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**Negative bias of processing ambiguously cued emotional stimuli**

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## **Abstract**

We daily cope with upcoming potentially disadvantageous events. Therefore, it makes sense to be prepared for the worst case. Such 'pessimistic' bias should be reflected in brain activation during emotion processing. Healthy subjects underwent functional neuroimaging while viewing emotional stimuli that prior were cued ambiguously or unambiguously concerning their emotional valence. Presentation of ambiguously announced pleasant pictures compared to *unambiguously* announced pleasant pictures resulted in increased activity in ventrolateral prefrontal, premotor and temporal cortex, and in caudate nucleus. This was not the case for the respective negative conditions. This indicates that pleasant stimuli after ambiguous cueing provided 'unexpected' emotional input, resulting in adaptation of brain activity. It strengthens the hypothesis of a 'pessimistic' bias of brain activation towards ambiguous emotional events.

*Key words: fMRI, emotion, ambiguous anticipation*

## **Introduction**

The emotional valence of an expected event provides the basis on which our brain develops behavioural strategies for quick and efficient adaptation to new circumstances. In everyday life we are often uncertain whether a future event will be pleasant or unpleasant. We then prepare ourselves mentally for the possible outcomes. From an evolutionary perspective, it is conceivable that we have come to prepare for, and thus cope better with, a potentially threatening environment by anticipating the worst case [1]. Thus, one may assume a negative or 'pessimistic' bias of anticipating an event of ambiguous emotional valence as reported earlier for the expectation period [2]. On the other hand, optimistic biases towards the general personal future were reported [3]. For currently faced events with ambiguous emotional impact, either positive or negative, we hypothesized a negative/'pessimistic' bias. In that case, presenting negative stimuli after an ambiguous anticipation period should not serve as relevant new information. Thus, we expected no relevant emotion specific cerebral activity changes compared to a condition of being prepared for a negative event known to be so, because the negative picture presentation just would confirm the negative presetting. On the other hand, a positive event occurring after ambiguously cued expectation of an emotional event should cause a mismatch between the hypothesized negatively biased anticipation and the pleasant presentation. Accordingly, in that case we expected activation in structures involved in emotion processing, mismatch detection and behaviour planning, because a 'remodelling' of the negative emotional presetting would have to take place. To test the hypothesis of a negative biased processing of ambiguous emotional impact, we applied an experiment in the context of functional magnetic resonance imaging (fMRI) measurements in which a visual cue signalled forthcoming emotional stimuli. Subjects were instructed to expect and then to perceive visual stimuli with prior unambiguous (pleasant, unpleasant/negative, neutral) or ambiguous (either unpleasant or pleasant) emotional valence. We compared brain activity during the presentation of pictures with the same valence (unpleasant and pleasant) after an ambiguous versus an explicitly pre-cued unambiguous anticipation period.

## **Materials and Methods**

### *Subjects and experimental design*

Sixteen healthy subjects (mean age 27.6 years, standard deviation 3.6, right-handed, 8 female) performed an emotion expectation task while being scanned with fMRI. The study was approved by the local ethics committee. The task comprised 56 trials in which emotional pictures were expected and then presented (fig. 1). The trials consisted of two main conditions: unambiguously and ambiguously announced emotional pictures.. For each trial of the unambiguously announced condition a small cue was presented depicting either a smiling ‘∪’ (‘pleasant’ (ps)), a non-smiling ‘∩’ (‘negative’ (ng) or ‘unpleasant’), or a neutral (nt) ‘-’ symbol and indicating the emotional valence of the pictures presented after a delay period. In the ambiguously announced condition (amb) ‘|’, either pleasant or unpleasant pictures appeared randomly. The cues were presented for 1000 ms followed by an anticipation period of 6920 ms (cue and anticipation together 7920 ms = 4 TRs; repetition time), during which a blank screen with a small fixation point was shown. Subsequently, emotional pictures of the International Affective Picture System (IAPS, [4]) were presented for 7920 ms (4 TRs). A baseline of 15840 ms (8 TRs) followed to allow the BOLD signal to level off before a new trial started. Altogether, 56 pre-cued pictures were shown in a randomized order, 14 for each condition: unambiguous positive, negative, neutral and ambiguous (7 positive and 7 negative). The subjects were instructed to expect the emotional stimuli after the cue and to be aware of the emotional valence signaled, and to subsequently look at the following picture. The stimuli were matched for complexity, content of faces, scenery, food and nature, and concerning intensity of positive and negative valence with the same difference in valence ratings from neutral [2]. The task was programmed with Presentation<sup>TM</sup> (Neurobehavioral Systems, USA).

### *fMRI acquisition and data analysis*

Imaging was performed with a 1.5 Tesla Siemens Sonata whole-body scanner (Erlangen, Germany) equipped with a head coil. The detailed general imaging parameters and the basic standard fMRI preprocessing procedures using BrainVoyager<sup>TM</sup> QX 1.10.1 (Brain Innovation, Maastricht, The

Netherlands) were reported in [2]. Nine predictors were used to build the design matrix of the experiment: four for the expectation (exp) conditions ng, ps, nt, amb, and five for the presentation (pres) conditions ng after ng exp, ng after amb exp, ps after ps exp, ps after amb exp, nt after nt exp. Expectation periods and picture presentation periods were modeled as epochs using the standard two-gamma hemodynamic response function. Three-dimensional statistical parametric maps were calculated for the groups with separate subject predictors using a general linear model and a random effects analysis (rfx). We used a cluster threshold of 135 voxel à 1×1×1 mm, for the analysis, corresponding to 5 voxel à 3×3×3 mm and set  $p < 0.005$ .

We examined whether brain areas react differentially to the presentation of positive or negative pictures depending on whether the pictures were *ambiguously* or *unambiguously* announced. We calculated the following contrasts in order to test our hypothesis that only the perception of ambiguously cued positive pictures requires additional brain processes in order to adapt to the new (better than expected) situation:

i. [Presentation of *positive* pictures after an ambiguous announcing cue] versus [*positive* pictures after unambiguous positive cue]; briefly: ([pres-amb-ps > pres-ps-ps]);

versus

ii. [Presentation of *negative* pictures after ambiguous announcing cue] versus [*negative* pictures after unambiguous *negative* cue]; briefly ([pres-amb-ng > pres-ng-ng]).

The comparison between i. and ii. represented the main analysis ([pres-amb-ps > pres-ps-ps]  $\diamond$  [pres-amb-ng > pres-ng-ng]).

The regions revealed with the first contrast (i.) were regarded exploratory and reported in the supplemental digital content (SDC) if complying with the hypothesized functions and if not being activated in the second contrast (ii.).

Furthermore, we calculated a conjunction analysis in order to reveal brain regions that are important for the adaptation process after an ambiguous announcing cue for both emotional valences (positive and negative):

iii. [Presentation of *positive* pictures after an ambiguous announcing cue] versus [*positive* pictures after *unambiguous* positive cue] AND [Presentation of *negative* pictures after ambiguous

announcing cue] versus [*negative* pictures after *unambiguously negative* cue]; briefly: ([pres-amb-ps > pres-ps-ps]  $\cap$  [pres-amb-ng > pres-ng-ng]).

The identification of the anatomical regions was based on the Talairach and Tournoux system [5]. An analysis restricted to the expectation period was reported earlier [2].

## Results

Fourteen of sixteen subjects were included in the analysis. Two subjects were excluded because of drowsiness in the scanner and a lack of concentration.

Aiming to identify those regions with a differing activity during the perception of ambiguously cued positive pictures in comparison with ambiguously cued negative pictures (contrasting i. minus ii.) revealed increased activity in the right ventrolateral prefrontal cortex (VLPFC; fig 2a), the right premotor cortex (PMC; fig 2b), the caudate/hippocampus and the middle temporal gyrus (MTG) in both hemispheres, the right precuneus, the left gyrus lingualis, and the left putamen (tab. 1). Calculating the reversed contrast (ii. minus i), for identifying regions reacting differentially to ambiguously announced negative pictures revealed no increased activity in any brain region.

The conjunction analysis aimed at uncovering those regions differing in activity dependent on whether positive and negative pictures were ambiguously or unambiguously cued (contrast iii.;  $p < 0.005$ ) revealed no activity in any brain region.

An exploratory analysis to uncover those regions which differ in activity dependent on whether positive pictures were ambiguously or unambiguously cued (contrast i., table S1 (SDC 1)) revealed activation in the anterior cingulate cortex (ACC, figure S1 (SDC 2)) and the dorsolateral prefrontal cortex (DLPFC; figure S2 (SDC 2)), which was not the case for the perception of ambiguously announced negative pictures (contrast ii.).

## Discussion

Perceiving ambiguously cued positive pictures in comparison with *unambiguously* cued positive pictures resulted in prominent changes in various hypothesized brain areas. In contrast, perceiving ambiguously cued negative pictures in comparison with *unambiguously* cued negative pictures did not

change brain activation. This implicates that in case of ambiguity, the positive valence of the pictures may have meant ‘unexpected’ information, which was not prepared for and onto which brain activation then had to adapt. On the other hand, the negative stimuli appeared to be ‘expected’ as no adaptive brain activity occurred. That provides neurobiological evidence for a ‘pessimistic’ bias in brain activation in response to events with ambiguous emotional impact, implicating that ambiguous expectation is associated with a preparation for the worse case [6].

The presentation of ambiguously announced positive pictures lead to brain activity changes in the VLPFC, a central region within emotion processing. The VLPFC was earlier reported to be involved in the integration of cognitive and emotional information [7], in processes of inner monitoring of emotions [8], in working memory [9,10], stimulus evaluation, and perceptual and conceptual processing [11]. These functions are reasonably involved in resetting a negative bias in order to deal with a positive event. Further, the mid-VLPFC, where the activity was observed here, is involved in active controlled judgments leading to the disambiguation of information in memory and perceptual processing [12]. Accordingly, one may interpret our finding in a way that the information provided with the pleasant pictures after ambiguous cueing could require more disambiguation than when being presented the negative pictures because these were implicitly expected. Further, we found bilateral activations in the MTG, which was earlier reported to be involved in higher order stimulus- and emotion-processing (e.g. [13,14]).

The PMC is involved in planning of voluntary motor action [15]. Hence, its involvement could be due to the hypothesized ‘remodelling’ of brain activity as potentially prepared motor reaction as ‘flight-or-fight-strategies’ have to be skipped with the appearance of an ‘unexpectedly’ positive picture. The same reason could explain the activation of the caudate, as part of the basal ganglia, showing visuomotor associations [16]. The caudate was shown to be part of dopamine-rich areas associated with reward and motivation [17], both functions that gain a new significance in case of the occurrence of a positive picture after a negatively biased ambiguous expectation. What is more, activity in the head of the caudate was shown to be linked to executive functions related to feedback receiving [18] and was associated with probabilistic classification [19], and information integration [20]. Taken together, the caudate may be involved in adapting brain activity when perceiving an



“unexpected” emotional event and in preparing the executive level in order to deal with the “new” circumstances.

When further regarding those regions with differing activity during the perception of ambiguously cued positive and negative pictures (in comparison with unambiguously cued positive and negative pictures; conjunction analysis), in order to reveal brain regions that are important for the adaptation process in general, we found no region to be activated, meaning that there are no common regions modulating the adaptation process regardless the emotional valence.

We expected an activation in the ACC, known for conflict monitoring and mismatch detection [21], or/and the DLPFC (executive functions and behaviour planning [22]). This was only the case when regarding those regions with differing activity during the perception of ambiguously cued positive pictures (in comparison with unambiguously cued positive pictures, see SDC); these regions were not activated in the respective negative condition, although the difference between both contrasts was not significant.

## **Conclusion**

Although subjects viewed pictures with the same positive emotional content, different activation patterns were observed dependent on whether the emotional valence was announced ambiguously or unambiguously. This presumably adaptive activation in case of ambiguity, not occurring with negative stimuli, confirms assumptions about a principal ‘pessimistic’ attitude towards upcoming events of ambiguous emotional impact for the individual.

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## Tables and Figures

**Table 1:** Activated regions in the contrast ‘presentation of positive pictures after ambiguous expectation versus positive pictures after unambiguous positive expectation’ compared with ‘presentation of negative pictures after ambiguous expectation versus negative pictures after unambiguous negative expectation’. Indicated are the cluster sizes in mm<sup>3</sup>, their central Talairach coordinates (x, y, z), and the maximal t-value of the voxels within each region. Abbreviations: R – right, L – left, VLPFC – ventrolateral prefrontal cortex, PMC – premotor cortex, TG – temporal gyrus.

**Figure 1:** Experimental task. The four conditions with the respective cues and the durations. Here, the cues are relatively enlarged for presentation reasons. In the experiment, they were about 1/40 of screen height.

**Figure 2:** Brain activation resulting from the contrast ‘presentation of *positive* pictures after *ambiguous (amb)* expectation versus *positive (ps)* pictures after *unambiguous positive* expectation’ compared with ‘presentation of *negative* pictures after *ambiguous* expectation versus *negative* pictures after *unambiguous negative* expectation’. The vertical gray bars represent the beginning of the expectation and presentation periods comprising each 4 volumes. Consider the time courses of BOLD signal changes showing differing activations in the presentation period of conditions with ambiguous (orange) and obvious positive cueing (yellow), despite both represented the perception of positive pictures: a) right (radiological convention) ventrolateral prefrontal cortex (VLPFC), b) right premotor cortex (PMC) and c) caudate body.

**Tables**

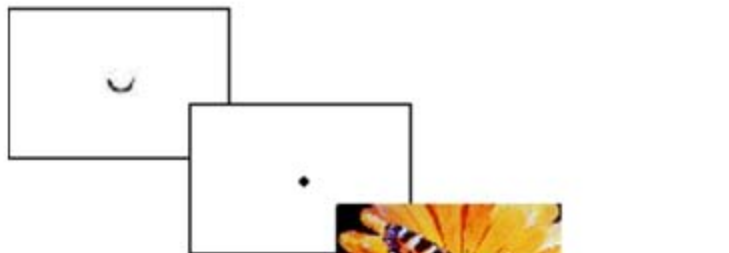
<b>Anatomical region</b>	<b>Brodmann Area (BA)</b>	<b>Voxel mm<sup>3</sup></b>	<b>Talairach coordinates .....x.....y.....z</b>			<b>t-max</b>
<b>(pres-amb-ps &gt; pres-ps-ps) &gt; (pres-amb-ng &gt; pres-ng-ng)</b>						
VLPFC R (fig. 2a)	45	635	49	19	9	4.89
PMC R (fig. 2b)	6	140	15	-10	55	5.26
Caudate L (fig. 2c)		198	-15	14	18	5.05
Hippocampus/Caudate Tail R		222	38	-26	-7	4.63
Putamen L		138	-25	-2	14	4.52
Middle TG R	37	850	49	-64	6	4.19
Middle TG R	22	278	49	-39	0	4.19
Middle TG L	37	163	-49	-64	9	4.17
Middle TG L	22	188	-61	-44	4	4.69
Precuneus R	31	580	13	-46	35	5.64
Gyrus lingualis L	18	723	-12	-77	4	6.18

Table 1

Supplemental Digital Content 1. doc

Supplemental Digital Content 2. tif

**positive**



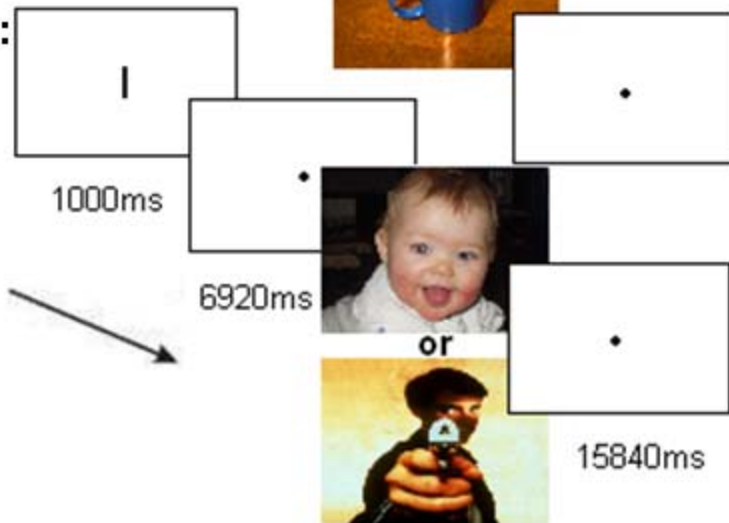
**negative**

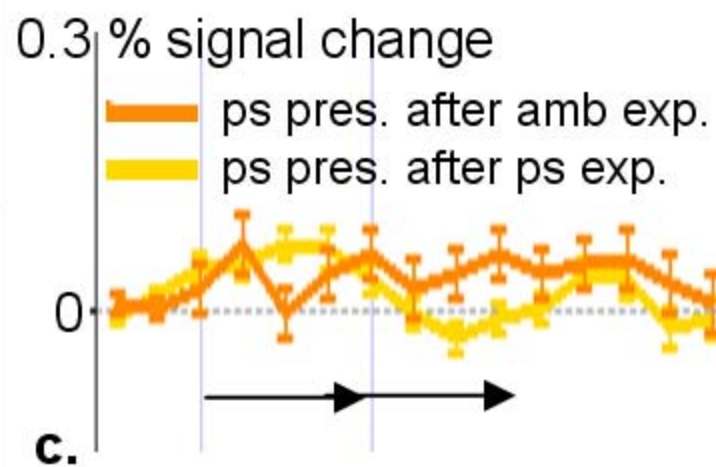
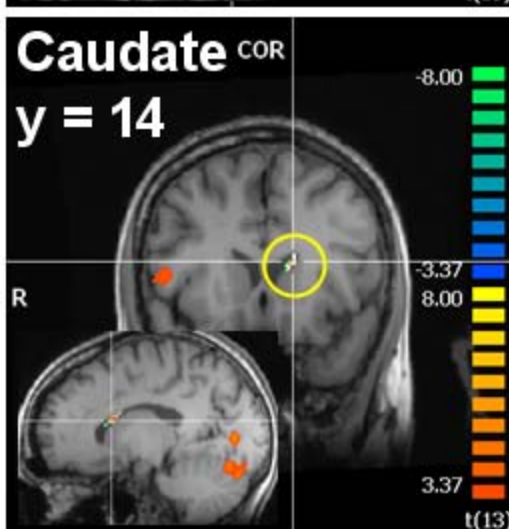
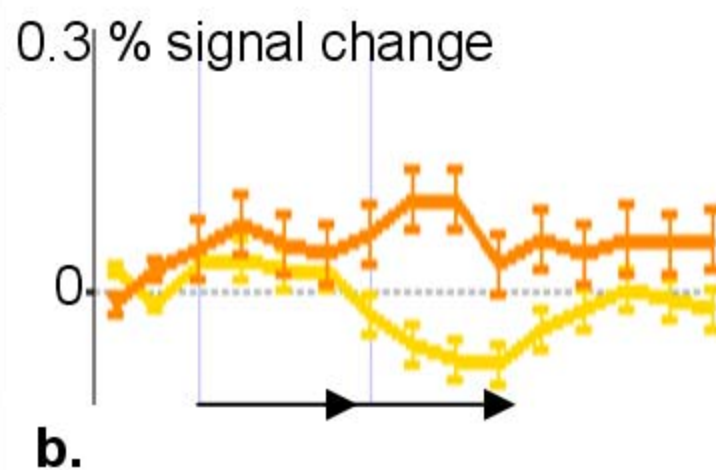
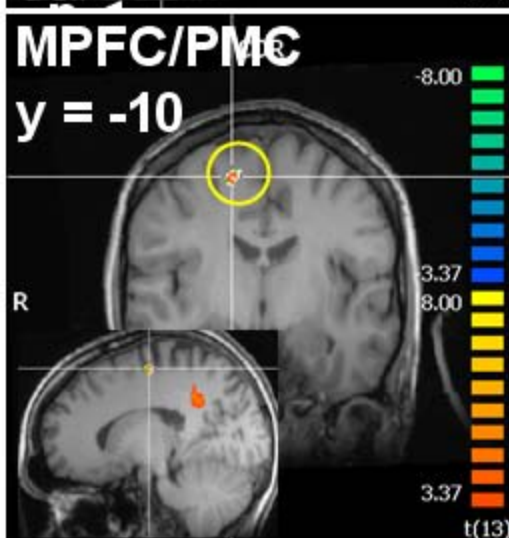
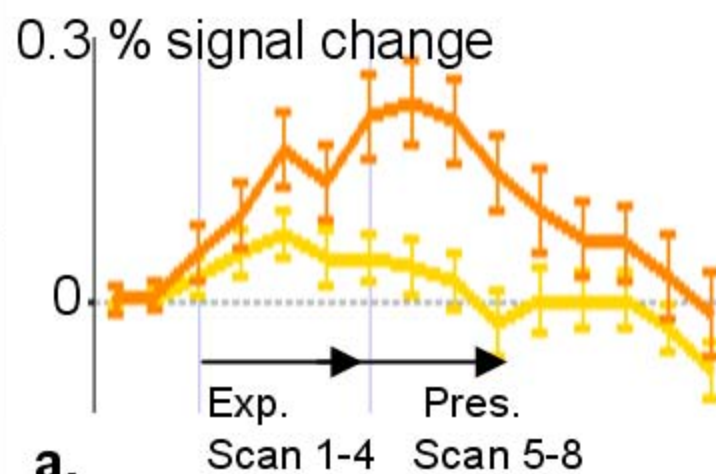
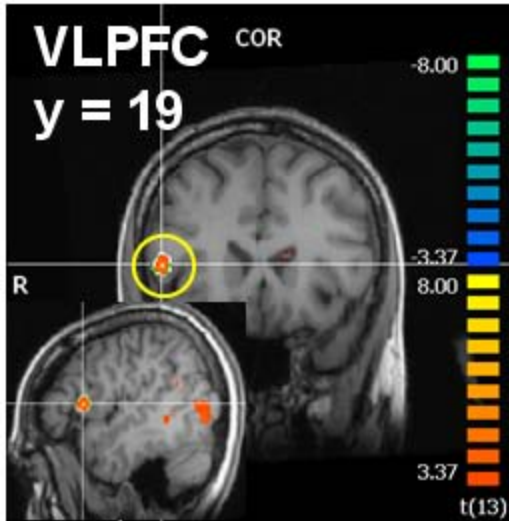


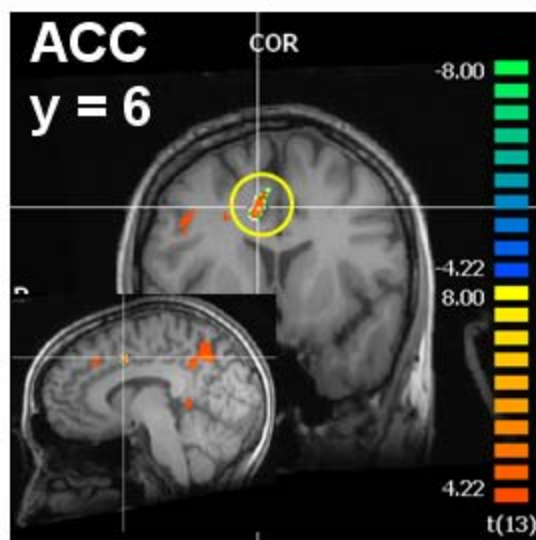
**neutral**



**ambiguous:  
positive or  
negative**



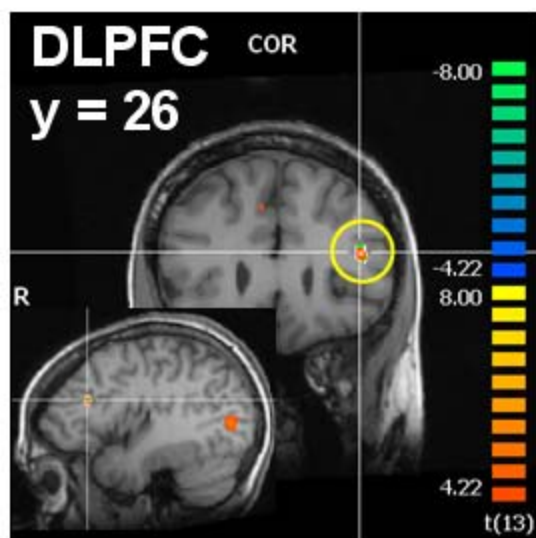
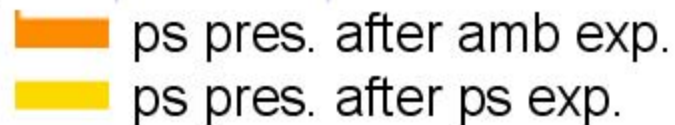




0.3 % signal change

0

**S1**



0.3 % signal change

0

**S2**

