Effects of age and gender on neural correlates of emotion imagery

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Abstract
Mental imagery is part of people's own internal processing and plays an important role in everyday life, cognition and pathology. The neural network supporting mental imagery is bottom-up modulated by the imagery content. Here, we examined the complex associations of gender and age with the neural mechanisms underlying emotion imagery. We assessed the brain circuits involved in emotion mental imagery (vs. action imagery), controlled by a letter detection task on the same stimuli, chosen to ensure attention to the stimuli and to discourage imagery, in 91 men and women aged 14–65 years using fMRI. In women, compared with men, emotion imagery significantly increased activation within the right putamen, which is involved in emotional processing. Increasing age, significantly decreased mental imagery-related activation in the left insula and cingulate cortex, areas involved in awareness of one's internal states, and it significantly decreased emotion verbs-related activation in the left putamen, which is part of the limbic system. This finding suggests a top-down mechanism by which gender and age, in interaction with bottom-up effect of type of stimulus, or directly, can modulate the brain mechanisms underlying mental imagery.

KEYWORDS
age, emotion, fMRI, gender, imagery, limbic system

1 INTRODUCTION

Imagine moving a body part: it will mimic real action execution and it will trigger activation of similar brain areas as for real execution of the same movements (Ehrsson et al., 2003). Imagine feeling tactile stimulation on the dorsal part of the right hand: this will cause activation in the contralateral primary and secondary somatosensory areas (Yoo et al., 2003). If you are invited to imagine hearing simple monotones, perceiving gustatory feelings, or odors, this will trigger activation in bilateral primary and secondary auditory areas (Yordanova et al., 2004), gustatory (Kobayashi et al., 2004), and olfactory (Djordjevic et al., 2005) regions in the brain, respectively.
What about to imagine an emotion? Emotion imagery involves many cognitive processes. Literature show that imagining an emotion requires: (a) verbal processing (if the emotion content to be imagined is presented verbally); (b) short-term memory (to hold in memory the description of the scenario); (c) more specifically, emotion imagery is based on the construction of an hypothetical scenario (executive functions are involved too); (d) the mental simulation of the perceptual aspect of the scenario, together with the semantic and affective information; (e) the simulation of possible causes and consequences of the imagined scenario (e.g., Kosslyn, 1980; Lang et al., 1980; Moulton & Kosslyn, 2009; Schacter et al., 2008).

To trigger emotion imagery different paradigms can be used. One is via verbal presentation of verbs describing emotions (and actions, for control condition) and the explicit instruction to mentally imagine the verbal content, and to report a pleasantness judgment of it (Grossman et al., 2002; Warrington & Weiskrantz, 1968).

In this paradigm, simulative processes evoke points (c) to (e) of the steps listed above. In addition, emotion conceptualization and simulation (based on personal past experiences) are also required. Several studies have addressed these processes, by using several paradigm like emotion language processing (e.g., Citron, 2012), tasks based on narrative comprehension (e.g., Oatley, 1995) or based on the presentation of situated scenarios (e.g., Wilson-Mendenhall et al., 2011). Impairments of these emotional processing steps are related to psychiatric disorders (e.g., Smith et al., 2019) and the study of the neural bases and cognitive mechanisms involved in emotion imagery could contribute in the understanding of affective disorders.

For example, in a previous functional magnetic resonance imaging (fMRI) study (Tomasino et al., 2014) we explicitly asked adult subjects to imagine emotion-related scenarios (as compared with action-related scenarios), and found that emotional imagery activated a right hemisphere neural network including the supramarginal (SMG) gyrus and the precuneus. Thus, emotional imagery activates areas involved in a first-person perspective (Cavanna & Trimble, 2006) and in generating subjectivity, for example, see Damasio (2010). Consistently, other results show that imagining ourselves engaged in emotional/abstract situations activate areas involved in social- and self-referential processing, as the posterior cingulate/precuneus, bilateral temporo-parietal junction together with the dorsomedial prefrontal cortex, bilateral temporal poles, and right amygdala (Frewen et al., 2011). Similarly, pleasant and unpleasant affective imagery activates the supplementary motor area, lateral cerebellum, and left inferior frontal gyrus (Sabatinelli et al., 2006), pleasant imagery activates the nucleus accumbens and the medial prefrontal cortex, and both pleasant and unpleasant imagery activates the amygdala (Costa et al., 2010).

Taken together, these studies indicate that mental imagery is modulated by the object of imagination, that is, bottom-up by the modality. Whether and how mental imagery (through its neural correlates) is modulated also by subjects’ related variables such as age and gender is poorly addressed. Specifically, it is unclear whether (a) age and gender effects on fMRI activation related to emotion imagery can be found, and (b) the potential age and gender effects are due to modifications that occur in affective processing, or alternatively at the level of affective conceptualization depth. As a last hypothesis, potential age and gender effects can be due to changes in emotion imagery abilities.

Studies addressing the age effect on mental imagery are few. At behavioral level, in the visual imagery domain, Stephen Kosslyn compared reaction times of adults and children aged 5-year-olds, 8-year-olds, and 14-year-olds while they generated, maintained, scanned, and rotated visual mental images (Kosslyn et al., 1990). Authors found that the processing components become differentiated into more specialized subsystems over age. Further evidence for adult age-related visual imagery differences was found in the ability to generate and manipulate visual mental images (Craig & Dirks, 1992). As far as motor imagery domain is concerned, studies indicate that such ability is subject to the age effect. Overall, the studies indicate that elderly participants can indeed have worse first-person motor imagery abilities as compared with younger participants (Mulder et al., 2007). Asking elderly and young participants to judge either the handedness of hand pictures (egocentric task) or the location of a marker placed on the same stimulus (allocentric task), it was found that the older group was less accurate and slower when imagining movements requiring biomechanically awkward hand postures (i.e., lateral hand orientations; De Simone et al., 2013).

Neuroimaging studies on age effect are even less and studies have small sample size. In one of the fMRI studies on motor imagery ability (Zapparoli et al., 2013), authors compared 24 young and 24 elderly participants asked to imagine finger movements, and found that occipito-temporo-parietal areas were over activated in the elderly participants. Authors (Zapparoli et al., 2013) concluded that what is changing with aging is the selection of strategies to solve the task, as the activation in visuo-spatial areas might reflect their use of visual imagery strategies (see Nedelko et al., 2010 for another fMRI study on motor imagery and aging). Thus, at this stage, despite the cognitive construct of emotion imagery needs to be probed in detail and investigate the covarying pattern with age the literature does not include sufficient data. We report preliminary data on 91 participants with different ages performing an emotion imagery task.

As to sex differences, this variable is known to impact on visuospatial ability: the literature shows that one of the most consistent sex differences, in favor of males, is found for the mental rotation paradigm (Parsons et al., 2004). It has been shown that sex affects the vividness of visual imagery (Campos & Sueiro, 1993). Authors compared visual imagery vividness ratings of 289 subjects of different age groups and found that females had greater imagery vividness than males, whereas age or the interaction term did not affect visual imagery vividness. On the motor imagery domain, vividness was found to be affected by age and to be similar between men and women, even if women performed better in timing (Subirats et al., 2018).

Data about age and gender effect on emotional imagery are lacking. Although it is well known the impact of emotion imagery on emotion processing and wellbeing, no study has been performed to determine the gender and aging related changes in brain network correlates of emotion imagery. As far age is concerned, in a previous
study (Tomasino et al., 2018) we found that imagery of emotion-related-as compared with action-related-scenarios in a sample of adolescents (age range 14–19 years) increased activation in the right supramarginal gyrus/rolandic operculum and in the right insula, and decreased activation in the right intraparietal sulcus. In an exploratory analysis, we compared adolescents’ data to the fMRI pattern found in older participants (Tomasino et al., 2014). We found a decreased activation for imagery of emotion-related scenarios in the left supramarginal gyrus for the older group (as compared with the adolescent group), and in the right superior frontal gyrus for the adolescents group (as compared with the older group). Given the paucity of fMRI data on emotional imagery, hypotheses can be generated by analyzing data on real emotion processing, in light of the above-mentioned parallelism between imagery and real perception. It is proposed that emotional stability is relatively conserved with aging (Lyoo & Yoon, 2017). Authors (Lyoo & Yoon, 2017) stratified 286 healthy subjects into three groups of the emotionally young, intermediate-aged, and old participants according to their performance on an emotion recognition task. Older subjects were better at recognizing happiness and worse at recognizing negative emotions. The intra-network functional connectivity of the visual and sensorimotor networks decreased with emotional aging, connectivity of the executive control network (ECN) increased with emotional aging and connectivity between the ECN and the default mode network was also greater in the older group.

The present study was designed to address the effects of age and gender on mental imagery using 3T fMRI measurements based on the blood oxygenation level dependent (BOLD) contrast. Ninety-one healthy volunteers, half males/half females, within the 14–65 years age range, were asked to imagine emotion-related scenarios (as compared with action-related scenarios) during the fMRI recordings. A letter detection task was used to ensure attention to the stimuli, by engaging subjects on a different task for discouraging imagery. The current study involves re-analysis of partially (N = 40 out of 91 subjects included in the present work) previously published data (Tomasino et al., 2014, 2018). We expect to observe correlations between age and gender and the pattern of brain activation. Nonetheless, we also expect to see some emotional imagery stability (Lyoo & Yoon, 2017). Our results thus can add new evidence about the trajectory of the brain functional organization of emotion (and motor as half of the stimuli are action-related) imagery. The investigation of the trajectory of neural networks underlying mental representation of emotion (and motor) imagery is crucial also from a psychopathology perspective, in light of the supposed special relationship between mental imagery and emotion and emotional disorders (Holmes & Mathews, 2010).

2 | MATERIALS AND METHODS

2.1 | Subjects

Ninety-one healthy volunteers (45 females, 46 males, 29.02 ± 12.04 years, age range 14–65 years) took part to the study, which was conducted in the IRCCS Scientific Institute “Eugenio Medea” of San Vito al Tagliamento, PN, Italy (FVG center) and in Bosio Parini, LC, Italy (BP center). The current study involves re-analysis of partially (N = 40 out of 91 subjects included in the present work) previously published data (Tomasino et al., 2014, 2018). While the proportions of females and males were equal, the age distribution was uneven (see Figure S1), with a wider percentage of younger (<30 years) compared with older (>30 years) subjects. All subjects were right-handed and monolingual native Italian speakers. The research protocol was approved by the competent Research Ethical Committee of the Research Institute IRCCS E. Medea, in accordance with the 2013 F taleza version of the Helsinki Declaration and subsequent amendments. A written informed consent to the study was obtained by all participants. In case of minors, parents gave consent (and minors gave assent).

2.2 | Experimental design

Magnetic Resonance Imaging (MRI) data were acquired using 3T Philips Achieva scanners (Philips, Best, The Netherlands) installed in the University Hospital of Udine (FVG center) and in the IRCCS “E. Medea” of Bosio Parini (BP center), equipped with 8 and 32 channel head-coils, respectively. The participants’ head movements were limited by restraining foam pads. The fMRI volumes (n = 612) were recorded using a T2*-weighted gradient echo planar imaging (FEPI) sequence with the following parameters: repetition time (TR) 2500 ms, echo time (TE) 35 ms, flip angle 90°, 30 axial slices with no gap, in-plane matrix 128 × 128, voxel size 1.79 mm × 1.79 mm × 3 mm, total scan duration 25 min and 30 s. The field of view coverage did not include the cerebellum and brainstem and, in the subjects with big brain size, could exclude portions of the temporal poles, amygdala, hippocampus, and parahippocampal gyrus. The morphological reference for the fMRI results was provided by a 3D T1-weighted MPRAGE turbo field echo (TFE) SENSE image with TR 8.2 ms, TE 3.76 ms, 190 axial slices with no gap, in-plane matrix 240 × 240, voxel size 1 mm³, total scan duration 8 min and 53 s.

The fMRI experiment was developed using the Presentation® software (Neurobehavioral Systems, Inc., Berkeley, California) and delivered in the MR scanner through MR-compatible VisuaStim goggles (Resonance Technology, Inc., Northridge, California). The subjects’ responses were collected using an MR-compatible hand Evoke Response Pad (Resonance Technology, Inc., Northridge, California). Prior to the fMRI experiment, outside the MR environment, all subjects were trained to perform the task.

A previously used (Tomasino et al., 2014, 2018) task was adopted. The fMRI experiment consisted of an event-related 2 × 2 full factorial design with task (Mental imagery task, I; Letter detection task, LD) and stimuli (action verbs referring to movements, e.g., to grasp, to write, Act; state/psychological abstract verbs, e.g., to hope, to believe, Sta/Psy) factors, each characterized by two levels. Subjects silently read the verbs and were explicitly asked to (a) form a mental image of
the verb content from a first person perspective, and to determine its pleasantness by responding to the question “Do you like it?” (I task); (b) identify a target letter in the word by responding to the question “Search: Is the ‘S’ present?” (LD task, 61% of the words [64% and 58% of Act and Sta/Psy verbs, respectively] included the letter “S”). Stimuli (n = 72) were equally divided into 36 Act verbs and 36 Sta/Psy verbs. These stimuli were previously validated in terms of capability to recall physical movement actions (Act verbs) or to trigger a psychological state/emotion (Sta/Psy verbs) (Tomasino et al., 2014, 2018). Stimuli were validated with a rating study (Tomasino et al., 2014). Unsurprisingly, the Act verbs (vs. Sta/Psy verbs) significantly differed in motor relatedness (t(35) = 132.7, p < .001), and in imageability (t(35) = 19.43, p < .001), since the perceptual and motor features are more rich and elaborated for Act vs. Sta/Psy verbs (Grossman et al., 2002). The Act and Sta/Psy stimuli had significantly higher relatedness to a psychological state/emotion (t(35) = –40.24, p < .001). The Act and Sta/Psy stimuli were matched for familiarity (t(35) = –9.5, p > .05, n.s.) and for length (t(35) = .55, p > .05, n.s.). Written frequencies differed (t(35) = 2.25, p < .05; Laudanna et al., 1995). This frequency effect was driven by two items in the Sta/Psy verbs list (i.e., to decide and to trust). After excluding these items, the written frequencies did not significantly differed across conditions (t(35) = 1.72, p > .05, n.s.).

As far as the distribution of the Sta/Psy stimuli (see Table S1) in the affective space(s), is concerned, arousal and valence were collected in a previous study (Bonivento et al., 2017) on a sample of three groups of subjects of different age. Subjects rated arousal—on a scale from 1 to 9 on the Self-Assessment Manikin (SAM) (Bradley & Lang, 1999) how much arousal was triggered by the action or feeling or state described by the verb (score 1–9, 1 = very calm; 9 = very aroused), and emotional valence—as on a scale from 1 to 9 on the SAM how much happy make them feel the action or feeling or state described by the verb (score 1–9, 1 = very happy; 9 = very unhappy). For the 16–19 years old subjects the Sta/Psy stimuli had an arousal mean of 4.4 ± 1.5 and a valence mean of 5.5 ± 2.1.

Previous studies (Tomasino et al., 2014, 2018) ascertained that this experimental paradigm is useful to elicit mental imagery in one task (I task) and to prevent subjects from selecting the content of the phrases (LD task). Indeed, in those studies, subjects were significantly slower for the I (as compared with the LD task) and for the I of action verbs (as compared with abstract). Furthermore, the pattern of RTs during the LD task—with a trend toward an increase when words were of increasing length but no influence of the position of the target letter “L” on RTs—is compatible with the notion that our subjects read all the stimuli during the LD task.

Since the behavioral effects of the task in terms of subjects’ decisions and response times (Tomasino et al., 2014) were replicated (Tomasino et al., 2018), in the present work subjects’ responses will not be further discussed.

Subjects responded by using the index/middle fingers of their dominant hand (i.e., the right one).

Each trial lasted 4 s and the intertrial interval, consisting of a fixation point, jittered between 3250 and 4000 ms with 250 ms steps. Event trials were randomly alternated with null events (n = 36) appearing as a prolongation of the intertrial period. This expedient helped to enhance the statistical power of the fMRI analyses by allowing the poststimulus undershoot of the BOLD response. Three pseudorandomized stimulus sequences were alternated. To avoid any priming effect, trial sequences were shuffled in the two tasks.

2.3 Data analyses

The preprocessing of fMRI volumes was performed using the open-source Statistical Parametric Mapping (SPM) software (version 12, https://www.fil.ion.ucl.ac.uk/spm) running on Matlab R2019a Update 4 (The Mathworks, Inc.). For each subject, the first six dummy volumes were excluded from the analyses. To reduce head motion artifacts, the remaining 606 fMRI volumes were spatially realigned to the first reference volume (originally the seventh fMRI volume) using a least squares approach and a rigid-body transformation. The mean of the resliced fMRI images was then used as reference for coregistration with the subject’s structural T1-weighted image. Then, the structural image was corrected from intensity biases and segmented (classified) into different tissue types. The segmentation step included the estimation of the forward deformation field for normalization of the subject’s brain volume to the standard Montreal Neurological Institute (MNI) space. The realigned fMRI volumes were then normalized to the MNI space, spatially resampled to 2 mm × 2 mm × 2 mm and smoothed using a 3D Gaussian kernel filter with 6 mm full width at half maximum (FWHM). The latter step was aimed to suppress high-frequency spatial noise and to reduce the interindividual differences in functional and gyral anatomy.

A voxel-based general linear model (GLM) activation analysis was performed on the preprocessed fMRI volumes of each subject using SPM12. The GLM design matrix included the experimental conditions given by the combinations of factors, (a) letter detection in action verbs (LD_Act), (b) letter detection in state/psychological verbs (LD_Sta/Psy), (c) mental imagery of action verbs (I_Act), and (d) mental imagery of state/psychological verbs (I_Sta/Psy), as well as fixation periods. For each stimulus condition, two regressors of interest were built through convolution of the corresponding train of events (0 s pulses starting at stimulus onset) with the canonical Hemodynamic Response Function (HRF) and its temporal derivative. Temporal high-pass filter with cutoff at 1/128 Hz and linear trend removal were applied. The six movement parameters (three for translation and three for rotation) resulting from the preprocessing realignment step were included as confounding regressors.

After restricted maximum likelihood (REML) estimation of the GLM β coefficients, the effects of each experimental condition were assessed by making inference on the corresponding β value with a two-sided t-test. Multiple conditions were compared using appropriate t-contrasts, that is, t-tests on the linear combination of the corresponding ß coefficients. The following GLM contrasts were considered: single imagery conditions (I_Act, I_Sta/Psy) versus rest, imagery task versus letter detection task (I_Act + I_Sta/Psy).
vs. (LD_Act + LD_Sta/Psy), abstract verbal stimuli versus motor verbal stimuli [(I_Sta/Psy + LD_Sta/Psy) vs. (I_Act + LD_Act)], as well as task × stimuli interactions [(I_Sta/Psy vs. I_Act) vs. (LD_Sta/Psy vs. LD_Act)]. Our main interest was to identify the brain regions involved in the imagination of emotional/psychological verbs with respect to motor verbs by using letter detection as reference condition.

The contrast images from all subjects were used in a set of second-level random-effects GLM analyses that allowed to make group inferences on the selected contrast while accounting for the interindividual variability. For each contrast, we employed a multiple regression design with linear age and sex as factors of interest and MR scanner/head-coil as confounding factor. Any nonlinear effects of age were assessed in a set of secondary GLM analyses, in which the linear age regressor was replaced with either a quadratic age regressor or a U-shaped age regressor (computed as the squared difference between each subject’s age and the median age). In these nonlinear age models, we purposely excluded the linear age regressor due to its high degree of non-orthogonality with the quadratic (or U-shaped) age regressor, which would have impeded a successful allocation of the explained variance between them. After GLM β estimation, we assessed the effects of age and sex on the subject-level fMRI activations using two-sided t-tests (p < .05 after cluster family wise error [cFWE] correction). The significant regions were then saved using the SPM Marsbar toolbox (version 0.44, http://marsbar.sourceforge.net/) for additional region of interest (ROI) analyses. For each ROI emerging from a specific contrast, we localized the ROI based on the automated anatomical labeling (AAL) atlas and computed the subjects’ contrast values (i.e., the linear combination of β coefficients) in the ROI. To this end, we masked the subjects’ contrast maps and averaged the values of the voxels within the ROI. The emerging ROI values were then represented as a function of age or sex, as appropriate. In view of the nonuniform age distribution within our sample, we tested the reliability of the brain clusters showing age-related fMRI activations, if any, via nonparametric statistics. Specifically, we assessed the association between age and subject-level fMRI activations via n = 5000 permutations, while considering gender and MR scanner/head-coil as covariates of no interest. For each contrast, significance was assessed on the corresponding nonparametric p-value map (p < .001). Since our main interest was to validate the results obtained using parametric statistics, in the results section we will merely report if the significant clusters from the T statistics were confirmed or not using the permutation-based statistics.

3 | RESULTS

Our main results focus on the effects of age and gender on the fMRI activations selectively induced by emotional versus motor imagery controlled by letter detection, expressed by the task × stimuli interaction (imagery of state/psychological vs. action verbs vs. letter detection of state/psychological vs. action verbs). The fMRI activations after removal of age, gender, and scanner effects are illustrated in the

3.1 | Age/gender effects on emotion imagery: The task × stimuli interaction

The fMRI activation induced by emotional (vs. motor imagery, controlled by letter detection) was significantly influenced by gender (p < .05, cFWE corrected). Indeed, females showed higher activation than males in a cluster within the right putamen located at the interface with pallidum (Figure 1; Table 1). Of note, this cluster showed a significant positive BOLD response to the same contrast in the entire group. No effects of age, neither linear nor quadratic, emerged on the fMRI activation pattern for the interaction term.

3.2 | Age/gender influences on the main effect task: Imagery versus letter detection

Our second result focuses on the effects of age and gender on the fMRI activations induced by the imagery ability, irrespective of the
imagery content, that is, type of stimulus, expressed by the main effect task.

Age linearly affected the fMRI activation patterns for the mental imagery task versus letter detection task. Two clusters in the left hemisphere, in the middle cingulate cortex and anterior insular cortex, progressively decreased their BOLD response with age \( (p < .05, \text{cFWE corrected}) \). These clusters were confirmed when nonparametric statistics were applied \( (p < .001) \). The emerged clusters were part of the brain regions with significant positive BOLD response in the entire group. Neither quadratic nor U-shaped age effects emerged \( (p < .05, \text{cFWE corrected}) \).

### 3.3 | Age/gender influences on main effect stimuli: Emotional versus motor verbs

The last result focuses on the effects of age and gender on the fMRI activations induced by the state/psychological abstract stimuli, irrespective of the cognitive operation exerted upon them, that is, type of task, expressed by the main effect stimuli.

Figure 3 shows that the left putamen showed a progressive decrease in its positive BOLD response with aging. This cluster resulted from both linear and quadratic age models \( (p < .05, \text{cFWE corrected}) \) and from nonparametric statistics \( (p < .001) \), but not from the U-shaped age model \( (p < .05, \text{cFWE corrected}) \).

### 3.4 | Group level fMRI activations

Figure 4 shows the brain regions significantly involved in the imagery task, emotional stimuli and task \( \times \) stimuli interactions \( (p < .05, \text{cluster-based family wise error corrected}) \), after removal of age, gender, and scanner effects. The anatomical localization and statistical information of the significant regions are reported in Table S2.

Imagery of both state/psychological (Figure 4, first row) and action verbs (Figure 4, second row) elicited the activation of a cluster in left inferior frontal cortex, including its orbital and triangular portions. Negative blood oxygenation level dependent (BOLD) responses...
to the imagery task were observed in bilateral portions of the precuneus, calcarine and mid cingulate cortices. Motor but not emotional imagery induced a deactivation of the superior parietal and supramarginal gyri in the right hemisphere.

The comparison between imagery and letter detection tasks (of both state/psychological and action verbs; Figure 4, third row) showed that imagery elicited higher BOLD responses than letter detection in bilateral inferior frontal cortex, middle temporal gyrus, left angular gyrus as well as subcortical regions like thalamus, pallidum, and caudate. On the contrary, bilateral middle frontal cortex and a big portion of parietal and occipital cortices showed higher BOLD responses to the letter detection task compared with the imagery task.

The comparison between emotional and motor items (in both imagery and letter detection tasks) showed a set of brain regions selective for the stimulus type (Figure 4, fourth row). Emotional verbs were associated with higher BOLD responses in the left midfrontal cortex, a big portion of parieto-occipital cortex and bilateral putamen, whereas motor verbs elicited higher BOLD responses in the inferior frontal cortex and supplementary motor area.

The task × stimuli interaction contrast (imagery of state/psychological vs. action verbs vs. letter detection of state/psychological vs. action verbs) showed that imagery of emotional stimuli was associated with (a) positive BOLD responses in the bilateral superior temporal gyrus and rolandic operculum, middle cingulate cortex and precuneus and in the right middle frontal cortex, insula, putamen, and supramarginal gyrus, (b) negative BOLD responses in bilateral portions of triangular inferior frontal cortex, insula, mid-cingulate cortex, and supplementary motor area and in the left middle temporal cortex.

4 | DISCUSSION

The present fMRI study is the first to identify the effect of gender and age on the neural correlates of emotion imagery. We carried out an fMRI experiment in which 91 healthy volunteers in a wide age range imagined of emotion-related scenarios (as compared with action-related scenarios).

4.1 | Gender effect on the right putamen by emotional imagery

Our main result is that the fMRI activation induced by emotional (vs. motor) imagery, controlled by letter detection, was significantly influenced by gender. Females showed higher activation than males in a cluster within the right putamen.

The putamen is part of the basal ganglia. It is known that, although motor function is the main processing in basal ganglia, these structures show segregation, in addition to motor control, also for cognitive and emotional function (e.g., for putamen, Oberhuber et al., 2013; Vinas-Guasch & Wu, 2017; Draganski et al., 2008). This view on functional organization is consistent with the anatomical segregation (Alexander et al., 1986) found in the basal ganglia. Indeed, different brain regions, such as the temporal lobe (Middleton & Strick, 1996), parietal lobe (Selemon & Goldman-Rakic, 1988; Stanton et al., 1988; Yeterian & Pandya, 1991), and the brainstem (Bostan & Strick, 2010), have topographically organized projections to the basal ganglia (Delong & Wichmann, 2007). For instance, Draganski et al. (2008) in a DTI study reported both segregated and also overlapping connections from cortical sites to different parts of basal ganglia. The putamen is part of the striatopallidum. The striatum is connected with the entire cortex via subregion-specific fronto-striatal loops (Haber, 2016). Parallel/segregated processing of different types of information characterize the striatum (e.g., Devan et al., 2011), given also its organization in two main subsectors: the ventral striatum (VS), which includes the nucleus accumbens, and the dorsal striatum (DS) that is strongly connected with dorsolateral and dorsomedial prefrontal regions (Di Martino et al., 2008; Postuma & Dagher, 2006). The striatum is hub that supports a variety of motor and cognitive function, as it can integrate emotional, cognitive, and sensory information (Waraczynski, 2006). In our study, we found that the this area is activated by emotional imagery, and that activation was higher for females. This result strengthens previous data.
showing an involvement of the striatum in imagery, emotion and language processing (e.g., Dzafic et al., 2016; Li, 2000; Makary et al., 2017; Radke et al., 2018; Vinas-Guasch & Wu, 2017) and it is not merely involved in action planning and execution. The striatum receives inputs from the amygdala (Alexander et al., 1986; Middleton & Strick, 2000; Pennartz et al., 2011), which in turns receives input from prefrontal areas. We found that gender modulates the fMRI activation during the sole imagery of emotional scenario of this area, as it was significantly higher in women. Behavioral differences in emotional processing exist: for example, women are able to recall more emotional autobiographical events as compared with men, are quicker in producing memories and generate more vivid memories (Fujita et al., 1991; Robinson, 1976).
4.2 | Age effects on the left insula and cingulate cortex by mental imagery

We found that mental imagery related activation, independent of its content (both emotion and action imagery), is affected by age. Of note, linear age modeling was found to be more sensitive in capturing age-related fMRI changes compared with quadratic age modeling.

Two clusters in the anterior insular cortex and in the left anterior midcingulate cortex (MCC), progressively decreased their BOLD response with increasing age. These two regions have a close functional relationship. They are considered input and output regions of the network involved in the processing of subjective feelings (Medford & Critchley, 2010). In particular, the insula is a key area for introspection during mental imagery (Skotnik & Linden, 2019). The role of the anterior insula is mediating awareness of one's internal states (Craig, 2002). This role is consistent with the task, since participants were instructed to determine the pleasantness of the produced mental image. The age-dependent decreased activation of this area may indicate that older participants need less activity in self-awareness areas, or that the ability to internally focus and monitor the ongoing internal state decreases with age. It has been shown that elderly adults are less likely to show measurable electrodermal skin conductance response to emotions compared with younger ones, regardless of the emotion subjective rating (Neiss et al., 2009). Similarly, the MCC activation is enhanced by emotion processing (Vogt et al., 2003) and it is activated by mental imagery (Damasio et al., 2000).

4.3 | Age effects on the left putamen by emotional versus motor verbs

Lastly, we found that the brain response to emotional stimuli, irrespective of the cognitive operation exerted upon them, that is, type of task, is moderated by age: the left putamen showed a progressive decrease in its positive BOLD response with aging. As already mentioned, the basal ganglia are involved in many functional domains including emotion processing (Obeso et al., 2000). fMRI studies on emotion-related words (Moseley et al., 2015) showed that the left putamen, among the orbitofrontal and frontopolar cortex, anterior cingulate gyrus, and insula, is involved in emotion word processing. We support and complement this result by adding further evidence that the emotion-related activation in the left putamen is subject to age effect, with a decreased activation with aging. It could be hypothesized that emotional words become less salient with aging, which is in line with evidence of lower emotion salience effects in attention and memory tasks in older compared with younger adults (Murphy & Isaacowitz, 2008). Given that the BOLD response to abstract emotional verbs decreases with aging in both imagery and letter detection conditions, this result could reflect a lower putamen responsiveness or attention to emotional words in older people.

5 | LIMITATIONS

Our study presents some limitations. For collecting a large sample, we used two different Philips 3T scanners. We included in the analysis one regressor specifying this variable, and checked that this did not influence our results. Future studies addressing age and gender (or other variables) effects will be conducted by using one scanner to avoid potential variance in the data.

The partial brain coverage of the fMRI sequence represents a further shortcoming of our study, which has prevented the robust identification of age or gender influences on the fMRI activations in brain regions with a known role in emotional processing, such as the amygdala and the hippocampi.

Second, although our sample size is large, the age distribution is imbalanced. To cope with this limitation, we validated the results concerning age effects on fMRI activations (based on T statistics) using nonparametric statistical tests. Nevertheless, future studies addressing age effects will be conducted by stratifying age classes better. In Tomasino et al., 2018, a group comparison between teenagers and adults showed that older adults showed decreased BOLD response in the left supramarginal gyrus and left superior frontal gyrus in the (imagery of emotion vs. motor verbs) contrast. Such effects were not maintained in the current dataset. Several methodological factors could have influenced this result such as sample size (24 adults vs. 16 teenagers in Tomasino et al., 2018’s study) versus a group of 91 subjects here, a higher mean age of the sample (here 29.02 ± 12.04 years) while in Tomasino et al., 2018’s study we compared a group of 16.34 ± 1.30 years versus a group of 24.87 ± 3.8 years. Lastly we used two different statistical approaches: a flexible factorial analysis in the former study and a multiple regression design with linear age and sex as factors here. Nonetheless, in the Appendix S1, it is reported that “The task × stimuli interaction contrast (imagery of state/psychological vs. action verbs vs. letter detection of state/psychological vs. action verbs) showed that imagery of emotional stimuli was associated with positive BOLD responses in the bilateral superior temporal gyrus and Rolandic operculum, middle cingulate cortex, and precuneus and in the right middle frontal cortex, insula, putamen, and supramarginal gyrus” which are the same regions activated by emotion imagery (vs. action), controlled for letter detection in the previous studies.

Finally, future studies will control for educational, socioeconomic, and developmental background differences that might covary with age stratification.

6 | CONCLUSION

Although progresses have been made in understanding the brain mechanisms underlying subjective emotional states, the neural bases of emotion imagery and their modulating factors remain largely unknown. Taken together, our fMRI results on emotion imagery indicate an influence of subjects’ related variables, such as participants'
age and gender, in interaction with bottom-up variables such as the object of imagination, or directly.

The present results hardly indicate on which component of emotional processing age and gender variables exert their effect. Modifications could occur in affective processing, or at the level of affective conceptualization depth, or in emotion imagery abilities. Our task was not designed to address this issue. Nonetheless, our task was designed to elicit explicit mental imagery, triggered through explicit instructions presented to the subjects. Certainly, the age and gender effects we found can be related to changes in emotion imagery abilities as the task evokes this type of processing. In addition, the task required participants to determine the pleasantness of the emotion image by responding to the question “Do you like it?”, and it has been argued that this question elicits deep semantic processing of emotion words (Grossman et al., 2002). Future studies are required to address this issue.

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CONFLICT OF INTEREST
The authors declare no conflict of interests.

DATA AVAILABILITY STATEMENT
Data will be made available from the authors upon request.

ETHICS STATEMENT
The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

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