Title:

The Neural Basis of Nostalgia

懐かしさの神経基盤に関する研究

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Note:

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1. Introduction

When something that is physically or mentally encountered cues memory retrieval, we sometimes experience a distinct emotional state called *nostalgia*. This term was originally introduced by a Swiss physician Johannes Hofer (1688/1934), as a Greek compound consisting of *nostos* (return) and *algos* (pain). He conceptualized nostalgia as a neurological disease characterized by adverse psychological and physiological symptoms, including persistent thinking of home, anxiety, irregular heartbeat, anorexia and insomnia, as displayed by many Swiss mercenaries who went on an expedition to foreign shores (Wildschut et al., 2006). In the modern era, nostalgia has been regarded as a predominantly (but not exclusively) positive emotional experience that is described as positive sentiment, bittersweet and wistful pleasure, accompanying autobiographical memory (AM) retrieval (Davis, 1979; Wildschut et al., 2006). Although the affective signature of nostalgia is rather mixed, many studies have reported that nostalgia is now thought to serve a psychologically adaptive function. For example, recent behavioral and psychophysiological studies of nostalgia have revealed that nostalgic experiences can decrease dysphoric states such as loneliness, depression and rumination about death (Wildschut *et al.*, 2006; Yamagami *et al.*, 2007; Routledge *et al.*, 2008; Zhou *et al.*, 2008), and can also decrease levels of peripheral proinflammatory cytokines such as the tumor necrosis factor-α and interferon-γ (Matsunaga et al., 2013). Furthermore, nostalgia can increase self-esteem, self-positivity and sense of social connectedness in young people (Sedikides, 2006), as well as sense of self-worth and desire to live in older adults who participate in reminiscence therapy, a clinical intervention that relies heavily on evoking nostalgic experiences (Yamagami et al., 2007). Such findings suggest that nostalgia can play a role in psychological resilience and everyday well-being.

One conceptual model of nostalgia proposes that nostalgic experiences are in fact a combination of autobiographical and affective experiences (Barrett et al., 2010), as theoretical studies of emotion have suggested that emotion can be constructed using information provided by memory, interoceptive information from inside one's body and sensory inputs from the outside world (Barrett, 2006; Moriguchi and Komaki, 2013). Previous studies have shown that a nostalgic experience can be triggered by remembering AMs in some way, such as through sensory inputs (smell, music and visual stimuli related to the past), conversation about the past and the experience of similar events (Barrett et al., 2010; Chrea et al., 2009; Davis, 1979; Wildschut et al., 2006). Although it is very important to clarify the neural basis of nostalgia, there have been only a few neuroimaging studies. Among them, one fMRI study examined the neural substrates of listening to music that evokes emotions such as tenderness, peacefulness and nostalgia, showing that experiencing these high valence/low arousal emotions activates various brain regions including hippocampus (HPC), parahippocampus, ventral striatum (VS), and ventromedial prefrontal cortex (VMPFC) as well as subgenual/rostral anterior cingulate cortex, somatosensory cortex and medial motor cortex (Trost et al., 2012). In addition, a positron emission tomography (PET) study examined odor-evoked AM that accompanies a sense of nostalgia, showing that such AMs are accompanied by activation of the precuneus and medial orbitofrontal cortex (Matsunaga et al., 2013). This study also showed the positive correlation between both of the activity, indicating the memory-reward relationship. Although, these studies show the activation of memory and reward systems as well as their co-activation in nostalgia experiences, it has not been clarified how the strength of memory-reward relationships is actually correlated with the subjective experience of nostalgia.

To address this issue, here, we conducted a functional magnetic resonance imaging (fMRI) study and performed the following analyses using visual stimuli, as distinct from previous studies, that are not inherently rewarding like food, money and sexual stimuli, but are related to childhood and highly likely to evoke nostalgic feelings. First, we confirmed the activity of memory and reward related areas. That is, we targeted HPC activity during nostalgic experiences, given that a previous fMRI study (Trost *et al.*, 2012) reported the involvement of HPC and this region is crucial for the retrieval of autobiographical events (Fink *et al.*, 1996; Ryan *et al.*, 2001; Maguire and Frith, 2003; Markowitsch *et al.*, 2003; Addis *et al.*, 2004; Cabeza *et al.*, 2004; Gilboa *et al.*, 2004; Piolino *et al.*, 2004; Svoboda *et al.*, 2006; Cabeza and St Jacques, 2007; Schacter and Addis, 2007; Viard *et al.*, 2007). Concerning the reward-related areas, we investigated the VS, VMPFC and substantia nigra/ventral tegmental area (SN/VTA) activity, since positive affects should be associated with these reward-system activity, which have been already demonstrated with numerous research paradigms (Diekhof et al., 2012; Kuhn and Gallinat, 2012). We also investigated the co-activation (positive correlation of the brain activity between two regions) of the HPC and reward related areas to confirm their interregional relationships during nostalgic experiences. Then, to examine the relationship between the memory-reward collaborative activity and the subjective experience of nostalgia, we investigated whether individual patterns of the memory-reward co-activation would be correlated to 'nostalgia tendency', that is the extent to which one tends to experience a remembrance as subjectively more nostalgic. If the co-operative activity of memory-reward systems is actually important for constructing nostalgia experiences, its strength would be correlated with the nostalgia tendency across individuals.

In addition to the above memory-reward co-activation in nostalgia, we also examined the implicit factors of nostalgia and their neural correlates. That is, we asked subjects to rate their emotions and memories accompanied by the experimental task, including the temporal remoteness of memory such as the age of memories that is an important factor of nostalgia (Davis, 1979) but has not ever been discussed so much in previous psychological studies (Wildschut *et al.*, 2006; Barrett *et al.*, 2010). Based on the data of ratings, we performed an exploratory factor analysis to extract the factors constituting nostalgia, and parametric modulation analyses with each factor.

2. Materials and Methods

2.1 Participants

Fifteen right-handed healthy young female undergraduates were recruited and completed the fMRI experiment as described below. One participant was removed from data analysis, as she reported that she had fallen asleep during the fMRI experiment. All statistical analyses were conducted using data from the remaining 14 participants (mean age ± SD = 22.1 ± 0.6 years). Participants had no history of psychiatric or neurological disorders. Only female participants were recruited because females have previously been shown to recall emotional AMs at a faster and higher rate than males (Davis, 1999), and because there are sex differences at the neural level related to emotional AM retrieval (Piefke et al., 2005). All participants provided their written informed consent prior to their participation. This study was approved by the Research Ethics Committee of Tokyo Metropolitan University and conducted in accordance with the Declaration of Helsinki.

2.2 fMRI experiment

We assumed that nostalgia would be induced by triggers common to a relatively homogeneous subset of individuals within the same culture, age, and sex groupings. For instance, most Japanese people experience similar events during the six years of compulsory education in elementary school. Memories of these times should contain common features, irrespective of the specific place in which participants grew up. All such individuals spent large amounts of time in a school building with a typical appearance, used certain types of school stationery typically depicted animated characters, and spent this unique period with friends of the same age. Since almost all of these experiences are limited to elementary school, people seldom have the same experiences after graduation. We therefore created visual stimuli for the fMRI task that depicted objects and scenes that are emotionally neutral by their nature but would induce nostalgic experiences once the stimuli were associated with the participants' childhood (nostalgic pictures) and the similar control pictures that would not induce nostalgia (Figure 1). As for details of stimulus preparation, see Supplementary information.

During the fMRI experiment, pictures falling into the four categories like Figure 1 were randomly presented for 8 s each. All pictures were presented only once and were interleaved with

8 s fixation crosses. Participants were not explicitly informed that they would be shown pictures specifically designed to arouse nostalgia, but were only instructed to view the pictures attentively. By this means, we could show that the induction of nostalgia can be a very basic and automated mental process such that it can be triggered implicitly. Presentation software (Neurobehavioral Systems) was used to display the pictures and to control presentation timing.

Scanning was conducted using a 3T MRI scanner (Achieva Quasar Dual, Philips). Blood oxygenation level-dependent (BOLD) T2*-weighted MR signals were measured using a gradient echo-planar imaging (EPI) sequence. Two hundred and ten volumes with nineteen contiguous slices of 6 mm thickness were acquired (TR = 4,000 ms, TE = 35 ms, flip angle = 90°, FOV = 230 mm^2, scan matrix = 128 × 128, total scan time = 840 s).

2.3 Post-scanning ratings

Immediately after the fMRI scan, participants were asked to view all of the pictures again on a computer screen and to retrospectively evaluate their experiences during scanning. These evaluations included: 1) two items pertaining to the object or scene depicted in each stimulus [‘How much do you know about the object/scene depicted in the picture?’ (recognizability) and ‘How familiar are you with the object or scene depicted in the picture?’ (familiarity)], 2) four items about the emotional experience that occurred when they saw each picture during scanning [‘How much did you feel nostalgia?’ (nostalgia), ‘How much did you feel happiness?’ (happiness), ‘How much did you feel attachment to the object or the scene?’ (attachment), and ‘How much did you feel sentimentality?’ (sentimentality)], and 3) four items about AMs retrieved in the scanner

[‘How important was the remembered AM?’ (personal significance), ‘How vivid was the remembered AM?’ (vividness), ‘How long ago did the remembered event occur?’ (age of memories), and ‘When did you last recall the AM?’ (age of last recall)]. These items were created based on previous behavioral studies of nostalgia (Davis, 1979; Wildschut *et al.*, 2006; Barrett *et al.*, 2010) to assess the psychological properties of nostalgia. All items were rated on a 5-point scale (1: not at all, 2: not much, 3: slightly, 4: quite, 5: extremely), except for the last two items which were rated on a 6-point scale [1: before entering elementary school (under 6 y/o), 2: early elementary grades (7-9 y/o), 3: late elementary grades (10-12 y/o), 4: junior high school (13-15 y/o), 5: high school (16-18 y/o), 6: university (19-present y/o)]. Scores for the last two items were later transformed into years prior to the day of the experiment.

2.4 Behavioral data analysis

To identify the separate qualitative aspects of the nostalgic experience, first we conducted a multiple regression analysis with subjective nostalgia intensity as the dependent variable and the nine items mentioned above as independent variables, using forward stepwise selection (n = 728; 52 pictures × 14 participants). We then selected significant explanatory variables on the basis of this analysis, and performed an exploratory factor analysis to extract interpretable subsets constituting the nostalgia construct. The maximum-likelihood method was used for factor extraction and the resulting factors were subjected to Promax rotation. We also calculated mean nostalgia scores (responses to the question ‘How much did you feel nostalgia?’) for all stimuli (52 pictures in total) for each participant and deemed this value to represent an individual’s ‘nostalgia tendency', as such values should reflect a tendency to experience one's subjective feelings of nostalgia. All behavioral data analyses were performed using SPSS statistical software version 17.0 (IBM SPSS).

2.5 fMRI data analysis

Image preprocessing and statistical analyses were performed using SPM8 (Wellcome Department of Cognitive Neurology, http://www.fil.ion.ucl.ac.uk/spm/). Functional images were realigned to the first volume to correct interscan movements. The slice timing in each volume shot was corrected. Functional images were then spatially normalized to the Montreal Neurological Institute (MNI) EPI template and smoothed with a Gaussian filter of 8-mm full width at half maximum.

Before conducting analyses using the fMRI data, we redefined the categorical membership of each picture according to participants' post-scanning nostalgia ratings, such that nostalgic pictures had scores of ≥ 3 (i.e., slightly/quite/extremely nostalgic) and control pictures had scores of ≤ 2 (i.e., not/not at all nostalgic). To analyze the fMRI time series data, we modeled two types of hypothetical hemodynamic event-related transient and sustained responses (Krendl et al., 2012). In the transient model, effects of interest were modeled by convolving each stimulus onset with the canonical hemodynamic response function (HRF), whereas in the sustained model, effects were modeled with the boxcar function convolved with the HRF. The former is useful for detecting fast neural response from the task-onset, while the latter is useful for detecting the lasting response over the task-block. We used this approach because midbrain dopamine neurons show transient activity increases in response to salient rewarding and novel events (Schultz, 1998; Shohamy and Adcock, 2010), while the HPC shows rather sustained activity during AM retrieval (Ryan et al., 2001). The convolved hypothetical hemodynamic curves in response to the four kinds of stimulus (nostalgic object, nostalgic scene, control object, and control scene) were entered into the two types of GLM model as explanatory variables, with motion parameters and discrete cosine filter models as a high-pass filter with a 128 s cut-off period as nuisance covariates. The two models were estimated to fit the time-series BOLD signals at each voxel. We then averaged the estimated parameters (beta values) into the nostalgia (object and scene) and control (object and scene) conditions.

2.6 Region of interest analysis

The bilateral HPC ROIs were first created using the Automated Anatomical Labeling (AAL) atlas (Tzourio-Mazoyer et al., 2002). We then separated the HPC into anterior and posterior portions in reference to a study examining the antero-posterior functional specialization of the HPC (Poppenk et al., 2013). Neuroimaging studies of AM retrieval have shown that the anterior HPC plays a role in the pattern completion of gist-like representations of an autobiographical event, whereas the posterior HPC is involved in the retrieval of spatially and temporally specific (pattern separated) representations (Nadel et al., 2013; Poppenk et al., 2013). The limit between anterior and posterior portions corresponded to $y = -21$mm (MNI coordinates) (Poppenk et al., 2013). In total, we generated 4 hippocampal ROIs: left anterior (L.aHPC), left posterior (L.pHPC), right anterior (R.aHPC) and right posterior (R.pHPC) portions.

The reward-related ROIs were identified by referring to a previous meta-analysis of the neural substrates of reward processing (Diekhof et al., 2012). This meta-analysis has shown that the SN/VTA plays a role in ‘reward anticipation’ whereas the VMPFC functions during the ‘reward outcome’ phase (or reward receipt phase), and the VS is involved during both anticipation and outcome phases. We defined the SN/VTA ROI as the intersection of the 8-mm radius sphere centered at (−4, −16, −14) and the midbrain mask as identified using PickAtlas software (Maldjian et al., 2003). As for the VMPFC ROI, we made an 8-mm radius sphere centered at (−2, 64, −2). For the VS ROIs, we calculated the centroid of the two VS coordinates reported in the meta-analysis, resulting in the 8-mm radius sphere centered at (−10, 11, −4) and (14, 13, −8). These 8 ROIs are depicted in Figure 2A.

We used MarsBaR software (version 0.42, http://marsbar.sourceforge.net/) to extract the mean parameter estimate within each of the 8 ROIs from individual beta images for nostalgia and control conditions (estimated by the transient and sustained hemodynamic GLM model), and compared these using paired t-tests between estimates for nostalgia vs. control events (i.e., we ran two t-test comparisons on the eight ROIs using estimates from both transient and sustained models, resulting in a total of 16 t-tests). Because we ran multiple comparison analyses, the statistical threshold was corrected as the family wise error rate [FWE; the Holm method (Holm, 1979)]. In addition to this hypothesis-driven ROI approach, we also performed a conventional whole-brain voxel-by-voxel analysis comparing the nostalgia and control conditions ($p < 0.001$ uncorrected, $k \geq 10$).

2.7 Relationships between the memory-reward co-activation and the nostalgia tendency

To demonstrate whether and how nostalgia-related neural activities in the memory and reward systems were related to one another, we investigated their co-activation. Co-activation means the positive correlation of brain activity between two regions, indicating the interregional relationships of the magnitudes of activity (Greenberg *et al.*, 2005).

We first regressed individual hippocampal activity (beta estimates of the HPC subregional ROIs that showed significant nostalgia-control differences) on the beta estimates of the four reward-related ROIs. We then ran multiple forward stepwise regression analyses in which HPC ROI activity was set as the dependent variable and activities in the four reward-related ROIs were set as the independent variables ($p < 0.05$, FWE corrected via the Holm method). We used these regression analyses to obtain most significant reward-related regions that showed co-activation with each subregion in the HPC (i.e., the L/R aHPC/pHPC).

Then, we conducted correlation analyses between the strength of interregional relationships and the individual nostalgia tendency scores (averaged nostalgia ratings of the pictures; see 2.4. Behavioral data analysis) to demonstrate that it is the memory-reward interrelationship which is important for nostalgic experiences. We first calculated individuals' 'memory-reward co-activation index' by computing the first eigenvalue through a principal component analysis (PCA) of the individual activation (beta estimates) in the hippocampal and reward-related regions. We then correlated these individual co-activation indices with participants' nostalgia tendency scores.

2.8 Correlation between the neural activity and the factors constituting nostalgia

To confirm the role of the selected ROIs in the generation of nostalgic experiences, we performed correlational (parametric modulation) analyses of the activation using the summed scores of each factor that composes nostalgia, as revealed by the aforementioned factor analysis (see 2.4 Behavioral data analysis). In this analysis, as well as the ROI analyses, we modeled two hypothetical hemodynamic responses (transient and sustained), and tested which ROI activation was correlated with each nostalgia factor. The search volume was restricted to the 8-mm radius sphere, centered at the peak coordinates within the ROI mask that showed differential brain activity in the voxel-by-voxel nostalgia vs. control contrast ($p < 0.05$, FWE corrected in SVC).

3. Results

3.1 Psychological aspects of nostalgic experiences

In post-scanning ratings of the pictures, participants reported that they had experienced nostalgia during scanning, such that the nostalgic pictures were in fact rated to be highly nostalgic, ($M = 4.5$, $SD = 0.6$), and the control pictures rated as low on this dimension ($M = 1.7$, $SD = 0.9$). There was a statistically significant difference (t (50) = 28.6, $p < 0.01$). This confirms that genuine nostalgic experiences were evoked in the scanner despite participants receiving no explicit guidance or warnings in this regard. We also confirmed that nostalgic pictures reminded participants of their remote past. Participants viewing the nostalgic pictures recalled events they experienced around 12.1 ($SD = 1.4$) years ago (around when participants were in elementary school), while they reported that the control pictures were associated with reminiscing back to an average of 5.4 (*SD*

= 2.7) years ago (around when participants were in high school) (*t* (13) = 15.8, $p < 0.01$).

A multiple regression analysis ($n = 728$) showed that Age of memories ($\beta = 0.35$), Happiness ($\beta = 0.31$), Attachment ($\beta = 0.135$), Sentimentality ($\beta = 0.134$), Personal significance ($\beta = 0.085$), and Age of last recall ($\beta = 0.092$) were significant predictors of Nostalgia (adjusted $R^2 = 0.77$, $p < 0.05$), whereas Recognizability ($\beta = 0.028$), Vividness ($\beta = 0.002$), and Familiarity ($\beta = -0.027$) were not. A subsequent exploratory factor analysis including the six significant predictors of Nostalgia scores revealed that these predictors were converged on two factors (Table 1). The first contained the four items of Attachment, Happiness, Personal significance and Sentimentality, and was termed "Emotional and personal significance". The second contained Age of memories and Age of last recall, and was termed "Chronological remoteness". The result is consistent with the notion that nostalgia is predicted by mixed but predominantly positive emotions, and is associated with getting back to "old times" (Davis, 1979; Wildschut *et al.*, 2006; Barrett *et al.*, 2010).

3.2 Neural activity for the nostalgia vs. control contrast

As predicted, hypothesis-driven ROI analysis revealed significant HPC and reward-related area activity for the nostalgic vs. control pictures comparison (Table 2 and Figure 2B). There was a significant difference of activity between nostalgia and control events (*t* (13) = 4.96, $p = 0.0042$, FWE corrected by Holm method) for the transient model in which we predicted reward-related SN/VTA activity. In this transient model, the other 7 ROIs did not show significant differences of activity between the two events (Table 2). For the sustained model in which we predicted the memory-related HPC subregions and reward-related regions activity, significant differential activity was observed between the two events in the L.aHPC (t (13) = 4.76, p = 0.0056), L.pHPC (t (13) = 3.85, p = 0.028), R.aHPC (t (13) = 3.63, p = 0.036), and in the L.VS (a reward-related region, t (13) = 3.68, p = 0.036). Other regions did not show significant activity after correction for multiple comparisons, including the SN/VTA (t (13) = –2.09), R.VS (t (13) = 1.30), VMPFC (t (13) = 2.49), and R.pHPC (t (13) = 3.00) (Table 2). These results support our hypothesis that nostalgia experiences involve both the reward and memory systems.

The additional whole-brain voxel-by-voxel analysis ($p < 0.001$ uncorrected, $k \geq 10$) revealed transient activity in the SN/VTA, right perirhinal cortex, right supplementary motor area and right cerebellum, and sustained activity in the right aHPC/parahippocampal cortex, left aHPC, left thalamus, left dorsolateral prefrontal cortex, right hypothalamus and bilateral cerebellum (Table 3).

3.3 Relationships between the HPC-VS co-activation and the nostalgia tendency

As expected, we found HPC and VS activation to be interrelated across individuals, such that individual differences in R.VS activity predicted such differences in bilateral aHPC activity [t (12) = 2.68, p = 0.02 for L.aHPC-R.VS and t (12) = 3.40, p = 0.01 for R.aHPC-R.VS], and that individual differences in L.VS activity predicted such differences in L.pHPC activity [t (12) = 4.60, p = 0.002, $p < 0.05$ FWE corrected by the Holm method], in the multiple regression analysis in which the activity of each HPC ROI (bilateral aHPC and L.pHPC) was regressed by the estimates of activity in the four reward-related regions. The HPC and VS showed concurrent, interrelated patterns of activity during the experience of nostalgia. Furthermore, to test for the collaborative activity of memory-reward systems in nostalgia, we calculated the individual strengths of the HPC-VS co-activations (first eigenvalue of each HPC-VS pairs' activity), and correlated these with individual nostalgia tendency scores. As a result, L.aHPC-R.VS co-activation scores were correlated with nostalgia tendency [Figure 2C, r (12) = 0.63, p = 0.047], while the co-activation of L.pHPC-L.VS and R.aHPC-R.VS were not significant [r (12) = 0.48, p = 0.079, r (12) = 0.52, p = 0.112, respectively, FWE corrected using Holm method]. This result indicates that HPC-VS co-activation makes an important contribution to the experience of nostalgia.

3.4 Factor-specific neural activity of nostalgia

We confirmed via the aforementioned factor analysis that nostalgia consists of two factors: Emotional and personal significance and Chronological remoteness. While Emotional and personal significance scores were correlated with transient activity in the caudal portion of the SN/VTA, Chronological remoteness scores were correlated with rostral SN/VTA activity [Table 4 and Figure 3, parametric modulation analyses; t (13) = 4.28, p = 0.023 and t (13) = 4.48 p = 0.024, respectively, with the SVC within a sphere region centered at the peak coordinates found at voxel-by-voxel analyses of the nostalgia vs. control contrast; (–4, –20, –20) and (–6, –16, –10)]. Furthermore, Emotional and personal significance scores were correlated with both the transient and sustained L.aHPC activity [parametric modulation analyses; t (13) = 4.26, p = 0.024, and t (13) = 5.81, p = 0.003 respectively, with spherical SVC centered at L.aHPC coordinate (–22, –10,

−22)], while there was no such relationship for Chronological remoteness scores. Thus, nostalgia appears to be composed of these two different factors, and that these different aspects of nostalgia are underpinned by a differential and fine spatial pattern of neural activation within the memory- and reward-related brain regions.

4. Discussion

Using multiple regression analysis, we demonstrated that nostalgia intensity is predicted by the age of memories, happiness, attachment, sentimentality, personal significance and age of last recall. This result indicates that nostalgia is not merely positive but instead has a rather mixed emotional profile (happiness accompanying sentimentality), and also indicates that remote and personally significant AMs, which dated from around elementary school in this study, are related to nostalgic experiences. On the other hand, vividness scores did not predict nostalgia intensity. This is probably because we used generic (rather than specific) visual stimuli to trigger nostalgic experiences and did not explicitly ask participants to remember their specific AMs from elementary school. A more speculative interpretation of this finding may be that nostalgic experiences can be triggered by retrieval success of gist-like AM representations (for lifetime periods and/or general events), which is modeled in an early stage of the AM reconstructive process (Conway and Pleydell-Pearce, 2000), before vivid and specific AM remembering occurs. In addition, we found that the nostalgic experience can be parsed into two dimensions, Emotional and personal significance (factor 1) and Chronological remoteness (factor 2). The emerged factor 'Emotional and personal significance' would be analogous to the proposed conceptual model of nostalgia (Barrett et al., 2010) that emphasizes both the affective and memory-related experiences. In addition to this factor, ‘Chronological remoteness’ emerged here as a distinct factor in the construction of nostalgic experiences. Interestingly, we could find different neural activity corresponding to these two factors within the nostalgia-related brain areas, that is, the L.aHPC and caudal SN/VTA play a key role in Emotional and personal significance, whereas the rostral SN/VTA activity is correlated with Chronological remoteness. A previous neuroimaging study provides a possible functional differentiation of the SN/VTA along its rostro-caudal axis, such that the caudal SN/VTA is modulated by reward while the more rostral portion of the SN/VTA is modulated by novelty (Krebs et al., 2011). Based on this, activity of the rostral SN/VTA implicates the involvement of novelty detection during nostalgic experiences (i.e., the retrieval of long-forgotten remote past should be experienced as novel relative to the retrieval of recent past). With regards to the L.aHPC, it appears to play a specific role in the retrieval of emotionally and personally significant information, as shown in a previous study in which HPC activity was modulated by the emotionality and personal significance of AMs (Addis et al., 2004).

Given that the HPC plays a crucial role in AM retrieval process (Fink *et al.*, 1996; Ryan *et al.*, 2001; Maguire and Frith, 2003; Markowitsch *et al.*, 2003; Addis *et al.*, 2004; Cabeza *et al.*, 2004; Gilboa *et al.*, 2004; Piolino *et al.*, 2004; Viard *et al.*, 2007), along with evidence that our participants did recall their remote past and feel strong nostalgic feelings in the scanner, the HPC activity we observed suggests that nostalgia requires more AM retrieval than observing non-nostalgic (control) events. Such HPC activity without an intentional retrieval demand suggests involvement of the involuntary AM retrieval (Berntsen and Hall, 2004) in nostalgic experiences.

Furthermore, rather anteriorly biased HPC activation (bilateral aHPC) is compatible with our behavioral results such that most of the objects and scenes depicted in the stimuli had been long forgotten and stored in long-term memory, and that their detailed information is therefore relatively degraded, in agreement with the previous findings that aHPC plays a role in the pattern completion of gist-like representations (Nadel et al., 2013; Poppenk et al., 2013). Of course, we assume that detailed AM representations triggered by personalized stimuli (such as the family photographs) can also induce nostalgia, and in such cases we speculate that both the gist-like and detailed AM retrieval processes would be involved in the involuntary induction of nostalgia and subsequent more detailed AM recollection.

We could also confirm interregional relationships between the memory and reward systems, as a co-activated pattern across participants for the HPC (bilateral anterior and left posterior) and VS. Furthermore, the strength of individual memory-reward interrelationships was correlated with individual subjective experience of nostalgia (a correlation of the nostalgia tendency with the L.aHPC-R.VS co-activation). This result shows that the memory and reward systems coproduce the subjective nostalgic experiences. Such interregional relationships during nostalgic experiences may be based on the intrinsic memory-reward network, that is, the hippocampal-VTA loop (Lisman and Grace, 2005) that enables hippocampal signals to activate the nucleus accumbens (a component of the VS) and the SN/VTA dopaminergic system. Although our data cannot show the direction of signal processing, the HPC, VS and SN/VTA activity and the HPC-VS co-activation suggest a possibility that the memory retrieval in HPC can trigger a series of reward processing through the hippocampal-VTA loop. Moreover, some studies have shown that reward-triggered involvement of this loop can enhance memory consolidation (Wittmann *et al.*, 2005; Adcock *et al.*, 2006). Although these studies have primarily focused on the processes of memory encoding, it has recently been predicted that involvement of this loop in retrieval could provide modulatory effects such as the re-encoding of the retrieved memory in accord with its expected utility and reinforcement learning (Scimeca and Badre, 2012). Based on this function of the hippocampal-VTA loop, we speculate that the memory and reward systems (i.e. the nostalgia-related network) might be involved in resilience as follows; Whenever nostalgia occurs, association between the retrieved AM and its reward value represented in the nostalgia-related network, would be reinforced by dopamine, and the contents of AM would be re-encoded and re-stored in the network. Such reinforced associations are expected to induce more positive and rewarding experiences than before, when nostalgia occurs again after the reinforcement of their association, suggesting that such experiences act as resilience to overcome adversity and support for strong motivation to live (Routledge *et al.*, 2008; Zhou *et al.*, 2008).

5. Conclusions

The present study confirmed the activation of memory (bilateral aHPC and L.pHPC) and reward (SN/VTA and L.VS) related areas, as well as their co-activation (L.aHPC-R.VS, R.aHPC-R.VS and L.pHPC-L.VS) in nostalgia experiences elicited by visual stimuli. Furthermore, we revealed the positive correlation between the memory-reward co-activation (L.aHPC-R.VS) and the nostalgia tendency, indicating that the memory and reward systems coproduce subjective experience of nostalgia. We also found that the two dimensions of nostalgic experiences —

Emotional and personal significance and Chronological remoteness — have differential neural correlates such that the caudal SN/VTA and L.aHPC are involved in the former and the rostral SN/VTA is involved in the latter. Taken together, the results show that the cooperative activity of memory and reward systems, where each of them has a specific role in the constructing factors of nostalgia, produces the experience of nostalgia.