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CLINICAL CASE

Using eye movement desensitization and reprocessing (EMDR) as a treatment for phantom breast syndrome: Case study[☆]



M.-J. Brennstuhl^{a,*}, C. Tarquinio^a, S. Montel^b, J. Masson^c,
F. Bassan^d, P. Tarquinio^d

^a EA 4360, Laboratory APEMAC, University of Lorraine, University Center for Research and Psychotherapy, île-du-Saulcy, BP 30309, 57006 Metz cedex 1, France

^b EA 2027, Laboratory LPN, Paris-8, 2, rue de la Liberté, 93526 Saint-Denis, France

^c EA 2089, Laboratory CURSEP, University of Picardie, chemin du Thil, 80025 Amiens, France

^d Private practice "Thionville psychothérapie", 27, boulevard Jeanne-d'Arc, 57100 Thionville, France

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KEYWORDS

Phantom breast syndrome;
Phantom limb pain;
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Post-traumatic stress disorder;
Psychotherapy

Summary

Purpose. – The aim of this research was to challenge the use of eye movement desensitization and reprocessing (EMDR) therapy in the treatment of the phantom breast syndrome.

Method. – Two patients agreed to participate in this study and were treated by EMDR therapy, focusing on two target types: traumatic events related to disease experience and phantom breast sensation. Quantitative evaluations were conducted before the first session, just after the last session and as a follow-up three and six months after. Intensity of the pain and intensity of the sensation were measured, as well as anxiety (through STAI) and depression (through CES-D). Qualitative evaluations completed these measures by paints of breast image made by the patients on the first and last sessions.

Results. – Results show the effectiveness of EMDR therapy on all quantitative measures, but also a qualitative and clinical change producing a modification of the body representation of patients and an effective reduction of the phantom breast syndrome.

Discussion. – Results show that EMDR approach can be an encouraging, non-invasive and relatively short strategy. While these results need to be completed by other studies covering a larger population and the use of a control group, they are still encouraging because they

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* Corresponding author.

E-mail address: mjo.b@live.fr (M.-J. Brennstuhl).

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suggest that a psychological treatment based on EMDR techniques and adapted to the specificity of phantom breast syndrome could be effective in bringing relief to patients.

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Introduction

Phantom breast syndrome (PBS) can be defined as a subjective experience of perceiving and sensing the presence of a breast or breasts after ablation by mastectomy (Aglioti et al., 1994; Rothmund et al., 2004). The phantom breast may appear in the form of more or less distinct sensations or pain, or both at the same time (Kroener et al., 1989; Kvekkeboom, 1996; Rothmund et al., 2004). The pain is most often described in terms of crushing, burning, stinging, stabbing or cutting in the breast whereas the patients most often talk about the sensations in terms of itching, numbness or even tightness.

For years, research studies have shown (Crone-Münzebrock, 1950; Kroener et al., 1989; Kvekkeboom, 1996) a risk of incidence of phantom breast syndrome during the first few years following surgery, whereas in phantom limb syndrome – documented more in-depth – the pain and sensations tend to decrease over time (Jensen et al., 1985).

In a review of the literature (Dijkstra et al., 2007), the authors showed that the average prevalence of the sensations after mastectomy was 36.5% (varying depending on the study from 0 to 66%) and the average prevalence of pain was 10.9% (varying depending on the study from 0 to 53%). Although the issue concerns many women suffering from breast cancer, there are still very few studies, whereas the consequences in terms of quality of life and depression are especially significant (Spyropoulou et al., 2008).

Since 1989, many publications (Tarquinio, 2007) have shown the effectiveness of the eye movement desensitization and reprocessing (EMDR) method, in particular in the field of psychotherapeutic treatment of post-traumatic stress disorder (PTSD). The effectiveness of EMDR for the treatment of trauma was evaluated as equal or superior to cognitive behavioral therapy (Rothbaum et al., 2005) supported by five meta-analyses (Bisson and Andrew, 2007; Bradley et al., 2005; Davidson and Parker, 2001; Maxfield and Hyer, 2002; Van Etten and Taylor, 1998). However, the approach has been developed further since then in order to determine indications in the treatment of several psychopathological disorders (De Jongh et al., 1999; Shapiro, 1989, 2001); that is the case, for example, for research dealing with the treatment of amputees suffering from a painful syndrome, and for whom pain decreased or even disappeared (Schneider et al., 2008).

The EMDR approach uses Shapiro's Adaptive Information Processing (AIP) model (Shapiro, 1995, 2001). That model is based on the precept of an information processing system whose role is to assimilate and integrate various (somatic, sensory, cognitive, behavioral and emotional) aspects of an experience. In highly stressful conditions, such as traumatic events, the system becomes unbalanced, thus hindering the integration of the experience in the autobiographical memory: consequently, the initial perceptions are stored in their

initial form with the distortions caused by the high-level of stress (Shapiro, 2002; Van der Kolk, 2002).

According to Shapiro (2002), these non-integrated experiences, or rather the unprocessed and dysfunctionally-stored mnemonic information, are at the origin of various psychological disorders and symptoms such as PTSD, anxiety disorders and depressive conditions. EMDR reactivates the natural information processing system and facilitates the adaptive resolution of the previously deformed material (Bergmann, 1998, 2000, 2010; Shapiro, 2002; Stickgold, 2002; Van der Kolk, 2002). This approach is based on specific processing (or targeting) framework, adapted to the typology of the disorders to be treated, whether PTSD, depression, anxiety disorders or painful syndromes (Shapiro, 1995).

Manifestations like PBS can, in that respect, result from memories of inadequately stored or chronically activated sensations or pain that continue to disturb the subject, even after treatment of the disease has ended (Flor et al., 1995; Whalley et al., 2007). It may also be a matter of emotionally disturbing, overwhelming or traumatizing memories related to the multiple traumatic events that a disease such as cancer inflicts on patients. Moreover, past psychological trauma is often reactivated by the context of disease or surgery (Basset et al., 2013). Those traumatic memories can play a major role in maintaining the PBS phenomenon. In actual fact, by association, the pain and sensations perceived in the phantom breast(s) are among the many cues that may revive the challenge the disease brought about in the past. As such, methods capable of processing traumatizing memories could prove to be effective in reducing the emotional dimensions associated with the disease and its course of development.

As a result, EMDR therapy applied to treating PBS could prove to be effective, provided that, on one hand, it processes the memories of unresolved negative experience that characterize the disease and, on the other hand, it deals with PBS as such, by offering a protocol centered on the pain and/or sensations reported by the patients.

The aim of this contribution is to present the two cases treated with a dual protocol. The first protocol – qualified as a standard protocol – will target more specifically events unique to a disease like cancer (diagnosis disclosure, treatment, postoperative follow-up, fear of dying, etc.). The second protocol – qualified as a pain protocol – will focus more specifically on treating the phantom breast syndrome.

Patients and methods

Participants

Two women, Paule (age 48, married, two children, secretary) and Nora (age 56, married, one child, teacher), having undergone a mastectomy of both breasts following a

diagnosis of cancer, participated in the study. Both patients directly contacted psychotherapists at the University Center for Research at the University of Lorraine (Metz, France) and the Center for Psychotherapy – C3PSY (Thionville, France). The patients had been operated 16 and 18 months earlier, respectively. Both gave their informed consent and accepted the treatment protocol and the data collection protocol. They also accepted to continue their medication for pain, which had been prescribed to them through the end of the study (paracetamol and codeine for both patients).

Paule had nine sessions, four in standard protocol and five in pain protocol, whereas Nora had 12 sessions, five in standard protocol and seven in pain protocol.

Procedure

After obtaining their informed consent, a brief clinical diagnostic interview was conducted using the Mini-International Neuropsychiatric Interview Plus 5.0.0.-R (Lecrubier et al., 1997) to explore the presence of axis I disorders based on the criteria established by the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (American Psychiatric Association, 2004).

As the patients presented no particular disorders, the study was pursued. After a few preliminary meetings to establish their case history, they were included in the evaluation process. The aim was to evaluate the subjects quantitatively and qualitatively before EMDR therapy (pre-test), after the treatment (post-test), then three and six months after the end of therapy.

For quantitative measures, we gave both participants a document including two scales evaluating depressive and anxiety disorders: the State-Trait Anxiety Inventory (STAI) and Center for Epidemiologic-Studies Depression (CES-D) scales, as well as the more specific PBS measurements.

STAI scale

The STAI scale (Spielberger et al., 1983) adapted and validated on a French population (Bruchon-Schweitzer and Paulhan, 1993) is made up of two distinct scales used to assess state and trait anxiety. We only used the State-Trait Anxiety Scale including 20 proposals (score varying from 20 to 80) and making it possible to establish what the subjects felt at the time. The scale allows the assessment of feelings of apprehension, tension, nervousness and worry. The score obtained is supposed to increase in the face of physical danger or psychological stress.

CES-D scale

The CES-D scale (Radloff, 1977), developed by the Center for Epidemiologic Studies, National Institute of Mental Health, is a self-administered questionnaire of 20 items evaluating depressive emotions. The participants were to indicate the frequency of the various symptoms using a scale of 0 (less than 1 day), 1 (1 or 2 days), 2 (3 to 4 days) and 3 (5 to 7 days) for the previous week. The CES-D has been translated into French and validated (Führer and Rouillon, 1989).

Measures specific to PBS

The measures specific to PBS are characterized by an assessment of the perception of pain and sensations in the

amputated breast(s). As such, during the two weeks prior to therapy, the two weeks following therapy, as well as three and six months later, we measured the intensity of the patients' pain and sensations in the following format:

- pain intensity: in a symptom journal, both patients recorded the intensity of their pain once a day using a numerical evaluation scale from 0 to 10, on which 0 corresponded to "no pain at all" and 10 to "the worst pain imaginable";
- sensation intensity: the intensity of the sensations was the second main evaluation criteria. In the same symptom journal, the patients recorded the intensity of the perceived phantom breast sensations once a day using a numerical evaluation scale from 0 to 10, on which 0 corresponded to "no sensation at all" and 10 to "the worst sensation imaginable".

The qualitative measurements consisted in producing drawings of their breasts, their shape, as well as graphically locating it by coloring the intensity of the pain and/or sensations. That graphic indicator made it possible to monitor the perception the two patients had of their breast(s) throughout the therapy. For information, the patients' graphic illustrations were produced before (pre-test) and after (post-test) EMDR therapy, so as to illustrate the differences existing in terms of perception of the sensations and/or pain of the phantom breast (Fig. 2).

Therapy

The number of EMDR sessions was determined by the number of targets to process. In our study, the therapy could focus on two types of targets. First of all, on currently disturbing memories related to the disease (its onset, its progress, its personal, family, social, and professional consequences, etc.) and treatment (mastectomy, radiotherapy, chemotherapy, etc.). Cancer diagnosis disclosure, the fear of dying, the fear of recurrence, the sacrifices and the mourning of a healthy body were among the many life events at the source of distress and whose psychotraumatic dimensions were unquestionable (intrusion, avoidance, etc.). For processing this type of target, the 8-phase standard protocol (Shapiro, 1989) was used. However, when EMDR therapy was directed at the sensations/pain of the amputated phantom breast (PBS), the protocol was adapted. Although the standard protocol is often identified and presented in the literature (Shapiro, 1989, 1995, 2001), the same is not true for the specific protocol that we present in Table 1 below.

In this study, the choice of bilateral stimulation focused on carrying out eye movements and tactile stimulations. As both methods were assumed effective (Servan-Schreiber et al., 2006; Shapiro, 2001), the choice was left up to the therapist and/or the patient. EMDR therapy consisted of weekly 90-minute sessions and was provided shortly after the participants were recruited. It ended when the participant no longer reported any pain at the end of the session, or did not report any additional decrease concerning the disturbance related to the targets associated with the trauma and the pain, or concerning the pain intensity (current pain target), during three sessions in a row.

Table 1 Phases of URG-EMDR protocol.

Phase 1	Therapist takes patient's medical history concerning the present situation, history of the disease, past challenges, and PBS symptoms
Phase 2	Therapist teaches patient about psychological trauma, PBS and psychotherapy: regarding the first aspect, the goal is to provide the patient with information about the psychological impacts that a disease like cancer can have. The goal is also to explain what PBS is. Teaching the patient about psychotherapy consists of presenting EMDR therapy in general and explaining the protocols that will be used and their specific character
Phase 3	Evaluation: therapist identifies the target, i.e. the pain and/or sensations currently perceived in the breast(s). "Describe how you perceive the pain and/or sensation now" (for pain, perceptions were in terms of tearing, cutting, stinging. For sensation, perception was in terms of tingling, squeezing, tickling). The patients are then advised to build a mental image of that perception. To do so, the patients may be helped by asking them "If the pain and/or sensation had a color, what color would it be? (red or black was often associated with rather strong sensation or pain intensities, while yellow or white, for example, was associated with weaker sensation or pain intensities). What shape or size would it be? Would it tend to be hot or cold? What material (wood, steel, etc.) might the area of pain or sensation be made of?" At that point, the patient could draw the shape of the breast, as she imagined it mentally. Such an aid also made it possible to position the area of pain and/or sensation graphically, to give it a shape and outline. Coloring the area at issue allowed the patient to express the intensity of the perception. The patients were then asked (negative cognition) "If you think of the pain and/or sensation in your breast(s), what are the words that come to mind and that say something negative about you or about the pain right now (example: I am powerless)? The patients then select an alternative positive cognition (example: I am in control) whose validity is measured using a scale from 1 ("completely false") to 7 ("completely true"). The patients are then asked to think of the pain and/or sensation while they think of the words of the negative cognition so as to say which emotion(s) they experienced (example: I'm afraid). Then, the patients were asked to think of the pain and/or sensation and the negative cognition so as to assess the strength of the pain and/or sensation on a Subjective Units of Distress Scale (SUD): the pain SUD ranging from 0 ("no pain at all") to 10 ("the worst pain imaginable") and the sensation SUD ranging from 0 ("no sensation at all") to 10 ("the worst sensation imaginable")
Phase 4	Target desensitization: therapist asks the patient to concentrate on the target image and the related aspects while simultaneously focusing on the bilateral stimulation introduced by the therapist. The bilateral stimulation refers to eye movements or tactile stimulations alternating from left to right, at an approximate frequency of two movements, sound or taps per second for about 45 seconds. Once that "series" is over, the patient briefly reports what came to mind. The procedure is repeated until the initial target memory no longer represents a disturbing source
Phase 5	Positive cognition installation: therapist teaches the patient to think of the target image and repeat the positive cognition while leading the patient through bilateral stimulation until her level of truth and belief are considered optimal
Phase 6	Body scan: therapist checks for any sign of residual discomfort or physical tension. If any of these signs are reported, the therapist teaches the patient to concentrate on her physical sensations while leading the patient through bilateral stimulation until the tension has decreased or disappeared
Phase 7	Session closure: therapist makes sure the patient is prepared to leave the session
Phase 8	Reevaluation during the following session: the patient comments on the targets processed previously and if need be, a new target is selected for the following session

Results

Both the patients had striking or traumatic memories related to the onset of their cancer, which needed processing and which established several targets to process in EMDR with the standard protocol.

For Paule, we processed four targets: the cancer diagnosis disclosure, the fear of dying, the fear of recurrence and the loss of her femininity. For Nora, we processed three targets: the discovery of the cancer upon palpating her breast, the cancer diagnosis disclosure and the fear of dying.

The painful perceptions were characterized in terms of squeezing, tearing, cutting, stabbing, ripping out, stinging,

twisting, cramps, tugging, flashes, crushing, contractions, throbbing. The sensations were differentiated from the painful perception and categorized by the patients in terms of tightness, stinging, numbness, squeezing, tingling, itching, heaviness, warmth and tickling. The distinction between pain and sensation appeared qualitatively different here.

Quantitative results

For both our patients, the results indicate EMDR therapy has a positive effect on all the scales, indicating a drop in the overall score for anxiety (STAI scale) and depression (CES-D

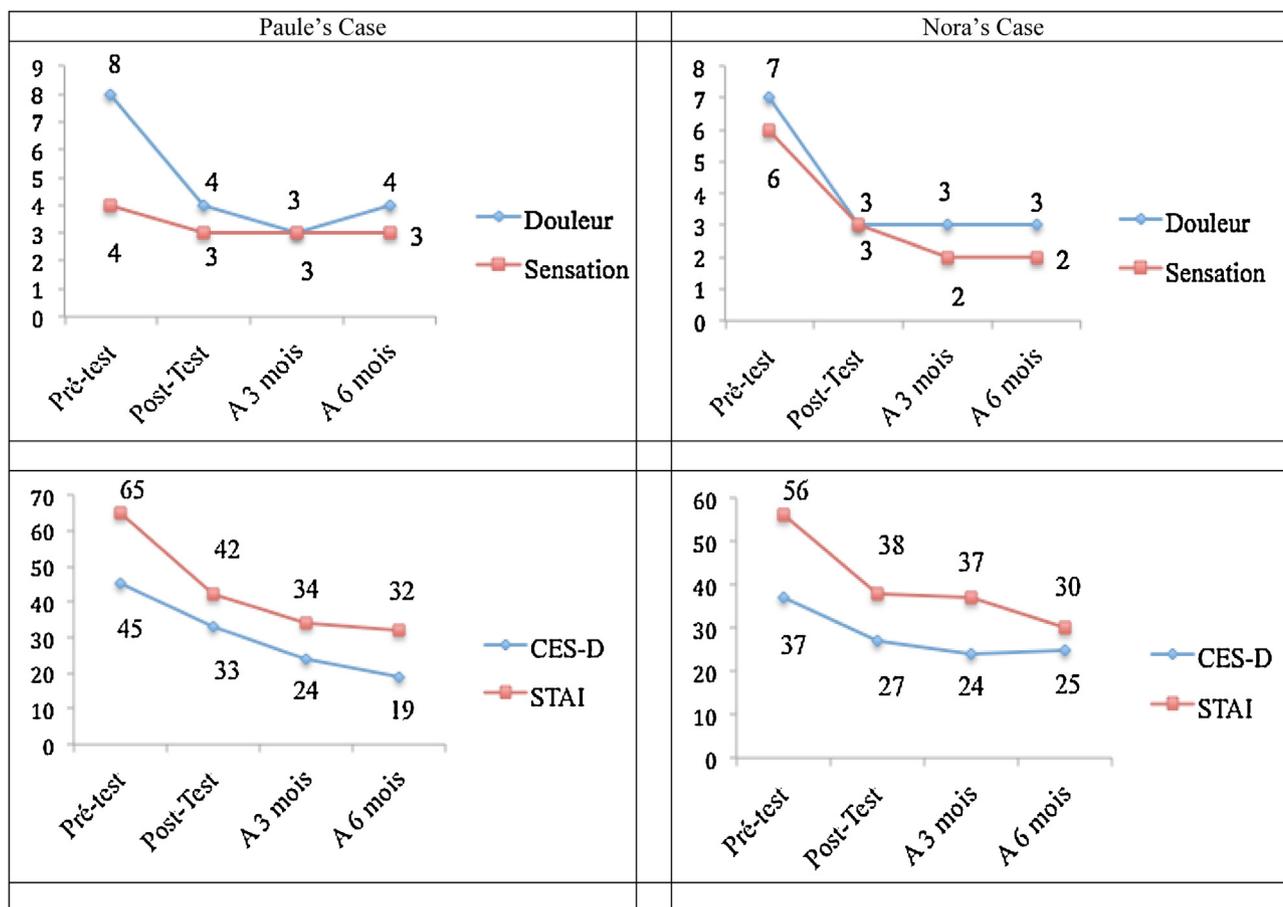


Figure 1 Pain intensity, sensation INTENSITY, STAI and CES-D on pre-test, post-test and at 3- and 6-month follow-ups.

scale), as well as for the intensity of PBS through a decrease in pain and sensation, as shown in Fig. 1.

For Paule, the pain intensity was halved after EMDR therapy, going from a score of 8 on the pre-test to a score of 4 on the post-test. That score then stabilized around 3–4 at the three- and six-month follow-ups.

The phantom breast sensation also decreased from a score of 4 on the pre-test, stabilizing at a score of 3 on the post-test as well as at the three- and six-month follow-ups.

Moreover, we observed a distinct decrease in Paule's emotions of depression and anxiety, through a decrease in the scores on the STAI and CES-D scales. In fact, Paule anxiety score went from 65 on the pre-test, to a score of 42 on the post-test, a score which continued to decrease at three (34) and six (32) months.

The same was true for the depression score that went from 45 on the pre-test to 33 on the post-test, and continued to decrease at three (24) and six (19) months after the therapy.

As for Nora, the results observed were similar. The pain intensity went from 7 on the pre-test to a score of 3 on the post-test, and remained stable at the three- and six-month follow-ups after the end of therapy. Likewise, the phantom breast sensation, higher than in Paule's case, went from 6 on the pre-test to a score of 3 on the post-test, and continued to decrease to a score of 2 at the three- and six-month follow-ups.

As for the anxiety and depression scores, the decrease was also significant. From a score of 56 on the STAI anxiety scale on the pre-test, Nora went down to a score of 38 on the post-test, and continued to decrease at the follow-ups three (37) and six (30) months after the end of therapy. The depressive emotions (CES-D) also decreased from a score of 37 on the pre-test to 27 on the post-test, stabilizing around 24–25 at the three- and six-month follow-ups.

Qualitative results

In addition to the quantitative results providing a quantified indication of the patients' progress thanks to their EMDR therapy, the use of breast drawings with colored areas highlighting the perception of phantom breast sensations and pain before and after therapy (Fig. 2) provides additional clinical indications.

It is actually possible to visually observe the work completed during the therapy.

For Paule, the substantial decrease in pain related to PBS before and after the therapy can be seen on the breast drawing where, although both breasts were still completely perceived at the time of the first EMDR session, they had totally disappeared from her body representation by the end of the last session. Furthermore, the breasts were almost entirely colored in red before the therapy, in particular



Figure 2 Breast drawings with areas colored to show perception of pain and sensations, before the therapy and at the end of therapy.

her more prominent left breast. After EMDR therapy, red had almost completely disappeared from the drawing, being replaced by thin yellow lines. The volume of her breast clearly decreased, and had totally disappeared after the therapy, while it went from a score of 4 to 3 on the PBS sensation scale.

For Nora, whose pain and sensations of PBS had been halved on the scales, a significant change can be observed with respect to the color used in the drawing, as well as a change with respect to the volume of her breasts. Although the pain and thus the red color had almost totally disappeared from the drawing after EMDR therapy, the volume of her breasts did not decrease as drastically as in Paule's case; for Nora, the score went from a phantom breast sensation of 6 on the pre-test to 3 on the post-test. Nevertheless, the volume of her breast appeared to be smaller, smoother and thinner, after EMDR therapy.

Discussion

The results obtained through the use of EMDR on Paule's and Nora's PBS are encouraging. After an average of 10 sessions, EMDR therapy actually enabled a significant decrease in the sensation and pain of PBS, as well as a decrease in the patients' anxiety and depression, whereas earlier treatment had not enabled any improvement. Associating a standard protocol targeting the traumatic events related to the disease with the use of a specific protocol targeting the phantom breast pain/sensations made it possible to treat the patients' experience as a whole. While the improvement in the anxiety and depressive affects enabled by the standard EMDR protocol supports the commonly accepted results pertaining to the effectiveness of EMDR on these disorders, as well as on PTSD, the addition of a protocol targeting pain/sensation is unprecedented. Nevertheless, this protocol becomes totally worthy of interest in a problematic disorder like phantom breast syndrome where sensations tend to appear in the first few years after surgery (Crone-Münzebrock, 1950; Kroener et al., 1989). Furthermore, based on these results, it can be observed that despite the substantial decrease in scores on the anxiety and depression scales, as well as the specific PBS measurements, the

representation of the breast does not necessarily decrease as intensely. That was especially the case for Nora, whose PBS measurements were halved, but whose breast was still represented as present in the drawings after EMDR therapy. The perception of body representation and the change in breast representation are therefore not necessarily quantifiable. The use of additional tools such as drawing and coloring is consequently worthwhile in conveying the representation that the patients have of their bodies, a subjectivity which is hard to objectify on purely quantitative scales.

Nevertheless, there is substantial research testifying to the link between the painful syndrome – as is the case with PBS – and the inappropriate storage or chronic activation of memories related to the perceptions of pain and sensations (Flor, 2002; Katz and Melzack, 1990). In the study presented here, we had put forth the hypothesis that EMDR used in processing traumatizing memories coupled with treating painful symptoms and sensations characteristic of PBS could be effective. Our results indicate that the EMDR approach can prove to be a promising, relatively brief and non-invasive treatment strategy. In fact, significant decreases were achieved with respect to PBS for the perception of pain and/or sensation. While the problematic nature of PBS remains specific and cannot be totally superimposed with the treatment of pain in a phantom limb, such results are comparable to those in the De Roos et al. (2010) study in which 40% of the patients were considered as totally pain-free after 3 months. These results are consistent with other studies dealing with the treatment of chronic pain of a phantom limb with EMDR in which 40% (Schneider et al., 2008) to 80% (Wilensky, 2006) of the participants were considered cured. Lastly, it should be noted that the scores obtained on the secondary evaluation criteria (STAI, CES-D) decreased significantly over time and remained stable at three and six months. Such a result suggests the link between PBS and the patients' psychological distress. In that respect, it should be recalled that we opted for a therapeutic strategy that consisted of distinguishing two types of targets. The first target related to the experience of the disease and the second target, more specifically related to the PBS symptoms. It is hard to say what contributed most to the decrease in the primary and secondary evaluation criteria. Whatever the case, it is not possible, in our

opinion, to aim at optimal remission in these patients without considering treatment of both aspects of the problem these types of patients have. In fact, what undoubtedly creates the specificity of PBS is that it occurs within the problematic context of cancer: a disease with challenges and stages during which many traumatic experiences accumulate and on which patients do not always have time to dwell, since each new day requires them to move forward and cope. In our study, the patients reported between 1 and 4 memories related to the period of the disease – a disease that often sounds like a death sentence in the popular imagination and in patients' psychic economy. Moreover, that fear of death never really leaves the patients, who even when in remission, always have the fear of recurrence hanging over their heads. As a result, the onset of every unusual symptom is often interpreted and contemplated as a warning sign of the disease, which brings back the patient's memory. That is most likely what is being expressed by the PBS symptoms (pain and sensations), which are all recall cues of the disease. In our opinion, once freed from the challenge of the disease itself, from the emotional baggage and from the distress it causes even years after the treatment, the terrain is clearer and more conducive to treating the symptoms of phantom breast sensation and pain. The dysfunctional mnemonic links between the "cancer" experience and possible psychic trauma in the history of diseases (Basset et al., 2013) calls for more global EMDR treatment, capable of improving the effect of the treatment even more.

In the study presented here, the two protocols had specific effects. Although the standard protocol, already substantially documented, allowed a decrease in the patients' distress related to the multiple traumatic events that a pathology such as this imposes on patients, that was not at all the case for the pain protocol more focused on the intensity of pain and sensation. In fact, beyond the primary and secondary evaluation criteria, and thanks to the use of drawing and coloring, we observed to what extent the cognitive representations of pain, as well as of the amputated breast(s), evolved with psychotherapy for all the patients. Little by little, the drawing that the patients made of their chest became consistent with the physical reality of the mastectomy. Over the course of the treatment and sessions, a sort of reorganization seems to have taken place. The same was true for the areas of pain and sensations which, most of the time, were reduced, and sometimes disappeared, in connection with a decrease in the intensity of the pain and sensation. EMDR, like other psychotherapies for that matter (if psychotherapies are considered as processes of change) activates and stimulates neuroplasticity (Melzack et al., 2001). In that respect, Melzack et al. propose the concept of a "neuromatrix", which produces a sort of neurosignature, in other words a sort of characteristic pattern of inputs indicating that the body is intact. This type of matrix functions in the absence of sensory input coming from the body's periphery, which creates the impression of having a limb, even when that limb has been removed. The neuromatrix, undoubtedly genetically determined, can also be shaped by experience. EMDR therapy is part of that active experience which, without a doubt, contributes to adjusting the neurosignature. Focusing on the amputated breast(s) at the time of treatment, as well as on the pain and sensations

are all components that can contribute to a kind of cortical reorganization and thus to the readjustment of the neurosignature. Furthermore, there is a known link between pain in a phantom limb and cortical reorganization (Flor, 2003) and the latter can be modified by a transformation of the sensory input in the neuronal network (Flor et al., 2001).

Conclusion

One of the limitations of the present study is the small size of the sample, which only enables the presentation of case studies. Furthermore, due to the absence of a control group (placebo), it is possible that the improvements reported are attributable to the passing of time rather than specifically to the therapy, even though the immediate post-test effect tends to testify to the operant aspect of the protocol. It is also possible that non-specific factors (hope, belief in effectiveness of the therapy, support, therapist's empathy, quality of the therapeutic bond) may have contributed to reducing the intensity of the pain and sensation. It is nevertheless noteworthy that our patients had been suffering from PBS for several months and that the prior psychological and pharmacological treatments had not achieved such effects. Although these results remain to be confirmed on a larger population, including a control group, they are still promising insofar as they suggest that psychological treatment based on EMDR techniques and adapted to the specificity of PBS could prove to be effective in providing relief to these patients.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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