests were excluded from statistical calculations. The maximum GH response was defined as the difference between the highest post-injection GH concentration and the baseline level. Blunted GH response was defined as a maximum GH response of less than 8 mU/l (Hunt et al., 1986; Balldin et al., 1993).

In the evening (not later than 20:00) of the day of admittance, some patients received small doses of alimemazine, propiomazin or clomethiazole (e.g. the evening before the CLON/GH tests at day 1). Starting after the first CLON/GH test, patients were treated for withdrawal symptoms with decreasing doses of clomethiazole ($n = 25$), oxazepam ($n = 2$), or a combination of chlorprotixen and carbamazepine ($n = 3$) together with vitamins during the treatment period (i.e. from day 1 to day 7). The medication was reduced each day and the dosages were minimal the day before the second challenge test. Medication was terminated each day at 20:00. No medication was given on the day of the challenge test until the test was completed. The above different types of medications have not been found to influence significantly baseline or CLON-induced changes in GH (Balldin et al., 1992b).

Male volunteers from the hospital staff acted as controls for the CLON/GH tests (for CLON$_{1.5}$: $n = 14$, mean age 44 years, range 33–54 years and for CLON$_{2.0}$: $n = 6$, mean age 28 years, range 23–34 years). The challenge tests were performed in a similar manner as described for the patient groups. According to statements during interview, the subjects were psychiatrically and somatically healthy and had no histories of previous psychiatric or major somatic illnesses. All controls were light social drinkers, with a reported weekly alcohol consumption of less than 100 g of pure ethanol, but none was a total abstainer. Laboratory data, including liver parameters etc. were all within the ranges for healthy individuals.

**Psychopathology**

The psychopathology of alcohol withdrawal was assessed on the days for the hormonal tests by trained staff members using the rating scale for Alcohol Withdrawal Psychopathology (AWIP; Bokström and Balldin, 1992). AWIP comprises 17 items and has a total range of scores of 0–102. For each item, scores of 0–2 are regarded as being within the normal range; 0 indicates absence and 6 extreme severity of the symptom. The items included in the AWIP rating scale are shown in Table 3.

Ten items of the AWIP rating scale have been found to be identical to items of the Montgomery–Åsberg Depression Rating Scale (MADRS; Montgomery and Åsberg, 1979; Table 3). The total range of scores for the latter is 0–60. A total MADRS score of 20–34 indicates moderate depression and a score of 35 or more severe depression according to the classification suggested by Snaith et al. (1986). AWIP has been found to have content validity (agreement with the DSM-III-R criteria for uncomplicated alcohol withdrawal; Bokström and Balldin, 1992), whereas concurrent validity has not been possible to assess, because there is no other scale that measures psychopathology in alcohol withdrawal (Bokström and Balldin, 1992). The validity of the MADRS has been demonstrated (Montgomery and Åsberg, 1979).

**Liver function**

For all patients, blood samples for assessment of liver function were obtained at the start of each challenge test and were used for determinations of serum concentrations of aspartate aminotransferase (ASAT), alanine aminotransferase (ALAT) and γ-glutamyltransferase (GGT). The laboratory upper reference limits for these liver parameters were 0.65, 0.65, and 0.90 μkat/l, respectively.

**Statistics**

All statistical calculations were performed using the statistical programme Stat View, Abacus. Within-group comparisons were performed with a paired $t$-test and between-group comparisons with an unpaired $t$-test. The Spearman rank correlation test (for absolute values) and Fisher’s exact test (for abnormal vs normal values) were used for evaluating associations between values of baseline GH concentrations/maximum GH responses to CLON and AWIP/MADRS scores or liver function test results. When baseline GH and GH responses to CLON were correlated with individual AWIP/
MADRS items, \( P < 0.01 \) was chosen as the level of significance, because of the large number of comparisons; otherwise \( P < 0.05 \) was used. In all tests, two-tailed levels of significance were used. The data are presented as means ± standard deviations (SD).

This study was approved by the Ethics Committee of the Göteborg University, Sweden and informed consent was obtained from all subjects.

RESULTS

There were no significant differences in any background data between the patient group CLON\textsubscript{1.5}, compared to CLON\textsubscript{2.0} (Table 1).

Some patients left hospital earlier than planned and could not therefore be retested at the end of the investigation period (day 7; CLON\textsubscript{1.5}; \( n = 3 \) and CLON\textsubscript{2.0}; \( n = 4 \)).

Urinary analyses for narcotic drugs and benzodiazepines showed no positive findings in any patient during the two test occasions. Blood glucose levels at the start of all CLON/GH tests were all well within the laboratory frame for fasting individuals.

Baseline serum GH concentrations and maximum GH responses to CLON for patients given CLON 1.5 \( \mu \)g and 2.0 \( \mu \)g, respectively, are shown in Table 2. Among patients with the CLON\textsubscript{1.5} dose, three patients had high baseline GH concentrations at day 1 (14.9, 19.7, and 20.2 mU/l) and two at day 7 (14.4 and 20.2 mU/l). Of 14 evaluable CLON/GH tests at day 1, 12 were blunted and at day 7 nine out of 12 were blunted (<8.0 mU/l; Fig. 1). Among patients with the CLON\textsubscript{2.0} dose, one patient had a high baseline GH concentration (28.7 mU/l) at day 1 and none at day 7. Of 12 evaluable CLON/GH tests at day 1, 11 were blunted. All GH maximum responses at the last test occasion (day 7; \( n = 9 \)) were found to be blunted (Fig. 2). There were no significant differences in baseline serum GH concentrations and maximum GH responses to CLON between the two patient groups at day 1 or at day 7. Neither were there any differences within each group comparing day 1 with day 7 (Table 2). Age was not found to correlate with maximum GH response to CLON for either patient or control groups (results not shown).

Patients and controls given CLON 1.5 \( \mu \)g were not found to be different in maximum GH responses [3.1 ± 5.7 (0–17.1) and 6.1 ± 9.1 (0–27.1) mU/l, respectively]. When administering the higher dose (CLON 2.0 \( \mu \)g), patients showed significantly lower maximum GH responses, compared to controls [3.9 ± 6.6 (0–22.8) vs 14.3 ± 12.5 (0.2–32.5) mU/l, respectively; \( P < 0.05 \)].

<table>
<thead>
<tr>
<th></th>
<th>CLON\textsubscript{1.5}</th>
<th></th>
<th>CLON\textsubscript{2.0}</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 1</td>
<td>Day 7</td>
<td>Day 1</td>
<td>Day 7</td>
</tr>
<tr>
<td>Baseline GH concentration (mU/l)</td>
<td>3.7 ± 2.8</td>
<td>3.0 ± 2.5</td>
<td>1.1 ± 2.3</td>
<td>0.7 ± 1.5</td>
</tr>
<tr>
<td></td>
<td>(( n = 14 ))</td>
<td>(( n = 12 ))</td>
<td>(( n = 12 ))</td>
<td>(( n = 9 ))</td>
</tr>
<tr>
<td>Maximum GH response (mU/l)</td>
<td>3.5 ± 6.1</td>
<td>5.0 ± 5.6</td>
<td>3.9 ± 6.6</td>
<td>2.0 ± 2.2</td>
</tr>
<tr>
<td></td>
<td>(( n = 14 ))</td>
<td>(( n = 12 ))</td>
<td>(( n = 12 ))</td>
<td>(( n = 9 ))</td>
</tr>
<tr>
<td>ASAT (( \mu )kat/l)</td>
<td>1.2 ± 1.0</td>
<td>0.7 ± 0.6</td>
<td>2.3 ± 4.3</td>
<td>0.8 ± 0.6</td>
</tr>
<tr>
<td></td>
<td>(( n = 16 ))</td>
<td>(( n = 14 ))</td>
<td>(( n = 13 ))</td>
<td>(( n = 9 ))</td>
</tr>
<tr>
<td>ALAT (( \mu )kat/l)</td>
<td>1.0 ± 1.3</td>
<td>0.9 ± 1.0</td>
<td>1.9 ± 3.3</td>
<td>1.3 ± 1.0</td>
</tr>
<tr>
<td></td>
<td>(( n = 16 ))</td>
<td>(( n = 14 ))</td>
<td>(( n = 13 ))</td>
<td>(( n = 9 ))</td>
</tr>
<tr>
<td>GGT (( \mu )kat/l)</td>
<td>1.5 ± 1.8</td>
<td>1.2 ± 0.7</td>
<td>3.6 ± 3.9</td>
<td>1.7 ± 1.7</td>
</tr>
<tr>
<td></td>
<td>(( n = 16 ))</td>
<td>(( n = 14 ))</td>
<td>(( n = 12 ))</td>
<td>(( n = 9 ))</td>
</tr>
</tbody>
</table>

Patients were investigated on days 1 and 7 after the end of a period of heavy alcohol intake. Values are means ± SD. There were no significant differences between the groups on day 1 or day 7 (unpaired \( t \)-test) or within each group (day 1 vs day 7; paired \( t \)-test).

ASAT, aspartate aminotransferase; ALAT, alanine aminotransferase; GGT, \( \gamma \)-glutamyltransferase.
Mean ± SD values for serum concentrations of ASAT, ALAT, and GGT for CLON\textsubscript{1.5} and CLON\textsubscript{2.0} patients at days 1 and 7 are given in Table 2. Data for all liver parameters from one patient in the CLON\textsubscript{1.5} group and one GGT value in the CLON\textsubscript{2.0} group are missing at day 1. There were, however, no significant differences between the groups at day 1 or at day 7, or within each group (day 1 vs day 7) in any of the liver enzyme levels. In the total patient group, values above the upper laboratory reference limit were observed in 15/29 (ASAT), 13/29 (ALAT), and 15/28 (GGT) patients at day 1. The corresponding figures for day 7 were: 7/23 (ASAT), 13/23 (ALAT), and 14/23 (GGT). There were no correlations between values for liver enzymes and baseline or maximum GH serum concentrations at day 1.

Scores for psychopathology at the start and end of the investigation period (days 1 and 7) for both patient groups are given in Table 3. There were no significant differences in psychopathology between the two patient groups on either day 1 or day 7. When comparing data on days 1 and 7 within each group, significant improvements were seen for several items in the AWIP scale (see Table 3).

The total sum of scores reflecting depression (MADRS) for both patient groups are shown in Table 4. There were significant differences within each group when comparing day 1 with day 7. However, there were no significant differences between the groups at day 1 or at day 7.

Twelve of 28 patients (42\%) displayed moderate (CLON\textsubscript{1.5}: n = 5 and CLON\textsubscript{2.0}: n = 7) and four severe depression (14\%; CLON\textsubscript{1.5}: n = 2 and CLON\textsubscript{2.0}: n = 2) at day 1 according to the classification suggested by Snaiht \textit{et al.} (1986). Only two patients (both in the CLON\textsubscript{2.0} group) showed moderate depression at day 7 (total sum of scores: 20 and 23).

In the CLON\textsubscript{1.5} group, baseline GH concentrations and maximum GH responses to CLON did not differ significantly between patients with (n = 7) or without (n = 5) depression at day 1 (according to the classification suggested by Snaiht \textit{et al.}, 1986;
Neither were such differences observed between patients with \( n = 8 \) or without \( n = 4 \) depression in the CLON\(_{2.0}\) group.

No correlations were found between values for baseline GH serum concentrations or maximum GH responses to CLON and sums of scores of reported and/or observed items in the withdrawal scale (AWIP) or the depression scale (MADRS), or scores of any of the individual items of the AWIP/MADRS scales on day 1 in either the CLON\(_{1.5}\) or the CLON\(_{2.0}\) group (data not shown). Furthermore, no relationships were found between baseline GH or maximum GH response to CLON and values for ASAT, ALAT or GGT on day 1 in either group.

**DISCUSSION**

The 30 alcohol-dependent patients in this study underwent CLON/GH tests immediately after...
ending a period of heavy alcohol drinking (day 1) and also a week later (day 7). The first investigation with challenge tests and assessments of psychopathology were performed at a time when patients had not yet started their medication for withdrawal symptoms. It may be argued that the hormonal and rating data obtained at day 7 could have been influenced by the medication. However, in earlier studies, different types of withdrawal medications were found not to influence baseline or CLON-induced changes in GH (Balldin et al., 1992b) or rating data (Bokström and Balldin, 1992). Furthermore, in the present study, the medication was reduced each day during the treatment period and the dosages were minimal the day before the second challenge test. Moreover, all challenge tests were performed after 8–9 h fasting and after 12–13 h without medication.

We investigated two groups of patients with similar background data in this study. The results revealed that 86% of the CLON<sub>1.5</sub> patients had blunted GH responses on day 1 and 75% on day 7. The figures for the patients given the higher CLON dose were 92 and 100% respectively. Thus, in spite of the fact that one patient group was given a higher dose of CLON, the proportion of blunted GH responses remained almost similar. This is further supported by the fact that there were no significant differences in maximum GH responses to CLON between the two patient groups either on day 1 or on day 7. This would suggest that administration of 1.5 or 2.0 µg CLON is equally effective in studies of α<sub>2</sub>-adrenoceptor function in alcohol dependence. On the other hand, the higher CLON dose caused increased maximum GH responses in healthy controls. Accordingly, when comparing data from patients with respective controls, we found that maximum GH responses to CLON were higher in controls compared to patients only for those given 2.0 µg CLON. In line with a study by Hoehe et al. (1988), our data suggest that a higher CLON dose is more likely to differentiate GH responders from non-responders in healthy individuals than in alcohol-dependent patients.

No associations were found between hormonal responses and liver function parameters obtained before the start of the period of medication for

### Table 4. Mean total scores of items reflecting depression

<table>
<thead>
<tr>
<th></th>
<th>CLON&lt;sub&gt;1.5&lt;/sub&gt;</th>
<th></th>
<th>CLON&lt;sub&gt;2.0&lt;/sub&gt;</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 1 (n = 15)</td>
<td>Day 7 (n = 12)</td>
<td>Day 1 (n = 13)</td>
<td>Day 7 (n = 9)</td>
</tr>
<tr>
<td>Reported scores</td>
<td>19.9 ± 8.0</td>
<td>5.3 ± 4.5***</td>
<td>17.5 ± 10.9</td>
<td>6.6 ± 8.5*</td>
</tr>
<tr>
<td>Observed scores</td>
<td>2.3 ± 1.9</td>
<td>0.6 ± 0.9**</td>
<td>1.5 ± 1.0</td>
<td>0.2 ± 0.4**</td>
</tr>
<tr>
<td>Total depression scores</td>
<td>22.2 ± 9.8</td>
<td>5.9 ± 5.1***</td>
<td>19.0 ± 11.3</td>
<td>6.8 ± 8.8*</td>
</tr>
</tbody>
</table>

Depression was assessed by the Montgomery–Åsberg Depression Rating Scale (MADRS; range for each item 0–6 and total range of scores 0–60), in alcohol-dependent patients investigated with clonidine (CLON)/growth hormone tests (1.5 and 2.0 µg CLON/kg body wt i.v. respectively) immediately after a period of heavy alcohol intake (day 1) and a week later (day 7). Values are means ± SD.

There were significant differences within each group comparing day 1 with day 7: *P < 0.05; **P < 0.01; ***P < 0.001 (paired t-test). No significant differences were found between the groups at day 1 or at day 7 (unpaired t-test).

### Table 5. Mean values for baseline growth hormone (GH) serum concentrations and clonidine (CLON)-induced maximum GH responses in alcohol-dependent patients with or without moderate/severe depression

<table>
<thead>
<tr>
<th></th>
<th>Baseline GH concentration (mU/l)</th>
<th>Maximum GH response (mU/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLON&lt;sub&gt;1.5&lt;/sub&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression (n = 7)</td>
<td>3.6 ± 2.6</td>
<td>3.3 ± 5.6</td>
</tr>
<tr>
<td>No depression (n = 5)</td>
<td>3.9 ± 3.4</td>
<td>3.9 ± 7.4</td>
</tr>
<tr>
<td>CLON&lt;sub&gt;2.0&lt;/sub&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression (n = 8)</td>
<td>0.3 ± 0.3</td>
<td>5.2 ± 7.8</td>
</tr>
<tr>
<td>No depression (n = 4)</td>
<td>2.7 ± 3.8</td>
<td>1.5 ± 2.4</td>
</tr>
</tbody>
</table>

Montgomery–Åsberg Depression Rating Scale scores were made according to the classification suggested by Snaith et al. (1986) one day after end of a period of heavy alcohol intake (day 1). There were no significant differences between the patient groups (unpaired t-test). Values are means ± SD.
withdrawal symptoms. Thus, the GH responses to CLON do not seem to be related to abnormal liver functions, either by altering the metabolism of CLON or that of GH.

The first rating for psychopathology was performed before starting the regular treatment for withdrawal symptoms. More than half (57%) of the patient group revealed signs of moderate to severe depression according to the classification suggested by Snaith et al. (1986), a figure in agreement with reports by Schuckit (1989) and Balldin et al. (1992c). Patients were retested again 1 week later (day 7) as it is known that symptoms of depression and anxiety usually remit within 1 or 2 weeks (Brown and Schuckit, 1988; Majumdar et al., 1988; Brown et al., 1991; Balldin et al., 1992c, Berggren et al., 1999; Fahlke et al., 1999). Through repeating the ratings for psychopathology at the end of the week, we could detect the existence of a dual diagnosis of alcohol dependence with a depressive/anxiety disorder. However, the results gave evidence for reduced psychopathology in all patients during the withdrawal period. At the end of the investigation, 28 patients were without depression. Only two patients showed remaining signs of moderate depression, but the sum of scores was lower compared to the first rating occasion (day 1: 28 and 27; day 7: 20 and 23, respectively). The slow decrease in psychopathology from the start to end of the study period does not suggest an additional syndrome of depression but may on the other hand indicate a slow and prolonged withdrawal period. Thus, taken together, this patient sample consisted only of individuals with a single diagnosis, i.e. alcohol dependence.

In the present study, we found no relationship between alpha-2-adrenergic function, reflected by GH response to CLON and psychopathology during the alcohol-withdrawal period. Thus, neither the items reflecting alcohol withdrawal (AWIP) nor the specific items reflecting depression (MADRS) were related to the degree of postsynaptic alpha-2-adrenergic function subsensitivity. There was also no relationship between this measure and symptoms of anxiety. Further evidence for a lack of association between psychopathology and alpha-2-adrenergic function was the finding that GH responses to CLON did not differ between patients with or without depression in the early withdrawal period. Furthermore, the fact that alpha-2-adrenergic function was also downregulated 1 week after the start of the withdrawal period, when the depressive symptoms had almost disappeared, strengthens the lack of association between alpha-2-adrenergic function and psychopathology in alcohol dependence. Although previous studies have shown blunted GH responses to CLON in patients with panic disorders or depression, but without concomitant alcohol dependence (Checkley et al., 1981, 1984; Charney et al., 1982; Siever and Uhde, 1984; Uhde et al., 1986; Charney and Hening, 1986; Anseau et al., 1988; Nutt, 1989; Curtis et al., 1989; Tancer et al., 1993; Coplan et al., 1995; Valdivieso et al., 1996), the results from the present study provide no evidence for a relationship between such psychopathological symptoms and postsynaptic alpha-2-adrenergic subsensitivity in alcohol dependence.

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