

Emotion

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Neurophysiological Traces of Interpersonal Pain: How Emotional Autobiographical Memories Affect Event-Related Potentials

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The automatic, involuntary reactivation of disturbing emotional memories, for example, of interpersonal pain, causes psychological discomfort and is central to many psychopathologies. This study aimed at elucidating the automatic brain processes underlying emotional autobiographical memories by investigating the neurophysiological dynamics within the first second after memory reactivation. Pictures of different individualized familiar faces served as cues for different specific emotional autobiographical memories, for example, for memories of interpersonal pain and grievances or for memories of appreciation in interpersonal relationships. Nineteen subjects participated in a passive face-viewing task while multichannel electroencephalogram was recorded. Analyses of event-related potentials demonstrated that emotional memories elicited an early posterior negativity and a stronger late positive potential, which tended to be particularly enhanced for painful memories. Source estimations attributed this stronger activation to networks including the posterior cingulate and ventrolateral prefrontal cortices. The findings suggest that the reactivation of emotional autobiographical memories involves privileged automatic attention at perceptual processing stages, and an enhanced recruitment of neural network activity at a postperceptual stage sensitive to emotional-motivational processing.

Keywords: evoked potentials, ERP, early posterior negativity (EPN), late positive potential (LPP), face processing

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Emotionally painful events and their later mnemonic reactivations are closely linked to subclinical psychological discomfort as well as to clinically relevant mental disorders. An extreme example is the posttraumatic stress disorder, in which traumatic autobiographical memories are spontaneously triggered and involuntarily retrieved (*Diagnostic and Statistical Manual of Mental*

Disorders, fourth edition; American Psychiatric Association, 1994). Likewise, retrieving and being occupied with painful emotional memories is central to other mental disorders such as, for example, depression or anxiety disorders. The reactivation of painful autobiographical memories can also be part of everyday life, when current stimuli, for example, a photograph of an ex-partner or a supposedly familiar voice, remind someone of past painful experiences, for example, frustrating conflicts or a bitter separation. In both clinical and nonclinical contexts, emotionally salient autobiographical memories (or fragments of them) are triggered in an automatic and involuntary manner. Neurophysiological methods, such as event-related potentials (ERPs), provide a sensitive measure to track fast and automatic brain processes, and therefore seem particularly suited for the investigation of the reactivation of emotional autobiographical memories.

Much of the previous neurophysiological research on the processing of emotional content has focused on ERPs in reaction to standardized emotionally arousing pictures that are assumed to trigger an immediate emotional response in participants. Viewing emotionally arousing stimuli (vs. neutral stimuli), provokes typical ERPs, such as the early posterior negativity (EPN) and the late positive potential (LPP). The EPN is typically observed in the difference wave between brain responses to emotional versus neutral stimuli, and emerges in a time window between 200 and 300 ms poststimulus with a temporo-occipital scalp distribution

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(e.g., Citron, Weekes, & Ferstl, 2013; Schupp, Schmäzle, Fleisch, Weike, & Hamm, 2013). The EPN reflects the sensory enhancement of emotionally relevant content and its automatic attention allocation (Olofsson, Nordin, Sequeira, & Polich, 2008; Schupp et al., 2013). The LPP appears from 400 ms poststimulus on as a relative positivity over central scalp electrodes for emotional compared to neutral stimuli (e.g., Cacioppo, Crites, Berntson, & Coles, 1993; Cuthbert, Schupp, Bradley, Birbaumer, & Lang, 2000; Schupp et al., 2000; Weinberg & Hajcak, 2010). The LPP is supposed to index sustained and more elaborative processing of emotionally salient stimuli (e.g., Foti, Hajcak, & Dien, 2009; Hajcak, MacNamara, & Olvet, 2010).

While extensive research elucidates the neurophysiological correlates of an immediate emotional response triggered by standardized emotionally arousing stimuli, only few studies address the neurophysiological correlates of emotional autobiographical memories reactivated by corresponding idiosyncratic stimuli. However, the latter would be a better approximation of the involuntary reactivation of disturbing autobiographical memories observed in everyday contexts and in clinical circumstances. The aim of the present study is to explore the neural signature of emotionally painful autobiographical memories that are reactivated by personally relevant, individualized stimuli.

To operationalize emotionally painful autobiographical memories, the present study uses a trauma-like mental condition found in clinical as well as in nonclinical populations, namely the presence of longstanding interpersonal grievances and pain, also referred to as *unfinished business* (UFB; Greenberg & Foerster, 1996; Greenberg & Malcolm, 2002; Paivio & Greenberg, 1995). Emotional UFB derives from autobiographically experienced painful, unsatisfying, frustrating, or even abusing interactions with a significant other person. It consists of persisting unresolved negative feelings toward that person (e.g., feeling betrayed or humiliated by an ex-partner, or feeling neglected by a parent). Like in other associative memory phenomena, different cues related to the original situation or person can automatically reactivate autobiographical emotional memories and cause emotional disturbances. Through this involuntary reactivation, UFB is a clinically relevant example of how past experiences may (negatively) impact a person's current functioning. Moreover, this mental condition is precisely operationalized by defined criteria (e.g., Greenberg & Foerster, 1996), and represents an excellent, reliable and yet ecologically valid trigger to explore the characteristics of emotionally painful autobiographical memories. Psychotherapy research demonstrated that specific in-session processes could be related to the successful resolution of UFB (Greenberg & Foerster, 1996; Paivio & Greenberg, 1995). In brief, the resulting empirically anchored model of resolution of UFB states that in-session processes such as the reactivation, exploration, and expression of interpersonal pain, as well as the restructuring of these feelings to shift view of self and other lead to the resolution of UFB (Greenberg & Malcolm, 2002). On a broader scale, it is hypothesized that therapeutic change in general results from the reactivation and updating of emotional autobiographical memories, so that new and healthier emotional experiences can be reconsolidated (Lane, Ryan, Nadel, & Greenberg, 2015). In this sense, the reactivation of emotionally painful memories represents an essential and intentional step within the process of therapeutic change. Both the intentional reactivation in psychotherapy and the involuntary, unwanted reactivation of emo-

tionally painful autobiographical memories (or fragments of them) outside the therapeutic setting rely on associative memory links between arousing stimuli and complex, rich, and personal memory representations.

Reactivating genuine emotionally painful autobiographical memories, that is, UFB, calls for personalized emotionally arousing stimuli. Previous experimental research on the neurophysiology of emotional memories often employed standardized, impersonal emotional cues or newly acquired emotional (i.e., experimental episodic instead of real autobiographical) representations to trigger emotional reactions or memories (see, e.g., Aguado et al., 2012, for experimentally learned emotional face stimuli; see, e.g., Daselaar et al., 2008, for standardized word-cued autobiographical recall in functional MRI [fMRI]). However, studies using standardized cues or experimentally acquired emotional memories do not capture the richness, personal relevance and impact associated with real autobiographical memories, and are therefore limited in their ecological validity (see Pascual-Leone, Herpertz, & Kramer, 2016, for a critique of standardized stimuli from a clinical point of view). The present study intends to trigger individual, personally relevant emotional autobiographical memories under controlled conditions. In the case of UFB, the respective memory representations and negative feelings—such as hurt or betrayal—are reactivated by specific cues related to the significant other with whom one has UFB, for example, his or her face, name or place of living. Among these cues, faces seem to be the primary ones to trigger mental representations linked to familiar persons (e.g., Abdel Rahman, Sommer, & Schweinberger, 2002; Bobes, Quinonez, Perez, Leon, & Valdes-Sosa, 2007; Tiedt, Beier, Lueschow, Pauls, & Weber, 2014; Vuilleumier & Pourtois, 2007).

Faces provide access to very different memory contents, for example, face-typical structural features, person-identity, and emotional-social significance such as closeness of relationship, as well as biographical knowledge and emotions associated with that person. Faces of emotionally significant persons can thus activate specific emotional autobiographical memory contents under well-controlled conditions (when compared to appropriate control faces). Electrophysiological research on faces and emotions has identified several ERP components with specific functional significance for emotional face processing. Among these are the N170 reflecting the structural encoding of faces (e.g., Bentin, Allison, Puce, Perez, & McCarthy, 1996; George, Evans, Fiori, Davidoff, & Renault, 1996), the above-mentioned EPN, the P3 reflecting task relevance and motivational significance (e.g., Polich & Kok, 1995), as well as the above-mentioned LPP.

A recent study investigated the ERPs elicited by neutrally looking faces that were associated with either emotional or neutral biographical knowledge, and that belonged to either well-known (famous) or previously unknown (newly learned) persons (Abdel Rahman, 2011). For well-known faces, the EPN and LPP were enhanced as a function of emotional biographical knowledge. Both the EPN and LPP effects were more pronounced when the emotional biographical knowledge was negative as compared to positive biographical knowledge. These results demonstrated that reminding participants of emotionally salient biographical information by presenting well-known faces captures automatic attention at a sensory level and leads to an enhanced and sustained further processing. Emotional biographical knowledge, especially when negative, thus plays a substantial, reinforcing role in the perceptual and postperceptual evaluative processing (Abdel Rah-

man, 2011). In an oddball paradigm with unfamiliar faces as standard and either previously learned and thus visually familiar faces or well-known faces of emotionally close persons as deviant stimuli, both types of deviant faces elicited a relative positivity around 500 ms with maximal amplitudes over centroparietal electrodes. Additionally, the emotionally relevant faces of close persons triggered a positivity with an earlier maximum at approximately 350 ms over frontal electrodes (Bobes et al., 2007). Here again, the results showed that the emotional significance of faces influences neural information processing at a relatively early time point, and that the related process can be dissociated from purely visual familiarity. In a recent set of passive face viewing paradigms, familiar faces of loved persons elicited higher P3 and LPP compared to unknown faces, which was interpreted as reflection of intense positive affect (Guerra et al., 2011, 2012; Vico, Guerra, Robles, Vila, & Anllo-Vento, 2010). Similarly, a magnetencephalography study using familiar and loved faces as retrieval cues for emotional autobiographical experiences found enhanced activity for loved faces from 300 ms on (albeit for female participants and left-sided sensors only, Tiedt et al., 2014). Source estimation studies suggest that the intracranial generators of the LPP in reaction to emotional visual stimuli are located in the posterior parietal and occipital cortex (Keil et al., 2002). Activity in these regions is thought to “reflect a relatively high level of visual processing, in which sustained attention is allocated to [. . .] emotionally salient cues” (Keil et al., 2002, p. 648). Combined electroencephalography (EEG) and fMRI recordings confirmed that the LPP reflects concurrent activity in multiple structures of the visual system, that is, across the lateral occipital, posterior parietal, and inferotemporal cortices (Sabatinelli, Lang, Keil, & Bradley, 2007). They also showed that the LPP correlated with activity in subcortical emotion processing structures such as the amygdala (Liu, Huang, McGinnis-Deweese, Keil, & Ding, 2012; Sabatinelli, Keil, Frank, & Lang, 2013). With regard to the EPN, source estimations have suggested that the EPN for emotional faces or words is generated in parieto-occipital cortical areas (e.g., Frühholz, Jellinghaus, & Herrmann, 2011; Keuper et al., 2014; see Jaspers-Fayer, Ertl, Leicht, Leupelt, & Mulert, 2012, for simultaneous EEG and fMRI analyses of the auditory EPN). However, studies employing both fMRI and EEG techniques have failed to establish significant relationships between modulation of the EPN and visual cortical blood-oxygenation-level-dependent signals in response to emotional pictures (e.g., Sabatinelli et al., 2013).

In summary, faces can trigger the activation of specific biographical representations, and previous literature points at specific functional significance of ERP components. Thus, ERPs elicited by personally and emotionally significant faces represent a well-suited technique to investigate the reactivation of emotional autobiographical memories. In the present study, faces of persons with whom one has longstanding interpersonal grievances (i.e., emotional UFB) served as triggers for painful autobiographical memories. We compared the neurophysiological reaction to these UFB-faces to the reaction to several control faces selected to control for facial familiarity, emotional arousal, and closeness of relationship. We assumed that the UFB-faces elicit stronger subjective feelings of discomfort, that is, unpleasantness, arousal, and weakness, as compared to control faces. Based on previous evidence for enhanced perceptual and postperceptual neurophysiological processing of emotionally salient contents, we hypothesized that the

reactivation of painful memories involves pronounced attentional processing on a sensory level, indexed by the EPN. We also expected an enhanced and sustained postperceptual evaluation, indexed by a stronger LPP. We assumed that the hypothesized EPN- and LPP-differences between the reactivation of emotionally painful and nonpainful memories involve differences in intracranial source configuration, which can be detected by topographic analyses of scalp surface potentials and by inverse source estimation methods. Additionally, differences were expected in the overall amount of brain activity, which can be detected by the calculation of the overall signal strength of the scalp electric potential.

Method

Participants

The sample consisted of 19 healthy adults, 17 females and two males, who reported suffering from UFB. Participants were recruited via mailing lists and announcements in psychotherapy training courses. Interested participants were contacted via telephone by a trained psychotherapist familiar with UFB to check for the presence of UFB which was operationalized according to Greenberg and Foerster (1996) as (a) the presence of lingering unresolved feelings such as hurt or betrayal, which were (b) related to a significant other person, (c) currently experienced, and (d) problematic for the experiencing person. Participants were aged from 26 to 42 years ($M = 30.9$, $SD = 4.6$), and had normal or corrected-to-normal vision. All participants had a degree in psychology and were trainees or practitioners in the field of psychotherapy. They participated in the present experimental setup as part of a larger study, which encompassed a psychotherapeutic intervention for the problem of UFB. Participants who were enrolled in psychotherapy training classes received course credit for participating. Exclusion criteria were nonfluency in German, psychopharmacological medication, and suicidality. The responsible research ethics board approved the study and all participants provided informed consent before participating.

Photograph-Viewing Task and Stimuli

To activate biographical emotional memory representations, photographs of different faces were presented while subjects were instructed to attend to their emerging emotional experience. The photographs showed (a) the significant other (UFB) with whom subjects had UFB, (b) an appreciated significant other (APR) with whom subjects had a similarly close but unproblematic relationship, (c) a familiar person (FAM) whom they knew as long as the UFB-person, and (d) pictures of two different unknown persons (UNP).

Participants provided digitized photographs of (a), (b), and (c). The unknown faces (d) were selected from Minear and Park (2004). The APR-picture served to match the UFB-person in importance and closeness of relationship. The FAM-person was displayed as a match in familiarity, that is, in length of relationship and freshness of memories. The pictures of the first unknown person matched the UFB-person in age and sex, and the second unknown person was introduced to ensure that neither the APR-nor the FAM-person, which might be of other sex as the UFB-person, was the only opposite sex picture in the set. The picture of

the second unknown person was only introduced for online balancing reasons during the passive-viewing task and was not included in further analyses. All faces had neutral-to-friendly expressions and looked straight into the camera. The photographs were edited using the software GIMP (i.e., GNU Image Manipulation Program, Version 2.8.2). All photographs were converted into gray-scale, and the face was cut out and shown on a white background. The stimuli were adjusted in terms of luminance and interpupillary distance (500 pixel) and displayed on a computer screen via the software E-Prime (Version 2.0) with stimulus duration of 2,000 ms and jittered interstimulus intervals of 1,000–1,500 ms. Each photograph was presented 30 times in a pseudo-randomized order with balanced positions within the presentation block. To monitor vigilance, a question mark was interspersed five times in each presentation block in reaction to which subjects were instructed to press the response key as soon as possible.

Self-Report Measures

After the picture viewing task, the Self-Assessment Manikin Scale (Bradley & Lang, 1994), a 9-point nonverbal pictorial Likert-scale, was displayed, and subjects were asked to rate their pleasure, arousal, and dominance associated with their emotional reaction to each photograph. For each of these three self-report variables, a one-way analysis of variance (ANOVA; conditions: UFB, APR, FAM, UNP) and planned contrasts between the UFB and each control condition (UFB vs. APR, CLO, UNP) were calculated. For the planned contrasts, effect sizes were estimated by r (e.g., Rosnow & Rosenthal, 2003).

EEG Recording

Multichannel EEG was recorded with a Nihon-Kohden Neurofax 1100 system from 70 scalp electrodes placed according to the extended 10/20 system. Two extra electrodes below the eyes were used to monitor eye movement artifacts. All channels were referenced online against the mean of C3 and C4 and digitally sampled at 500 Hz. All impedances were kept below 20 Ω , online filters were set at 0.016 Hz (high pass) and 150 Hz (low pass).

EEG Data Preprocessing

EEG data preprocessing was performed offline using Brain Vision Analyzer Version 2.0 (Brain Products GmbH, Gilching, Germany). Eye movement artifacts were identified and subsequently removed with the help of an independent component analysis (Jung et al., 2000; Makeig, Bell, Jung, & Sejnowski, 1996). Epochs with remaining artifacts were manually excluded from further analysis. Channels containing much physiological or electronic noise were interpolated by averaging data from adjacent electrodes (Perrin, Pernier, Bertrand, Giard, & Echallier, 1987). A bandpass filter from 0.5 to 18 Hz and a 50-Hz notch filter were applied. Next, all data was recomputed against average reference. ERPs were calculated by segmenting data in epochs of 1,000 ms post stimulus and averaging data separately for each subject and condition. An average of 25.5 artifact-free segments could be included for each participant and condition (range: 19–30).

EEG Analyses

ERP signal consistency. To define start and end points of the ERP epochs to be further analyzed, a topographic consistency test (Koenig & Melie-Garcia, 2010) was conducted. This procedure tests whether the overall ERP signal that can be characterized by a scalp electric field and thereby by an electric topography significantly different from noise in the data. It uses randomization-based statistics to compare the overall signal strength (global field power [GFP], see below) of the measured ERP signals to the GFP in shuffled and averaged data, that is, under the null hypothesis (for a detailed description of this procedure, see Koenig & Melie-Garcia, 2010).

Topographic differences. To detect time windows with significant differences between the scalp electric fields (topographies) of the four picture type conditions (UFB, APR, FAM, UNP), a topographic analysis of variance (TANOVA) was computed. TANOVA is a nonparametric randomization test for differences between whole electric field topographies. When applied to amplitude-normalized data (as in the present study), qualitative differences between electric field maps can be analyzed independently of their field strength. In contrast to ERP voltage waveform analyses at individual electrodes, TANOVA takes the spatial and temporal characteristics of the entire electric field into account and is reference-independent (e.g., Koenig & Gianotti, 2009; Michel & Murray, 2012; Murray, Brunet, & Michel, 2008). For time windows with significant topographic differences, pairwise topographic comparisons between the UFB and each control condition were conducted and illustrated by t -maps of the topographic differences. For each comparison, the maximum absolute t -value was extracted to order the four conditions according to their topographic similarity. Increasing t -values (and corresponding significance levels) would indicate increasing topographic dissimilarity between conditions.

Amplitude differences. To compare differences in the overall electric field strength (amplitude) between conditions, GFP (Lehmann & Skrandies, 1980) was computed. In average referenced data, GFP equivalents the standard deviation across all sensors at a given time point (Koenig, Kottlow, Stein, & Melie-Garcia, 2011; Michel & Murray, 2012). It constitutes a reference-independent measure of scalp field strength, which can be plotted as a waveform as a function of time.

The separation of topographic and amplitude differences has the following advantages: Significant topographic differences with normalized data must result from an at least partially different location and/or orientation of active intracranial sources and thereby indicate that at least partially different brain functions are involved (Koenig et al., 2011). Significant amplitude differences without topographic differences would indicate that similar, but differently strong sources are active (Koenig et al., 2011). All TANOVA and GFP analyses were based on randomization statistics and performed using the software RAGU (i.e., Randomization Graphical User Interface, Koenig et al., 2011). The number of randomization runs was set to 5,000. Similar to earlier studies, the TANOVA and GFP analyses were computed for every time point. However, to avoid errors due to alpha accumulation, only effects lasting over 25 ms were considered as significant (Murray et al., 2004; Ortigue et al., 2004; Stein et al., 2006).

Source estimation. Because topographic differences (as indicated by the TANOVA) must result from differences in the configuration of intracranial sources, a source-analysis method was employed to estimate the putative responsible intracranial generators. Epochs in which the TANOVA detected significant topographic differences were further explored with standardized low-resolution electromagnetic tomography (sLORETA, Pascual-Marqui, 2002). The sLORETA software (publicly available free academic software at <http://www.uzh.ch/keyinst/loreta.htm>) computes the cortical three-dimensional distribution of current density with exact localization, albeit with low spatial resolution (i.e., adjacent neuronal sources are highly correlated). The computations are made in a realistic head model (Fuchs, Kastner, Wagner, Hawes, & Ebersole, 2002), using the Montreal Neurological Institute (MNI) 152 template with the solution space restricted to cortical gray matter (Lancaster et al., 2000). The correspondent intracerebral volume comprises 6,239 voxels at 5-mm spatial resolution. In the present study, the sLORETA method was applied to the mean current density data of each of the two timeframes displaying significant topographic differences. Because our design asked for an ANOVA with repeated measures on four levels (UFB, APR, FAM, UNP), which was not implemented in sLORETA, normalized and log-transformed current density values for each voxel, condition and participant were exported from sLORETA to Matlab. The Matlab script is available in the online supplemental material. In Matlab, mean current density data for each of the two timeframes with significant topographic differences were computed for each participant, condition and voxel. Then, ANOVAs with repeated measures were performed on this mean current density data using the *fitrm* function in Matlab and specifying the within model with one four-leveled factor. The aim being to localize the observed TANOVA effects, only those voxels presenting TANOVA-analogue patterns of activation were considered and a significance threshold of $p < .05$ per voxel was applied. Clusters with three or more adjacent significant voxels were reported. Because sLORETA was restricted to epochs that had already shown significant topographic differences, it was not used to test for significant differences but rather to illustrate the already established significant differences. No further correction for multiple comparisons was applied.

Results

Self-Report Measures

Figure 1 shows the means and standard deviations for the Self-Assessment Manikin Scale scores of valence, arousal, and dominance. As the self-report data of one participant were not registered, only data of $N = 18$ participants were entered in the analyses. One-way ANOVAs yielded significant picture type effects for valence, $F(1.70, 28.97) = 34.05$, $p < .001$ (with Greenhouse–Geisser correction), arousal, $F(3, 15) = 23.27$, $p < .001$, and dominance, $F(1.93, 32.78) = 20.98$, $p < .001$ (with Greenhouse–Geisser correction). Planned contrasts of the UFB condition against the other conditions showed that faces in the UFB condition elicited significantly less pleasant feelings: UFB versus APR, $F(1, 17) = 100.00$; effect size $r = .92$; UFB versus FAM, $F(1, 17) = 29.83$; $r = .80$; UFB versus UNP, $F(1, 17) = 9.41$; $r = .60$; all $p < .01$, more arousal: UFB versus APR., $F(1,$

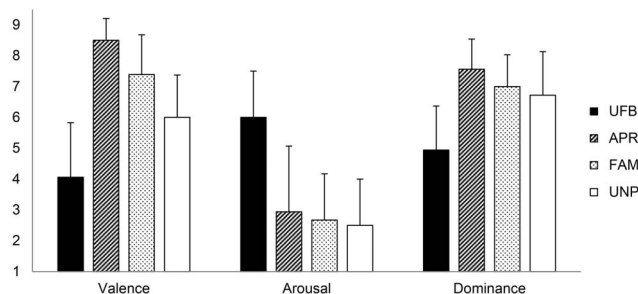


Figure 1. Means and standard deviations of the Self-Assessment Manikin Scale scores for valence, arousal, and dominance in reaction to the four picture types: unfinished business (UFB; black), appreciated persons (APR; shaded), familiar persons (FAM; dotted), and unknown persons (UNP; white).

17) = 25.75; $r = .78$; UFB versus FAM, $F(1, 17) = 65.39$; $r = .89$; UFB versus UNP, $F(1, 17) = 68.17$; $r = .89$; all $p < .001$, and less feelings of dominance: UFB versus APR, $F(1, 17) = 43.21$; $r = .85$; UFB versus FAM, $F(1, 17) = 25.38$; $r = .77$; UFB versus UNP, $F(1, 17) = 14.41$; $r = .99$; all $p \leq .001$.

EEG Measures

ERP signal consistency. The topographic consistency test (Koenig & Melie-Garcia, 2010) showed that in the majority of conditions, the ERP signal turned into an inconsistent signal, that is, with a bad signal-to-noise ratio, at around 950 ms, which was set as the end point of the analyzed epoch.

Topographic differences. The TANOVA revealed significant ($p < .05$; duration > 25 ms) topographic differences between the four different conditions (UFB, APR, FAM, UNP) in two timeframes, from 258 to 284 ms (mean $p = .004$) and from 602 to 628 ms (mean $p = .003$). Electrical scalp topographies for these timeframes for each condition, as well as pairwise comparisons between the UFB condition and each control condition and resulting t -value maps and significance levels are shown in Figure 2. For the EPN timeframe (258 to 284 ms), a conclusive pattern of order of conditions emerged: Topographic comparisons between the UFB condition against each control condition indicated that the topographic difference was small and nonsignificant between UFB and APR ($p = .453$; max. absolute $t = 3.29$), bigger and significant between UFB and FAM ($p = .026$; max. absolute $t = 3.24$), and biggest and significant between UFB and UNP ($p = .0106$; max. absolute $t = 4.43$). For the LPP time frame (602 to 628 ms), the topographic comparisons between the UFB condition and each control condition indicated a similar pattern of order of conditions. The topographic difference was smallest and with a trend toward significance between UFB and APR ($p = .0638$; max. absolute $t = 3.44$), bigger and significant between UFB and FAM ($p = .0146$; max. absolute $t = 4.10$), and biggest between UFB and UNP ($p = .0010$; max. absolute $t = 4.54$). The TANOVA effects thus revealed an order of conditions from UFB to APR to FAM to UNP. To allow for visual inspection of the ERP waveforms and for comparison with results of studies employing conventional ERP analyses, Figure 3 depicts the ERP waveforms at selected electrodes, separately averaged for each condition.

Source estimation. To estimate brain regions that might be responsible for the significant topographic differences in the time

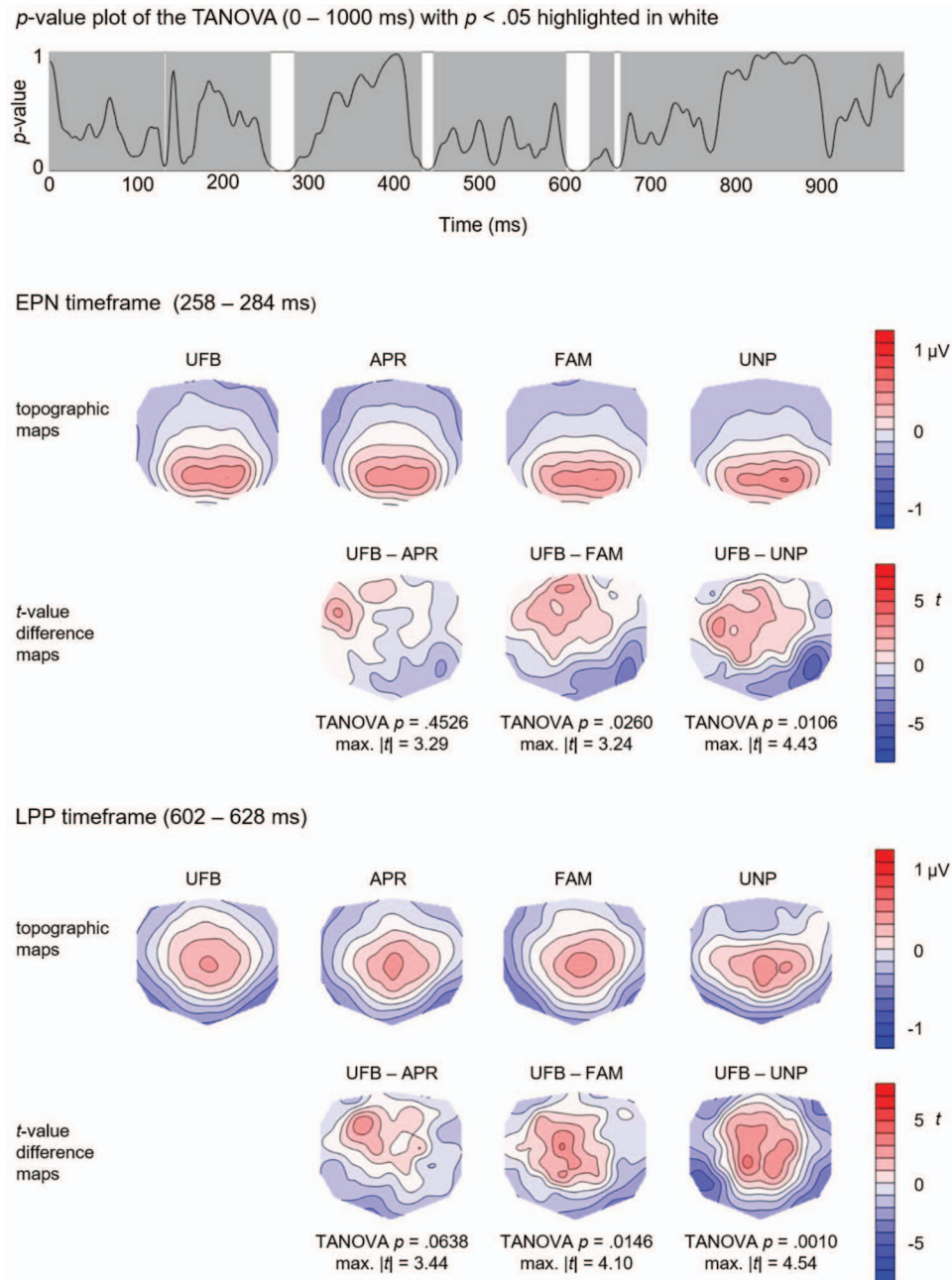


Figure 2. Illustration of topographic analysis of variance (TANOVA) results. Top: Temporal spread of *p*-levels in the overall TANOVA analysis. The *p* value (y-axis) is plotted as a function of time (x-axis); timeframes of *p* < .05 are highlighted in white. Middle and bottom: Topographic results for the early posterior negativity (EPN) timeframe (258–284 ms) and the late positive potential (LPP) timeframe (602–628 ms). Each upper panel shows the topographic maps for each of the four conditions, and the respective lower panel displays the *t*-value maps of topographic differences between the unfinished business (UFB) condition and each control condition. The increasing *t*-values indicate the increasing topographic dissimilarity between UFB and appreciated person (APR), familiar person (FAM), unknown person (UNP) conditions, respectively. Relative positivity is depicted in red and relative negativity in blue color. More saturated colors indicate higher microvolt or *t*-values, respectively. See the online article for the color version of this figure.

windows of the EPN (258–284 ms) and LPP (602–628 ms), the sLORETA model was applied to these time windows. As explained above, the analyses were restricted to those voxels presenting a TANOVA-like activation pattern (i.e., $UFB > APR > FAM > UNP$, or $UFB < APR < FAM < UNP$, respectively). For the EPN-time window (258–284 ms), the statistical analysis revealed significant sLORETA differences corresponding to the activation pattern of $UFB > APR > FAM > UNP$ in a cluster of eight adjacent voxels in the right pre- and postcentral gyri (Brodmann areas [BAs] 3, 4, and 6), and in a cluster of three adjacent voxels in the right inferior parietal lobule (BA 40). With an opposite activation pattern ($UFB < APR < FAM < UNP$), a cluster of six adjacent voxels was found in the right superior temporal gyrus (BA 22). The MNI coordinates of the absolute maximal F value of each cluster are listed in Table 1.

For the LPP time window (602–628 ms), the statistical analyses revealed three clusters with the Current Source Density (CSD) activation pattern of $UFB > APR > FAM > UNP$. The biggest cluster (43 adjacent voxels) was centered around the left inferior

frontal gyrus (BA 45), spanning pre- and postcentral structures of BAs 4, 6, 9, and 44 (see Figure 4). A cluster of 27 adjacent voxels was identified in the cingulum (BAs 23, 24, 31), with significant voxels in both left and right cingulate gyrus and spanning right precuneus (BA 7; see Figure 4). A third cluster (four adjacent voxels) with the above-mentioned activation pattern was located in the right posterior cingulate (BA 29) and parahippocampal gyri (BA 30). Additionally, sLORETA identified four clusters with the opposite CSD activation pattern of $UFB < APR < FAM < UNP$. In the right hemisphere, a big cluster of 26 adjacent voxels was located in the precentral gyrus (BA 4), spanning postcentral and inferior frontal gyri (BAs 3, 6, 42, 43, and 44; see Figure 4). Two additional right lateralized clusters were identified in the anterior cingulate gyrus (ACC, five adjacent voxels, BA 32) and in right ACC and medial frontal gyrus (two adjacent voxels, BAs 9 and 32). In the left hemisphere, clusters with the CSD activation pattern of $UFB < APR < FAM < UNP$ were localized in the left medial frontal gyrus (seven adjacent voxels, BA 10) spanning the ACC (BA 32), in the left medial frontal and superior gyri (three

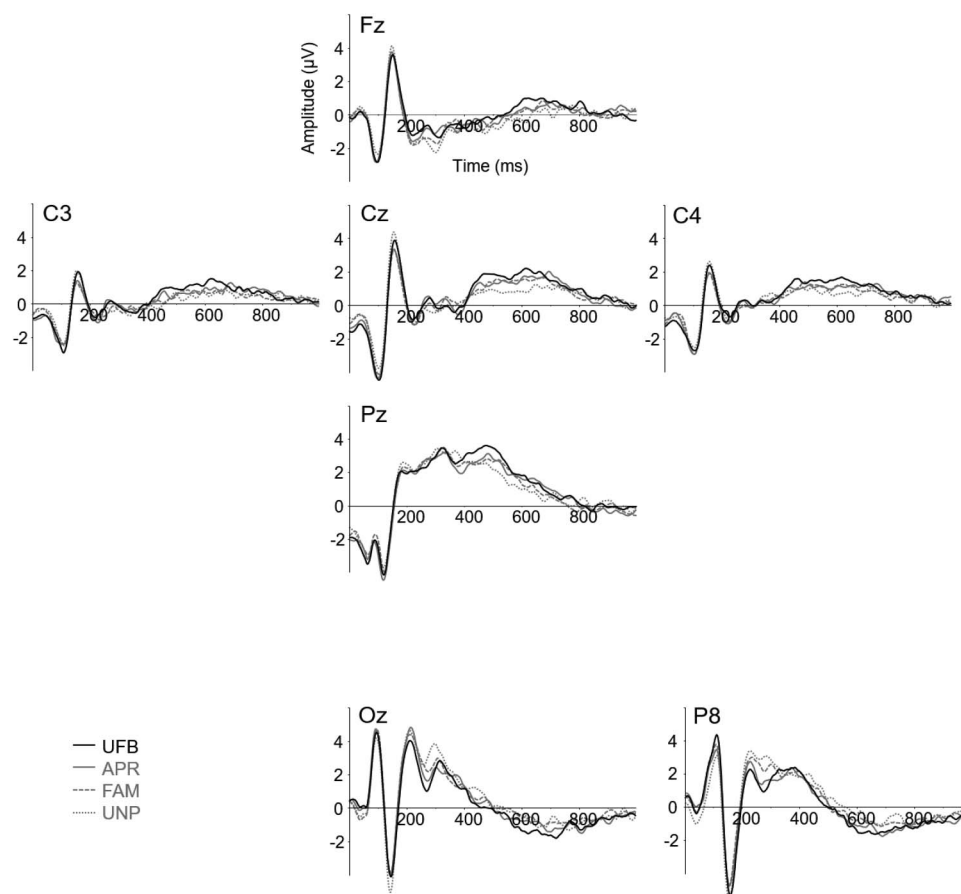


Figure 3. Average-referenced event-related potential (ERP) waveforms in reaction to faces of persons with whom participants had emotional “unfinished business” (UFB, solid black line), faces of appreciated persons (APR, solid gray line), faces of familiar persons (FAM, dashed gray line), and faces of unknown persons (UNP, dotted gray line). Top: Midline and central electrodes Fz, Cz, Pz, C3, and C4 are shown to descriptively illustrate the waveform shapes related the LPP component. Bottom: Occipital and parietal electrodes Oz and P8 are shown to descriptively illustrate the waveform shapes related to the early posterior negativity component. Negativity is plotted downward.

Table 1
Local Maxima of Standardized Current Density for the Contrasts Reflecting Topographic Analysis of Variance–Like Activation Patterns in the Early Posterior Negativity Time Window From 258 to 284 ms

Local maximum with TANOVA-like activation pattern	R/L	BA	MNI coordinates of local maximum			F_{\max}	Voxel/cluster
			x	y	z		
UFB > APR > FAM > UNP							
Postcentral gyrus	R	3	65	-20	40	4.48	8
Inferior parietal lobule	R	40	60	-30	30	3.59	3
UFB < APR < FAM < UNP							
Superior temporal gyrus	R	22	65	-45	10	3.71	6

Note. MNI = Montreal Neurological Institute; R/L = right/left hemisphere; BA = Brodmann area; UFB = unfinished business; APR = appreciated persons; FAM = familiar persons; UNP = unknown persons.

adjacent voxel, BA 10), and in the left inferior parietal lobule (two adjacent voxels, BA 40). The MNI coordinates of the absolute maximal F value of each cluster are listed in Table 2.

Amplitude differences. The GFP analyses indicated significant ($p < .05$; duration >25 ms) amplitude differences between the four conditions from 474 to 526 ms (mean $p = .001$), and from 582 to 628 ms (mean $p = .004$). In both timeframes, highest amplitudes were found in the UFB condition, and lowest amplitudes in the UNP condition, with APR and FAM conditions lying in between.

Discussion

This study investigated the neurophysiological traces of emotionally painful autobiographical memories. Such memories were

reactivated by personally relevant, idiosyncratic stimuli, that is, photographs of a person with whom one had long standing interpersonal grievances (emotional UFB).

As expected, we found time windows that fall within the typical latencies of the EPN and LPP to be sensitive to the emotionality associated with autobiographical memories. This was demonstrated by significant differences in electrophysiological scalp topography during the EPN timeframe and by significant differences regarding topography as well as signal strength (GFP) in the LPP timeframe. Because the effects fell within the typical latencies of the EPN and LPP, respectively, they were referred to as “LPP” and “EPN.” In both cases, the neurophysiological investigation revealed a meaningful pattern of conditions; suggesting that the neurophysiological reaction varied as a function of emotionality,

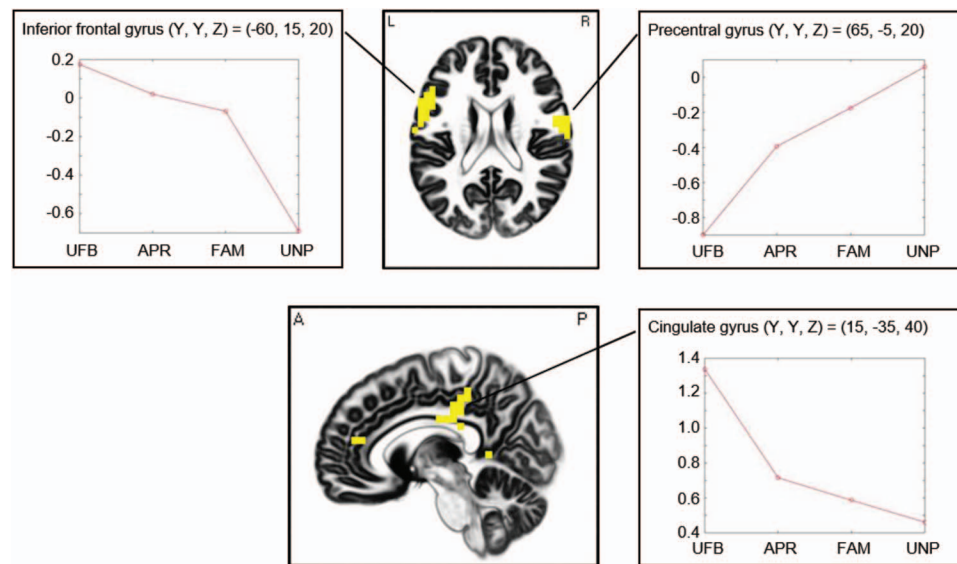


Figure 4. Illustration of source estimation of the topographic analysis of variance (TANOVA)-like effects in the late positive potential (LPP) time window (602–628 ms) for the three biggest clusters. Brain slices depict voxels with TANOVA-like Current Source Density (CSD) activation patterns (only significant effects are displayed). Line charts depict the corresponding Current Source Density (CSD) activation in the voxel with the maximal F value in the respective cluster, that is, in the left inferior frontal gyrus (left), in the right precentral gyrus (upper right), and in the right cingulate gyrus (lower right). L = left; R = right; A = anterior; P = posterior; UFB = unfinished business; APR = appreciated person; FAM = familiar person; UNP = unknown person. See the online article for the color version of this figure.

Table 2

Local Maxima of Standardized Current Density for the Contrasts Reflecting Topographic Analysis of Variance–Like Activation Patterns in the Late Positive Potential Time Window From 602 to 628 ms

Local maximum with TANOVA-like activation pattern	R/L	BA	MNI coordinates of local maximum			F_{\max}	Voxel/cluster
			x	y	z		
UFB > APR \geq FAM > UNP							
Cingulate gyrus	R	31	15	-35	40	6.44	27
Inferior frontal gyrus	L	45	-60	15	20	4.12	43
Posterior cingulate gyrus	R	30	10	-45	5	3.41	4
UFB < APR < FAM < UNP							
Precentral gyrus	R	4	65	-5	20	5.87	26
Superior frontal gyrus	L	10	-15	65	15	4.81	3
Medial frontal gyrus	L	10	-10	55	15	4.12	7
Anterior cingulate gyrus	R	32	15	35	25	3.54	4

Note. MNI = Montreal Neurological Institute; R/L = right/left hemisphere; BA = Brodmann area; UFB = unfinished business; APR = appreciated persons; FAM = familiar persons; UNP = unknown persons.

and that the reactivation of painful autobiographical memories went along with a specific, partly unique neurophysiological signature.

Reactivating emotional autobiographical memories enhanced the EPN, which is assumed to reflect automatic, involuntary allocation of attention to emotionally salient stimuli. Starting at about 250 ms, seeing faces linked to emotional autobiographical memories (UFB) elicited a stronger negativity over posterior electrodes (with a slightly right-lateralized maximum) than the control conditions. Importantly, EPN enhancement varied as a function of emotionality of the autobiographical memories. Reactivating painful memories as triggered by a face (UFB) was topographically most different from viewing faces of completely unknown persons (UNP), and second most different from viewing a familiar (FAM) face. The EPN in response to the face of an appreciated person (APR) was insignificantly smaller than the EPN in response to an UFB person. These results suggest that the EPN indicated the emotional salience of memories associated with the displayed face stimuli. Emotionally and personally salient faces, that is, those associated with either painful (UFB) or very pleasant (APR) autobiographical memories, involved a stronger EPN than emotionally more neutral faces of familiar, but not emotionally close, or unknown persons. The enhancement of the EPN in reaction to the faces conveying richest autobiographical information is in line with a recent study that demonstrates that neutral faces conveying self-relevant information leads to a more pronounced EPN than faces linked to other-related information, whereas subtle differences in the emotional content of the associated information does not affect the EPN (Klein, Iffland, Schindler, Wabnitz, & Neuner, 2015). The observation of an enhanced EPN is in line with a recent review (Pourtois, Schettino, & Vuilleumier, 2013) and meta-analysis (Lindquist, Wager, Kober, Bliss-Moreau, & Barrett, 2012) on the neural processing of emotional stimuli, highlighting that the amplitude of neural response to emotionally salient stimuli is consistently enhanced along the sensory pathway. The present results extend this principle of sensory enhancement to the processing of stimuli that draw their emotional relevance solely from their association with specific autobiographic memories. Importantly,

the surface features of the face stimuli which were used to reactivate memories (stimulus luminance, interpupillary distance, facial expression) as well as their “unemotional” memory characteristics (familiarity, freshness of memories) were held constant or controlled, and only the inherent, idiosyncratic emotional impact of each face was systematically varied. The current study replicates and extends the findings of Abdel Rahman (2011) who reported an enhanced EPN as a function of emotional biographical knowledge linked to face stimuli, albeit without personalized stimuli and with different ERP analysis methodology. In that study, both negative and positive affective knowledge involved a stronger EPN than emotionally neutral knowledge, with negative knowledge provoking even more enhanced EPN (Abdel Rahman, 2011). The present findings suggest that emotional autobiographical memories attract a prioritized processing at a basal and preconscious level of automatic attention allocation. This privileged sensory processing probably induces a more efficient mode of processing for emotionally salient stimuli (Pourtois et al., 2013).

The main generators of the emotionality-driven EPN effect were localized in right-hemispheric pre- and postcentral structures as well as in the right inferior parietal lobule, where the CSD signal increased with increasing emotionality (UFB > APR > FAM > UNP) and—with an opposite activation pattern (UFB < APR < FAM < UNP)—in the right superior temporal gyrus. Electrophysiological studies tracking the intracranial sources for EPN effects are still rare, and existing studies rely mostly on standardized arousing word or picture stimuli assumed to trigger an immediate emotional response (Frühholz et al., 2011; Keuper et al., 2014). Such studies reported enhanced activity in parietal and occipital areas in the EPN time window linking this to more resourceful higher order visual processing (Frühholz et al., 2011). The present study did not investigate the immediate emotional response to standardized emotional stimuli, and did not localize the intracranial sources of the EPN per se, but aimed at identifying those intracranial sources that differed as a function of emotionality of reactivated individual autobiographic memories. Consequently, the localization of this emotionality-driven effect comprised signal increases outside the typical visual processing stream, which might

account for the uniqueness of autobiographical memories. For instance, enhanced activation in the inferior parietal lobule is in line with the inferior parietal lobule's involvement in representing naturally acquired memories (e.g., Maddock, Garrett, & Buonocore, 2001) and signal increases in pre- and postcentral structures might suggest that reactivation of painful autobiographical memories involves richer and more vivid sensory details (Cabeza & St Jacques, 2007).

Reactivating painful emotional autobiographical memories enhanced the LPP, which is usually interpreted as an indicator for the sustained and more elaborative processing of intrinsically relevant emotional information (e.g., Hajcak et al., 2010). Starting at about 470 ms, significant GFP differences in the absence of topographic effects indicated that the same intracranial generators, but with different strengths, were active across conditions. The strongest network activity was found in the UFB condition, followed by the APR, the FAM, and the UNP condition. In a later time window from approximately 600 ms on, significant GFP and topographic differences indicated strongest network activity in the UFB condition again, as well as a different configuration of intracranial sources in the UFB condition as compared to the control conditions. The topographic differences consisted of a relatively stronger positivity over central electrodes in reaction to UFB-faces triggering painful emotional memories. Topographic analyses showed a clear enhancement of the LPP as a function of emotionality associated with the respective faces as trigger for autobiographical memory. Reactivating painful memories (UFB) was topographically most close to remembering an appreciated person (APR), second most close to remembering a familiar person (FAM), and most different from viewing unknown persons (UNP). Painful autobiographical memories (UFB) tended to elicit a different topography than pleasant autobiographical memories (APR), suggesting that autobiographical interpersonal pain has a unique neural signature in the LPP time window. This is in line with a recent report of LPP enhancement in response to neutral faces that were experimentally associated to socially threatening information (e.g., rejection, humiliation; Klein et al., 2015) and extends these findings showing for the first time that specific emotional autobiographical representations linked to neutrally looking faces also modulate the LPP. A stronger LPP effect in reaction to neutrally looking faces has been interpreted as an indicator for postperceptual evaluation of emotional significance (Abdel Rahman, 2011), or, in another study with faces of different expressions, as an indicator for social relevance (Bublitzky, Gerdes, White, Riemer, & Alpers, 2014). Our findings extend the vast body of research that has found a stronger LPP in reaction to emotionally arousing stimuli (e.g., Foti et al., 2009; Schupp et al., 2000) to stimuli that draw their emotional salience solely from their association with emotional autobiographic memories.

Source estimations localized the intracranial generators of the enhanced LPP for emotionally painful memory representations in left-lateralized regions of the ventrolateral prefrontal cortex with a peak activation in the inferior frontal gyrus, and in the right cingulate, posterior cingulate and parahippocampal cortices (CSD activation in these clusters: UFB > APR > FAM > UNP). These structures displaying high activations in the UFB condition have repeatedly been related to the processing of autobiographical memories and their idiosyncratic emotional significance. The posterior cingulate cortex (PCC) as well as left-sided ventrolateral

prefrontal cortices (VLPFC) have been identified as part of a "core" network for autobiographical memory retrieval (Svoboda, McKinnon, & Levine, 2006). PCC activation has been linked to remembering familiar people (Maddock et al., 2001), to the subjective experience of emotional salience and reward (Kable & Glimcher, 2007; Maddock, Garrett, & Buonocore, 2003), and to the personal significance of emotional memories and autobiographical memories (Addis, Moscovitch, Crawley, & McAndrews, 2004; Touryan et al., 2007). VLPFC and particularly the left inferior frontal gyrus have been shown to be specifically implicated in the involuntary retrieval of experimentally acquired "traumatic" memories (Clark, Holmes, Woolrich, & Mackay, 2016). It has been hypothesized that the left inferior frontal gyrus might "flag" traumatic events during encoding and direct one's attention toward such "flagged" memory representations during recall (Clark et al., 2016). While the present study is not designed to investigate brain activation during encoding of highly emotional or traumatic events, it supports the notion that the left inferior frontal gyrus is implicated in the processing of highly emotional, biographically salient and painful memories.

A decrease in CSD activation in the UFB condition as compared to control conditions was localized in clusters centered around the right precentral gyrus, in the anterior cingulate gyrus, and in the left medial and superior frontal gyrus (CSD activation pattern: UFB < APR < FAM < UNP). The precentral cluster spans the premotor cortex, which is associated with the preparation and execution of motor responses, and the anterior cingulum as well as the medial and superior frontal gyrus that are part of a medial frontal network involved in social cognition, mentalizing and metacognition (Amodio & Frith, 2006). Relative deactivation of these brain areas during the LPP time window might be indicative of an allocation of limited neural resources to rather emotional aspects of memory contents compared to demanding higher order cognition. Painful emotional autobiographical memories attract prioritized processing along the information-processing stream. One might speculate that this happens to the expense of "cold" cognitive processing in the LPP time window, and that the missing resources in this cognitive domain hinder the generation of a more adaptive way of dealing with these memories. Taken together, the LPP-findings illustrate that painful autobiographical memories display a unique activation pattern on the neurophysiological level, which is characterized by increased processing in motivational networks and reduced activation in higher order cognitive processing. This interpretation is in line with a clinical perspective on emotional UFB. Indeed, emotional UFB consists of unresolved, overwhelming, potentially "trauma-like" negative lingering feelings, which are often reexperienced over and over again in a similar, dysfunctional way. Their resolution demands the integration of emotional and cognitive processing to make new meaning of the emotional experience (Greenberg & Malcolm, 2002).

As exemplified above, the present source estimation findings fit with functional brain imaging studies that elucidate where emotional autobiographical memories are instantiated in the brain. A growing body of literature suggests that the experience of emotion and emotional memories need to be characterized at the level of distributed and interconnected brain networks, or functional brain circuits, and not just at the level of specific loci of brain activity (Barrett, 2017; Pessoa, 2017; Wager et al., 2015). Patterns of distributed network activity and connectivity vary dynamically

from moment to moment, and their particular functional state determines how they contribute to a psychological function. Brain imaging studies conceptualize a distributed functional network spanning the medial prefrontal cortex, posterior cingulate gyrus, and temporal structures as “default mode network” (Buckner, 2012; Buckner, Andrews-Hanna, & Schacter, 2008) which is central to constructing emotional memories (Barrett, 2017). Dynamic activations in this network seem, among others, engaged when remembering autobiographical memories, or when representing first-person experience (Barrett & Satpute, 2013). The present study found an activity pattern of estimated sources (UFB > APR > FAM > UNP) in the LPP timeframe that partly overlaps with such a network. While the data of the present study do not allow for a more specific illumination of functional brain circuits or identification of connectivity between networks, prospective studies may answer the question of how emotional disturbances such as emotional UFB are characterized at the level of distributed and interconnected functional brain networks.

As hypothesized, participants reported less subjective feelings of pleasantness, more arousal and less feelings of dominance when they were reminded of painful biographical memories by faces of persons with whom they had UFB. It seems almost trivial that the reactivation of painful biographical memories, triggered by the UFB-face, induced unpleasant feelings, emotional arousal and feelings of weakness. Nevertheless, this finding is noteworthy as it was obtained in an experimental setting, where we controlled for surface features of the stimuli as well as for their “unemotional” memory characteristics, and varied only the emotional impact that was associated with stimulus. We employed individualized stimuli, allowing for the ecologically valid investigation of personal, autobiographical memories. The present subjective rating results are in line with previous studies investigating positive emotions that were elicited by personally known loved faces. They showed that the valence scale differentiated between loved and unknown faces, and that valence, arousal and dominance differed between filial and romantic love (Guerra et al., 2011, 2012; Vico et al., 2010). The present self-report results not only extend these findings to painful emotions, but also underline the potential of faces for the individualized, effective, and well-controlled activation of emotional autobiographical memories.

To rule out the alternative explanation that the enhanced EPN and LPP in the UFB condition reflected a mere valence or arousal effect (e.g., Cuthbert et al., 2000), the following supplementary analyses were made. With regard to subjective ratings of valence, the descriptive order of conditions (APR > FAM > UNP > UFB) did not parallel the order of conditions found in the topographic analyses (UFB–APR–FAM–UNP), which renders unlikely the alternative explanation of a mere valence effect. Supplementary analyses within each condition explored if valence ratings covaried systematically with the electrical topography in the EPN or LPP time window (by calculating the channel-wise covariance of valence with the scalp field data and testing the significance with randomization-based resampling techniques, Koenig, Melie-Garcia, Stein, Strik, & Lehmann, 2008). Neither for the EPN time window, nor for the LPN time window, were the subjective ratings of valence significantly correlated with the topographies.

With regard to subjective ratings of arousal, the descriptive order of conditions (UFB > APR > FAM > UNP) paralleled the order of conditions in the topographic analyses. Still, if the topo-

graphic effects were due to a mere arousal effect, such an arousal effect should also be present within each condition, that is, within each condition, participants with higher arousal responses to the respective face should display enhanced EPN or LPP responses to that specific face. We explored this possible alternative interpretation by conducting supplementary analyses in which we correlated, within each condition, the individual subjective ratings of arousal with the individual electric topographies in the EPN time window, and in the LPP time window, respectively. No significant correlations between subjective arousal ratings and ERP topographies were found, neither within the EPN time window, nor within the LPP time window. Thus, the present data did not support the interpretation of a pure valence or arousal effect.

Some limitations of the present study need to be acknowledged. The participant sample consisted of healthy, mainly female, and psychologically educated persons, so that the results can only be generalized to a limited extent. Source estimations were restricted to cortical structures, so that subcortical structures that might play an important role in the processing of emotionally painful memories may have remained undetected. In our paradigm using individualized face stimuli to reactivate autobiographical memories, it was challenging to assess the relatively early EPN with regard to exact source localizations. For future studies on ERPs of emotional, autobiographical memory processing, source localization might be further improved by exploiting simultaneously measured MEG data (Keuper et al., 2014). The ratings of subjective feelings in reaction to the face stimuli captured only the broad dimensions of valence, arousal, and dominance, which might not adequately illustrate the emotional richness and complexity of autobiographical memories. Future studies should include subjective ratings of more specific emotions such as sadness, disgust, or anger, or of motivational directions such as approach or withdrawal, and relate these more specific subjective ratings to neurophysiological processing.

In summary, the present study provides evidence for distinct neurophysiological signatures for emotionally salient autobiographical memories as compared to other autobiographical memories and to new representations. Our results demonstrate a way to achieve a high internal as well as ecological validity using idiosyncratic, highly personalized stimuli to trigger genuine emotional memories in a well-designed experiment. The ERP results indicate that the reactivation of emotional, autobiographical memories involves a privileged automatic attention allocation at perceptual processing stages (EPN). At a postperceptual stage (LPP), our results show an enhanced recruitment of neural network activity, which is sensitive to emotional-motivational processing, while some aspects of higher order cognition seem to be selectively reduced at that stage. Effects on a subjectively reportable level, that is, feelings of unpleasantness, arousal, and weakness in reaction to stimuli triggering painful memories complement the electrophysiological findings. These results can have implications for therapeutic approaches aiming at treating disorders related to painful autobiographical memories. Successful psychotherapy should not only foster emotional change on postcognitive levels, but might also target modifications at very basic, automatic information processing steps. One possibility to facilitate such change might be the application of mainly “bottom-up”-driven interventions in psychotherapy, such as exposure (e.g., Foa & Kozak, 1986; Rachman, 1980) or experiential, emotion-focused interven-

tions (e.g., Greenberg, 2004; Greenberg & Safran, 1987) that aim at the holistic activation of emotional representations at various levels (i.e., perceptual, bodily felt, experiential, verbal, etc.). Drawing upon the present results, one might recommend intervening purposefully at nonconscious processing stages of emotionally disturbing associative memory phenomena.

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