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GABA\textsubscript{A} Agonist Reduces Visual Awareness: A Masking–EEG Experiment

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Abstract

Consciousness can be manipulated in many ways. Here, we seek to understand whether two such ways, visual masking and pharmacological intervention, share a common pathway in manipulating visual consciousness. We recorded EEG from human participants who performed a backward-masking task in which they had to detect a masked figure form its background (masking strength was varied across trials). In a within-subject design, participants received dextromethorphan (a $N$-methyl-D-aspartate receptor antagonist), lorazepam (LZP; a GABA\textsubscript{A} receptor agonist), scopolamine (a muscarine receptor antagonist), or placebo. The behavioral results show that detection rate decreased with increasing masking strength and that of all the drugs, only LZP induced a further decrease in detection rate. Figure-related ERP signals showed three neural events of interest: (1) an early posterior occipital and temporal generator (94–121 msec) that was not influenced by any pharmacological manipulation nor by masking, (2) a later bilateral perioccipital generator (156–211 msec) that was reduced by masking as well as LZP (but not by any other drugs), and (3) a late bilateral occipital temporal generator (293–387 msec) that was mainly affected by masking. Crucially, only the intermediate neural event correlated with detection performance. In combination with previous findings, these results suggest that LZP and masking both reduce visual awareness by means of modulating late activity in the visual cortex but leave early activation intact. These findings provide the first evidence for a common mechanism for these two distinct ways of manipulating consciousness.

INTRODUCTION

Consciousness can be manipulated in many ways. A visual stimulus can be rendered invisible through physical manipulations such as masking or rivalry, by physiological manipulations like TMS, or via pharmacological interventions such as anesthesia. Different as these methods may seem, they all share that consciousness sensations are—partly or fully—abolished. Does that mean that these manipulations all have a common neural pathway?

A problem with research on consciousness is that different neural correlates of consciousness are proposed, depending on the type of manipulation used, the kind of neural signals recorded, and the interpretation of behavioral results (for reviews, see Tononi & Koch, 2008; Seth, 2007; Dehaene, Changeux, Naccache, Sackur, & Sergent, 2006; Lamme, 2006; Crick & Koch, 2003). A fruitful way out of this conundrum may be to seek for the common factor between these proposals. More specifically, the search for a final common pathway for all types of manipulations of consciousness may lead the way toward understanding what consciousness actually is. Here, we seek to understand whether a common pathway can be found for two very different ways of manipulating visual consciousness: pharmacological intervention that is considered to affect conscious level and backward-masking, a technique that manipulates conscious content.

With a pharmacological intervention, it is possible to specifically manipulate neurotransmitters by antagonizing or agonizing their receptors. Different theories are proposed on which neurotransmitter or receptor is important for consciousness and several candidates have been suggested, including acetylcholine (Perry, Walker, Grace, & Perry, 1999) and $N$-methyl-D-aspartate (NMDA; Flohr, Glade, & Motzko, 1998). However, to induce anesthesia, the most common way to pharmacologically reduce consciousness level, various other receptors such as receptors for GABA, glycine, and muscarine (Alkire, Hudetz, & Tononi, 2008) can be targeted. How can such a variety of pharmacological interventions produce the same effect: loss of consciousness?

The answer may be found in the effects on neural activity when these receptors are manipulated. One suggestion is that anesthesia disrupts cortical communication, causing a loss of integration of information (Alkire et al., 2008; Tononi, 2004). Crucially, the same might be true for visual masking. A stimulus becomes less perceptible or even invisible through the presentation of a second stimulus—the “mask”—shortly after the first. Accumulating evidence suggests that when stimuli are effectively masked, recurrent processing in visual cortex is reduced.
whereas feedforward activity remains relatively unaffected (Boehler, Schoenfeld, Heinze, & Hopf, 2008; Fahrenfort, Scholte, & Lamme, 2007; Lamme, Zipser, & Spekreijse, 2002; Di Lollo, Enns, & Rensink, 2000). Therefore, a pharmacological intervention (known to affect conscious level) and masking (known to affect conscious content) might both disrupt cortical communication, although a direct link between both manipulations of consciousness has so far not been demonstrated. Here, we try to find out whether a subanesthetic pharmacological intervention and backward-masking have similar effects.

We recorded EEG while subjects discriminated between trials containing a figure or no figure under various masking strengths (ranging from fully “seen” figures to fully “unseen” figures). This task was performed on separate days, on each of which we either administered dextromethorphan (DM; an NMDA receptor antagonist), lorazepam (LZP; a GABA_A receptor agonist), scopolamine (SCO, a muscarine receptor antagonist), or a placebo (PLC). This experimental setup allowed us to explore the existence of a common neural pathway for two different ways of manipulating visual consciousness.

METHODS
Participants
Twenty-two participants (all women, mean age = 21.54 years, SD = 2.65 years) with no relevant psychiatric or neurological history participated in the experiment. They all had normal or corrected-to-normal vision. Written informed consent was obtained from each participant during a screening session. The ethical committee of the Psychology Department of the University of Amsterdam approved the experiment. Two participants were excluded from analysis because they were experiencing extreme side effects of the LZP. Therefore, all reported analyses are based on the remaining 20 participants.

Masking Task
In this experiment visual awareness was manipulated using a backward-masking paradigm in combination with a pharmacological manipulation. In separate sessions, different drugs that operate on different synaptic mechanisms were administered to study their effects on subjective stimulus visibility. In the backward-masking task, each trial started with a fixation (300 msec) after which the target stimulus was presented for 16.7 msec. Participants had to detect whether the target contained oriented line elements that all had the same orientation (no-figure trials) or contained an orientation-defined square (figure trials). To manipulate the visibility of the target, a texture-defined pattern mask (of varying strengths) or an isoluminant gray screen with no texture (no mask) was presented for 500 msec immediately after the target. Participants had to indicate within 1500 msec after the target stimulus which stimuli they had perceived (see Figure 1A).

The presentation of the stimuli was rendered unpredictable by using a jitter for the fixation duration (added random 300–550 msec). Participants were instructed to fixate throughout the task. Participants indicated their response through pressing a button with their left hand for “figure present” or a button with their right hand for “no-figure trial” (buttons were counterbalanced across subjects). Participants were instructed to guess if they did not see the target.

Stimuli
The target stimuli consisted of textures with oriented line elements. The oriented line elements had either the same direction (no-figure trials) or were oriented in a 45° angle relative to the background to form an orientation-defined square (figure trials). In total, background and figure line segments could appear in four different orientations (22.5°, 67.5°, 112.5°, and 157.5°). The orientations were counterbalanced across trials so that local stimulation of the visual cortex was on average identical for no-figure and figure trials (for a similar procedure, see Fahrenfort et al., 2007; Scholte, Witteveen, Spekreijse, & Lamme, 2006; Caputo & Casco, 1999; Lamme, Van Dijk, & Spekreijse, 1992).

The orientations of the line elements in the mask differed from the line elements in the preceding target stimuli. We created multiple levels of masking strength (11 in total) by changing the color of the line elements in the mask from black to light gray while keeping the background color constant. The lighter the line elements, lower the contrast of the mask; hence, the easier it was to detect the target. These multiple levels of masking strength spanned the range from invisible, where the mask had the same color (black) and luminance as the target and performance was at chance level (“full mask”), to visible, when there was no mask presented (“no mask”). This also allowed us to discover whether increasing masking strength lead to a linear reduction of the neural activity or whether masking had a more an “all-or-none” effect. In addition, a subjective 75% mask condition (“subjective mask”) was selected out of the intermediate masks based on performance on the backward-masking task in the screening session. Stimuli were presented using Presentation (Neurobehavioral Systems, Inc., Albany, CA).

Procedure
The experiment consisted of a screening session and four morning test sessions (10–14 hr), which occurred on separate days with a minimum interval between each session of 1 week.

In the screening session, participants were screened on the contraindications for the different drugs and practiced the backward-masking task. During the practice, they received feedback on their detection after each trial.
After the practice, the participants performed five blocks of 176 trials of the backward-masking task. On the basis of their detection performance on this task, the “subjective mask” was set to a performance of 75% correct. In each test session, a different drug was administered at a dosage selected to have mild psychogenic and sedating effects (Boroojerdi, Battaglia, Muellbacher, & Cohen, 2001). The following agents were used (within subjects): (i) DM (120 mg, 40 ml of Dampo syrup), a potent non-competitive NMDA receptor antagonist (Wong, Coulter, Choi, & Prince, 1988); (ii) LZP (1.5 mg, pill), a short-acting benzodiazepine that at this dose produces functional potentiation in specifically the GABAA receptors (Sybirska et al., 1993); and (iii) SCO (1.5-mg dermal patch behind the ear), a muscarinic receptor antagonist (Frey et al., 1992). Because the intake differed for all three drugs, the subjects received a pill, syrup, and a patch behind the ear in each session. As a result, two PLCs and one condition-dependent active drug were administered per visit. In the PLC condition, all three substances were PLCs. The order of the drug conditions was counterbalanced across sessions, and participants were blind to this order. Participants were instructed to have a good night’s sleep, abstain from alcohol- and caffeine-containing products 24 hr before and after testing. At 10:00 a.m., the drug was administered. Immediately after drug intake, participants practiced a block of 216 trials. The task and EEG recording commenced ∼120 min after ingestion of the medication to maximize the levels of drug during the task (Boroojerdi et al., 2001). During the task, participants performed 2160 trials (with a short break after each block of 216 trials) with a breakdown of 480 no-mask trials, 480 full-mask trials, 480 subjective mask trials, and an additional 80 trials for the intermediate masking strengths. For the analyses of the intermediate masks, we binned three levels of the intermediate masks, because each condition only contained 80 trials. As a result, three masking strength conditions were created (easy, medium, and strong), which all contained 240 trials. In each condition, 50% of the trials contained a figure. The order of the trials was random; each block contained a similar distribution of the conditions. During each session, participants filled in a set of five visual analogue scales (Bond & Lader, 1974) that assessed their subjective state before medication ingestion, after 2 hr and then 3 hr into testing, and on completion of testing. The mean score of these scales (length = 100 mm) assessed complementary aspects of sedation (alert/drowsy, excited/calm, clear headed/muzzy, energetic/lethargic, and

Figure 1. Task design and behavioral results. (A) Schematic description of a trial. Participants indicated whether a figure was present or not. The target visibility was manipulated, spanning the range from weakly masked to strongly masked. (B) Detection performance as expressed in mean d-prime for no-mask, subjective mask, and full-mask stimuli per drug. The targets were more difficult to detect with LZP compared with PLC. (C) With increasing masking strength detection performance also decreased and, again, participants’ performance decreased significantly more with LZP.
quick/slow), where a high value indicates that participants feel subjectively more sedated (Danion, Zimmermann, Willard-Schroeder, Grangé, & Singer, 1989).

**Behavioral Analysis**

On the basis of the individual ability to discriminate at 75% accuracy between figure and no-figure trials, we created the participant-specific subjective mask. Here, we fitted the individual performance for the different intermediate masks with a Weibull psychometric function, using the Psignifit toolbox (bootstrap-software.org/psignifit/) version 2.5.6 for Matlab (The MathWorks, Inc., Natick, MA) that implemented the maximum likelihood method for curve fitting (Wichmann & Hill, 2001).

Forced-choice detection performances expressed in d-prime were tested for significance using paired sample t tests and repeated-measures ANOVA with Drugs (PLC and one of DM, LZP, or SCO) and Masking (no, subjective, full, weak, medium, strong mask) as within-subject factors. The ratings on the visual analogue scales were analyzed with repeated-measures ANOVA with Drug (PLC vs. DM or LZP or SCO) and Time (drug intake, 2 hr, 3 hr, end of experiment) as within-subject factors. Because we were interested in the effects of drugs in comparison with PLC, we compared each drug with PLC separately.

**EEG Analysis**

We recorded the EEG data from the scalp using a BioSemi ActiveTwo 64-channel active EEG system (BioSemi, Amsterdam, the Netherlands) sampled at 2048 Hz and referenced to two ear electrodes. Four external electrodes were placed around the eyes (two horizontal and two vertical, referenced to their counterpart) to account for eye movements. We filtered the data with a high-pass filter of 0.1 Hz, a low-pass filter of 30 Hz, and a notch filter of 50 Hz. After filtering, the data were downsampling to 256 Hz. Ocular correction was performed with an independent component analysis (Hyvärinen, Karhunen, & Oja, 2001). The EEG data were segmented based on the target position. A segment consisted 100 msec before target presentation (baseline) and 400 msec after target presentation. If a segment contained EEG activity outside the −75 and +75 μV range or contained voltage steps larger than 50 μV or had an activity lower than 0.5 μV and an amplitude larger than 2.5 SD of the maximum amplitude, it was removed from further analysis. Baseline correction was applied to the −100 to 0 msec interval before stimulus presentation. Spherical interpolation was used to create a signal for the removed channels. To estimate current source densities (CSD), spline laplacian distributions were calculated (Perrin, Pernier, Bertrand, & Echallier, 1989). With CSD, deep sources are filtered out and greater weight is put onto local sources in the superficial cortex (Nunez & Srinivasan, 2006).

After the CSD transform, ERP averages were calculated per drug and masking strength (no, subjective, full mask, and binned intermediate masks). Analyses were conducted on difference waves, obtained by subtracting the ERP average of no-figure trials from the ERP average of figure trials. Because a mask followed both trials, any direct influence of the mask was subtracted out, ensuring that the two brain signals only differed in the presence or absence of a figure (see also Fahrenfort, Scholte, & Lamme, 2008; Fahrenfort et al., 2007; Scholte et al., 2006; Caputo & Casco, 1999; Lamme et al., 1992).

To increase the independence of data, we performed a split half procedure, which randomly divided the data. This split half procedure boosts the reliability of the effects that are found by precluding coincidental significance of sources that are identified visually (Pollick & Mumford, 2009). Half of the trials were used to select those electrodes that showed a difference between figure and no-figure trials in the no-mask PLC condition using the subtraction method described above. The selected electrodes were then pooled to increase the signal-to-noise ratio. This procedure results in the following ROIs: an occipito-temporal ROI (P5, P7, PO7, P6, P8, PO8), an occipital ROI (Az, Oz, POz), a perioccipital ROI (O1, PO7, PO3, Oz, O2, PO4, PO8), a central ROI (P1, P2, Pz, Cz), and an occipital temporal parietal ROI (O1, P5, P7, PO7, PO3, O2, P6, P8, PO4, PO8). The other half of the trials was then used for statistical analyses and for selecting the moments of significant deflections per ROI. The moments of significant deflections per ROI (referred to as a neural event) were ascertained by sample-by-sample paired t tests between figure and no-figure trials. Multiple comparison correction with respect to the number of time points being tested was performed to limit the false discovery rate (see Figure 2).

To explore the effect of drugs and masking on the neural events, we contrasted the mean amplitude of the difference wave per condition at each neural event. If a neural event consisted of two ROIs with both a positive and a negative deflection, we took the average of the absolute value of both. For statistical analyses, we used a repeated-measures ANOVA on the mean activity values for each neural event, with Drugs (PLC vs. DM, LZP, SCO) and Masking Strength (weak, medium, strong) as within-subject factors. Post hoc paired sample t tests were used to compare conditions more directly. Preprocessing was performed using Brain Vision Analyzer (Brain Products, Munich, Germany). Statistical analyses and visualization of the time courses were done using Matlab.

**RESULTS**

**Behavioral Effects: LZP Reduces Stimulus Visibility**

Figure trials were easily discriminated from no-figure trials in the no-mask condition (see Figure 1B), as evidenced by detection performance (expressed as d-prime) close to 7. Crucially, masking strongly reduced stimulus visibility. When the subjective-mask was presented, the
d-prime dropped to approximately 2, whereas it was at chance level with the full mask (main effect for Masking, all Fs(2, 38) > 354.8, p < .001). When looking at the effect of Drug on stimulus visibility, only LZP differed significantly from PLC (main effect for Drugs, F(1, 19) = 35.56, p < .001). LZP reduced the detection performance in the no-mask and subjective-mask conditions (assessed with paired sample t tests (t(1, 19) = 4.40, p < .001 and t(1, 19) = 6.60, p < .001, respectively), but not in the full-mask condition, because the full-mask already reduced stimulus visibility to chance level for all conditions. In contrast, the other two drugs had no significant effect on stimulus visibility (DM, F(1, 19) = .49, p = .492; SCO, F(1, 19) = .23, p = .636).

Next, we were interested in how the variation in masking strength influenced stimulus visibility. To test whether there was a linear or all-or-none relationship between masking and detection performance, we analyzed the effect of the clustered intermediate masks (weak, medium, strong) on performance. As can be seen in Figure 1C, for all drugs, increased masking strength reduced the detection performance (main effect for Masking Strength, F(2, 38) > 55.5, p < .001; linear contrast, F(2, 38) = 51.92, p < .001). However, only LZP significantly affected detection behavior, as demonstrated by better performance for the intermediate masks with PLC than with LZP (main effect of drugs, F(1, 19) = 13.83, p < .001). For DM and SCO, no significant differences were observed from the PLC (all Fs < 0.487 and all ps > .49). Overall, these findings indicate that increasing the strength of the mask gradually decreases stimulus visibility and that administering LZP further increases the difficulty of perceiving the targets at all levels of masking strength.

**EEG Results**

Because detection rates were impaired only with LZP, follow-up EEG analyses were first performed for the PLC and LZP conditions (supplementary analysis showed no effects of DM and SCO on the EEG; see Figure 6). To capture the neural processes involved during the detection of the figure, the ERPs for no-figure trials were subtracted from the ERPs for figure trials (see Methods). Figure 2 shows the course of neural processing of the subtracted ERPs (indicated as the difference) for the no-mask trials in the PLC condition only. On the basis of visual inspection of the data (see Methods) and results from previous studies (Fahrenfort et al., 2007, 2008), the following three neural events were distinguished: (1) an early neural event observed at occipito-temporal and occipital electrodes at ~94–121 msec, the early event; (2) a later event at ~156–211 msec at peri-occipital and central electrodes, the middle event; and (3) a large positive deflection at occipital-temporal parietal electrodes, at ~293–386 msec, the late event.

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**Full and Subjective Mask and LZP Reduce Activity of the Later Two Neural Events, but Not of the Early Neural Event**

First, we determined the effect of full or subjective mask on the above-outlined three neural events. We contrasted the mean amplitude of the difference wave for full mask and no mask (see Methods). First of all, the fully masked figure did not elicit any additional activity compared with the fully masked no-figure trials, showing that full masking has a very profound effect on figure-related activity (see Figure 3). In the subjective mask condition, we observed typical EEG–masking findings in that late activity was reduced by masking (Koivisto & Revonsuo, 2010; Boehler et al., 2008; Del Cul, Baillet, & Dehaene, 2007; Fahrenfort et al., 2007). Paired sample t tests revealed that masking specifically diminished activity for the later two neural events, but not or at least much less so for the early event (see Figure 4B). This suggests that the activity at these later events is important for stimulus visibility. Interestingly, LZP had similar effects on figure-related neural processing, because it reduced activity for the two later neural events, while leaving activity on the early event
relatively unaffected. The reduction in neural activity due to LZP was most pronounced at the middle neural event (see Figure 4).

**Increasing Masking Strength Influences Activity at the Middle Event Linearly**

Additionally, we compared the effects of the binned intermediate masks (weak, medium, strong) per neural event (see Methods and Figure 5A). A linear effect for Masking Strength was found only at the middle event (main effect linear contrast for masking strength, $F(1, 19) = 5.74, p < .03$), reflecting that increasing masking strength led to decreased neural activity in the 156–211 msec range. This effect was reduced with LZP compared with PLC (main effect for Drug, $F(1, 19) = 6.14, p < .02$). The neural activity at the middle event seems therefore important for stimulus visibility, as it was this activity that reduced with increasing masking strength and reduced even more with LZP, similar to what we observed in our behavioral results. At the other two neural events, there were no effects of LZP or masking strength (all $F$s(1, 19) < .994, all $p$s > .347).

**Correlating the Reduced Neural Activity at the Events with Stimulus Detection Behavior**

To test this, we calculated Spearman’s rank correlations between the mean amplitude per neural event for masking...
strength (weak, medium, strong) and the detection rate. As depicted in Figure 5B, a significant correlation was found only for the middle event with PLC (rho = .262, p < .044) and no correlation with LZP (rho = .139, p > .290). This suggests that subjects with higher detection rates were correlated with larger deflections at this time window. No correlations were observed in the other events (all rhos < -.15, all ps > .261).

No Eye Movement Differences between Masking and Drugs Conditions
To ascertain that the observed effects were not due to different patterns of eye movements across conditions, we performed exactly the same analysis as for the EEG data on the raw EOG signal for the horizontal EOG and vertical EOG channels over time. For both the horizontal and vertical EOGs, we did not observe any significant differences between the relevant drugs and masking conditions, which highlight that blinks or eye movements did not affect our EEG results.

DM and SCO Did Not Affect the Neural Activity
As a control, all EEG analyses were also performed for the two other drugs (DM and SCO); however, just as for the behavioral data, no significant differences were observed when compared with PLC (see Figure 6).

No Correlation between Sedation and Reduced Visual Awareness
To assess the influence of the pharmacological intervention on changes in subjective mood ratings of sedation, we analyzed the visual analogue scales (Bond & Lader, 1974; see Methods). Overall, subjects felt more sedated in the drug conditions compared with PLC, and the sedation increased over time (interaction drug and time, all Fs > 3.11, ps < .03; Figure 7). In the LZP condition, the sedative effect was strongest (main effect Drug, F(1, 16) = 24.01, p < .01). To assess whether this may have contributed to the effects we reported, the Spearman’s rank correlations were calculated between the difference in sedation (LZP minus PLC: an average of the second and third time point) and the difference in EEG activity for both the no-mask and subjective-mask condition. Moreover, the specificity of the reduction in neural activity, being that only the later neural events were affected, already suggests that there was not an overall reduction in neural activity due to sedation only (see Figure 4). No positive correlations were observed (all rhos < .16, all ps > .54). The absence of reliable and consistent positive correlations between sedation scores and

Figure 5. Effect of masking strength on the middle event for LZP and PLC. (A) For PLC increasing masking strength reduced the neural activity in a linear manner. (B) The scatter plot for the middle event shows a positive correlation between the size of the deflection and detection performance.

Figure 6. ERPs for DM, SCO, and LZP compared with PLC. The difference waves (figure − no-figure trials) averaged for all active electrodes for DM, SCO, LZP, and PLC (no mask). No significant differences are observed between DM and PLC or between SCO and PLC. LZP, however, did reduce the neural activity significantly compared with PLC.
neural measures suggests that the sedative effects of LZP cannot explain the reported neural results.

DISCUSSION

In this study, we combined a masking paradigm with a pharmacological intervention to study the neural mechanisms underlying visual awareness. Behaviorally, both LZP (GABAA receptor agonist) and masking reduced visual awareness as evidenced by decreased detection performance. With respect to neural activity, the effects for these two distinct ways of manipulating visual consciousness appeared very similar with respect to timing and scalp topography. For both manipulations, the early evoked neural activity (<120 msec) was relatively intact, whereas the neural activity after ~150 msec was decreased.

This effect of masking is in line with several previous studies in humans that also demonstrated that masking disrupts late activity, while leaving early activity intact (Koivisto & Revonsuo, 2010; Boehler et al., 2008; Fahrenfort et al., 2007, 2008; Del Cul et al., 2007; Lamme et al., 2002; Lamme & Roelfsema, 2000). Additionally, our results seem similar to average response times in early visual areas with macaque intracranial recordings with very comparable stimuli (Lamme & Roelfsema, 2000). Therefore, the early figure–no-figure difference might reflect sustained activity resulting from feedforward processing, although it cannot be ruled out that some feedback is already incorporated at this interval (Foxe & Simpson, 2002).

The observed reduced neural activity in the 156–211 msec range seems similar to the visual awareness negativity (Koivisto & Revonsuo, 2010). Visual awareness negativity is described as a posterior negativity around 200 msec that emerges across different manipulations of visual awareness, including masking, change blindness, and the attentional blink (Koivisto & Revonsuo, 2010). In addition, we found that in the 156–211 msec range the amount of disruption depended on the strength of the mask: The stronger the mask, the more the neural activity was reduced (see Del Cul et al., 2007, for comparable findings). This reduction was correlated with a decrease in detection behavior and was mostly effected with LZP, stressing the importance of this activity in visual awareness. Previous studies have also demonstrated that this activity correlated with perception and detection performance (Koivisto & Revonsuo, 2010; Fahrenfort et al., 2008). Furthermore, it seems in line with studies showing contextual modulation in this time frame in V1 and higher areas possible due to recurrent processing (Lamme et al., 1992, 2002; Lamme, Zipser, & Spekreijse, 1998; Lamme, 1995). These recurrent processing loops in the visual cortex seem to serve integration of information from distant receptive fields and provide perceptual organization.

The observed late positive neural activity (297–387 msec) has also been found in other studies on visual awareness and might be involved in the transition of visual perception to a reportable stage (Lamy, Salti, & Bar-Haim, 2009; Del Cul et al., 2007; Sergent, Baillet, & Dehaene, 2005). However, in this study, it did not correlate with stimulus visibility and was less affected by LZP. Therefore, it might reflect more higher-level cognitive processes (Donchin & Coles, 1988), either decision-related processes (Koivisto & Revonsuo, 2010; Eimer & Mazza, 2005; Nieuwenhuis, Aston-Jones, & Cohen, 2005) or processes related to nonspatial attention (Koivisto & Revonsuo, 2010; Boehler et al., 2008).

To our knowledge, this is the first study to show that LZP affects neural activity in a specific way in that it has a selective effect on late activity and not on the early activity of the ERP, that is, on figure-ground selective signals and mainly in the 156–211 msec range and thereby reducing conscious content. Similar results have been observed in studies that affected conscious level using anesthesia. For example, in a study where monkeys were anesthetized with isoflurane, an anesthetic that binds to NMDA, GABA, and glycine receptors, while activity in the primary visual cortex (V1) was simultaneously recorded. Anesthesia did not reduce early feedforward activation of V1 receptive fields; orientation selectivity of cells was not affected. What was abolished were the later recurrent interactions between V1 and higher-level visual areas (Lamme et al., 1998). In another study with anesthetized rats, a selective reduction of synchronization in the long-range anterior–posterior coherence was observed, whereas the local anterior coherence was not affected (Imas, Ropella, Wood, & Hudetz, 2006). Furthermore, a breakdown of cortical effective connectivity was found in humans when loss of consciousness was induced with midazolam, also a GABAA receptor agonist (Ferrarelli et al., 2010). Our results thus add that apart from manipulating conscious level, a pharmacological intervention can also influence conscious content.

Behavioral effects of LZP on visual processing have been observed previously (Lorenceau, Giersch, & Seriès, 2005; Giersch & Herzog, 2004; Beckers, Wagemans, Boucart, &
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