Author's response to reviews

Title: Toward a new computer-based and easy-to-use tool for the objective measurement of motivational states in humans: A pilot study

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Author's response to reviews: see over
Bordeaux, June 10, 2014

Dear Editor,

We have revised the manuscript (MS: 2034778144121030) entitled: “Toward a new computer-based and easy-to-use tool for the objective measurement of hedonic and motivational states in humans: A pilot study”. Both referees recommended some changes to improve the manuscript. We have now addressed each concern in the point-by-point answers below and modified the manuscript accordingly. Changes in the revised text have been highlighted in yellow.

We thank the reviewers for their evaluation and thoughtful suggestions. The overall result is a much improved manuscript, and for that we are in debt with the reviewers.

Please do not hesitate to contact me if there are any questions about our resubmission.

Sincerely,

PR. B. AOUIZERATE
Responses to the reviewer 1

Major Compulsory Revisions

Comment 1.

A. However, my primary concern is that it is unclear what exactly the computer task measures, and how this can be said to be an assay of hedonic and motivational states. The metrics (judgment of image size and presentation duration) are shown to be altered by satiety state, but it is not intuitive what this result means exactly. We thank the reviewer for this comment. As also requested by the reviewer 2, we have now clarified this point, especially in: i) the title, as follows: “Toward a new computer-based and easy-to-use tool for the objective measurement of motivational states in humans: A pilot study”; ii) the introduction section, as follows (page 5, line 8): “Therefore, our pilot study had as objective the development and use of a new experimental computer-based and easy-to-use test based on the presentation of visual food cues for the objective and quantitative measurement of motivational states in humans. We explored the influence of both incentive salience and physiological hunger on the visual and time perception.”; and, iii) the discussion section, as follows: a) (page 14, line 2) “Therefore, hunger is able to specifically produce modifications in the perception of food pictures, an effect presumably related to changes in their incentive effects.”; b) (page 14, line 6) Our data illustrate the interaction between the physiological hunger and motivation.”; and, c) (page 14, line 17) “Our global evaluation of the appetitive value of the food images used in our study accounted for their incentive value.”

B. For example, do these satiety-related effects arise because attentional processes are altered (as in the dot-probe tasks that have been shown to change as a function of satiety state)? This was not investigated in our study. For this reason, we have now added a paragraph in the limitation section of the manuscript specifically addressing this relevant point, as follows (page 16, line 14): “previous findings have shown the allocation of attentional resources in response to the salience and relevance of food-related stimuli [19,40,41]. In particular, it has been demonstrated that the attentional processing for food stimuli is influenced by fasting [20,42,43]. Our study assessed the accuracy of perception, as reflected by the PSE. However, we did not assess the precision of perception, which reflects, at least in part, the participant's attentional engagement.”

C. Further, do the authors' metrics relate to traditional indicators of hedonic and motivational states, such as liking ratings or actual amount of food consumed? I suggest the authors conduct an additional validation experiment - or at the very least elaborate on this within the manuscript. As mentioned in the manuscript, two VAS were administered to the participants in order to assess the appetitive (incentive) properties of food images and the hunger levels, respectively. Detailed information about the exact question raised has been now provided in the text, as follows (page 8, line...
17): “Each subject had to answer the following question: “How hungry are you?” and rate hunger levels by placing a mark on a horizontal line, 100 mm in length, anchored by the word descriptors “Not at all” on the left end (0) and “Extremely” on the right end (100). An additional VAS evaluating the appetitive properties of the viewed food pictures was administered although only at the end of the last experimental session, so that the exact objective of the study remained unknown to the participants, thereby limiting potential response bias. The following question was asked: “How much did you consider the presented food images appetitive?”. The subject was invited to place a mark on the horizontal line anchored by word descriptors similar to those cited above for the VAS assessing hunger levels. For both VAS, the score was determined by measuring the distance in millimeters from the left end of the line to the mark that the subject drew [28,29].” Moreover, we need to point out that all the subjects consumed the same amount of food, which was administered to them by the experimenter at the beginning of each experimental session in satiety. Finally, following the suggestion of the reviewer we have now discussed more in detail how our metrics relate to traditional indicators of motivational states in the discussion section, as follows: a) (page 13, line 12) “To our knowledge, this is the first study using psychophysical methods for the development of a test based on perception for the objective and quantitative assessment of motivational states in humans”; b) (page 14, line 2) “Therefore, hunger is able to specifically produce modifications in the perception of food pictures, an effect presumably related to changes in their incentive effects. This is suggested by studies showing that visual and time perceptions are both modulated by the affective state in response to the presentation of food or word-related stimuli [21,26]”. Finally, emotions were not evaluated in our work. This has been clarified in the following sentence (page 15, line 2): “Thus, although emotional responses were not specifically assessed in our study, it cannot be ruled out that hunger will affect not only the incentive, but also the hedonic characteristics of the food pictures.”

D. Additionally, this manuscript will benefit from a comparison of the authors’ tasks to other computer-based tasks that have been shown to be modulated by satiety state (e.g., the dot probe task, reinforcement tasks, food selection or shopping tasks). We thank the reviewer for this comment. We have now added the following information in the revised text (page 4, line 20): “There are other computer-based tests that primarily refer to: i) food reinforcement tasks for the study of motivated responses and effort toward food [15,16]; ii) food tasting tasks for the evaluation of the hedonic experience and pleasantness elicited by food intake [17,18]; and, iii) visual probe tasks with food images for the exploration of cognitive aspects and especially the attentional capture according to the motivational characteristics of food pictures [19,20]. Thus, to date little attention has been paid to methods assessing motivational states in relation with the perception. While the manipulation of the emotional valence of words has recently been documented to create substantial changes in the size or time perception [21], the perceptual processing of motivationally significant stimuli such as food, which could putatively be linked to hunger levels, has not been investigated.”
Comment 2.

A second primary concern is that – as the authors highlight in their discussion of study limitations – the pattern of results they observed do not converge. For example, in Task A, the PSE results do not correspond to those of the PSD. Tasks A and B are also not altered by satiety in the same direction. As such, the result summary (Paragraph 2 of Discussion) does not represent the overall pattern of the data. The complexity of the results should be discussed from the outset, rather than at the end of the Discussion – perhaps by an acknowledgment that not all metrics show the expected changes following satiety, and a proposal for which metrics should be used moving forward. In response to the reviewer comment, we have added the following (page 15, line 15): "measurements of the PSD showed that hunger specifically induces an overestimation of the size of the viewed food images under fasting while assessments of PSE revealed similar changes in the size perception although occurring indifferently for both types of stimuli in fasting. This partial discrepancy between the PSD and PSE could be possibly due to the chosen psychophysical parameters, especially the size of the step, which might be too large for identifying with the PSE small perceptual differences between food and control stimuli in a sample of healthy subjects free from any pathology of the reward system. An alternative explanation is the smaller number of subjects performing the task A than those participating in the task B for which the PSE and the PSD concordantly showed that under fasting the time of presentation was perceived shorter for food but not for control images."

Moreover, in order to improve the understanding of the results of PSE and PSD we have provided more detailed information in the results section, as follows: i) (page 11, line 4) “For task A, assessments of the PSE revealed negative values on the logarithmic scale for both types of stimuli “F” and “C” in either fasting or satiety (Figure 3A). This means that the subjects considered the images “F” or “C” equal in size to their respective devalued counterparts “D” while the images “F” or “C” were in reality smaller in size than “D”. Therefore, the subjects overestimated the size of both stimuli “F” and “C” relative to their respective devalued counterparts “D” under either fasting or satiety. However, there was a tendency toward a difference in the PSE between fasting and satiety conditions, regardless of the type of the viewed stimuli “F” or “C” [condition effect, F(1,23)=3.65, p=0.07]. The PSE of both images “F” and “C” tended to have more negative values on the logarithmic scale under fasting as compared to satiety (Figure 3A). Therefore, the overestimation seemed more marked under fasting than in satiety for both types of stimuli “F” and “C” when compared to their respective devalued counterparts “D.”; and, ii) (page 12, line 9) For task B, measurements of the PSE for the stimuli “F” and “C” varied differently across fasting and satiety conditions [stimulus x condition interaction, F(1,26)=4.34, p<0.05]. The PSE for the images “F” had a positive value on the logarithmic scale in fasting (Figure 3B). In other words, the subjects considered the stimuli “F” equal in time of presentation to their devalued counterparts “D” while the stimuli “F” were in reality greater in time of presentation than “D”. Therefore, in fasting, the
subjects underestimated the duration of presentation of the stimuli “F” when compared to their devalued counterparts “D”. Opposite results were observed for the stimuli “C”. The PSE for the images “C” showed a negative value on the logarithmic scale in fasting (Figure 3B). This means that the subjects perceived the stimuli “C” equal in time of presentation to their devalued counterparts “D” while the stimuli “C” were in reality smaller in time of presentation than “D”. In other words, in the fasting condition, the subjects overestimated the duration of presentation of the stimuli “C” when compared to their devalued counterparts “D”. The PSE for the images “F” was significantly greater than that of the images “C” in fasting (p<0.02) (Figure 3B). Therefore, relative to their respective devalued counterparts “D”, the duration of presentation of the stimuli “F” was estimated significantly smaller than that of the stimuli “C” under fasting.

Minor Essential Revisions

Comment 3
In the introduction, the authors cite major depression as an example of a reward-related pathology. This is not intuitive; addictions might be a more appropriate examplar. We respectfully disagree with the reviewer and find relevant to mention major depression, since this pathology is characterized by anhedonia, which is the loss of motivation for pleasurable activities or for primary reinforcements like food. We have now added “addiction” (page 4, line 2) or (page 17, line 7) among the pathological conditions that are characterized by profound disturbances of reward processes.

Comment 4
In the methods section, the description of the devalued images would benefit from elaboration. For example, why were devalued images introduced (as opposed to a direct comparison between the food items and the control geometric figures)? We thank the reviewer for this remark, however we need to point out that size comparison requires close figures of similar shapes, ie. food-food or controls-controls and that a direct comparison between food items and control geometric figures is not appropriate. We have now clarified in the text why devalued images were used, as follows (page 7, line 1): “Devalued images were used since earlier studies demonstrated that the visual characteristics, particularly in terms of colors, have an impact on the affective reaction to salient cues, thereby influencing the size and time perception [22-26]”.

Comment 5
In either the methods or results sections, please explain why some participants were dropped (30 enrolled vs. 24 for Task A and 27 for Task B). As also requested by the second reviewer, we have now addressed this point, as follows (page 9, line 22): “Of the study population, data of the first 6 subjects enrolled for task A that served for gradual psychophysical parameter adjustments (step size,
initial ratio “F”/“D” or “C”/“D”) were excluded from the final analyses. For task B, data of 3 subjects were excluded because pictures were abnormally displayed on the computer screen when these 3 subjects passed the test.”

Comment 6
In the discussion, the limitations and conclusion paragraphs need to be checked for grammar and spelling (e.g., ‘Emotionnally [sic] salient’, ‘Loose [sic] its accuracy’). The text has been corrected for grammar and spelling errors (page 15, line 12) and (page 16, line 4).

Discretionary Revisions
Comment 7
The authors’ discussion of neuroimaging findings involves a fair amount of reverse inferences. The authors may consider rephrasing these. This point has been taken into account in the revised text, as follows (page 14, line 18): “However, numerous functional neuroimaging studies have shown that the presentation of visual food stimuli is associated with the activation of frontal-limbic loops [13,14] that are highly involved in processing the hedonic significance of the environmental stimuli [36,37].”
Responses to the reviewer 2

Comment 1. In the abstract, ‘possibly helping further explore biological substrates and estimate the clinical efficacy of therapeutic responses...’ does not appear to be related to the results and is too far-stretched to be mentioned here. We thank the reviewer for this remark. This sentence has been removed from the abstract.

Comment 2. In background

a) Para 1: ‘Reward-related pathologies’ is not a commonly used term. It is not uncertain if this is an established term. If to be used, it has to be clearly defined to the reader. We have now replaced this uncommon term in: i) the abstract (page 3, line 3): “in human diseases that are characterized primarily by serious disturbances in reward processing.”; ii) the introduction (page 4, line 1): “highly disabling pathologies, such as major depression, addiction and obesity, in which reward function is especially disrupted”, or iii) the discussion section (page 15, line 21): “free from any pathology of the reward system.”

b) Para 1: ‘Eating-related disorder’ gives the impression that you are referring to eating disorders. This needs to be more clearly defined. We have now replaced this term by obesity in the text of the manuscript in: i) the introduction section (page 4, line 2); and, ii) the conclusive part (page 17, line 8).

c) Para 2: ‘Directional and activational aspects’ : Although explained, the terms used are not immediately intuitive. Would you be referring to appetitive motivation and physiological/homeostatic hunger? We have now clarified these concepts as follows (page 4, line 5): “Motivation (i.e. wanting), as one of the two components of reward beside the hedonic experience and sensory pleasure (i.e. liking), relies on the brain process involved in the attribution of incentive salience and that generates the desire to consume appetitive food [4-9]. The motivation to obtain and eat food is modulated by the sensations of hunger, as reflective of the physiological need to introduce calories [4-9].”

d) Para 4: The objective is defined as ‘development for measurement of hedonic and motivational states in human.’ As mentioned in para 3, various methodological approaches have been used to study hedonic and motivational states e.g. examining emotions, taste sensitivity, monetary cues. The objective needs to specify that this study uses food visual cues as the key approach. We have now changed the text, as follows (page 5, line 8): “Therefore, our pilot study had as objective the development and use of a new experimental computer-based and easy-to-use test based on the presentation of visual food cues for the objective and quantitative measurement of motivational states in humans.” There are various motivational processes and the objective needs to specify the specific motivational process this study is examining e.g. hedonic hunger,

We have taken this comment into consideration in the introductive section (page 5, line 11): “We explored the influence of both incentive salience and physiological hunger on the visual and time perception.” but also in the title in which “hedonic” has been removed.

e) What are your hypotheses for this study? We have now added the following sentence (page 5, line 16): “We hypothesized that fasting specifically causes changes in the perception of either the size or the presentation duration of the food images.”

Comment 3. In materials and methods

a) Subjects: If possible, please provide details of the body mass indices of the subjects. It is known that BMI is strongly associated with hedonic feeding and motivational states. We agree with this remark, but it should be pointed out that as already mentioned in the manuscript we enrolled healthy, normal body weight subjects for the study. We have now included the following information in the methods (page 6, line 6): “The Body Mass Index (BMI) calculated for each participant before entering the study was systematically comprised between 18.5 and 24.9 kg/m2 (mean BMI = 21.80 kg/m2 ± sem = 0.32).”

b) Experimental sessions: It is unclear why two sessions in satiety is required. We have now clarified this point (page 8, line 8): “Two experimental sessions in satiety were carried out 3-4 days apart in order to ensure that the behavioral responses to the tasks remained stable over time”.

c) Experimental sessions: It is unclear how the additional VAS can be used to evaluate the appetitive properties of the food pictures. It would help to list the questions being asked to the subjects, so as to differentiate this from the first VAS used to assess hunger levels.

Taking into account this comment and the comment of reviewer 1 concerning this point we have changed the text as follows (page 8, line 17): “Each subject had to answer the following question: “How hungry are you?” and to rate hunger levels by placing a mark on a horizontal line, 100 mm in length, anchored by the word descriptors: “not at all” on the left end (0) and “Extremely” on the right end (100). An additional VAS evaluating the appetitive properties of the viewed food pictures was administered although only at the end of the last experimental session, so that the exact objective of the study remained unknown to the participants, thereby limiting potential response bias. The following question was asked: “How much did you consider the presented food images appetitive?”. The subject was invited to place a mark on the horizontal line anchored by word descriptors similar to those cited above for the VAS assessing hunger levels. For both VAS, the score was determined by measuring the distance in millimeters from the left end of the line to the mark that the subject drew [28,29].”

d) Data analysis: It is unclear what the difference is between PSE and PSD and the implications of the difference. It will be useful to also describe them in more layman terms. Do they measure hedonic or motivational states? We have taken this important point into consideration. We have now
improved the explanation concerning the use and meaning of these 2 experimental variables. This is now clearly stated in the revised text as follows (page 9, line 7): “Two experimental variables were considered as a measurement of perceptual changes that are putatively reflective of changes in motivational states. First, the point of subjective equality (PSE) calculated for each category of stimuli “F” and “C” is the ratio “F”/“D” or “C”/“D” for which the stimulus “F” or “C” was judged equal to “D” in terms of size or presentation time and it is estimated by averaging reversal points within both staircases [27]. Second, the percentage of subjective discrimination (PSD) determined for each type of stimuli “F” and “C” corresponds to the percentage of responses where the stimulus “F” or “C” was judged greater than “D” during the trials where the stimulus “F” or “C” was physically equal to “D”, in terms of size or duration of presentation (Figure 2). This latter variable is expected to show changes in either size or time perception similar to those found with the PSE. For instance, if the PSE for the stimuli “F” has a positive value, it means that the stimuli “F” are considered equal to their devalued counterparts “D” whereas the stimuli “F” are in reality greater than “D” in either size or presentation time. Therefore, the stimuli “F” were underestimated as compared to “D”. Consequently, the corresponding PSD will have a value below 50%.”

Comment 4. In results

a) Hunger levels of study population: ‘Appetitive properties of food pictures on VAS showed relatively high scores...’. What is this relative to? Please specify. We have now modified this sentence as follows (page 10, line 16): “Ratings of appetitive properties of food pictures on VAS showed a mean score of 6.39 (± sem = 0.45).”

b) Visual and time perception changes: Why was the sample size different for task A and task B? This needs to be accounted for as the difference may bias the results.

The difference in sample size was due to technical reasons that we have now described (page 9, line 22): “Of the study population, data of the first 6 subjects enrolled for task A that served for gradual psychophysical parameter adjustments (step size, initial ratio “F”/“D” or “C”/“D”) were excluded from the final analyses. For task B, data of 3 subjects were excluded because pictures were abnormally displayed on the computer screen when these 3 subjects passed the test.”

The difference in sample size is now also discussed as follows (page 15, line 15): “measurements of the PSD showed that hunger specifically induces an overestimation of the size of the viewed food images under fasting while assessments of PSE revealed similar changes in the size perception although occurring indifferently for both types of stimuli in fasting. This partial discrepancy between the PSD and PSE could be possibly due to the chosen psychophysical parameters, especially the size of the step, which might be too large for identifying with the PSE small perceptual differences between food and control stimuli in a sample of healthy subjects free from any pathology of the reward system. An alternative explanation is the smaller number of subjects performing the task A than those
participating in the task B for which the PSE and the PSD concordantly showed that under fasting the
time of presentation was perceived shorter for food but not for control images."

c) Again, the rationale behind having two satiety sessions needs to be specified. We have now
clarified this point (page 8, line 8): “Two experimental sessions in satiety were carried out 3-4 days
apart in order to ensure that the behavioral responses to the tasks remained stable over time”.

d) It may not be surprising that the PSE and PSD are not correlated with hunger levels or
appetitive values because VAS is a subjective, not objective assessment tool. We thank the
reviewer for this comment, however for task A, we found correlations between the PSE calculated for
either the food or control images and the hunger levels assessed by VAS in the fasting condition, as
described in the results section (page 11, line 16).

Comment 5. In Discussion

a) Para 2: ‘effect related to changes in both the internal emotional and motivated states’
What does this refer to and how is this judged? Emotions are not measured in this study. Which
motivational state would this be referring to? We have clarified this important point and several
sentences have been modified in the discussion section. The changes in perception that we observed
are probably related to the incentive effects of food images (page 14, line 2). Emotions were not
evaluated in our work. This has been clarified in the following sentence (page 15, line 2): “Thus,
although emotional responses were not specifically assessed in our study, it cannot be ruled out that
hunger will affect not only the incentive, but also the hedonic characteristics of the food pictures.”

b) Para 3: ‘mesencephalic dopamine system.....’ It is not clear how this sentence is linked with
the earlier sentence on physiological need. We have taken this point into account and changed
several sentences, as follows (page 14, line 6): “Our data illustrate the interaction between the
physiological hunger and motivation. Prolonged fasting is associated with an increased activity within
the hypothalamus [30] but also evokes midbrain activation in response to the anticipated experience of
a forthcoming meal [31]. Such activation is assumed to mediate the motivational aspects related to the
expectation of food [4-7,32,33]. The motivation is characterized by the assignment of attractive and
desirable properties to an external stimulus such as a food image and it is mediated by the release of
dopamine within the mesolimbic pathways [4-7,32,33].”

c) Para 3: If the VAS does account for both incentive and affective properties, a reference needs
to be provided. As now clearly explained in the methods, the VAS used for the figures evaluated the
appetitive properties of the figures. Their appetitive value accounted for their incentive properties (see
page 14, line 17). Therefore, no reference has been inserted.

d) Para 3: The phenomenon ‘alliesthesia’ is described. How does the current study relates to
this. Does the VAS measures emotions? Describing questions asked in the VAS may help to
clarify this. We thank the reviewer for this remark. We have now removed the sentence addressing the concept of alliesthesia, since emotions were not evaluated in this study.

e) Para 4 under limitations: ‘geometric figures in colour could possibly.....therefore induce changes in size perception...’ I thought the devalued counterparts for geometric figures were also used in the experiment. Wouldn’t that counterbalance this effect? For task A (size), the PSE measured for food and controls images revealed that under fasting both categories of stimuli were overestimated in size (page 15, line 10): “Therefore, it can be assumed that the geometric figures in color relative to their devalued counterparts in grayscale could possibly acquire emotional salience, as seen for the food images, and consequently induce changes in size perception under fasting, as suggested by the effects of affective states on size estimation [21].”

Minor revisions: 1. Under Discussion para 2
a) ‘paralleled by modifications...’ the word modifications does not appeared to be suitable in this case. It has been replaced by “changes” (page 13, line 16).