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The Behavioral and Cognitive Effects of Two Benzodiazepines Associated with Drug-Facilitated Sexual Assault*

ABSTRACT: Recently, sexual assaults have included the use of benzodiazepines to impair the victim. Our aim was to examine the physiological, cognitive, and behavioral effects of flunitrazepam (FN) and clonazepam (CLO). In the first study, ten healthy volunteers received a single oral dose of 2 mg of FN. Mini Mental State Examination (MMSE), behavioral reports and staff observations were then collected. In the second study, ten healthy volunteers received a single oral dose of 3 mg of CLO. Vitals signs, performance on the MMSE and Digit Symbol Substitution Test, and behavioral changes were examined. FN significantly decreased systolic and diastolic blood pressure 4 h post drug ingestion with diastolic remaining low at 6 h. CLO was associated with changes in temperature and decreased systolic pressure. FN affected memory and attention 4 h following ingestion. CLO affected memory and attention throughout the study (6 h), and psychomotor performance was decreased 2 h post ingestion. In both studies, subjects were disinhibited and did not perceive their own impairment.

KEYWORDS: forensic science, flunitrazepam, clonazepam, drug-facilitated sexual assault, cognitive effects, behavioral effects, physiological effects

Recent data indicate that approximately 75% of all rapes are categorized as date or acquaintance rape (1). Increasingly, these incidents, as well as assaults by strangers, involve the use of various drugs to impair the victim. One of these drugs is flunitrazepam (Rohypnol®) (FN), a quick-acting benzodiazepine hypnotic that is colorless, odorless, and tasteless. A second agent is clonazepam (Klonopin™) (CLO), a rapidly absorbed benzodiazepine anticonvulsant. FN has been prescribed in several European countries since the 1970s but is not legally available in the United States. CLO, however, is currently approved in the United States, which may explain its potential use in drug-facilitated sexual assault. Typically, these drugs are slipped into the victim's alcoholic drink, potentiating the effects of the drugs. Benzodiazepines are chosen because they cause drowsiness, diminish cognitive and motor skills, and most importantly produce amnesia for the event, thus impairing recall of the assault (2). As a result, many victims do not immediately report these incidents and valuable information for possible prosecution is lost. Researchers are developing assays, however, that can measure the metabolites of these drugs in hair and urine, allowing for the potential for evidence collection long after drug administration (3–5).

Anecdotal reports describe significant amnesic effects of benzodiazepines. The cognitive effects of FN have been studied in substance abusers, patients with insomnia, and healthy populations. Several studies have also examined FN's abuse potential, since the opioid-dependent population often prefers this agent. For example, Mintzer and Griffiths compared the behavioral effects of FN and triazolam in sedative drug abusers (6). They found that FN produced an earlier onset and longer duration of memory deficits (based on digit symbol substitution and word recall/recognition) and psychomotor performance (based on balance and hand eye coordination) than triazolam. They also noted that FN had the highest ratings on subjective measures of "liking" and interest in taking it again. In another study, Farre, Teran, and Cami examined the acute cognitive effects of FN in healthy volunteers in an attempt to understand the preference (7). Subjects were given either FN (0.5 or 2 mg) or triazolam (0.25 or 0.5 mg). Cognitive testing was completed at 0.5, 1, 1.5, 2, 3, 4, and 6 h after drug administration. The battery included simple reaction time; a digit symbol substitution test (a measure evaluating the recognition and recording of visual information); a balance task; Maddox-wing device (a measure of psychomotor impairment); and visual analog scales. They found that 2 mg of FN produced the greatest impairment in reaction time, psychomotor skill, balance, and digit symbol performance followed by 0.5 mg of triazolam, 0.25 mg of triazolam, and finally by 0.5 mg FN. In addition, FN and triazolam both caused a decrease in diastolic blood pressure and FN caused a decrease in body temperature.

Since FN is effective in treating insomnia, other studies have examined this agent's effect on sleep and side effect profile. Smirne et al. studied the effects of FN (1, 2, and 4 mg doses) on vigilance, attention, memory, and learning in healthy volunteers (8). Subjects

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took the medication, were instructed to go to sleep, and were tested 3.5 h later and the next morning (i.e., 10 h after administration). The authors concluded that the 4 mg dose impaired vigilance, attention, immediate memory, and short-term complex memory. Bareggi et al. studied the cognitive effects of three doses of FN (1, 2, or 4 mg) as it relates to plasma level (9). Healthy volunteers were given either a placebo or one of the three FN doses. Cognitive tests included measures of reaction time (psychomotor sedation), number inversion test (attention), digit span (working memory) prose and immediate recall (memory), and trigrams (learning). Utilizing the same paradigm in their previous study, they found that only the 4 mg dose of FN significantly affected psychomotor sedation, attention, and working memory at the first testing (8). In the morning, both doses of FN only significantly affected delayed recall. Dujardin et al. compared the effects of zolpidem and FN on sleep structure and cognitive functions in patients suffering from insomnia (10). Cognitive tests were completed four times on the day following administration of the drug. These tests included the sign crossing test, dichotic listening test, digit span, visual recognition test, and free recall. The authors concluded that 1 mg of FN significantly affected selective attention and short-term memory compared to 10 mg of zolpidem or placebo.

Ott, Rohloff, Aufdembrinke, and Finchte reported the results of a double-blind study of amnesic effects in healthy male volunteers who received single doses of lormetazepam (1 or 2 mg), FN (2 mg), or placebo (11). Examining anterograde and retrograde amnesic effects with immediate and delayed recall and recognition, they found that FN was associated with the most anterograde memory deficits. Fossen, Godlibsen, Loyning, and Dreyfus completed two studies with healthy volunteers comparing the effects of zopiclone (7.5 mg) to FN (2 mg), nitrazepam (5 mg), and placebo on memory (12). Following drug administration, the subjects were tested on Days 1, 7, 8, 14, 15, 21, 22 and 28. Assessments examined long-term (retention test) and short-term memory (paired associates and visual memory test). They concluded that, compared to placebo, all three drugs produced some memory problems, especially on the day the drug was taken, but that FN caused significantly more impairment in short-term memory than zopiclone. The memory impairment was most notable on the visuospatial subtest of the visual memory test. The cognitive effects of FN also evidenced a trend toward disturbance in long-term memory and the induction of potential amnesia. Overall, existing data indicate that FN affects motor skills, including balance and eye-hand coordination, and cognitive functions, including short-term memory, attention, and vigilance.

There is limited research on the cognitive effects associated with CLO. Many of the studies or reviews focus on its side effects in epileptic populations (13,14). Two studies examined the psychomotor effects of CLO, however, in healthy volunteers. Wildin et al., in a double-blind study comparing clobazam (10 or 20 mg) to CLO (0.5 or 1 mg), found that CLO produced significantly greater effects on psychomotor performance than clobazam (15). Van der Meyden et al. also compared clobazam (20 mg) to CLO (2 mg) on psychomotor performance in healthy volunteers and reported that CLO produced a significantly lower choice reaction time and alertness than clobazam (16). The existing data suggest that CLO significantly affects motor skills.

The primary goals of our two studies were to develop a sensitive and accurate method for measuring the presence of FN (Study 1) and CLO (Study 2) in urine and hair. During the process of collecting the biological data in healthy volunteer subjects, however, several interesting effects were identified in the safety data (i.e., physiological, cognitive, and behavioral) and are the focus of this paper. Based on qualitative clinical observations and assessments with the Mini Mental State Examination (MMSE, 17) in the first study of FN, we included more specific tests to measure cognitive and behavioral effects in the second study of CLO. This study is the first to examine behavioral data.

Study 1

Methods

Following a description of all procedures, subjects provided informed consent as approved by the University of Illinois at Chicago's Institutional Review Board. The first study collected hair and urine samples in healthy volunteers who were given a single oral dose of 2 mg of FN. The study included ten subjects with a mean age of 35 ($\pm$10.70) years. Eight females and two males participated in this study. Eight subjects were Caucasian, one African American, and one Asian. All subjects completed at least a high school education. Hair and urine samples were collected at baseline prior to receiving the medication and 6 h after taking the medication. Vital signs and objective observations of behavior were recorded at baseline, as well as 4 h and 6 h post FN ingestion. As part of the safety measures, subjects completed the MMSE 4 and 6 h after receiving FN. This measure was included to ensure that each subject was lucid and able to safely return home. In total, staff closely observed subjects for 8 h following drug administration. Subjects also returned several times during the following four weeks to provide urine and hair samples. Again, while the primary aim of the first study was to develop a sensitive and precise assay for detecting the elimination of FN in hair and urine (3,4), the focus of this report is to examine the immediate physiological, cognitive, and behavioral effects of FN.

Results

Physiological Data—Using a repeated measures ANOVA, there were no significant differences in temperature $F(2,8) = 0.577$, $p = 0.584$, pulse $F(2,8) = 0.500$, $p = 0.624$ and respiration $F(2,8) = 0.162$, $p = 0.853$ between baseline, 4 and 6 h post drug administration. However, we found a significant decrease in systolic blood pressure between baseline and 4 h post FN ingestion, $t(9) = 4.20$, $p = 0.002$(standing); $t(9) = 3.31$, $p = 0.009$ (lying). There was also a significant increase in standing systolic blood pressure between 4 and 6 h post FN $t(9) = 2.418$, $p = 0.039$. At 6 h post FN, both standing and lying systolic blood pressure were not significantly different from baseline. There were no differences in standing diastolic blood pressure between baseline, 4 h, and 6 h post drug administration, $F(2,8) = 2.029$, $p = 0.194$. There was a significant decrease in lying diastolic blood pressure between 4 and 6 h post FN $t(9) = 2.57$, $p = 0.030$ (see Figs. 1 and 2).

Cognitive Data—Although we did not obtain a baseline MMSE measure, the score on the MMSE was significantly lower at 4 h

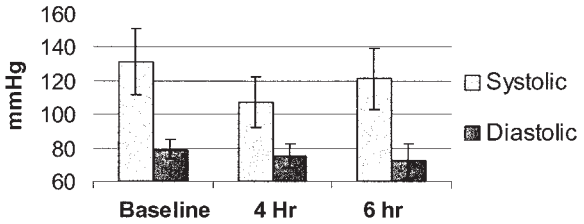

FIG. 1—*Study 1–FN mean standing blood pressure.*

compared to 6 h post FN $t(9) = 3.04$, $p = 0.01$ (see Fig. 3). Specifically, FN adversely affected items on the MMSE addressing orientation, attention and calculation, and recall.

Behavioral Data—One week after the study, we collected descriptions of the subject's experience while under the influence of FN. Staff behavioral observations were not formally collected as part of the data, but were ascertained as anecdotal reports.

Subjects consistently reported the first indication of the effects of FN was a sense of drowsiness. One subject reported, "my vision was slightly tunneled; I got very tired very quickly." Subjects fell asleep between 15 to 90 min after FN ingestion and usually slept during the remainder of the study.

All but two of the subjects reported they were sleepy or "spacey" the remainder of that day. "I felt like I do after alcohol consumption, tired physically, sluggish, and a little sensitive to light." Most subjects reported napping on and off and then going to bed early. Two subjects stated the remainder of their day was normal. One of the subjects, however, reported feeling energized the next day until 2:00 p.m. when they then became tired.

Subjects reported slowed thought processes and a loss of concentration, requiring extra concentration to accomplish various tasks. One subject reported having difficulty recalling words. Subjects reported confusion or spaciness.

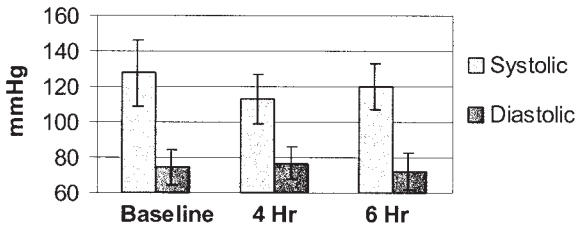

FIG. 2—*Study 1–FN mean lying blood pressure.*

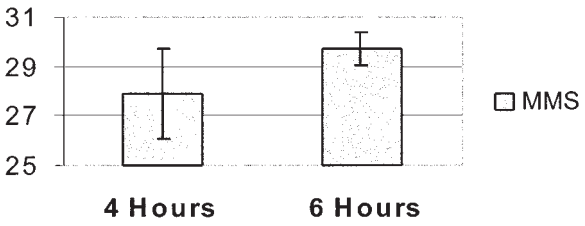

FIG. 3—*Study 1–FN mean MMSE scores.*

The subjects were asked if they had received feedback from others (staff, family, or friends) that differed from their experience. This was equally divided. Although some subjects reported no differences between their experience and what others observed, several subjects reported an inability (or at least difficulty) in remembering who they spoke to or what they did. In fact, anecdotal reports from staff identified behaviors (including decreased inhibition) that the subjects were unable to recall. These reports included subjects who subjectively reported no change other than drowsiness.

There were several discrepancies between staff and subject reports. One subject was not able to find the door in a small office. Another subject was unaware that while they ate cereal, they were missing their mouth and spilling it all over the floor. One subject remembered going to sleep and waking at the end of the study. However, staff reported the subject was walking, talking, and appeared very alert at times throughout the day. Subjects were less inhibited; one subject stated she was warm and attempted to remove her blouse before staff intervened.

Most subjects identified no difficulty in their cognitive processes. Only two of the subjects stated that they felt their ability to make decisions was impaired: "I feel like I had a harder time making decisions and was more willing to go along with suggestions or decisions made by others." However, through staff observation several subjects exhibited impaired judgment and decision-making. Several subjects felt that being in the protective environment of the study did not require decisions on their part and therefore they did not notice a change.

When asked about their experience taking the first MMSE at 4 h post FN ingestion, the subjects were equally divided between believing that they had difficulty and that they had no difficulty. One subject had trouble with the entire MMSE, while others reported problems with recall of three items and repeatedly subtracting 7 from 100. One subject had no recall of the first MMSE: "I remember only one vaguely and remember that I did it very playfully." All subjects reported no difficulty with the final MMSE.

The subjects were asked if they had any additional comments about their experience of taking FN. Several expressed amazement and surprise at the "patchy" amnesia. One subject commented that it felt the same as receiving anesthesia during a tooth extraction. One subject experienced a sense of weaving even while standing still. Two subjects reported an enhanced sense of taste. One subject concluded, "I can see how someone could lose their inhibitions."

The individual behavioral and cognitive data are summarized in Table 1. Memory disturbance was present in all subjects, and the remaining symptoms varied across the subjects.

TABLE 1—*Study 1: Individual behavioral and cognitive data.*

Sub.	Initial Drug Effect	Confusion	Concentration Problems	Memory Disturbance	Impaired Judgment & Decision Making
A	Drowsy	−	−	+	−
B	Drowsy	−	+	+	−
C	Sleepy & drowsy	+	+	+	+
D	Drowsy	+	−	+	+
E	Sleepy & drowsy	−	−	+	+
F	Drowsy	+	−	+	+
G	Sleepy	−	−	+	−
H	Sleepy	+	−	+	+
I	Sleepy	−	+	+	−
J	Drowsy	+	−	+	+

+ Denotes positive.
− Denotes negative.

While safety was the focus of the staff observations in this study, given the number of discrepancies between subject's perceptions and staff's verbal reports, we included a more formal system for collecting staff observations in Study 2.

Study 2

Methods

Following a description of all procedures, subjects provided informed consent as approved by the University of Illinois at Chicago's Institutional Review Board. The second study collected hair and urine samples in healthy volunteers who were given a single oral dose of 3 mg of CLO. The study included ten subjects with a mean age of 38 (±9.72) years. Six females and four males participated in this study. Five subjects were Caucasian, one African American, one Hispanic, and three Asian. All subjects completed at least a high school education. Hair and urine samples were collected at baseline prior to receiving the medication and 6 h after taking the medication. Subjects also returned several times during the following four weeks after drug administration to provide urine and hair samples. On the study day, vitals (sitting blood pressure, pulse, and temperature) were taken 1, 2, and 6 h post CLO. Only sitting blood pressure was obtained since orthostatic changes are not associated with this medication. In total, subjects were observed for approximately 8 h following drug administration.

Based on the earlier experience with the FN study, we incorporated some additional assessments for the CLO study that included a baseline MMSE (17) and the Digit Symbol Test (DS) of the Wechsler Adult Intelligence Scale (18) at baseline, 2 h or *C*max (maximum concentration) and 6 h post drug administration. We continued to use the MMSE because it is a quick assessment of cognitive function. The DS task was added because it tests psychomotor performance, which is influenced by coordination, speed, and attention and is relatively unaffected by intellectual skill, memory, or learning (19). We recorded observations of staff who monitored the subjects from baseline to discharge from the hospital. When the subjects returned the following day to provide urine and hair samples, we also collected their subjective reports of the experience with a questionnaire developed by one of the authors (MJS).

Results

Physiological Data—Using a repeated measures ANOVA, there were no significant differences in pulse between baseline, 1, 2, and 6 h post CLO $F(3,7) = 0.477$, $p = 0.708$. There was, however, a significant increase in temperature from baseline to 1 h post CLO, $t(9) = 3.7$, $p = 0.005$, and a significant increase in temperature from baseline to 6 h post CLO, $t(9) = -3.3$, $p = 0.008$. There were no significant differences in temperature between baseline and 2 h post CLO, $t(9) = 1.76$, $p = 0.113$ (see Fig. 4).

While there were no differences in diastolic blood pressure across the four time points, there were significant differences in systolic blood pressure. A paired samples t-test comparing each of the time points revealed a significant decrease in systolic blood pressure between baseline and 1 h post CLO $t(9) = 3.84$, $p = 0.004$, between baseline and 2 h post CLO $t(9) = 6.11$, $p = 0.000$, and between baseline and 6 h post CLO $t(9) = 2.78$, $p = 0.021$ (see Fig. 5).

Cognitive Data—There were significant differences on the MMSE across the three time points. Thus, when we conducted paired samples t-test to compare each of the time points, there was a significant decrease in the total MMSE score between baseline and 2 h post CLO $t(9) = 4.23$, $p = 0.002$, and again between baseline and 6 h post CLO $t(9) = 2.45$, $p = 0.037$. There was a significant increase in total MMSE scores between 2 h post and 6 h post CLO $t(9) = -3.51$, $p = 0.007$ (see Fig. 6). The item requesting subjects to remember three items and repeat them later was significantly worse 2 h post CLO compared to baseline $t(9) = 6.68$, $p = 0.000$. The ability to complete serial sevens or spell "world" backwards (two alternative options to test attention) was also significantly worse at 2 h post CLO compared to baseline $t(9) = 2.37$, $p = 0.045$. Finally, the item addressing orientation to time was significantly worse at 2 h post CLO compared to baseline $t(9) = 1.96$, $p = 0.081$.

There were also significant differences on the DS task across the three time points. There was a significant decrease in total score on the DS between baseline and 2 h post CLO $t(9) = 3.98$, $p = 0.003$ with a significant increase in total score on the DS between 2 h post CLO and 6 h post CLO $t(9) = -3.68$, $p = 0.005$. The scores on the DS, however, were not significantly different between baseline and 6 h post CLO (see Fig. 7).

Behavioral Data—One of the first indications that CLO was affecting subjects was their report of feeling lightheadedness or dizzy

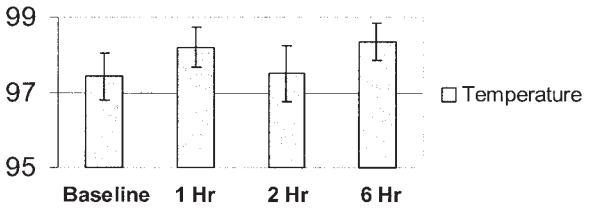

FIG. 4—*Study 2–CLO mean temperature.*

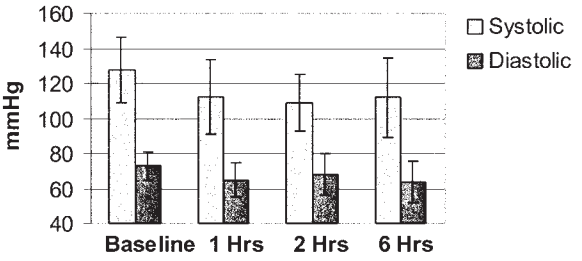

FIG. 5—*Study 2–CLO mean sitting blood pressure.*

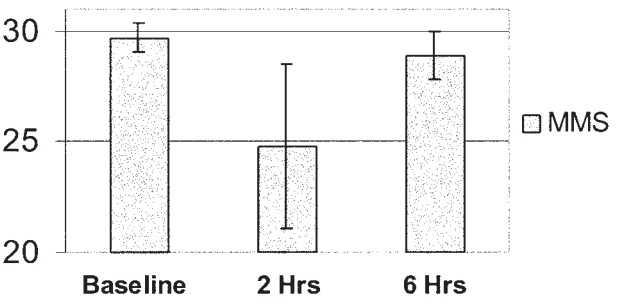

FIG. 6—*Study 2–CLO mean MMSE scores.*

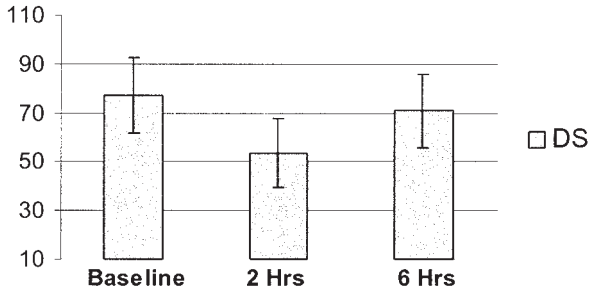

FIG. 7—*Study 2–CLO mean DS scores.*

(i.e., "I got up to go to the bathroom, I got dizzy and lightheaded"). Subjects also reported a sense of drowsiness soon after the administration of CLO, feeling "woozy after 15 minutes." All of the subjects slept during the study. It was difficult to arouse two subjects throughout the entire study period, and two others slept lightly during the study period. One subject believed that she remained awake during the entire study period, but has no recall of doing the second MMSE and DS test.

The second study had a MMSE and DS scheduled at *C*max. The baseline MMSE and DS were experienced as "pretty basic" with only minor difficulties with the serial sevens/spelling and recall of three objects. One subject, however, ". . . had more trouble at baseline, especially remembering the three objects. Maybe it was anxiety."

Six of the 10 subjects had no memory at all of the second set of evaluations. Even after being informed they had taken a second set, several of the subjects were surprised. "I have no memory. I thought we only took two." "Are you kidding me!"

The final set of cognitive tests was experienced as more difficult than baseline for the majority of subjects. They reported that the DS and recall on the MMSE was the most difficult. On the DS one subject ". . . noticed my eye-hand coordination wasn't tracking . . . " Another subject reported, "I had to force myself to get the answers." One subject ". . . remembered the three items from the morning." In fact, some only remembered the third set of tests with prompting by the investigator during follow-up.

The study did not specifically require the subjects to concentrate except during the cognitive testing. However, several subjects talked of a decreased ability to concentrate: "I was reading the paper and was not able to concentrate, I thought 'I am going down.'" They expressed a sense of having to consciously pull their thinking up in order to make decisions. "I couldn't concentrate, I couldn't think. I had to really work at it. I was lost." Other subjects just went to sleep and we have no sense of this symptom in these subjects.

When asked about their perception of the remainder of the day, most of the subjects identified problems with motion. Over half of the subjects actually used the term "wobbly." "My mind was fine but my body was not in sync." "I noticed I was a little off balance and stumbled. Even today I think if I didn't pay attention, I'd stumble."

More than half the subjects perceived no changes in their decision-making process. "No, boredom was the biggest problem." Two subjects acknowledged an awareness of increased suggestibility, reporting the experience as "more liberating, like being under the influence of alcohol; more freedom, less inhibitions." The difference between the subjects' perception of what was happening during the study, the objective feedback from others, and subjects' memories are marked. One subject took notes during the study, stating he was doing so to remember what happened. He appeared to be writing without difficulty, but when staff looked at the paper it was illegible. The next day the subject could not recall taking notes at all, and was not able to locate his notepad!

Another subject was reading a book periodically during the study day. According to staff she even seemed to be turning the pages at the appropriate times. The next day she reported a loss of memory of what she had read just prior to the study beginning. "I had to re-read everything. I have no memory of reading anything else, and I hear I read all afternoon. I don't remember."

One of the most disturbing experiences for several of the subjects was the loss of an awareness of the normal passage of time. "My first memory is 2:30 p.m." "I don't remember going to sleep. I remember getting a bagel, but I don't remember eating it." "There is a space I lost track of, about 3 h." One subject summed up the whole experience: "I felt a little dizzy, like a heaviness sort of. Then after that I don't remember anything."

Additionally, one subject identified the same experience later during the study day: "we talked about going to the store. I lost all track of time. I said, 'Let's go.' He looked at me strangely and said, 'I've already been there and back.'"

The individual behavioral and cognitive data are presented in Table 2. All but one subject described their initial reaction as sleepy, woozy, or lightheaded. The symptoms of ataxia and general memory impairment were present in all subjects. However, there were three subjects who did not have impaired judgment or decision-making. Those same subjects also did not report a loss of time.

In closing, regardless of all the reports of loss of time, memory problems, and difficulty concentrating, the overall perception of

TABLE 2—*STUDY 2: Individual behavioral and cognitive data.*

Sub.	MMSE % Change ↓	DS % Change↓	Initial Drug Effect	Ataxia	Recall of 2nd Testing	Memory Disturbance	Impaired Judgment & Decision Making	Loss of Time
A	26%	39%	Woozy	+	+	+	+	+
B	3%	33%	Sleepy	+	−	+	+	+
C	20%	37%	Woozy	+	−	+	+	+
D	7%	18%	Dizzy	+	+	+	−	−
E	43%	71%	Dizzy	+	−	+	+	+
F	13%	49%	Dizzy	+	−	+	+	+
G	7%	12%	Lightheaded	+	−	+	+	+
H	16%	34%	None reported	+	−	+	+	+
I	3%	19%	Lightheaded	+	+	+	−	−
J	21%	4%	Lightheaded	+	+	+	−	−

+ Denotes positive.
− Denotes negative.

the subjects was that they were not very affected. In fact, one subject continues to emphatically deny that the cognitive tests were completed on three occasions. As one subject stated, "I did not have the sense that something was strange. I kept thinking 'When is this drug going to take effect?' I didn't feel doped up. I'm usually a real relaxed guy, but today I feel kind of smooth."

Discussion

This research examined the physiological, cognitive, and behavioral effects of a single dose of FN (2 mg) or CLO (3 mg) in healthy volunteers.

We found that FN significantly decreased blood pressure 4 h following administration. Interestingly, diastolic pressure remained low 6 h following ingestion, while systolic pressure returned to baseline levels. A previous study found a similar effect on diastolic pressure (7). In this same study, it was also found that FN caused a decrease in body temperature. However, in our study FN did not alter temperature, pulse, or respiration. Mattilla et al. and Rao et al. attributed diastolic blood pressure changes in their subjects administered benzodiazepine intravenously to peripheral vascular resistance and a decrease in cardiac output (20,21).

By contrast, CLO was associated with changes in temperature and systolic blood pressure. Temperature increased 1 h following CLO administration, returned to baseline level at 2 h, and again increased at 6 h. To our knowledge, this has not been found in other studies, and there are no clear explanations for these changes. While CLO also decreased systolic blood pressure throughout the entire study period, unlike FN, there were no effects of CLO on diastolic blood pressure.

As measured by the MMSE, we found that FN produced significant cognitive impairments related to memory and attention. Four hours post drug ingestion, the subjects had difficulty with orientation, repeatedly subtracting seven from 100 or spelling words backwards (attention and calculation), and remembering three objects after a several- minute delay (recall). In the second study, we found similar impairments on the MMSE at both the 2 and 6 h assessments. At the 2 h measure, the subjects had difficulty on the same three items (i.e., orientation, recall, and attention and calculation). Unlike the previous study, where cognitive performance returned to baseline level, CLO continued to significantly impact performance 6 h following administration, perhaps related to this agent's longer half-life. Although the level of impairment was statistically significant from baseline at the end of the study, all subjects were accompanied home without difficulty.

In the second study, we also examined a measure of psychomotor performance with the DS test and found that it was significantly decreased 2 h following drug ingestion and returned to baseline levels by 6 h.

Subjectively and behaviorally, FN and CLO appeared to cause significant drowsiness, sluggishness, and confusion. Consistent with performance on the MMSE, subjective reports identify difficulty concentrating and problems with memory. In both studies, there were difficulties with memory and concentration. Thus, several subjects did not recall events following ingestion, including the second test administration. Subjects' psychomotor performance was also significantly impaired.

In both studies, the memory impairments were most striking when examined in the context of subjects' lucidity and directability. Based on observation, subjects were clearly fatigued; however, they could be engaged and were attentive. While many subjects denied being affected by the drug, during formal testing they were very impaired and subjective reports on the questionnaire the next day were clearly in conflict with staff observation and documentation. In both studies, some subjects were clearly disinhibited and did not accurately perceive their own level of impairment. Due to the small sample size and diverse symptoms reported, we are unable to establish any explanations for the individual differences in symptoms exhibited. In Study 1, there were no observable patterns in symptoms. In Study 2, it appears that three subjects manifested similar symptom patterns that included impaired decision making, loss of time, and their ability to recall the second testing. We explored several potential explanations (i.e., weight, body mass index, and age) for this pattern but were unable to support a hypothesis. It is, however, apparent that, although there were individual differences, all subjects were affected in some way.

Although there is previous research examining the cognitive impairments associated with these drugs, this study is the first to document their influence on behavior. Weaknesses of this study, however, include the small sample size and the anecdotal nature of these observations. At this point, we are unaware of any reliable and valid questionnaires to more accurately assess this information. Therefore, we relied on our experience from the first study to develop a questionnaire.

Those working with victims of drug-facilitated sexual assault in hospital emergency rooms or crisis centers have likely experienced victims' confusion and inability to recall information. This may be combined with the victim's belief that they were not impaired. Our study clearly documents in a controlled, safe setting that there are significant behavioral and cognitive effects of these drugs. This study provides evidence that CLO, which is available in the United States, also has the potential for the misuse observed with FN. It is also important to note that these drugs are usually combined with alcohol, almost certainly amplifying their effects (22,2). While both FN and CLO impact cognitive, behavioral, and physiological functions, it is clear that victims under the influence of these agents are able to function and interact. Further, while they may perceive a loss of time, they often have no recall of events and their behavior.

This information is clinically relevant because it provides evidence that validates the victim's experience. An important element of recovery from trauma is to understand what happened and to process the fear associated with the event (23). These are only preliminary findings, but our hope is that this study provides support of the powerful effects of these drugs, which are often unrecognized by the victim and those around them.

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