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# The Neural Bases of Event Monitoring across Domains: a Simultaneous ERP-fMRI Study

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The ability to check and evaluate the environment over time with the aim to detect the occurrence of target stimuli is supported by sustained/tonic as well as transient/phasic control processes, which overall might be referred to as event monitoring. The neural underpinning of sustained attentional control processes involves a fronto-parietal network. However, it has not been well-defined yet whether this cortical circuit acts irrespective of the specific material to be monitored and whether this mediates sustained as well as transient monitoring processes. In the current study, the functional activity of brain during an event monitoring task was investigated and compared between two cognitive domains, whose processing is mediated by differently lateralized areas. Namely, participants were asked to monitor sequences of either faces (supported by right-hemisphere regions) or tools (left-hemisphere). In order to disentangle sustained from transient components of monitoring, a simultaneous EEG-fMRI technique was adopted within a block design. When contrasting monitoring versus control blocks, the conventional fMRI analysis revealed the sustained involvement of bilateral fronto-parietal regions, in both task domains. Event-related potentials (ERPs) showed a more positive amplitude over frontal sites in monitoring compared to control blocks, providing evidence of a transient monitoring component. The joint ERP-fMRI analysis showed that, in the case of face monitoring, these transient processes rely on right-lateralized areas, including the inferior parietal lobule and the middle frontal gyrus. In the case of tools, no fronto-parietal areas correlated with the transient ERP activity, suggesting that in this domain phasic monitoring processes were masked by tonic ones. Overall, the present findings highlight the role of bilateral fronto-parietal regions in sustained monitoring, independently of the specific task requirements, and suggest that right-lateralized areas subtend transient monitoring processes, at least in some task contexts. 

Keywords: EEG-fMRI, face processing, tool processing, sustained monitoring, transient monitoring, cognitive control

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Q6

#### Neural Bases of Event Monitoring

#### INTRODUCTION

116 Flexible goal-directed behaviors require an adaptive cognitive 117 control system that selects task-relevant contextual information 118 and optimize their processing. A key cognitive control function 119 supporting efficient systems is monitoring. This ability refers to 120 a set of checking and evaluating processes, directed to assess 121 stimuli or responses. As such, it represents a multifaceted 122 function, recruited in a variety of apparently unrelated tasks 123 and encompassing different sub-processes. For instance, in 124 experiments on performance monitoring, it denotes the ability 125 to continuously check action outcomes in order to detect 126 errors and adjust future action selection (Ridderinkhof and 127 Ullsperger, 2004; Ullsperger et al., 2014). In time monitoring 128 paradigms, it includes processes devoted to continuous updating 129 of temporal/probability information in order to anticipate 130 the occurrence of an upcoming stimulus and prepare motor 131 response (Coull et al., 2000; Vallesi et al., 2007b, 2009; Coull, 132 2009). In prospective memory paradigms, it involves the active 133 maintenance of task goals and the check of the environment to 134 detect prospective targets (Guynn, 2003; Smith, 2003). 135

In all these tasks, monitoring is supported by both 136 sustained/tonic and transient/phasic processes. When the 137 occurrence of target stimuli/events is expected over time, 138 sustained control processes should be instantiated, which 139 promote and prepare individuals to their detection. In the 140 same context, however, the occurrence of single stimuli 141 elicits more transient control processes, since each of them 142 should be assessed one-by-one. While the sustained monitoring 143 processes are ubiquitous and span multiple trials, the transient 144 monitoring processes operate within a trial. To give some 145 examples: performance monitoring tasks requires the continuous 146 assessment of whether ongoing actions match expected goals; 147 on the other hand, it involves more transient responses, such 148 as error detection and subsequent action adjustments. Similarly, 149 in time monitoring tasks, temporal expectations bias response 150 preparatory processes over time. However, the actual onset of 151 each target stimulus update these expectations in a more trial-152 by-trial basis (Coull et al., 2016). In prospective memory tasks, 153 individuals are engaged in the sustained maintenance of the 154 prospective goal and, at the same time, they must check stimuli 155 item-by-item in order to detect targets. This dual process is 156 engaged especially in non-focal prospective tasks, that require 157 the detection of a stimulus feature unrelated to the ongoing task 158 (McDaniel et al., 2015; Cona et al., 2016). The two qualitatively 159 different cognitive controls processes might be assimilated to 160 the proactive and reactive modes theorized by Braver (2012). 161 They might act in a "semi-independent" manner, thus they may 162 be both engaged simultaneously or one could dominant on the 163 other, in distinct moments in time, according to the experimental 164 requirements (Gonthier et al., 2016). 165

Functional magnetic resonance imaging (fMRI) studies have provided evidence on distinct neural mechanisms subserving sustained and transient attentional control processes (Braver et al., 2003; Reynolds et al., 2009; McDaniel et al., 2013). These studies have used a mixed blocked/event design to disentangle between sustained and transient brain responses. By this

methodological approach, block-related (sustained) functional 172 brain activity and event-related (phasic) activity were extracted. 173 Findings converged in showing a fronto-parietal network as the 174 principal contributor of sustained attentional control processes. 175 Specifically, in a prospective memory task, Reynolds et al. (2009) 176 found that the activity of bilateral cortical regions of the middle 177 frontal gyrus, namely the anterior (BA 10/46) and dorsolateral 178 (BA 46/9) prefrontal cortex, regions of the superior and inferior 179 parietal lobe (BA 7/40), and the anterior cingulate cortex were 180 modeled as a sustained process, spanning the entire task block. 181 Regions specifically engaged in item checking, in a transient 182 (event-related) fashion, did not emerge. A selective transient 183 response of the middle temporal gyrus was only found when the 184 target was encountered. Similarly, McDaniel et al. (2013) found 185 that bilateral areas, including the dorsolateral prefrontal cortex 186 (middle frontal gyrus, BA 46), the anterior cingulate area (BA 187 32), the inferior frontal junction (precentral gyrus, BA 47/44), 188 the frontal eye fields (precentral/middle frontal gyrus, BA 6), and 189 superior parietal lobule (BA 7), were involved in sustained top-190 down attentional control. The transient brain response elicited by 191 target trials involved the activity of some of the aforementioned 192 fronto-parietal regions, namely, the left inferior frontal junction 193 (BA 44), the frontal eye fields (BA 8/6) and the bilateral inferior 194 parietal lobule (BA 40) plus the left anterior cingulate gyrus (BA 195 32), the bilateral anterior insula (BA 47) and ventral parietal 196 cortex, which are likely involved in stimulus-driven processes. 197 No evidence of transient processes related to non-target trials 198 was provided. This is surprising, if one considering that, in a 199 task requiring event monitoring, each stimulus (not just the 200 targets) should undergo transient checking/evaluating processes 201 (cf. Vallesi, 2014). Therefore, a question remains unexplored: are 202 the transient item checking processes (i.e., the reactive control 203 processes) obscured by more sustained monitoring processes 204 because of the sluggish temporal resolution of fMRI? 205

To address this point, we designed an event monitoring 206 experiment where participants were required to check series of 207 visual stimuli over time for detecting the occurrence of target 208 events (see also Poth et al., 2014). This event monitoring ability 209 is crucial in many everyday activities, such as in the work of 210 security officers who have to continuously inspect individuals 211 as well as objects to identify critical targets and ensure the safe 212 movement of a mass of people. In order to unveil the presence of 213 sustained as well as transient monitoring processes, we conducted 214 a simultaneous EEG-fMRI study. This multimodal technique 215 is the gold-standard for characterizing spatial and temporal 216 dynamics of brain activity over different time scales, within the 217 same experimental session (Laufs, 2008; Mulert and Lemieux, 218 2009; Ullsperger and Debener, 2010; Huster et al., 2012; Jorge 219 et al., 2014). In the current study, a blocked EEG-fMRI design was 220 specifically devised. The co-registration approach allowed us, on 221 the one hand, to capture the functional changes of brain regions 2.2.2 associated with sustained activity across trials and inter-stimulus 223 intervals (fMRI data) and, on the other hand, to capture the fast 224 brain responses elicited by each event (ERP data). By doing so, 225 we could disentangle tonic and phasic brain responses which are 226 likely to at least partially overlap in space and time. By coupling 227 block-related fMRI data and ERP data we were able to detect 228

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brain regions, among those showing a sustained activity, which 229 actually intervened in a stimulus-driven fashion. Moreover, the 230 simultaneous EEG-fMRI recording helps overcoming the limit 231 of examining long-lasting and phasic components in separate 232 blocks, as in previous studies. As such, this approach represents a 233 possible alternative to mixed (Visscher et al., 2003; Petersen and 234 Dubis, 2012) or "hybrid" (Braver et al., 2003) block/event-related 235 fMRI designs. 236

Another missing point in the literature is whether there is a
unique fronto-parietal circuit that mediates sustained monitoring
processes, common to different task/material to be processed.
Previous findings suggest that this possibility is very likely.
However, direct evidence supporting this point is limited.

Along this line, a block-design fMRI experiment (Benn 242 et al., 2014) represents an encouraging attempt to differentiate 243 between long-lasting monitoring components and trial-by-trial 244 ones and to compare monitoring processes involved in different 245 domains (numerical and visuo-spatial). The authors contrasted 246 non-monitoring blocks to blocks that required monitoring 247 information either over time or trial-by-trial. The conjunction 248 analysis showed that an extensive fronto-parietal network was 249 associated with monitoring over time in both domains. These 250 results suggested that domain-independent processes constituted 251 the long-lasting component of monitoring. Compared to non-252 monitoring blocks, the trial-by-trial monitoring condition in 253 the numerical domain activated the right superior parietal, 254 left inferior parietal and bilateral superior and medial frontal 255 gyri. Unfortunately, no evidence about the discrete, trial-by-256 trial monitoring component was collected in the visuo-spatial 257 domain. Furthermore, areas activated in both sustained and 258 transient monitoring were not investigated. 259

Recently, the domain-general nature of monitoring has 260 been corroborated by an event-related potential (ERP) study. 261 Here, participants had to monitor either verbal or spatial 262 information while performing a concurrent verbal or spatial task, 263 respectively (Capizzi et al., 2016). Stimuli in monitoring blocks 264 elicited a more pronounced positivity over frontal and parietal 265 scalp regions compared to stimuli in non-monitoring blocks, 266 which was interpreted as reflecting greater attentional resources 267 needs to maintain the focus of attention on the monitoring 268 requirements. 269

To elucidate whether the same fronto-parietal network would 270 be recruited independently of the material to be monitored, in the 271 current event monitoring experiment participants were asked to 272 monitor the occurrence of different stimulus materials, within the 273 same experimental session. To better dissociate the hemispheric 274 contribution according to the domain, materials known to be 275 processed by differently lateralized brain regions were used. 276 Namely, in the control condition (i.e., non-monitoring blocks) 277 participants performed a categorization task involving either 278 faces or tools. While the processing of faces is usually subtended 279 by dominant right temporal-occipital areas (e.g., Busigny et al., 280 2010; Frässle et al., 2016; for a recent review Yovel, 2016), the 281 processing of tools mostly relies on a dominant left-lateralized 282 283 fronto-parietal network (Grafton et al., 1997; Chao and Martin, 2000; Proverbio et al., 2013; Orban and Caruana, 2014; Perini 284 et al., 2014). In monitoring blocks, they were also asked to 285

monitor the occurrence of specific stimuli (i.e., faces or tools), 286 which constituted the target stimuli. Since the probability of 287 the target occurrence slightly varied across experimental blocks, 288 participants had to continuously monitor stimuli over time in 289 order to efficiently detect them. 290

Our primary hypothesis was that monitoring processes are 291 mediated by a network of fronto-parietal cortical areas, with 292 an important node in the lateral prefrontal cortex (Henson 293 et al., 1999; Vallesi et al., 2007a,b, 2009; Shallice et al., 2008; 294 Vallesi and Crescentini, 2011), and that these areas operate in 295 a domain-independent fashion. By comparing blocks requiring 296 monitoring to blocks not requiring this process, we expected that 297 the activation of fronto-parietal areas would emerge, similarly for 298 the two domains (i.e., faces and tools). The second hypothesis was 299 that some of these fronto-parietal areas reflect sustained/tonic 300 monitoring processes, whereas some others support more 301 transient/phasic ones. By integrating block-related fMRI and ERP 302 measures we expected to differentiate the neural bases of these 303 two monitoring components. 304

### MATERIALS AND METHODS

#### **Participants**

Twenty-two students from the University of Padua took part in 309 the study. Data from two participants were discarded because 310 of excessive head movements (>  $\pm 3$  mm in any translation 311 direction) and two others because of low task performance 312 (accuracy level < 2.5 standard deviations). Therefore, the results 313 are reported here for 18 participants (12 female; mean age: 23 314 years; age range: 20-28 years). They were all right-handed, as 315 indicated by the Edinburgh Handedness Inventory (Oldfield, 316 1971; mean laterality score: 89.4, range: 70-100), and reported 317 normal or corrected-to-normal visual acuity (MRI-compatible 318 glasses were used when appropriate). The study was approved by 319 the Bioethical Committee of the Azienda Ospedaliera di Padova 320 and was conducted according to the guidelines of the Declaration 321 of Helsinki. All participants signed a written informed consent 322 prior to their participation and were paid 25 euro after the 323 experiment. 324

### Stimuli

Stimuli consisted of pictures of faces and tools. The face pictures 327 were downloaded from publicly available internet databases, 328 after obtaining appropriate permissions when required 329 (http://agingmind.utdallas.edu/download-stimuli/face-database/, 330 Minear and Park, 2004; http://www.macbrain.org/resources.htm 331 Tottenham et al., 2009; http://mmlab.ie.cuhk.edu.hk/archive/ 332 facesketch.html, Wang and Tang, 2009). All pictures were 333 cropped and resized in ovals of 184 (width)  $\times$  272 (height) pixels. 334 Hair and gender-related features (such as beard and make-up) 335 were removed. Overall, a total of 50 face pictures were created, 336 half female and half male. They belonged to different races, 337 white/Caucasian, black/African-American, Hispanic, Middle-338 East, Indian. In addition, 20 pictures of Chinese individuals and 339 20 of older Caucasian adults were included as target stimuli to 340 be monitored. Faces were selected that have a neutral expression 341 and as few as gender-related features as possible. 342

The tool pictures were obtained via accurate selection on the 343 web. Familiar tools (e.g., scissors, comb, guitar) were collected, 344 that is, manipulable objects with a clear affordance, which 345 implicitly suggests a motor interaction. The tool pictures were 346 resized to maintain either the width or the height of the faces. 347 Overall, a set of 50 tool pictures was selected, belonging to 348 15 unimanual and 15 bimanual categories. Twenty pictures of 349 cooking tools (e.g., whisk, frying pan) and 20 of working tools 350 (e.g., screwdriver, drill) were included as target stimuli to be 351 monitored. 352

All pictures were converted in gray scale using the GIMP software (http://gimp.org). Luminance values were equalized across all images using the SHINE toolbox (Luminance Histogram Matching; Willenbockel et al., 2010), implemented in Matlab. Overall, a total of 280 face pictures and 280 tool pictures were presented across the whole experiment.

A pilot study was carried out on 12 subjects to ensure that 359 all stimuli were easily recognizable and correctly categorized as 360 female/male faces and unimanual/bimanual objects with at least 361 90% of accuracy. In addition, a set of 40 scrambled images (272 362  $\times$  272 pixel) were created by averaging the pixels of 20 randomly 363 selected pictures and were used during rest/fixation phases. All 364 images were presented centrally on a 64 (width)  $\times$  40 (height) cm 365 screen (InVivo Esys Display, Gainesville, FL, USA),  $1,280 \times 800$ 366 pixel resolution, on a white background. Faces were 9 (width)  $\times$ 367 14 (height) cm of size and objects were contained in a 14 (width) 368  $\times$  14 (height) cm square. The screen was placed at the head of 369 the bore and the images were visible to the participants through 370 a double mirror system mounted on the head coil, with the head 371 of participants lying 150 cm from the monitor. 372

#### **Procedure and Task**

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An illustrative picture of the experimental procedure is 375 reported in Figure 1. Four types of blocks were pseudo-376 randomly presented, namely monitoring blocks and non-377 monitoring blocks containing faces (hereafter named "Mon 378 Faces" and "NonMon Faces," respectively), monitoring blocks 379 and non-monitoring blocks containing tools (hereafter named 380 "Mon Tools" and "NonMon Tools," respectively). The entire 381 experiment contained 10 blocks of each type (Mon Faces, 382 NonMon Faces, Mon Tools, and NonMon Tools), which were 383 grouped in 5 scanning runs of 8 blocks each (2 for each type). 384 Each run consisted of alternating cycles of fixation (A) and 385 task (B) blocks presented in an ABAB succession. Fixation 386 blocks (denoted by a centrally presented scrambled image) lasted 387 randomly 8, 10, 12, 14, or 16 s (mean duration 12 s); task blocks 388 were 40 s long and included 14 trials, containing 7 female and 389 7 male faces, or 7 unimanual and 7 bimanual tools. Monitoring 390 blocks included from 2 to 6 target stimuli. Each stimulus was 391 presented centrally for 800 ms, followed by a blank with an 392 inter-stimulus interval continuously varying between 1,900 and 393 2,100 ms. This small random variation of the inter-trial interval 394 ensured that the stimuli were not locked to multiples of the 395 slice acquisition frequency, minimizing the influence of any 396 residual MRI artifact in the EEG trace. Stimulus presentation 397 and response collection were controlled by Eprime 2 software 398 (Schneider et al., 2002). 399

In Face blocks participants had to decide whether the face 400 gender was female or male. In Tool blocks they were asked 401 to decide whether the object is generally manipulated with 402 one hand (unimanual objects) or with both hands (bimanual 403 objects). Responses were given by pressing one of two buttons 404 with the two index fingers lying on two-button MRI-compatible 405 response boxes. All possible combinations between category 406 (female/male, unimanual/biamanual) and responding hand were 407 counterbalanced across participants. In addition to this ongoing 408 task, in half of the experimental blocks participants were asked 409 to perform a monitoring task, namely they had to detect specific 410 categories of faces or tools (targets). In Mon Faces blocks they 411 were asked to detect either Chinese faces or faces of people older 412 than 50 years; in Mon Tool blocks they were asked to detect 413 either cooking tools or working utensils (in Italian: "attrezzi da 414 lavoro"). The two target categories never appeared together in 415 the same block. Each block was preceded by an instruction screen 416 (2 s in the fixation block, 6.5 s in the task blocks) that indicated 417 the task to be executed, the target category to be monitored, and 418 reminded the stimulus-response mappings. In order to verify that 419 participants correctly detected the target stimuli, at the end of 420 Mon blocks they were asked to estimate the approximate number 421 of targets. The numbers from 1 to 6 appeared, two at a time, 422 and participants had to press the response button (beneath the 423 left or right index) corresponding to the number of targets that 424 they had estimated. Participants were instructed not to count but 425 to focus on target detection. Furthermore, they were informed 426 that the Monitoring blocks had a 100% probability to contain at 427 least 1 target stimulus in order to encourage the involvement of 428 monitoring processes. 429

A practice session was performed the day before, outside the scanner. During this session one sample of each type of block was presented and trial-by-trial feedbacks on participants' accuracy were provided. If participant's overall accuracy was below 80%, the practice was repeated until she/he reached this criterion. The experimenter clarified any doubt on the experimental session and ensured that the instructions were clearly understood. 430

FMRI Signal Acquisition and Preprocessing 438 MR images were acquired using a 3T Ingenia Philips whole-439 body scanner (Philips Medical Systems, Best, The Netherlands) 440 equipped with a 32-channel head-coil, at the Neuroradiology 441 Unit of the Azienda Ospedaliera of Padova. Functional volumes 442 were obtained using a whole head T2\*-weighted echo-planar 443 image (EPI) sequences (repetition time, TR: 2,000 ms; echo time, 444 TE: 35 ms; 25 axial slices with ascending acquisition; voxel size: 445  $2.4 \times 2.4 \times 4.8$  mm; flip angle, FA: 90°; field of view, FOV: 230 446 mm, acquisition matrix:  $84 \times 80$ ; SENSE factor: 2 in anterior-447 posterior direction). 448

Special care was taken to ensure that frontal areas and 449 cerebellum would be included in the imaging volume. Small foam 450 cushions were placed around the participant's head to minimize 451 head movements and to ensure a comfortable position; they also 452 wore earplugs to reduce acoustic noise. A total of 282 EPI images 453

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<sup>&</sup>lt;sup>1</sup>The Italian word specifically refers to tools usually found in a toolbox and used to fix or build things, not to general tools, such as scissors. 456

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blocks (8–16 s). The top of the figure depicts an example of trial sequence within a two monitoring (Mon) blocks. Faces and tools were displayed for 800 ms in each trial and appeared in separate blocks. In the figure, the target stimulus in the Face Mon block is represented by a Chinese face, whereas in the Tool Mon block is the picture of a blender. In the non-monitoring (NonMon) blocks the subject has to categorize the picture as female/male face or unimanual/bimanual tool. In the Mon blocks the subjects has to perform the categorization task and to detect to the target stimuli.

were acquired for each of the five runs. Two dummy scans at the beginning of each run were not acquired. High-resolution T1weighted anatomical images (TR/TE: 8.1/3.7; 180 sagittal slices; FA: 8°; voxel size:  $0.49 \times 0.49 \times 1$  mm; FOV: 220 mm; acquisition matrix: 220 × 220) were acquired after the functional runs.

The fMRI data pre-processing and statistical analyses were performed using SPM12 (Statistical Parametric Mapping software; Wellcome Department of Cognitive Neurology, London, UK; http://www.fil.ion.ucl.ac.uk/spm). Functional images were spatially realigned to compensate for participants' head movements during the experiment using a 4th degree B-Spline interpolation and a mean image of the realigned volumes was created. For normalization, the 6-parameter rigid-body transformation from the mean image to the anatomical image was concatenated with a transformation from the anatomical image to the standard Montreal Neurological Institute (MNI) template (2 mm<sup>3</sup> voxel-size) and applied to all volumes. Normalization to MNI was performed by combining registration and tissue classification into a single generative model, which also includes parameters that account for image intensity non-uniformity. The functional images were then spatially smoothed with an 8 mm full-width-at-half-maximum Gaussian filter. 

#### **EEG Signal Acquisition and Preprocessing**

The EEG signal was recorded using a MR-compatible system (Brain Products, Munich, Germany), connected to 64 sintered Ag/AgCl ring electrodes, equipped with current-limiting  $5-k\Omega$ resistors and mounted on an elastic cap (BrainCap MR) according to the extended 10–20 system. Reference and

ground channels were located over FCz and AFz, respectively. An electrode placed in the middle of participants' back, approximately 4 cm left to the spine, was used to acquire the electrocardiographic (ECG) signal. Impedance values were kept below 5 k $\Omega$ . Raw data were band-pass filtered between 0.016 and 250 Hz digitized at a sampling rate of 5 kHz. The EEG was monitored while scanning using online correction software (RecView 1.4, Brain Products). Overall, the EEG recording procedure was performed according to safety and data quality guidelines provided by Mullinger et al. (2013). 

The EEG data preprocessing was performed using either BrainVision Analyzer 2.1 (Brain Products) or EEGLAB 12.0 (Delorme and Makeig, 2004), implemented in Matlab, according to each specific preprocessing step. The gradient artifact (GA) was removed from EEG data using the fMRI artifact slice template removal (FASTR) algorithm (Niazy et al., 2005), implemented in EEGLAB (FMRIB plug-in). A total of 31 consecutive volume artifacts were included in the averaging window for computing the artifact template. The gradient residual artifacts were removed by the Optimal Basis Set (OBS) procedure (Niazy et al., 2005). The resulting EEG signal was low-pass filtered by applying a windowed sinc FIR filter, with a cut-off frequency of 40 Hz, a Kaiser Window type with a beta of 5.65, a maximum pass-band deviation of 0.001 and a transition band of 10 Hz (Widmann et al., 2014). The ballistocardiographic (BCG) artifact was removed using a semi-automatic procedure implemented in BrainVision Analyzer. As an initial step, the R peaks of every heart pulse were automatically detected and marked on the ECG channel. Visual inspection 

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was then conducted on the whole ECG signal to ensure the
correct positioning of all the peaks. Finally, the artifact was
removed from all EEG channels by means of an average template
subtraction, analogously to the procedure implemented for the
GA (Allen et al., 1998, 2000; Niazy et al., 2005).

The EEG signal was then down-sampled to 500 Hz. The 576 BCG artifact residuals, ocular movements and muscle artifacts 577 were removed by means of an Independent Component Analysis 578 (ICA; Debener et al., 2007; Mantini et al., 2007), based on 579 an extended Infomax algorithm (Bell and Sejnowski, 1995). 580 The continuous EEG signal was segmented in epochs ranging 581 from -200 ms before stimulus onset to 1,000 ms after stimulus 582 presentation. The resulting epochs were then baseline-corrected 583 using a time window from -200 to 0 ms. Data were re-referenced 584 to the average of all electrodes, with the exception of the ECG 585 channel. To allow a reliable integration with fMRI block analysis, 586 all trials belonging to a block were included in the ERP average. 587 Afterwards, the resulting block-by-block ERPs were averaged for 588 each condition, namely NonMon Faces, Mon Faces, NonMon 589 Tools, Mon Tools. 590

# 592 DATA ANALYSIS

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#### 594 Behavioral Data Analysis

Accuracy and response times (RTs) on the female/male and 595 unimanual/bimanual tasks were examined in order to investigate 596 the effect of Monitoring (NonMon, Mon) and Domain (Faces, 597 Tools). Due to the non-normal distribution of accuracy data, the 598 non-parametric Friedman's ANOVA was performed. Post-hoc 599 600 Wilcoxon signed-rank tests were then run on pairs of conditions to reveal significant differences between pair of conditions. A 601 602  $2 \times 2$  repeated measure ANOVA model was used to test the effect of Monitoring and Domain factors on mean RTs. For all 603 the behavioral analyses, the significance level was set at  $\alpha = 0.05$ 604 and corrected for multiple comparisons in post hoc tests using the 605 Bonferroni procedure. The partial eta squared ( $\eta^2$ ) was computed 606 to quantify the effect size. Statistical analyses were conducted 607 using the SPSS 22 software (IBM). 608

#### **FMRI Data Analysis**

For each participant, first-level analyses were performed using 611 a General Linear Model (GLM). Five task-related regressors 612 entered the GLM, one for each block type (Mon Tools, NonMon 613 Tools, Mon Faces, NonMon Faces and Fixation), which were 614 convolved with a canonical Hemodynamic Response Function 615 (HRF). Six additional regressors derived from the motion 616 correction step were also included in the design matrix as 617 regressors of no-interest, to account for variance associated with 618 head movements. Slow signal drifts were removed using a 240 s 619 high-pass filter. The hemodynamic response for each of the four 620 experimental conditions was contrasted with the average of the 621 hemodynamic response in the Fixation blocks, used as baseline. 622 The second-level (i.e., group) SPM maps were generated from the 623 individual contrast maps using a random-effect model. Namely, 624 a 2 (Domain: Faces, Tools) × 2 (Monitoring: Mon, NonMon) 625 full-factorial ANOVA was performed and the following specific 626 t-contrasts were computed: Faces > Tools and Tools > Face 627

(collapsed for Monitoring factor), Mon Faces > NonMon Faces 628 and Mon Tools > NonMon Tools (collapsed for Domain factor). 629

Moreover, a conjunction analysis was performed to investigate 630 those voxels which were commonly activated in Mon compared 631 to NonMon in Face and Tool blocks. The whole brain was 632 considered in the analysis. The statistical significance of the 633 blood oxygenation level-dependent (BOLD) response changes 634 was set at p < 0.05 using a voxel-level family-wise error (FWE) 635 correction for multiple comparisons. A cluster-size threshold 636 of 20 contiguous voxels was further applied (Lieberman and 637 Cunningham, 2009). The anatomical regions corresponding to 638 MNI coordinates of the peak voxels within each cluster were 639 extracted by referring to the probabilistic Anatomical Automated 640 Labeling (AAL) atlas, implemented in SPM12 (Tzourio-Mazoyer 641 et al., 2002, http://www.gin.cnrs.fr/AAL2). The "whereami" 642 toolbox of AFNI (Cox, 2012) was used to find the likely 643 Brodmann area (BA) for each cluster. 644

#### **ERP Data Analysis**

The mean global field power (GFP) was computed for 647 each subject and condition. This measure summarizes the 648 contribution of all electrodes point-by-point and indexes global 649 modulations in the strength of the electric field (Lehmann and 650 Skrandies, 1980). Mathematically, it equals the root mean square 651 of the average-referenced amplitude values across all electrodes 652 at a given point in time. The extraction of ERP components 653 was time-centered on the interval where differences between 654 conditions in GFP emerged based on paired *t*-tests (Figure S1). 655 Analogously, the electrodes to be considered for each ERP 656 component were determined by examining the topographical 657 distribution of *t*-tests (t-maps), which resulted from contrasting 658 individual ERP averages between pairs of conditions. The ERP 659 components were quantified in terms of peak amplitude, peak 660 latency or mean amplitude. The effects of Monitoring and 661 Domain factors were assessed by means of  $2 \times 2$  repeated-662 measure ANOVAs. 663

#### **EEG-fMRI** Integration

The relationship between the ERP and the fMRI responses 666 was investigated using the integration-by-prediction method 667 (Debener et al., 2006; Mulert et al., 2008; Eichele et al., 2009). 668 This method, which was developed for event-related designs, in 669 this study was adapted to a block design. First of all, all five runs 670 were concatenated. To build the correct concatenation model, 671 the high-pass filter and temporal non-sphericity calculations 672 were corrected to account for the original run lengths. The 673 ERP components that were found to be associated with the 674 monitoring process in the conventional analyses were considered 675 for the integration analysis. As it will be detailed in the result 676 section, for each block the mean voltage amplitude either of 677 the frontal or the parietal ERP components was extracted and 678 entered into two separate GLMs as parametric modulators of the 679 BOLD response. For example, the mean ERP amplitude extracted 680 from a Mon Face block over frontal electrode sites modulated the 681 estimated BOLD response in that block. 682

Overall, 4 ERP regressors were included in the first-level 683 GLM, together with the 11 conventional regressors (4 for 684

Neural Bases of Event Monitoring

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experimental conditions, 1 for fixation, and 6 for movement 685 parameters). Before entering the model, each ERP regressor 686 was orthogonalized with respect to its conventional regressor 687 by mean centering it. This procedure allows the detection of 688 hemodynamic responses specifically related to variations in the 689 ERP response and not to some general feature of the task 690 experimental condition (Debener et al., 2006; Mulert et al., 691 2008; Eichele et al., 2009). Afterwards, the ERP regressors were 692 convolved with the canonical HRF function. At the group 693 level, the relationship between ERP amplitudes and BOLD 694 responses was assessed using a 2  $\times$  2 full-factorial ANOVA 695 model. The t-contrasts between the ERP-related regressors were 696 697 generated. Namely, the activations obtained from the Mon Faces > NonMon Faces and Mon Tools > NonMon Tools contrasts 698 were used as inclusive masks, in order to identify the brain 699 regions associated with the ERP components within the clusters 700 of voxels emerged from the conventional fMRI analysis. 701

#### RESULTS

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#### 705 Behavioral Results

Both data on accuracy and RTs confirmed the presence of 706 a Monitoring cost (lower performance in Mon compared to 707 NonMon blocks). Mean values are summarized in Table 1. The 708 Friedman's test showed significant differences in accuracy on 709 the categorization task across conditions [ $\chi^2_{(3, 18)} = 36.27, p <$ 710 0.001). Post hoc Wilcoxon's tests on pairs of variables revealed 711 that the accuracy in Mon blocks was lower than accuracy in 712 NonMon blocks, for both Faces (Z = 3.59, p < 0.001) and 713 714 Tools (Z = 3.74, p < 0.001). No differences in accuracy emerged between Faces and Tools (both Zs < 1.34, ps > 0.178). The 2 715  $(Faces, Tools) \times 2$  (MonNon, Mon) ANOVA performed on mean 716 717 RTs yielded a significant main effect of Monitoring  $[F_{(1, 17)} =$ 60.57, p < 0.001,  $\eta^2 = 0.781$ ] and a significant Monitoring  $\times$ 718 Domain interaction  $[F_{(1, 17)} = 11.41, p = 0.004, \eta^2 = 0.402]$ . The 719 interaction revealed that while the Monitoring cost was present 720 in both domains, it was higher in Tools compared to Faces  $[t_{(17)}]$ 721 = 3.38, p < 0.004]. The mean accuracy in the estimation of the 722 number of targets reported at the end of each monitoring block 723 was 92.7% (SD = 21.5) for Faces and 98.3% (SD = 3.8) for Tools 724 (Z = 1.00, p = 0.317).725

### FMRI Results

In Tables 2, 3 the results of the 2  $\times$  2 full-factorial ANOVA 728 (p < 0.05, voxel-level FWE correction) are reported. Specifically, 729 the Table 2 contains the between Faces and Tools t-contrasts. 730 731 Compared to the Tools, the Faces yielded a positive activation of the right fusiform gyrus and of the amygdala, bilaterally 732 (Figure 2A, top panel). Compared to the Faces, the Tools 733 processing activated a broader set of brain regions encompassing 734 the fusiform gyrus bilaterally (mainly in the left hemisphere), 735 the middle temporal gyrus and the middle occipital gyrus 736 bilaterally, the left inferior parietal lobule (IPL), comprising 737 the supramarginal gyrus and the intra-parietal sulcus (IPS), 738 the right inferior temporal gyrus, the left inferior frontal gyrus 739 (pars triangularis), and the right cerebellum (Figure 2A, bottom 740 panel). 741

**TABLE 1** | Mean response times (RT) and percentage of accurate responses(ACC) on the Non-Monitoring (NonMon) and Monitoring (Mon) blocks by Stimulusmaterial (Face, Tools).

	Fac	ces	Tools			
	ACC (%)	RT (ms)	ACC (%)	RT (ms)		
NonMon	97.3 (3.9)	583 (94)	98.6 (1.0)	573 (64)		
Mon	93.8 (3.5)	643 (112)	93.1 (2.9)	658 (102)		

Standard deviation values are reported in parentheses

**TABLE 2** | Brain regions showing significant fMRI activations (voxel-level  $P_{\rm FWE}$  < 0.05) in the Faces vs. Tools blocks.

Anatomical region	Side	BA	Cluster size	MNI coordinates (mm)			T-values
				x	У	z	
Faces > Tools							
Amygdala	R		187	22	-6	-14	7.98
Fusiform gyrus	R	37	58	38	-56	-18	7.77
Amygdala	L		38	-18	-6	-18	5.42
Tools > Faces							
Fusiform gyrus	R	37	1,103	32	-46	-8	15.28
Fusiform gyrus	L	37	5,260	-30	-46	-12	14.83
Middle temporal gyrus	L	37		-48	-62	_4	14.36
Middle occipital gyrus	L	19		-42	-80	8	12.12
Middle occipital gyrus	R	19	816	30	-72	34	8.62
Middle occipital gyrus	R	39		42	-78	10	8.13
Inferior temporal gyrus	R	37	202	50	-58	-6	8.61
Supramarginal gyrus	L	40	93	-58	-32	34	6.67
Inferior parietal lobule	L	40		-54	-32	44	5.01
Inferior frontal, triangular part	L	45	61	-52	30	12	6.55
Cerebellum	R		46	28	-76	-48	6.49
Inferior parietal lobule	L	40	192	-36	-50	56	6.14
Inferior parietal lobule	L	40		-38	-42	48	5.75

L and R stand for left and right hemisphere, respectively. MNI coordinates and t-values are reported for all peaks observed within a cluster. Anatomical labels derived from the Anatomical Automated Labeling (AAL) atlas.

The contrast between Mon and NonMon blocks showed the 785 recruitment of extensive clusters of voxels including bilateral 786 frontal and parietal cortical regions, consistently associated with 787 sustained control processes in previous studies (Table 3 and 788 Figure 2B). The activated regions were very similar between 789 the two domains. The conjunction analysis revealed the areas 790 commonly involved in both domains (Table 3 and Figure 2B, 791 bottom panel). Specifically, in the frontal right hemisphere, the 792 inferior portions of the middle frontal gyrus (MFG), the inferior 793 frontal gyrus (IFG, pars opercularis), and the dorsolateral portion 794 of the superior frontal gyrus (SFG) were activated. At the parietal 795 level, the angular gyrus, portions of the IPL, comprising the 796 supramarginal gyrus, and a smaller cluster in the right precuneus 797 were found. In the left hemisphere, the activity mainly included

Anatomical region

Faces: Mon > NonMon

Superior parietal lobule

Inferior parietal lobule

Inferior parietal lobule

Supplementary Motor

Superior frontal gyrus,

Supplementary Motor

Inferior parietal lobule

Inferior frontal gyrus,

Middle frontal avrus

Middle frontal gyrus

Inferior frontal gyrus,

Inferior frontal gyrus,

Middle frontal gyrus

Tools: Mon > NonMon

Supplementary Motor

Middle frontal gyrus

Inferior frontal gyrus,

dorsolateral

triangular part

Precentral gyrus

Superior parietal lobule

Inferior parietal lobule

Inferior parietal lobule

Inferior parietal lobule

Middle cingulate gyrus

Mon > NonMon (Conjuction)

Superior frontal gyrus,

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Area

Area

dorsolateral

Angular gyrus Inferior parietal lobule

opercular part

triangular part

triangular part

Insula

Insula

Area

Insula

Insula

Precuneus

Precuneus

Angular

Precuneus

Precentral avrus

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TABLE 3 | Brain regions showing significant fMRI activation (voxel-level P<sub>EWE</sub> < 799 0.05, unless otherwise specified) in the Monitoring vs. Non-Monitoring blocks. 800

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L 40

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Side BA Cluster MNI coordinates

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#### TABLE 3 | Continued

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(Continued)

Anatomical reg	ion Side	BA	Cluster size	MNI coordinates (mm)			T-values
				x	У	z	
Supplementary N Area	Notor L	6		-16	2	64	5.35
Superior parietal	lobule L	7	486	-28	-64	48	7.98
Inferior parietal lo	bule L	40		-40	-48	40	6.80
Angular gyrus	R	7	436	34	-62	48	7.11
Inferior parietal lo	bule R	40		48	-40	46	6.01
Inferior frontal gy opercular part	rus, R	9	524	42	10	32	7.02
Middle frontal gy	rus R	9		42	30	32	7.01
Middle frontal gy	rus R	46		40	34	22	5.40
Inferior frontal gy triangular part	rus, L	44	652	-40	20	26	6.87
Inferior frontal gy triangular part	rus, L	45		-50	24	28	6.69
Precentral gyrus	L	6		-44	2	36	6.23
Insula	L	47	85	-32	26	0	6.57
Middle frontal gy	rus L	10	56	-30	50	16	6.19
Precuneus	R	7	84	8	-66	46	6.07
Insula	R	47	24	32	26	-4	5.46
Mon Faces > N	onMon Face	es-ER	P modula	tion*			
Inferior parietal lo	bule R	40	63	46	-50	42	3.35
Middle frontal gy	rus R	9	85	48	24	34	3.31
Middle frontal gy	rus R	9		38	26	32	2.61

L and R stand for left and right hemisphere, respectively, MNI coordinates and t-values are reported for all peaks observed within a cluster. Anatomical labels derived from the Anatomical Automated Labeling (AAL) atlas.

\*Voxel-level uncorrected p < 0.005, k > 52.

890 more ventral PFC regions (i.e., the pars triangularis of the IFG), 891 and a small cluster peaking in a frontopolar portion of the 892 MFG. Moreover, a medial portion of the SFG corresponding 893 to the supplementary motor area (pre-SMA) and extending to anterior cingulate cortex (ACC), and a portion of the precentral 894 gyrus corresponding to the inferior frontal junction (IFJ, i.e., the 895 896 intersection between the precentral sulcus and the inferior frontal sulcus) were also active in Mon blocks. At the parietal level, the 897 activation clusters in the left hemisphere comprised portions of 898 the superior parietal lobule (SPL) and IPL. Both the right and the 899 left parietal clusters contained the IPS. Smaller clusters involved 900 the insula bilaterally. 901

Differential patterns of activations for Mon vs. NonMon 902 blocks between Face and Tools were explored through second 903 level interaction t-contrasts (weights for the Mon Face, NonMon 904 905 Face, Mon Tools, NonMon Tools blocks: 1 -1 -1 1 and -1 1 1 -1). This analysis revealed that no regions exhibited differential 906 907 monitoring-related activations between the two domains.

## **ERP** Results

As expected, a large negative peak was evoked at the onset 910 of the pictures of faces over parieto-occipital and temporo-911 occipital electrodes (Figure 3A). This peak clearly represents a 912

Area	L	6	577	-6	10
Superior frontal gyrus, dorsolateral	R	6		20	10
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939 N170 component. The amplitude of the peak was contrasted 940 across experimental conditions. Based on previous literature 941 (Itier and Taylor, 2004; Rossion and Jacques, 2008), and on 942 temporal and spatial information derived from the GFP and 943 the t-maps (Figure S1), the latency of the maximum negative 944 peak was extracted from 140 to 210 ms in PO7, P7, PO8, P8, 945 TP9, TP10 electrodes. The amplitude mean over a 12 ms time-946 window around the identified peak latency was measured. The 2 947 (NonMon, Mon) × 2 (Faces, Tools) ANOVA yielded a significant 948 main effect of Domain  $[F_{(1, 17)} = 74.85, p < 0.001, \eta^2 = 0.815],$ 949 which statistically confirmed the presence of a larger negative 950 peak for Faces. Moreover, a Monitoring × Domain interaction 951 emerged  $[F_{(1, 17)} = 6.96, p = 0.017, \eta^2 = .815]$  that revealed a 952 decrease of the N170 amplitude in Mon blocks compared to 953 NonMon blocks only in the Face domain (p = 0.039). The mean 954 latency of the peak was 177 ms (SD = 10) and 178 ms (SD = 955 10) for Faces in the NonMon and Mon blocks respectively, and 956 181 (SD = 9) and 184 (SD = 10) for Tools. The ANOVA on 957 mean latencies showed a main effect of Domain  $[F_{(1, 17)} = 7.71]$ , 958 p = 0.013,  $\eta^2 = 0.312$ ], which confirmed that the peak emerged 959 slightly earlier for Faces.

960 The GFP exhibited an increased strength of the electric field 961 in the Tool blocks compared to Face blocks from 240 to 340 ms 962 (Figure S1). The t-maps revealed that this modulation mainly 963 affected the following electrodes: FC1, FCz, FC2, C1, Cz, C2, 964 CP1, CPz, and CP2. The waveforms of picture-evoked potentials 965 plotted over these electrodes showed a negative deflection 966 that characterized the responses to tools compared to faces 967 (Figure 3B). Therefore we named this ERP component as "tool 968 negativity." The mean ERP amplitude of this component was 969

extracted for each subject and condition in these electrodes, from 240 to 340 ms, and submitted to a 2 × 2 ANOVA. This analysis yielded a significant main effect of Domain [ $F_{(1, 17)}$  = 38.80, p < 0.001,  $\eta^2 = 0.695$ ] which confirmed larger negative ERP responses for Tools. Moreover, a main effect of Monitoring [ $F_{(1, 17)} = 7.58$ , p = 0.014,  $\eta^2 = 0.308$ ] revealed more positive ERP waveforms in Mon blocks.

The GFP revealed that differences between Mon and NonMon blocks emerged from 320 to 520 ms over frontal as well as parietal sites in both domains, as confirmed by the t-maps (**Figure S1**). The frontal ERP component was characterized by a positive deflection in the Mon blocks compared to NonMon blocks (**Figure 4A**), whereas the parietal component was characterized by a negative deflection in the Mon blocks (**Figure 4B**). Given its spatio-temporal trend, the latter component might be assimilated to a P3. Based on the t-maps, the frontal component was quantified in terms of mean ERP amplitude over F3, F1, Fz, F2, and F4 electrodes, whereas the parietal component was quantified in terms of mean ERP amplitude over PO3, POz, and PO4 electrodes.

To sum up, two monitoring-related ERP components emerged, a frontal positivity and a parietal negativity. The 2 × <sup>1017</sup> 2 ANOVA on the frontal ERP component showed a main effect of Monitoring  $[F_{(1, 17)} = 48.18, p < 0.001, \eta^2 = 0.739]$  that revealed that the pictures evoked more positive ERPs over frontal electrode sites in Mon compared to NonMon blocks. In addition, a main effect of Domain emerged  $[F(1, 17) = 8.20, p = 0.011, \eta^2$ = 0.325] that showed that the ERPs (P3) were more positive for Faces compared to Tools. No significant interaction was found  $[F_{(1, 17)} = 2.66, p = 0.121, \eta^2 = 0.136]$ . On the other hand, the Tarantino et al



the stimulus. The t-maps in panel A represent the topographical distribution of t-tests values obtained from the difference between ERP averages in Face and Tool blocks from 140 to 210 ms (A), and from the difference between ERP averages in Tool and Face blocks from 240 to 340 ms (B). 7-test values range from -10 to +10.

analysis of ERP amplitude over parietal sites yielded a significant effect of Monitoring  $[F_{(1, 17)} = 51.19, p < 0.001, \eta^2 = 0.751]$  that revealed an amplitude decrease in Mon compared to NonMon blocks. Neither the main effect of Domain  $[F_{(1, 17)} = 0.179, p]$ = 0.678,  $\eta^2 = 0.01$ ] nor the Monitoring × Domain interaction  $[F_{(1, 17)} = 0.478, p = 0.498, \eta^2 = 0.027]$  were significant. 

In all the above reported analyses, both fMRI and ERP, Target and Non-Target trials in the Mon blocks were collapsed. In order to examine the presence of differences in the event-related brain activity between Non-Target and Target trials within the Mon blocks compared to the NonMon trials, we analyzed the ERP amplitude in the 320–520 ms time window by means of two  $3 \times 2$ ANOVAs (only on correct trials; Figure S2). The analysis yielded a significant main effect of the trial type in both frontal  $[F_{(1,4,11,4)}]$ = 24.75, p < 0.001,  $\eta^2 = 0.593$ ] and parietal [ $F_{(1.4, 11.4)} = 10.99$ ,  $p = 0.001, \eta^2 = 0.393$ ] electrodes. The post hoc test showed significant differences in ERP amplitude between NonMon and Non-Target trials (ps < 0.001) and between NonMon and Target trials (ps < 0.003), but not between Non-Target and Target trials (ps > 0.093), in both scalp areas. These results demonstrated that the amplitude of the two examined ERP components did not differ between Target and Non-Target trials. A main effect 

of Domain emerged only in frontal sites, as in the previous block analyses  $[F_{(1, 17)} = 7.01, p = 0.017, \eta^2 = 0.292]$ . No significant interactions emerged (ps > 0.290).

#### **ERP-fMRI** Results

The monitoring-related ERP components which emerged in the conventional analyses were integrated with BOLD responses. Specifically, the mean amplitude of the ERPs over frontal electrodes (F1, F3, Fz, F2, and F4) in each block, from 320 to 520 ms, were entered in the first-level GLM as additional regressors (i.e., parametric modulator). Moreover, the mean ERP amplitude over parietal electrodes (PO3, POz, and PO4) in the same time-window was considered as a parametric modulator in a separate GLM (see the Statistical analysis section for details). No activations survived the p < 0.05 voxel-level FWE correction. Typically, EEG-BOLD coupling yields weak results since they derive from the residual effects after the mean BOLD responses are removed (Liu et al., 2016). Therefore we lowered the voxel-level significance threshold to a p < 0.005 uncorrected (Mulert et al., 2008). To control for multiple comparisons, the extent-threshold necessary to obtain a cluster-level FWE correction (p < 0.05) was derived from a Monte-Carlo simulation with 



**FIGURE 4** Grand-average waveforms of stimulus-locked ERPs for each Monitoring condition (Non-Monitoring vs. Monitoring), separated by Domain (Faces vs. Tools), over frontal (A) and parietal (B) electrodes. The zero time point corresponds to the onset of the picture. The t-maps represent the topographical distribution of *t*-tests in the 320–520 ms time window. *T*-test values range from –6 to +6.

10,000 iterations (Slotnick and Schacter, 2004; https://www2.bc. edu/sd-slotnick/scripts.htm). Following this simulation, a cluster extent of a minimum of 52 contiguous voxels was considered. The activation of two right-lateralized clusters emerged when contrasting ERP regressors in Mon Faces vs. NonMon Faces (Table 3 and Figure 5). Namely, the activity of the right IPL, including the SMG, and of the right MFG were more activated in Mon compared to NonMon blocks and this activity was modulated by the frontal positivity potential. No clusters of voxels survived the chosen statistical threshold in the Tool domain and when considering parietal electrodes. 

### Task Difficulty

In order to check whether the increased sustained activity in the Monitoring condition was the expression of task-difficulty rather than monitoring processes per se, we correlated functional changes in brain activity with RTs (Burgess et al., 2003). Namely, the mean RTs for each block were entered into the design matrix as parametric modulator instead of the ERPs. The same significance criterion was adopted (p < 0.005 uncorrected, cluster extent threshold = 52 voxels). At the second level analysis, a 2  $\times$  2 full-factorial ANOVA model was built. The Mon > Ong contrast revealed that only one cluster was modulated by RTs, namely the posterior portion of the left inferior and middle temporal lobe (k = 146, peak coordinates = -48, -58, -10; -50, -60, 0; -42, -58, 2). This area fell outside the mask created by the original contrast (Mon > Ong, fMRI results), meaning that 



**FIGURE 5** | Brain activations modulated by the ERP amplitude over frontal electrodes (F1, F3, Fz, F2, F4) at p < 0.005 (voxel-level uncorrected) and  $k \ge 52$ .

task difficulty cannot account for the increased brain response in the Monitoring condition. The involvement of the posterior temporal lobe was likely linked to the sematic retrieval process that supported the categorization tasks, especially for tools (Whatmough et al., 2002; Kellenbach et al., 2003; Whitney et al., 2012).

# DISCUSSION

The goal of the present study was twofold: (1) to investigate the neuroanatomical correlates of sustained and transient control processes mediating monitoring, and (2) to elucidate whether these brain structures are influenced by the nature of the tobe-processed material or are domain-independent. We referred 1254

to monitoring as the process of checking the environment 1255 over time for detecting the occurrence of target events (event 1256 monitoring). To address the first study goal, the EEG-fMRI 1257 coregistration technique was applied to a blocked experimental 1258 design, in which blocks requiring monitoring were contrasted 1259 to blocks not requiring monitoring. This approach enabled 1260 us to simultaneously capture both tonic (block-related fMRI) 1261 and phasic (event-related potentials) brain responses associated 1262 with the monitoring requirements. Conventional fMRI and 1263 ERP analyses were performed along with fMRI-ERP integration 1264 analyses (Debener et al., 2006; Mulert et al., 2008; Eichele et al., 1265 2009). Namely, the block-by-block variations of ERPs were 1266 coupled with the corresponding block-by-block BOLD signal. To 1267 address the second goal, a within-subject design was used, in 1268 which participants were asked to monitor either faces or tools, 1269 in separate blocks. Task-domain specificities of monitoring were 1270 examined by comparing brain activity between the two types 1271 of blocks. These two stimulus materials were chosen because 1272 their processing is known to engage differently lateralized neural 1273 substrates. 1274

The conventional fMRI results showed a set of fronto-1275 parietal regions in Mon compared to NonMon blocks 1276 commonly active in both domains, confirming our expectations 1277 that event monitoring has a domain-general nature. The 1278 electrophysiological results revealed that the transient 1279 component of monitoring, elicited by the onset of each 1280 event (i.e., the stimulus-evoked or reactive control processes) 1281 were represented by ERP amplitude modulations from 320 1282 to 520 ms after stimulus onset. The frontal ERP modulation 1283 correlated with the BOLD signal in the right IPL and right MFG 1284 for the face domain. No significant activations were detected for 1285 tool monitoring. A more detailed discussion of the functional 1286 significance of the results is provided below. 1287

#### 1289 Monitoring vs. Non-monitoring

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The fMRI findings confirmed previous evidence that points to the 1290 involvement of a fronto-parietal cortical network in monitoring 1291 the occurrence of target events over time (Reynolds et al., 2009; 1292 Vallesi et al., 2009; Vallesi and Crescentini, 2011; McDaniel et al., 1293 2013; Benn et al., 2014; Vallesi, 2014). This network included 1294 the pre-SMA, the IFG, and lateral portions of the MFG at the 1295 frontal level, and the angular gyrus, the supramarginal gyrus 1296 and portions of the SPL at the parietal level. The activation 1297 of these areas reflected the action of tonic processes, which 1298 span multiple trials, across ITIs, and are not just instantiated at 1299 trial onsets. The conjunction analysis extended this evidence by 1300 showing that a similar bilateral set of fronto-parietal regions was 1301 recruited in Mon blocks compared to NonMon blocks in both 1302 stimulus domains. These results revealed the domain-general 1303 nature of the sustained control processes involved in monitoring 1304 and converged with the study of Benn et al. (2014) that found 1305 that long-lasting monitoring was associated with the bilateral 1306 activity of a fronto-parietal network of areas for both numerical 1307 and visuo-spatial domains. 1308

The bilateral involvement of the fronto-parietal areas suggested that these processes required the cooperation multiple cortical areas between the two hemispheres. Furthermore, the fact that the identified areas belong to distinct 1312 functional resting networks led us to speculate that multiple 1313 control networks, not just the fronto-parietal one, were engaged 1314 for implementing the task. For example, the IPS and the IFG 1315 have been consistently found to represent central nodes of 1316 two attentional control systems, that are the "dorsal attention 1317 network" (DAN) and the "ventral attention network" (VAN; 1318 Corbetta and Shulman, 2002; Fox et al., 2005; Corbetta et al., 1319 2008), respectively. The former system, IPS, SPL and frontal-1320 eye-field, is hypothesized to play a key role in the top-down 1321 allocation of attention to goal-relevant and expected stimuli. The 1322 latter system, which is based on right-lateralized frontal areas 1323 comprising the temporo-parietal junction, extending into IPL, 1324 the IFG/MFG, the frontal operculum and the anterior insula, 1325 is thought to support stimulus-driven orienting of attention 1326 to relevant but unanticipated stimuli. Both systems integrate 1327 endogenous and exogenous signals, therefore there is not a strict 1328 dichotomy between them (Macaluso and Doricchi, 2013). The 1329 bilateral IPS activation in our study denoted the involvement 1330 of important nodes of the DAN, and specifically the top-down 1331 adjustment of the attentional focus according to the task goal 1332 (Langner and Eickhoff, 2013). On the other hand, the role of the 1333 right IFG might be attributed to the detection of relevant stimuli 1334 (Corbetta et al., 2008). Collectively, these two areas might have 1335 underlined the attention control requirements of our monitoring 1336 task 1337

The involvement of the bilateral PFC (including both dorsal 1338 and ventral regions) cannot be fully explained by attentional 1339 control processes. The sustained coactivation of these areas 1340 suggested the intervention of additional tonic/proactive control 1341 component, such as the maintenance of task goals (Shallice 1342 and Burgess, 1991; Bunge et al., 2001; Miller and Cohen, 2001; 1343 Sakai and Passingham, 2003). Indeed, goal representations, which 1344 contain information regarding task requirements (e.g., detect 1345 cooking tools), needed to be maintained in an active state 1346 throughout the block in order to boost the target checking 1347 process. 1348

The activation of the pre-SMA cluster might have mediated 1349 the selection between task-set representations (Rushworth et al., 1350 2002; Crone et al., 2006; Vallesi et al., 2015)<sup>2</sup>. Indeed, in 1351 the monitoring blocks two task-sets must be managed: the 1352 categorization task and the target detection task. Therefore, the 1353 pre-SMA involvement could be not strictly related to monitoring 1354 processes but also to dual-task requirements. 1355

The IFG and the IPS bilaterally, together with the pre-SMA 1356 and the insula, has been found to be part of the working memory 1357 network (Wager and Smith, 2003 for meta-analyses; Owen et al., 1358 2005; Rottschy et al., 2012). In the monitoring task, working 1359 memory might have likely played a role in updating task goals 1360 as new information becomes available. However, it could also be 1361 related to the updating of counting. Although participants were 1362 instructed not to use the counting strategy, we cannot exclude 1363 they were actually engaged in it. 1364

<sup>&</sup>lt;sup>2</sup>We can rule out a role of pre-SMA in controlling or preparing motor outputs (Nachev et al., 2008) since the monitoring task does not require immediate extra motor responses.

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Importantly, in order to identify which cortical areas among 1369 those active across the entire block mediated phasic monitoring 1370 processes, the individual block-by-block ERP mean amplitude 1371 was entered into the GLM as a parametric modulator. This 1372 analysis revealed that, for face monitoring, two right-lateralized 1373 regions, namely the IPL and the MFG, covaried with the frontal 1374 ERP modulations. According to our hypotheses, these areas 1375 are active throughout the block but in a more phasic manner 1376 relative to the rest of the fronto-parietal network. Their transient 1377 activation might subserve a more trial-related evaluation of the 1378 events. Notably, the anatomical location of these areas were very 1379 close to the IPL and the inferior-middle frontal gyrus reported in 1380 1381 a previous fMRI study focusing on monitoring spatial trajectories (Vallesi and Crescentini, 2011). The authors demonstrated that 1382 these areas were maximally activated in predictable trajectories, 1383 suggesting that the more the external contingencies match 1384 expectations, the higher their activity is. Taking together the 1385 findings of the present study and those of this earlier one, 1386 we may infer that the activity of these areas is linked with 1387 match/mismatch operations, which compare the actual stimulus 1388 to the expected one. 1389

The modulations in ERP amplitude, evoked by the onset of 1390 each event, highlighted the role of phasic processes also involved 1391 in monitoring blocks. In particular, a frontal ERP component 1392 was modulated in terms of an increased positivity in Mon 1393 compared to NonMon blocks. This ERP result was consistent 1394 with the findings in a similar study on event monitoring 1395 (Capizzi et al., 2016) and in previous studies focused on strategic 1396 monitoring in prospective memory (Cona et al., 2012, 2015a). 1397 Such positive deflection has been interpreted as reflecting the 1398 general recruitment of greater resources devoted to maintain the 1399 1400 focus of attention on the monitoring requirements.

When the individual block-by-block ERP mean amplitude was 1401 entered in fMRI analyses as parametric modulator in the GLM 1402 in the tool monitoring blocks, no activation cluster survived 1403 the statistical threshold. We may interpret this null result as 1404 reflecting the fact that in the tool domain a weaker transient 1405 activity, masked by a stronger sustained one, was engaged relative 1406 to faces. The stronger BOLD activity reported in monitoring tools 1407 compared to the faces, and the higher monitoring cost observed 1408 in response times, corroborate this tentative explanation. Further 1409 research needs to disambiguate this point. 1410

The operational definition of monitoring adopted in the 1411 current study might be strongly related to the constructs 1412 of vigilant attention and prospective memory (e.g., Kliegel 1413 et al., 2008; Langner and Eickhoff, 2013). Unlike typical 1414 vigilant attention tasks, however, our monitoring manipulation 1415 implies a categorization task and not simple detection or 1416 discrimination operations. Furthermore, in order to counteract 1417 the right frontoparietal deactivation associated with the increased 1418 time spent performing low demanding attention task (Coull 1419 et al., 1998) and to discourage the automatic processing, the 1420 monitoring task was inserted in an ongoing task. Unlike 1421 prospective memory tasks, the goals to be fulfilled were explicitly 1422 updated at the beginning of each block so that memory 1423 demands were minimized. In addition, the frequency of the 1424 target occurrence was higher than in typical prospective memory 1425

paradigms and the block duration shorter. Yet, some processes 1426 are likely to be commonly engaged in these two types of 1427 tasks. Indeed, vigilant attention is mediated by a mainly right-1428 lateralized network of cortical structures (including middle and 1429 ventrolateral PFC, intraparietal sulcus and insula) as well as 1430 subcortical ones. In prospective memory, the dorsal fronto-1431 parietal network, including precuneus and DLPFC, is associated 1432 with a strategic monitoring process (Cona et al., 2015b for 1433 a meta-analysis). This process reflects the allocation of top-1434 down attentional and memory processes required, respectively, 1435 to maintain the intention active in mind and to monitor 1436 the environment for detecting the PM cues (i.e., the stimuli 1437 associated with the intention to execute). 1438

#### Faces vs. Tools

The fMRI results confirmed that the processing of the two 1441 stimulus materials chosen for investigating the supra-ordinate 1442 nature of monitoring was subserved by a differently lateralized 1443 brain network. As expected, face processing was subtended 1444 by mainly right-lateralized areas compared to tool processing, 1445 whereas tools were processed by more left-lateralized regions. 1446 Specifically, faces compared to tools elicited the activation of the 1447 portion of the right fusiform gyrus, corresponding to the fusiform 1448 face area, which is devoted to face detection and recognition 1449 (Kanwisher et al., 1997; Kanwisher and Yovel, 2006; Frässle et al., 1450 2016). 1451

In addition, the contrast revealed a significant activation of 1452 the amygdala, bilaterally. The significantly higher activation of 1453 the amygdala in the presence of neutral faces is likely linked to 1454 the processing of socially-relevant features of faces, in this case 1455 race (Todorov and Engell, 2008; Todorov, 2012). Interestingly, 1456 it has been found that the amygdala is affected by habituation 1457 when ingroup but not outgroup faces are presented (Hart et al., 1458 2000). This phenomenon is part of the "other-race" face effect 1459 (Platek and Krill, 2009), and it has been proposed to result 1460 from an implicit and automatic process due to cultural learning 1461 (Lieberman et al., 2005). Since in our study faces belonging to 1462 different races were displayed, the activation of the amygdala 1463 suggests an implicit categorization of race (but the risk of reverse 1464 inference should be acknowledged here). The conventional ERP 1465 results confirmed the presence of a well-known face-selective 1466 component in face processing, the N170 over occipito-temporal 1467 and temporo-parietal electrodes (Itier and Taylor, 2004; Rossion 1468 and Jacques, 2008; Nguyen and Cunnington, 2014). 1469

As compared to faces, the tool processing engaged the 1470 activity of wider sets of clusters, more extended in the left 1471 hemisphere, which comprised the fusiform gyrus, the middle 1472 occipital gyrus and the middle temporal gyrus. This pattern of 1473 areas was coherent with the involvement of the lateral occipital 1474 complex (LOC), located on the lateral bank of the fusiform gyrus 1475 and extending ventrally and dorsally, which mediates object 1476 recognition processes (Grill-Spector and Malach, 2001; Perini 1477 et al., 2014). The data confirm that the object-sensitivity of 1478 the LOC is stronger in the left hemisphere when objects are 1479 compared to faces (Haist et al., 2010). 1480

Additionally, the tool processing activated the left IPL, 1481 comprising the supramarginal gyrus and the IPS. These parietal 1482

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regions, together with the middle temporal gyrus, store the representations of the movements associated with the object's use and are automatically engaged by viewing manipulable objects with a clear affordance (tools), independently of an overt motor output (Chao and Martin, 2000; Creem-Regehr and Lee, 2005). In particular, the left IPL stores hand-postures that can be used for planning object-directed actions (van Elk, 2014). Altogether, these findings suggest the involvement of both the ventral and the dorsal visual streams, deputed to the functional identification of an object, that is to its perceptual recognition and to its use, respectively (Goodale and Milner, 1992; Valyear and Culham, 2010).

The fact that monitoring in the tool blocks required longer 1495 response times is likely related to the specific task requirements. 1496 Indeed, the categorization of tools according to their use is 1497 more complex than the categorization of faces according to the 1498 race or age. The activation of the left inferior frontal gyrus in 1499 tools' processing might reflect the implicit use of some linguistic 1500 functions to support the categorization task (such as naming, 1501 Lupyan et al., 2012; Lupyan and Mirman, 2013). Furthermore, the 1502 activity of the left inferior frontal gyrus might be associated with 1503 the selection of semantic knowledges (Thompson-Schill et al., 1504 1997). 1505

The electrophysiological counterpart confirmed these 1506 inferences. Specifically, the ERP marker of tool processing was 1507 represented by a negative deflection over central and pericentral 1508 electrodes at 240-340 ms, significantly larger for tools than faces. 1509 This negativity reminds the anterior negativity found in a passive 1510 viewing task where tools were compared to graspable objects, 1511 whose role was attributed to the automatic access to motoric 1512 object properties (Proverbio et al., 2011). 1513

Taken together, the fMRI and ERP results on face and tool processing were coherent with the previous literature in showing an opposite lateralization of face and object processing and validate our choice of stimuli.

# 1519 CONCLUSIONS

The present research provides direct neuroimaging evidence of 1521 the domain-general nature of the sustained monitoring processes 1522 by showing that the same set of fronto-parietal cortical areas 1523 were co-activated when monitoring the environment for different 1524 types of events. Remarkably, the integration of fMRI and ERP 1525 findings offered a novel window into the attempt to detect the 1526 1527 neural bases of a transient monitoring component overlapping with the sustained one. Indeed, while the bilateral fronto-parietal 1528 1529

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activation subtend the monitoring processes in a sustained 1540 manner, only right-lateralized clusters, at least in the face domain, expressed the phasic/transient component of the monitoring 1542 process.

## **AUTHOR CONTRIBUTIONS**

VT and AV conceived the experimental design. VT and SF 1547 created the task and the stimuli set. VT, IM, and SF collected the 1548 data. VT performed the EEG analyses. IM provided engineering 1549 support to MR set-up and performed fMRI and EEG-fMRI 1550 analyses. FC provided medical supervision and constructive 1551 suggestions to the experimental setting. AV provided significant 1552 feedbacks and contribution throughout all study phases. VT and 1553 IM drafted the manuscript. All authors provided substantial and 1554 critical revisions of the manuscript, approved the final version of 1555 the manuscript and agree to be accountable for all aspects of the 1556 work 1557

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### SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: http://journal.frontiersin.org/article/10.3389/fnhum. 2017.00376/full#supplementary-material

**Figure S1** | In (**A**), the mean Global Field Power (GFP) between Faces and Tools is contrasted in Non-Monitoring (left) and Monitoring (right) blocks. In (**B**), the mean GFP between Non-Monitoring and Monitoring blocks is contrasted in Face (left) and Tool (right) blocks. The gray frames mark the time-windows in which paired *t*-test denoted significant differences ( $\rho < 0.05$ ).

**Figure S2 |** Grand-average waveforms of faces-locked ERPs (left) and tools-locked ERPs (right) in Non-Monitoring blocks compared to NonTarget and Target stimuli in Monitoring blocks. **(A)** depicts frontal electrodes, parietal **(B)** depicts parietal electrodes.

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**Conflict of Interest Statement:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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