High-Dose Benzodiazepine Users' Perceptions and Experiences of Anterograde Amnesia

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Associations between criminal activity and the use of psychotropic substances are well established. Flunitrazepam, specifically, has been suspected of triggering, *per se*, violent criminal behavior and severe memory disturbances in the form of anterograde amnesia. However, data from investigations of this relationship are scarce and have been primarily derived from forensic institutions, where there may be a reporting bias. This study was a qualitative exploration of high-dose benzodiazepine users' experiences of anterograde amnesia symptoms and their beliefs about their behavior during the phases of memory impairment in a nonforensic setting. Users subjectively reported experiencing symptoms of anterograde amnesia, especially after combining short-acting benzodiazepines with alcohol, but only rarely when using slow-onset, long-acting compounds. They perceived their experiences as unpleasurable, unpredictable, and embarrassing. Their awareness developed with time, triggered by descriptions of disinhibited and erratic behavior by others. Users described being victimized during phases of anterograde amnesia in addition to engaging in violent and criminal activities themselves. Although unable to recall, many participants believed that they had been able to make rational decisions while intoxicated with flunitrazepam, disregarding notions of diminished insight. In light of the varying terminology used for the phases of memory disturbance and these findings, we suggest that forensic experts additionally explore evaluees' beliefs about amnestic periods and their self-perceptions about their behaviors during these episodes, when evaluating high-dose benzodiazepine-dependent patients.

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Since their introduction to pharmaceutical markets in 1960,[1,2] benzodiazepines have developed into one of the most commonly prescribed classes of psychotropic agents internationally, a trend that only recently is reported to have stabilized.[3–5] In light of their sedative, anxiolytic, anticonvulsant, and muscle relaxant properties and their resulting usefulness across various medical specialties and for multiple indications, either as monotherapy or as an adjunctive medication, this finding is unsurprising.[6–8] The beneficial effects of this medication class, reported to consist of more than 50 different compounds exhibiting similar pharmacologic but different pharmacodynamic and pharmacokinetic properties, remain undisputed.[9–11] These substances bear the potential for serious adverse effects, such as the risk of dependence with long-term use, and is a source of great concern.[12–14] Analyzing pharmacy records in Switzerland and Germany, it is estimated that 16 to 20 percent of the general population in these countries have benzodiazepine dependence.[15,16] Furthermore, although most patients (49.3%) in Switzerland receive long-term regimens of benzodiazepines (≥90 days) in low or normal doses, there is a significant number of patients (8.2%)

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that use them in very high doses, exceeding at least twice the maximum recommended dose.[15]

The harmful consequences of benzodiazepine abuse are not entirely dose related. The group of patients with high-dose, long term, and otherwise problematic use of benzodiazepines, such as mixing them, escalating their dosage repeatedly to relieve symptoms associated with physical or mental disorder, using them for recreational purposes, and obtaining them by illegal means, seems to have difficulty benefiting from recommended therapeutic approaches focused on long-term abstinence through discontinuation.[17–21] Frequent relapse exposes this subgroup to the harms associated with benzodiazepine misuse, including injuries from falls, traffic accidents, and other accidents, as well as acute and chronic cognitive impairments, such as sedation, drowsiness, deficits in learning, psychomotor slowing, and anterograde amnesia.[22–24] Especially worrisome are the consequences of disinhibition, memory disturbances and anterograde amnesia (loss of memory for events occurring forward in time) that are known to correlate with benzodiazepine dose[25,26] and may contribute to endangerment of self or others.[27]

Few studies have specifically investigated high-dose benzodiazepine users, but it has been suggested that unlike methadone maintenance treatment (MMT), which may militate against the commission of crime, there may actually be an association between the use of benzodiazepines and disinhibited, aggressive behavior, as well as feelings of invincibility and criminal activity (in the form of shoplifting, property crime, drug dealing, violence, and intoxicated driving).[28] The relationship between the use of disinhibiting psychotropic substances and illegal activity is well established.[29–31] The short-acting fast-onset benzodiazepine flunitrazepam (Rohypnol; not available in the United States) has been particularly implicated in triggering violent criminal and sexual behavior, impulsive decision-making, and anterograde amnesia.[32] However, there are only limited data available, primarily coming from forensic institutions where there may be a reporting bias, especially with regard to symptoms of amnesia. This present qualitative interview-based study sought to explore high-dose benzodiazepine-dependent patients' experiences of anterograde amnesia in a nonforensic setting. We focused on this group's perceptions and beliefs surrounding their behavior and insight, both before and after episodes of memory disturbance. We believe that these considerations would be important when assessing individuals in a forensic capacity and attempting to ascertain their level of insight into their own behavior during intoxicated and associated amnestic periods.

Ethics Statement

Ethics approval for the study (E-23_2009) was received from Zurich's Cantonal Ethics Committee Kantonale Ethikkommission Zürich (www.kek.zh.ch). In line with the approved protocol, written consent was obtained from all participants and identifying information was removed from the transcripts. Transcripts were further assigned a code number. An Excel file (Microsoft) containing the demographic information without names was maintained separately.

Methods

Participants

Participants were identified and recruited from the in- and outpatient units of the Psychiatric University Hospital Zurich between 2011 and 2012, using a mixed method of purposeful and saturation sampling principles. Patients with a diagnosis of (high-dose) benzodiazepine dependence according to International Classification of Diseases (ICD)-10 and with use of benzodiazepines over an extended period of more than a 40 mg diazepam dose equivalent per day and otherwise problematic use, such as mixing benzodiazepines, dosage escalation, use for recreational purposes, or illegal obtainment strategies, were eligible for inclusion. Exclusion criteria were vastly insufficient language skills and acute intoxication. The members of our research group approached potential participants, who were identified by treating physicians. Initially, every eligible patient from the dual diagnosis ward and the outpatient center for the treatment of substance use disorders was asked to participate in the study. After the first 10 interviews, we sought subjects from general treatment settings to ensure that a wide range of views were represented and to achieve greater variation of themes and motives. For each patient, the full chart with a complete biographical and psychiatric history was available to extract demographic data.

Interviews

Forty-one patients agreed to participate in single, face-to-face, unstructured, in-depth interviews that lasted approximately 60 to 90 minutes. Interviews were conducted outside the regular treatment setting by members of our research group (M.-T.G. and M.S.) who had gathered experience in one-to-one qualitative procedures (M.-T.G. and M.S.) as well as in treatment of substance abusing individuals (M.G.). Participation was voluntary with a compensation of 5 Swiss francs offered in the form of a cash payment in the outpatient setting or as a gift card for the same amount in the inpatient setting. All participants were informed of their right to end the interview at any time if they wished to do so and were assured that information from the interview would not be shared with their treatment providers or with anyone else, such as legal authorities. Following recommended guidelines for conducting qualitative research, the interviewers began with narrative opening questions, and the various topics were further pursued as they occurred naturally in the participant's narrative. However, a self-developed topic guide provided a flexible interview framework to explore beliefs that were not spontaneously covered. Specific topics covered in the interviews were, for example: what are the views of participants on benzodiazepines (initiation, reasons for use, obtainment strategies, and perceptions of cessation and withdrawal)? What are perceived effects of these substances (side effects if any and experiences of anterograde amnesia ("blackouts"), disinhibition, and criminality)? Great care was taken to ask open-ended and neutrally worded questions to avoid eliciting socially desirable responses, especially with regard to violent and criminal behavior. Furthermore, appropriate nonjudgmental and nonleading probes (e.g., the echo probe, the "uh-huh" probe, and the tell-me-more probe) were used during the interviews to explore perceptions that were not covered spontaneously in patients' initial narratives. We allowed themes and motives identified in earlier interviews to be explored in subsequent interviews, combining the principles of maximum variation and complexity reduction to widen the scope of results and examine previous assumptions.

Analysis

All interviews were digitally recorded with Dictamus for iOS (Apple Computer) and then transcribed verbatim and assigned a code number. Data collection and analyses were conducted simultaneously until saturation had been reached. Mayring's qualitative content-analysis approach[33,34] was taken to evaluate findings, allowing the data to "speak for themselves" rather than approaching them within existing hypotheses. Interviews were coded using an inductive qualitative procedure. Categories obtained were discussed in the research team (M.L., A.B., M.G., and C.C.) to validate ratings and achieve consensus on a biweekly basis. M.L. applied the final code, with confirmation of consistency through blind dual coding of transcripts with M.G. and C.C.

Prior to submission of this manuscript to the Journal of the American Academy of Psychiatry and the Law, representative quotations were translated from German into English by ML and proofread by native English speakers (Corinna Fales of New York and Anish Dube of Los Angeles).

Results

Participants' characteristics, diagnosis, and consumption patterns are described in Table 1. All participants were adults. The mean ± SD age of the participants was 39.5 ± 9.2 years (median, 39.0; range, 21–65 years).

Twenty-five of the 41 high-dose benzodiazepine-dependent participants had experienced symptoms of anterograde amnesia. Most commonly, participants had developed individual terminology to describe these phenomena, referring to their memory disturbances as blackouts, film-tears, absences, or simply holes. Subjects were more eager than expected to share their perceptions and beliefs surrounding this topic, often describing not just their own experiences but pointing out disturbances they had witnessed in others or recounting stories other users had told them. Content analysis of the interviews yielded several major themes, which are noted below with verbatim quotations from the participants.

Interview Responses

Anterograde amnesia is most often experienced after use of a fast-onset, short-acting benzodiazepine in combination with alcohol. With the exception of one narrative, participants associated anterograde amnesia with the use of the fast-onset, short-acting benzodiazepines midazolam (Dormicum) and flunitrazepam (Rohypnol) or a combination of these substances and alcohol.

Table 1 Characteristics of Study Participants

Characteristic	*n* (%)
Demographic	
Gender	
Male	31 (75.6)
Female	10 (24.4)
Employment status at the time of interview	
Employed	12 (29.3)
Unemployed	11 (26.8)
Retired	1 (2.4)
On disability pension	16 (39.0)
No data	1 (2.4)
Substance use	
Years of benzodiazepine use	
<5	14 (34.1)
5–9	12 (29.3)
>10	14 (34.1)
Not available	1 (2.4)
Age at first benzodiazepine use, years	
<25	15 (36.6)
25–39	18 (43.9)
>40	7 (17.1)
Could not recall	1 (2.4)
Maximum dosage of benzodiazepines as diazepam equivalents, mg	
<50	14 (34.1)
50–99	14 (34.1)
>100	13 (31.7)
Number of additional substances used	
0	4 (9.8)
1	8 (19.5)
>1	29 (70.7)
Comorbid psychiatric disorders	
Number of comorbid psychiatric diagnosis groups except SUD (F2, F3, F4, F6, F9)	
0	10 (24.4)
1	15 (36.6)
>1	16 (39.0)
Comorbid psychiatric diagnosis groups except SUD	
F2: Schizophrenia, schizotypal, delusional, and other non-mood psychotic disorders	1 (2.4)
F3: Mood [affective] disorders	21 (51.2)
F4: Anxiety, dissociative, stress-related, somatoform and other nonpsychotic mental disorders	12 (29.3)
F6: Disorders of adult personality and behavior	14 (34.1)
F9: Behavioral and emotional disorders with onset usually occurring in childhood and adolescence (e.g. ADHD)	1 (2.4)
Anterograde amnesia	
Present	25 (61.0)
Absent	14 (34.1)
No data	2 (4.9)
Most commonly associated benzodiazepine (n = 25)	
Flunitrazepam	2 (8)
(With alcohol)	1 (4)
Midazolam	7 (28)
(With alcohol)	3 (12)
Oxazepam	1 (4)
Unavailable/other combination	11 (44)
Delinquency associated with anterograde amnesia (n = 25)	
Yes	15 (60)
No	5 (20)
Unknown	5 (20)

N = 41. SUD, substance use disorder.

> Ms. 37: When I took a lot of it [midazolam], I could not remember the next day what I had done. I just had holes.
>
> Mr. 17: You have to understand, alcohol enhances the effects of benzos. If I take alcohol additionally, then it gets more [the blackouts]. Formerly, when I just had alcohol, it never happened.

In this context, slow-onset, long(er) acting benzodiazepines, for example, diazepam or clonazepam, as well as other substances (e.g., cannabis), were not mentioned.

> Mr. 36: Blackouts I only had from alcohol. . . . Now I don't drink alcohol anymore and don't have blackouts. . . . About blackouts, I only heard from people who take or inject Dormicum. I have heard that they are lashing out and don't know what they are doing. But with Xanax [alprazolam], that does not happen.
>
> Ms. 38: But I noticed fast that, with the combination of Temesta [lorazepam] and alcohol, I would do things I would not normally do, like going to my former boyfriend and ringing the doorbell like crazy. On the next day I still knew this, felt ashamed, and was really embarrassed. . . . Another time, I went and waited at a bank and fell asleep. I still remember this; with [Temesta] I don't have such blackouts, but it is just embarrassing. You do things you would otherwise not do.

Anterograde amnesia occurs more frequently after initiating use of fast-onset, short acting benzodiazepine. Furthermore, some participants believed that they had experienced symptoms of anterograde amnesia more frequently immediately after they had begun using midazolam and flunitrazepam, describing an increasing tolerance effect.

> Ms. 30: It was at the very beginning, the first two or maybe three times that I experienced that. I still remember how it happened. I was sitting at the bus terminal and later I was at home, and I have no recollection at all of how I got home. . . . Later, there was something very similar: I was in Affoltern, and then later I was at the outskirts of a forest, and later at home. And at this stage how I got there, I cannot remember. It was only these two times, and then once a third, but I have no recollection of that at all. But otherwise I have never experienced blackouts.
>
> Mr. 23: In the beginning I could only bear little amounts of Dormicum. For example, I fell asleep in the middle of the street. I got robbed and lost my IDs, things like that. You automatically fall into a hole the next morning, because you don't know what you have done and where you have been. . . . At least in the beginning. Over time, the body starts to adapt.

The duration of memory disturbance caused by the use of fast-onset, short-acting benzodiazepines is highly subjective and unpredictable for users. Participants described experiencing episodes of anterograde amnesia that ranged from seconds, minutes, and hours to days. Most commonly, subjects reported that they had no recollection of the day after

the intake of fast-onset, short-acting benzodiazepines. For many participants, there was neither a clear dose effect nor consistent results linked to the route of administration, thus making it difficult to predict the time of the memory disturbance. In some cases, island memories remained.

> Ms. 24: When you inject it [midazolam], then you either have a three-second blackout, or sometimes it is very different. It is rather strange; sometime I inject four benzos and have a three-second blackout, and I am fit afterward, and sometimes I inject just one and have a blackout for half a day.
>
> Mr. 35: You will be completely surprised to hear this! I had downright half hour mental blackouts and did not get what was going on for half an hour. Checked out, gone.
>
> Mr. 9: It was during the time when you wanted to get really wasted. . . . And there were memory gaps, very unpleasant. Sometimes you are missing just a few hours, but sometimes it is days. . . .

Anterograde amnesia is an actively discussed topic among users, preventing some from initiating use. It became apparent that the particular adverse effects of midazolam and flunitrazepam use were hotly discussed topics among participants, encouraging some from abstaining from using these types of benzodiazepines altogether. Very few subjects reported perceiving memory disturbances as pleasurable.

> Ms. 37: I also had a friend who was using Dormicum. He walked on the highway at night. Then they picked him up and brought him back. But later they found him again on the highway. Shit like that. That can be really dangerous. Another friend of mine got run over by a bus while he was intoxicated with Dormicum.
>
> Mr. 2: I know people who, when they combine benzodiazepines with alcohol get active, starting to shoplift and then later do not know about it. I had that less. I always knew what I was doing, although I was taking so much I never experienced such brain failures. . . . But I have heard from friends who went on real raids. They shoplifted and did this and that . . . and on the next morning they woke up and did not know how they got this stuff. . . .
>
> Ms. 24: A friend of mine killed his best friend on "Dormies" [midazolam] and he could not remember it. He was considered to have diminished capacity and got off without a huge punishment, but I don't want something like that happening to me. . .. But of course the desire is there, in the end it is Dormi and it smashes phat.

Awareness of episodes of anterograde amnesia develops only after time and is pointed out by other parties. Most of the participants were at first unaware of episodes of anterograde amnesia, even when they were told so by close friends or relatives, and often questioned these parties' stories or tried to verify the facts themselves. However, over the course of time, subjects increasingly sought these parties' aid in filling memory gaps.

> Ms. 37: For example I took two Dormicum and I was sure that I went to sleep right after it. On the next day, a friend told me, that we had a great time the evening before, that I had been in his room and was jumping all over. . . . I thought he was kidding me; I did not believe him at all. But apparently there had been other people around and they confirmed this. . . .
>
> Mr. 16: On one evening I got home to my mom at 3 o'clock and I asked her when are we going to have lunch and she told me: it is 3 o'clock; lunch is long over. And I had to assure myself by checking on the Teletext that it really was 3 o'clock which baffled me quite a bit. . . . A filmtear is like a dream you wake up from, but you cannot remember it at all.

In this sample, some subjects became aware of anterograde amnesia only because they got detained for their behavior by either the health or legal authorities.

> Mr. 20: I did not realize a lot when I had my accident. I only remember that it banged a few times. When police interviewed me, they asked me how many collisions I had caused, but I did not know. The cop then wrote on his protocol "refuses to make a statement." I then told him, that I really did not know it. I only knew that I had hit something, that something went wrong. I have no idea what had happened to the other car, I still don't have it, I still have a blackout.

Behavior during episodes of anterograde amnesia is perceived to be mostly, but not always, unexplainable. Despite some island memories, most subjects reported that they had learned of their behavior through third parties. In most cases, the reported behavior came as a complete surprise to the subjects and was viewed as not in line with their self-conception or normal behavior. Nearly all had developed an explanatory model and viewed this alteration of their behavior as a result of strong disinhibition and memory impairment by flunitrazepam or midazolam. Disinhibited, impulsive behavior was thereby viewed foremost to have negative consequences on interpersonal relationships and social interactions, whereas forgetfulness was regarded to impair overall daily functioning, with some overlap between the two. Some participants regarded these behaviors as so distressing that they gave them as a reason to discontinue fast-onset, short acting benzodiazepines.

> Mr. 23: You are just starting to do completely absurd things. For example, you are getting undressed somewhere, because you have the feeling, that you are somewhere in a dream, you act as a clown, you make obscene comments. You are provoking other people, you have sex with people you do not know. . . . This is at least what other people were

describing to me. . . . I think that suddenly things get to the surface that are bothering you deep inside yourself. The brutal thing is just, that you do not know what you are doing.

Ms. 37: For example, I cheated on my boyfriend while I was using Dormicum. I got pregnant and had to have an abortion. Just because I was so drugged.

Increased involvement in violent and criminal activities as well as becoming a victim are reported by some during periods of anterograde amnesia. Almost two-thirds of subjects (16 of 25) who had experienced symptoms of anterograde amnesia following the use of flunitrazepam or midazolam reported either aggressive or violent behavior leading to personal injury.

Mr. 23: With respect to aggression, there is less of a threshold . . . I got banned from the premises of Pfarrer Sieber [a charitable organization]. Someone turned me in, and I took a chair and threw it at him. Nothing major. I am just scared, that I could knock someone down or stab someone without remembering anything the next morning.

Ms. 24: . . . and then you get a blackout, and that is the real problem; however, until this event I did not care: The protocol of the police says, and I don't remember this, that I broke into the police station at Urania and that I physically beat up a female officer. Apparently, I went into the police station, went straight toward that officer and apparently really beat her up, just beat her. I have no clue how that happened . . . All I remember is that I injected Dormicum and shut my eyes, next time I opened them I was in the psychiatric hospital.

They also reported increased criminal activity, most commonly in the form of property offenses. Again, these behaviors were associated with a perceived decrease in inhibition threshold.

Mr. 30: . . . I cannot really recall what I did. Maybe on the street or in other places. You are going into a store, stealing things you do not really want. You are doing things, you don't really want to do. Especially when you mix it with alcohol. Then you are doing bad things, really bad things. And on the next day, you have a blackout and no clue what you have done. Once I woke up with 600 CHF [Swiss francs] in my wallet. And then I got really scared. What I had done, I don't know. Did I rob someone? Did I hurt someone? What did I do? And then there were the opposite situations, where I had been picked to pieces, because I had been smashed. No wallet and no shoes. Watch gone, glasses gone. Everything gone.

Unsurprisingly, nearly the same number of participants described that they themselves had become victims during times of amnesia.

Mr. 22: People noticed soon that when I had taken 2 or 3 Dormicum, that after an hour or so I would not realize anything anymore and then some of them started to steal my stuff out of my apartment and later, of course, they pretended not to remember who had wrapped up my belongings.

Participants view their insight into the consequences of their actions at times of anterograde amnesia as not necessarily diminished. Many subjects perceived themselves as capable of making reasonable decisions while intoxicated with flunitrazepam or midazolam and while experiencing symptoms of anterograde amnesia. This theme was more often reported by subjects who had engaged in criminal activity while being intoxicated than by those who had done not so.

Ms. 13: I did not do anything bad. In the moment, you know what you are doing. Nobody can tell that they did not know what they were doing. In many people it might decrease the inhibition threshold, but somewhere everybody has his limits, that you don't cross, no matter what, whether you had alcohol or other things. That is my opinion!

Ms. 27: . . .I believe, during the specific moment you always know what you are doing, what is right, and what is not. I would never shoot someone because I am on Seresta (oxazepam) or benzos. But afterward, you don't know what you have done. That is why people can tell you a lot of things afterward.

Disinhibition and memory impairment results in shame, embarrassment, and anxiety in users. Most participants felt uneasy about disinhibition and sedation on the one hand and symptoms of anterograde amnesia on the other. The latter was viewed especially as a major strain on interpersonal relationships and was seen as a source of shame and embarrassment. Although some participants viewed the disinhibiting and memory-impairing effects of fast-onset, short acting benzodiazepines as beneficial to engaging in criminal activity, the majority expressed great concern about the possibility of committing criminal acts and not remembering them.

Mr. 40: I took on the street 2 mg Rohypnol often together with alcohol. Especially when you were living on the street it enabled you to steal very well. Sometimes I got out of Coop and Migros (supermarkets) with two full bags of groceries. Sober, I could not have stolen a chocolate bar, but on Rohypnol, you just pick stuff up. And you come through with that. You just don't care. . . .

Mr. 23: For example you are going to the bank, and you are withdrawing 50 CHF. On the next day, you figure out that in fact you withdrew 150 CHF, because meanwhile you had gone to the bank again, but did not realize it. On the next day, you want to withdraw another 50 CHF, but then you are being told that you don't have enough funds left, because you had been there the day before. Such things are of course devastating and . . . embarrassing . . . .

Ms. 24: I am primarily suicidal, but when. . .I am on benzos, then the suicidal thoughts change to thoughts of mur-

der and then I focus on one person and want to kill that person. . . . And I don't want to kill someone just because I don't get a punishment, when I am on Dormicum. But the risk is there, and since I have encountered that in my environment, I have some respect for them."

Conclusions

For this article, we explored high-dose benzodiazepine-dependent patients' experiences of anterograde amnesia and specifically, their beliefs about their behaviors and their insight into their actions during and after episodes of memory disturbance. To our knowledge, few studies have examined this problem in depth, particularly in this subgroup. The present study is unique because:

It involved a qualitative approach with in-depth interviews instead of quantitative surveys.

It was conducted outside the regular treatment setting in a confidential atmosphere with limited feedback to treating therapists and none to legal authorities.

The sample was nonforensic patients with no strategic advantage in feigning amnesia except for reasons of social desirability and positive self-image.

The study revealed that most of the high-dose benzodiazepine-dependent patients believed that they had experienced symptoms of anterograde amnesia or at least memory disturbances, most often when combining the use of fast-onset, short-acting benzodiazepines like flunitrazepam and midazolam, with alcohol. These perceptions are consistent with research investigating the combined effects of benzodiazepines and alcohol on memory.[35,36] Since both substances have been reported to produce symptoms of anterograde amnesia on their own, it has been suggested that the likelihood of these impairments is increased when they are combined.[37] Furthermore, it has been noted that although anterograde amnesia is a common effect of all benzodiazepines, albeit with various times of onset and durations depending on the particular pharmacokinetics, dose, and route of administration,[26] fast-onset, short-acting benzodiazepines such as midazolam and flunitrazepam produce an exceptionally dense, though temporary, anterograde amnesia.[38] This finding may be one reason why participants in this study associated short-acting benzodiazepines with anterograde amnesia, but made no such connections with slow-onset, long-acting benzodiazepines, like clonazepam.

We also found that participants believed that they experienced symptoms of anterograde amnesia more frequently close to the initiation of short-acting benzodiazepine use, suggesting the development of tolerance with subsequent use. Indeed, research investigating the effects of flunitrazepam in healthy volunteers found that, when the drug was administered as a hypnotic over a period of three consecutive nights, anterograde amnesia for tasks performed when participants were awakened during the night was reported the morning after memory tests, but levels of forgetfulness were reduced over the course of the three nights, suggesting a tolerance effect.[26,39]

As would be expected, the duration of memory disturbance caused by the use of fast-onset, short-acting benzodiazepines was highly subjective and unpredictable, especially for users who mixed different benzodiazepines, had limited understanding of equivalent dosage calculations, and relied on illegal ways of obtaining the drugs. However, we were surprised to find that anterograde amnesia was actively discussed among high-dose benzodiazepine users, was frequently considered an adverse effect, and was not perceived as pleasurable. Some participants pointed out that they had witnessed this effect in others or had heard negative stories about it, preventing them from initiating use of benzodiazepines with these specific pharmacokinetic properties. This finding again underscores that patients rely foremost on their personal experiences and subjective beliefs when making decisions concerning substance use.[40–42]

In light of the diverse terminology used by participants for the phases of memory disturbances and the notion of some participants that they were initially completely unaware of anterograde amnesia symptoms and developed an awareness of them only after being confronted by third-party observations, careful exploration of this subject in general psychiatric and in forensic assessments seems necessary. Although in the early stages, this finding has implications for patients' ability to profit from certain (cognitive behavioral) psychotherapeutic approaches used in substance use treatment settings (e.g., the ability of patients to fill out relapse forms),[43] and indeed there is research exploring the value of adjunctive cognitive behavioral therapy during the discontinuation phase of long-term benzodiazepine users.[44] In the later

stages, it may result in under- or over-diagnosing of anterograde amnestic states and consequently may have profound effects on sentencing.[45,46] In the present study, we found that participants who had learned of their behavior from others perceived their behavior as inexplicable and inconsistent with their self-conception or normal behavior. Instead, they linked their behavior to the strong disinhibiting effects of these substances, especially compared with alcohol. These statements are consistent with reports on the pharmacokinetic properties of various benzodiazepines.[47,48]

Though disinhibited behaviors were perceived to impair social functioning and interpersonal relations, they were infrequently associated with violent or criminal behavior. Furthermore, it is noteworthy that impaired memory was perceived by participants as increasing the likelihood of personal injury or personally becoming a victim of crime. Given that only some high-dose benzodiazepine users also reported violent behavior and increased criminal activity when abusing short-acting, fast-onset benzodiazepines, our participants' perceptions contradict the notion that these substances, *per se*, result in agitated, aggressive, and criminal behavior in all subjects.[49] Our findings are consistent with previous reports that individuals with impaired impulse control and symptoms such as hostility are more likely to exhibit paradoxical aggressive reactions when using benzodiazepines with pharmacokinetics comparable to those of flunitrazepam.[32,50–52]

The participants' narratives also suggest that patients retrospectively perceived themselves as capable of making reasonable decisions, not only while under the influence of flunitrazepam or midazolam, but also when they had experienced symptoms of anterograde amnesia and had no recollection of the events in question. Although participants believed themselves to be disinhibited, at the same time, they did not feel that they lacked insight into their actions and believed they were still able to differentiate "right" from "wrong." We are unaware of any studies investigating this subject among high-dose benzodiazepine-dependent individuals, but research among nonbenzodiazepine-dependent surgical patients has repeatedly shown that when fast-onset, short-acting benzodiazepines are administered in combination with analgesics, the result is conscious sedation, a state in which relatively normal communication with patients remains possible, but one where patients later have little or no recollection of the surgical procedure itself.[53–55] Furthermore, our findings are consistent with data showing that healthy volunteers have little insight into their cognitive impairments after having received midazolam.[54] We hesitate to suggest a specific course based on our findings, but feel that forensic experts should be aware that users may not perceive themselves as having diminished insight as a result of concomitant use of fast-onset, short-acting benzodiazepine and other substances. Finally, our findings underscore substantial distress and suffering from the shame, embarrassment, and anxiety related to the continued use of fast-onset, short-acting benzodiazepines in this sample of high-dose benzodiazepine-dependent users. Because these patients are more likely to fail current discontinuation strategies, we suggest exploring treatment alternatives to minimize further harm in this heavily burdened subgroup.[18]

Limitations of This Study

Participants interviewed in this sample often had various comorbid psychiatric conditions, most frequently mood and personality disorders. Furthermore, most were also using at least one other substance of abuse, commonly alcohol. Our sample, though heterogeneous, nevertheless reflects clinical reality, especially in forensic settings where it is estimated that 70 percent of all patients receive a dual-diagnosis.[56,57] We were unable to verify objectively either the occurrence of anterograde amnesia or the combination and amount of ingested substances that might have contributed to it, limiting the generalizability of the study. However, this sample's descriptions are generally consistent with results from quantitative research on this subject,[38,58] and the aim of qualitative research is not necessarily to generalize beyond an exploration of common themes and motives. Finally, interviews were conducted solely at the Psychiatric University Hospital Zurich, representing the perceptions and beliefs about benzodiazepines of primarily a Swiss sample. Since it is known that subjective experiences are influenced by the social and cultural context in which they occur, it is conceivable that findings could differ in other countries, or even in other Swiss cities. Although the street value of different benzodiazepines, reportedly a reflection of desirability, fluctuates across communities,[59] worldwide reports on the abuse of this class of medication indicate that especially benzodiazepines such as fl-

unitrazepam with a fast onset of action tend to be associated with disinhibited and erratic behavior in vulnerable individuals. Thus, the opinions expressed do not reflect solely the subjective experiences of this nonforensic sample, but suggest the importance of pharmacokinetic properties over social and cultural factors.[32,60–62]

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