The neurochemical correlate of consciousness: exploring neurotransmitter systems underlying conscious vision

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Citation for published version (APA):

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Chapter 3. GABA concentration in visual cortex predicts dynamics of bistable perception

Sometimes, perception fluctuates spontaneously between two distinct interpretations of a constant sensory input. These “bistable” perceptual phenomena provide a unique window into the neural mechanisms that create the contents of conscious perception. Models of bistable perception posit that mutual inhibition between stimulus-selective neural populations in visual cortex plays a key role in these spontaneous perceptual fluctuations. However, a link between neural inhibition and bistable perception has not yet been established experimentally. We relate perceptual dynamics in three distinct bistable visual illusions (binocular rivalry, motion-induced blindness and structure from motion) to measurements of gamma-aminobutyric acid (GABA) concentrations in human visual cortex (as measured with magnetic resonance spectroscopy). As predicted by a model of neural interactions underlying bistability, higher GABA concentrations in visual cortex were correlated with longer percept durations in all three illusions. Thus we show that GABA, the main inhibitory neurotransmitter, shapes the dynamics of bistable perception. These results pave the way for future studies into the competitive neural interactions across the visual cortical hierarchy that elicit conscious perception.

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Introduction
One of the most fruitful approaches to studying the neural mechanisms underlying consciousness is through manipulating visual awareness and studying the effect of these manipulations on visual processing. A number of tasks can be used to this end, but a specific class of stimuli called “bistable” perceptual phenomena (Leopold & Logothetis, 1999) are particularly elegant because they induce switches in visual awareness while physical stimulation remains constant. These phenomena contain ambiguous sensory information that induces competition between conflicting interpretations, causing conscious perception to spontaneously switch between rivaling percepts. These ambiguous stimuli therefore allow neural events that correlate with consciousness to be isolated from the constant visual input, with the goal of understanding the precise conditions that give rise to consciousness.

Previous studies have demonstrated the involvement of both lower-level and higher-level areas in bistable perception, for example, with binocular rivalry (BR). BR occurs when the eyes are presented with monocular stimuli using a stereoscope or anaglyph glasses: this causes conscious perception to alternate between the monocular images, as opposed to become an integration of the information from each eye. During BR activity at primary visual areas (including retinotopic visual cortex and lateral geniculate nucleus) partially reflects the currently dominant percept (Haynes & Rees, 2005; Logothetis, Leopold, & Sheinberg, 1996; Polonsky, Blake, Braun, & Heeger, 2000), suggesting a local locus. Yet, higher brain regions, such as the right superior parietal lobe (rSPL), show activity which correlates with perceptual switches (Kanai, Carmel, Bahrami, & Rees, 2011; Lumer, 1998). Others have suggested also the involvement of parietal and frontal cortex in bistable perception, but the nature of the role of these areas in the perceptual dynamics is under debate (Knappen, et al., 2011; Sterzer & Kleinschmidt, 2007). Another intriguing bistable phenomenon is motion-induced blindness (MIB). MIB occurs when one or more salient, fixed target(s) are surrounded by a pattern with global movement: this causes the target(s) to disappear from consciousness for periods of up to a few seconds at a time (Bonnehe, Cooperman, & Sagi, 2001). An fMRI study demonstrated that the target and mask are processed by separate pathways during MIB, with subjective disappearances of the target correlating in opposite directions to modulations of activity in each pathway (Donner, et al., 2008). This suggests that an interaction between multiple processing pathways, at different levels, is necessary to account for the properties of bistable perception. Furthermore, several models postulate that these bistable perceptual dynamics result from reciprocal inhibitory interactions between stimulus-selective neural populations (Blake, 1989; Blake & Logothetis, 2002; Hering, 1964; Lehky, 1988; Noest, et al., 2007).

If this is true, one may expect a central involvement of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) in bistable perception. Therefore, as a proxy of cortical inhibition, we measured GABA concentrations in human participants by means of magnetic resonance spectroscopy (MRS). With MRS it is possible to measure neurotransmitter concentrations in vivo. Previous research has demonstrated that there are consistent relationships between GABA concentration in visual cortical areas and performance on visual tasks involving inhibition. These studies have found that when inhibitory activity impedes target processing, reduced GABA levels improve task performance. On the other hand,
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when inhibitory activity facilitates target processing, reduced GABA levels impair
task performance (Edden, et al., 2009; Yoon, et al., 2010).

We measured from a region encompassing retinotopic visual cortex (calcarine
sulcus) which has been shown to modulate during perceptual alternations in BR,
Tong & Engel, 2001). We also measured from a high-level area in the right
dorsolateral prefrontal cortex (rDLPFC), which is thought to be involved in bistable
perception (Knappen, et al., 2011; Sterzer & Kleinschmidt, 2007). We used a
computational model of perceptual bistability (Noest, et al., 2007) to derive specific
predictions about the effect of GABAergic inhibition on the perceptual dynamics.

Methods

Participants

Eighteen participants (all males) reporting no history of psychiatric or neurological
afflictions participated in the MRS visual illusion experiment. Female participants
were excluded from our MRS sample, as cortical GABA levels vary during the
menstrual cycle (Epperson, et al., 2002). All participants had normal or corrected-to-
normal vision, and normal color perception. They gave written informed consent.
Four participants were excluded from the analysis due to low signal to noise ratio in
the MRS signal. All MRS analyses are based on the remaining fourteen participants
($M = 22.71$ years of age, $SD = 1.52$ years). The experiment was approved by the
Psychology Department’s ethical committee at the University of Amsterdam.

Stimuli and Perceptual Tasks

Binocular Rivalry

The BR stimulus consisted of a superimposed orthogonal red-green grating (Figure
3.1A), modified from a stimulus used previously (Knappen, et al., 2011). The stimulus
rotated in a clockwise direction around a small yellow central fixation point at a
speed of 1 Hz. Participants wore anaglyph glasses which filtered the superimposed
stimulus so that each eye was presented a monocural grating (i.e., each eye viewed a
grating orthogonal in orientation and opposite in color). Participants indicated their
percept through pressing and releasing the mouse buttons (left for green; right for
red; no button while the grating was a mixture of red and green). The mean and
median percept duration of the dominant percepts were calculated to capture the
BR dynamics.

Motion-induced Blindness

The MIB stimulus consisted of two yellow target dots presented on a moving mask of
blue crosses (Figure 3.1B) on a black background, slightly modified from stimuli used
in a previous study (Donner, et al., 2008). The target dots had a visual angle of 0.5°,
and subtended 2.5° of visual angle to the left and right of a small red central fixation
point. The mask was a square grid which measured 17° of visual angle in width and
length that subtended 3.6° of visual angle and rotated around its center at a speed
of 1 Hz. The direction of rotation was reversed after each block. To minimize effects
of lateral masking and thus ensure pure MIB effects in driving target disappearance,
the target was separated from the mask by a “protection zone” subtending about 2°
around the target. Participants indicated their perception of each target separately,
with the left and right target mapped onto corresponding mouse buttons (pressing a button indicated target disappearance; releasing indicated reappearance). In this way perceptual dynamics were recorded separately for each target. The dynamics of MIB were quantified by means of two different measures: rate and duration. Rate was computed as the number of target disappearances per minute (“switch rate”). MIB duration was computed as the mean and median duration of all target disappearances (“invisible duration”) and reappearances (“visible duration”). Subsequently, the switch rate, mean and median percept durations of the two separate targets were averaged.

Structure from Motion

The SFM stimulus was a rotating sphere (sphere size 4.5 degree) that consisted of 1850 black and white dots (dot size 0.011 degree) presented on a mean-luminance grey background, as used previously (de Jong, Knapen, & van Ee, 2012) (Figure 3.1C). A green fixation dot was presented in the center of the sphere. The sphere rotated 80 degrees per second and this rotation could either be perceived as clockwise (CW) or counterclockwise (CCW). Participants acted as passive observers, indicating spontaneous shifts in their perception by pressing and releasing mouse buttons (left for CW; right for CCW; no button when the direction was unclear). This condition will be referred to as “SFM Spontaneous”. On even-numbered blocks, participants were instructed (except for two) to actively accelerate the alternations of perception (“SFM Accelerated”). To provide a more robust measure of the participant’s perceptual dynamics, we initially combined the data from both these conditions, yet also looked at the two conditions separately. To capture the SFM dynamics, we calculated the mean and median percept duration of the dominant percepts.

![Figure 3.1. Bistable visual illusions](image)

(A) Binocular rivalry (BR): Differences between the eyes’ images cause observers to alternately perceive the left and right eye’s images. (B) Motion-induced blindness (MIB): A moving mask of blue crosses causes the highly salient yellow targets to transiently disappear from awareness. (C) Structure from motion (SFM): A rotating dotted sphere that can be perceived to rotate clockwise (CW) or counterclockwise (CCW) and causes spontaneous switches in perceived rotation direction.

Reaction Time Task

As a control task, we measured in a separate session reaction times (RT) with a computerized adjusted version of the Hick paradigm (Jensen, 1987). In the task one square was presented on the computer screen. After a jittered interval between 700 ms and 2000 ms (with steps of 100 ms) a plus sign appeared in the square. Subsequent to appearance of the cue (plus sign), participants had to react as quickly
as possible by pressing a button on a standard keyboard with the index finger of the dominant hand. When participants failed to make a response within the response time period of 1200 ms, a feedback screen was shown for 500 ms with the text “you did not press”. Then a blank, inter-stimulus screen was shown for 1500 ms, whereafter the next trial started again with an empty square. Participants were instructed and motivated by the experimenters to react as fast as possible.

Experimental Procedure
The experiment consisted of two sessions. At the start of the first session participants were screened and gave their written informed consent. In this first session the visual illusion were presented. The BR and MIB illusion were presented in five 90-seconds blocks and the SFM illusion in ten 90-seconds blocks with short breaks in between. The stimuli were displayed on a 60 Hz, 32-bit Iiyama Vision Master Pro 450 CRT monitor with a resolution of 1024 x 768 pixels, using Presentation (Neurobehavioral Systems, Inc, Albany, CA, USA), viewed at a distance of 100 cm. The order of presentation of the illusions was counterbalanced across participants. Participants were explicitly instructed to keep their gaze at fixation while attending to the illusions.

During a second session, which was between 1-2 months after the first session, a 3 Tesla Philips Achieva MRI scanner (Phillips Healthcare, Best, Netherlands) with an eight-channel headcoil was used to collect MRS measurements for each participant. A three-dimensional (3D) turbo field echo acquisition (number of slices = 150; slice thickness = 1 mm; repetition time (TR) = 8.2 ms; echo time (TE) = 3.8 ms; field of view = 256 x 256 x 160 mm; matrix size = 256 x 256; voxel resolution: 1 x 1 x 1 mm) was used to place the spectroscopy voxels according to the individual’s anatomical landmarks. The visual cortex (VC) voxel had a volume of 30 x 25 x 20 mm, and was centered bilaterally on the calcarine sulcus (Figure 3.2A). The right dorsolateral prefrontal cortex (rDLPFC) voxel had a volume of 30 x 20 x 25 mm. The center was placed on the middle frontal gyrus with the posterior border of the voxel anterior to precentral sulcus (Figure 3.2A). Voxels were placed with care to exclude cerebral spinal fluid (CSF) from the ventricles or the cortical surface.

Edited 1H J-difference spectra were acquired for each voxel using a GABA-specific sequence of the MEGA-PRESS method (Waddell, Avison, Joers, & Gore, 2007). Scanning each voxel took approximately 12 minutes, during which time 384 transients were collected from each voxel; TE = 73 ms; TR = 2000 ms. During the odd transients, a 15.64 ms sinc-center editing pulse (64 Hz FWHM) was applied at 1.9 ppm and 4.6 ppm in an interleaved manner, to specifically excite GABA and suppress water, respectively. During the MRS scan, participants viewed the same section of a movie without audio. The total MRS acquisition lasted approximately 1 hour.

Quantification of GABA
The MRS measurements allowed us to quantify the concentration of GABA and Glx (combined signal of glutamate and glutamine) from the VC and rDLPFC. The even and the J-difference (odd-even) acquisitions were analyzed with the linear combination (LC) Model (Provencher, 2001). Total creatine (tCr) and N-acetyl-aspartate (NAA) were quantified from the even acquisitions, while GABA, Glx and again NAA were quantified from the difference acquisitions (Figure 3.2B). GABA and
Glx were normalized to the difference spectra NAA, while the even spectra NAA was normalized to tCr. This procedure calibrated signal amplitude across even and difference acquisitions within each subject, enabling GABA and Glx concentrations to be expressed in units of tCr (Waddell, et al., 2007; Waddell, et al., 2011). The GABA and Glx concentrations were corrected for the proportion of grey matter volume within each voxel, using FAST segmentations from the FSL toolbox (Smith, et al., 2004).

**Figure 3.2 Spectroscopy details**

(A) MRS voxel locations: visual cortex voxel (VC) and right dorsolateral prefrontal cortex (rDLPFC) voxel. (B) Example spectrograph output for the even and difference acquisitions from the VC voxel.

**Statistical Analysis**

Percept durations shorter than 200 ms were removed from analysis. Visual GABA concentrations were correlated with mean and median percept durations for three illusions using non-parametric Spearman rank correlations. Since GABA and Glx concentrations correlated within the rDLPFC voxel (Rho = 0.697, p = 0.006) and not in the VC voxel, we ran partial correlations to isolate the unique contribution of each neurotransmitter within the rDLPFC (Jocham, Hunt, Near, & Behrens, 2012). Permutation tests were conducted with 10,000 iterations to test these correlations for significance. Our computational model provided specific predictions for the direction of the effects (Figure 3.3). Therefore, all reported analyses regarding the GABA concentration were tested one-sided.

**Neural Model**

We implemented a neural model of bistability (Noest, et al., 2007), in which both adaptation and inhibition govern the activity dynamics of two interacting visual cell assemblies (see Figure 3.3A). The model consisted of two populations of neurons ($X_1$ and $X_2$), which were driven by two distinct stimulus components of constant strength ($I_1$ and $I_2$), and competed by mutual inhibition ($\gamma$). These two populations of neurons had intrinsic dynamics due to slow adaptation and stochastic variability (“noise”), governed by the following pair of differential equations:

$$\tau \frac{dX_1}{dt} = I_1 - (1 + A_1)X_1 - \gamma S[X_2] + N(0, \sigma_{x1})$$

$$\tau \frac{dX_2}{dt} = I_2 - (1 + A_2)X_2 - \gamma S[X_1] + N(0, \sigma_{x2})$$
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where \( S[X_i] \) corresponds to a sigmoidal transformation (using a Naka-Rushton function) of the “local fields” described by \( X_i \) (Noest, et al., 2007), \( N \) corresponds to normally distributed noise, and \( A_i \) describes adaptation. The adaptation dynamics is given by:

\[
\tau_A \frac{\partial A_i}{\partial t} = -A_i + \alpha S[X_i]
\]

Simulating this model with continuous inputs \( X_1 \) and \( X_2 \) yielded spontaneous fluctuations in the activity of \( X_1 \) and \( X_2 \), which, in turn, produced spontaneous alternations between dominance of the two populations of visual cortical neurons.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \tau )</td>
<td>Timescale of X population activities</td>
<td>1.0</td>
</tr>
<tr>
<td>( \tau_A )</td>
<td>Timescale of adaptation</td>
<td>125.0</td>
</tr>
<tr>
<td>( \alpha )</td>
<td>Gain of Adaptation</td>
<td>4.0</td>
</tr>
<tr>
<td>( \gamma )</td>
<td>Inhibition Gain</td>
<td>3.0 [2.6, 3.4]</td>
</tr>
<tr>
<td>( \sigma_{X_1, X_2} )</td>
<td>Standard deviation of noise in X-popolations</td>
<td>0.003, [0.0, 0.015]</td>
</tr>
<tr>
<td>( X_1, X_2 )</td>
<td>Input strength</td>
<td>1.0, [0.95, 1.05]</td>
</tr>
</tbody>
</table>

Table 3.1 Model parameters used in simulations.

Numbers are the parameters used for simulations reported in this paper. Numbers in parentheses indicate the range of parameters used.

Simulations were run using a fixed step size integration procedure implemented in the gnu scientific library, and were run in python, see Figure 3.3BC.

Results

Model Simulations

Our model simulations show that stronger cortical inhibition (likely mediated by GABA\(_A\) receptors in the cortex) should slow down perceptual dynamics, that is, induce longer durations of individual percepts and fewer alternations between distinct percepts (Figure 3.3BC).

Figure 3.3. Neural computational model

(A) Neural computational model of bistability as reciprocal inhibition between competing visual cell assemblies (Noest, et al., 2007). (B) Simulations of the computational model with different levels of the inhibition. Percept durations increase and alternation rate decreases with stronger inhibition. (C) Cumulative percept duration histograms of model simulations for different levels of inhibition strength.
**GABA Concentration**

We observed significant correlations between GABA levels in the visual cortex and the dynamics of bistable perceptual phenomena in all three illusions. In line with the model predictions (Figure 3.3), observers with higher GABA concentrations in visual cortex experienced slower perceptual dynamics (Figure 3.4 and Table 3.2). Specifically, positive correlations are observed between GABA concentrations in visual cortex and the mean and median percept (invisible) durations for all three illusions. For MIB we do not observe a correlation between GABA and visible duration or disappearance rate, but only find a positive correlation between invisible duration and visual GABA (see Discussion).

![Figure 3.4. Correlations between percept duration and GABA concentration in visual cortex](image)

Higher GABA concentrations in visual cortex correlated with longer mean percept duration for BR, mean invisible duration for MIB and mean percept duration for SFM (Combined for Spontaneous and Accelerated condition). *p < .05, **p < .01.

However, top-down influences from high-level cortex on sensory areas may play an important role in bistable perception dynamics (Leopold & Logothetis, 1999; Sterzer & Kleinschmidt, 2007). Therefore we instructed our participants to attempt to actively control their percept duration of one of the illusions, SFM (Figure 3.1C), by trying to increase the rate of perceptual changes. Human observers are capable of voluntarily controlling their perception even without resorting to eye movements (Brouwer & van Ee, 2006). Also in our experiment, participants were able to accelerate their percept: percept durations were shorter than during spontaneous perceptual switches ($t_{(15)} = 3.39, p < .001$) (see Figure 3.5).

![Figure 3.5. SFM Spontaneous and Accelerated median percept durations](image)

Participants were able to accelerate their percept durations in the SFM Accelerated condition compared to the SFM spontaneous condition. Error bars indicate SEs **p < .01.
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When we then looked at the relationship with visual GABA, only the percept durations of the SFM Spontaneous condition correlated significantly with the visual GABA concentrations. The accelerated perceptual durations did not exhibit a significant positive correlation with GABA in either visual cortex or rDLPFC. For BR and MIB there were also no significant correlations for GABA in the rDLPFC. This highlights the specificity of the correlations found in visual cortex (see Table 3.2).

<table>
<thead>
<tr>
<th></th>
<th>VC</th>
<th>rDLPFC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GABA</td>
<td>Glx</td>
</tr>
<tr>
<td></td>
<td>Rho</td>
<td>P</td>
</tr>
<tr>
<td>BR Median</td>
<td>0.506</td>
<td>0.021</td>
</tr>
<tr>
<td>Mean</td>
<td>0.508</td>
<td>0.027</td>
</tr>
<tr>
<td>SFM Median</td>
<td>0.636</td>
<td>0.006</td>
</tr>
<tr>
<td>Mean</td>
<td>0.636</td>
<td>0.006</td>
</tr>
<tr>
<td>Sponta. Mean</td>
<td>0.569</td>
<td>0.034</td>
</tr>
<tr>
<td>SFM Median</td>
<td>0.486</td>
<td>0.078</td>
</tr>
<tr>
<td>SFM Mean</td>
<td>0.301</td>
<td>0.342</td>
</tr>
<tr>
<td>Accel. Median</td>
<td>0.322</td>
<td>0.308</td>
</tr>
<tr>
<td>MIB Mean</td>
<td>0.526</td>
<td>0.022</td>
</tr>
<tr>
<td>Invisible Median</td>
<td>0.451</td>
<td>0.039</td>
</tr>
<tr>
<td>MIB Mean</td>
<td>-0.169</td>
<td>0.587</td>
</tr>
<tr>
<td>Visible Median</td>
<td>-0.031</td>
<td>0.925</td>
</tr>
<tr>
<td>MIB Rate</td>
<td>-0.167</td>
<td>0.712</td>
</tr>
</tbody>
</table>

Table 3.2. Spearman Rank correlations
Spearman Rank correlations for all three illusions with GABA and Glx in visual cortex (VC) and right dorsolateral prefrontal cortex (rDLPFC). Significance was assessed with permutation testing, 10,000 iterations.

**Glx Concentration**
To further assess the specificity of our GABA results, we also measured “Glx”: the combined concentration of glutamate and glutamine, a metabolite of glutamate. We found a significant negative correlation between visual Glx and SFM mean duration, but only when the Spontaneous and Accelerated conditions were combined. Visual Glx did not correlate for the two conditions separate or with the other two bistable phenomena (see Table 3.2). We did observe positive correlations with Glx in rDLPFC in that MIB visible durations correlated positively with Glx. It could be that visible durations depend on top-down processes, in that more excitation in the rDLPFC could induce longer visible durations, reflected in a positive correlation (see Discussion).

**Reaction Time**
To assess the specificity of our GABA results, we measured reaction times (RT) with a computerized adjusted version of the Hick paradigm. We then calculated the Spearman rank correlation between the mean RT and visual GABA concentrations. As depicted in Figure 3.6, we did not observe a significant correlation (Rho = 0.042, p
= 0.887), suggesting that the observed correlations between GABA and perceptual dynamics are specific.

**Figure 3.6. Reaction time (RT) control experiment**

No correlation between visual GABA concentration and reaction times in the Hick paradigm.

**Discussion**

Here we show that GABA, the main inhibitory neurotransmitter, shapes the dynamics of conscious perception during perceptual bistability. As predicted by a computational model of the neural interactions underlying bistable perception, we demonstrate that higher GABA concentrations in visual cortex predict slower dynamics in perceptual bistability. Taken together, our results provide strong support for the mutual inhibition account of perceptual bistability (Blake, 1989; Blake & Logothetis, 2002; Hering, 1964; Lehky, 1988; Noest, et al., 2007).

GABA mediated inhibition is a generic property of cortical circuits, and many perceptual phenomena involve interactions between populations of excitatory and inhibitory neurons in the visual cortex (Carandini & Heeger, 2011; Moreno-Bote, Rinzel, & Rubin, 2007; Shapley, Hawken, & Ringach, 2003). Therefore, such a general role of visual cortical GABA concentration in different perceptual phenomena would be expected. However, MRS measurements do not distinguish between pre- or post-synaptic GABA, and the concentration is extracted from a relative large voxel. Therefore, whether the measured GABA concentrations reflect inhibitory network properties could still be questionable. Yet, recent studies have found MRS-measured GABA concentrations to be strongly correlated to the evoked response of the same region, suggesting that MRS measurements do reflect network properties. (Muthukumaraswamy, Edden, Jones, Swettenham, & Singh, 2009; Muthukumaraswamy, Evans, Edden, Wise, & Singh, 2012). Additionally, the present results are consistent with previous MRS studies that link visual GABA concentrations to performance on visual tasks that depend on inhibition such as orientation discrimination (Edden et al., 2009) and orientation-surround suppression (Yoon et al., 2010).

Different bistable illusions have many similarities in terms of their perceptual dynamics (Brascamp, van Ee, Noest, Jacobs, & van den Berg, 2006; Carter & Pettigrew, 2003; Klink, van Ee, & van Wezel, 2008). These similarities have prompted the assumption that they depend on common shared underlying mechanisms (Carter & Pettigrew, 2003; Leopold & Logothetis, 1999). The present results suggest
that the dependence on GABAergic inhibition in visual cortex may be this generic mechanism.

Interestingly, in MIB, we only observed a correlation between visual GABA and invisible duration; we did not find this for disappearance rate and visible duration. But, in MIB, the rate of perceptual fluctuations depends on both visible and invisible durations. Hence, invisible duration and disappearance rate are not necessarily anti-correlated due to the presence of this third parameter, the target-visible duration, which may decouple the first two (Donner, et al., 2013). In terms of underlying neural interactions; these different parameters (rate, visible and invisible duration) seem to be governed by neural interactions at different levels of the visual cortical hierarchy (V1-V3 vs. V4) (Donner, et al., 2013), and our visual MRS voxel captured mainly V1 and is unlikely to have sampled V4 GABA concentrations. Similarly, for SFM we found that V1 GABA mainly correlated with spontaneous percept dynamics and not with the accelerated percepts. Apparently, observers are able to influence perceptual dynamics through mechanisms that are not reflected by V1 GABA concentrations. Further research, using smaller MRS voxels to sample different levels in the visual hierarchy or a pharmacological manipulation of GABAergic processing (see Chapter 4) is necessary to further elucidate the relationship between bistable perception and GABA.

Moreover, only visible duration correlated with Glx in rDLPFC, suggesting that visible durations might depend on top-down processes. But caution should be taken with interpreting these results since it is not possible to disentangle the glutamate from glutamine at 3 Tesla, and therefore the Glx reflects a combined signal of these two compounds. Furthermore, it is unclear whether correlations between Glx and behavior rest on faster AMPA or slower NMDA functioning. Further research could address this question on the involvement of Glutamate in bistable perception using pharmacological glutamate manipulations of either AMPA and / or NMDA receptors.

Evidence suggests that higher-level cortical association areas, such as posterior parietal cortex and frontal areas also play a role in bistable perception. The nature of the role of these areas in the perceptual dynamics is under debate (Knapen, et al., 2011; Sterzer & Kleinschmidt, 2007). Frontal cortex could be involved in ways that are not expressed in GABA concentration. For instance, it might send excitatory (glutamatergic) feedback signals during bistable perception, which, in turn, bias the ongoing competition in visual cortex (Desimone & Duncan, 1995; Miller & Cohen, 2001), perhaps in concert with ascending neuromodulatory systems (Harris & Thiele, 2011). Regarding the role of parietal areas in bistable perception, continuous theta burst stimulation (cTBS) applied to the posterior intraparietal sulcus leads to longer percept durations in the SFM illusion (Kanai, et al., 2011). Interestingly, independent findings show that cTBS increases GABA concentrations (Stagg, et al., 2009).

In summary, our MRS results link individual differences in the dynamics of conscious perception to the neurotransmitter systems that underlie these processes. Our results open new lines for further research into the relationship between neurotransmitter systems and the dynamics of conscious perception.