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ABSTRACT

Objective: Visual pursuit should be tested with a mirror in patients with disorders of consciousness. This stimulus was indeed more efficient than a person or an object, and the auto-referential aspect was supposed to be the key feature. The present study tested the hypothesis that the mirror was more efficient because of its self-aspect.

Methods: The mirror was compared (1) to the patient's picture and to the picture of a famous face, in 22 patients in minimally conscious state and (2) to the patient's picture and a fake mirror, which had dynamical and bright aspects of the mirror, without reflecting the face, in 26 other patients in minimally conscious state.

Results: The mirror was more efficient than the patient's picture, which was not statistically different from the famous face. The second part of the study confirmed the statistical difference between the mirror and the picture. However, the fake mirror was neither statistically different from the mirror nor from the picture.

Conclusions: Although our results suggest that the hypothesis proposed by previous studies was partly wrong, they confirm that the mirror is the best stimulus to use when assessing visual pursuit.

Introduction

Different disorders of consciousness (DOC) can follow a coma period. Patients with unresponsive wakefulness syndrome, previously coined as vegetative state (UWS/VS (1)), show eye-opening periods, without any sign of consciousness of themselves or of the environment. Patients in minimally conscious state (MCS (2)) show subtle but reproducible signs of consciousness of themselves or of their environment. MCS has been subcategorized in MCS− and MCS+. While the former show signs of consciousness that are not supported by language comprehension, the latter are able to understand simple orders (3). This distinction is reflected in the cerebral metabolism of those patients, as the language network metabolism is relatively preserved in patients in MCS+, as compared to MCS− (4). Patients emerge from the MCS when they are able to functionally communicate and/or to functionally use different objects, on two consecutive assessments (2). Behavioural assessments are the first tool to diagnose these patients, and the Coma Recovery Scale-Revised (CRS-R (5)) is recognized as the most appropriate scale to distinguish the different states (6). This scale assesses different functions through six subscales, namely auditory, visual, motor and oromotor/verbal functions, communication and arousal. Different studies have highlighted the importance of the visual subscale (7), and more particularly of one of its items, the visual pursuit (8), in identifying patients in MCS. Moreover, the visual pursuit is one of the three most frequently observed items in patients in MCS (9). As required

in the CRS-R guidelines, visual pursuit is assessed by moving a mirror in front of the patient's face according to a standardized procedure. The patient is asked to follow the mirror, and a visual pursuit is considered present if the patient succeeds at least twice. While the creators of the CRS-R did not explicitly explained why they recommended to use a mirror instead of any other object, one could reasonably assign this choice to the reflection of the patient's face. Indeed, self-face is a particular stimulus which is known to be very attraction-grabbing (10), even if its distractive power might be only observed in specific conditions (11). Actually, different studies showed the superiority of the mirror to elicit visual pursuit in patients with DOC, as compared to a moving person or object (12,13). Mirror was thus supposed to be more efficient because of the self-referential aspect. Indeed, it is known that the self-referential stimuli are more susceptible to catch the patient's attention (12–15). However, to our knowledge, no study has directly addressed this question. Other aspects of the mirror could be a reason for this superiority, such as familiarity of the displayed face or the physical characteristics of the mirror (i.e. brightness and dynamical aspects).

The present study aimed at understanding the reason of the mirror superiority in visual pursuit assessment in patients in MCS. The first objective was to determine if it was due to the self-referential aspect of the mirror. The second objective was to disentangle the self-referential aspect from the physical characteristics of the mirror.

Methods

Severely brain-damaged patients with DOC were enrolled in the study. Inclusion criteria were the presence of a visual pursuit and a diagnosis of MCS (based on the presence of at least one sign of MCS during the CRS-R). Patients subsequently diagnosed as EMCS during the CRS-R assessment (i.e. showing functional communication or use of objects) were excluded. Patients were assessed in a comfortable position, in a bed or in a chair. Visual pursuit was tested according to the CRS-R guidelines. Each stimulus was presented in front of the patient's face, and slowly moved towards left, right, up and down, for a 45-degree angle. The procedure was done twice, leading to eight movements for each stimulus. The sequence of the directions was randomly determined before the testing of each patient (i.e. pure random by drawing lots). Visual pursuit was considered as present when the patient followed the stimulus at least two times out of the eight performed movements. A complete CRS-R assessment was then performed to diagnose the current state of the patient.

Each part of the study tested three different stimuli, presented in a randomized order to the patient. The first part of the study was designed to assess the self-referential and the familiar aspects of the mirror. Visual pursuit was thus tested with a mirror, a picture of the current patient's face and a picture of Marilyn Monroe's face (a familiar face which is not self-referential). Pictures and mirror were of similar size and shape. The second part of the study was designed to disentangle the self and physical characteristics of the mirror. Visual pursuit was here tested with a mirror, a picture of the current patient's face and a fake mirror. The fake mirror reproduced the brightness and the dynamical aspect of the mirror, without reflecting the patient's face. The patient's picture was still used in order to confirm the superiority of the mirror in the second part of the study, and to directly compare the auto-referential and the physical aspects of the mirror.

This study was approved by the Ethics Committee of the Medical School of the University of Liège, and written informed consent was obtained from the legal surrogate of the patients.

Hypotheses were based on the literature on visual pursuit in patients with MCS, suggesting that the mirror is more efficient in triggering visual pursuit because of the self-aspect. In the first part of the study, the mirror was expected to be as efficient as a self-picture, but more efficient than a familiar picture. In the second part of the study, the mirror was expected to be as efficient as the self-picture, but more efficient than a fake mirror. Two different dependent variables were included in the analyses: the occurrence of visual pursuit (a binary variable: presence or absence of visual pursuit) and the number of movements followed by the patient (a discrete variable from zero to eight). Binary variables were analysed with a Cochran test. Comparisons of proportions with Bonferroni correction for multiple comparisons were used as *post-hoc* to the Cochran test. Discrete variables were analysed with Friedman ANOVA and Wilcoxon tests (with Bonferroni correction for multiple comparisons). In the second study, to assess if the different aspects of the mirror (self and physical properties) have an additional or interactive effect, a Wilcoxon test comparing visual pursuit probabilities (pMirror, pPicture, pFakeMirror) was used. The probabilities were based on the number of observed visual pursuits, divided by eight (the total number of trials for each stimulus). For example, if the patient followed the mirror six times out of the eight trials, the probability was 0.75 (=6/8). This was done for each stimulus in each patient. The pMirror was compared to [(pPicture + pFakeMirror) − (pPicture × pFakeMirror)] with the Wilcoxon test. If the comparison was statistically significant, it could be assumed that the effect was interactive.

To assess a possible difference between patients included in the two studies, group comparisons were made with Mann–Whitney U-tests for the continuous variables (i.e. age and time since onset), and Fisher exact tests for binary variables (i.e. traumatic/non-traumatic aetiology, MCS+/MCS−).

To assess possible confounding variables in the self-referential aspect, patients from both groups (first and second study) were brought together. The effects of MCS subcategorization (MCS− or MCS+), chronicity (assessed before three months post-onset, or after 28 days post-onset) and of aetiology (traumatic or non-traumatic) were assessed by Wilcoxon tests comparing self-picture and mirror in different subgroups: MCS−, MCS+, traumatic, non-traumatic, acute and chronic. The effect of age and time since onset was assessed by Spearman correlations with the number of pursuits elicited by the picture.

Analyses were run in Statistica12 (Statsoft).

Results

The first study, assessing the auto-referential and familiar aspects, included 22 patients in MCS [median age (interquartile range, IQR) = 50 (30) years old, 9 women, 12 MCS+, median time since injury (IQR) = 7 (48) months, 14 chronic (more than 3 months post-injury)]. Aetiology was traumatic in 11 patients and non-traumatic in 11 patients (4 anoxic/hypoxic and 7 non-anoxic). The global model on the ability to elicit sufficient visual pursuit was statistically significant (Cochran test: $Q = 15.27$, DF = 2, $p < 0.001$). *Post hoc* proportions comparison tests identified significant differences between the mirror and the patient's picture ($p = 0.005$) and between the mirror and the Marilyn Monroe's picture ($p < 0.001$). However, no statistical difference was observed between pictures ($p > 0.99$; see Figure 1). When looking at the number of visual pursuits elicited by each stimulus, the global model was significant (Friedman ANOVA: χ^2 (22,2) = 10.31, $p = 0.006$; see Figure 2). Wilcoxon tests showed significant differences between mirror and patient's picture ($Z = 2.69$, $p = 0.021$) and between mirror and familiar picture ($Z = 2.89$, $p = 0.012$). No difference was observed between self and familiar pictures ($Z = 0.58$, $p > 0.99$).

The second study disentangling auto-referential and physical characteristics of the mirror included 26 other patients in MCS [median age (IQR) = 38 (34) years old, 9 women, 8 MCS +, median time since injury (IQR) = 15 (44) months, 21
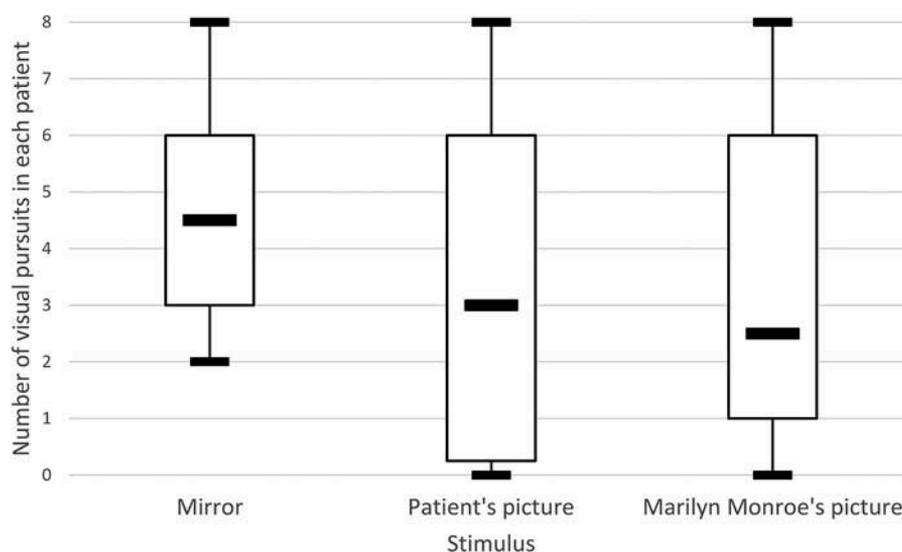
Figure 1. Percentage of patients in minimally conscious state showing visual pursuit, according to the three different stimuli tested in the first part of the study.
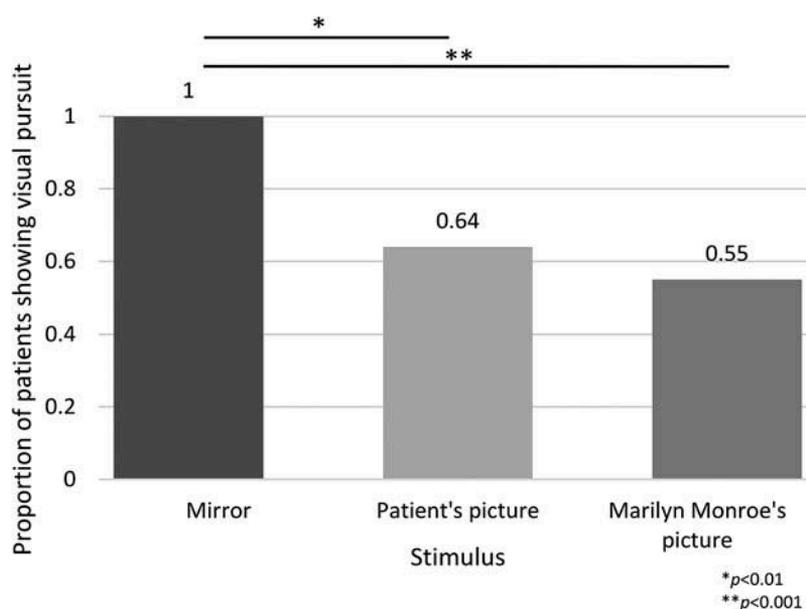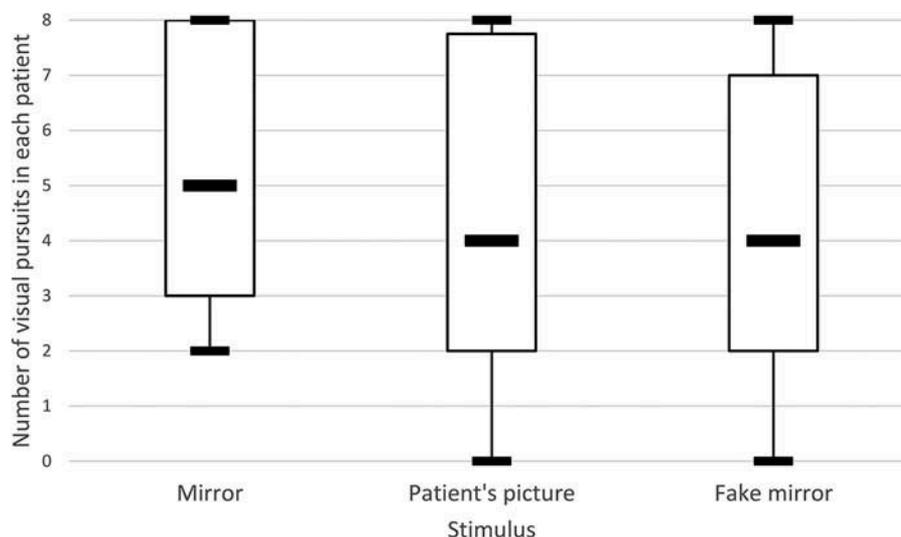

Figure 2. Boxplot of number of visual pursuits elicited by the three stimuli used in the first study (mirror, self-picture, Marilyn Monroe's picture). Used values are median, IQR and range.

chronic (more than 3 months post-injury)]. Aetiology was traumatic in 14 patients and non-traumatic in 12 patients (3 anoxic/hypoxic and 9 non-anoxic). This second group was not different from the first one regarding age ($U = 215$, $p = 0.158$) and time since onset ($U = 227$, $p = 0.2284$). No difference was observed between groups according to the diagnosis (MCS– vs. MCS+, $p = 0.1429$) or to the aetiology (traumatic vs. non-traumatic, $p = 0.7725$). The global model on the ability to elicit visual pursuit in the second group of patients was statistically significant (Cochran test: $Q = 6.75$, DF = 2, $p = 0.034$). However, we only found a significant difference between the mirror and the patient's picture ($p = 0.028$), as observed in the first part of the study. The fake mirror was neither statistically different from the mirror ($p = 0.223$) nor from the patient's picture ($p = 0.815$; see

Figure 3). When looking at the number of visual pursuits elicited by each stimulus, the global model was significant (Friedman ANOVA: χ^2 (26,2) = 12.67, $p = 0.002$; see Figure 4). Wilcoxon tests showed significant differences between mirror and patient's picture ($Z = 2.64$, $p = 0.025$). No difference was observed between patient's picture and fake mirror ($Z = 0.95$, $p > 0.99$), nor between mirror and fake mirror ($Z = 1.99$, $p = 0.139$). The investigation of the additional or interactive effect of the properties of the mirror showed that the mirror was efficient because of an additive effect of both characteristics, and not an interactive effect ($Z = 0.26$, $p = 0.795$).

The difference between mirror and picture was observed in the traumatic subgroup ($Z = 2.77$; $p = 0.006$), non-traumatic subgroup ($Z = 2.66$; $p = 0.008$), acute subgroup ($Z = 2.14$;

Figure 3. Percentage of patients in minimally conscious state showing visual pursuit, according to the three different stimuli tested in the second part of the study.
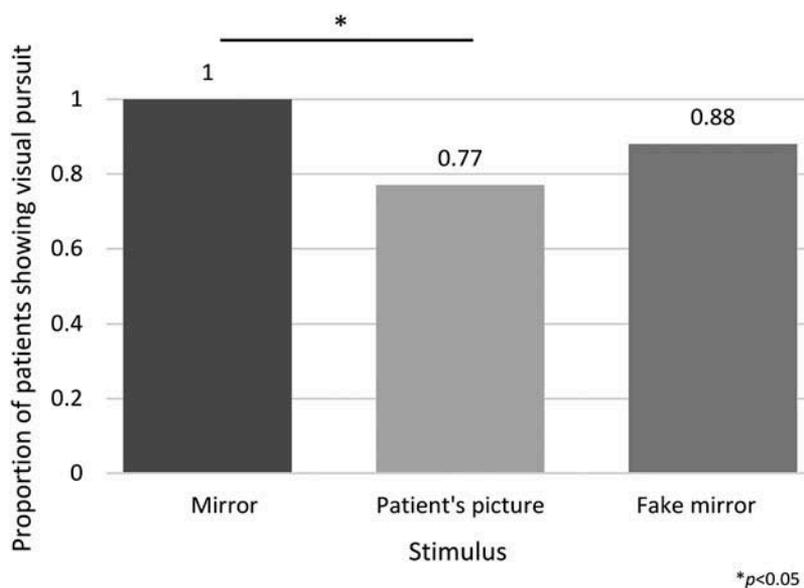
Figure 4. Boxplot of number of visual pursuits elicited by the three stimuli used in the second study (mirror, self-picture, fake mirror). Used values are median, IQR and range.

$p = 0.032$), chronic subgroup ($Z = 3.09$; $p = 0.002$) and MCS– subgroup ($Z = 3.25$; $p = 0.001$). No difference was found in MCS+ subgroup ($Z = 1.87$; $p = 0.062$): using a mirror or a picture produced a similar number of pursuits. However, the detection of a visual pursuit according to the CRS-R criteria was still significantly higher with a mirror than with the picture (100% vs. 75%, $p = 0.017$). Regarding age and time since onset, they did not correlate with the number of visual pursuits observed with the picture ($R = 0.06$, $p = 0.98$ and $R = 0.11$, $p = 0.472$, respectively).

Discussion

Visual pursuit is a key marker of the MCS (2). Literature showed that an adequate assessment (i.e. using a mirror) increased the probability to detect visual pursuit (12,13).

Indeed, the mirror proved to be more efficient than a person or an object. Authors argued that the reflection of one's face was the reason of the mirror efficiency. However, physical properties of the mirror, such as brightness and the reflection of a dynamic image, could also explain this superiority. Hence, the present study aimed at addressing this question, by comparing a mirror to pictures and to a fake mirror.

Regarding the familiarity, our results showed that the mirror was more efficient than the pictures in detecting visual pursuit, whether it be the patient's face or a familiar face. This effect was observed in the detection of a visual pursuit according to the CRS-R criteria as well as in the number of observed pursuits (out of the eight performed trials). We can thus assume that the mirror not only is more likely to identify the presence of visual pursuit but also elicits more pursuits, attracting the patient's gaze more often than the pictures.

Actually, according to recent results in healthy subjects, mirror was presumed not to be more attractive than an object (i.e. eliciting a larger number of visual pursuits), but to elicit smoother visual pursuits (16). This might increase the probability for the clinician to detect the visual pursuit (16). Further investigations are needed in patients with DOC to confirm the results obtained in healthy subjects. Whatever, in our study, results brought evidence that the mirror superiority was not completely due to the auto-referential effect. If it was the case, testing visual pursuit with a mirror or a picture of the patient's face would have produced similar responses. Moreover, no significant difference was observed between both pictures, suggesting that the auto-referential effect was not stronger than the familiarity effect in attracting attention. This is line with previously reported effect in healthy controls, showing that the own face was not more attractive than a highly familiar face to catch the attention (17).

In the second part of the study, the mirror revealed once again more efficient than the patient's picture, confirming that the auto-referential aspect did not fully explain the efficiency of the mirror. Although the fake mirror attracted more visual pursuits than the picture, and less than the mirror, the differences did not reach significance. Regarding the additional or interactive effect of the mirror properties (i.e. self-referential and attracting physical properties), our results showed that the efficiency of the mirror might be due to an additive effect. The mirror superiority might be due the conjoint presence of those features, but there is no emergent property, no supra-additive effect due to the interaction between these features, which would explain the efficiency of the mirror. Finally, the non-significant but numerical difference observed between fake mirror and self-picture could suggest that the self-aspect might not be the most determinant factor in the mirror attractiveness. Further studies are needed to explore which of the aspects is the more important: the self or the physical properties. One could wonder if the assessment of visual pursuit would not only reflect the assessment of a reflex, if the mirror was efficient because of physical properties such as brightness. Indeed, in the literature, it has been evoked that patients who show a visual fixation to a brightly coloured object as the only sign of consciousness have a cerebral metabolism comparable to patients who are in UWS/VS (18). The presence of such a behaviour might then not ensure that the patient is in MCS. One could thus doubt that the visual pursuit of a bright object is a sign of consciousness. However, the previously cited study only included five patients, and the results should then be taken with care. Furthermore, another study on visual fixation showed that mirror was more efficient than a light to elicit visual fixation (15). This implies that the bright aspect is not sufficient, and the self-aspect seems to play a role in attracting gaze. An effect of the self could only appear with at least a residual consciousness. Moreover, in our study, results did not show that a fake mirror, without self-aspect but with physical properties, was as efficient as a mirror, and more efficient than a picture. While the fake mirror was numerically between mirror and picture, no significant difference was determined. Future

studies should tackle this question, and investigate the effect of the dynamics and the brightness of the mirror, and their respective weights. Indeed, unfortunately, our methodology was not designed to disentangle the physical properties.

In both studies, pictures represented the patient in the current state. Some patients might then have some difficulties in recognizing themselves, as severe brain injury could affect one's appearance, and their face might not correspond to their self-representation anymore. This dissonance between self-representation and the current picture was impossible to standardize, as patients were at different stages, and had different stories and kind of injuries. However, no difference was found between acute and chronic patients: both had better results with the mirror than with the picture. The same results were observed between traumatic and non-traumatic subgroups, suggesting that the efficiency of the mirror was not especially affected by a modified appearance. The fact that the supposed difficulty of self-recognition was not found when using the mirror could be due to the compensatory effect of the brightness and the dynamics. These physical properties might have kept on grabbing attention even if the image was not pleasant or expected by the patient.

The superiority of the mirror as compared to the picture was found in each subgroup regarding aetiology, chronicity and diagnosis, excepted in patients in MCS+: in these patients, mirror and picture elicited comparable number of pursuits (i.e. how many pursuits were detected out of the eight trials), suggesting a similar efficacy. But surprisingly, when looking at the detection of a visual pursuit as defined by the CRS-R guidelines (i.e. if at least 2/8 trials are succeeded), mirror was still more efficient than the picture. It implies that, with patients in MCS+, the clinician would be more likely to detect a visual pursuit according to the CRS-R guidelines when using a mirror. However, it seems that once the patient follows the current picture, a greater number of visual pursuits (out of the eight trials) should be observed. These results might indicate that some patients in MCS+ are able to sustain a behaviour during repeated assessments even in the absence of physical properties retaining attention (i.e. brightness and/or dynamic of the mirror). This is in line with the hypothesis of patients in MCS+ showing higher level of consciousness (3). Another explanation might be that patients in MCS+ are more conscious of their reflection in the mirror, and decide not to look at them too long.

In our setting, the use of a current picture permitted to make the mirror equivalent to the picture, and to directly deal with the main question: was the superiority of the mirror due to one's face? Other studies using pictures of the patient before the onset might also be of interest but would answer another question: was the patient more attracted by the past than by the current appearance? Future studies might address this question.

Limitations

The small amount of included patients is the main limitation in this study, and further investigations should be carried out

to provide stronger results. The sample size also prevented the investigation in each study of the effect of potential confounding variables, such as the aetiology, time since onset or sub-categorization MCS+/MCS−. Moreover, diagnosis was based on a single assessment, while we know that diagnosis can fluctuate across different assessments, and that a diagnosis of MCS− after a single assessment is wrong in 57% of patients (19). It is thus possible that some patients in our study were considered in MCS− whereas they would have been able to follow simple commands on another day or time.

Finally, future studies should use technological devices to better assess visual pursuit. Although the CRS-R provides clear guidelines about visual pursuit assessment, clinical evaluation might still be biased because of human subjectivity. However, eye tracker use is very difficult in patients with DOC because they are non-collaborative and non-communicative, by definition. Some research is focusing on the use of such devices (20,21) and promising new methods without the need of calibration are currently developed (22,23). Future studies should include such objective assessment to provide stronger results.

Conclusion

Our results confirm that the mirror is the best stimulus to test visual pursuit, as recommended by the CRS-R (5), and showed by previous studies (12,13). However, the reason invoked by those authors, the auto-referential aspect of the mirror, does not seem to be the main characteristic attracting attention. The mirror attractiveness was indeed mediated by the conjoint presence of auto-referential and physical aspects (brightness and dynamics), with a possible preponderance of the latter ones. When disentangling these two different physical properties, there was no stimulus able to be as efficient as the mirror.

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Declaration of interest

The authors report no conflicts of interest.

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