The effect of benzodiazepines on attention has been the object of few investigations. Studies using the spatial cueing paradigm (Posner’s paradigm) have reported inconsistent results, which are likely due to methodological and/or dose differences but suggest impaired disengagement of attention from the cue to the target. The authors investigated the effect of a benzodiazepine (diazepam) on attentional shifting in the temporal domain. The attentional blink effect refers to difficulties in detecting a target if it follows the identification of a previous target occurring within a temporal window of 200–400 ms. The authors assessed whether the duration of the attentional blink was affected by diazepam. Streams of 15 real-world scenes displaying a road were presented for 50 ms each. A city name (target) appeared at Serial Positions 2, 3, or 4 of each stream. A vehicle (probe) appeared at different intervals following the city name. In a dual-task condition, participants were asked to report the city name and whether a vehicle was present. In a control condition, participants had to report only the presence of a vehicle and ignore the city name. Thirty-six healthy volunteers were assigned to 3 groups (placebo, diazepam 0.1 mg/kg, or 0.3 mg/kg). Diazepam increased both the magnitude and duration of the attentional blink effect. Participants treated with a high dose of diazepam needed more than 600 ms to detect a vehicle following identification of the name. Results suggest that diazepam at a therapeutic dosage affects attentional shifting in the temporal domain and impairs dual-task performance.

Keywords: benzodiazepines, attention, attentional blink, dual-task performance

Many everyday activities entail the ability to process different information or to perform different tasks simultaneously and/or in rapid succession. Usually, situations requiring divided attention, or dual tasks, can be accomplished easily when one of the tasks can be performed automatically (e.g., listening to the radio while driving). Things become more difficult, and interference may occur, when two tasks involve controlled processes and require substantial attentional resources (e.g., speaking in a cellular phone while driving). Interference is all the more pronounced when the two tasks involve the same sensory channel (e.g., vision in both tasks). The main explanation for this is that automatic processes can be accomplished in parallel with unlimited capacity, but controlled processes are performed serially with capacity limitations (for a review, see Pashler, 1998). The ability to perform a dual task is based on several factors, such as, for instance, the degree of automaticity of one of the tasks, the speed of information processing, or the time for focal attention, having already been allocated to a primary task (or initial target), to be reallocated to a subsequent task (or second target). Though it has been speculated (Treisman & Gelade, 1980) that switching attention from one to another target is relatively fast in the spatial domain, on the order of 50 ms in visual search tasks, attentional modulation in the temporal domain operates at much slower speeds, on the order of 400 to 500 ms (Ward, Duncan, & Shapiro, 1996; Ward, Duncan, & Shapiro, 1997).

Research on the temporal dynamics of visual attention has identified a robust pattern of interference referred to as the attentional blink (Raymond, Shapiro, & Arnell, 1992). In the typical paradigm, visual events are presented at a rapid rate at the same spatial location (e.g., 10–20 items per second). Performance is compared in two conditions. In the dual-task condition, participants are required to identify a first target specified by a physical characteristic (e.g., the single white letter of the sequence) and to detect the pres-
ence of a second target (e.g., the letter X) occurring at various intervals following the first target. In the control condition, participants are asked to detect the second target and to ignore the first target. Participants are able to detect or identify a single target, but when the task involves multiple targets performance is impaired. Participants experience difficulties in reporting the second target if it occurs in a temporal window of about 400 ms following the first target. This phenomenon has been called the **attentional blink effect** (Chun & Potter, 1995; Raymond et al., 1992).

The present study was designed to investigate the effect of a benzodiazepine (diazepam) on selective attention and dual-task performance in the temporal domain. Acute benzodiazepine administration has been described as causing impairments in several cognitive domains such as memory (causing anterograde amnesia and difficulties learning new material; Boucart, Biederman, Cuervo, Danion, & Wagemans, 2002; Curran & Gorenstein, 1993; Curran, Schifano, & Lader, 1991; Danion et al., 1989; Legrand et al., 1995; Vidalilhet et al., 1994), visuospatial abilities (Beckers, Wagemans, Boucart, & Giersch, 2001; Giersch, 1999; Giersch, Boucart, Danion, Vidalilhet, & Legrand, 1995; Giersch, Boucart, Speeg-Schatz, Kauflman-Muller, & Danion, 1996; Wagemans, Notebaert, & Boucart, 1998) and oculomotricity (Masson et al., 2000; Speeg-Schatz et al., 2001). Although benzodiazepines are known to produce sedation, drowsiness, and psychomotor slowing (for a review, see Stewart, 2005), few studies have examined the effect of benzodiazepines on attentional processes. Spatial attention shifting can be investigated by the Posner’s paradigm. In this classic paradigm, three squares are displayed horizontally: one central and two peripheral squares. A cue, which can be exogenous (e.g., an abrupt change in luminance of one of the peripheral squares) or endogenous (a central arrow), indicates the probable location of a target (a star or a letter). Trials in which the target appears at the cued location are called “valid.” Trials in which the target appears at the opposite location of the cue are called “invalid.” Response times to the detection of the target are shorter in valid trials. A cost in response times is observed when attention is drawn to the location of the cue and the target appears at another location (invalid trials). This cost is thought to reflect attentional disengagement from the cue to the target. With a spatial cueing paradigm Johnson, Weingartner, Andreasson, and George (1995) reported that response times following both exogenous and endogenous cues were slowed by triazolam as compared with response times in placebo-treated participants. In particular, the response time difference for valid, as compared with invalid, trials was larger for triazolam than for placebo, suggesting that triazolam selectively impairs attentional disengagement and/or attention shifting mechanisms, but the lack of a neutral condition complicates the interpretation of the results. A later study by Carter, Maddock, Chaderjian, and Post (1998) was designed to replicate and extend the findings of Johnson et al. (1995). They included a neutral condition in addition to the valid and invalid cue trials. They were thus able to examine drug effects on the operation of engagement (determined by the facilitation for valid relative to neutral trials) and the operation of disengagement (on the basis of the cost in response times for invalid relative to neutral trials). In this study, the benefit of valid cueing was greater for participants treated with triazolam than for placebo-treated participants. The authors suggested that triazolam might lead to an increase in facilitation or a reduction in inhibition for automatic attentional orientation mechanisms. The discrepancy between the two studies may be due either to changes in the paradigm (the inclusion of neutral trials) and/or to the difference in the dose of triazolam used across the studies (a lower dose was used for Carter et al.’s 1998 study).

Mintz and Griffiths (2003) compared the effects of an anticholinergic drug (scopolamine) and a benzodiazepine (lorazepam) on two attention tasks involving inhibitory processes (the Stroop color–word interference task and negative priming). In the Stroop task, naming the color of an incongruent color word (e.g., the word green printed in yellow) requires suppression or inhibition of the irrelevant dimension. Negative priming in this paradigm refers to the increase in response time to name the color in which a word is printed when the color to be named on a given trial is the color word that was to be suppressed (or inhibited) on the immediately preceding trial (e.g., the word green printed in red is preceded by the word red printed in blue). They found that, as compared with placebo-treated observers, neither drug affected negative priming, and the magnitude of interference in the Stroop task was equivalent in the placebo and the lorazepam (2 mg/70 kg) groups.

More recently, Coull, Jones, Égan, Frith, and Maze (2004) reported that midazolam impaired performance in a target detection task that was presented in the presence or absence of loud white noise. According to Gorissen and Eling (1998), diazepam intake has no detrimental effect on attentional resources. The authors found that learning of word pairs was diminished following diazepam intake, but no disproportionate learning costs were found during dual-task conditions. Yet, Boucart, de Visme, and Wagemans (2000) found that diazepam could lead to depletion of attention resources and therefore affect dual-task performance. Boucart et al. (2000) examined the effect of two benzodiazepines (lorazepam and diazepam) on the attentional blink effect. In that study, the stimuli were streams of isolated pictures of objects. In the dual-task condition, participants were asked to (a) identify the single picture of the stream appearing on a blue background (the other pictures appeared on a grey background) and (b) detect the presence of a second target (a globe). In the single-task control condition, participants were asked only to detect the presence of a globe and to ignore the picture on a blue background. The authors found that the attentional blink was more pronounced in magnitude and duration for benzodiazepine-treated participants, especially those treated with diazepam, than for placebo-treated participants. They suggested that the larger attentional blink effect for diazepam than for lorazepam was unlikely to be due to sedation, because performance was equivalent for both benzodiazepine- and placebo-treated participants in the single-task control condition and because the doses (lorazepam 0.038 mg/kg and diazepam 0.3 mg/kg) were equally sedative (Dundee, McGowan, Lilburn, McKay, & Hegarty, 1979). Although both diazepam and lorazepam interact with gam-
ma-aminobutyric acid type A receptors, a differential effect of these two benzodiazepines on cognitive processes has been previously reported. For instance, lorazepam has been found to impair both explicit and implicit memory, whereas diazepam affects only explicit memory (Legrand et al., 1995; Vidalh et al., 1994), and lorazepam is more detrimental than diazepam on perceptual integration (Beckers et al., 2001; Giersch et al., 1995, 1996; Wagemans et al., 1998). The present study used the Rapid Serial Visual Presentation (RSVP) paradigm in a more ecologically valid situation with photographs of scenes as stimuli in conditions simulating driving. It was aimed at investigating the effect of different doses of a benzodiazepine (diazepam) on attentional switching and at examining the magnitude of dual-task impairments as a function of the dose.

### Method

#### Participants

Thirty-six healthy volunteers (18–35 years of age) were recruited from a student population. They were native French speakers, and all were drivers. They had no medical illness or history of alcoholism, drug abuse, or tobacco consumption of more than 10 cigarettes per day. They were not chronic users of benzodiazepines and had not taken any concomitant medication for at least 21 days. Forbidden drugs and medications were checked from a urine sample. Participants were instructed to abstain from beverages containing caffeine or alcohol for the 24 hr prior to the study. All participants were tested in the morning after an overnight fast. They all had normal or corrected-to-normal vision. Written informed consent was obtained from all volunteers before they entered the study. The study was approved by the Ethical Committee of Lille.

Participants were randomly assigned to one of three parallel groups of 12 participants each: a placebo group (mean age 24.5 years; 8 women, 4 men), a diazepam 0.1 mg/kg group (mean age 25.2 years; 5 women, 7 men), or a diazepam 0.3 mg/kg group (mean age 26.2 years; 6 women, 6 men). These dosages were chosen so that the peak plasma concentration of diazepam would correspond to the average plasma concentration under the usual given doses in medical practice (Greenblatt et al., 1981; Rutherford et al., 1978). Randomization was performed with six equal blocks of 6 participants. Diazepam was provided by Roche (Milan, Italy). In order to give the accurate dose, we administered the oral drug solution with drops (three drops per milligram). The placebo was made of extract of bitter orange peel and syrup provided by Cooper Laboratories (Brindas, France). Diazepam and placebo drops were prepared by an unblinded nurse with 100 ml of water in an opaque, lidded tumbler. The drug was given to the volunteers by another nurse to preserve the double-blind procedure.

#### Stimuli and Apparatus

The stimuli were colored photographs of natural scenes depicting roads (an example is shown in Figure 1) and 10 well known French city names of five letters each. Two different scenes were used as stimuli. At a viewing distance of 35 cm the mean angular size of the display was 26.2° horizontally × 8.2° vertically. The mean angular size of the city names, written in uppercase letters, was 6.5° × 1.6° of visual angle. The stimuli were centrally displayed on the screen of a Dell computer.

### Experimental Procedure and Drugs

Biodisposition of diazepam varies widely among individuals. To ensure that the experiment was conducted at the optimal blood concentration of the drug, we scheduled two visits: We performed pharmacokinetics more than 10 days before the experiment in order to measure the metabolic abilities of each participant. For each dosage (0.1 and 0.3 mg/kg), measured on different days, a blinded nurse collected 11 blood samples to measure the blood concentration of diazepam before intake of the drug and at 20, 30, 40, 50, 60, 75, 90, 120, 180, and 240 min after intake. The blood samples of placebo-treated participants were destroyed except for the first one, which was analyzed to check for lack of benzodiazepines. According to the study design pharmacokinetics data were analyzed by a blinded physician who provided the T_max (time of optimal concentration) for each participant to the researcher. The experiment (including practice trials) started 10 min before T_max. For placebo-treated participants, an unblinded physician provided the blinded researcher with a virtual T_max obtained randomly. The drug concentration as a function of time is displayed in Figure 2.

A fixation dot was displayed centrally for 500 ms and followed by a stream of 15 photographs of a scene that were also centrally displayed. Each photograph in the stream was displayed for 50 ms, separated by a 17-ms blank interval except for the city name (the target), which appeared for 100 ms. The city name appeared randomly at Serial Positions 2, 3, or 4 in the stream. The probe (a vehicle) appeared randomly at Serial Positions 2 (84 ms), 4 (218 ms), 6 (352 ms), 8 (486 ms), or 10 (620 ms) after the city name. A mask composed of randomly distributed colored rectangles signaled the end of each stream. An example of a stream is displayed in Figure 1.

Performance was compared in two conditions: (a) In the dual-task condition, participants were asked to identify the city name (the target) and to detect the presence of a vehicle (the probe). (b) In the single-task control condition, participants were asked to detect the presence of a vehicle and to ignore the city name. Participants were presented with 100 streams with the probe present (10 city names × 5 serial positions of the probe × 2 lateral positions [left/right] of the probe) and 100 streams with the probe absent in each condition. At the end of each stream participants typed their responses (the city name and yes or no for the probe in the dual-task condition and only yes or no for the probe in the single-task condition) on the keyboard of the computer. Participants were instructed to give the exact name of the city and to type the word “rien” (nothing) if they did not identify or remember the name. Given that practice reduces
the attentional blink effect (Maki & Padmanabhan, 1994), all participants started with the dual-task condition. Participants were given 20 trials as practice on the dual task prior to the experiment.

Results

The data are displayed in Figure 3 for each treatment group. An analysis of variance was conducted (using SYSTAT 8.0) on the detections of the probe (the vehicle) and on the correct identifications of the city name. The between-subjects factor was the group determined by the treatment (placebo, diazepam 0.1 mg/kg, or diazepam 0.3 mg/kg). The within-subject factors were the task condition (dual-task vs. single-task) and the serial position of the probe relative to the target (2, 4, 6, 8, or 10).

Target Identification

The percentage of correct identifications of the city name was high, above 88%, for the three treatment groups. It was significantly higher for the placebo group than for the diaz-
epam 0.3 mg/kg group (96.5% vs. 88.5%), $F(1, 22) = 25.6$, $p < .001$, but there was no significant difference between the placebo group and the diazepam 0.1 mg/kg group (96.5% vs. 95.0%).

**Probe Detection**

The percentage of false alarms (i.e., a yes response for the vehicle when it was absent) was higher in the dual-task condition than in the single-task condition (3.3% vs. 0.6%), $F(1, 33) = 17.2$, $p < .001$. There was no significant main effect of the group for false alarms.

For correct probe detections a significant main effect of group was found, $F(2, 33) = 23.6$, $p < .001$. Accuracy in probe detection was higher for placebo-treated participants than for participants in the benzodiazepine groups (see Figure 2). There was also a significant main effect of task condition, $F(1, 33) = 71.3$, $p < .001$. Accuracy was higher in the single-task than in the dual-task condition. The main
effect of probe serial position was also significant, $F(4, 132) = 16.9, p < .001$: Accuracy increased as the target-probe lag increased. A significant interaction was observed between task condition and probe serial position, $F(4, 132) = 10.8, p < .001$. Performance was stable across probe serial position in the single-task condition, whereas a strong impairment in probe detection was observed in the dual-task condition: the attentional blink effect. Task condition interacted significantly with group, $F(2, 33) = 10.8, p < .001$. This interaction resulted from a larger impairment in probe detection in the benzodiazepine groups than in the placebo group in the dual-task condition, $F(2, 33) = 23.6, p < .013$, whereas performance was not significantly affected by drug in the single-task condition, $F(2, 33) = 2.2, ns$. In the single-task condition performance was lower for the diazepam 0.3 mg/kg group than for the placebo group, $F(1, 22) = 5.9, p < .023$, but no significant difference was found between the placebo group and the diazepam 0.1 mg/kg group, $F(1, 22) = 1.1, ns$, and between the diazepam 0.1 mg/kg group and the diazepam 0.3 mg/kg group, $F(1, 22) = 3.3, p < .08$. As can be seen from Figure 2, the magnitude of the attentional blink effect, measured by the difference in performance in the dual-task condition and the single task condition for all serial positions of the probe, was larger for benzodiazepine-treated participants than for placebo-treated participants. Comparison of the different groups showed that the magnitude of the attentional blink effect was larger for the diazepam 0.1 mg/kg group than for the placebo group, $F(1, 22) = 6.4, p < .019$. The largest magnitude of the attentional blink was found for the diazepam 0.3 mg/kg group: diazepam 0.3 mg/kg versus placebo, $F(1, 22) = 59.0, p < .001$, and diazepam 0.3 mg/kg versus diazepam 0.1 mg/kg, $F(1, 22) = 14.4, p < .001$. The three way interaction between group, task condition, and probe serial position was significant, $F(8, 132) = 2.4, p < .019$. It resulted from a shorter attentional blink effect in the placebo group (218 ms corresponding to Serial Positions 2 and 4), followed by the diazepam 0.1 mg/kg group (352 ms); the longest duration of the blink was found for the diazepam 0.3 mg/kg group (more than 620 ms).

Because menstrual or estrous cycle phase might affect responses to medication, we checked for an effect of gender on the benzodiazepine-treated groups. There was no main effect of gender in either the 0.1 mg/kg group, $F(1, 10) = 0.2, ns$, or the 0.3 mg/kg group, $F(1, 10) = 1.9, ns$. Gender did not interact with condition: 0.1 mg/kg, $F(1, 10) = 1.7, ns$; 0.3 mg/kg, $F(1, 10) = 0.1, ns$; and no significant interaction was found between gender and serial position of the probe: 0.1 mg/kg, $F(4, 40) = 0.2, ns$; 0.3 mg/kg, $F(4, 40) = 1.0, ns$.

Discussion

The main results are the following: (a) Performance for target identification was high, more than 88% correct, in the three treatment groups. (b) In the single-task condition, performance in probe detection was slightly lower, but still above 90% correct, in the diazepam 0.3 mg/kg group than in the placebo group. (c) An attentional blink effect was found in the dual-task condition. (d) The magnitude and duration of the attentional blink increased with the dose of benzodiazepine. (e) Dual-task performance was degraded twice as much for the diazepam 0.1 mg/kg group and four times as much for the diazepam 0.3 mg/kg group as for the placebo group.

Though sedation might have played a role in the lower performance for probe detection in the diazepam 0.3 mg/kg group, performance varied little in the three groups in the single-task condition, and the target was identified with high accuracy in the three groups, suggesting that sedation was not the critical factor for the strong attentional blink effect observed in the benzodiazepine-treated groups.

Previous studies using RSVP methodology on words or pictures have shown that high-level recognition performance can be obtained when words or pictures are presented for 100 ms each, as long as they are separated by a substantial interstimulus interval and/or no pattern masking (for reviews, see Intraub, 1999, and Potter, 1999). The attentional blink effect was weak in the placebo-treated group as compared with healthy participants in previous studies using letters as stimuli, in which the duration of the blink was usually on the order of 400 ms (Chun & Potter, 1995; Raymond et al., 1992). Placebo-treated observers missed the probe in about 10% of the streams when it followed the city name by 218 ms. There is good evidence that the masking parameters of Target 1 modulate the magnitude of the attentional blink effect. Reducing the effectiveness of a visual mask following Target 1 or increasing the discriminability between Target 1 and the other items of the stream tends to reduce the magnitude of the attentional blink effect (Chun & Potter, 1995; Grandison, Ghirardelli, & Egret, 1997; Raymond et al., 1992; Raymond, Shapiro, & Arnell, 1995; Seiffert & Di Lollo, 1997). In the present study, no mask was displayed following Target 1, and the exposure time of the word was relatively long (100 ms). It can be argued that the use of invariant streams (the same scene repeated 15 times) was not optimal to induce an attentional blink effect, but Bachmann and Sikka (2005) reported a substantial attentional blink effect with perceptually continuous objects (two target letters appearing within streams of capital Is).

Several accounts have been proposed for the attentional blink effect. (a) The memory account (Chun & Potter, 1995; Giesbrecht & Di Lollo, 1998; Jolicour, 1999; Vogel, Luck, & Shapiro, 1998) suggests that the attentional blink effect may be the result of attentional processing inherent to identification and consolidation of Target 1. The operation of consolidation of Target 1 monopolizes attentional resources for some time (several hundred milliseconds), thus reducing the processing of subsequent stimuli (distractors and the probe) because of capacity limitations. (b) The interference account (Isaak, Shapiro, & Martin, 1999) is based on a competition between Target 1, the probe, and items temporally surrounding the targets for the same perceptual and cognitive resources. When the probe occurs within Target 1’s processing time, all critical items compete for processing resources, thus reducing the accuracy of report of the probe. When the interval between Target 1 and
the probe is longer than 500 ms, Target 1 is no longer engaging processing resources, and a response has been selected. (c) The attentional account (Ward et al., 1996, 1997) proposes that the blink reflects the time for focal attention, having already been allocated to an initial target, to be reallocated to a subsequent target. Consistent with this idea, neglect patients, who are thought to be impaired in attentional orienting (the operation of disengagement of attention from an invalid cue to a target displayed at different spatial locations), exhibit a longer attentional blink effect (about four times longer) than control participants (Husain, Shapiro, Martin, & Kennard, 1997).

The magnitude and the duration of the blink increased with the dose of diazepam. The strong attentional blink effect observed in the diazepam 0.3 mg/kg group confirms previous results (Boucart et al., 2000) observed with streams of isolated pictures as stimuli, but a single dose of diazepam was used in that study.

The attentional blink involves short-term memory. Target 1 has to be stored for less than 1 s (the duration of the stream) before being reported. Studies on the effect of benzodiazepines on memory usually use tasks involving relatively long-term memory. For instance, in studies of implicit memory, participants are presented with a series of words or pictures in a study phase and with a second series of old (presented in the study phase) and new items in a test phase occurring several minutes later. In studies of explicit memory, participants are presented with a list of words that they have to recall several minutes later. These studies have repeatedly demonstrated that lorazepam, but not diazepam, impairs explicit memory (priming), whereas both benzodiazepines impair explicit memory (Buffet-Jerrott & Stewart, 2002; Curran & Gorenstein, 1993; Danion et al., 1989; Legrand et al., 1995; Schifano & Curran, 1994; Sellal et al., 1992; Vidalhiet et al., 1994). The fact that diazepam-treated participants, treated with a high dose, were able to report accurately more than 85% of the target names suggests that short-term memory, within 1 s, is spared under diazepam.

The effect of benzodiazepines on attentional processes has been the object of few investigations (for a review, see Buffet-Jerrott and Stewart, 2002). Ward et al. (1996, 1997) compared the attentional blink effect to the dwell time (i.e., the duration of interference between two events). They measured the time course of interference in a divided attention task. Two displays composed of two stimuli (two letters and two digits) were presented in different spatial locations (e.g., horizontal for letters and vertical for digits), separated in time. Attention was engaged on an item (e.g., one of the letters) by requiring its identification. At varying intervals after the presentation of the first display, a second pair of stimuli (e.g., two digits) was presented for identification. The results showed a deficit in identification accuracy when participants were required to report two objects (one letter and one digit) if the temporal interval was shorter than 450 ms. They proposed that interference between relevant objects under RSVP conditions may reflect the time for focal attention, having already been allocated to an initial target, to be reallocated to a subsequent target. Although inconsistent data have been reported with the spatial cueing paradigm (Carter et al., 1998; Johnson et al., 1995) the increased duration and magnitude of the attentional blink under diazepam is likely to reflect impairment in shifting attention from one target to a second target in the temporal domain.

Conclusion

Attentional deficits in the spatial domain have been reported for participants treated with benzodiazepines but with inconsistent results. The present study was designed to investigate attentional impairments in the temporal domain in conditions simulating driving, in which observers had to read the name of a city and to detect a vehicle appearing left or right of fixation at short temporal intervals. We showed that diazepam, at therapeutic dosage, impairs shifting of attention when participants have to process two events occurring in rapid succession.

References


