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Assessing subjective and psychomotor effects of the herbal medication valerian in healthy volunteers

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Abstract

Valerian is the common name given to the genus *Valeriana*, an odiferous, herbaceous perennial plant widely distributed in the temperate regions of Asia, Europe, and North America. It is among the most widely used herbal medicines in the world. Numerous clinical studies have demonstrated valerian's ability to improve sleep; however, to the best of our knowledge, no study has systematically assessed subjective and psychomotor/cognitive effects of valerian in young healthy adults across a range of doses. In the present study, we sought to determine whether valerian extract (*Valeriana officinalis*) altered mood and/or impaired psychomotor/cognitive performance in young healthy volunteers. We examined the effects of valerian extract (600, 1200, and 1800 mg) and 10 mg diazepam (positive control) compared to placebo in 10 young healthy volunteers. Dependent measures included subjective and psychomotor variables. The valerian extract had no significant effects on any of the dependent measures. Diazepam, though, produced subjective effects as measured by four different rating scales, and impaired psychomotor/cognitive performance. The data suggest that acute administration of valerian does not have mood-altering or psychomotor/cognitive effects in young healthy volunteers.

Keywords: Valerian; *Valeriana officinalis*; Herb; Mood; Psychomotor performance; Diazepam; Benzodiazepine; Sedative–hypnotic; Human

1. Introduction

There has been a considerable increase in the worldwide use and proliferation of herbal medicines. Medicinal herbs now constitute the most rapidly growing segment of the U.S. alternative medicine market (Matthews et al., 1999; McCabe, 2002), with over 29,000 herbal substances presently available for use in the United States (Kaye et al., 2000). Valerian, the common name given to the genus *Valeriana*, is among the most widely used herbal medicines (Fugh-Berman and Cott, 1999; Kemper, 1999). It is an odiferous, herbaceous perennial plant widely distributed in the temperate regions of Asia, Europe, and North America. There are approximately 250 different species (Beaubrun and Gray, 2000), but common valerian (*Valeriana officinalis* L.) is the one most often cultivated for medicinal uses (Leathwood and Chauffard, 1982/1983). The herb is primarily used for its putative sleep-enhancing and sedating (calming) effects (McCabe, 2002). Several neurobiological mechanisms have been postulated to mediate its sedative and hypnotic effects, including agonist effects at the human A_1 adenosine receptor (Schumacher et al., 2002) and benzodiazepine receptor (Ortiz et al., 1999) and potentiation of GABAergic transmission via both GABA release and inhibition of GABA reuptake (Santos et al., 1994; Ortiz et al., 1999). Studies with nonhumans tend to support valerian as a central nervous system depressant. In mice, valerian has been shown to reduce locomotion (Torrent et al., 1972; Wagner et al., 1980; Hendriks et al., 1985), potentiate barbiturate-induced sleeping time (Hendriks et al., 1985; Leuschner et al., 1993), and produce weak anticonvulsive effects (Dunaev et al., 1987; Leuschner et al., 1993).

In humans, a number of placebo-controlled, randomized, double-blind clinical trials have demonstrated that valerian affects sleep, including improvements in sleep quality and duration and decreased latency to sleep onset (Leathwood et al., 1982; Gessner and Klasser, 1984; Kamm-Kohl et al., 1984; Leathwood and Chauffard, 1985; Balderer and Borbely, 1985; Schulz et al., 1994; Vorbach et al., 1996; Donath et al., 2000). There have been two placebo-controlled,

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randomized, double-blind clinical trials that have examined the extent to which valerian has anxiolytic effects. In a study by Andreatini et al. (2002) with 36 outpatients suffering from generalized anxiety disorder, chronic dosing of valerian produced a significant reduction in the psychic anxiety subscale (i.e., consisting of anxious or depressed mood and cognitive or concentration disturbances) of the Hamilton anxiety scale (HAM-A) (Hamilton, 1959), suggesting that valerian may have a potential anxiolytic effect on the psychological symptoms of generalized anxiety disorder. In a study by Cropley et al. (2002) with 54 healthy volunteers, chronic dosing of valerian reduced physiological reactivity and self-reported ratings of pressure during mental stress tasks. Four placebo-controlled, randomized, double-blind studies have assessed whether and to what extent valerian affects psychomotor and cognitive performance. However, the methodology of some of these studies (e.g., using very low doses of valerian (Kohnen and Oswald, 1988), combining valerian with other substrates (Gerhard et al., 1996), examining residual effects the morning after administration (Kuhlmann et al., 1999) have not definitively resolved the issue as to whether valerian has impairing effects. A recent, well-designed study with psychomotor tests sensitive to detecting impairment in sedative drugs failed to find any psychomotor or cognitive impairment in elderly volunteers after acute administration of 400 and 800 mg of valerian (Glass et al., 2003). This study also failed to find any subjective effects, including effects (e.g., euphoria) that are thought to influence the likelihood of abuse of a substance.

The purpose of the present study was to systematically characterize the subjective and psychomotor/cognitive effects of valerian in young adult volunteers, using a range of doses that included a dose higher than doses used in the other studies that have assessed these parameters. Characterization of the subjective and psychomotor/cognitive effects of valerian is important for several reasons. First, as mentioned above, it is widely used; valerian was among the 10 most popular herbal medications sold in the United States in 1998 (Fugh-Berman and Cott, 1999; Kemper, 1999). As a result, it is widely used by people who may be engaging in activities, such as working and driving. Second, there has been recent concern that some herbal medications are being used recreationally for their mood-altering effects (Yates et al., 2000). Thus, it is important to begin to characterize the subjective effects of valerian, including abuse liability-related effects. Finding significant effects on psychomotor function, cognition, and mood would be significant from a public policy/regulatory standpoint since valerian is widely available and unregulated.

2. Methods

2.1. Subjects

The study was approved by the local Institutional Review Board. Participants were recruited from the university and surrounding community, primarily via newspaper ads and posters. Before participating, volunteers signed a written consent form describing the details of the study. In the consent form, subjects were informed that the purpose of the experiment was to study the effects of herbal medications and/or prescription drugs on mood and psychomotor functioning in healthy volunteers. They were told that the oral drugs that might be used were drugs commonly used in medical settings and might come from one or more of six classes: sedative/tranquilizer, antihistamine, stimulant, opiate, alcohol, or placebo. They were also told that the herbal medications that might be used were herbs used for sleep or relaxation, enhancing mood, improving mental functioning, or increasing energy. Volunteers initially participated in a structured telephone interview (acquiring data on age, sex, medical condition, and self-reported alcohol, cigarette, and marijuana use). Individuals meeting criteria (21–39 years old, fluent in English, high school diploma or equivalent, within 20% of ideal body weight, reporting some level of current recreational drug use, and no current medical problems) were invited for a personal interview with a member of our research staff, skilled in psychiatric/drug screening. At the screening interview, subjects' drug-use history and psychiatric and medical status were assessed, to determine if there were contraindications to their participating in the study (Derogatis et al., 1973; Derogatis, 1994). Volunteers completed the following questionnaires: (1) "Health Questionnaire," a locally developed questionnaire detailing their medical and drug-use history; (2) Michigan Alcoholism Screening Test (Selzer, 1971); and (3) Symptom Checklist 90-R, a checklist designed to assess their current level of psychiatric symptomatology (Derogatis et al., 1973; Derogatis, 1994). They also participated in a semistructured psychiatric interview, which included the use of the following: (1) Behavioral Pharmacology Research Group Screening Interview Checklist (a locally developed checklist addressing such issues as drug dependency and mental disorders, such as anxiety and depression); (2) Structured Clinical Interview for DSM-IV Axis I Disorders—Clinician Version (First et al., 1997); (3) DSM-IV (American Psychiatric Association, 1994). Exclusion criteria included past or current medical conditions that would contraindicate study participation; history of or current substance use disorder, as defined by DSM-IV criteria; a score of 4 or more on the Michigan Alcoholism Screening Test; current emotional or psychiatric problems; current or past DSM-IV Axis I psychiatric disorder; and pregnancy or intention to become pregnant. Additionally, if volunteers had applied to, been accepted to, or were currently enrolled in medical, nursing, dental, pharmacy, veterinary, or physician's assistant school, they were excluded from our study. The rationale behind this exclusion criterion is that we did not wish to expose these people to drugs that have abuse potential and to which they may one day have easy access. None of the subjects had a history of drug abuse or dependence (American Psychiatric Association, 1994). However, subjects did have to report

some level of recreational drug use, as opposed to being completely naïve to such drugs. We did not want to use completely drug-naïve volunteers for two reasons. First, we did not want to be the first individuals giving a drug (i.e., lorazepam) to drug-naïve individuals. Second, we believed that using drug-naïve participants might affect the results in this small population study. They might react in a totally different way from subjects with some history of recreational drug use, and they might not understand what certain subjective effects terms meant (such as "high" and "coasting"). Five men and five women (age range: 21–35 years; mean age: 26.6 years) completed the study. One subject withdrew from the study after completing four sessions for reasons unrelated to the study. Volunteers received payment for their participation in the research study.

2.2. Design

A randomized, placebo-controlled, double-blind, crossover trial consisting of five sessions was conducted. Volunteers ingested 90 ml of water with five identical (color and size) capsules containing standardized valerian root extract (Lichtwer Pharma, Eatontown, NJ, USA) (600, 1200, or 1800 mg), 10 mg diazepam, or placebo (cornstarch). Capsule weight was measured using a digital scale, and cornstarch was added when necessary to standardize capsule weight. We chose 1800 mg as the highest dose of valerian extract, based on the PDR for Herbal Medicine's maximum daily dose recommendation of 1800 mg per day (*PDR for Herbal Medicines*, 2000). Diazepam, a prototypic sedative, was chosen as a positive control because valerian is an herb with putative sedative effects.

2.3. Sessions

Each session was approximately 6 h in duration and conducted from 1000 to 1600 h in the Psychomotor Performance Laboratory on an outpatient basis. Sessions were spaced at least 1 week apart. Upon arrival at the laboratory, urine toxicology screening (Cloned Enzyme Donor Immunoassay Technique, Boehringer Mannheim, Indianapolis, IN), pregnancy testing (for all female participants), and breath alcohol testing were conducted. While in a semi-recumbent position on a hospital bed, subjects completed several subjective effects forms and psychomotor tests. Capsule administration was supervised by an anesthetist. Subjects were told, "The capsules you are about to ingest may or may not contain a drug." Because of the distinctive odor of the valerian extract, a rubber adjustable nose clip was given to subjects to wear during capsule administration, and maintenance of the blinding procedure was assessed 15 and 300 min postingestion using an odor detection/liking questionnaire. The questionnaire assessed the extent to which subjects detected an odor on a scale of 1–5 (1 = *I did not smell an odor*; 5 = *I smelled a very strong odor*) and the extent to which subjects liked the odor (0 = *dislike a lot*; 50 = *neutral*; 100 = *like a lot*) on a 100-mm line. Mood and psychomotor performance were assessed before and at fixed time intervals after capsule ingestion, in each of the five sessions of the experiment. Heart rate and arterial oxygen saturation were monitored throughout the study for safety reasons.

2.4. Dependent measures

The subjective effects and psychomotor/cognitive performance measures used in this study are tools that we have used in previous studies and have been sensitive in detecting the effects of various drugs, including alcohol, opioids, barbiturates, benzodiazepines, nitrous oxide, and volatile inhaled general anesthetics.

2.4.1. Subjective effects measures

Five subjective effects questionnaires were used. First, a computerized, short form of the Addiction Research Center Inventory (ARCI), a true/false 49-item questionnaire designed to differentiate among different classes of psychoactive drugs, was used (Haertzen, 1966; Martin et al., 1971). The ARCI yielded scores for five different scales: PCAG, sensitive to sedative effects; BG and AMP, sensitive to amphetamine-like effects; LSD, sensitive to somatic and dysphoric changes; and MBG, often described as euphoria. Second, a locally developed visual analog scale (VAS), consisting of twenty-six 100-mm lines, each labeled with an adjective (e.g., "coasting ['spaced out']," "dreamy," "lightheaded"), was used. Endpoints were labeled "not at all" and "extremely." Third, a locally developed drug effect/drug liking/take again questionnaire assessed three things: (1) the extent to which subjects currently felt a drug effect on a scale of 1–5 (1 = *I feel no effect from it at all*; 5 = *I feel a very strong effect*), (2) the extent to which subjects currently liked the drug effect (0 = *dislike a lot*; 50 = *neutral*; 100 = *like a lot*), and (3) the extent to which subjects would want to take the drug received again on another session (if given the opportunity) (0 = *definitely would not*; 50 = *do not care*; 100 = *definitely would*) on a 100-mm line. The extent to which subjects liked the drug effect overall and would want to take the drug received again on another session (if given the opportunity) was also assessed at the end of the session and 24 h later at home. Fourth, a locally developed adjective rating scale, derived in part from the Single Dose Questionnaire (Fraser et al., 1961), assessed somatic and side effects of psychotropic drugs. The scale consisted of 14 items (e.g., "drive [motivated]," "headache," "nodding") that the subject rated on a five-point scale from 0 (*not at all*) to 4 (*extremely*). The scale was used to measure possible side effects of the valerian root extract. The fifth subjective effects measure was a locally developed Post-Session questionnaire, which subjects were asked to fill out at home 24 h after the session. Subjects rated the extent to which they felt 20 symptoms (e.g., "anxious," "difficulty concentrating," "unusual

drowsiness'') since they left the laboratory, on a scale from 0 (*not at all*) to 4 (*extremely*). The ARCI and the adjective rating scale were administered at baseline and 60, 120, 180, 240, and 300 min post-capsule ingestion. The other subjective effects tests were administered at baseline and 15, 30, 60, 90, 120, 150, 180, 210, 240, 270, and 300 min post-capsule ingestion.

2.4.2. Psychomotor/cognitive performance

Five psychomotor tests were used. First, the Digit Symbol Substitution Test (DSST), a 1-min paper-and-pencil test, required the subject to replace digits with corresponding symbols according to a digit–symbol code listed on the top of the paper (Wechsler, 1958). The dependent measures were total number of symbols drawn and number of symbols drawn correctly. The test assessed functions including perception, decision-making, and motor abilities (Wetherell, 1996). It was administered at the same time points as the VAS and drug effect/drug liking/take again questionnaire. Second, a 1-min computerized logical reasoning test, similar to the Logical Reasoning Test (LRT) developed by Baddeley (1968), consisted of true/false statements about the juxtaposition of the two letters A and B (e.g., A is preceded by B—true or false). The dependent measures were the total number of statements answered and the number of statements answered correctly. The test assessed higher mental processes such as reasoning, logic, and verbal ability. Third, a 1-min eye–hand coordination test required the subject to track a randomly moving target (a circle) on the computer screen using a computer mouse (Nuotto and Korttila, 1991). The dependent measure was the number of seconds that a small plus sign, which was controlled by the mouse, deviated by more than 1 cm from the center of the target circle. Fourth, the backward digit span test (Wechsler, 1958), a computerized memory test, presented digits on the screen to subjects, which they were to reproduce in backward order. Successful completion of the first trial (in which one digit was presented) initiated a succeeding trial in which the number of digits was incremented by one. The dependent measure was the number of trials successfully completed. The LRT, eye–hand coordination test, and backward digit span test were administered at the same time points as the ARCI and the adjective rating checklist. A locally developed memory test presented a sequential list of 15 words on the computer in approximately 30 s. Subjects were then given 120 s to write down as many words as they could remember in any order. The list was presented 120 min after capsule ingestion, and subjects were asked to recall the list immediately after its presentation, as well as 180 min later. Different word lists were used for all sessions. The test measured immediate and delayed free recall.

2.5. Data analysis

Two sets of repeated measures analysis of variance (ANOVA) were used for statistical treatment of the data. For the sake of brevity, we will refer to both herb and drug conditions as drug conditions in this article. The first analysis compared peak and/or trough effects of the five drug conditions. Only postingestion values were included in this analysis, and values were determined for each subject independent of time point. The second analysis included the factors drug condition (5 levels) and time (2–12 levels). F values were considered significant for $P < .05$ with adjustments of within-factors degrees of freedom (Huynh–Feldt) to protect against violations of symmetry. Tukey post hoc testing was done on the first set of ANOVAs, comparing each of the four active drug conditions to placebo, and on the second set of ANOVAs, comparing drug responses to placebo at each time point.

3. Results

3.1. Subjective effects measures

The valerian extract, relative to the placebo capsules, had no significant effect on any of the subjective effects measures. Table 1 presents the mean peak and/or trough values (S.E.M.) of subjective effects measures that were sensitive to one or more of the active drug conditions. In addition, statistically significant effects of the drug or Drug × Time analysis are noted in the table. On the ARCI, 10 mg diazepam significantly increased peak PCAG scores and significantly decreased trough BG scores relative to placebo. Peak LSD scores showed statistical significance (P=.04); however, post hoc testing revealed no significant difference between placebo and the drug conditions. Peak AMP and MBG scores did not show significant drug effects in this study. Ten milligrams diazepam significantly increased peak VAS ratings of ''coasting,'' ''dizzy,'' ''dreamy,'' ''floating,'' ''heavy or sluggish fee ling,'' ''lightheaded,'' ''sedated,'' and ''sleepy'' and signifi cantly decreased trough ratings of ''in control of body'' and ''in control of thoughts'' relative to placebo. Peak ratings of ''difficulty concentrating'' showed statistical significance (P=.007), but post hoc testing revealed no significant difference between placebo and the drug conditions. Peak/trough ratings of ''hungry'' and peak ratings of ''confused,'' ''difficulty concentrating,'' ''down [depressed],'' ''drunk,'' ''elated [very happy],'' ''feeling bad,'' ''feeling good,'' ''having plea sant bodily sensations,'' ''having pleasant thoughts,'' ''having unpleasant bodily sensations,'' ''having unpleasant thoughts,'' ''high,'' ''nauseous,'' ''stimulated,'' and ''tingling'' did not show significant drug effects in this study. Peak ratings of ''feel drug effect'' were significantly increased by 10 mg diazepam relative to placebo. Peak ratings of ''drug liking'' and ''take drug again'' showed statistical significance (P=.02 and P=.01, respectively), but post hoc testing revealed no significant difference between placebo and the drug conditions. Ratings of ''drug liking'' and ''take drug again'' were not significant either at the end of the session or 24 h following the session. On the adjective rating

Table 1
Subjective effects measures that showed statistical significance ($P \leq .05$)

	PLC	600 VAL	1200 VAL	1800 VAL	10 DZP
ARCI					
PCAG[a]	5.8	5.9	7.1	6.5	10.2
	(0.9)	(1.0)	(1.0)	(0.9)	(0.9) *
BG[b]	4.9	4.7	4.6	4.7	2.2
	(0.5)	(0.5)	(0.5)	(0.6)	(0.6) * *
LSD[c]	3.9	3.8	4.5	4.5	4.9
	(0.7)	(0.5)	(0.7)	(0.7)	(0.7)
VAS					
Coasting	5.1	6.6	9.5	9.1	24.0
(“spaced out”)	(2.5)	(5.4)	(4.6)	(4.8)	(7.2) *
Difficulty	16.2	7.7	8.7	12.4	29.9
concentrating[a,c]	(6.2)	(5.3)	(5.5)	(4.8)	(8.9)
Dizzy	0.3	0.6	2.7	2.4	12.6
	(0.2)	(0.4)	(1.6)	(1.9)	(4.1) *
Dreamy[a]	3.1	6.7	9.4	4.7	33.5
	(1.2)	(5.3)	(4.5)	(2.2)	(8.7) *
Floating[b]	1.5	2.4	2.1	0.5	21.7
	(1.0)	(2.2)	(1.6)	(0.2)	(9.2) *
Heavy or sluggish	13.2	11.8	17.8	10.0	44.2
feeling[a]	(6.8)	(6.0)	(8.4)	(5.5)	(11.0) *
In control	88.9	92.2	88.3	85.0	69.1
of body[a]	(6.2)	(4.8)	(6.5)	(9.8)	(7.1) * *
In control	89.4	90.8	89.1	85.8	75.3
of thoughts	(6.1)	(5.2)	(6.5)	(9.8)	(7.1) * *
Lightheaded[a]	2.7	5.3	3.8	6.2	25.2
	(1.9)	(2.3)	(1.5)	(2.9)	(7.5) *
Sedated[a]	16.4	10.8	15.7	15.1	34.3
	(9.1)	(6.2)	(7.8)	(7.1)	(9.4) *
Sleepy[a]	34.3	30.2	29.9	25.8	62.3
	(7.9)	(7.2)	(7.0)	(6.2)	(9.9) *
Drug effect/drug liking/take again					
Feel drug[a]	1.7	1.7	2.0	2.1	3.4
	(0.3)	(0.2)	(0.3)	(0.3)	(0.3) *
Like drug[c]	53.6	51.6	55.6	60.4	60.4
	(1.9)	(0.8)	(2.4)	(3.7)	(3.9)
Take again[c]	56.1	55.5	58.3	63.0	63.7
	(1.9)	(1.2)	(2.2)	(3.6)	(4.0)
Adjective rating scale					
Nodding[a]	0.1	0.1	0.1	0.1	1.3
	(0.1)	(0.1)	(0.1)	(0.1)	(0.4) *

Shown are mean peak or trough scores or ratings (S.E.M.) of subjective effects measures for each of the five drug/herb conditions (PLC = placebo; VAL = valerian; DZP = diazepam). Results from time course analyses in which significant drug or Drug × Time effects were obtained are also included.

[a] Time course analysis: significant drug or Drug × Time effect; post hoc testing determined 10 DZP significantly different from placebo.

[b] Time course analysis: significant drug or Drug × Time effect; but post hoc testing determined no significant difference between placebo and drug conditions.

[c] Peak analysis: $P \leq .05$; but post hoc testing determined no significant difference between placebo and drug conditions.

* Peak analysis: $P \leq .05$; post hoc testing determined 10 DZP significantly different from placebo.

** Trough analysis: $P \leq .05$; post hoc testing determined 10 DZP significantly different from placebo.

scale, peak ratings of “nodding” were significantly increased by 10 mg diazepam. Peak ratings of “carefree,” “drive [motivated],” “dry mouth,” “flushing,” “good mood,” “headache,” “nodding,” “numb,” “skin itchy,” “sweating,” “turning of stomach,” “vomiting” did not show significant drug effects in this study. Post-Session questionnaire ratings of “anxious,” “clumsy,” “coasting [spaced out],” “confused,” “difficulty concentrating,” “down [depressed],” “dreaminess,” “dry mouth,” “excessive hunger,” “excessive thirst,” “feel good,” “feel bad,” “headache,” “heavy or sluggish feeling,” “lightheaded,” “nausea,” “skin itchy,” “unusual drowsiness,” “unusual stimulation,” and “vomiting” showed no significant drug effects in this study.

When time course data were analyzed, significant drug and/or Drug × Time effects were obtained with 10 mg diazepam on a number of subjective effects measures. In the ARCI, time course analyses revealed a statistically significant increase in PCAG scores relative to placebo following diazepam administration. BG scores showed statistical significance (P=.01), but post hoc testing revealed no significant difference between placebo and the drug conditions. Eight of the 26 VAS adjectives showed significant drug and/or Drug × Time effects. Diazepam significantly increased ratings of “difficulty concentrating,” “dreamy,” “heavy or sluggish feeling,” “lightheaded,” and “sedated” and significantly decreased ratings of “in control of body” relative to placebo. Duration of effects was generally 90 or 120 min, and onset of effects tended to occur at 30–60 min after capsule administration. Ratings of “floating” and “sleepy” showed statistical significance (P=.002 and P=.002, respectively), but post hoc testing revealed no significant difference between placebo and the active drug conditions. The mean rating of “feel drug effect” was significantly increased up to 210 min after diazepam administration. Diazepam significantly increased ratings of “nodding” at the 60- and 120-min time points on the adjective rating scale.

Four subjects detected an odor with one or more of the valerian conditions (two with all of them, one with 600 mg valerian, and one with 1200 mg valerian). However, the difference between placebo and the drug conditions on odor detection and liking ratings was not statistically significant.

3.2. Psychomotor/cognitive performance

The valerian extract relative to placebo had no statistically significant effect on psychomotor performance. Table 2 illustrates the trough (DSST/LRT) effects on the psychomotor tests that were sensitive to one or more of the drug conditions. Because short- and long-term memory were assessed only once each in a session, trough effects could not be assessed, and the effects shown are main effects of Drug. In addition, statistically significant effects of the drug or Drug × Time analysis are noted in the table. Trough

Table 2
Psychomotor/cognitive performance measures that showed statistical significance ($P \leq .05$)

	PLC	600 VAL	1200 VAL	1800 VAL	10 DZP
DSST					
DSST (number of symbols drawn)[a]	49.4 (2.4)	50.7 (2.4)	49.9 (2.4)	49.7 (2.2)	37.1 (2.7) *
DSST (number drawn correctly)[a]	48.8 (2.3)	50.3 (2.6)	49.5 (2.3)	49.3 (2.2)	35.5 (3.1) *
Logical reasoning test					
LRT (number of statements answered)[a,b]	17.1 (1.0)	16.2 (0.8)	17.2 (1.0)	15.7 (0.8)	14.3 (1.1)
LRT (number answered correctly)[a]	15.2 (1.5)	14.9 (1.1)	15.4 (1.4)	14.7 (0.7)	12.3 (1.4)
Memory test					
Short-term memory	9.8 (0.9)	8.3 (0.9)	9.1 (0.6)	8.6 (0.8)	7.7 (0.7) **
Long-term memory	6.9 (0.8)	6.0 (0.9)	5.9 (0.7)	5.6 (0.7)	3.6 (0.7) **

Shown are mean trough scores (DSST, LRT) and mean number of words recalled (memory) (S.E.M.) for each of the five drug/herb conditions (PLC = placebo; VAL = valerian; DZP = diazepam). Results from time course analyses in which significant drug or Drug × Time effects were obtained are also included.

[a] Time course analysis: significant drug effect or Drug × Time effect; post hoc testing determined 10 DZP significantly different from placebo.

[b] Trough analysis: $P \leq .05$; but post hoc testing determined no significant difference between placebo and drug conditions.

* Trough analysis: $P \leq .05$; post hoc testing determined 10 DZP significantly different from placebo.

** Average analysis: $P \leq .05$; post hoc testing determined 10 DZP significantly different from placebo.

measures of total number of symbols drawn and number drawn correctly in the DSST were significantly lower in the 10-mg diazepam condition than in the placebo condition. The trough measure of total number of statements answered in the logical reasoning test showed statistical significance (P=.04), but post hoc testing revealed no significant difference between placebo and the drug conditions. The trough measure of number of statements answered correctly in the logical reasoning test did not show significant drug effects in this study. Diazepam significantly impaired both immediate (7.7 words versus 9.8 words recalled in the placebo condition) and delayed (3.6 words versus 6.9 words recalled in the placebo condition) free recall. Peak scores on the eye–hand coordination test (i.e., seconds outside circle) and trough scores on the backward digit span test did not show significant drug effects in this study.

Time course analyses revealed statistically significant Drug × Time effects on the DSST and LRT. Significant impairment was obtained on the DSST, both on total number of symbols drawn and number drawn correctly, following diazepam administration. Tukey post hoc testing revealed that these effects occurred at 30–120 min post-ingestion. Significant impairment was also obtained on the logical reasoning test, both on total number of statements answered and number answered correctly, at 60 min following diazepam administration.

4. Discussion

The purpose of our study was to (1) determine if valerian had psychomotor- or cognitive-impairing effects and (2) determine if it had any subjective effects, including those that might be considered abuse liability-related in nature. Such effects might include increased VAS ratings of "sedated (calm, tranquil)," "having pleasant bodily sensations," "elated (very happy)," and drug liking. The sensitivity of the test battery was confirmed by the detection of sedation caused by a moderate dose of diazepam (both via subjective effects and psychomotor/cognitive tests). Diazepam significantly increased subjective effects measures on four different rating scales and impaired several indices of psychomotor/cognitive performance. Valerian had no significant effect on either subjective or psychomotor/cognitive effects, going up to a dose that was higher than doses tested in other studies that assessed the subjective and psychomotor/cognitive effects of this herb.

The present study, using young healthy volunteers, replicated the results of Glass et al. (2003), which used older healthy volunteers and also failed to detect sedative or impairing effects of valerian. The results of both studies suggest that acute doses of valerian do not produce subjective effects indicative of sedation or psychomotor impairment. In addition, we did not observe any subjective effects of valerian indicative of abuse liability-related effects (e.g., drug liking). Glass et al. (2003) also failed to detect any abuse liability-related subjective effects from valerian (e.g., elated). The results of both studies suggest that valerian, using an acute-dosing regimen, does not have abuse liability in a non-drug-abusing adult population.

Acute doses of valerian, up to 1800 mg, administered in the morning, did not produce subjective effects or psychomotor/cognitive impairment. We would not want to conclude from this study, however, that valerian has no subjective or impairing effects. It is possible that acute valerian has subtle sedative and impairing effects and that our sample size lacked adequate statistical power to detect differences between the valerian conditions and placebo. However, given that our battery did detect impairment from a moderate dose of diazepam, the effects of acute valerian are almost certainly insignificant. It may also be the case that chronic dosing is needed to detect effects of valerian. Schulz et al. (1997) suggested that valerian's effects on sleep topography might take 2–4 weeks to develop. In a study by Donath et al. (2000), effects on sleep structure and quality were obtained after 2 weeks of valerian treatment, but not after single-dose administration. In another study by Andreatini et al. (2002), a significant reduction in the HAM-A psychic anxiety subscale was detected when valerian

(mean daily dose: 81.3 mg) was administered chronically for 4 weeks. If chronic dosing is needed to begin to see effects, then it is also possible that subjective effects may emerge, including those that could be considered abuse liability related. It is also conceivable that the effects of valerian may be more apparent in people who have sleeping difficulties (e.g., insomnia). Support for this notion comes from a clinical study in which valerian produced greater improvements in self-reported poor sleepers than in individuals reporting no sleep difficulties. The time of day may have also influenced our results. In most of the studies assessing the hypnotic effects of valerian, the herb was administered at night, usually 1 h before bedtime. It may be the case that, had our study been conducted in the evening hours (after subjects had not slept for a number of hours), sedative effects of valerian would have emerged.

In conclusion, acute doses of valerian do not appear to produce subjective effects or impairment in healthy volunteers who consume up to 1800 mg in the morning. Further research is needed to examine such factors as subject population (e.g., people with insomnia), time of day, and chronic dosing to determine whether there are indeed conditions in which valerian is capable of producing subjective or impairing effects.

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