JYU DISSERTATIONS 415

Qianru Xu

Change Detection in the Surrounding World

Evidence from Visual and Somatosensory Brain Responses

UNIVERSITY OF JYVÄSKYLÄ
FACULTY OF EDUCATION AND
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Editors
Noona Kiuru
Department of Psychology, University of Jyväskylä
Päivi Vuorio
Open Science Centre, University of Jyväskylä

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ABSTRACT

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Change detection is crucial for our daily lives. There are two research traditions for change detection: (1) change detection that investigates changes between two successively presented pictures with a time interval inserted, for which attention is considered necessary; and (2) deviance detection, which refers to the detection of changes that violate certain regularities in serially presented stimuli and can be conducted in an unattended condition. In **Study I**, I reviewed contradictory results from studies that applied attentive visual search and change detection tasks to study emotional bias in the perception of facial expressions. Three possible contributing factors that have significant impacts on the contradictory results were proposed, namely, differences in stimuli, differences in experimental settings, and differences in underlying cognitive processes. In Studies II and III, using magnetoencephalography, I investigated deviance detection in regularity formed by serially presented facial expressions and the location of electrical pulses. In **Study II**, I investigated to what extent the automatic encoding and change detection of paracentrally presented facial expressions is altered in dysphoria. The brain responses demonstrated that with both happy and sad faces, changes could be detected automatically. However, dysphoric individuals exhibited a negative perceptual bias toward sad faces in addition to a general deficit in the pre-attentive deviance detection processing. In **Study III**, a novel oddball task was introduced to investigate brain responses to unpredictable and predictable rare somatosensory events. The results showed that rare stimuli elicited two main brain activity components in the primary and secondary somatosensory areas contralateral to the stimulation. However, the results linked only the earlier component, at 30–100 ms after stimulus onset, to the prediction error signals. The results of **Study III** also highlighted the need to disentangle the effects of stimulus rareness and predictability in future studies. Overall, this dissertation brings together two relatively separate but related research domains of change detection. In addition to reviewing evidence of change detection, this dissertation provides empirical evidence of deviance detection in both the visual and somatosensory modalities and raises suggestions for future research on both types of change detection.

Keywords: change detection, deviance detection, facial expression, dysphoria, magnetoencephalography, somatosensory, predictability

TIIVISTELMÄ (FINNISH ABSTRACT)

Xu, Qianru
Muutoksen havaitseminen ympäröivässä maailmassa: Tuloksia näkö- ja tuntojärjestelmän aivovastemittauksista
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Muutoksen havaitseminen on välttämätöntä jokapäiväisessä elämässämme. Muutoksen havaitsemista voidaan tutkia kahden vaihtelevan ärsykkeen välillä tai sarjallisesti esitettyjen ärsykkeiden säännönmukaisuudessa. Osatutkimuksessa I tein katsauksen ristiriitaisiin tuloksiin, joita oli saatu käyttämällä tarkkaillun visuaalisen etsinnän ja muutoksen havaitsemisen tehtäviä, ja joilla oli tutkittu emotionaalista vääristymää kasvonilmeiden havaitsemisessa. Osatutkimuksen I tuloksena ehdotan, että kolmella tekijällä (erot ärsykkeissä, kokeellisissa tilanteissa ja tutkimuskohteena olevissa kognitiivisissa prosesseissa) on merkittävä vaikutus tulosten ristiriitaisuuteen. Osatutkimuksessa II selvitin aivomagneettikäyrämittauksien avulla muutoksen havaitsemista poikkeamiin sarjallisesti esitetyissä kasvonilmeissä ja osatutkimuksessa III poikkeamiin tuntoärsykkeen paikassa. Osatutkimuksessa II tutkin masennusoireiden vaikutusta automaattiseen kasvojen havaintoon ja muutoksen havaitsemiseen kasvonilmeissä. Aivovasteet osoittivat, että sekä iloisissa että surullisissa kasvoissa muutokset havaittiin, vaikka tutkittavat eivät tarkkailleet niitä. Tutkittavilla, joilla oli masennusoireita, ilmeni sekä negatiivinen havaintovääristymä surullisiin kasvoihin liittyen että yleinen heikentyminen muutoksen havaitsemissa. Osatutkimuksessa III käytettiin uudenlaista koetilannetta, jolla tutkittiin aivovasteita ennustamattomiin ja ennustettavissa oleviin muutoksiin tuntoärsykkeissä. Tulokset osoittivat, että muutokset tuntoärsykkeissä aiheuttivat kaksi erillistä aivovastekomponenttia tuntoaivokuorella. Tulokset viittasivat kuitenkin siihen, että ainoastaan aiempi komponentti, joka esiintyi 30–100 ms ärsykkeen esittämisen jälkeen, liittyi ennustamattoman ärsykkeen havaitsemiseen. Osatutkimus III myös osoitti tarpeen tulevaisuudessa pyrkiä erottamaan ärsykkeen harvinaisuuden ja ennustettavuuden vaikutukset aivovasteissa. Kokonaisuudessaan tämä väitöskirjatyö tuo yhteen kaksi melko erillistä, mutta toisiinsa kytkeytyvää muutoksen havaitsemisen tutkimusaluetta. Muutoksen havaitsemiseen liittyvän katsauksen lisäksi tämä väitöskirja tarjoaa empiiristä tutkimustietoa muutoksen havaitsemisesta näkö- ja tuntojärjestelmissä ja tarjoaa ehdotuksia jatkotutkimukseen.

Avainsanat: muutoksen havaitseminen, poikkeavan ärsykkeen havaitseminen, kasvonilme, dysforia, aivomagneettikäyrä, somatosensorinen, ennustettavuus

Author
Qianru Xu, M.Ed
Department of Psychology
Kärki, Mattilanniemi 6
P. O. Box 35
FI-40014 University of Jyväskylä
Jyväskylä, Finland
qianru.q.xu@jyu.fi
ORCID: 0000-0003-1579-6972

Supervisors
Associate Professor Piia Astikainen, Ph.D.
Department of Psychology
University of Jyväskylä
Jyväskylä, Finland

Professor Jarmo Hämäläinen, Ph.D.
Department of Psychology
University of Jyväskylä
Jyväskylä, Finland

Reviewers
Associate Professor Jukka Leppänen, Ph.D.
Department of Psychology and Speech-Language Pathology
University of Turku
Turku, Finland

Senior Lecturer Elia Valentini, Ph.D.
Department of Psychology
University of Essex
Colchester, UK

Opponent
Associate Professor Jukka Leppänen, Ph.D.
Department of Psychology and Speech-Language Pathology
University of Turku
Turku, Finland

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Now, it is the end of this era, but also the beginning of a new chapter.

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LIST OF ORIGINAL PUBLICATIONS

I Xu, Q., Ye, C., Gu, S., Hu, Z., Yi, L., Li, X., Huang, L., & Liu, Q. (2021). Negative and positive bias for emotional faces: Evidence from the attention and working memory paradigms. *Neural Plasticity*, *2021*, 8851066.

II Xu, Q., Ruohonen, E.M., Ye, C., Li, X., Kreegipuu, K., Stefanics, G., Luo, W., & Astikainen, P. (2018). Automatic processing of changes in facial emotions in dysphoria: A magnetoencephalography study. *Frontiers in Human Neuroscience. 12*, 186.

III Xu, Q., Ye, C., Hämäläinen, J.A., Ruohonen, E.M., Li, X., & Astikainen, P. (2021). Magnetoencephalography responses to unpredictable and predictable rare somatosensory stimuli in healthy adult humans. *Frontiers in Human Neuroscience. 15*, 641273.

Taking into account the instructions and comments from coauthors, the author of this thesis contributed to the original publications as follows: In **Study I**, the author developed the concept of the review. In **Study II**, the author analyzed and interpreted the data. In **Study III**, the author conceived the experiments, performed the data acquisition, and analyzed and interpreted the data. For all three studies, the author drafted and revised the manuscript.

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ORIGINAL PAPERS

1 INTRODUCTION

When driving on the road, we need to constantly detect multiple changes, such as signal light shifts or pedestrians stepping in front of the car, and the failure to detect these changes can lead to dire consequences. Although we are sometimes blind to overt changes, it is also quite easy for us to detect sudden changes that violate certain regularities based on repetition. For example, imagine that you are sitting on the metro, becoming numb to the black walls flashing by your eyes; at that moment, the sudden appearance of the metro LED advertisement is likely to attract your attention. Change detection thus exists everywhere and is essential for coping with our daily lives, and any abnormalities in change detection can correlate with clinical symptoms (e.g., depression, autism, attention deficit hyperactivity disorder; Gomot et al., 2006; Ruohonen, Alhainen, & Astikainen, 2020; Türkan, Amado, Ercan, & Perçinel, 2016).

In research, two types of change detection can be distinguished: (1) change detection in a general sense, which focuses on changes between the pre- and post-representation (e.g., between two static pictures) when a time interval separates the two representations (Luck & Vogel, 1997; Maurage et al., 2008; Rensink, 2002; Rensink, O'Regan, & Clark, 1996; Simons & Rensink, 2005); and (2) deviance detection, which refers to the automatic detection of changes in stimuli that violate certain regularities based on repetition (Näätänen, Gaillard, & Mäntysalo, 1978; Näätänen & Kreegipuu, 2012; Pazo-Alvarez, Cadaveira, & Amenedo, 2003; Stefanics, Kremláček, & Czigler, 2014). The existence of change detection and deviance detection are supported by significant empirical evidence in the visual modality, but while deviance detection is also widely studied in the auditory modality, our knowledge is still limited for the other modalities (e.g., somatosensory) and the relationship between change detection and the processing of emotional information (e.g., facial expression). In this dissertation, I introduce these two types of change detection and present empirical evidence for both the visual and somatosensory modalities. I will further introduce and discuss emotional bias in both types of change detection and present possible clinical applications based on the results of this research, especially for individuals with depressive symptoms (i.e., dysphoric individuals).

1.1 Change detection

The world around us constantly changes. Therefore, we should be good at intuitively detecting changes. But the truth is that we sometimes overlook even undisguised changes. One of the most famous examples of this comes from what is known as the invisible gorilla experiment (Simons & Chabris, 2000). In this study, participants were shown a video clip of two teams of actors dressed in different colors playing a casual game of basketball. During the game, an actor dressed as a gorilla passes through the crowd and is on screen for a total of 5 s. The experiment's participants were asked to count the number of passes made by one of the teams (for example, the team wearing white T-shirts). Interestingly, the results were that nearly half of the participants did not notice the gorilla in the video (Simons & Chabris, 2000).

According to a literature review authored by Rensink (2002), research on change detection dates back to the mid-1950s, and many studies conducted since then have suggested that focused attention is needed for successful change detection (for reviews, see Rensink, 2002; Simons & Rensink, 2005). In the laboratory, studies of attended change detection usually follow a design logic where a stimulus array is presented first, and then a change occurs (i.e., one or several elements are added, removed, or altered) in the subsequent stimulus array, and the observers are usually told to respond whenever they detect a change (Rensink, 2002). The change detection task (also known as the one-shot task, the forced-choice detection task, the match-to-sample probe recognition task, or the visual short-term memory task), which was developed by Phillips (1974) and popularized by Luck and Vogel (1997), is one of the most commonly used tasks for investigating change detection. This task generally comprises four parts: pre-stimulus fixation, memory array, retention interval, and probe array. Typically, in half of the related trials, the probe array and memory array are exactly the same, and in the other half of the trials, one of the memory items in the probe array differs from the memory array; the participant's task is to detect whether a change has occurred (Phillips, 1974). Because perceiving the difference between the two arrays before and after the change (i.e., between the memory array and the probe array) requires the involvement of attention and memory, this approach has also become a primary investigative tool for studying visual working memory (VWM; Luck & Vogel, 2013; Pailian & Halberda, 2015) or exploring the relationship between attention and VWM for obtaining a better understanding of basic human cognition (Fukuda & Vogel, 2009; Liang, Chen, Ye, Zhang, & Liu, 2019; Lu et al., 2017; Souza & Oberauer, 2016; Ye et al., 2020; Ye, Hu, Ristaniemi, Gendron, & Liu, 2016; Zhang et al., 2018).

Many studies have emphasized the importance of attention as a necessity (Rensink, 2002; Simons, 2000; Simons & Rensink, 2005), but attention alone has been regarded as insufficient for the successful detection of change. For example, studies have found that change blindness (i.e., the failure of an observer to perceive obvious changes; Simons & Rensink, 2005) can happen in the central visual field of attention (Levin & Simons, 1997; O'Regan, Deubel, Clark, & Rensink, 2000). In principle, to detect a change, the visual system relies mainly on two distinct mechanisms (Kanai & Verstraten, 2004). The first mechanism, which has a parallel and unlimited capacity, accounts for detecting low-level transients, which means an immediate and automatic sensation of certain changes. This mechanism depends on sensory memory and works only in limited situations (e.g., with a short interstimulus interval [ISI] or without any other interference, such as intervening masks; Pashler, 1988; Phillips, 1974). However, the change detection task generally inserts a blank array (i.e., an intervening mask) between the memory and probe arrays and thus relies on the VWM to compare the different stimulus arrays. Because VWM is limited in capacity, change blindness can happen even if focal attention has been given to the location of the change (Kanai & Verstraten, 2004).

Rensink (2000, 2002) provided a broad theoretical account of visual change detection, attention, and memory called the coherence theory. The coherence theory states that focused attention acts as a hand that "grabs" noticed visual features and places them in VWM. Thus, only information that is the subject of focused attention can stay stable across brief disruptions (e.g., saccadic eye movements) and be successfully detected after a change. When attention is released or when an object is not the subject of focused attention, it will be in a volatile form and easily replaced by new input (Hollingworth, Williams, & Henderson, 2001; Rensink, 2000, 2002). Therefore, changes should be noticed and encoded only as long as attention is maintained on an object.

1.2 Deviance detection as indexed by mismatch negativity

Although the importance of focal attention has been frequently emphasized in the above-mentioned research trends in change detection (Rensink, 2002; Simons & Rensink, 2005), we can still detect some changes without attention. This automatic change detection is especially apparent when the changes violate certain regularities or expectations, so this detection is also called deviance detection (Näätänen et al., 1978; Näätänen & Kreegipuu, 2012; Pazo-Alvarez et al., 2003; Stefanics et al., 2014). It should be noted that a relatively stable environment has to be established for successful deviance detection (Kujala & Näätänen, 2003). In other words, deviance detection happens when a stimulus violates expectations formed by a repeated stimulus.

In experimental research, deviance detection in serially presented stimuli can be studied with a relatively simple test called the oddball paradigm. An oddball paradigm usually contains two kinds of stimuli: the standard stimulus and the deviant stimulus. The standard stimulus has a relatively high probability of occurrence (usually greater than 80%), while the deviant stimulus has a small probability of occurrence. During the task, a repetitive standard stimulus is infrequently replaced by a deviant stimulus, and the participants are asked to respond to the deviant stimulus. The oddball task can also be applied in an unattended manner in which the stimuli are presented in the same way, but participants need to focus their attention on another task (e.g., listening to an audiobook when presented with a visual oddball task or watching a movie when presented with an auditory oddball task).

Over the past several decades, many studies have demonstrated that stimuli that violate the rules of a stimulus sequence (deviant stimuli) elicit more pronounced responses in event-related brain activity than regular (standard) stimuli in both attended and unattended stimulus conditions (for reviews, see Fitzgerald & Todd, 2020; Fong, Law, Uka, & Koike, 2020; Näätänen, Kujala, & Light, 2019). This brain activity, obtained by subtracting the activity elicited by the standard stimulus from the activity elicited by the deviant stimulus, is called mismatch negativity (MMN or MMNm when measured with magnetoencephalography [MEG]; Näätänen, Paavilainen, Rinne, & Alho, 2007; Näätänen et al., 1978). MMN was originally found in the auditory modality (Näätänen et al., 1978). Responses that are analogous to the auditory MMN (aMMN) have also been studied in the other sensory systems, such as with visual MMN (vMMN) (e.g., Astikainen, Cong, Ristaniemi, & Hietanen, 2013; Astikainen & Hietanen, 2009; Ruohonen et al., 2020; Stefanics, Csukly, Komlósi, Czobor, & Czigler, 2012; for reviews, see Czigler, 2007; Kimura, Schröger, & Czigler, 2011; Kremláček et al., 2016; Stefanics et al., 2014), and somatosensory mismatch response (sMMR, which has positive polarity in some electroencephalographic [EEG] measurements; e.g., Shinozaki, Yabe, Sutoh, Hiruma, & Kaneko, 1998; Spackman, Boyd, & Towell, 2007; Strömmer et al., 2017; Strömmer, Tarkka, & Astikainen, 2014). aMMN is often observed over the bilateral temporal and frontal areas in scalp topography at a latency of approximately 100–200 ms after the onset of the deviant sound, and it is typically elicited by changes in sound frequency, intensity, location, or duration (for reviews, see Garrido, Kilner, Stephan, & Friston, 2009; Näätänen et al., 2007; Winkler, 2007). The neural generators of aMMN have been mainly attributed to the auditory cortex, but the exact location may change depending on the acoustic features elicited. Furthermore, in addition to the thalamus and the hippocampus, the frontal area is also suggested as a generator of aMMN, at least in some species (Alho, 1995; Fishman, 2014; Näätänen et al., 2007). Later studies have hinted at a hierarchical cortical network including the primary auditory cortex, superior temporal gyrus, and inferior frontal gyrus that may be involved in auditory change detection (Garrido et al., 2009). vMMN, on the other hand, is elicited at approximately 100−200 ms post-stimulus but also in a later latency range up to 400 ms after the stimulus onset, depending on the stimuli and changing features (Czigler, 2007; Kremláček et al., 2016; Stefanics et al., 2012). vMMN have been mainly located in the occipital cortex (Kimura, Ohira, & Schröger, 2010; Susac, Heslenfeld, Huonker, & Supek, 2014), and the frontal cortex has also been located as a source (Kimura et al., 2010).

Compared to its counterparts in the auditory and visual modalities, sMMR has been less studied. Previous studies have typically shown sMMR at approximately 100−200 ms after stimulus onset in the frontocentral regions that are contralateral to the stimulation. Sometimes, a deviant somatosensory stimulus also elicits other components, either in the earlier latency, at approximately 30−70 ms (Akatsuka et al., 2005; Shinozaki et al., 1998; Strömmer et al., 2014, 2017) or a lateral positive polarity response at 150−250 ms latency (Spackman et al., 2007). Studies have also shown that nociceptive MMN exhibit a topography and later latency similar to the non-nociceptive sMMR, which was most pronounced on the bilateral temporal regions around 182 ms after the stimulus onset (Hu, Zhao, Li, & Valentini, 2013; C. Zhao, Valentini, & Hu, 2015). It is also worth noting that MMN is not only sensitive to changes of the stimuli's basic physical features (e.g., intensity or frequency of sound or color or orientation of a visual object), it also shows sensitivity to more complicated, abstract regularities such as the representation of sequential regularities (Kimura, Widmann, & Schröger, 2010; Stefanics, Kimura, & Czigler, 2011) and the relationship of the physical features (e.g., the direction of the frequency change between a pair of sounds; Saarinen, Paavilainen, Schöger, Tervaniemi, & Näätänen, 1992; for a review, see Paavilainen, 2013).

There are two major competing hypotheses presented for the elicitation of MMN: the adaptation hypothesis and the memory trace hypothesis (also known as the memory comparison hypothesis or the model adjustment hypothesis; for reviews, see Fitzgerald & Todd, 2020; Garrido et al., 2009; May & Tiitinen, 2010; Näätänen, Jacobsen, & Winkler, 2005). The adaptation hypothesis explains MMN elicitation as a neural adaptation and regards MMN not as an independent component but rather as a result of attenuated and delayed N1 response. The N1 response is an obligatory response typically observed as a negative deflection that peaks approximately 100 ms after stimulus onset. It is generated in the primary auditory cortex and is associated with early auditory processing (Garrido et al., 2009; Näätänen et al., 2005). The adaptation hypothesis also proposes that when processing a sequence of stimuli, the replaying of frequently repeated stimuli causes an adaptation in the neurons responding to it that results in a delayed and attenuated N1 response, whereas rare stimuli are not affected by this adaptation effect and therefore elicit a larger response (Jääskeläinen et al., 2004; May & Tiitinen, 2010).

Conversely, the memory trace hypothesis considers MMN to be an independent component that reflects a mismatch between the new input signal and the memory trace of the preceding input (Näätänen, 1992; Näätänen et al., 2005). That is, when the brain receives a stimulus, it compares the new input with the memory template formed based on the previous stimulus sequence. When the brain detects that the new input stimulus is inconsistent with the memory template, an MMN is generated. In agreement with the memory trace account, researchers have proposed a further model adjustment hypothesis, suggesting that MMN reflects the online modification of a model formed in the brain when new input does not match the existing memory trace (Näätänen & Winkler, 1999; Winkler, Karmos, & Näätänen, 1996).

More recently, the generation of MMN has been linked to a more general theory: predictive coding framework (Figure 1). In this framework, deviance detection is described as a hierarchical and bidirectional inference process in the brain that integrates forward and backward connections to form predictions and minimum prediction errors. That is, neural networks constantly learn the statistical regularities of the surrounding stimulus environment and make predictions of future events. When the input information does not match the prediction, the lower sensory areas send a prediction error signal into the higher areas to modify the prediction (Fong et al., 2020; Friston, 2005; Garrido et al., 2009; Stefanics et al., 2014). This new prediction is then sent backward to the lower areas, where it is again compared with new sensory input signals. The MMN is thus suggested to be an electrophysiological marker for prediction error and the reflection of a mismatch between the new input and the predicted input based on prior representations (Carbajal & Malmierca, 2018; Wacongne, Changeux, & Dehaene, 2012). The predictive coding theory has gained more and more attention in recent years, and it has been considered a unifying framework for the adaptation and model adjustment hypotheses (Garrido et al., 2008, 2009). As indicated by dynamic causal modeling, the perceptual learning of stimulus trains is affected by both within and between cortical source connections, and neither of the contradictory accounts just discussed (i.e., adaptation vs. memory-based/model adjustment) are sufficient alone to explain MMN generation (Garrido et al., 2008, 2009).

It has been posited that the generation of MMN involves two basic processes: (1) the prediction error signal elicited by the difference between the unpredicted and predicted events, and (2) the effect of refractoriness or adaptation (Czigler, Sulykos, & Kecskés-Kovács, 2014; Kremláček et al., 2016). Therefore, to conclude that the brain response obtained in an oddball task is the real reflection of prediction error, it is necessary to separate the MMN from the refractoriness or adaptation and obtain a so-called genuine MMN (Male et al., 2020; Stefanics et al., 2014). Adaptation, refractoriness, and other terms such as "habituation" and "neural fatigue" have also appeared in previous studies (Grill-Spector, Henson, & Martin, 2006; Stefanics et al., 2014), but it has been stated that the interchangeable use of different terms led to the interpretive error, and therefore, a better term to use is "adaptation" (O'Shea, 2015; Stefanics, Kremláček, & Czigler, 2016). Therefore, in this dissertation, I will use adaptation to refer to the repetition effect. In the oddball condition, because standard and deviant stimuli have different probabilities (i.e., standard stimuli occur more frequently than deviant stimuli), neurons responding to the standard stimuli show more widespread adaptations, while the neurons stimulated by deviant stimuli are still "fresh" (Stefanics et al., 2014). Therefore, a larger event-related potential (ERP) response for deviant stimuli could be caused by the adaptation to standard stimuli instead of the genuine MMN. One common way to separate the effect of adaptation is to use the equal probability condition (also called the many-standards condition; Ruhnau, Herrmann, & Schröger, 2012; Schröger & Wolff, 1996). In the equal probability control condition, several stimuli are presented in a random order but without consecutive repetitions. The probability of each stimulus is the same as the probability of the deviant stimulus in the oddball condition. Therefore, the genuine MMN can be calculated as the difference between the responses to the deviant in the oddball condition and the same stimulus in the equal probability condition (Stefanics et al., 2014).

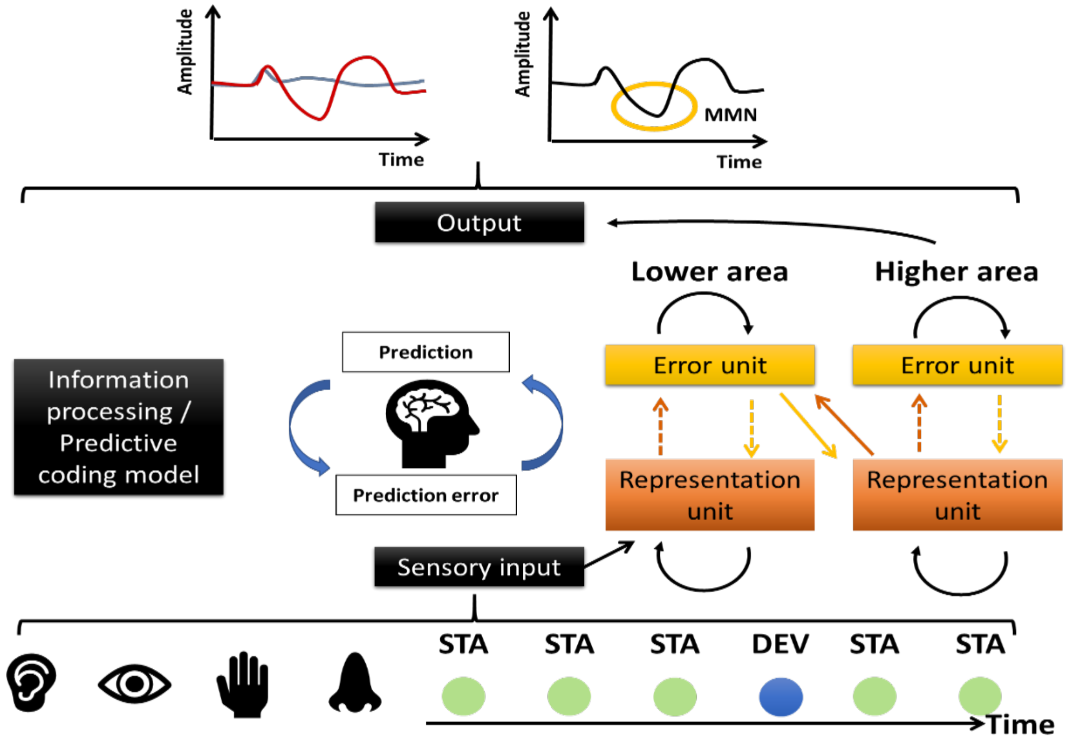

FIGURE 1 The predictive coding framework and mismatch negativity (MMN). Generally, the brain constantly learns statistical regularities from surrounding environmental stimuli and makes predictions of future events from the different modalities shown in the lower panel (visual, auditory, somatosensory, and olfactory). In the brain (middle panel), the signal processing is considered hierarchical, containing bottom-up forward and top-down backward loops. Within these loops, the representation units send out predictions, while the error units return the prediction error. The MMN (upper panel) is obtained by subtracting the activity elicited by the standard stimulus from the activity elicited by the deviant stimulus. It has been suggested as an electrophysiological marker for prediction error, and it arises when prior predictions do not match with new input (i.e., deviant stimuli).

In addition, several other criteria have been suggested as presuppositions to all analogs of the MMN (Male et al., 2020). First, the physical differences between the deviant and standard stimuli should be controlled to avoid interference from differences in stimulus properties. This can be done by either comparing brain responses to the same physical stimuli (possibly with a flip-flop design where two stimuli series are applied, with reversed assignment of standard and deviant stimulus properties) or averaging across conditions to counterbalance the different stimulus features between standard and deviant stimuli (Susac et al., 2014). Second, MMN can be obtained outside of the focus of attention. Therefore, a true analog of the MMN, or the genuine MMN, should be obtainable in an unattended manner. This issue is important in terms of both theory and methodology (Stefanics et al., 2014). Given the theoretical considerations, it has been suggested that attention affects the precision of the prediction error and therefore influences prior expectations (Clark, 2013; Friston, 2010). Given the methodological consideration, attention or attended stimuli can elicit other components (such as a posterior N2 and P300; Czigler & Csibra, 1990) and thus confound the MMN. However, when applying an unattended oddball condition, special considerations and controls over the difficulty of the distraction task are needed. For example, studies have argued that an auditory task (e.g., listening to an audiobook playing in the background) is insufficient to distract an individual's attention from the foveally presented stimuli when MMN is obtained in the visual modality (Stefanics et al., 2012).

1.3 Change detection in facial expressions

Facial expressions, or emotional expressions, are among the most essential and efficient communication tools in our social lives. The common view holds that facial expressions are configurations of different facial muscle movements that are used to signal or reveal one's emotional state (Barrett, Adolphs, Marsella, Martinez, & Pollak, 2019). Facial expressions play an important role in social reward and decision-making, and they signal others about potential threats in the environment (Anderson, Christoff, Panitz, De Rosa, & Gabrieli, 2003; Bechara, 2004). In social situations, as in other scenarios (e.g., driving an automobile), we need to constantly monitor and detect changes in the expressions of others to assess their attitudes. Therefore, the capability to correctly and successfully detect changes in others' facial expressions is significant for appropriate behavioral responses.

Cognitive studies have postulated that in visual attention, emotional signals (including facial expressions) are processed by specialized brain circuits that facilitate the processing of emotional stimuli over neutral stimuli, and thus, emotional signals are more likely to capture our attentional resources (Nummenmaa & Calvo, 2015; Vuilleumier, 2002, 2005). For example, experiments have consistently shown that faces showing smiling or angry expressions are more likely to stand out from a group of faces than those with neutral expressions (e.g., Becker, Anderson, Mortensen, Neufeld, & Neel, 2011; C. H. Hansen & Hansen, 1988; Juth, Lundqvist, Karlsson, & Öhman, 2005; Öhman, Lundqvist, & Esteves, 2001; for reviews, see Frischen, Eastwood, & Smilek, 2008; Kauschke, Bahn, Vesker, & Schwarzer, 2019; Nummenmaa & Calvo, 2015). However, whether different expressions capture our attentional resources differently or whether certain expressions are more likely to be detected remains controversial.

Based on the valence (i.e., the pleasantness or unpleasantness of stimuli) of an emotional expression, the results of previous studies can be divided into two main categories—negative bias and positive bias—which are still controversial (for negative bias, see Fox et al., 2000; C. H. Hansen & Hansen, 1988; Horstmann, Scharlau, & Ansorge, 2006; Pinkham, Griffin, Baron, Sasson, & Gur, 2010; for positive bias, see Becker et al., 2011; Juth et al., 2005; Williams, Moss, Bradshaw, & Mattingley, 2005). Negative bias in facial expressions refers to the processing advantage that negative faces (e.g., angry, fearful, sad, or disgusted faces) have over positive faces (i.e., a happy expression). Conversely, a positive bias refers in emotional face processing to a preference for positive faces (i.e., happy ones; Kauschke et al., 2019). From the points of view of evolution and social functions, both negative and positive biases appear to be important. Negative expressions (e.g., angry or fearful faces) signal potential interpersonal conflicts, and successfully detecting them could mean avoiding harm to one's body and mind (Nummenmaa & Calvo, 2015). In other circumstances, positive expressions (e.g., happy faces) can facilitate the integration of individuals into a shared environment and help with building cooperative relationships (Fredrickson, 2004). Nonetheless, both positive and negative biases have been supported by empirical evidence from repeated studies, particularly those using the so-called visual search task (also known as a face-in-the-crowd task when using faces as stimuli; Figure 2A; Becker et al., 2011; C. H. Hansen & Hansen, 1988) or the change detection task (Figure 2B; Curby, Smith, Moerel, & Dyson, 2019; Jackson, Wu, Linden, & Raymond, 2009).

A visual search task is a classical and important exercise that mimics finding a target object or identifying people given the types of multifarious information received in everyday life (Frischen et al., 2008; Treisman & Gelade, 1980). For example, C. H. Hansen and Hansen (1988) first found attentional bias toward angry faces using black-and-white photographs that resulted in shorter response times (RTs) and a lower error rate for angry faces versus happy and neutral faces. However, many subsequent experiments have brought into question C. H. Hansen and Hansen's (1998) results (Purcell, Stewart, & Skov, 1996), and some have even yielded completely opposite results (Calvo & Marrero, 2009; Calvo & Nummenmaa, 2008; Juth et al., 2005; Williams et al., 2005). The most representative contradictory results are from Becker et al. (2011), who used photographs and realistic computer-graphic faces to control confounding variables in previous attentional bias studies. In their study, the results across seven experiments found no support for efficiently detecting angry faces but did find a positive bias toward happy faces. Moreover, they suggested that the positive bias in their studies could not be attributed to low-level visual confounds (Becker et al., 2011). Overall, while many other contributing factors exist, meta-analysis results have revealed that by using different stimuli, a more consistent positive bias is found with photographic faces, whereas schematic faces showed more consistent results for negative bias (Nummenmaa & Calvo, 2015). In change detection, studies have revealed a similar phenomenon, finding both negative and positive advantages in VWM performance (for negative bias, see Jackson, Wolf, Johnston, Raymond, & Linden, 2008; Jackson et al., 2009; Langeslag, Morgan, Jackson, Linden, & Van Strien, 2009; Sessa, Luria, Gotler, Jolicœur, & Dell'acqua, 2011; for positive bias, see Curby et al., 2019; Spotorno, Evans, & Jackson, 2018; Xie et al., 2017). For example, by using the change detection task, Jackson et al. (2009) first examined how expression and identity interact with one another (face identity was task-relevant, while expression was task-irrelevant). Their results consistently showed enhanced VWM performance with different set sizes, durations, and face sets (Jackson et al., 2009). With schematic faces, other researchers limited cognitive resources by manipulating the encoding time and set size, and they found better performance with angry faces at a short exposure time (150 ms) and a large set size of five stimuli (Simione et al., 2014). Similarly, researchers have found that participants could better maintain fearful faces in VWM than neutral faces during the change detection task (Sessa et al., 2011). Moreover, studies have shown enhanced VWM storage for fearful faces as compared to neutral faces (Sessa et al., 2011; Stout, Shackman, & Larson, 2013).

Similar to the visual attention study, the opposing positive bias has been observed with the change detection task. For example, one study found superior memory sensitivity for not only fearful faces but also happy faces as compared to neutral faces (Lee & Cho, 2019). Moreover, by adding location information to the change detection task, researchers found that the relocation accuracy for happy faces was significantly enhanced compared to angry faces (Spotorno et al., 2018). Studies have also found that, while no memory differences occurred between different emotional faces (approach-oriented positive faces versus avoidance -oriented negative faces), high-capacity participants tended to retain more positive faces than negative ones, which was reflected in a significant correlation between affective bias and participants' VWM capacity (Xie et al., 2017). In summary, with the involvement of attention and VWM, a similar phenomenon (i.e., the contradictory advantage effects of different emotional expressions) has been reported in change detection studies.

However, while deviance detection has been less studied, it has shown more consistent results of negative bias compared to studies using visual search or change detection tasks. For example, using an oddball task (e.g., Figure 2C) in which participants were instructed to concentrate on an auditory task while neutral (standard, 80% probability), sad (deviant, 10% probability), and happy (deviant, 10% probability) faces were randomly presented, one study found that vMMN elicited by the sad facial expression was greater than that elicited by the happy facial expression (L. Zhao & Li, 2006). Another study recorded ERPs to peripherally presented emotional faces when participants were instructed to respond to a change in a cross pattern presented in the center of the screen (Stefanics et al., 2012). The results showed that rare changes in facial emotions (both fearful and happy faces used as standards and deviants) elicited vMMN at bilateral occipitotemporal sites, and the vMMN with fearful faces showed bigger responses than with happy faces over the right hemisphere at 90−120 ms, 195−275 ms, and 360−390 ms intervals, whereas a happy face advantage was only observed over left temporal areas at 360−390 ms. These findings indicate an automatic negative bias toward fearful faces (Stefanics et al., 2012). However, some other studies have not found any differences between the ERPs with happy and fearful faces (i.e., fearful and happy deviant faces elicited equal differential responses relative to neutral standard faces; Astikainen & Hietanen, 2009; Astikainen et al., 2013). These results suggest that deviance detection of facial expression occurs even when the faces are outside of the focus of attention. However, despite the accumulation of evidence in recent years and the advancement of new research methods, we still have only limited knowledge about the impact of individual differences (e.g., effects of mental disorders such as depression) on the automatic processing of emotional faces.

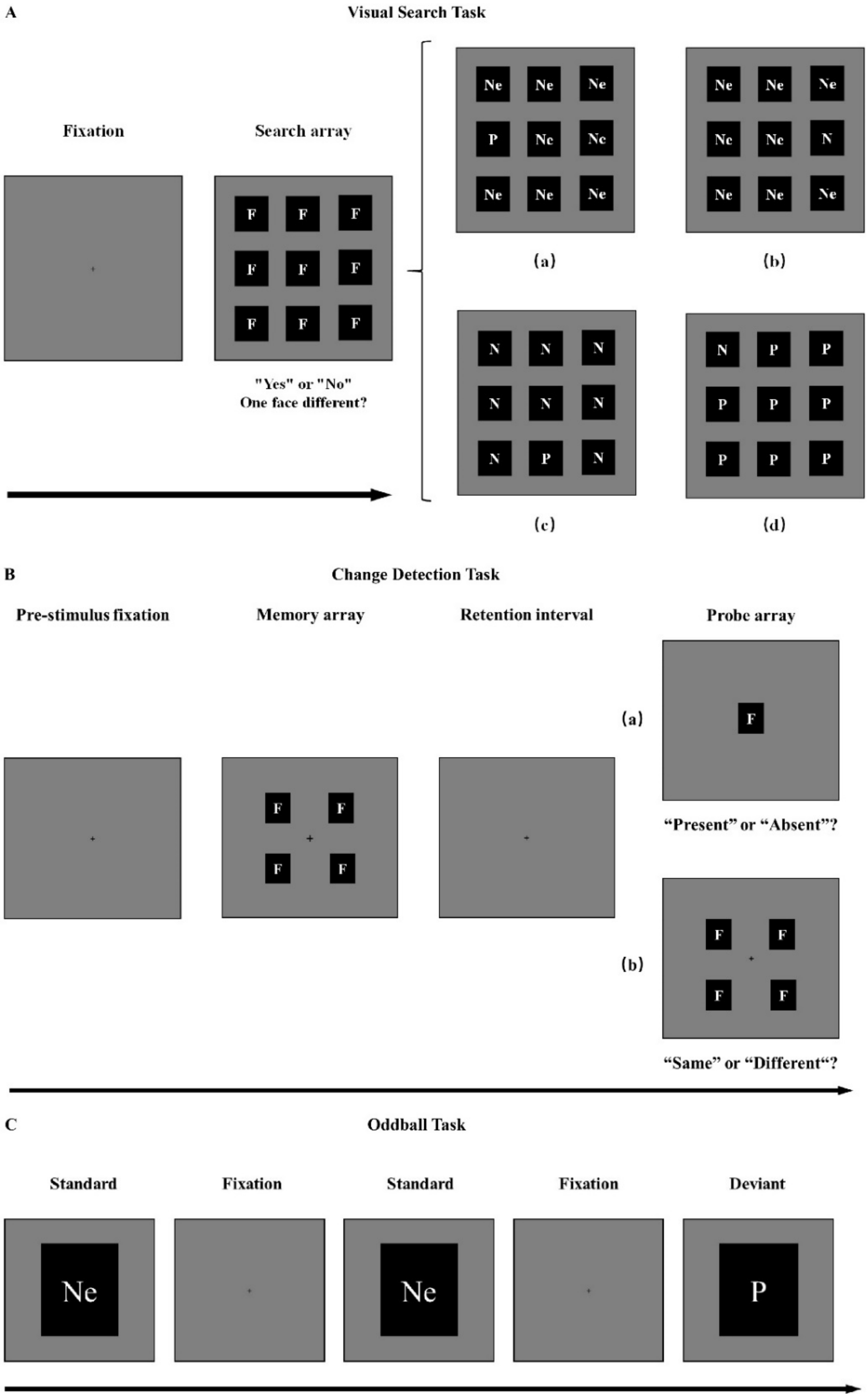

FIGURE 2 Schematic of the general procedure used in different tasks to study emotional bias processing. (A) Visual search task; (B) Change detection task; (C) Oddball task. F: neutral or emotional faces; P: positive faces (i.e., happy facial expressions); N: negative faces (i.e., angry, fearful, sad, or disgusted facial expressions). The figure is modified from Xu, Ye, Gu, et al. (2021).

1.4 Change detection and negative bias in depression

Depression is a common and frequently recurrent mental disorder. According to the World Health Organization, more than 300 million people worldwide suffer from depression. Depression can become a serious problem for functioning in an individual's normal life, causing the person to suffer greatly and perform poorly at work, at school, and in the family. In the worst cases, depression can lead to suicide.

Unlike in healthy populations, where negative and positive bias is still controversial, the negative bias in depression has been well documented. It has been suggested that negative bias plays a critical role in initiating and maintaining depression. Specifically, depressed individuals are more likely to maintain attention and memory on negative information, which exposes them to recurrent depression (Beck, 1967; Beck, 2008). This view has also been supported by empirical studies in which depressed individuals exhibited a pronounced bias toward negative stimuli, especially sad faces (Bistricky, Atchley, Ingram, & O'Hare, 2014; Dai & Feng, 2012; Gotlib, Krasnoperova, Yue, & Joormann, 2004). Depressed participants are also more likely than control participants to perceive neutral stimuli, including neutral faces, as negative (Delle-Vigne, Wang, Kornreich, Verbanck, & Campanella, 2014). In addition, depressed participants were also particularly less accurate in recognizing neutral faces as compared to happy and sad faces, whereas no such differences were found in controls (Leppänen, Milders, Bell, Terriere, & Hietanen, 2004). This result suggests that depression-prone individuals display an impairment in recognizing neutral faces and may therefore interpret neutral faces as emotionally meaningful.

Despite a limited number of studies, evidence has been provided of negative bias in the change detection and VWM domain. For instance, one study examined whether the memory bias for negative faces previously shown in depressed individuals could be generalized from long-term to short-term memory. The results showed that compared to healthy individuals, depressed individuals demonstrated impaired memory for all types of facial emotions, as well as memory deficits for face identity, regardless of whether the faces had happy, angry, or neutral expressions (Noreen & Ridout, 2010). By using a change detection task for emotional faces, one study showed that the storage of sad faces was better in the melancholic group, but not in non-melancholic and control groups (Linden, Jackson, Subramanian, Healy, & Linden, 2011). Similarly, another study found that although the depressed group had worse overall identity recognition performance compared to the control group, depressed individuals actually did better at recognizing faces with sad expressions in the encoding phase compared to happy expressions, whereas no such difference was found in the control group (Zhou, Liu, Ye, Wang, & Liu, 2021). Another study divided depressed participants into groups with either high-level or low-level suicidal ideations. Unlike the negative bias found in other studies, the researchers in this study found pain avoidance motivation (i.e., the tendency to avoid psychological pain or painful feelings) in the high-level suicidal ideation group; that is, they tended to retain fewer negative faces in VWM (Xie, Li, Zou, Sun, & Shi, 2018). Taken together, these studies examined facial identity recognition in change detection and found mood-congruent memory biases or overall deficits in individuals with depression.

Similarly, and related to depression, visual deviance detection in emotional faces has also revealed abnormalities in emotional processing. For example, Chang et al. (2010) used schematic faces (neutral faces as standard; happy and sad faces as deviant) in an oddball condition with both depressed and control participants. Despite the absence of negative bias (no difference in vMMN between sad and happy faces), a weaker vMMN was induced in depressed patients than in the healthy participants. Furthermore, the depressed group did not show the same face inversion effect (it is much more difficult to identify inverted faces than upright ones; see, e.g., Savage & Lipp, 2015) that healthy participants had, suggesting that information processing of overall face configuration is impaired in depressed patients (Chang, Xu, Shi, Zhang, & Zhao, 2010). However, a recent study (Ruohonen et al., 2020) found a negative bias in a depressed group, as indexed by enlarged P1 responses in the oddball condition for sad deviant faces compared to neutral standard faces. Follow-up measurements at 2 and 39 months showed that this negative bias normalized when the depressive symptoms were reduced with the help of psychological intervention. Furthermore, in the auditory modality, another study compared responses to different acoustic emotional prosodies presented in an oddball task. The results showed that sad aMMN was absent in depressed participants, while no differences were found for happy or angry aMMN when compared with the healthy participants (Pang et al., 2014). In conclusion, while the evidence for negative bias is still controversial in deviance detection processing, depressed participants seem to exhibit generally impaired deviance detection.

1.5 The use of magnetoencephalography (MEG) in change detection processing

MEG records the magnetic field changes induced by electrical currents in the human brain. Although MEG is sometimes seen as equivalent to EEG, MEG devices provide better source localization information while allowing for a high degree of temporal resolution. Furthermore, MEG is not as affected by the electrical conductivity of different brain tissues (e.g., skull and scalp) as EEG is. Consequently, the MEG topography tends to be clearer and less affected by physiological signals other than EEG (Baillet, 2017; P. Hansen, Kringelbach, & Salmelin, 2010). MEG, therefore, has an irreplaceable value and role, both in terms of scientific and clinical value, and the study of magnetic brain signals is increasingly becoming a research trend in the field of cognitive neuroscience (Baillet, 2017).

Several studies have used the MEG technique to explore the neural processes and corresponding source localization with change detection tasks (Becke, Müller, Vellage, Schoenfeld, & Hopf, 2015; Luria, Balaban, Awh, & Vogel, 2016; Robitaille, Grimault, & Jolicœur, 2009). For example, Robitaille et al. (2009) first used a combined EEG-MEG in a study that located the parietal areas as the source of brain activity for VWM maintenance during a change detection task. This finding was confirmed by a subsequent study (Becke et al., 2015) demonstrating that the posterior parietal cortex was the main source, and the ventral extrastriate cortex was also identified as a contributor.

Studies related to deviance detection that used MEG are relatively more numerous and have been used in studies much earlier than the change detection study investigating VWM. As early as 1984, there had been attempts to use MEG devices to study deviance detection processing in the auditory modality and to locate the source of aMMN in the primary auditory cortex (Hari et al., 1984). For the visual modality, the neural generators of vMMN have been located in bilateral middle occipital gyrus, peaking at around 150 ms for color change information (Urakawa, Inui, Yamashiro, & Kakigi, 2010). Furthermore, studies using images of neutral and happy faces have found face-sensitive neuromagnetic vMMN responses at approximately 90−120 ms after stimulus onset, and the involvement of the occipital, temporal, and parietal regions have been identified (Susac, Ilmoniemi, Pihko, Ranken, & Supek, 2010).

The deviance detection process of somatosensory stimuli has also been investigated using the MEG technique. For example, by recording and comparing the change detection process of electrical and tactile stimuli, studies have found that both types of stimuli significantly evoked responses in the contralateral primary and secondary somatosensory cortex, but only tactile stimulation evoked sustained bilateral primary somatosensory cortex activation (Hautasaari, Kujala, & Tarkka, 2019).

However, studies using the MEG technique are still very limited for both the visual and somatosensory modalities. For example, to my knowledge, no study has yet explored the deviance detection process for facial expressions in depressive participants using MEG, and the source localization of automatic somatosensory deviance detection and the factors influencing it are still unclear. Therefore, more studies are needed to further investigate change detection and deviance detection using the combined advantages of the temporal and spatial resolutions of MEG.

1.6 Purpose of the research

The purpose of my studies was to investigate change detection requiring the involvement of attention and change detection that is independent of attention. Three studies aimed at gaining an understanding of the influence of emotional facial expressions, depressive symptoms, and stimulus predictability on change detection were conducted. In addition to the traditional visual modality, the less frequently studied somatosensory modality was also examined. Some common factors that jointly influence the two types of change detection and multiple sensory modalities will be explored further in the discussion section.

Study I reviewed previous contradictory results regarding negative and positive biases toward emotional faces in the field of visual attention and VWM. Specifically, two typical tasks—the visual search task in attention and the change detection task in VWM—were compared. Previous literature review papers have discussed the contradictory findings in existing visual attention studies (Frischen et al., 2008; Kauschke et al., 2019; Nummenmaa & Calvo, 2015). However, to the best of my knowledge, no studies have yet combined the findings of visual search tasks with those of change detection tasks and discussed the common factors that may have contributed to their contradictory outcomes. Therefore, in **Study I**, I aimed to list the distinct behavioral and neural levels of evidence, particularly for those using change detection tasks in VWM. With these summaries, I expected to find possible reasons for the existing controversial results and provide new guidelines and suggestions for future emotional bias studies.

Study II investigated whether the automatic encoding and deviance detection of paracentrally presented facial expressions is altered with dysphoria. Here, "dysphoric" refers to individuals with an elevated number and level of depressive symptoms. Unlike the contradictory results of different emotional biases in healthy individuals, negative bias in depressed individuals has been well documented (for reviews, see Delle-Vigne et al., 2014; Mathews & MacLeod, 2005). Therefore, I expected to specifically observe a negative bias toward sad faces in the dysphoric group. In addition, I expected that rare changes in facial emotions presented in the paracentral vision without attention would result in amplitude modulations of responses corresponding to the vMMN and facial expression processing (e.g., P1, N170, and P250, as shown in Chang et al., 2010).

Study III investigated the effects of stimulus predictability on the somatosensory deviance detection process. In order to conclude that the brain response obtained in an oddball task is the real reflection of prediction error, it is necessary to separate MMN from adaptation. However, compared to its counterpart in the auditory and visual modalities, it is more difficult to apply a control condition (e.g., equal probability condition) in the somatosensory modality. This is because, for instance, a deviant probability of 10% would require 10 stimulation locations for a location change task. To my knowledge, no previous studies have applied such a control condition in the somatosensory domain with human participants. Therefore, brain responses to unpredictable and predictable rare events were recorded for comparison with frequent events. I expected that the stimulation would elicit activity in two main time windows, as indicated by previous studies (Hautasaari et al., 2019; Strömmer et al., 2014, 2017), at approximately 30–70 ms and 100–200 ms after stimulus onset. I also expected that both the early and later responses would reveal a larger amplitude with rare stimuli than with FRE. Larger responses to specifically the unpredictable rare stimulus were expected to reflect the prediction error, while larger responses to both unpredictable and predictable rare stimuli were expected to reflect stimulus rarity in comparison to somatosensory FRE. For the source localization results, I expected activity in the sensory cortices contralateral to the stimulation (i.e., the primary somatosensory cortex [SI] and/or the secondary somatosensory cortex [SII]).

2 METHODS

2.1 Participants

The participants in this study (adults 21–43 years old) were recruited via email lists, advertisements on the notice board at the University of Jyväskylä, and advertisements in the local newspaper. Ten control group participants in **Study II** overlapped with **Study III**. Before the experiment, a phone interview was conducted to confirm the inclusion and exclusion criteria described below. Each participant received one movie ticket as compensation for their participation.

The recruits for **Study II** were 13 healthy participants (nine females and four males aged 21–43 years) and 10 dysphoric participants (six females and four males aged 21–36 years old). The inclusion criteria for all participants were right-handedness; normal vision or vision corrected to normal; no neurological disorders, use of illegal drugs, or extensive consumption of alcohol (in women, defined as more than 16 doses per week, and in men, more than 24 doses per week); and no psychiatric disorders other than depression or anxiety for the dysphoric group. In the dysphoric group, one participant reported having a comorbid anxiety disorder, one reported a previous anxiety disorder diagnosis, and one reported a previous anxiety disorder combined with an eating disorder. They were included in the study because depression and anxiety are frequently comorbid. Prior to the experiment, all participants completed the Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996). An exclusion criterion for healthy participants was a BDI-II score of 10 or higher. The inclusion criterion for dysphoric participants was a BDI-II score of 13 or higher in the range of 13–36 (mean = 22.4, SD = 7.26). All but one of the participants had a past medical diagnosis of depressive disorder (one with mild depression [F32.0], four with moderate depression [F32.1], one with severe depression [F32.2], two with moderate episodes [F33.1], and one who did not remember which depression diagnosis was given). Six participants were currently receiving medication for their depression; three of them were taking selective serotonin reuptake inhibitors (SSRIs), and the other three took SSRIs combined with bupropion.

In **Study III**, the 15 healthy participants (12 females and three males aged 21–43 years) included 10 participants who had been recruited after participating in **Study II**. Inclusion criteria were 18–45 years of age, right-handedness, and self-reported normal senses (vision corrected with eyeglasses was allowed). Exclusion criteria were current or previous neurological or psychiatric disorders, use of illegal drugs, or extensive use of alcohol (for women, more than 16 doses per week, and for men, more than 24 doses per week). Similar to **Study II**, a Finnish-language version of the BDI-II (Beck et al., 1996) was completed by the participants, and a maximum score of 10 on the BDI-II was allowed for inclusion as a healthy participant.

2.2 Research ethics

All procedures were conducted in accordance with the Declaration of Helsinki. Ethical approvals were obtained from the Ethical Committee of the University of Jyväskylä for **Study II** and **Study III** before the participants were recruited for the experiments. All participants volunteered to be part of the experiments and signed an informed consent form before the study began. Researchers informed participants in both written and oral forms about the study before each measurement. This information specifically included what their participation in the research involved, what the purpose was for the research, and how the data they provided will be handled and stored. The participants were informed of their ability to withdraw from the study at any time without any consequences. All participants' brain responses (MEG data, **Study II** data, and **Study III** data) and behavioral data (**Study II**) were stored separately from the key code in an encrypted folder labeled with the participant ID on a server at the University of Jyväskylä. Only researchers involved in these studies have access to these files. Questionnaires were preserved with participants' IDs in locked cabinets in a secure environment within the University of Jyväskylä's office space. All written informed consent forms are stored separately in another locked cabinet in a secure environment. The code key associating the IDs with the contact information of participants was stored in an encrypted folder on the server at the University of Jyväskylä. The key code will be destroyed five years after data collection. All the researchers involved in these studies received sufficient training to guarantee good scientific practices. Requests to access the data outside the research group are granted only for anonymized data.

2.3 Stimuli and procedures

In **Study II**, the stimulus materials and experimental design were essentially similar to the EEG experimental procedure used by Stefanics et al. (2012). The stimulus materials were selected from Pictures of Facial Affect (Ekman & Friesen, 1976). All stimuli were black-and-white photographs measuring 3.7° wide by 4.9° high, with only facial features preserved (five male faces, five female faces). All stimuli were presented on a dark-gray background screen at a viewing distance of 100 cm from the participant. The stimulus array consisted of four simultaneously presented faces on the four corners of an imaginary square (eccentricity, 5.37°). All the faces presented with the same expression (happy or sad). Two of the faces were male, and the other two were female. The identities of faces in the same location changed from trial to trial, which meant that the identities of faces in the same location in adjacent trials would never be the same. There was a cross in the middle of the screen that randomly changed in length.

The experimental design was a modified oddball task (Figure 3). During the task stimulus array, the four emotional faces were presented for 200 ms with an interval of 450–650 ms before the next emotional array appeared. Participants were asked to look at the cross in the middle of the screen and report any changes to the cross by pressing a button (the cross changed at random, averaging 11 times per minute). Faces and crosses never changed at the same time. Every 500 stimuli were divided into separate blocks, each containing 450 standard stimuli and 50 deviant stimuli. In two of the blocks, sad faces were used as standard stimuli (presented with 90% probability), and happy faces were used as deviant stimuli (presented with 10% probability), while the other two blocks were reversed. Deviant faces were randomly assigned among the standard faces, and there were at least three standards (up to 15) before the first deviant appeared or between every two deviant trials. Participants were allowed to take breaks between each block, and the order of presentation of the blocks was randomized and counterbalanced among the participants.

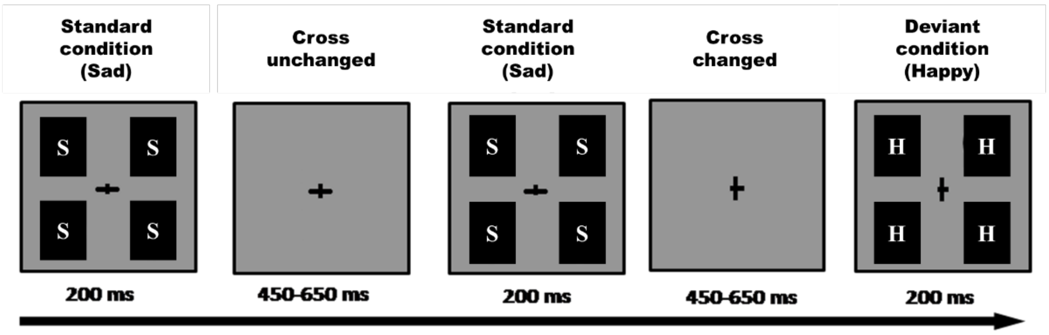

FIGURE 3 Illustration of the pattern of stimulus presentation used in Study II. Four faces of different individuals with the same facial expression (either happy or sad) were presented on the screen for 200 ms, followed by a random interval of 450–650 ms, during which one of the lines in the cross in the fixation point could change in length. The participant's task was to detect this change and respond by pressing a button. Occasionally, the emotional expression in the faces changed (deviant condition).

In **Study III**, the stimulation was delivered as a 200 µs electrical pulse through four flexible metal ring electrodes. The left index and little fingers were stimulated on the cathode above the proximal phalanx and the anode above the distal phalanx. The intensity of the stimulation was adjusted separately according to the threshold of each finger for each subject. Stimulation was started at a very low intensity and then gradually brought up in 0.1 mA steps to a higher intensity until the participant sensed the stimulus with an oral report. This procedure was repeated three times for each of the stimulated fingers. The threshold was defined as the mean values of the time before the three oral reports. The applied intensities in the experiment were 1.5 times the subjective sensory threshold intensity.

The stimulation procedure of **Study III** was a novel modified oddball task in which a standard stimulus (frequent stimulus, FRE) was pseudorandomly replaced by two rare stimuli. The first unpredictable rare stimulus (UR) was always stimulation to both fingers simultaneously, and the second rare stimulus (predicted rare stimulus [PR]) was to the finger that had not been stimulated by the FRE (Figure 4). The main experiment had two primary stimulus conditions, condition A and condition B. In condition A, FRE stimulated the little finger and PR stimulated the index finger, whereas in condition B, the stimulus assignment of FRE and PR were reversed. During further analysis, the responses of conditions A and B were averaged, which allowed the physical features of the FRE and PR to be counterbalanced. The UR was always a double stimulus (stimulating the index and little fingers at the same time) in both conditions. In order to investigate the effects of the physical features of the stimuli for traditional sMMR, an additional experiment was conducted with condition C for four participants after the presentation of conditions A and B. In condition C (Figure 4), FRE stimulated both the index and little fingers, while UR and PR stimulated the index and little fingers, respectively. Similar to the main task, the responses of conditions B and C were averaged during further analysis to counterbalance the physical features of FRE and UR. There were a total of 1,000 somatosensory stimuli for each condition, with an 80% probability of the FRE and a 10% probability of one of the two rare stimuli, UR or PR. The ISI was 500 ms. The stimulus presentation was controlled by Presentation software (Neurobehavioral Systems, Inc., Berkeley, CA). Participants were instructed not to attend to somatosensory stimuli but to focus on a silent movie playing on a screen approximately 1 m from them.

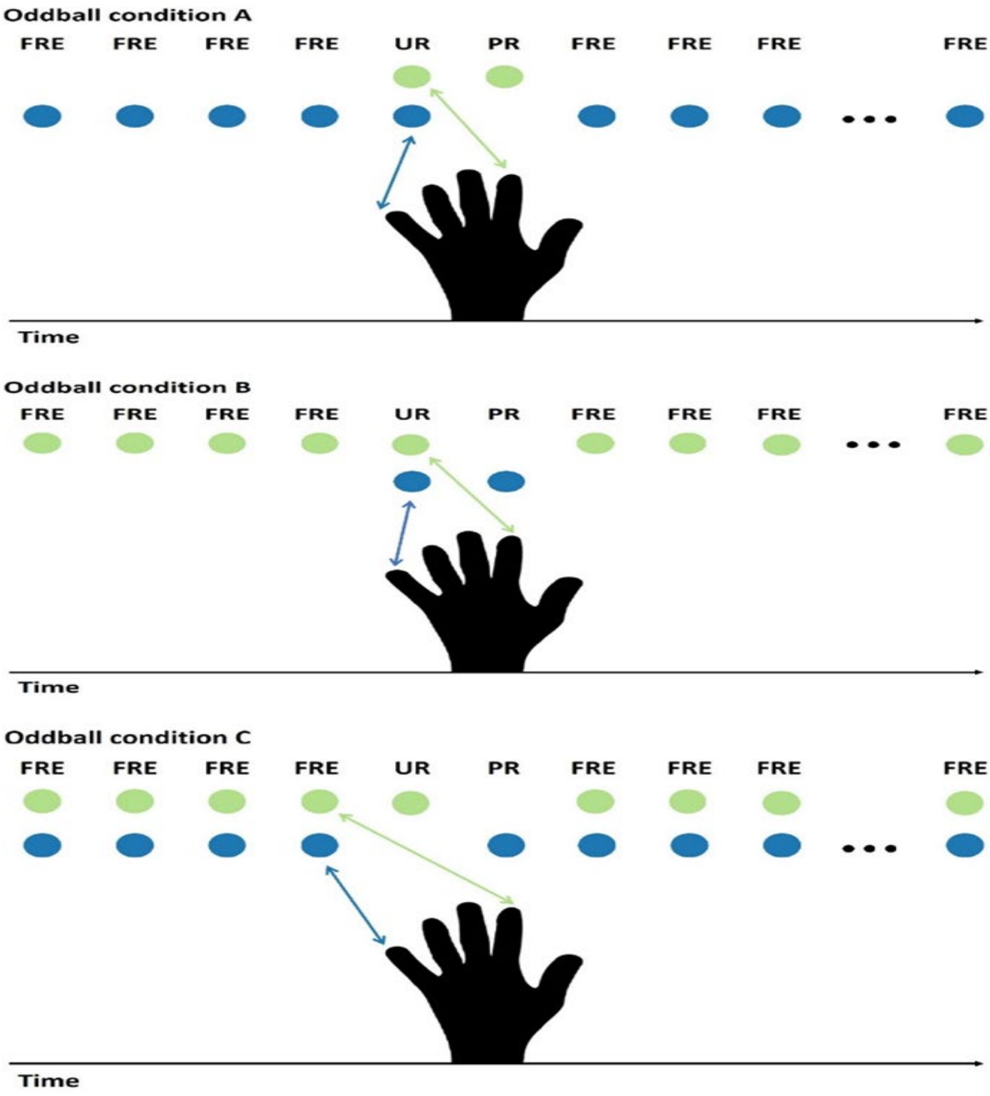

FIGURE 4 Illustration of the stimulus presentation for all three conditions used in Study III. FRE: Frequent stimulus; UR: unpredictable rare stimulus; PR: predictable rare stimulus. The figure is modified from Xu, Ye, Hämäläinen, et al. (2021).

2.4 MEG data acquisition and preprocessing

Study II and **Study III** were recorded with a 306-channel whole-head system (Elekta Neuromag TRIUX system; Elekta AB, Stockholm, Sweden) consisting of 204 planar gradiometers and 102 magnetometers in a magnetically shielded room at the MEG Laboratory, University of Jyväskylä. The MEG device was adjusted to the 68° upright position, and a 2 minute recording of the empty room was made before the measurement. All participants first reconfirmed that they were free of any metallic materials that might affect the experiment. For monitoring participants' head positions during the measurement, three anatomical landmarks and five head position indicator (HPI) coils were determined with an ISOTRAK three-dimensional digitizer (Polhemus, Colchester, VT) before the experiment started. The three anatomical landmarks were defined as the nasion and two preauricular points, while the five HPI coils were placed behind both ears, on both temples, and on the forehead. Additionally, over 100 other points on the scalp were digitized to provide a more accurate representation of the individual head shape. Six additional electrodes were used to record electrooculogram (EOG) and electrocardiogram (ECG) signals for removing artifacts of eye movements and heartbeats in the further data analyses: the vertical EOG electrodes were placed above and below the right eye; the horizontal EOG electrodes were placed at the outer canthus of each eye; and two ECG electrodes were placed one between the two clavicles and one below the right clavicle. In addition, a ground wristband was wrapped around the left carpal bone of the participant. During the MEG recording, the participant was instructed to sit still on the chair with their head inside the helmet-shaped device and their hands placed naturally on the table. The head position with respect to the sensors in the helmet was checked at the beginning of each block according to the magnetic fields produced by currents fed into five indicator coils at predetermined locations on the scalp. The continuous MEG signal was recorded with an online bandpass filter of 0.1–330 Hz and a sampling frequency of 1,000 Hz.

For both **Study II** and **Study III**, the spatiotemporal signal space separation (tSSS) method (Supek & Aine, 2014; Taulu, Simola, & Kajola, 2004) in MaxFilter 3.0 software (Elekta Neuromag, Helsinki, Finland) was used to remove external interference from the MEG data. The MaxFilter software was also applied for head movement correction and transforming the head origin to the same position for each participant. Bad channels were automatically detected and marked in **Study II** and manually marked in **Study III**. Then, the MEG data were analyzed using Brainstorm software (Tadel, Baillet, Mosher, Pantazis, & Leahy, 2011).

In Study II, recordings were filtered offline by a bandpass filter between 0.1 and 40 Hz. Eye blink and heartbeat artifacts were identified and removed in Brainstorm using the signal space projection (SSP) method. Epochs with values exceeding ± 200 μV in EOG channels were also removed from further analysis. Magnetometer data were analyzed for a more direct comparison to prior ERP studies and, in particular, to the results from Stefanics et al. (2012). The data were segmented into epochs from a 200 ms pre-stimulus baseline to 500 ms from the stimulus onset, and a DC offset baseline correction was applied within the 200 ms pre-stimulus period. Trials were averaged separately for happy standard, happy deviant, sad standard, and sad deviant stimuli for each participant. Based on the inspection from the grand-averaged data and prior findings (Peyk, Schupp, Elbert, & Junghöfer, 2008; Stefanics et al., 2012; Taylor, Bayless, Mills, & Pang, 2011), I mainly defined three major responses, M100, M170, and M300, corresponding to three time windows at 55–125 ms, 155–255 ms, and 280–350 ms post-stimulus. Two (M100, M300) or four (M170) regions of interest (ROIs) for the peak amplitude analysis of each response were identified for each respective component (Figure 4). The ROIs were located at bilateral occipital regions for M100, bilateral temporal and occipital sites for M170, and bilateral occipital sites for M300. Peak amplitudes were calculated as the maximum or minimum values in the corresponding time window for each component and ROI using a custom MATLAB script. The peak latencies for each component were identified as the corresponding times for each peak. Because two participants' data did not show M300 responses (one in the control group and the other in the dysphoric group), they were excluded from the analysis for this response. Both the peak amplitudes and latency values were sent on to the subsequent analysis.

In **Study III**, a notch filter of 50 Hz and a low-bandpass filter of 60 Hz were applied as previously described (Hautasaari et al., 2019). Eye blink and heartbeat artifacts were attenuated with SSP in Brainstorm by visually inspecting and removing the corresponding SSP components separately for gradiometers and magnetometers. The data were then segmented into epochs according to the stimulus events, from a 100 ms pre-stimulus baseline to 500 ms from the stimulus onset. A DC offset baseline correction was calculated and removed as the 100 ms pre-stimulus period for each epoch. The responses were then averaged with the number of trials in each condition for each stimulus type (FRE, UR, PR). Only the FRE epochs immediately before UR were averaged and further processed to equalize the number of each stimulus type. In addition, conditions A and B were combined to counterbalance the physical features of FRE and PR; that is, FRE, UR, and PR were further weighted averaged across conditions A and B based on the number of trials for each stimulus type. For sensor-level comparisons in **Study III**, planar gradiometer channel pairs at each sensor location were combined using root mean squares (RMS). For source-level analysis, the FSAverage_2016 anatomy template was used for magnetic resonance imaging (MRI) co-registration due to the lack of individual MRI data. To make the template a better match for each participant's head shape, I warped the anatomy templates to match the shape defined by the digitized points. The noise covariance matrix was estimated from an empty room recording made on the same day or on neighboring days. For the MEG forward model, the sensor-weighted overlapping sphere model (Huang, Mosher, & Leahy, 1999) was used for the representation of the cortical surface with 45,000 dipoles. The unconstrained depth-weighted minimum-norm estimates (wMNE) were applied for the inverse solution. The current density maps produced by the wMNE were then normalized with a Z-score transformation with respect to the baseline period, from −100 to 0 ms before the stimulus onset. The norm of the vectorial sum of the three orientations for the unconstrained source maps was used in the subsequent statistical analyses.

2.5 Statistical analyses

In **Study II**, behavioral results were first calculated for the hit rate and false alarms. The hit rate was calculated as the ratio of the number of button presses to the actual number of cross changes within 100–2000 ms after the event. The false alarm rate was calculated as the ratio of the number of button presses without a cross change to the actual number of cross changes within a 100–2000 ms interval after the event. The reaction times, hit rates, and false alarm rates were then sent to the repeated-measures analysis of variance (ANOVA) for a within-subjects factor of stimulus block (sad vs. happy standard) and a between-subjects factor group (control vs. dysphoric).

For the sensor-level results in **Study II**, peak amplitudes and peak latencies were analyzed separately at different ROIs and different time windows with three-way repeated-measures ANOVA, using the within-subject factors of emotion (sad vs. happy) and stimulus type (standard vs. deviant) and the between-subjects factor of group (control vs. dysphoric). In addition, specifically for M300, a lateralization index was calculated to investigate the possible lateralization. The lateralization index was calculated as Lateralization index = (Left − Right)/(Left + Right) for each stimulus type (all values from the right hemisphere were multiplied by −1 to correct the polarity difference, as applied in a prior study; Morel, Ponz, Mercier, Vuilleumier, & George, 2009). A three-way repeated-measures ANOVA with the within-subjects factors of emotion (sad vs. happy) and stimulus type (standard vs. deviant) and the between-subjects factor of group (control vs. dysphoric) was applied. For all significant ANOVA results, either two-tailed paired t-tests or independent-samples t-tests with a bootstrapping method using 1,000 permutations (Good, 2005) were conducted as the post hoc analysis. Additionally, partial eta squared (η^2_p) measures were used for effect size estimates in ANOVA. Cohen's d (Cohen, 1988) was computed with pooled standard deviations for effect size estimates in the t-test. Whenever a significant interaction effect with the between-subject factor of group was found, two-tailed Pearson correlation coefficients with a bootstrapping method using 1,000 permutations were used to evaluate the correlation between the BDI-II score and the brain response in question. The significance level was set to $p < .05$ for all tests.

In **Study III**, sensor-level analyses were carried out in Brainstorm by calling the spatiotemporal cluster-based permutation test functions from the Fieldtrip toolbox (Maris & Oostenveld, 2007). Time windows for the analysis were restricted based on visual inspections of the maximum of the global field power from the grand-averaged response and previous somatosensory studies (Hautasaari et al., 2019; Strömmer et al., 2014, 2017). Accordingly, two time windows were selected for further investigation: one at 30–100 ms latency after stimulus onset (labeled M55) and the other at 130–230 ms latency (labeled M150) after stimulus onset. Over the corresponding time ranges for each component, the contrast between the PR and FRE, the UR and FRE, and the UR and PR were conducted separately in each time window. Channel cluster alpha was set as 0.05, and the number of permutations was 1,000, with no minimum cluster size determined. This cluster-based permutation test is based on the permutation distribution of the maximum cluster-level sum, which is beneficial for controlling the multiple comparison problem.

For a source-level analysis in **Study III**, previous MEG studies in the ignore condition have suggested that sMMR is mainly elicited in the primary somatosensory cortex (SI) and/or the secondary somatosensory cortex (SII) (Akatsuka, Wasaka, Nakata, Kida, Hoshiyama, et al., 2007; Akatsuka, Wasaka, Nakata, Kida, & Kakigi, 2007; Hautasaari et al., 2019; Naeije et al., 2016, 2018). Therefore, based on the prior studies and the results verified in our grand-averaged source maps, two ROIs were defined, namely SI (G_postcentral: postcentral gyrus) and SII (Lat_Fis-post: posterior ramus of the lateral fissure), based on the Destrieux atlas (Destrieux, Fischl, Dale, & Halgren, 2010). Only the contralateral somatosensory cortices (i.e., contralateral SI [cSI] and the contralateral SII [cSII]) to the stimulation were used because little or no activation occurs in the ipsilateral areas with the same scale. The norm of the vectorial sum of the three orientations for an unconstrained source map within the 30–100 ms and 130–230 ms after stimulus onset were exported from Brainstorm into the SPSS program for further analysis. One-way repeated-measures ANOVA with stimulus type (FRE, UR, PR) as the within-subjects factor was conducted separately for each ROI and time window. The Greenhouse–Geisser correction (*p*-value after Greenhouse–Geisser correction, [p_{corr}]) was applied when the sphericity assumption was not met. When ANOVA results showed significance, post hoc analyses using a two-tailed paired t-test were conducted between different stimulus pairs. For controlling the multiple comparison problems, the Bonferroni correction was used for both ANOVA and post hoc analyses (*p*-value after Bonferroni correction, p_{corr}). Similar to **Study II**, partial eta squared (η^2_p) measures were used for effect size estimates in ANOVA, while Cohen's d with pooled standard deviations (Cohen, 1988) was used for the effect size estimate in the t-test. The significance level was set to $p < .05$ for all tests.

3 OVERVIEW OF THE ORIGINAL STUDIES

3.1 Study I: Literature review of negative and positive biases for emotional faces: Evidence from attention and working memory tasks

Previous studies have summarized most of the work that has explored the priority effects of different emotions in visual search (e.g., Becker et al., 2011; Kauschke et al., 2019; Xu, He, Ye, & Luo, 2019). Therefore, in **Study I**, which was a narrative review, I only summarized and listed studies investigating the emotional bias effect in VWM, especially for those adopting the change detection task (including 20 studies; see Table 1). Based on these results, I suggested three possible contributory factors that have significant impacts on the contradictory conclusions regarding different emotional bias effects: stimulus choice, experimental setting, and cognitive process.

3.1.1 Differences in stimulus choice

For stimulus choice, two factors may have influenced the results of the different experiments, that is, the choice of the schematic versus real faces and the stimulus arousal.

Both photographs of real faces and schematic faces are widely used stimuli for visual search and change detection tasks. However, a more consistent negative bias occurs with schematic faces, while photographs of real faces show more evidence of a positive bias (for reviews, see Kauschke et al., 2019; Nummenmaa & Calvo, 2015). Studies have attributed this contradictory pattern to the differences in the visual salience of stimuli (i.e., the perceptual prominence of a picture or part of a picture compared to other parts in terms of physical features such as luminance, contrast, etc.) at the perceptual level rather than to differences in emotion per se (Calvo & Nummenmaa, 2008; Nummenmaa &

Calvo, 2015). These studies have even shown contradictory results when using different stimulus sets with a similar procedure (Savage, Becker, & Lipp, 2016; Savage, Lipp, Craig, Becker, & Horstmann, 2013). This concern also applies to the change detection task. However, in change detection tasks, there is a lack of research exploring the effects of the physical features of the stimulus. The type of stimulus database used also varies from study to study, making it difficult to directly compare different studies (Table 1). It is worth noting that it is difficult to explain some of the negative bias (e.g., sad/fearful bias) with low-level visual confounds in stimulus choice because studies have shown that happy faces (especially happy faces with exposed teeth) are usually more visually salient (Calvo & Nummenmaa, 2008; Savage et al., 2013). However, special attention needs to be paid to the potential impact of the mouth or eyes areas, as these characteristics themselves can significantly affect the results (Calvo & Nummenmaa, 2008; Horstmann, Lipp, & Becker, 2012).

Furthermore, I argued that differences in arousal are the direct cause of many previously inconsistent findings. “Stimulus arousal” refers to the intensity of the metabolic and neural activations of the independent or co-active appetitive or aversive system (Lang, Bradley, & Cuthbert, 1998). In visual search tasks, studies have found that the degree of arousal from a picture’s material was highly correlated with the participants’ response as the direction of their corresponding bias (Lundqvist, Juth, & Öhman, 2013). In change detection studies, although lacking a direct comparison to emotional arousal between positive and negative faces, studies have suggested that different intensities of the angry face will lead to different contralateral delay activity (CDA) responses (Sessa et al., 2018). The CDA component has been widely used as an ERP marker of the number of items stored in VWM (Adam, Robison, & Vogel, 2018; Feldmann-Wüstefeld & Vogel, 2019; Fu, Ye, Liang, Li, & Liu, 2020; Hao, Becker, Ye, Liu, & Liu, 2018; Li, Zhang, Liang, Ye, & Liu, 2020; Liang et al., 2020; McCollough, Machizawa, & Vogel, 2007; Vogel & Machizawa, 2004; Ye, Zhang, Liu, Li, & Liu, 2014). Its amplitude increases as the number of objects stored in the VWM increases, and therefore, the results of Sessa et al.’s (2018) study indicate that arousal does affect VWM performance. However, not all previous studies with change detection tasks have measured and controlled for stimuli arousal levels (Table 1).

3.1.2 Differences in experimental settings

In terms of the experimental setting, I suggest that three main factors contribute to the inconsistency of previous results, namely, (1) visual display size and corresponding display time; (2) the manner of stimulus presentation; and (3) differing demands in experiments.

First, in both the visual search and change detection tasks, the visual display set size is an essential index concerning behavioral results, such as the search slope (the function of RT and display set size) in the visual search task and numbers of VWM representations in the change detection task. Although it cannot be applied to all the controversial results from previous studies, the stimulus array usually appeared longer in studies that showed positive bias (e.g., meaning no time limit in the visual search task, see Juth et al., 2005; Williams et al., 2005; or the change detection task with 4000 ms condition in Curby et al., 2019). Conversely, results supporting a negative bias usually present the stimulus for a shorter period of time (e.g., asked participants to respond within a limited time frame in the visual search task, see Öhman et al., 2001; Pinkham et al., 2010; or change detection task with 1000 ms condition in Curby et al., 2019).

Second, given that multiple stimuli are usually presented simultaneously, both the visual search and change detection tasks are very context-dependent processes. In visual search, target and distractors present simultaneously. Therefore, differences in the processing of distracting stimuli affect the search for target stimuli. For example, studies have shown that attention disengagement from the distractor face (Fox et al., 2000) and the use of heterogeneous or homogenous identities as a background both affect visual search performance (Craig, Becker, & Lipp, 2014). With the change detection task, although direct evidence is lacking, it has been shown that different expressions have different filtering efficiencies, which may affect the detection of target stimuli (Stout et al., 2013; Ye et al., 2020; Ye et al., 2018).

Third, I argue that the controversial results in emotional bias were partly due to the demands placed by the experiment and the participants' own strategies in understanding the task instructions. For example, some of the visual search studies that supported negative bias did not specify the target stimulus before the experiments were conducted with participants (Fox et al., 2000; C. H. Hansen & Hansen, 1988; Horstmann, 2009). On the contrary, studies in favor of positive bias have often asked participants to find target stimuli for specific emotions (Becker et al., 2011; Calvo, Nummenmaa, & Avero, 2008; Juth et al., 2005). Although previous studies have suggested employing a fixed target (i.e., give a specific expression at the beginning of the experiment and ask the participant to search for this target expression across trials) to avoid discrepancies caused by different strategies across participants, this experimental setting also made the search task more difficult to distinguish from the recognition task. A similar impact from experiment instruction can also occur in VWM studies using the change detection task. For example, previous studies have shown that when participants needed to remember the stimuli more deeply—for example, in a relocated task (Spotorno et al., 2018)—or when a longer encoding time was provided (Curby et al., 2019), the happy face advantage in memory appeared.

3.1.3 Different stages in the cognitive process

Finally, with both visual search and change detection, the participants must finish several cognitive processes to accomplish the task. Thus, it is possible that different biases actually occur at different stages, but the behavioral outcomes do not reflect this difference.

In visual attention research, the process of a visual search task conventionally contains two distinct but interrelated stages: the pre-attentive stage and the attentive or post-attentive stage. The pre-attentive stage occurs before the attentional selection of a target stimulus, whereas the attentive or post-attentive process involves direct focus on a target stimulus (Smilek, Frischen, Reynolds, Gerritsen, & Eastwood, 2007). A "decision efficiency" stage has also been proposed using an eye-movement technique in a visual search. It tracks the time between fixing the gaze on the target stimulus and decision-making (Calvo et al., 2008). One possibility for the contradictory results in a visual search is that an automatic bias toward negative emotions exists in the early pre-attentive stage, whereas a positive bias is revealed in the later recognition and/or decision-making stages. Consistent with this point of view, the use of an emotion classification task combined with the EEG technique revealed that in the early stage, N170 showed more responses to negative faces—such as angry, fearful, and sad faces. By contrast, happy faces tended to correlate with facilitation in categorization (reflected by P3b) and decision-making (reflected by a slow positive wave in the later stage; Calvo & Beltrán, 2013).

As for VWM studies, the change detection task process comprises four stages: encoding, consolidation, maintenance, and retrieval (Ye, 2018). Perception representations are created and consolidated into VWM during the encoding and consolidation stages. Meanwhile, the consolidation stage comprises two different phases (Ye, 2018; Ye et al., 2017, 2019). In the early consolidation phase, individuals automatically create low-precision representations. Subsequently, in the late consolidation phase, individuals can voluntarily create high-precision representations. After the stimulus disappears, participants need to maintain VWM representations and then retrieve them in subsequent tasks in order to complete the entire cognitive process of VWM. Studies have indicated that different expressions did not have any effect at the encoding stage, but emotional faces (both angry and happy) showed greater resource allocation at the maintenance stage (Langeslag et al., 2009). More importantly, the encoding stage in VWM overlaps with the processes in attention research; however, previous studies have not been able to dissociate attention from VWM. Therefore, whether attention or VWM is responsible for this discrepancy is difficult to discern.

TABLE 1 Studies on visual working memory (VWM) using emotional faces in the change detection task

Study [a]	N	Expression	Stimulus type/ Stimulus set [b]	Stimulus arousal	Set size	Encoding time (ms)	Task [d]	Behavior /Neural index	Results [e]
Becker et al. (2014): Exp. 1	64	Neutral, angry	Photograph /- [c]	-	4	10000	Detect identity present/ absent	Hit rate, false alarm rate, *d*', bias (c)	Angry > neutral
Brenner et al. (2014)	29	Positive (very happy, somewhat happy), neutral, Negative (sad, fearful, and angry)	Photograph /NimStim	-	1	200	Detect expression same/ different	Acc, RT, P100, N170, N250, theta power	Negative > positive
Curby et al. (2019): Exp. 1	40	Fearful, neutral	Photograph /NimStim, KDEF, CVL	-	5	1000/4000	Detect probe same/ different	K	1000 ms: no effect; 4000 ms: fearful< neutral
Curby et al. (2019): Exp. 2	41	Fearful, neutral	Photograph /NimStim, KDEF, CVL	-	5	1000/4000	Detect probe same/ different	K	1000 ms: no effect; 4000 ms: fearful< neutral
Curby et al. (2019): Exp. 3	82	Fearful, neutral	Photograph /NimStim, KDEF, CVL	-	2,4,6	4000	Detect probe same/ different	K	Fearful < neutral

continues

TABLE 1 continues

Study [a]	**N**	**Expression**	**Stimulus type/ Stimulus set [b]**	**Stimulus arousal**	**Set size**	**Encoding time (ms)**	**Task [d]**	**Behavior /Neural index**	**Results [e]**
Curby et al. (2019): Exp. 4a	42	Neutral, happy, fearful, angry	Photograph /Radboud	Happy =fearful; fearful ≠angry; happy ≠angry	5	4000	Detect probe same/ different	K	Fearful, angry < happy
Jackson et al. (2008)	35	Angry, happy, neutral	Photograph /Ekman & Friesen	Happy= angry	1,2,3,4	2000	Detect identity present/ absent	*d*', fMRI	Angry > happy; angry > neutral
Jackson et al. (2009): Exp. 1	24	Angry, happy, neutral	Photograph /Ekman & Friesen	-	1,2,3,4	2000	Detect identity present/ absent	*d*', K-iterative (K_{it})	Angry > happy; angry > neutral
Jackson et al. (2009): Exp. 2	18	Angry, happy, neutral	Photograph /Ekman & Friesen	Angry = happy	2,4	2000	Detect identity present/ absent	*d*', K-iterative (K_{it})	Angry > happy; angry > neutral
Jackson et al. (2009): Exp. 3	26	Angry, neutral	Photograph /Ekman & Friesen	-	2,4	4000	Detect identity present/ absent	*d*', K-iterative (K_{it})	Angry > neutral
Jackson et al. (2009): Exp. 5	40	Angry, happy, neutral	Photograph /Ekman & Friesen, KDEF	Morphed to the same intensity	2,4	2000	Detect identity present/ absent	*d*', K-iterative (K_{it})	Angry > happy; angry > neutral

continues

TABLE 1 continues

Study [a]	**N**	**Expression**	**Stimulus type/ Stimulus set** [b]	**Stimulus arousal**	**Set size**	**Encoding time (ms)**	**Task** [d]	**Behavior /Neural index**	**Results** [e]
Jackson et al. (2012): Exp. 1	25	Angry, happy	Photograph /Ekman & Friesen	-	2	2000	Detect identity present/ absent	*d'*, RT	Angry = happy
Jackson et al. (2012): Exp. 2	27	Angry, happy	Photograph /Ekman & Friesen	-	2	2000	Detect identity present/ absent	*d'*, RT	Angry face was boosted by intervened emotional word, but happy face was not affected by it
Jackson et al. (2014): Exp. 1	22	Angry, happy	Photograph /Ekman & Friesen	Angry= happy	1,2,3,4	2000	Detect identity present/ absent	Hits, false alarm rate, *d'*, RT	Angry > happy
Jackson et al. (2014): Exp. 2	13	Angry, happy	Photograph /Ekman & Friesen	Angry= happy	1,2,3,4	2000	Detect identity present/ absent	Hits, false alarm rate, *d'*, RT	Angry = happy
Jackson et al. (2014): Exp. 3	25	Angry, happy	Photograph /Ekman & Friesen	Angry= happy	2	2000	Detect identity present/ absent	Hits, false alarm rate, *d'*, RT	No effect of word valence for happy faces, but negative intervening word boosted angry face WM performance
Langeslag et al. (2009)	29	Angry, happy, neutral	Photograph /Ekman & Friesen	Angry= happy	1,3	2000	Detect identity present/ absent	Pr, Br, RT, P1, N170, P3b, N250r	Angry > neutral; happy > neutral

continues

TABLE 1 continues

Study [a]	**N**	**Expression**	**Stimulus type/ Stimulus set** [b]	**Stimulus arousal**	**Set size**	**Encoding time (ms)**	**Task** [d]	**Behavior /Neural index**	**Results** [e]
Lee and Cho (2019): Exp. 1	32	Fearful, happy, neutral	Photograph /KUFEC	Feaful: 4.2 Happy: 4.46	4	1200	Detect identity same/ different	d'	Fearful, neutral group > happy, neutral group; fearful > neutral; happy> neutral
Lee and Cho (2019): Exp. 2	32	Fearful, happy, neutral	Photograph /KUFEC	Feaful: 4.2 Happy: 4.46	4	1200 (300 ms for each face)	Detect identity same/ different	d'	Fearful, neutral group > happy, neutral group; fearful > neutral
Lee and Cho (2019): Exp. 3	32	Fearful, happy, neutral	Photograph /KUFEC	Feaful: 4.2 Happy: 4.46	4	1200 (300 ms for each face)	Detect identity same/ different	d'	Fearful, neutral group = happy, neutral group; fearful > neutral
Linden et al. (2011): Exp. 1	20	Angry, happy, neutral, sad, fearful	Photograph /Ekman & Friesen	Angry, fearful higher than all other condition, sad & happy > neutral	2	2000	Detect identity present/ absent	d'	Angry > fearful; happy > fearful; neutral > fearful

continues

TABLE 1 continues

Study [a]	**N**	**Expression**	**Stimulus type/ Stimulus set** [b]	**Stimulus arousal**	**Set size**	**Encoding time (ms)**	**Task** [d]	**Behavior /Neural index**	**Results** [e]
Liu et al. (2020)	38	Happy, sad	Photograph /CFEES	Happy= sad	2	2000	Detect identity present/ absent	Hits, CR, FA, RTs, *d'* N170, VPP, N250, P3b, LPP	Happy > sad
Maran et al. (2015): Exp.1	24	Angry, happy, anxious, neutral	Photograph /NimStim	No difference in perceived intensity	4	2000	Detect identity present/ absent	*d'*	Neutral arousing condition: angry > happy; angry > anxious; angry > neutral; happy > anxious. Negative arousing condition: equalized VWM performance for all expression
Maran et al. (2015): Exp.2	30	Angry, happy, anxious, neutral	Photograph /NimStim	No difference in perceived intensity	4	2000	Detect identity present/ absent	*d'*	Neutral arousing condition: angry> happy; angry> anxious; angry> neutral. Positive arousing condition: equalized VWM performance for all expression

continues

TABLE 1 continues

Study [a]	**N**	**Expression**	**Stimulus type/ Stimulus set** [b]	**Stimulus arousal**	**Set size**	**Encoding time (ms)**	**Task** [d]	**Behavior /Neural index**	**Results** [e]
Sessa et al. (2011)	28	Fearful, neutral	Photograph /Ekman & Friesen, KDEF	-	2,4	200	Detect identity same/ different	d', K, K_{it}, RT, CDA	Fearful > neutral
Sessa et al. (2018)	29	Neutral, subtle angry, full angry	Photograph /KDEF	Morphed from neutral to full angry	2	500	Detect expression same/ different	Mean proportion of correct responses, CDA	Full angry > neutral > subtle angry
Simione et al. (2014): Exp. 1	19	Angry, happy, neutral	Schematic face	-	4	150/400	Report the expression at the probed location	Acc	Emotion > neutral, but no difference between angry and happy
Simione et al. (2014): Exp. 2	20	Angry, happy, neutral	Schematic face	-	3,5	150	Report the expression at the probed location	Acc	Angry > neutral; angry > happy
Spotorno et al. (2018): Exp. 1	48	Angry, happy	Photograph /Radboud	-	1,2,3,4	1500 ×set size	Drag the face to the original location	Acc, precision, swap error, oculomotor activity	Happy > angry

continues

TABLE 1 continues

Study [a]	**N**	**Expression**	**Stimulus type/ Stimulus set** [b]	**Stimulus arousal**	**Set size**	**Encoding time (ms)**	**Task** [d]	**Behavior /Neural index**	**Results** [e]
Spotorno et al. (2018): Exp. 2	48	Angry, happy	Photograph /Radboud database	-	4	6000	Drag the face to the original location	Acc, precision, swap error, oculomotor activity	Happy > angry
Švegar et al. (2013)	24	Afraid, angry, disgusted, happy, neutral, sad, surprised	Photograph /AKDEF, KDEF	-	6	2000	Detect expression same/different	Percentage of correct answers; RT	Happy > all the other emotions while no difference among other emotions
Thomas et al. (2014): Exp. 1	25	Angry, happy, neutral	Photograph /Ekman & Friesen	-	4	2000	Detect identity present/absent	*d*', RT	Angry > happy
Thomas et al. (2014): Exp. 2	32	Angry, happy, neutral	Photograph /Ekman & Friesen	-	4	2000	Detect identity present/ absent	*d*', RT, eye movement	Angry > happy
Xie et al. (2017): Exp. 1	60	Positive set (5 happy + 1 neutral); negative set (5 sad + 1 neutral)	Schematic face	Positive = negative	4	500	Localize the changed face	K	Positive = negative. K (neutral color) > K (emotional face); higher WM capacity maintain more happy faces

continues

TABLE 1 continues

Study [a]	**N**	**Expression**	**Stimulus type/ Stimulus set** [b]	**Stimulus arousal**	**Set size**	**Encoding time (ms)**	**Task** [d]	**Behavior /Neural index**	**Results** [e]
Xie et al. (2017): Exp. 2	42	Positive set (5 happy + 1 neutral); negative set (5 sad + 1 neutral)	Schematic face	Positive = negative	4	500	Localize the changed face	K	Positive = negative. K (emotional face) > K (neutral line drawing symbols); higher WM capacity maintain more happy faces
Zhou et al. (2021)	31	Happy, sad	Photograph /CFEES	Happy= sad	2	2000	Detect identity present/absent	Hits, CR, FA, RTs, *d*' N170, VPP, P3b, LPP	Happy = sad

[a] The missing experiment here is due to the sub-experiment unrelated to the change detection paradigm or the main topic of this review, e.g., Experiment 2 in Becker et al. (2014) is more related to race than emotional processing; Experiment 4 in Jackson et al. (2009) is a discrimination task; Experiment 2 and 3 in Linden et al. (2011) are emotional classification task and arousal/valance rating task, respectively.

[b] We listed here both the stimulus material types (photograph or schematic face) and the stimulus set of photographs for a better comparison between different stimulus databases. The main database used in previous studies included: Ekman & Friesen set (Ekman & Friesen, 1976); KDEF, Karolinska Directed Emotional Faces database (Lundqvist, Flykt, & Öhman, 1998), AKDEF, Averaged Karolinska Directed Emotional Faces (Lundqvist & Litton, 1998); NimStim database (Tottenham et al., 2009); CVL Face Database (Solina, Peer, Batagelj, Juvan, & Kovač, 2003); Radboud Face Database (Langner et al., 2010); KUFEC, Korea University Facial Expression Collection (Kim, Choi, & Cho, 2011); CFEES, Chinese facial expression of emotion system (Liu, Hou, & Yu, 2012).

[c] "-" means the information was not reported in the relevant publications.

[d] Here we classified the tasks into four types based on what the researchers reported in relevant studies: 1) detect identity present/absent, 2) detect identity same/different, 3) detect expression same/different; 4) detect probe same/different. "Present/absent" refers to studies using multiple stimuli in the encoding array, with only one single stimulus in the central of the probe array, and the main task of the participant was to report whether or not the single probe was presented in the memory array; "Same/different" refers to studies using multiple stimuli (or single stimulus in

the probe array but the face present in one of the locations from the study array rather than central space) both in the memory array and the probe array, and participants needed to indicate whether the probe array was identical to the memory array or whether one of the faces had changed. "Detect identity" refers to the expression irrelative to the study, and participants only needed to detect whether the identity had changed, whereas "Detect expression" meant that the participants needed to detect whether the expression on the probe array was identical to the memory array while the identity stayed unchanged or needed to be ignored. Additionally, "Detect probe" refers to the relevant study that did not emphasize detecting the expression or the identity but required participants to determine whether the whole probe face (both identity and expression) was identical to the memory items. In addition, a few studies have used a similar but not the classical change detection task, we decided to include those studies here for a better comparison. For those studies, we have only presented the specific tasks reported in the relevant studies without placing them in any of the above categories.

[e.] Only the main and most consistent results are reported here. " > " refers to the bias toward the former expression compared to the latter one; " < " refers to the bias toward the latter expression compared to the former one; " = " refers to no significant difference between the two expressions.

Abbreviations:

Column 1 (Study): Exp., Experiment

Column 2 (N): N, participants numbers

Column 9 (Behavior/Neural index): Acc, accuracy; RT, reaction time; d', VWM performance index, d' = Z(hit rate) – Z(false alarm rate); K, VWM capacity index, K= set size × (hit rate – false alarm rate); fMRI, functional magnetic resonance imaging; K-iterative (Kit), calculated by an iterative procedure, please see details in Jackson et al. (Jackson et al., 2009); Pr, discrimination index, Pr = hit rate – false alarm rate; Br, response bias index, Br = false alarm rate/(1-Pr), Please see more details for Pr and Br in Langeslag et al. (Langeslag et al., 2009); CR, correct rejections; CDA, contralateral delay activity, also known as sustained posterior contralateral negativity, SPCN, neural index of VWM maintenance.

Column 11 (Comments): rSTS, right superior temporal sulcus; rPFC, right prefrontal cortex; IFS, inferior frontal sulcus; rGPi, right globus pallidus internus.

The table is modified from Xu, Ye, Gu, et al. (2021).

3.2 Study II: Automatic processing of changes in facial emotions in dysphoria: A magnetoencephalography study

In **Study II**, I investigated unattended change detection of paracentrally presented emotional faces in dysphoric (i.e., participants with depressive symptoms) and control groups.

The behavioral results showed that both groups of participants were able to accomplish the task well and showed neither a significant interaction effect nor a main effect in either accuracy (hit rate and false alarm) or reaction time. The mean reaction time was 386 ms. The mean hit rates were greater than 98%, and false alarms were below 1% for both groups.

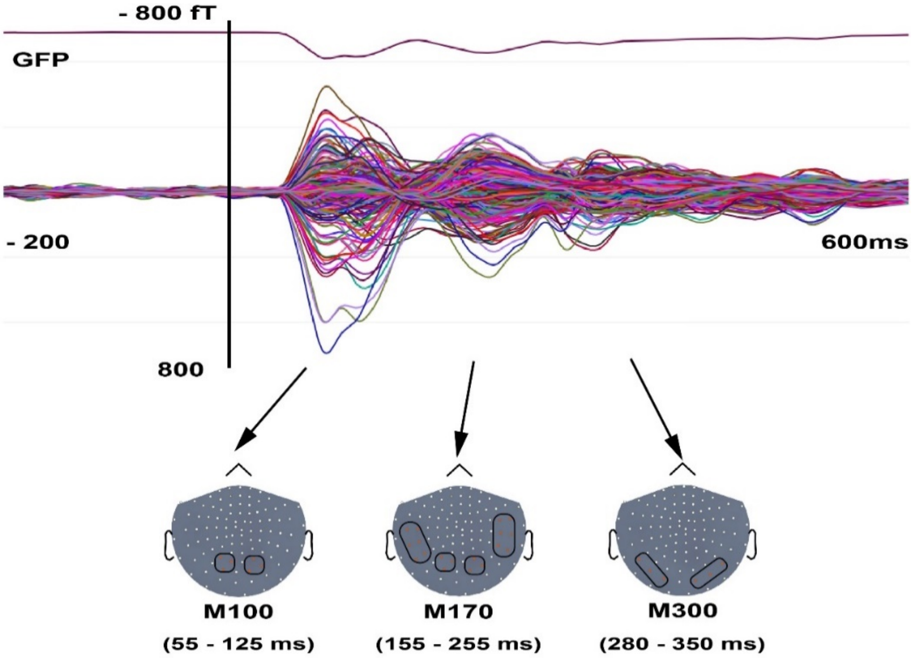

FIGURE 5 Butterfly view of the grand-averaged responses to happy standard stimuli in all participants. Event-related fields reflecting three stages of face processing (M100, M170, and M300). The results for all other stimuli (happy deviant, sad standard, sad deviant) showed similar patterns. Magnetometer sensors and the regions of interest used for analyses are marked with black frames on M100, M170, and M300. Each participant's peak values were extracted from the time windows of 55–125 ms, 155–255 ms, and 280–350 ms after stimulus onset for M100, M170, and M300, respectively. The top line of the graph is the global field power (GFP; i.e., the sum of the square of all channels at each time point) plotted as a function of time.

The grand-averaged event-related fields (ERFs) showed a prominent M100, M170, and M300 within 55–125 ms, 155–255 ms, and 280–350 ms in both groups (Figure 5). The response latencies showed no significant main or interaction effects. For peak amplitude values, enhanced amplitudes with deviant faces reflecting the magnetic counterpart of the vMMN responses were found for all time intervals, indexing deviance detection even though the faces were presented paracentrally and unattended. The M170 peak amplitudes (Figure 6) were also modulated by the emotion, reflected by response amplitudes that were larger with sad faces than happy faces. The details of the significant results are reported in Table 2.

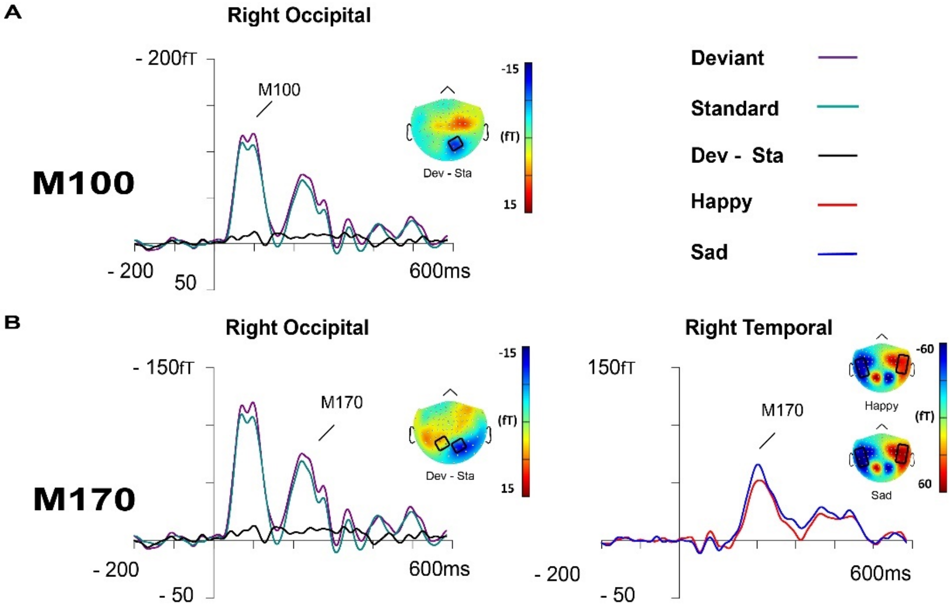

FIGURE 6 Grand-averaged ERFs demonstrating M100 and M170. (A) Grand-averaged ERFs demonstrating the M100 waveforms for deviant, standard, and deviant minus standard differential responses at the right occipital ROI. The topography of vMMN (deviant − standard) is depicted as the mean amplitude value of activity 55–125 ms after stimulus onset. (B) Grand-averaged ERFs demonstrating the M170: waveforms for deviant, standard, and deviant minus standard differential responses at the right occipital ROI, and responses to happy and sad faces at the right temporal ROI. Topographic maps are depicted as the mean amplitude value of the activity 155–255 ms after stimulus onset. ERF: Event-related field; ROI: region of interest; vMMN: visual mismatch negativity. The figure is modified from Xu et al. (2018).

Group differences were found for M300 (Figure 7). In the dysphoric group, the amplitudes were larger for sad than happy deviant faces at left occipital ROIs, while no such difference was found in the control group. Conversely, at right occipital ROI, the control group showed larger M300 amplitudes for deviant faces than standard faces, while no amplitude difference between stimulus types was found in the dysphoric group. Group difference was also found in vMMN amplitude between dysphoric and control group at right occipital in M300. To further explore the results of M300, I tested the correlation effect for BDI-II scores and M300 responses. However, there were no significant correlations between BDI-II scores and M300 response amplitudes in either the left or right ROIs for all stimulus types. The same applied to the correlations calculated separately for the dysphoric group, nor were results found for the lateralization index. The details of the significant results are reported in Table 2.

TABLE 2 Summary of ANOVA results for the peak amplitude values of each component in Study II

Component	ROI	Effect [a]	F (df, df error) [b]	*p*	η_p^2
M100	Left occipital	–	–	–	–
	Right occipital	Stimulus type	F(1,21) = 30.22	< 0.001	0.59
M170	Left temporal	Emotion	F(1,21) = 3.46	0.077	0.14
	Right temporal	Emotion	F(1,21) = 8.52	0.008	0.29
	Left occipital	Stimulus type	F(1,21) = 9.29	0.006	0.31
	Right occipital	Stimulus type	F(1,21) = 12.81	0.002	0.38
M300	Left occipital	Emotion × Stimulus type × Group	F(1,19) = 4.52	0.047	0.19
		Emotion × Stimulus type	F(1,19) = 4.48	0.048	0.19
		Emotion × Group	F(1,19) = 4.34	0.051	0.19
	Right occipital	Stimulus type × Group	F(1,19) = 5.15	0.035	0.21
		Stimulus type	F(1,19) = 5.40	0.031	0.22

[a] Only significant or marginally significant effects are reported.

[b] Two participants did not show M300 responses (one in the control group, and one in the dysphoric group) and were excluded from the statistical analysis; therefore, the df error in M300 was 19. df: degrees of freedom.

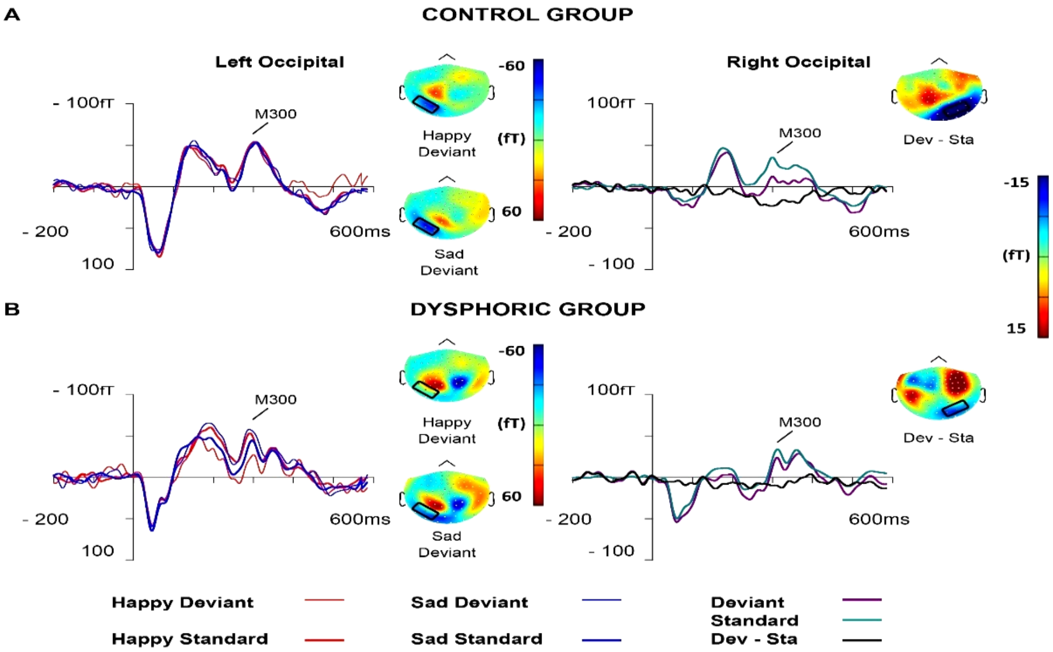

FIGURE 7 Grand-averaged ERFs for the M300 response and corresponding topographic maps in the (A) control and (B) dysphoric groups. Waveforms of the ERFs to happy deviant, happy standard, sad deviant, and sad standard stimuli at the left occipital ROIs and deviant, standard, and deviant minus standard differential responses at the right occipital ROIs in the control and dysphoric groups. Note that for M300 at the left occipital ROI, there was an interaction effect of emotion × stimulus type × group, indicating that sad deviant faces induced more activity than happy deviant faces in the dysphoric group but not in the control group. At the right occipital ROIs for M300, an interaction effect of stimulus type × group was found, indicating that the responses to deviant faces were lower in amplitude than the responses to standard faces in the control group, but no such difference was found in the dysphoric group. ERF: Event-related field; ROI: region of interest. The figure is modified from Xu et al. (2018).

3.3 Study III: Magnetoencephalographic responses of healthy adult humans to unpredictable and predictable rare somatosensory stimuli

Study III introduced a new passive oddball task that can investigate somatosensory responses to unpredictable and equally rare predictable events. In principle, the increased activity related to the UR stimulus, when compared with PR and FRE stimuli, could be associated with prediction error. The results showed that for both the sensor-level and source-level results, there were two main components, M55 and M150, within the time windows of 30–100 ms and 130–230 ms, respectively.

The cluster-based permutation test at the sensor level revealed significant differences between UR vs. FRE, PR vs. FRE, and UR vs. PR for M55 (30–100 ms). However, for M150 within 130–230 ms, significant differences were found between UR vs. FRE, and PR vs. FRE, but no significant cluster was observed for the UR vs. PR comparison. The details of the significant results are reported in Table 3.

TABLE 3 Summary of the cluster-based permutation test results at the sensor level

Component /Time window [a]	**Stimulus contrast**	**Largest cluster time point** [b]	**Cluster region** [c]	**Cluster size** [d]	**p-value**
M55 (30–100 ms)	UR > FRE	42 ms	Right frontoparietal and temporal areas	2204	0.002
	PR > FRE	96 ms	Right parietal and temporal areas	324	0.010
	UR > PR	38 ms	Right frontoparietal and temporal areas	1731	0.002
M150 (130–230 ms)	UR > FRE	185 ms	Right frontal areas	1706	0.002
	PR > FRE	161 ms	Right frontal and parietal regions	1404	0.002

[a] The cluster-based permutation tests were conducted separately for each stimulus contrast (UR vs. FRE, PR vs. FRE, UR vs. PR) in time windows of 30–100 ms and 130–230 ms. Only results that revealed significant clusters are reported here.

[b] Largest cluster time point denotes the time point (after stimulus onset) that the maximum number of sensors were connected to each other.

[c] Cluster regions are the sensor spaces showing the most pronounced difference in topographies from corresponding time windows.

[d] The cluster size denotes the connected data points of the corresponding cluster.

FRE: Frequent stimulus, UR: unpredictable rare stimulus, PR: predictable rare stimulus.

The source-level analysis results are in line with sensor-level results, suggesting that M55 elicited increased activity in response to the rare events (both UR and PR stimuli) compared to the frequent events in both the cSI and the cSII areas (Figures 8–9). In addition, both ROIs showed more source strength for the UR than the PR. However, for M150, consistent with the sensor-level results, both the PR and the UR induced more activity than did the FRE in both ROIs, but no difference was found between the UR and PR in either the cSI or the cSII areas.

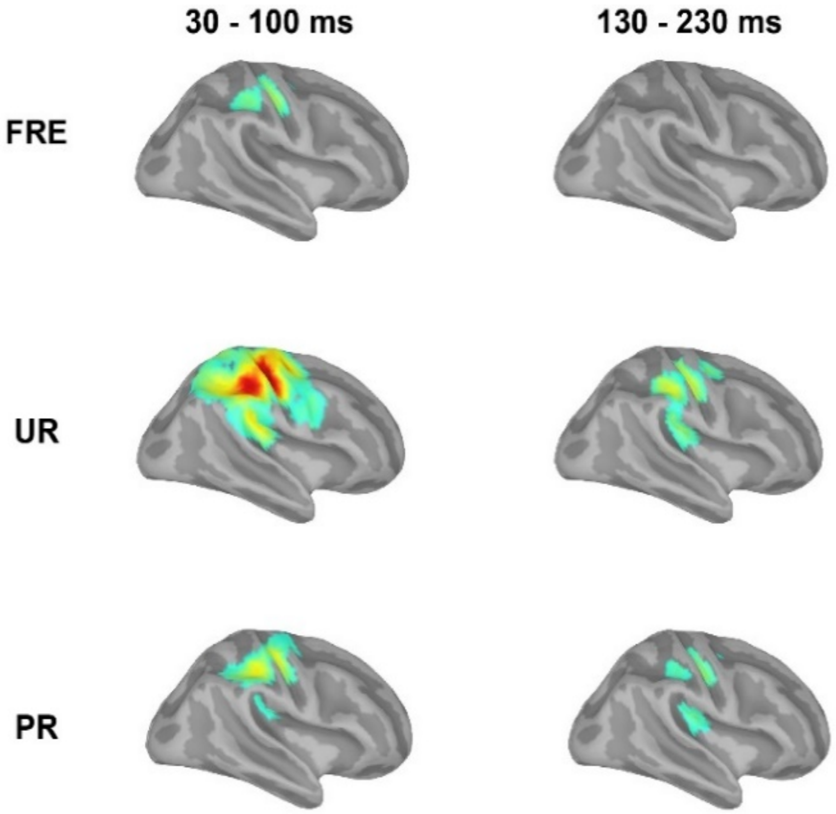

FIGURE 8 Right-side view of grand-averaged source activation in the time windows of 30–100 ms (M55) and 130–230 ms (M150) after stimulus onset for each stimulus type. For visualization purposes, only the sources with a value > 40% of the color bar maximum are displayed here. FRE: Frequent stimulus, UR: unpredictable rare stimulus, PR: predictable rare stimulus. The figure is modified from Xu, Ye, Hämäläinen, et al. (2021).

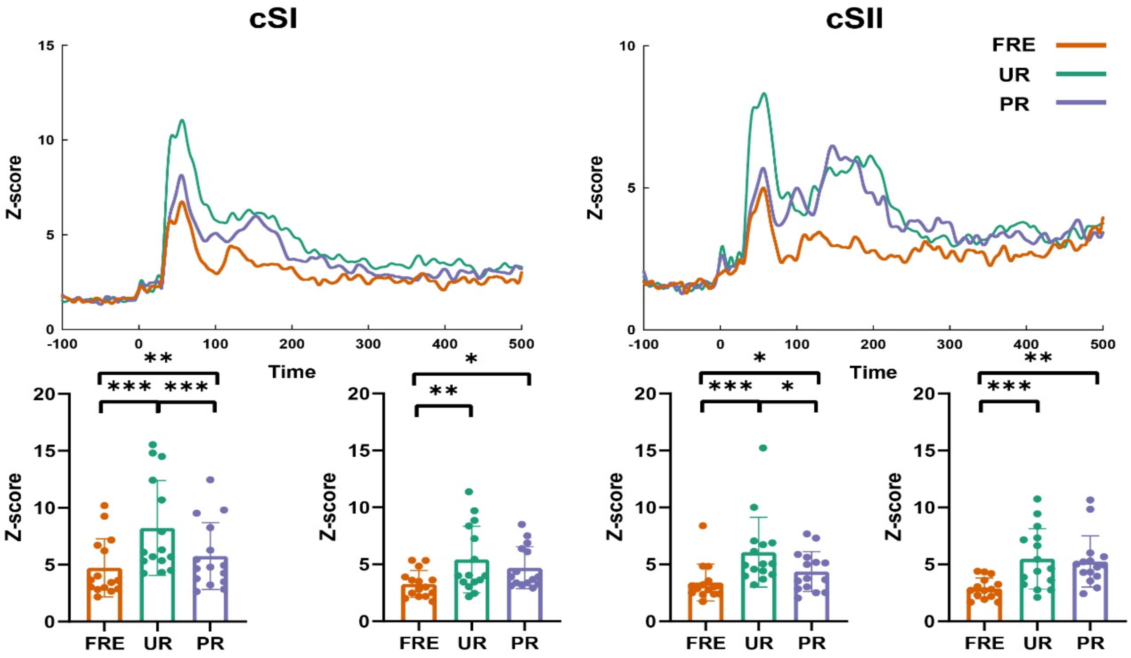

FIGURE 9 The summary of results from the source-level analyses. Upper panel: The cortical time series for all three conditions (FRE, UR, PR) in the cSI (left panel) and cSII (right panel). Lower panel: The bar graph of the source strength comparison for all three conditions (FRE, UR, PR) in the cSI (left panel) and cSII (right panel). Error bars represent the standard error of the mean, and the dots represent the values of the individual participants. FRE: Frequent stimulus; UR: unpredictable rare stimulus; PR: predictable rare stimulus; cSI: contralateral primary somatosensory cortex; cSII: contralateral secondary somatosensory cortex. The figure is modified from Xu, Ye, Hämäläinen, et al. (2021).

For control of the physical features between UR and FRE, control condition C with four of the original 15 participants were conducted. A descriptive figure of the averaged response with a 95% confidence interval (95% CI) derived from single trials for each participant is presented in Figure 10. Visual inspection of the grand-averaged waveforms indicated that both UR and FRE showed two main components corresponding to M55 (30–100 ms) and M150 (130–230 ms). Specifically, the UR seemed to induce a larger amplitude than the FRE in both time windows. As these data stem from only a small sample (n = 4) without statistics, we cannot provide convincing evidence for elicitation of the genuine sMMR. However, visual observation suggests that the responses to the UR are numerically larger than the responses to the FRE for at least some participants. This finding was observed in three of the four participants for M55 and two of the four for M150.

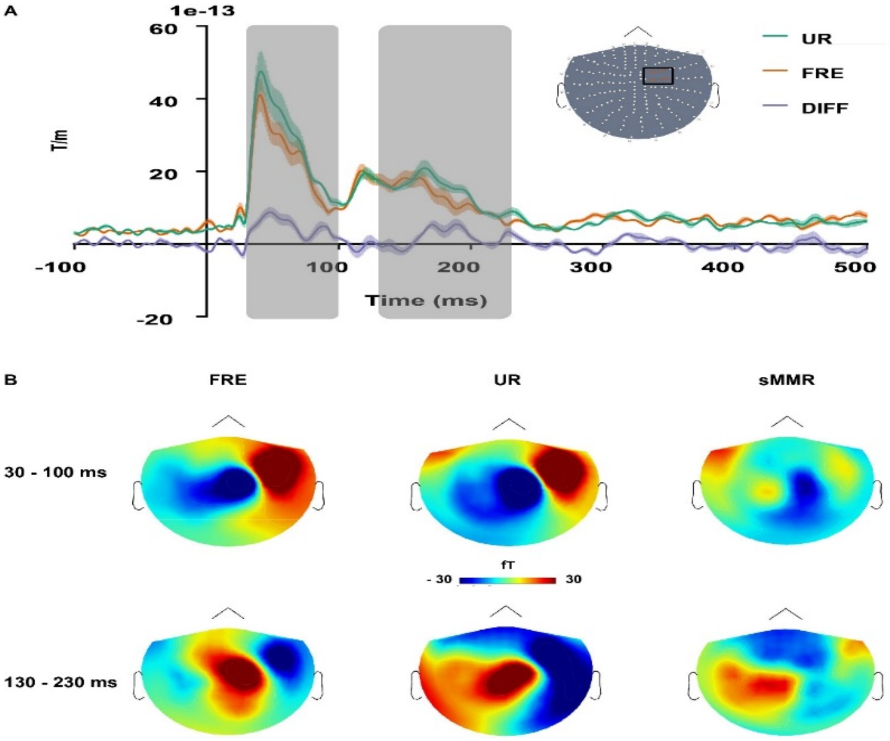

FIGURE 10 Sensor-level grand-averaged results of four participants (conditions B and C averaged; thus, physical features for the FRE and UR are counterbalanced). (A) Grand-averaged waveforms (n = 4) with 95% CI averaged from the eight most pronounced sensors (marked with red dots in the black frame on the sensor map). Orange line: frequent stimulus (FRE); green line: unpredictable rare stimulus (UR); purple line: somatosensory mismatch response (sMMR, obtained by subtracting the FRE from the UR). The gray shaded areas indicate the time window for M55 (30–100 ms) and M150 (130–230 ms), analyzed in the main text. (B) Topographical maps of the FRE, UR, and sMMR for M55 and M150 extracted as mean amplitude values from the time windows of 30–100 ms and 130–230 ms, respectively. Upper panel: Topography of M55 (30–100 ms). Lower panel: Topography of M150 (130–230 ms). The figure is modified from Xu, Ye, Hämäläinen, et al. (2021).

4 DISCUSSION

This dissertation investigated change detection using two static images that appeared successively with a time interval inserted, along with the change detection (i.e., deviance detection) in which a change violates certain regularities based on a series of repeated stimuli. The first kind of change detection is usually considered necessary to have the involvement of focal attention and VWM, while deviance detection can occur pre-attentively. In this dissertation, I first reviewed the evidence for attentive change detection and visual search in facial expression stimuli. Second, I empirically investigated unattended deviance detection in serially presented facial expressions. Brain responses were compared between participants with depressive symptoms and non-depressed controls. Third, I investigated pre-attentive deviance detection of somatosensory stimuli, particularly the effect of stimulus predictability on brain responses.

In **Study I**, a literature review was conducted to summarize the previous contradictory results regarding negative or positive bias toward emotional faces when using a visual search or change detection task. These two tasks are considerably similar and share some common contributing factors in stimulus choice and experimental setting that may have had significant impacts on the contradictory conclusions (negative bias vs. positive bias) of previous studies. Furthermore, because many contradictory results came from behavioral studies in which the underlying mechanism could not be investigated, another possibility is that the varying emotional bias results might derive from the different advantages at the different stages of attention or VWM processes.

In **Study II**, magnetic brain responses were recorded to investigate the deviance detection processing of paracentrally presented facial expressions in both dysphoric and healthy individuals. The magnetic counterpart of the vMMN was elicited at all stages of face processing (M100, M170, M300), indexing automatic deviance detection of deviant faces. The M170 amplitude was also modulated by emotion, and the response amplitudes were larger for sad faces than happy ones. Group differences were found for M300, which reflected an automatic negative bias toward sad faces and a general deficit in automatic deviance detection processing in dysphoria.

In **Study III**, the MEG technique was again used to investigate brain responses to unpredictable and predictable rare somatosensory events. A novel stimulus protocol was introduced wherein somatosensory FRE were occasionally replaced by two consecutively presented rare stimuli (UR and PR). This design allowed for testing whether the brain responses reflected prediction error, as suggested by the predictive coding theory, or only the rareness (probability of presentation) of stimulus. Two main components, M55 and M150, were found for each stimulus type on the contralateral somatosensory cortices. The sensor-level and source-level results revealed a similar pattern in which components had a bigger response with the UR and PR than the FRE. However, a greater response for the UR than for the PR only appeared in M55, and no such difference was found for M150 between the UR and PR. The results of **Study III** indicate that M55, but not M150, possibly signals the prediction error.

Overall, the results suggest that special attention should be paid to the influence of stimulus selection, experimental setting, and distinguishing between different cognitive processes in studying the change detection and visual search process of facial expressions. In addition, depressive symptoms and stimulus predictability can affect the automatic processing of deviance detection.

4.1 Change detection of the emotional face in visual modality: Contradictory evidence from visual search and change detection tasks

In **Study I**, I mainly focused on studies of visual search and change detection tasks with different emotion faces, and I proposed three possible factors responsible for the mixed results in prior studies: stimulus choice, experimental setting, and cognitive process. A recent review by Becker & Rheem (2020) listed five necessary points of guidance for future researchers using the visual search task to study facial expressions. In addition to their guidance, I offer several other suggestions to address the problems that are common in visual search and change detection tasks. Below, I first discuss the limitations and recommendations of the existing tasks related to the visual search and change detection tasks in order to minimize discrepancies. I then propose some possible directions for future research.

4.1.1 Choice of emotional stimuli

Above all, in studies of change detection and visual search, researchers need to be more careful in the selection of stimulus materials, especially regarding the control of low-level physical features and stimulus arousal. The degree of arousal resulting from the stimulus itself should be defined and evaluated more comprehensively. Collecting the participants' own arousal evaluations for each experimental stimulus in the study is also important because arousal, as such, is subjective. Moreover, I offer three other suggestions for the selection of emotional stimuli.

First, future research should pay more attention to the selection of photographs and schematic faces in terms of physical features. Therefore, more advanced technology or accurate methods of further controlling physical features—for example, using computer-generated techniques to create human-like pictures (Spencer-Smith et al., 2001)—is needed in future work. The application of dynamic facial expressions along with body expressions also offers possible directions for future exploration (Becker et al., 2011; Gilbert, Martin, & Coulson, 2011; Krumhuber, Kappas, & Manstead, 2013).

Second, both attention and VWM studies have considered the use of neutral faces to be a baseline setting for comparison with emotional faces. However, neutral faces are more likely to be perceived as negative than positive (Kauschke et al., 2019). This tendency may lead to imbalance in a search array or the encoding stage of a memory array. Moreover, the use of fearful and angry faces for the threat effect should also be interpreted with caution. Although fearful and angry faces have both usually been classified as threatening faces in previous studies (e.g., Fox et al., 2000; Horstmann, 2009; Öhman et al., 2001), they actually contain different information. The threat source of anger is basically the face per se, while fear serves as a reminder of the threat in the viewers' environment (Curby et al., 2019; Davis, Somerville, Ruberry, Shin, & Whalen, 2011). Therefore, future studies should discuss fearful and angry faces separately rather than simply categorizing both as threatening stimuli.

Third, previous studies have shown that emotional states or mental illnesses (e.g., depression, anxiety, worry) can affect attention and VWM (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007; Long, Ye, Li, Tian, & Liu, 2020; Ruohonen et al., 2020; Stout, Shackman, Johnson, & Larson, 2015; Zhou et al., 2021). However, knowledge is currently limited about the influence of emotional states on the results of visual search or change detection tasks that use emotional face stimuli. Therefore, future studies could further explore the emotional states' effects on individuals' processing of attentional or memory tasks.

4.1.2 Standardization of the experimental setting

Based on my summary, the experimental settings for both tasks evidently require further standardization. For example, when testing different visual matrix sizes, future studies should also consider the timing of stimulus presentation and explore the effects of different combinations of stimulus set sizes and times with both tasks. In addition, experimental instructions should be carefully controlled to prevent the involvement of unnecessary cognitive processes.

Furthermore, most prior studies have used visual search and change detection tasks to investigate emotional face processing in attention and VWM; however, some other tasks can investigate similar topics in these fields. For example, in the field of attention, the dot-probe task (Cooper & Langton, 2006), rapid serial visual presentation task (RSVP; Luo, Feng, He, Wang, & Luo, 2010), and visual crowding task (Gong & Smart, 2021) can also explore emotional face attentional bias. Similarly contradictory results on emotional bias have also been found in studies using the RSVP task (for negative bias, see Maratos, Mogg, & Bradley, 2008; for positive bias, see Miyazawa & Iwasaki, 2010). Some studies even have found that VWM and the attentional blink observed in the RSVP task seem to share the same neural processing and storage capacity mechanisms (Simione et al., 2012, 2014). In addition to the change detection task, another appropriate task to test emotional bias is the N-back task (Kensinger & Corkin, 2003; Tamm, Kreegipuu, Harro, & Cowan, 2017), which can measure several high-level cognitive processes (e.g., updating, interference; Szmalec, Verbruggen, Vandierendonck, & Kemps, 2011). A growing body of research has used N-back tasks or other tasks to explore emotional faces' potential differential impact in comparison to neutral faces (for a review, see Schweizer et al., 2019). Thus, future research can examine whether task types modulate emotional bias in attention and VWM. Likewise, many of the issues mentioned in this paper (e.g., selection of stimulus materials) are applicable to other attention or VWM studies.

4.1.3 Controlling and tracking cognitive processes

Future studies also need to explore the causes of the positive and negative biases underlying different cognitive processes. This exploration will require that future studies define and divide different processing stages (e.g., pre- and post-attentive stages in visual attention; the encoding stage and maintenance stage in VWM) into corresponding tasks. EEG and MEG techniques have advantages with their temporal resolution and ability to track the effects of certain experimental manipulations in different stages (Baillet, 2017; Langeslag et al., 2009). Future studies can succeed in this regard by combining traditional behavioral indicators with other neuroscience techniques. Specifically, they can combine different ERP/ERF indicators (e.g., N2pc in visual attention studies, CDA in VWM studies, and some other face or emotion-related component such as P1, N170) or combine EEG with eye movements to generate fixation-based ERPs (Kulke, 2019).

In VWM studies, both attention and memory play vital roles; therefore, different emotional advantages may already exist in the attention process than in the memory process. This makes it rather difficult to determine whether attention or memory processes caused the mixed results in VWM studies of emotional advantages. Future studies could try to separate the attention-related process from the VWM-related process (e.g., separating the encoding stage by using EEG/MEG techniques) when exploring emotional face advantages in VWM. Alternatively, future studies could include attention and VWM in the same context (e.g., using similar stimuli and experimental settings) and examine the associations between visual attention and VWM. For example, one previous study showed a high correlation between the reciprocals of VWM capacity and the visual search slope by using line drawing objects (Alvarez & Cavanagh, 2004). Therefore, a joint study of these two tasks could be a feasible alternative for better studying the role that attention plays in the emotional biases of VWM.

4.2 Change detection of the unattended emotional face in visual modality: Evidence from healthy and dysphoric individuals

The main goal of **Study II** was to examine emotional encoding and deviance detection of unattended and paracentrally presented facial emotions in dysphoria. MEG recordings showed prominent M100, M170, and M300 responses corresponding to the responses found in previous ERP studies conducted with healthy participants and using similar stimulus conditions as were applied here (Stefanics et al., 2012). In addition, M170 was modulated by emotion, reflected in a greater response to sad faces than to happy ones. Moreover, group differences were found for the M300 component, which showed both negative bias and impaired pre-attentive deviance detection brain responses in dysphoria.

The most significant results were from M300, which was different between the groups in both investigated ROIs. First, at the left occipital ROI, the dysphoric group showed a larger response amplitude for deviant sad faces than deviant happy faces, while no such difference was found in the control group. This negative bias toward sad faces seems to be associated with deviance detection, as the deviant stimulus responses, but not the standard stimulus responses, were larger for sad faces than happy ones in the dysphoric group. This is a novel finding and extends previous studies of the attentive condition (e.g., Bistricky et al., 2014; Chen et al., 2014) to an ignore condition. Second, at the right occipital ROI, the control group showed lower M300 amplitudes for deviant faces as compared to standard faces (i.e., vMMN), while no difference in amplitudes between stimulus types was found in the dysphoric group. This finding indicates that, in addition to the negative bias, there is a general deficit in change detection processing in dysphoria. This finding is also consistent with one prior study that used an ignore oddball condition in which they observed a late vMMN (at 220–320 ms) in the control group but not in the depression group (Chang et al., 2010). However, as with many other previous studies, their study applied standard neutral faces and deviant emotional faces as stimuli, which means that the effects of emotional processing and deviance detection cannot be distinguished. In **Study I**, the differential responses of vMMNs were calculated for responses to the same emotion. Therefore, the physical features were controlled between the deviant and standard stimuli and allowed for separating the vMMN and emotional modulation responses.

The present finding of the altered emotional vMMN in dysphoria is in line with prior results found in schizophrenia, in which diminished brain responses to unattended emotional faces were also reported (Csukly, Stefanics, Komlósi, Czigler, & Czobor, 2013). It has also been suggested that vMMN can serve as the neural indicator of affective reactivity in autism spectrum disorder, given that vMMN responses to unattended emotional faces showed a correlation with Autism-Spectrum Quotient scores (Gayle, Gal, & Kieffaber, 2012). However, in **Study I**, no correlation between the M300 amplitude and BDI-II was found. The lack of correlation could be due to the small sample size applied in this study. An alternative explanation could be that the M300 alteration in my study reflects more of the trait-dependent factors in depression rather than state-dependent factors of depression.

Beyond the findings related to dysphoria in M300, **Study I** also revealed the pre-attentive deviance detection and emotion processing that conforms to the entire participant group. Standard and deviant faces elicited a differential response (i.e., vMMN) also in the early stages of face processing, in the latency range of M100 and M170 peaks. My study is in line with prior EEG and MEG studies in which vMMN to facial expression was also elicited at the P1 time window (Susac et al., 2010) and N170 or P2 time window (Astikainen & Hietanen, 2009; Chang et al., 2010; L. Zhao & Li, 2006). Although the deviance-related responses occurred in all three time windows and were modulated by stimulus rarity, the underlying mechanisms behind these responses and the functional significance they manifested could be different. For example, P1/M100 has been suggested to reflect the encoding and categorization of the structure of the face, and N170/M170 seems to reflect both emotional modulation and face structure (e.g., J. Liu, Harris, & Kanwisher, 2002; Susac et al., 2010). However, because I cannot separate the effects of rareness from these face-related components in the current results, it remains unclear whether the vMMN shown here was reflecting special visual or face-related processing (i.e., P1, N170, and P2/P250) or the rareness processing as such. As far as I know, only one previous study used independent component analysis to directly address this question and separated the vMMN and N170 components within the time window of 100–200 ms (Astikainen et al., 2013). However, neither that study (Astikainen et al., 2013) nor other prior studies examined vMMN in relation to the functional independence of other components' responses, such as P1/M100 or P2/P250/M300.

Notably, **Study II** was not designed to determine whether the vMMN responses reflected a prediction error signal (i.e., the genuine vMMN). Therefore, it is limited in separating the effects of neural adaptation and prediction error signals. However, pictures of several male and female models were used in this study, and the face identity successively appearing in the same location was always different, which avoided the interference of adaptation from low-level visual features of a particular face. One previous study addressed this adaptation issue directly by presenting an immediate repetition of an emotional expression as a deviant stimulus (i.e., inserting a sudden repetition of a face in a sequence of alternating happy and fearful faces; Kimura, Kondo, Ohira, & Schröger, 2012). This stimulus condition allowed for observation of neural responses to regularity violations, and they found that prediction error related signals were elicited 250 ms after the stimulus onset. Therefore, the first two stages (M100 and M170) in my study may reflect neural adaptation to repeatedly presented standard stimuli, while the later M300 response may reflect a genuine vMMN. However, this assumption needs to be further confirmed in future studies.

The effect of emotion was found in the second stage (M170) of face processing. The N170 ERP component has been posited to index a structural encoding of faces (Bentin, Allison, Puce, Perez, & McCarthy, 1996). However, it remains controversial whether this response is modulated by facial expressions (e.g., Batty & Taylor, 2003; Miyoshi, Katayama, & Morotomi, 2004) or not (e.g., Eimer & Holmes, 2002; Holmes, Vuilleumier, & Eimer, 2003). In **Study II**, sad faces induced greater responses than happy faces at a right temporal ROI, which demonstrates an emotional modulation in the M170 response. This result is also in line with previous studies showing different response amplitudes for happy and sad faces (Chen et al., 2014; Lynn & Salisbury, 2008; L. Zhao & Li, 2006). It is noteworthy, however, that while there was no emotion × group interaction effect, nearly half of our participants had depression symptoms, which might have affected the results. Previous studies have found a smaller N170 response in depressed participants as compared to healthy controls (Dai & Feng, 2011), which suggests that depression may also alter the N170/M170 responses. In addition, even in healthy participants, sad faces elicited a larger vMMN than happy faces (L. Zhao & Li, 2006), but because that study also used deviant faces that were emotional and standard faces that were always neutral, it is possible that the modulation found for N170 contained the effects of both emotion processing and deviance detection. It has been contested in prior literature whether the N170 is sensitive to emotion and if it is modulated by attention (for a review, see Hinojosa, 2015). However, **Study II** and a similar study conducted by Stefanics et al. (2012) suggest that N170 can be elicited without the involvement of attention and is modulated by facial expressions.

Study II is limited in its explanation of source localization. Due to the lack of individual MRI data and in order to have a better comparison with the results from Stefanics et al. (2012), I restricted analysis to the sensor level. The ROI selected in this study was also based on the control participants, who served as the reference group in this study for comparison with the dysphoric group. Future studies should further investigate potential differences in the source localization of dysphoric and control groups, especially for M300. Furthermore, it is possible that some existing effects were not observable with the relatively small sample size used in this study, which warrants replication of the study with larger participant groups. It is also worth mentioning that the dysphoric group had depressive symptoms during the measurement (scores of 13 or higher measured with the BDI-II), and nearly all of them (9 out of 10 participants) had a diagnosis of depression. However, the diagnoses were not confirmed at the start of this study. Therefore, future studies should further explore potential source localization in clinical depression and in patients with different subtypes.

4.3 Change detection in somatosensory modality: Differences in processing of unpredictable and predictable stimuli

In **Study III**, a novel stimulus protocol was introduced in which a frequently presented somatosensory stimulus (FRE) was occasionally replaced by two consecutively presented and equally rare stimuli (UR and PR) that differed in predictability. This design allowed for testing whether brain responses reflected a prediction error, as suggested by predictive coding theory, or only rareness (probability of presentation) of the stimulus. The results reflected two main components, M55 and M150, for each stimulus type: the FRE, UR, and PR stimuli. Sensor-level analyses showed that for both components, activity was greater in amplitude for the UR and PR than the FRE. Furthermore, M55, but not M150, had a larger response amplitude to the UR than the PR. The results of the source-level results are in line with this, showing that a greater response for UR than PR was found only in M55, not in M150, although both UR and PR were larger than FRE in both time windows. Furthermore, in line with our hypothesis, the source-level results are most pronounced in the contralateral somatosensory areas (i.e., cSI and cSII).

The time frames were consistent with previous studies (e.g., Akatsuka et al., 2005; Hautasaari et al., 2019; Shinozaki et al., 1998) showing that electrical stimulation of the fingers induced mainly two components, one at 30–100 ms latency, and the other at 130–230 ms latency. Spatiotemporal cluster-based permutation tests were used to investigate sensor-level effects in a data-driven manner. Visual observation of the sensor-level signal and the sensor cluster contrasts between the stimulus types suggest that M55 showed a right-lateralized response (contralateral to stimulation). Both rare stimuli (UR and PR) elicited a significantly greater response than FRE, and these responses were larger for UR than PR. This pattern may represent a prediction error signal. M150 also seems to be right-lateralized, and greater responses were elicited by both rare stimuli than by FRE. But unlike M55, M150 showed no statistically significant cluster for the UR versus PR contrast. This finding is surprising because some previous studies linked the later response (between 100–200 ms post-stimulus), but not the earlier one, to prediction error signals (sMMN/sMMR; e.g., Akatsuka et al., 2005; Hautasaari et al., 2019; Kekoni et al., 1997; Shinozaki et al., 1998; Strömmer et al., 2014, 2017). In contrast, my data, which controlled for the rareness of the unpredictable and predictable stimuli, dissociates this later component from prediction error because UR and PR elicited similar responses.

These findings were supported and further enlightened by the source-level analyses, which showed that the rare electrical stimulation, as compared to the FRE, induced greater responses before 100 ms (M55, 30–100 ms after stimulus onset) and between 100–200 ms (M150, 130–230 ms after stimulus onset), involving the activity of both the SI and SII areas. However, a greater response was observed for UR than for PR only with M55, whereas no difference was found in the response amplitudes between UR and PR for M150. Although there is some variation in whether activity is identified from SI, SII, or both, previous studies have primarily localized deviance detection related responses in SI and/or SII with the oddball condition. For instance, studies that applied the source localization method for sMMR suggest that the early component originated from the SI, while the later component originated from the SII (Akatsuka, Wasaka, Nakata, Kida, Hoshiyama, et al., 2007; Akatsuka, Wasaka, Nakata, Kida, & Kakigi, 2007). Also, the posterior parietal cortex (PPC) and areas 1 and 3b in the SI were linked to deviance detection at approximately 50–120 ms after stimulus onset. Deviance detection related activity was also found on the bilateral SII cortex in a few participants (Yamashiro et al., 2014). Both the electrical and tactile stimuli also elicited SI activation for an early response within 40–58 ms and a later response (110–185 ms) in the SII area (Hautasaari et al., 2019). Simultaneous SI and SII responses, rather than a strictly hierarchical or serial approach, have also been found as early as 20–30 ms (Karhu & Tesche, 1999), suggesting that the SI and SII could process somatosensory stimuli in a parallel manner. Taken together with the results from **Study III**, the available evidence suggests that both the SI and SII could contribute to deviance detection and are possibly linked to the prediction error.

The main finding of **Study III** is that the results suggest that M55, but not M150, may signal the prediction error. Thus, the results raised questions regarding the interpretation of previous studies indicating that the responses to sMMR at a 100–200 ms latency reflected a prediction error. For example, several studies have also found larger responses to deviant stimuli than to standard stimuli at an early latency (within the 100 ms post-stimulus latency; Akatsuka et al., 2005; Hautasaari et al., 2019; Kekoni et al., 1997; Shinozaki et al., 1998; Strömmer et al., 2014, 2017). However, most of those studies did not consider the early response to be analogous to sMMR. It is notable that previous studies have not directly compared the activity to predictable and unpredictable rare stimuli with the same probability. Therefore, the differential response at 100–200 ms found in these previous studies (Akatsuka et al., 2005; Akatsuka, Wasaka, Nakata, Kida, Hoshiyama, et al., 2007; Akatsuka, Wasaka, Nakata, Kida, & Kakigi, 2007; Hautasaari et al., 2019; Mima, Nagamine, Nakamura, & Shibasaki, 1998; Shinozaki et al., 1998; Strömmer et al., 2014, 2017) may possibly have merely reflected the rareness of the deviant stimulus, while the earlier responses before 100 ms could reflect a prediction error. Consistent with this assumption, previous studies that used the global/local oddball paradigm (a paradigm that contains two temporal regularities and thus can confirm the hierarchical processing of the predictive coding framework) also found a prediction error related response peaking at 70–100 ms over the posterior bank of postcentral sulcus (Naeije et al., 2016, 2018). Recordings of local field potentials in the somatosensory cortex of rabbits also revealed similar and even earlier latencies (i.e., 20–40 ms and 80–100 ms) for somatosensory deviance detection processing (Astikainen, Ruusuvirta, & Korhonen, 2001). Similarly, results from the auditory modality have also supported this idea. For example, the auditory middle latency responses (MLRs) elicited within 50 ms following stimulus onset have been studied in the context of a predictive coding framework (e.g., Althen et al., 2011; Grimm et al., 2011; Recasens et al., 2014) and are suggested to be correlated to stimulus-specific adaptation (Grimm, Escera, & Nelken, 2016).

Study III highlighted the need to control stimulus rareness or disentangle stimulus rareness and predictability in future studies. However, it is limited in its interpretation regarding M55 because of the effect of low-level features.

Therefore, a control condition C was conducted with small subsamples, and the results suggest that the differences in low-level physical features were probably not the only reason for the greater responses to the UR than FRE in the larger sample. Future studies using both single-cell and neural network level recordings are needed to understand whether the early latency brain responses (e.g., the M55 reported here and MLRs) in the somatosensory and auditory modalities have functional similarities and to further explore the underlying mechanism behind the early component.

4.4 General discussion

This dissertation investigated change detection from a general view and the detection of deviance stimuli that violate certain regularities based on repetition. Various influencing factors of change detection are discussed in both fields. Specifically, by comparing the results from the visual search and change detection tasks, **Study I** reviewed the contradictory results on emotional bias and proposed some potential factors that could have led to the contradictory results on positive or negative bias. **Study II** investigated the deviance detection of emotional faces in both dysphoric and healthy individuals. In **Study III**, the deviance detection in the somatosensory modality was examined in healthy participants using a novel paradigm that allows for responses to be compared to stimuli presented with the same probability when their predictability is manipulated.

In general, although both research traditions of change detection have been widely studied using the same term, the paradigm used and possibly the underlying mechanisms for these cognitions are separate. The former have mainly used behavioral approaches to explore change detection in the context of attention and VWM. While the CDA component has sometimes been recorded in the context of change detection tasks, it is widely used in VWM studies as an indicator of VWM performance rather than focusing on the change detection process per se. Conversely, the research community of deviance detection has mainly focused on brain signals such as EEG/MEG activities. In principle, the change detection task mentioned in this dissertation is similar to the equiprobability control condition applied for the oddball tasks, with standard and deviant stimuli both presented as a 50% probability. However, the relationships between the two types of change detection and the mechanisms behind them need to be further explored.

For both types of change detection, the physical features of the stimuli and the adaptation of the experimental procedures should be carefully controlled. As I discussed in **Study I**, the visual salience and stimulus arousal per se could affect visual search and change detection tasks. This also applies to the oddball condition, where the MMN is obtained by calculating the difference in the responses elicited by the two kinds of stimuli. Therefore, the stimuli's physical differences in oddball tasks can affect not only responses to emotional stimuli but also deviance-related responses. This dissertation provides a way to separate the emotion-related responses from the responses that reflect deviance detection (i.e., comparing responses to deviant and standard stimuli of the same emotion, which is possible when the two stimuli are applied as both standard and deviant stimuli in two stimuli series). However, it is still difficult to disentangle responses to emotional and physical feature processing for emotional faces. Furthermore, both the pre-attentive and attentive change detection processes require further confirmation that emotional information in faces is actually processed. Therefore, in emotional face processing, it is important to introduce a control condition (e.g., using inverted faces, scrambled faces, or other better-controlled faces in physical features).

Another methodological issue that merits further consideration is distinguishing a rareness-related effect from a prediction error. In addition to the somatosensory modality stressed in **Study III**, it is equally important when exploring the deviance detection of emotional faces and in the visual and auditory modality in general. Although some studies have employed certain control conditions (e.g., equiprobability condition; Astikainen et al., 2013; Kovarski et al., 2017) to study facial expressions related vMMN, existing studies (in both the somatosensory modality and in studies of facial expression) are few in number. The underlying mechanisms and roles of different emotional stimulus types (e.g., different facial or body expressions) and sensory stimuli (e.g., non-painful and painful stimuli) need to be further explored in future studies.

Finally, by moving beyond these methodological challenges, both types of change detection have potential value in their applications. For the deviance detection related studies, it has been well documented that the MMN could serve as a neural marker for some mental disorders, such as schizophrenia and depression (Ruohonen, 2020; Ruohonen et al., 2020; Toshihiko, Shogo, & Toshiaki, 2013). However, the utilization of sMMR and vMMN (especially with emotional stimuli) is still limited in clinical populations (for a review, see Kremláček et al., 2016). Emotional stimuli such as the emotional faces could be potential markers for some mental disorders, such as social phobia or autism. sMMR, on the other hand, has been suggested as a potential clinical tool, especially for certain developmental disorders in which somatosensory discrimination impairment plays a role (e.g., developmental coordination disorder and autism; Näätänen, 2009).

Conversely, change detection tasks have recently been used and validated to improve direct change detection performance as well as the quantity and quality of VWM (Buschkuehl, Jaeggi, Mueller, Shah, & Jonides, 2017; Moriya, 2019). Both of these aspects have significance. For the improvement of change detection ability, as indicated by many studies, experts in specific fields will be more sensitive to changes in the relevant domain (e.g., drivers showed better performance in detecting changes in driving-related situations; football players showed better performance in detecting changes in football images, e.g., Gaspar, Neider, Simons, McCarley, & Kramer, 2013; Werner & Thies, 2000; N. Zhao et al., 2014). Therefore, the change detection task could be a low-cost training method for special occupations such as air traffic controller. As for the enhancement of VWM, the change detection task has its own benefit because it can be specifically used to improve VWM capacity and targeting in the processing of multiple memory items (Buschkuehl et al., 2017). In summary, by refining the influencing factors addressed in this dissertation, both tasks could have further clinical applications and help researchers gain a better understanding of human emotional face and somatosensory processing.

YHTEENVETO (SUMMARY)

Muutoksen havaitseminen ympäröivässä maailmassa: Tuloksia näkö- ja tuntojärjestelmän aivovastemittauksista

Aivan ihmiskunnan historian alusta saakka me ihmiset olemme eläneet monimutkaisessa ympäristössä. Kyky tutkia ympäristöä ja havaita muutoksia siinä on elintärkeä selviytymiselle. Ottaen huomioon muutoksen havaitsemisen tärkeyden, ei ole yllättävää, että sitä on tutkittu laajasti. Tutkimusta on tehty lähinnä kahdessa traditiossa. Toinen tutkii muutoksen havaitsemista lähinnä näköjärjestelmässä tilanteessa, jossa kaksi toisistaan hieman poikkeavaa kuvaa esitetään vuorotellen. Tällaisen muutoksen havaitsemisen on yleensä ajateltu vaativan tarkkaavuutta ja visuaalista työmuistia. Toinen taas tutkii poikkeavien ärsykkeiden havaitsemista tilanteessa, jossa toistuva ärsyke muodostaa jonkin säännönmukaisuuden. Tällaisen muutoksen havaitsemisen on ajateltu olevan riippumatonta tarkkaavuudesta. Aivojen sähköinen jännitevaste nimeltään poikkeavuusnegatiivisuus (engl. mismatch negativity) voidaan mitata vasteena sarjassa esiintyvään poikkeavaan ärsykkeeseen. Viime aikoina poikkeavan ärsykkeen havaitseminen ja poikkeavuusnegatiivisuusvaste on yhdistetty ennakoivan koodaamisen teoriaan. Vaikkakin poikkeavan ärsykkeen havaitsemista on tutkittu laajasti kuulojärjestelmässä, ilmiötä ei tunneta yhtä hyvin näkö- ja tuntojärjestelmässä.

Tässä väitöskirjatyössä tein ensinnäkin katsauksen kirjallisuuteen, jossa on tutkittu tarkkailtua muutoksen havaitsemista kasvoärsykkeissä. Toiseksi tutkin empiirisesti ei-tarkkailtua muutoksen havaitsemista sarjallisesti esitetyissä kasvoissa, joissa vaihteli kasvon ilme. Masentuneiden ja ei-masentuneiden tutkittavien aivovasteita vertailtiin. Kolmanneksi selvitin tuntoärsykkeiden esitietoista muutoksen havaitsemista ja erityisesti ärsykkeen ennustettavuuden vaikutusta aivovasteisiin.

Osatutkimuksessa I tein kirjallisuuskatsauksen aiempaan ristiriitaiseen tutkimustietoon negatiivisesta ja positiivisesta tarkkaillun tiedonkäsittelyn vääristymästä liittyen tunnepitoisiin kasvoihin. Käyttäytymis- ja aivovastetutkimukset, joissa käytettiin visuaalisen etsinnän ja tarkkaillun muutoksen havaitsemisen tehtäviä, otettiin mukaan katsaukseen. Katsaukseen perustuen ehdotan, että kolme tekijää saattavat vaikuttaa siihen, että aiemmat tulokset ovat olleet ristiriitaisia havaintovääristymiin liittyen: ärsykevalinta, kokeellinen tilanne ja tutkittavana oleva kognitiivinen alaprosessi. Katsauksessa ehdotan myös uusia tutkimussuuntia ja ohjeita tulevaisuuden tutkimuksiin.

Osatutkimuksessa II selvitin magneettiaivokäyrämittauksin esitietoista muutoksen havaitsemista kasvonilmeissä masentuneilla ja ei-masentuneilla tutkittavilla. Poikkeavuusnegatiivisuusvaste ilmeni muutoksiin periferiassa esitettyihin kasvokuviin kaikissa kasvojen prosessointivaiheissa (aivovastekomponentit M100, M170, M300) ilmentäen automaattista muutoksen havaitsemista. M170 vasteen amplitudi muuntui kasvonilmeen mukaan, siten että vaste oli suurempi surullisiin kuin iloisiin kasvoihin. Ryhmäeroja löydettiin

M300 vasteessa. Masennusryhmässä vaste oli amplitudiltaan suurempi surullisiin kuin iloisiin poikkeaviin kasvoihin vasemman takaraivolohkon alueella ilmentäen negatiivista vääristymää, jota ei havaittu ei-masentuneilla kontrolleilla. Toisaalta masennusryhmällä ei havaittu poikkeavuusnegatiivisuutta, mikä ilmeni kontrolliryhmällä oikealla takaraivonlohkolla. Aivovasteet siis ilmentävät esitietoista muutoksen havaitsemista tunnepitoisissa kasvoissa kontrolleilla, mutta masentuneilla sama toiminto on heikentynyt ja siinä on heillä myös negatiivinen vääristymä surullisiin kasvoihin.

Osatutkimuksessa III magneettiaivokäyrämittausta käytettiin tutkimaan aivovasteita ennustettaviin ja ennustamattomiin tuntoärsykkeisiin. Otin käyttöön uudenlaisen ärsykejärjestelyn, jossa sormiin esitetyn toistuvan tuntoärsykkeen korvasi välillä kaksi peräkkäin esitettyä harvinaista ärsykettä (ärsytys toisiin sormiin), jotka erosivat toisistaan ennakoitavuuden suhteen. Tämä asetelma mahdollisti selvittää ilmentävätkö aivovasteet poikkeaviin ärsykkeisiin ennakointivirhettä, kuten ennakoivan koodaamisen teoria esittää, vai pelkästään ärsykkeen harvinaisuutta (esittämistodennäköisyyttä). Kaksi pääasiallista aivovastetta löytyi kaikkiin ärsyketyyppeihin: M55 ja M150. Näiden vasteiden lähteet paikantuivat aivojen tuntoaivokuorelle. Sekä sensori- että lähdetason analyysit osoittivat, että molemmat aivovasteet olivat amplitudiltaan suurempia harvoin esitettyihin kuin toistuviin ärsykkeisiin. M55-vaste oli kuitenkin suurempi ennakoimattomiin kuin ennakoitavissa oleviin harvinaisiin ärsykkeisiin. Samanlaista eroa ei havaittu M150 vasteen kohdalla. Nämä tulokset viittaavat siihen, että M55 ilmentää ennakoimisvirhettä, mutta M150 liittyisi ärsykkeen harvinaisuuteen. Tulokset tuovat myös esiin tarpeen kontrolloida ärsykkeen esitystodennäköisyys tai pyrkiä erottamaan ärsykkeen harvinaisuuteen ja ennakoitavuuteen liittyvät vaikutukset tulevissa tutkimuksissa.

Tämä väitöskirjatyö tuo yhteen kaksi melko erillistä, mutta toisiinsa kytkeytyvää muutoksen havaitsemisen tutkimusaluetta. Muutoksen havaitsemiseen liittyvän katsauksen lisäksi tämä väitöskirja tarjoaa empiiristä tietoa muutoksen havaitsemisesta näkö- ja tuntojärjestelmissä ja tarjoaa ehdotuksia jatkotutkimukseen. Jatkotutkimuksen tulee kiinnittää huomiota esimerkiksi ärsykkeiden valintaan ja koeasetelmallisiin kysymyksiin. Yksilöllisiä eroja, joita tässä tutkimuksessa selvitettiin masennusoireisiin liittyen, tulisi myös laajemmin tutkia muutoksen havaitsemisen yhteydessä.

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ORIGINAL PAPERS

I

NEGATIVE AND POSITIVE BIAS FOR EMOTIONAL FACES: EVIDENCE FROM THE ATTENTION AND WORKING MEMORY PARADIGMS

by

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Review Article

Negative and Positive Bias for Emotional Faces: Evidence from the Attention and Working Memory Paradigms

Qianru Xu,[1,2] **Chaoxiong Ye**,[1,2] **Simeng Gu**,[1,3] **Zhonghua Hu**,[1] **Yi Lei**,[1] **Xueyan Li**,[4] **Lihui Huang**,[5] **and Qiang Liu**[1]

[1]*Institute of Brain and Psychological Sciences, Sichuan Normal University, Chengdu, China*
[2]*Department of Psychology, University of Jyvaskyla, Jyväskylä, Finland*
[3]*Department of Medical Psychology, Jiangsu University Medical School, Zhenjiang, China*
[4]*School of Foreign Languages, Dalian University of Technology, Dalian, China*
[5]*Faculty of Education, Sichuan Normal University, Chengdu, China*

Correspondence should be addressed to Chaoxiong Ye; cxye1988@163.com

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Visual attention and visual working memory (VWM) are two major cognitive functions in humans, and they have much in common. A growing body of research has investigated the effect of emotional information on visual attention and VWM. Interestingly, contradictory findings have supported both a negative bias and a positive bias toward emotional faces (e.g., angry faces or happy faces) in the attention and VWM fields. We found that the classical paradigms—that is, the visual search paradigm in attention and the change detection paradigm in VWM—are considerably similar. The settings of these paradigms could therefore be responsible for the contradictory results. In this paper, we compare previous controversial results from behavioral and neuroscience studies using these two paradigms. We suggest three possible contributing factors that have significant impacts on the contradictory conclusions regarding different emotional bias effects; these factors are stimulus choice, experimental setting, and cognitive process. We also propose new research directions and guidelines for future studies.

1. Introduction

In the processing of visual information, attention and memory are two cognitive processes that play pivotal roles in human life, and they are extremely important aspects of psychology and cognitive neuroscience research. Previously, however, these two topics have been studied separately; for example, memory studies have not tended to explore the effect of selective attention on memory encoding, while attention studies have often neglected the consequence of past experience [1]. In recent years, a growing body of research has begun to explicitly link visual attention to visual working memory (VWM, which could also be called "visual short-term memory," VSTM). These studies have reached a broad consensus that attention and VWM are intimately linked [2–4]. This consensus is unsurprising, given that the definitions of "attention" and "VWM" already overlap significantly.

As defined by Olivers et al. [2], visual attention describes a process during which individuals select relevant information and ignore irrelevant information. By contrast, VWM describes the process during which individuals temporarily retain relevant information and suppress irrelevant information. In addition to the similarity of their definitions, the visual attention and VWM processes may have many overlapping mechanisms, such as the activation of many similar brain regions (e.g., the supplementary motor area and frontal eye fields, the lateral prefrontal cortex, the anterior cingulate, the superior and inferior parietal cortex, and the occipital area) and a similar capacity limitation (for about four units or chunks), as well as similar control processes (for a review, see [3]). Therefore, exploring the relationship between visual attention and VWM is highly significant for obtaining a better understanding of basic human cognition [5–11].

Emotional processing, another major cognitive function for humans, has attracted considerable interest in both the visual attention and VWM fields. Regarding visual attention, many studies have examined attentional bias toward emotional stimuli, which can be further divided into negative bias and positive bias (for negative bias, see [12–15]; for positive bias, see [16–18]; for reviews, see [19, 20]). (The phenomenon of negative and positive bias has been studied extensively using a variety of emotional materials, such as faces, scenes, and words [19, 21]. However, we mainly focus in this paper on previous studies that have used emotional faces for the following reasons. First, humans are experts in assessing faces [22]. Compared to other stimuli, faces more easily attract visual attention, and they are more likely to be stored in the human VWM than other complex stimuli [23]. Second, the same facial identity can reflect different types of emotions with little physical difference between the emotions, while other emotional stimulus materials (e.g., different emotional scenes) differ greatly in physical features between emotions [24]. Finally, due to the short history of researching VWM as such [25, 26], the study of the emotional bias effect on VWM began only decades ago, mostly using emotional faces as materials [27–29].) “Negative bias” refers to the processing advantage of negative stimuli (e.g., angry, fearful, sad, or disgusted faces) over positive stimuli (i.e., happy faces); conversely, a “positive bias” refers to the preference for positive stimuli (i.e., happy faces) in emotional processing [19, 21]. Interestingly, VWM studies have revealed a similar phenomenon, finding both negative and positive advantages to VWM performance (for negative bias, see [27, 28, 30, 31]; for positive bias, see [32–34]). These controversial results are derived mainly from two kinds of paradigms, namely, the *visual search paradigm* in visual attention studies and the *change detection paradigm* in VWM studies. Some previous review papers have discussed the contradictory findings of previous visual attention studies (e.g., [19, 20, 35–37]). However, to our knowledge, no studies have yet combined the findings of visual attention studies with those of VWM studies to discuss the possible factors that have contributed to their contradictory outcomes. Therefore, in this paper, we conduct a literature review on previous studies that have investigated the different emotional bias effects in (a) visual attention studies using the visual search paradigm and (b) VWM studies using the change detection paradigm. Our purposes in conducting this work are to list the distinct behavioral and neural levels of evidence, to discuss the possible reasons behind the existing controversial results, and to provide new guidelines and suggestions for future emotional bias studies.

2. Controversial Results in Different Expressions

2.1. Behavior and Neural Evidence with Different Emotional Faces in the Visual Search Paradigm

2.1.1. Negative Bias. With their use of a visual search paradigm, Hansen and Hansen [12] first found an attentional bias toward angry faces presented as black-and-white photographs, with the bias reflected in a shorter response time (RT) and a lower error rate for angry faces versus happy and neutral faces (see Figure 1 for an illustration of the stimulus conditions; see Supplementary Materials for more detailed introduction of this paradigm and frequently used behavioral and neural indexes). However, this result soon met with challenges from other studies because of the extraneous dark areas in Hansen and Hansen’s black-and-white stimuli [38]. Nevertheless, even with better control of the stimuli, some follow-up studies still found an attentional bias toward angry faces (e.g., [15, 39, 40]). In addition to angry faces, fearful faces (commonly referred to as “threatening faces”—together with angry faces) have been suggested to have a similar automatic attention capture as angry faces [39]. Indeed, a fearful face seems even easier to detect than an angry face [41]. The attentional bias toward angry and fearful faces, taken together, has been called the “threat superiority effect.” This threatening bias is more widely validated by schematic face studies (e.g., [13, 42, 43]) than by studies using photographs of real faces. However, some studies have suggested that the attentional bias toward threatening faces in schematic experiments was actually an attentional bias to sad faces because the participants were more likely to label the corresponding stimulus material as “sad faces” [13].

In addition to behavioral studies, studies using other techniques have also supported the threat superiority effect. Using the eye tracking technique—which allows for relatively direct and continuous measurement of overt visual attention—a previous study using schematic faces found that, in the context of neutral faces, participants took a longer time and more fixations to fixate on the emotional face target if it was a positive face versus a negative face [44]. Another study using photographs found that participants fixated on more distractors before first fixating on a happy face target compared to an angry face target [45]. The use of electroencephalogram (EEG) technology in previous studies confirmed that angry face targets induced earlier and greater N2pc (N2-posterior-contralateral) than did happy face targets [46]. An enhanced contralateral delay activity (CDA) (also known as sustained posterior contralateral negativity [SPCN]) then indicated that angry faces might involve more subsequent processing than was required for happy faces. Moreover, lateralized early posterior negativity (EPN) showed that angry faces already induced greater negativity than happy faces at 160 ms, indicating early threat-relevant information processing.

2.1.2. Positive Bias. Although early research found evidence supporting the bias toward happy faces, this phenomenon has not received sufficient attention. Most studies tended to regard it as a perceptual confounder rather than an emotional factor (see, e.g., [16]). However, further accumulation of relevant evidence [17, 18, 47–49] has renewed interest in this phenomenon. For example, Becker et al. [18] used photographs and realistic computer-graphic faces to control all the confounding variables that have arisen in previous attentional bias studies, and they found no support for efficiently detecting angry faces; however, they did find a robust positive bias effect across seven experiments. They suggested that the

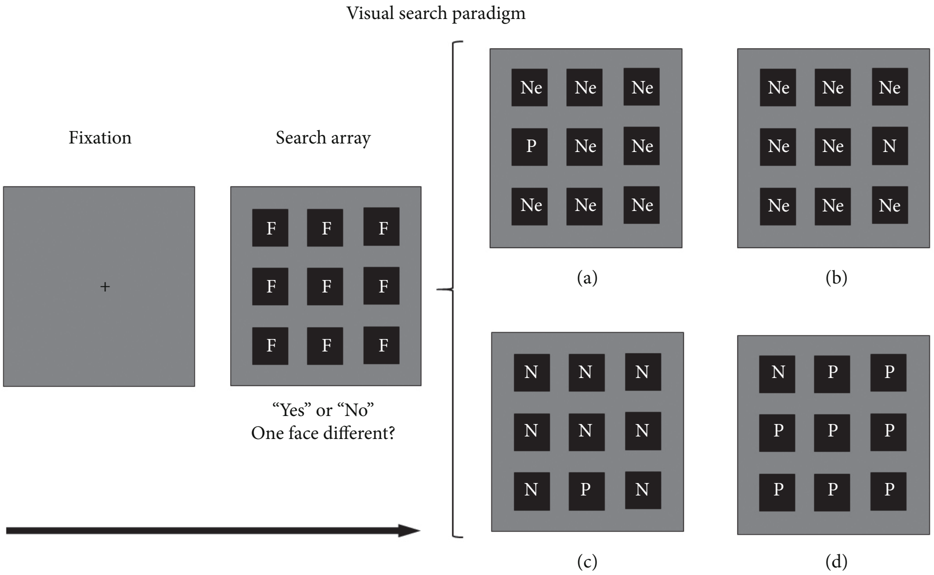

Figure 1: Illustration of a visual search paradigm. Participants needed to detect whether one face differed from the other faces. The letter F denotes a face in the search array. Usually, in half of the trials, all faces show the same expression, while in the other half of the trials, one face shows a different expression from the other faces. The trials containing different kinds of expressions (as presented in panels (a)–(d)) have usually occurred in four versions: (a) one positive face with a neutral face background (P: positive face; Ne: neutral face); (b) one negative face with a neutral face background (N: negative face; Ne: neutral face); (c) one positive face with a negative background (P: positive face; N: negative face); (d) one negative face with a positive background (N: negative face; P: positive face). Note that the set size in each search array can differ across studies. Negative face: angry, fearful, sad, or disgusted expression face; positive face: happy expression face; neutral face: neutral expression face.

positive bias in their studies could not be attributed to low-level visual confounders [18]. Unlike the negative bias, which yielded a robust effect with schematic stimuli, little evidence supported the positive bias with schematic faces [19]. Only one study showed a positive bias when the distractors were changed to a heterogeneous (i.e., using different identities in the search array) background instead of a homogenous (i.e., using the same identity in the search array) background [50].

Similarly, several other neuroscience studies have supported the positive bias. For example, studies using the eye-tracking technique have provided evidence for an attentional bias toward happy faces. Calvo et al. [48], in their study, showed that happy targets were detected faster than any other expressions (e.g., surprised, disgusted, fearful, angry, or sad). Conversely, and in contrast to previous studies [44, 45], angry faces were detected more slowly and less accurately than were happy, surprised, disgusted, and fearful faces [48]. However, compared to studies on the search advantage of angry faces, fewer EEG studies have supported a bias toward happy faces, which only indirect evidence has implied. For example, one study [51] suggested that the widely used stimuli in previous studies (e.g., happy and angry faces) are not equal in biological relevance to observers. Therefore, the authors used baby faces as positive stimuli and compared the results with angry adult faces (as negative stimuli) in an attention task. Their results indicated that positive and negative stimuli induced similar modulations in P1 amplitude and with corresponding topography and source localization, suggesting that both positive and negative stimuli have similar advantages in capturing attention at the neural level [51].

2.2. Behavior and Neuroscience Evidence with Different Emotional Faces in the Change Detection Paradigm

2.2.1. Negative Bias. Using the change detection paradigm (see Figure 2 for an illustration of the stimulus conditions; see Supplementary Materials for more detailed introduction of this paradigm and frequently used behavioral and neural indexes), Jackson et al. [27] first examined how expression and identity interact with one another (face identity was task relevant while expression was task irrelevant). Their results consistently showed enhanced VWM performance with different set sizes, durations, and face sets. With schematic faces, other researchers limited the cognitive resources by manipulating the encoding time and set size, and they found better memory performance for angry faces with short exposure time (150 ms) and a large set size of stimuli (five items) [52]. Similarly, researchers found that participants could better maintain fearful faces in VWM than they could retain neutral faces [30, 53]. Research has also shown enhanced VWM storage for fearful faces compared to neutral faces [30, 54].

The use of EEG confirmed that threatening faces (both fearful and angry faces) showed an enhanced N170 response and higher theta power compared to both positive faces (very happy and somewhat happy faces) and neutral faces, both at the encoding stage and at the early maintenance interval after

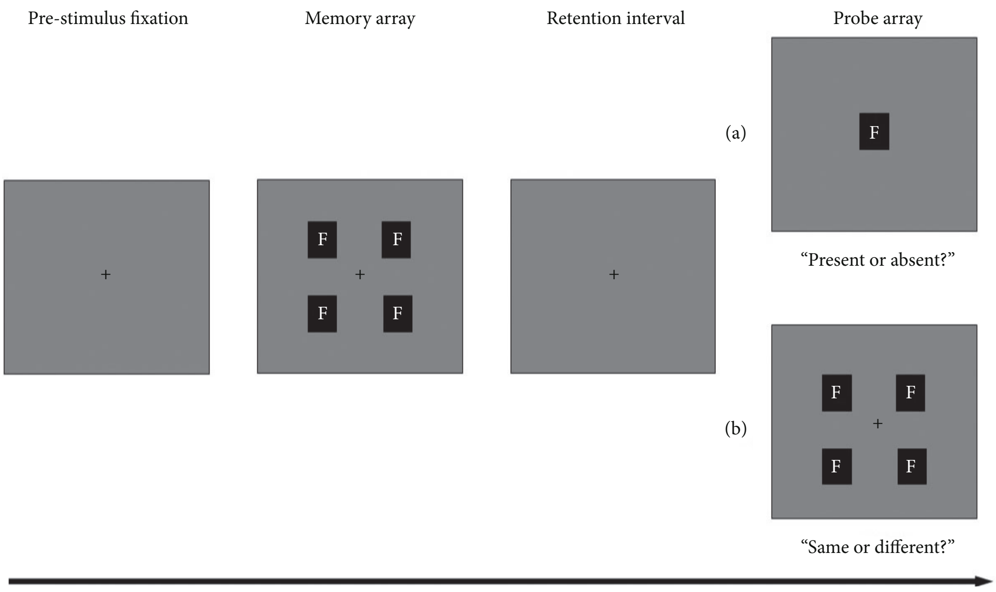

FIGURE 2: Two versions of the change detection paradigm. Participants need to detect (a) whether the single probe is present or absent in the memory array or (b) whether the probe array is identical to the memory array or one of the faces has changed. The letter F denotes a face, which can be emotional (positive or negative) or neutral in different studies. Note that the set size in the search array can differ across studies. Negative face: angry, fearful, sad, or disgusted expression face; positive face: happy expression face; neutral face: neutral expression face.

the memory array disappeared [55]. Sessa et al. [30] found that fearful faces showed an enhanced CDA compared to neutral faces, which suggested an increased maintenance for a fearful face in VWM than for a neutral face. With a similar experimental setting as their own study, Jackson et al. [28] found the results of functional magnetic resonance imaging (fMRI) supported a benefit of angry faces in the change detection paradigm. Compared to happy and neutral faces, angry faces significantly enhanced blood oxygen level-dependent responses—particularly in three areas of the right hemisphere: the prefrontal cortex, the superior temporal sulcus, and the globus pallidus internus [28].

2.2.2. Positive Bias. Although initial studies have generally reported a negative bias in VWM, the happy face benefit (or threatening face cost) has appeared in recent studies [32–34, 53, 56]. One study that used photographs [53] found superior memory sensitivity for fearful faces but also for happy faces compared to neutral faces. Interestingly, by manipulating memory array and encoding time, Curby et al. [34] found worse VWM performance for fearful faces than for neutral and happy faces, which suggested a fearful face cost in VWM compared to happy and neutral faces. The addition of location information to the change detection paradigm also revealed that the relocation accuracy for happy faces was significantly enhanced compared to angry faces [33]. Studies using schematic faces have also found that, although no memory differences occurred between different emotional faces (approach-oriented positive faces versus avoid-oriented negative faces), high-capacity participants tended to maintain more positive (e.g., happy) than negative (e.g., sad/angry) faces, and this was reflected in a significant correlation between affective bias and the participants' VWM capacity [32].

However, as with the attention studies, the positive advantage in VWM has found less support from neuroscientific evidence. Compared to happy faces, sad faces tend to significantly attenuate facial identity recognition, a finding supported by the exhibited components of N170, N250, P3b, vertex positive potential, and late positive potential [57]. This finding can be partially verified by the overall emotional advantage effect. For example, using the EEG technique, researchers examined the event-related potential (ERP) components of P1, N170, P3b, and N250r in a VWM task [58]. Their results showed that none of these ERP components were modulated by emotional faces during the encoding stage. During maintenance, a decreased early P3b and increased N250r for emotional faces were observed when compared to neutral faces, but no difference in ERP components was apparent between positive and negative faces.

Overall, the development processes and evidence patterns of the change detection paradigm and visual search paradigm are quite similar. The findings of a negative bias have a relatively longer history and greater support from empirical research using cognitive neuroscience techniques. By contrast, the findings of a positive bias have mostly resulted from recent behavioral studies with better control over the potential confounding variables. However, scant neuroscience evidence has supported the positive bias for either the attentional or the VWM studies.

3. Possible Contributing Factors for Emotional Bias

The findings above show that both attention and VWM studies have revealed some controversial results regarding emotional bias. Some studies have discussed and listed several potential contributors for the emotional bias in attention (e.g., [19, 20, 35, 36]). However, to the best of our knowledge, no study has summarized the positive and negative face advantages in VWM. Therefore, we have summarized and listed these advantages in Supplementary Table 1 (including 20 papers with 36 experiments), especially regarding the adoption of the change detection paradigm [27, 28, 30–34, 52, 53, 55–65]. Based on the table summarized by previous studies on visual attention (see [18] for a summary of the visual search paradigm; see [19] for more general methods) and our table for VWM (see Supplementary Material Table 1), we found some common factors responsible for the contradictions in these two areas—especially for studies using the visual search and change detection paradigms. Below, we discuss these possible contributing factors separately, using three aspects: stimulus choice, experimental setting, and cognitive process.

3.1. Differences in Stimulus Choice. In both visual search and change detection paradigm, the experimental materials used for different studies often differ. Previous controversial results could therefore simply reflect the different choices in stimulus materials.

3.1.1. Schematic Faces versus Real Faces. Both photographs of real faces and schematic faces are widely used stimuli in the visual search and change detection paradigms. However, a more consistent negative bias occurs with schematic faces, while photographs of real faces show more evidence of a positive bias for visual attention (for reviews, see [19, 37]). Thus, the choice of stimulus (schematic or real faces) used in an experiment is crucial. Similarly, in the field of VWM, as we mentioned in the previous section, different studies using different stimuli have yielded different results.

For visual attention, a schematic face undoubtedly allows for better control of physical features than can be achieved with photographs. However, the representative expressions of a schematic face are limited, and they lack ecological validity. Thus, schematic faces have been criticized for presenting differences in the perceived configuration of the stimulus itself, rather than reflecting a direct response to emotions [66–68]. For example, some researchers have emphasized that the attentional bias toward angry faces in the visual search paradigm using schematic faces resulted from perceptual grouping, in which participants perceived happy faces as a group more easily than angry faces; therefore, angry faces were more salient when happy faces served as distractors [68]. Photographs of real faces are more ecologically valid; however, the results differ significantly for visual search studies. Previous studies have even found different results based on individual differences and different stimulus sets as the materials in the visual search paradigm [69]. Moreover, when using photographs, various settings of the eyes and mouth may be potential influencing factors. For example, emotional bias can be obtained from the eye characteristics alone (for bias toward angry faces, see [70]; for bias toward happy faces, see [18]). Whether the teeth are exposed also leads to different results as well [71]. However, these factors undeniably also serve as the major composition of the expression per se; thus, one cannot entirely attribute this controversy to perceptual differences, especially for photographs.

Similarly, in the change detection paradigm, the results for schematic faces have also tended to favor either a negative bias or an overall affective bias, which may also relate to problems that we mentioned earlier in attention studies. Different studies using photographs have used various sets of stimulus materials (see Supplementary Table 1). For example, the series of experiments by Jackson et al. [27] used the Ekman set [72] and the Karolinska Directed Emotional Faces (KDEF) database [73], while the materials used by Curby et al. [34] were a collection of four stimulus databases (the NimStim database [74], the KDEF database [73], the CVL Face Database [75], and the Radboud Faces Database [76]). These variations in stimulus materials from different studies complicate any direct comparison of the two effects. Besides, the stimuli used in previous studies did not rule out the effect of some subtle issues that we mentioned above, such as potential influences from the eyes or mouth regions. Although we cannot conclude that different results are due to the use of different stimuli (e.g., the study by Jackson et al. [27] validated an angry face advantage in both image databases), neither can we completely reject the possibility that different memory advantages are irrelevant to the choice of stimulus material.

3.1.2. Stimulus Arousal. "Stimulus arousal" refers to the intensity of metabolic and neural activations of the independent or coactive appetitive or aversive system [77]. Arousal, combined with emotional valence and dominance, has been suggested as a universal, three-dimensional conceptualization of the emotional stimuli [78] in which arousal and valence are culture-free, accounting for major proportion variance in emotional judgment [79, 80]. Reasonably, then, a fair comparison of different expressions requires similar fundamental parameters used in different stimuli. We have found controversial results in previous studies using faces with different emotional valences (i.e., negative and positive biases). Thus, we suggest that stimulus arousal may, in part, be considered responsible for these past results.

A recent meta-analysis of attention studies found a larger negative bias effect for high-arousal scenic or verbal emotional stimuli than for low-arousal stimuli [21]. Although this meta-analysis did not include the factor of face stimuli, other studies have suggested that the degree of arousal also affects the processing of different expressions [81]. For example, in the study by Lundqvist et al. [81], the authors reanalyzed their previous studies (e.g., [16, 82, 83]) and found that the degree of arousal from a picture was highly correlated with the participants' response as the direction of their corresponding superiority effect. At the same time, the researchers asked the participants to rescore the degree of arousal to the photographic stimuli widely used in the visual search research, and they predicted attentional bias based on the arousal score collected from the original stimulus set. The predicted result ultimately fit well with previous studies [81]. Thus, these findings suggest that the contradiction between negative and positive bias in the visual search paradigm is based on the degree of arousal in response to picture stimulation.

No VWM studies have directly investigated the effect of emotional arousal on memory bias toward positive or negative faces. However, although lacking a direct comparison to emotional arousal between happy and angry faces, one study found that different intensities of angry expressions evoked different CDA amplitudes [61]. Specifically, full expressions had a higher amplitude than both subtle (intermediate intensity angry face, morphed from the continuum between neutral and intense angry face) and neutral expressions, while neutral faces had a higher amplitude than subtle expressions, suggesting that different intensities of emotional faces may affect VWM [61]. Studies have also suggested a reduced overall working memory performance when people need to memorize several high-arousal stimuli simultaneously [84]. Taken together, these results indicate that arousal could at least partly affect VWM performance. However, not all previous studies have measured and controlled for a stimulus's arousal level (see Supplementary Table 1; e.g., [55, 56]), and variations exist in the definition of arousal across different studies, i.e., some studies used intensity as their index (e.g., [34]) while others used arousal (e.g., [58]).

In brief, the choice of stimulus material, as well as stimulus arousal, affects the results of both the visual search and the change detection paradigms. However, some studies have used similar materials and obtained different results (e.g., both used schematic faces or photographs but obtained different results), suggesting that differences in stimulus material choices are not the only reason for the inconsistent results. Thus, differences in experimental settings can also account for some variance in results. We further discuss this issue below.

3.2. Differences in Experimental Settings. The visual search and change detection are different paradigms; however, several aspects in the experimental settings are similar and affect the experimental results for both paradigms. We next discuss the possible experimental settings that may affect the results of the emotional bias from three main perspectives.

3.2.1. Visual Display Size and Corresponding Time. In both the visual search and change detection paradigms, the visual display set size is an essential index concerning behavioral results, such as the search slope (the function of RT and display set size) in the visual search paradigm and number of VWM representations in the change detection paradigm. Thus, both the display set size and the amount of time given to participants to process the task matter.

Previous attention studies have shown that varying the time settings can lead to differences in the composition of an individual's attention [85]. Using an attention task, researchers have found that a probed stimulus presentation time of 100 ms accompanies an attentional bias toward negative stimuli (such as angry faces in an angry–neutral stimuli pair and neutral faces in a neutral–happy stimuli pair), and this trend was reversed when the presentation time was extended to 500 ms [86]. Although this hypothesis may not explain all the previous studies on the visual search paradigm, the time setting seems to affect the results of emotional bias. For example, in studies supporting a negative bias, participants have usually needed to respond in a limited time [15, 42]. However, in studies supporting a positive bias, participants have usually not had specific time limits for their responses. These trials ended when participants pressed a button (e.g., [16, 17]) or when the interval time was much longer than participants needed (e.g., 10 s in [18] or 30 s in [71]).

VWM studies have found more direct evidence supporting the effect of display size and corresponding time. For example, one study found that high perceptual processing competition (e.g., 150 ms exposure time for encoding) revealed an emotional face advantage (i.e., both happy and angry faces had an advantage over neutral faces). By contrast, an angry face advantage emerged when the competition between stimuli was further increased by increasing the stimulus set size [52]. Furthermore, with the same set size of five, a previous study found a VWM performance cost for fearful faces compared to neutral faces, but only with a longer encoding duration (4,000 ms), as it showed no differences with a shorter encoding duration (1,000 ms [34]: Experiment 1 and Experiment 2). Consistently, the advantage of happy faces compared to angry and fearful faces has also been extractable from a long encoding time condition (4,000 ms [34]: Experiment 4a). These results suggest that the emotional bias in VWM may be affected by the set size and stimulus exposure time of memory array. However, we should note that as the processing time of a single stimulus reduces or extends, the VWM representations might risk being confounded with representations of perception or long-term memory.

3.2.2. The Manner of Stimulus Presentation. The visual search is a very context-dependent process; therefore, discussions of targets should not be isolated from those of background stimuli. This concept is also true for the process of the change detection paradigm in which multiple stimuli are usually presented simultaneously, rather than sequentially. Consequently, differences in the manner of the stimulus presentation for the target and the distractor or background stimuli may also contribute to variations in the results on emotional bias.

For example, the presentation of happy and angry faces in the same visual search array could result in different processing speeds for distractors instead of targets [13, 87]. This hypothesis is mainly applicable to situations where opposite emotions are used as the distractors. For example, one study set a homogenous condition in which all stimuli were presented with the same emotional face. The authors found that participants responded more slowly to all-negative faces than to all-positive and neutral faces [13]. From this point of view, the faster processing of angry target stimuli can be explained by the faster processing of happy distractor stimuli, whereas the slower perception of happy target stimuli can be explained by the degree to which negative faces cause attentional difficulties in attention disengagement from the distractors. Thus, the different setting in distractors may ultimately result in processing differences for both types of target stimuli. In addition, the use of heterogeneous or homogenous identities as a background can also lead to different results. For example, while previous schematic faces had yielded more consistent results for a negative bias, a positive bias emerged when a heterogeneous background was used [50]. However, this phenomenon does not fully explain the results obtained with photographs because some studies with a heterogeneous background showed a positive bias [16, 18], while others showed a negative bias [40, 45].

The effect of the manner of presentation may be generalized to the findings of VWM studies. Previous studies can be roughly divided into two kinds of settings in terms of stimulus presentation, namely, different identities with the same expression [27, 28] and the same identity with a different expression [52, 56]. Although these settings do not appear to directly cause different results, differences in stimulus presentation have occurred across studies despite the use of a similar experimental paradigm. In addition, the change detection paradigm typically involves two stimulus arrays, a "memory array" and a "probe array." The patterns of both arrays affect the experimental results, and the results may also be influenced by the visual search process itself—either at the memory array or the probe array. Besides memory maintenance, memory filtering is another essential aspect of studying VWM. The manipulation of fearful and neutral faces as targets or distractors in a change detection task has revealed in previous studies that—in general—fearful faces are more challenging to filter than are neutral faces, thereby reflecting a larger CDA amplitude in the fearful-distractor-with-neutral-target condition [54]. Follow-up behavioral and fMRI studies found similar result patterns [88, 89]. Ye et al. [90], who used the CDA component, found that participants with high VWM capacity were able to filter all the facial distractors from VWM, regardless of their expression, while low-capacity participants failed to filter the neutral and angry faces but efficiently filtered happy faces. In addition, a follow-up study used a similar paradigm and found that participants in the personal relative deprivation group failed to filter out neutral or angry facial distractors but succeeded in filtering out happy facial distractors from VWM [91]. All these studies suggest that the expression types of stimuli modulate both storage and distractor filtering in VWM. From this point of view, the use of the same or different emotional faces in a memory array could also lead to different results.

3.2.3. Differing Demands in Experiments. Another important aspect in experimental settings relates to the observers. We human beings, as subjective animals with our own thoughts, may also be indirectly affected by how experimenters provide instructions and by our own understanding of an experiment. As Supplementary Table 1 shows, although the paradigm remains basically the same, the participants' task can be further divided (e.g., detect whether identity is present or absent, detect whether identity is the same or different, detect whether the expression is the same or different, and detect whether the probe is the same or different). Therefore, the demands placed by the experiment and the participants' own strategies in understanding the task instructions could partially affect the results of emotional bias.

Previous studies using a visual search have suggested employing a fixed target to avoid the discrepancies caused by different strategies across participants. That is, the specific target would be given an emotion (e.g., happy face) at the beginning of the task, and the participants were then asked to constantly search for this target emotion across trials [35]. Although this type of control reduces the variation in subjects' own search strategies, we argue that it also makes the search task more difficult to distinguish from the recognition task. Unlike the controversial results on the visual search, which require a rapid but less in-depth process, expression recognition studies have more consistently supported positive bias [37]. Most of the previous visual search studies supporting negative bias also did not specify the target stimulus before conducting their experiments with participants [12, 13, 43]. On the contrary, studies in favor of positive bias have often asked participants to find target stimuli for specific emotions (i.e., they used a fixed target [16, 18, 47]). These results also raise concerns that some of the positive bias findings might be confounded with the interference of face recognition.

A similar impact from experiment instruction can also occur in VWM studies using the change detection paradigm. For example, the information that participants were required to remember has differed across studies (see column 8 in Supplementary Table 1). Some studies have regarded emotional information as a form of task-independent information [27, 28, 30, 34], while others have regarded the expression as task-related information [31, 32, 52]. Although this setup difference may not directly explain the observed discrepancy, a deeper processing of emotional information seems to be more likely to trigger positive bias. For example, in a relocated task [33], or when a longer encoding time was provided [34], the happy face advantage emerged in VWM.

These results suggest that different experimental settings may involve different cognitive resources. Therefore, by moving beyond these methodological challenges, a more likely explanation for the conflicting results of previous studies is that negative bias and positive bias act at different cognitive stages.

3.3. Different Stages in the Cognitive Process. In both the visual search and the change detection paradigms, the participants must finish several cognitive processes to accomplish their whole task. In attention research, the process of the visual search paradigm has, conventionally, contained at least two distinct but interrelated stages: the preattentive stage and the attentive or postattentive stage. The preattentive stage occurs before the attentional selection of a target stimulus. In this stage, the process does not require attentional allocation to the stimulus, whereas the attentive or postattentive process involves the direct focus on a target stimulus [92]. Calvo et al. [48], who used eye movement techniques, proposed a third stage of visual search for emotional faces called "decision efficiency." The decision efficiency stage occurs immediately before decision-making, as the varying decision times between fixing the gaze on the target stimulus and making a choice have shown for different emotional faces

[48]. For VWM studies, the change detection paradigm process comprises four stages: the encoding stage, the consolidation stage, the maintenance stage, and the retrieval stage [93]. The encoding stage in VWM overlaps with the processes in attention research, during which, perception representations are created and then consolidated into VWM representations during the consolidation stage. After the stimulus disappears, the participants need to "maintain" VWM representations and then "retrieve" them in subsequent tasks to complete the whole cognitive process of VWM. In addition, the VWM consolidation comprises two different stages [94–96]. In the early consolidation stage, individuals automatically create low-precision representations. Subsequently, in the late consolidation stage, individuals can voluntarily create high-precision representations.

For visual search studies, one possibility is that an automatic bias toward negative emotions exists in the early preattentive stage, whereas the positive bias is revealed in the later recognition and/or decision-making stages. Consistent with this point of view, the use of an emotion classification task combined with the EEG technique has revealed that N170, in the early stage, showed a higher response to negative faces—such as angry, fearful, and sad faces. By contrast, happy faces tended to correlate with facilitation in categorization (reflected by P3b) and decision-making (reflected by a slow positive wave in the later stage) [97]. LeDoux [98] concluded from animal model studies that the fear response could comprise two pathways. In the subcortical pathway, information is sent rapidly and directly to the amygdala. By contrast, in the cortical path, information is sent to the cortex for subsequent analysis before reaching the amygdala. Therefore, the subcortical pathway activates the amygdala in advance and enables a ready state for fearful information. Thus, once information on the cortical path is transmitted to the amygdala, the individual can respond immediately. Therefore, the amygdala can combine limited information for a rough but rapid assessment of threat stimulation at the early stage. This first stage of quick evaluation is likely the neural mechanism that produces the superiority effect of threat stimuli (angry and fearful faces). However, other emotional information (i.e., a happy face) may reach the cortical path with more comprehensive processing. Studies have confirmed that although happy faces can also activate the amygdala, the effect is mainly observed at the later stimulus presentation time [99]. On the contrary, Becker and Rheem [36] have an opposite view and suggest that threatening faces are privileged at a later stage because of the difficulty of attention disengagement. For either order, however, future studies will need to separate the different stages, as this may help to shed light on the real reasons for the discrepancies in previous results.

Similarly, for VWM studies, although memory usually requires more in-depth processing of task-related information, different emotional information could also affect VWM at different processing stages. For example, different expressions did not show any effect at the encoding stage, but emotional faces (both angry and happy) showed a greater resource allocation at the maintenance stage [58]. Information with different emotional valences also influences VWM via different neural bases [100]. More importantly, previous studies have not been able to dissociate attention from VWM. Therefore, whether attention or VWM is responsible for this discrepancy is difficult to discern.

In conclusion, after controlling for the effects of stimulus materials and experimental procedures, further delineation of different cognitive processing stages may be an effective way to resolve previous conflicts.

4. Summary and Prospects

In this paper, we have mainly considered studies on attention and VWM using different emotional faces, and we have proposed three possible factors that could explain the mixed results of the previous studies. A recent study by Becker and Rheem [36] listed five necessary points of guidance for future researchers who use the visual search paradigm to study expressions. (Extracted from the conclusion of Searching for a Face in the Crowd: Pitfalls and Unexplored Possibilities ([36], p. 635). "(a) Vary the crowd size so that search slopes can be assessed. (b) Account for the speed with which distractors are rejected by considering the target-absent search rates or ensure that all of the distractor arrays are equivalent. (c) Ensure that participants are processing the stimulus signal of interest rather than low-level features that are correlated with this signal. (d) Vary the distractors and targets in ways that keep participants from learning to use any low-level features to complete the task. (e) Jitter the positions of the items in the crowds so that textural gestalts cannot be exploited.") In addition to their guidance, we offer several other suggestions for addressing the problems common to both the visual search paradigm and the change detection paradigm. We first discuss the limitations and recommendations of the existing paradigms related to the visual search and change detection paradigms in order to minimize discrepancies. We then propose some possible directions for future research.

4.1. The Choice of Emotional Stimuli. Above all, in studies of change detection and visual search, researchers need to be more careful in the selection of stimulus materials, especially regarding the control of low-level physical features and stimuli's arousal. The degree of arousal resulting from the stimulus itself should be defined (e.g., distinguish between arousal and intensity) and evaluated comprehensively. Collecting the participants' own arousal evaluations for each experimental stimulus within the study is also important since arousal as such is subjective. We offer three other suggestions for the selection of emotional stimuli.

First, future research should pay more attention to the selection of photographs and schematic faces. Therefore, more advanced technology for further control of facial expression—for example, using computer-generated techniques to create human-like pictures [101]—is needed in future work. The application of dynamic facial expressions, as well as body expressions, also offers possible directions for future exploration [40, 102, 103].

First, future research should pay more attention to the selection of photographs and schematic faces in terms of physical features. Therefore, more advanced technology or accurate way for further control of physical features—for example, using computer-generated techniques to create human-like pictures [101]—is needed in future work. In addition, the application of dynamic facial expressions, as well as body expressions, also offers possible directions that future research should explore [18, 102, 103].

Second, both attention and VWM studies have considered the use of neutral faces as a baseline setting for comparison with emotional faces. However, neutral faces are more likely to be perceived as negative than positive [19]. This tendency may lead to imbalance in a search array or the encoding stage of a memory array. The use of fearful and angry faces for the threat effect should also be interpreted with caution. Although fearful and angry faces have usually been classified into the same category as threatening faces by previous studies (e.g., [13, 42, 43]), they actually contain different information. The threat source of anger is basically the face per se, while fear serves as a reminder of the threat in the viewer's environment [34, 104]. Therefore, future studies should discuss fearful and angry faces separately, rather than simply categorizing both of them as threatening stimuli.

Third, since emotional faces (e.g., angry faces) are already a source of emotional information per se, another question that future studies should address is whether the currently available results are due to emotional states triggered by expression stimuli. The answer to this question may be negative, mainly because emotional induction usually takes time and needs to remain relatively stable. In typical visual search and change detection paradigms, different emotional faces (positive and negative) often randomly appear in the same trial or in adjacent trials, which can create difficulty for the participants to form a stable emotional state. Thus, emotional states should not be the main cause of the previous controversial studies. However, this suggestion does not negate the effects of emotional states on an individual's processing of attentional or memory tasks. Indeed, previous studies have shown that emotional states or mental illnesses (e.g., depression, anxiety, and worry) can affect attention and VWM [64, 65, 88, 105–109]. However, knowledge is currently limited regarding the influence of emotional states on the results of the visual search or change detection paradigms that use emotional face stimuli. This area should therefore be explored further in future research.

4.2. Standardization of the Experimental Setting. Based on our summary, the experimental settings for both paradigms evidently require further standardization. For example, when testing different visual matrix sizes, future studies should also consider the timing of the stimulus presentation and explore the effects of different combinations of stimulus set sizes and times for both paradigms. The experimental instructions should also be carefully controlled to prevent the involvement of unnecessary cognitive processes.

Most previous studies have used the visual search paradigm and change detection paradigm to investigate emotional face processing in attention and VWM; however, some other paradigms can investigate similar topics in these fields. For example, in the field of attention, the dot-probe paradigm [86], rapid serial visual presentation task (RSVP) [110], and visual crowding paradigm [111] can also explore attentional bias to emotional faces. Similar contradictory results have also been found for emotional bias in studies using the RSVP paradigm (for negative bias, see [112]; for positive bias, see [113]). Some studies have even suggested that VWM and the attentional blink observed in the RSVP paradigm might share the same neural processing and storage capacity mechanisms [52, 114]. In the VWM field, the N-back task [115] is also an appropriate paradigm for testing emotional bias. A growing body of research has used N-back tasks or other tasks to explore the potential differential impact of emotional faces versus neutral faces (for a review, see [116]). Thus, future research should examine whether paradigm types modulate emotional bias in attention and VWM. Likewise, many of the issues mentioned in this paper (e.g., selection of stimulus materials) are applicable to other attention or VWM studies.

4.3. Controlling and Tracking Cognitive Processes. Future studies also need to explore the causes of the positive and negative biases underlying different cognitive processes. This exploration will require that future studies define and divide the different processing stages in corresponding paradigms. Future studies can succeed in this regard by combining traditional behavioral indicators with other neuroscience techniques. Specifically, they can combine different ERP indicators (e.g., N2pc in visual attention studies and CDA in VWM studies) or combine EEG with eye movements to generate fixation-based ERPs [117].

In VWM studies, both attention and memory play vital roles; therefore, different emotional advantages may already exist in the attention process rather than in the memory process. This makes determining whether attention or memory processes caused the mixed results from VWM studies in emotional advantages rather difficult. Future studies can try to separate the attention-related process from the VWM-related process when exploring emotional face advantages in VWM. Alternatively, future studies could include attention and VWM in the same context (e.g., using similar stimuli and experimental settings) and examine the associations between visual attention and VWM. For example, previous study showed a high correlation between the reciprocals of VWM capacity and the visual search slope with line-drawing objects [118]. Therefore, a joint study of these two paradigms could be a feasible alternative to better study the role that attention serves in the emotional bias of VWM.

5. Conclusion

This review of the literature supports the view that the mixed results from previous studies could have been arisen due to differences in stimuli, experimental settings, and processing stages at the neural level. The empirical research and the theoretical background indicate that both negative and positive biases are likely. However, if we eliminate the influence of the stimulus materials and experimental settings, a more likely explanation would be that both biases occur but in different cognitive stages. Researchers should adapt more comparable and well-designed paradigms to provide new evidence of positive and negative bias for emotional faces in future studies. A combination of neuroscience techniques and advanced data analysis should be also applied to this field to provide a better understanding of the mechanism behind the advantage effect of different expressions. We believe that the adoption of these suggestions will help to settle the controversy of positive/negative emotional bias in visual attention and VWM.

Conflicts of Interest

There is no interest conflict among the authors.

Authors' Contributions

QX and CY developed the concept of the review. QX wrote the first draft of the manuscript. CY supervised the review and assisted in paper revision. QL, SG, LY, HZ, XL and LH provided critical revisions. All authors read and approved the submitted version.

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Supplementary Materials

Supplementary Material 1 summarizes the paradigms and measures used in visual search and change detection paradigm. Supplementary Table 1 lists the key setups and results in previous VWM studies, especially on the adoption of the change detection paradigm. *(Supplementary materials)*

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Supplementary Material

Negative and Positive Bias for Emotional Faces: Evidence from the Attention and Working Memory Paradigms

Qianru Xu[1,2], Chaoxiong Ye[1,2]*, Simeng Gu[1,3], Zhonghua Hu[1], Yi Lei[1], Xueyan Li[4], Lihui Huang[5], Qiang Liu[1]

1 Institute of Brain and Psychological Sciences, Sichuan Normal University, Chengdu, China;
2 Department of Psychology, University of Jyvaskyla, Jyväskylä, Finland;
3 Department of Medical Psychology, Medical School in Jiangsu University, Zhenjiang, China;
4 School of Foreign Languages, Dalian University of Technology, Dalian, China;
5 Faculty of Education, Sichuan Normal University, Chengdu, China;

*** Correspondence to:**

Chaoxiong Ye, Ph.D.
Institute of Brain and Psychological Sciences,
Sichuan Normal University, Chengdu, 610000, China
Email: cxye1988@163.com

Paradigms and Measures Used in Visual Search and Change Detection Paradigm

The visual search paradigm (also called the “face in the crowd paradigm” when using faces as stimuli) mimics the process of detecting target objects or people from multifarious information of everyday lives [1,2]. In a classic visual search paradigm experiment (see Figure 1 in the main text), each trial contained a face array, and half of the trials contained a target stimulus (i.e., one face showed different expressions than the other faces) while the other half of the trials did not contain a target stimulus (i.e., all the faces showed the same expression). Participants are asked to detect whether a face presented different expressions from the other faces. For the analysis of results, the reaction time (RT), accuracy rate (ACC), error rate, and search slope (the function of RT and set size) are behavioral indices to evaluate participants' efficiency in detecting the search target. The shallower the search slope of a target stimulus, the more efficient the search. Moreover, the search slope can also indicate whether the processing method uses a parallel or serial search approach [2]. In addition to the behavioral index, Luck and Hillyard [3] found an event-related potentials (ERPs) component called N2-posterior-contralateral (N2pc) which has been commonly used by recent studies as an indicator to track the visual selective attention process. N2pc is mainly distributed in the posterior-contralateral electrodes, appearing 200–300 ms after stimulus presentation (for a review, see [4]). The latency of the N2pc indicates the time point at which attention focused on the target item, while amplitude can reflect the amount of attention on the target [4,5]. Additionally, several other ERP components—such as N170, early posterior negativity (EPN), and late positive potential (LPP)—have usually been used to indicate emotional processing in visual attention tasks (for a review, see [6]).

VWM research on emotional bias has widely used the change detection paradigm. This paradigm (also called the “visual short-term memory task” [see [7]] or the “match-to-sample probe recognition task” [see [8]]) generally comprises four parts: pre-stimulus fixation, memory array, retention interval, and probe array (see Figure 2 in the main text). Typically, in half of the related trials, the probe array and memory array are exactly the same, and in the other half of the trials, one of the memory items in the probe array differs from the memory array, and the participant's task is to detect whether or not a change has occurred. Generally, the change detection paradigm asks participants to temporarily store the memory array across a blank delay period and then compare the memory array with the probe array. Accuracy, Cowan's K[1] [9], and *d'*[2] [10], are common behavioral indicators in the change detection paradigm. Cowan's K is often used to measure individuals' VWM capacity. It is an estimated index of the number of items successfully stored in an individual's VWM. Meanwhile, *d'* is an index of VWM performance. It is obtained from the signal detection theory, representing the distance between the z-transforms of the hit rate and false alarm rate [10]. Also, researchers have identified an ERP component called

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[1] K = *set size* × (hit rate – false alarm rate).

[2] *d'* = Z(hit rate) – Z(false alarm rate).

“contralateral delay activity” (CDA, also known as “sustained posterior contralateral negativity,” SPCN; [11]) as a neural indicator of VWM maintenance. The CDA’s amplitude increases with the number of items in an individual’s VWM during the maintenance of memory material, and it reaches an asymptote once approximately three to four simple objects have been stored, reflecting the limitation of an individual’s VWM capacity [12]. In addition, N170, N250 (which usually reflects the repetition effect) and P3b (the subcomponent of P300, which is sensitive to the resource allocation process) have also been suggested to relate with VWM emotional processing (e.g., [13,14]).

Supplementary Table 1: Studies on emotional face in visual working memory (VWM) by using change detection paradigm.

Study [a]	N	Expression	Stimulus type/ Stimulus set [b]	Stimulus arousal	Set size	Encoding time (ms)	Task [d]	Behavior /Neural index	Results [e]	Comments
Becker et al. (2014)[15]: Exp. 1	64	Neutral, angry	Photograph /- [c]	-	4	10000	Detect identity present/ absent	Hit rate, false alarm rate, *d′*, bias (c)	Angry > neutral	Test gender effect
Brenner et al. (2014)[16]	29	Positive (very happy, somewhat happy), neutral, Negative (sad, fearful, and angry)	Photograph /NimStim	-	1	200	Detect expression same/ different	Acc, RT, P100, N170, N250, theta power	Negative > positive	
Curby et al. (2019)[8]: Exp. 1	40	Fearful, neutral	Photograph /NimStim, KDEF, CVL	-	5	1000/4000	Detect probe same/ different	K	1000 ms: no effect; 4000 ms: fearful < neutral	
Curby et al. (2019)[8]: Exp. 2	41	Fearful, neutral	Photograph /NimStim, KDEF, CVL	-	5	1000/4000	Detect probe same/ different	K	1000 ms: no effect; 4000 ms: fearful < neutral	Also test inverted face
Curby et al. (2019)[8]: Exp. 3	82	Fearful, neutral	Photograph /NimStim, KDEF, CVL	-	2,4,6	4000	Detect probe same/ different	K	Fearful < neutral	Test emotional state, and attentional control

Study [a]	N	Expression	Stimulus type/ Stimulus set [b]	Stimulus arousal	Set size	Encoding time (ms)	Task [d]	Behavior /Neural index	Results [e]	Comments
Curby et al. (2019)[8]: Exp. 4a	42	Neutral, happy, fearful, angry	Photograph /Radboud	Happy = fearful; fearful ≠ angry; happy ≠ angry	5	4000	Detect probe same/ different	K	Fearful, angry < happy	
Jackson et al. (2008)[17]	35	Angry, happy, neutral	Photograph /Ekman & Friesen	Happy = angry	1,2,3,4	2000	Detect identity present/ absent	*d'*, fMRI	Angry> happy; angry> neutral	Emotion effect showed on rSTS, rPFC (IFS), and rGPi
Jackson et al. (2009)[7]: Exp. 1	24	Angry, happy, neutral	Photograph /Ekman & Friesen	-	1,2,3,4	2000	Detect identity present/ absent	*d'*, K-iterative (K_{it})	Angry > happy; angry > neutral	
Jackson et al. (2009)[7]: Exp. 2	18	Angry, happy, neutral	Photograph /Ekman & Friesen	Angry = happy	2,4	2000	Detect identity present/ absent	*d'*, K-iterative (K_{it})	Angry > happy; angry > neutral	High or low-arousal music was played during the experiment
Jackson et al. (2009)[7]: Exp. 3	26	Angry, neutral	Photograph /Ekman & Friesen	-	2,4	4000	Detect identity present/ absent	*d'*, K-iterative (K_{it})	Angry > neutral	
Jackson et al. (2009)[7]: Exp. 5	40	Angry, happy, neutral	Photograph /Ekman & Friesen, KDEF	Morphed to the same intensity	2,4	2000	Detect identity present/ absent	*d'*, K-iterative (K_{it})	Angry > happy; angry > neutral	16 participants performed with Ekman face set, 24 performed with KDEF face set

Study [a]	N	Expression	Stimulus type/ Stimulus set [b]	Stimulus arousal	Set size	Encoding time (ms)	Task [d]	Behavior /Neural index	Results [e]	Comments
Jackson et al. (2012)[18]: Exp. 1	25	Angry, happy	Photograph /Ekman & Friesen	-	2	2000	Detect identity present/ absent	*d′*, RT	Angry = happy	Intervening neutral words vs. no words during maintenance
Jackson et al. (2012)[18]: Exp. 2	27	Angry, happy	Photograph /Ekman & Friesen	-	2	2000	Detect identity present/ absent	*d′*, RT	Angry face was boosted by intervened emotional word, but happy face was not affected by it	Intervening negative, positive, or neutral words during maintenance
Jackson et al. (2014)[19]: Exp. 1	22	Angry, happy	Photograph /Ekman & Friesen	Angry= happy	1,2,3,4	2000	Detect identity present/ absent	Hits, false alarm rate, *d′*, RT	Angry > happy	Emotional faces presented at encoding phase.
Jackson et al. (2014)[19]: Exp. 2	13	Angry, happy	Photograph /Ekman & Friesen	Angry= happy	1,2,3,4	2000	Detect identity present/ absent	Hits, false alarm rate, *d′*, RT	Angry = happy	Emotional faces presented at retrieval phase
Jackson et al. (2014)[19]: Exp. 3	25	Angry, happy	Photograph /Ekman & Friesen	Angry= happy	2	2000	Detect identity present/ absent	Hits, false alarm rate, *d′*, RT	No effect of word valence for happy faces, but negative intervening word boosted angry face WM performance	Intervening a word valence categorization during maintenance
Langeslag et al. (2009)[13]	29	Angry, happy, neutral	Photograph /Ekman & Friesen	Angry= happy	1,3	2000	Detect identity present/ absent	Pr, Br, RT, P1, N170, P3b, N250r	Angry > neutral; happy > neutral	

Study [a]	**N**	**Expression**	**Stimulus type/ Stimulus set** [b]	**Stimulus arousal**	**Set size**	**Encoding time (ms)**	**Task** [d]	**Behavior /Neural index**	**Results** [e]	**Comments**
Lee and Cho (2019)[20]: Exp. 1	32	Fearful, happy, neutral	Photograph /KUFEC	Feaful: 4.2 Happy: 4.46	4	1200	Detect identity same/ different	*d′*	Fearful, neutral group > happy, neutral group; fearful > neutral; happy > neutral	Half of participants performed fearful and neutral faces, while half performed happy and neutral faces
Lee and Cho (2019)[20]: Exp. 2	32	Fearful, happy, neutral	Photograph /KUFEC	Feaful: 4.2 Happy: 4.46	4	1200 (300 ms for each face)	Detect identity same/ different	*d′*	Fearful, neutral group > happy, neutral group; fearful > neutral	Memory array stimuli presented sequentially
Lee and Cho (2019)[20]: Exp. 3	32	Fearful, happy, neutral	Photograph /KUFEC	Feaful: 4.2 Happy: 4.46	4	1200 (300 ms for each face)	Detect identity same/ different	*d′*	Fearful, neutral group = happy, neutral group; fearful > neutral	Memory array stimuli presented sequentially and a blank interval of 300 ms appeared between images

Study [a]	N	Expression	Stimulus type/ Stimulus set [b]	Stimulus arousal	Set size	Encoding time (ms)	Task [d]	Behavior /Neural index	Results [e]	Comments
Linden et al. (2011)[21]: Exp. 1	20	Angry, happy, neutral, sad, fearful	Photograph /Ekman & Friesen	Angry, fearful higher than all other condition, sad & happy > neutral	2	2000	Detect identity present/ absent	*d′*	Angry > fearful; happy > fearful; neutral > fearful	Also test 20 melancholiac depression and 20 non-melancholic depression participants, and sad face benefits showed in melancholic group
Liu et al. (2020)[14]	38	Happy, sad	Photograph /Chinese facial expression of emotion system	Happy = sad	2	2000	Detect identity present/ absent	Hits, CR, FA, RTs, *d′* N170, VPP, N250, P3b, LPP	Happy > sad	

Study [a]	N	Expression	Stimulus type/ Stimulus set [b]	Stimulus arousal	Set size	Encoding time (ms)	Task [d]	Behavior /Neural index	Results [e]	Comments
Maran et al. (2015)[22]: Exp.1	24	Angry, happy, anxious, neutral	Photograph /NimStim	No difference in perceived intensity	4	2000	Detect identity present/ absent	d'	Neutral arousing condition: angry > happy; angry > anxious; angry > neutral; happy > anxious. Negative arousing condition: equalized VWM performance for all expression	Under unpleasant/ neutral affect emotional state

Study [a]	N	Expression	Stimulus type/ Stimulus set [b]	Stimulus arousal	Set size	Encoding time (ms)	Task [d]	Behavior /Neural index	Results [e]	Comments
Maran et al. (2015)[22]: Exp.2	30	Angry, happy, anxious, neutral	Photograph /NimStim	No difference in perceived intensity	4	2000	Detect identity present/ absent	*d′*	Neutral arousing condition: angry > happy; angry > anxious; angry > neutral. Positive arousing condition: equalized VWM performance for all expression	Under pleasant/neutral affect emotional state
Sessa et al. (2011)[23]	28	Fearful, neutral	Photograph /Ekman & Friesen, KDEF	-	2,4	200	Detect identity same/ different	*d′*, K, K_{it}, RT, CDA	Fearful > neutral	
Sessa et al. (2018)[24]	29	Neutral, subtle angry, full angry	Photograph /KDEF	Morphed from neutral to full angry	2	500	Detect expression same/ different	Mean proportion of correct responses, CDA	Full angry > neutral > subtle angry	
Simione et al. (2014)[25]: Exp. 1	19	Angry, happy, neutral	Schematic face	-	4	150/400	Report the expression at the probed location	Acc	Emotion > neutral, but no difference between angry and happy	

Study [a]	**N**	**Expression**	**Stimulus type/ Stimulus set [b]**	**Stimulus arousal**	**Set size**	**Encoding time (ms)**	**Task [d]**	**Behavior /Neural index**	**Results [e]**	**Comments**
Simione et al. (2014)[25]: Exp. 2	20	Angry, happy, neutral	Schematic face	-	3,5	150	Report the expression at the probed location	Acc	Angry > neutral; angry > happy	
Spotorno et al.(2018)[26]: Exp. 1	48	Angry, happy	Photograph /Radboud	-	1,2,3,4	1500 ×set size	Drag the face to the original location	Acc, precision, swap error, oculomotor activity	Happy > angry	
Spotorno et al.(2018)[26]: Exp. 2	48	Angry, happy	Photograph /Radboud database	-	4	6000	Drag the face to the original location	Acc, precision, swap error, oculomotor activity	Happy > angry	Test the effect of the maintenance time
Švegar et al. (2013)[27]	24	Afraid, angry, disgusted, happy, neutral, sad, surprised	Photograph /AKDEF, KDEF	-	6	2000	Detect expression same/different	Percentage of correct answers; RT	Happy > all the other emotions while no difference among other emotions	
Thomas et al. (2014)[28]: Exp. 1	25	Angry, happy, neutral	Photograph /Ekman & Friesen	-	4	2000	Detect identity present/absent	d', RT	Angry > happy	Compare the uniform memory array and singleton memory array

Study [a]	N	Expression	Stimulus type/ Stimulus set [b]	Stimulus arousal	Set size	Encoding time (ms)	Task [d]	Behavior /Neural index	Results [e]	Comments
Thomas et al. (2014)[28]: Exp. 2	32	Angry, happy, neutral	Photograph /Ekman & Friesen	-	4	2000	Detect identity present/ absent	*d′*, RT, eye movement	Angry > happy	The procedure was same as the singleton condition in Exp.1, but they also monitored the eye movement here and verbal suppression was omitted.
Xie et al. (2017)[29]: Exp. 1	60	Positive set (5 happy + 1 neutral); negative set (5 sad + 1 neutral)	Schematic face	Positive = negative	4	500	Localize the changed face	K	Positive = negative; K (neutral color)> K (emotional face); higher WM capacity maintain more happy faces	WM capacity measured by color

Study [a]	N	Expression	Stimulus type/ Stimulus set [b]	Stimulus arousal	Set size	Encoding time (ms)	Task [d]	Behavior /Neural index	Results [e]	Comments
Xie et al. (2017)[29]: Exp. 2	42	Positive set (5 happy + 1 neutral); negative set (5 sad + 1 neutral)	Schematic face	Positive = negative	4	500	Localize the changed face	K	Positive = negative; K (emotional face)> K (neutral line drawing symbols); higher WM capacity maintain more happy faces	WM capacity measured by line-drawing symbols
Zhou et al. (2021)[30]	31	Happy, sad	Photograph /Chinese facial expression of emotion system	Happy = sad	2	2000	Detect identity present/absent	Hits, CR, FA, RTs, d' N170, VPP, P3b, LPP	Happy = sad	Depressed group: sad > happy

Abbreviations:
Column 1 (Study): Exp., Experiment
Column 2 (N): N, participants numbers
Column 9 (Behavior/Neural index): Acc, accuracy; RT, reaction time; d', VWM performance index, d' = Z(hit rate) – Z(false alarm rate); K, VWM capacity index, K= set size × (hit rate – false alarm rate); fMRI, functional magnetic resonance imaging; K-iterative (Kit), calculated by an iterative procedure, please see details in Jackson et al. [7]; Pr, discrimination index, Pr = hit rate – false alarm rate; Br, response bias index, Br = false alarm rate/(1-Pr), Please see more details for Pr and Br in Langeslag et al. [13]; CR, correct rejections; CDA, contralateral delay activity, also known as sustained posterior contralateral negativity, SPCN, neural index of VWM maintenance.
Column 11 (Comments): rSTS, right superior temporal sulcus; rPFC, right prefrontal cortex; IFS, inferior frontal sulcus; rGPi, right globus pallidus internus
a. The missing experiment here is due to the sub-experiment unrelated to the change detection paradigm or the main topic of this review, e.g., Experiment 2 in Becker et al. [15] is more related to race than emotional processing; Experiment 4 in Jackson et al. [7] is a discrimination task; Experiment 2 and 3 in Linden et al. [21] are emotional classification task and arousal/valance rating task, respectively.
b. We listed here both the stimulus material types (photograph or schematic face) and the stimulus set of photographs for a better comparison between different stimulus databases. The main database used in previous studies included: Ekman & Friesen set [31]; KDEF, Karolinska Directed Emotional Faces database

[32], AKDEF, Averaged Karolinska Directed Emotional Faces [33]; NimStim database [34]; CVL Face Database [35]; Radboud Face Database [36]; KUFEC, Korea University Facial Expression Collection [37]; Chinese facial expression of emotion system [38].

c. "-" means the information was not reported in the relevant publications.

d. Here we classified the tasks into four types based on what the researchers reported in relevant studies: 1) detect identity present/absent, 2) detect identity same/different, 3) detect expression same/different; 4) detect probe same/different. "Present/absent" refers to studies using multiple stimuli in the encoding array, with only one single stimulus in the central of the probe array, and the main task of the participant was to report whether or not the single probe was presented in the memory array; "Same/different" refers to studies using multiple stimuli (or single stimulus in the probe array but the face present in one of the locations from the study array rather than central space) both in the memory array and the probe array, and participants needed to indicate whether the probe array was identical to the memory array or whether one of the faces had changed. "Detect identity" refers to the expression irrelative to the study, and participants only needed to detect whether the identity had changed, whereas "Detect expression" meant that the participants needed to detect whether the expression on the probe array was identical to the memory array while the identity stayed unchanged or needed to be ignored. Additionally, "Detect probe" refers to the relevant study that did not emphasize detecting the expression or the identity but required participants to determine whether the whole probe face (both identity and expression) was identical to the memory items. In addition, a few studies have used a similar but not the classical change detection task, we decided to include those studies here for a better comparison. For those studies, we have only presented the specific tasks reported in the relevant studies without placing them in any of the above categories.

e. Only the main and most consistent results are reported here. " > " refers to the bias toward the former expression compared to the latter one; " < " refers to the bias toward the latter expression compared to the former one; " = " refers to no significant difference between the two expressions.

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II

AUTOMATIC PROCESSING OF CHANGES IN FACIAL EMOTIONS IN DYSPHORIA: A MAGNETOENCEPHALOGRAPHY STUDY

by

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Automatic Processing of Changes in Facial Emotions in Dysphoria: A Magnetoencephalography Study

Qianru Xu[1,2], Elisa M. Ruohonen[2], Chaoxiong Ye[1,2], Xueqiao Li[2], Kairi Kreegipuu[3], Gabor Stefanics[4,5], Wenbo Luo[1,6]* and Piia Astikainen[2]

[1] Research Center of Brain and Cognitive Neuroscience, Liaoning Normal University, Dalian, China, [2] Jyväskylä Centre for Interdisciplinary Brain Research, Department of Psychology, University of Jyväskylä, Jyväskylä, Finland, [3] Institute of Psychology, University of Tartu, Tartu, Estonia, [4] Translational Neuromodeling Unit, Institute for Biomedical Engineering, University of Zurich–ETH Zurich, Zurich, Switzerland, [5] Laboratory for Social and Neural Systems Research, Department of Economics, University of Zurich, Zurich, Switzerland, [6] Laboratory of Emotion and Mental Health, Chongqing University of Arts and Sciences, Chongqing, China

It is not known to what extent the automatic encoding and change detection of peripherally presented facial emotion is altered in dysphoria. The negative bias in automatic face processing in particular has rarely been studied. We used magnetoencephalography (MEG) to record automatic brain responses to happy and sad faces in dysphoric (Beck's Depression Inventory $\geq$ 13) and control participants. Stimuli were presented in a passive oddball condition, which allowed potential negative bias in dysphoria at different stages of face processing (M100, M170, and M300) and alterations of change detection (visual mismatch negativity, vMMN) to be investigated. The magnetic counterpart of the vMMN was elicited at all stages of face processing, indexing automatic deviance detection in facial emotions. The M170 amplitude was modulated by emotion, response amplitudes being larger for sad faces than happy faces. Group differences were found for the M300, and they were indexed by two different interaction effects. At the left occipital region of interest, the dysphoric group had larger amplitudes for sad than happy deviant faces, reflecting negative bias in deviance detection, which was not found in the control group. On the other hand, the dysphoric group showed no vMMN to changes in facial emotions, while the vMMN was observed in the control group at the right occipital region of interest. Our results indicate that there is a negative bias in automatic visual deviance detection, but also a general change detection deficit in dysphoria.

Keywords: automatic, change detection, dysphoria, emotional faces, magnetoencephalography

Edited by:
Xiaolin Zhou,
Peking University, China

Reviewed by:
Jan Kremláček,
Charles University, Czechia
Qinghua He,
Southwest University, China
István Czigler,
Hungarian Academy of Sciences,
Hungary

****Correspondence:***
Wenbo Luo
luowb@lnnu.edu.cn

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INTRODUCTION

Depression is a common and easily recurring disorder. Decades ago, Beck (1976) suggested that negatively biased information processing plays a role in the development and maintenance of depression. According to his theory, a dysphoric mood is maintained through attention and memory functions biased toward negative information, and these cognitive biases also expose individuals to recurrent depression (Beck, 1967, 1976).

Previous empirical studies have indeed demonstrated a negative bias in attention and memory functions in depression (Ridout et al., 2003, 2009; Linden et al., 2011; for reviews see, Mathews and Macleod, 2005; Browning et al., 2010; Delle-Vigne et al., 2014). Depressed participants have a pronounced bias toward negative stimuli as well as toward sad faces (Gotlib et al., 2004; Dai and Feng, 2012; Bistricky et al., 2014).

Brain responses, such as electroencephalography (EEG) and magnetoencephalography (MEG) responses, allow face processing to be studied in a temporally accurate manner. Previous studies have demonstrated that different evoked EEG/MEG responses reflect different stages of face perception (Bourke et al., 2010; Luo et al., 2010; Delle-Vigne et al., 2014). P1 (or P100) in event-related potentials (ERPs) and its magnetic counterpart M100 are thought to reflect the encoding of low-level stimulus features and are also modulated by emotional expressions (e.g., Batty and Taylor, 2003; Susac et al., 2010; Dai and Feng, 2012). P1 is also affected by depression: sad faces elicited greater responses than neutral and happy faces in the depressed group reflecting an attentive negative bias in depression (Dai and Feng, 2012). The following N170 component in ERPs and the magnetic M170 both index the structural encoding of faces (Bentin et al., 1996; Liu et al., 2002). This component has also shown emotional modulation in some studies (for positive results, see e.g., Batty and Taylor, 2003; Miyoshi et al., 2004; Japee et al., 2009; Wronka and Walentowska, 2011; and for negative results, see, e.g., Eimer and Holmes, 2002; Herrmann et al., 2002; Eimer et al., 2003; Holmes et al., 2003). In addition, depression alters the N170/M170: some ERP studies have found a smaller N170 response in depressed participants than in healthy controls (Dai and Feng, 2012), while others have found no such effects (Maurage et al., 2008; Foti et al., 2010; Jaworska et al., 2012). Negative bias has been reported as a higher N170 amplitude for sad faces relative to happy and neutral faces in depressed participants (Chen et al., 2014; Zhao et al., 2015). The P2 component (also labeled as P250), a positive polarity ERP response approximately at 200–320 ms in the temporo-occipital region, is followed by the N170 and reflects the encoding of emotional information (Zhao and Li, 2006; Stefanics et al., 2012; Da Silva et al., 2016). It has also a counterpart in MEG responses, sometimes labeled M220 (e.g., Itier et al., 2006; Schweinberger et al., 2007; Bayle and Taylor, 2010). In an ERP study with an emotional face intensity judgment task, depressed participants showed larger P2 amplitude for sad faces than happy and neutral ones, reflecting a negative bias in their attentive level, which was not found in the control group (Dai and Feng, 2012).

Although the negative bias in depression is well documented in settings involving sustained attention (for reviews see, Mathews and Macleod, 2005; Browning et al., 2010; Delle-Vigne et al., 2014), few studies have focused on automatic processing of emotional stimuli in depressed participants. Since our adaptive behavior relies largely on preattentive cognition (Näätänen et al., 2010), it is important to investigate emotional face processing in preattentive levels in healthy and dysphoric participants.

Studies based on the electrophysiological brain response called visual mismatch negativity (vMMN), a visual counterpart of the auditory MMN (Näätänen et al., 1978), have demonstrated that automatic change detection is altered in depression (Chang et al., 2010; Qiu et al., 2011; for a review, see Kremláček et al., 2016). vMMN is an ERP component elicited by rare "deviant" stimuli among repetitive "standard" stimuli over posterior electrode sites approximately at 100–200 ms post stimulus but also in a later latency range, up to 400 ms after the stimulus onset (e.g., Czigler et al., 2006; Astikainen et al., 2008; Stefanics et al., 2012, 2018; for a review, see Stefanics et al., 2014).

Related to depression, three studies have investigated the vMMN to changes in basic visual features (Chang et al., 2011; Qiu et al., 2011; Maekawa et al., 2013; for a review, see Kremláček et al., 2016), and one to changes in facial emotions (Chang et al., 2010). In study by Chang et al. (2010), centrally presented schematic faces were applied as stimuli (neutral faces as standard stimuli and happy and sad faces as deviant stimuli). The results showed that the early vMMN (reflecting mainly modulation of the N170 component) was reduced compared to the control group and the late vMMN (reflecting mainly modulation in P2 component) was absent in the depression group. This study thus demonstrated no negative bias, but a general deficit in the cortical change detection of facial expressions. Since in this study neutral faces were always applied as standard stimuli and emotional faces as deviant stimuli, it is unclear whether the modulations in ERPs were due to facial emotion processing as such or due to change detection in facial emotions. This applies nearly to all vMMN studies with facial expressions as the changing feature, as visual and face-sensitive components are known to be modulated by emotional expression (e.g., Batty and Taylor, 2003). This problem is particularly difficult when a neutral standard face and an emotional deviant face are used in the oddball condition, as the exogenous responses are the greatest to emotional faces (e.g., Batty and Taylor, 2003). This problem can be solved using only emotional faces in the oddball condition and analyzing the vMMN as a difference between the responses to the same facial emotion (e.g., a happy face) presented as deviant and standard stimuli (see Stefanics et al., 2012). This analysis method allows separating the vMMN, which reflects change detection, and the emotional modulation of visual and face-sensitive components.

In the present study, we investigated automatic face processing and change detection in emotional faces in two groups of participants: those with depressive symptoms (Beck's Depression Inventory $\geq$ 13; here referred to as the dysphoric group) and in gender- and age- matched never-depressed control participants. The stimuli and procedure were similar to those reported previously by Stefanics et al. (2012), but instead of happy and fearful faces, we applied happy and sad faces. We chose happy and sad faces since impairments in the processing of both of these have been in previous studies associated to depression (happy faces: Fu et al., 2007; sad faces: e.g., Bradley et al., 1997; Gollan et al., 2008), and because these facial emotions make it possible to study mood-congruent negative bias in depression. Recordings of MEG were applied, which provide excellent temporal resolution and relatively good spatial resolution; in addition, its signal is less disturbed by the skull and scalp than the EEG signal (for a review, see Baillet, 2017).

Importantly, during the stimulus presentation the participants conducted a task related to stimuli presented in the center of the screen, while at the same time, emotional faces were presented in the periphery. In most of the previous studies of unattended face processing, face stimuli have been presented in the center of the visual field (e.g., Zhao and Li, 2006; Astikainen and Hietanen, 2009), as well as in the study where depression and control groups were compared (Chang et al., 2010). Centrally presented pictures might be difficult to ignore, and in real life, we also acquire information from our visual periphery. We hypothesize that rare changes in facial emotions presented in the peripheral vision in a condition in which participants ignore the stimuli will result in amplitude modulations in responses corresponding to the vMMN. We expect that the experimental manipulation of the stimulus probability will elicit the vMMN in three time windows reflecting the three stages of facial information processing. This hypothesis is based on previous ERP studies applying the oddball condition in which amplitude modulations in P100, N170, and P2 have been found (Zhao and Li, 2006; Astikainen and Hietanen, 2009; Chang et al., 2010; Susac et al., 2010; Stefanics et al., 2012). In addition to stimulus probability effects, modulations by facial emotions are expected in the MEG counterparts of N170 and P2 (Miyoshi et al., 2004; Zhao and Li, 2006; Japee et al., 2009; Chen et al., 2014; Hinojosa et al., 2015). However, it is not clear if the first processing stage, M100, can be expected to be different in amplitude for sad and happy faces. In ERP studies, the corresponding P1 component have been modulated in amplitude for happy and fearful faces (Luo et al., 2010; Stefanics et al., 2012), but there are no previous studies contrasting sad and happy face processing in a stimulus condition comparable to the present study. Importantly, based on prior studies we expect that a group difference can be found for vMMN at the time windows for P1, N170, and P2, but it might not be specific to sad or happy faces (Chang et al., 2010). A depression-related negative bias, larger responses to sad than happy faces specifically in the dysphoric group, is also expected. Studies that have used attended stimulus conditions suggest that the negative bias is present in the two later processing stages (i.e., N170 and P2, Dai and Feng, 2012; Chen et al., 2014; Zhao et al., 2015; Dai et al., 2016; also, for a negative bias in P1, see Dai and Feng, 2012).

MATERIALS AND METHODS

Participants

Thirteen healthy participants (control group) and ten participants with self-reported depressive symptoms (dysphoric group) volunteered for the study. The participants were recruited via email lists and notice board announcements at the University of Jyväskylä and with an announcement in a local newspaper. Inclusion criteria for all participants were age between 18 and 45 years, right handedness, normal or corrected to normal vision, and no self-reported neurological disorders. Inclusion criteria for the participants in the dysphoric group were self-reported symptoms of depression (13 scores or more as measured with the BDI-II) or a recent depression diagnosis. The exclusion criteria for all participants were self-reported anamnesis of any psychiatric disorders other than depression or anxiety in the dysphoric group (such as bipolar disorder or schizophrenia) and current or previous abuse of alcohol or drugs.

All but one of the participants in the dysphoric group reported having a diagnosis of depression given by a medical doctor in Finland. According to their self-reported diagnoses, one participant had mild depression (F32.0), four had moderate depression (F32.1), one had severe depression (F32.2), two had recurrent depression with moderate episode (F33.1), and one did not remember which depression diagnosis was given. One participant reported to have a comorbid anxiety disorder, one reported a previous anxiety disorder diagnosis, and one reported a previous anxiety disorder combined with an eating disorder. They were included in the study because comorbidity with anxiety is high among depressed individuals. Because in some cases the diagnosis had been given more than 1 year ago, the current symptom level was assessed prior to the experiment with Beck's Depression Inventory (BDI-II, Beck et al., 1996).

According to the BDI-II manual, the following normative cutoffs are recommended for the interpretation of BDI-II scores: 0–13 points = minimal depression, 14–19 points = mild depression, 20–28 points = moderate depression, and 29–63 points = severe depression (Beck et al., 1996). Based on these cut-off values, there were four participants with mild depression, four participants with moderate depression, and two participants with severe depression. The BDI-II scores and demographics are reported in **Table 1**. Written informed consent was obtained from the participants before their participation. The experiment was carried out in accordance with the Declaration of Helsinki. The ethical committee of the University of Jyväskylä approved the research protocol.

Stimuli and Procedure

The visual stimuli were black and white photographs (3.7° wide × 4.9° tall) of 10 different models (five males and five females) from Pictures of Facial Affect (Ekman and Friesen, 1976). Stimuli were presented on a dark-gray background screen at a viewing distance of 100 cm. Each trial consisted of four face stimuli randomly presented at four fixed locations at the corners of an imaginary square (eccentricity, 5.37°) and a fixation cross in the center of the screen. The four faces were presented at the same time, each face showing the same emotion (either happy or sad). On each panel, two male and two female faces were presented. The duration of each stimulus was 200 ms.

An oddball condition was applied in which an inter-stimulus interval (ISI) randomly varied from 450 to 650 ms (offset to onset). The experiment consisted of four stimulus blocks in which frequent (90%; standard) stimuli were randomly interspersed with rare (10%; deviant) stimuli. In two experimental blocks, sad faces were presented frequently as standard stimuli, while happy faces were presented rarely as deviant stimuli. In the other two blocks, happy faces were presented as standard stimuli and sad faces were presented as deviant stimuli. Each block contained 450 standard stimuli and 50 deviant stimuli, and the order of the four blocks were randomized across participants.

The participants' task was to fixate to the cross in the center of the screen, ignore the emotional faces, and respond by pressing a button as soon as possible when they detected a

TABLE 1 | Characteristics of the participants.

Variable		Group	
		Dysphoric	Control
N		10	13
Mean age (SD)		25.10 (4.51)	26.69 (7.65)
Level of education[a]	2	6	6
	3	4	7
Female/male		6/4	9/4
Time of diagnosis (within 6 months/within year/over a year ago		2/2/5	
Currently on psychotropic medication		6	0
Duration of antidepressant medication less than 1 year/1 year or more		2/4	
Antidepressant type		3 SSRIs, 3 SSRIs + bupropion[b]	
With a history of psychotropic medication		4	0
Currently in psychotherapy treatment for depression		2	0
With a history of psychotherapy		4	0
Currently have psychiatric diagnoses other than depression		1[c]	0
With a history of psychiatric diagnoses other than depression		2[d]	0
Mean BDI-II score (SD) [range]		22.40 (7.26) [13–36]	2.38 (2.40) [0–7]

[a]Levels of education were coded as follows: 2 = middle level (high school or equivalent); 3 = high level (bachelor or higher degree). [b]SSRIs, selective serotonin reuptake inhibitors. [c]One of the participants also suffered from anxiety at the time of the study. [d]Two of the participants had a self-reported previous anxiety disorder, and one of them was diagnosed with anorexia in youth.

change of the cross in the screen center. The change in cross was a lengthening of its horizontal line or vertical line with a frequency of 11 changes per minute. Face and cross changes never co-occurred.

Data Acquisition

The visually evoked magnetic fields were recorded with a 306-channel whole-head system (Elekta Neuromag Oy, Helsinki, Finland) consisting of 204 planar gradiometers and 102 magnetometers in a magnetically shielded room at the MEG Laboratory, University of Jyväskylä. The empty room activity was recorded for 2 min before and after the experiment to estimate intrinsic noise levels. It was confirmed that all the magnetic materials that may distort the measurement had been removed from participants before the experiment. The locations of three anatomical landmarks (the nasion and left and right preauricular points) and five Head Position Indicator coils (HPI-coils, two on the forehead, two behind the ears, and one on the crown), as well as a number of additional points on the head were determined with an Isotrak 3D digitizer (Polhemus^{TM}, United States) before the experiment started. During the recording, participants were instructed to sit in a chair with their head inside the helmet-shaped magnetometer and their hands on a table. The vertical electro-oculogram (EOG) was recorded with bipolar electrodes, one above and one below the right eye. The horizontal EOG was recorded with bipolar electrodes placed lateral to the outer canthi of the eyes.

Data Analysis

MEG Data

First, the spatiotemporal signal space separation (tSSS) method (Taulu et al., 2005; Supek and Aine, 2014) in the MaxFilter software (Elekta-Neuromag) was used to remove the external interference from the MEG data. The MaxFilter software was also applied for head movement correction and transforming the head origin to the same position for each participant. Then, the MEG data were analyzed using the Brainstorm software (Tadel et al., 2011). Recordings were filtered offline by a band-pass filter between 0.1 and 40 Hz. To avoid potential artifacts, epochs with values exceeding $\pm 200\ \mu\mathrm{V}$ in EOG channels were rejected from the analysis. Next, eye blink and heartbeat artifacts were identified based on EOG and electrocardiographic (ECG) channels using a signal-space projection (SSP) method (Uusitalo and Ilmoniemi, 1997) and removed from the data. To compare the results more directly with the previous ERP studies and to the results of Stefanics et al. (2012) in particular, data from magnetometers were analyzed. The data were segmented into epochs from −200 ms before to 600 ms after the stimulus onset and baseline corrected to the 200 ms pre-stimulus period. Trials were averaged separately for happy standard, sad standard, happy deviant, and sad deviant stimuli for each participant, the number of accepted trials being 651 (*SD* = 13.57), 639 (*SD* = 23.45), 83 (*SD* = 3.18), and 81 (*SD* = 4.69), respectively. The percentage of accepted trials for happy and sad deviants, and happy and sad standards were 83% (*SD* = 3.18%), 81% (*SD* = 4.69%), 72% (*SD* = 1.51%), and 71% (*SD* = 2.61%), respectively. There were no group differences in the number of accepted trials (all p-values > 0.34).

The peak amplitude values for each participant, separately for each stimulus type and emotion, were measured in three time windows: 55–125 ms, 155–255 ms, and 280–350 ms post-stimulus, corresponding to the three major responses, M100, M170, and M300, found from the grand-averaged data (**Figures 1–3**). Based on prior findings (Peyk et al., 2008; Taylor et al., 2011; Stefanics et al., 2012), we defined two (M100, M300) or four (M170) regions of interest (ROIs) for the peak amplitude analysis for each response (**Figure 3**). For M100, the peak amplitudes were averaged across sensors at bilateral occipital regions (Left ROI: MEG1911, MEG1921, MEG2041; Right ROI: MEG2311, MEG2321, MEG2341). For M170, the peak amplitudes were averaged across sensors at bilateral temporal and occipital sites (Left temporal ROI: MEG1511, MEG1521, MEG1611, MEG1641, MEG1721, MEG0241; Right temporal ROI: MEG1321, MEG1331, MEG1441, MEG2421, MEG2611, MEG2641; Left occipital ROI: MEG1911, MEG1921, MEG2041; Right occipital ROI: MEG2311, MEG2321, MEG2341). For M300, the peak amplitude values were averaged across sensors at occipital sites (Right ROI: MEG1721, MEG1731, MEG1931; Left ROI: MEG2331, MEG2511, MEG2521). In addition to peak amplitudes, the peak latencies were also measured for each component from the same sensors as used in the amplitude analysis. Since two participants' data did not show M300 responses (one in control group and another in dysphoric group), they were excluded from the analysis for this response.

Behavioral Data

For the behavioral task, the analysis included hit rate and false alarm calculations. The hit rate was calculated as the ratio between button presses in a 100–2,000 ms interval after the event and the actual number of cross-changes. The false alarm rate was calculated as the ratio between button presses that were not preceded by a cross-change in a 100–2,000 ms interval before the event and the actual number of cross-changes.

Statistical Analyses

Repeated-measures analysis of variance (ANOVA) was used to analyze the reaction time and accuracy (hit rate and false alarm) for the cross-change task. A within-subjects factor Stimulus Block (Sad vs. Happy standard) and a between-subjects factor Group (Control vs. Dysphoric) were applied.

Peak amplitudes and peak latencies separately at different ROIs in three time windows were analyzed with a three-way repeated-measures ANOVA with within-subjects factors Stimulus Type (Standard vs. Deviant) and Emotion (Sad vs. Happy), and a between-subjects factor Group (Control vs. Dysphoric).

In addition, because the visual inspection of the topographic maps of the M300 showed that there might be differences in the lateralization of the responses in dysphoric and control groups, we further studied this possibility using the lateralization index. First, all peak values from the right hemisphere ROI were multiplied by −1 to correct for the polarity difference (also see Morel et al., 2009; Ulloa et al., 2014). Then, using these rectified response values, the lateralization index was calculated for responses to each stimulus type (Happy Deviant, Happy Standard, Sad Deviant, Sad Standard) as follows: Lateralization index = (Left − Right)/(Left + Right). A three-way repeated-measures ANOVA with the within-subjects factors Stimulus Type (Standard vs. Deviant) and Emotion (Sad vs. Happy), and the between-subjects factor Group (Control vs. Dysphoric) was applied.

Besides, possible differences in the lateralization of the M300 response were investigated separately for happy and sad, as well as for deviant, and standard stimulus responses with repeated-measures ANOVAs. Furthermore, because small sample size can limit the possibility to observe existing significant differences in multi-way ANOVAs, we also compared lateralization indexes separately for the happy (Deviant happy − Standard happy) and sad (Deviant sad − Standard sad) vMMN between the groups with independent samples *t*-tests (bootstrapping method with 1,000 permutations; Supplementary Materials).

For all significant ANOVA results, *post hoc* analyses were conducted using two-tailed paired *t*-tests to compare the differences involving within-subjects factors and using independent-samples *t*-tests for between-subjects comparisons, both with a bootstrapping method using 1,000 permutations (Good, 2005).

For all analyses, η_p^2 presents effect size estimates for ANOVAs and Cohen's d for *t*-tests. Cohen's d was computed using pooled standard deviations (Cohen, 1988). In addition, we conducted the Bayes factor analysis to estimate whether the null results in *post hoc* analyses were observed by chance (Rouder et al., 2009). The Bayes Factor (BF_{10}) provides an odds ratio for the alternative/null hypotheses (values < 1 favor the null hypothesis and values > 1 favor the alternative hypothesis). For example, a BF_{10} of 0.5 would indicate that the null hypothesis is two times more likely than the alternative hypothesis.

Whenever a significant interaction effect with the factor Group was found, two-tailed Pearson correlation coefficients were used to evaluate the correlation between the BDI-II score and the brain response. Bootstrap estimates of correlation were performed with 1,000 permutations.

The significance level was set to $p < 0.05$ for all tests.

RESULTS

Reaction Time and Hit Rate

For the reaction time and accuracy, neither significant main effects nor interaction effects were found (all *p*-values > 0.17). The mean reaction times were 384 ms (*SD* = 53) and 394 ms (*SD* = 69) for happy and sad standard stimulus blocks, respectively, and the mean reaction time for the whole experiment was 386 ms (*SD* = 61). The hit rate for blocks with happy faces as the standard stimuli was 98.86% (*SD* = 0.02), and 98.74% (*SD* = 0.02) for blocks with sad standard faces. The mean hit rate was 98.79% (*SD* = 0.02) for the whole experiment. The mean false alarm was below 1% both for happy and sad standard stimulus blocks, and the mean of the experiment was 0.96% (*SD* = 0.01). The mean reaction times were 380 ms (*SD* = 16) and 393 ms (*SD* = 27) for the control and dysphoric groups, respectively. The hit rate was above 98% for both groups (*M* = 99.1%, *SD* = 0.02 for the control group; *M* = 98.4%, *SD* = 0.02 for the dysphoric group). The mean false alarm rates were 0.978% (*SD* = 0.01) for the control group and 0.931% (*SD* = 0.004) for the dysphoric group, respectively.

Evoked Magnetic Fields

The grand-averaged evoked fields showed characteristic M100, M170, and M300 responses for both happy and sad faces presented as standard and deviant stimuli (**Figures 1**, **2**). Butterfly views of the standard and deviant responses and each individual participant's responses (for the standards only) are shown separately for happy (**Figure 1**) and sad stimuli (**Figure 2**) for the control and dysphoric groups. The topographic maps for each response type are shown in **Figure 3A**, and the ROIs for each response are shown in **Figure 3B**.

The response latencies are reported in **Table 2**. There were no significant main effects or interaction effects in response latencies.

The peak amplitude values are reported in **Table 3**. Next, the results of the amplitude analyses are reported separately for each component.

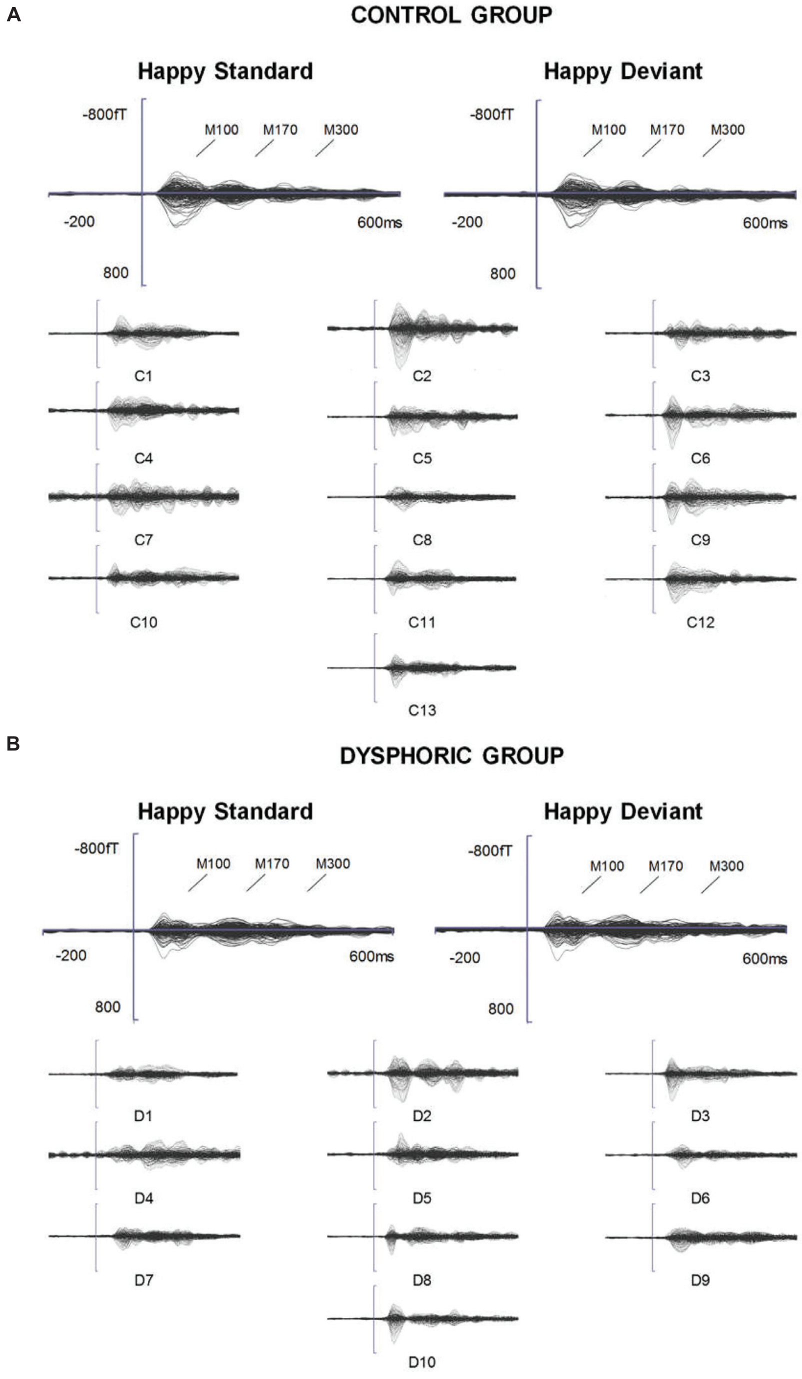

FIGURE 1 | ERFs reflecting three stages of face processing (M100, M170, and M300). **(A)** Butterfly view of the grand-averaged responses to happy standard and happy deviant faces in the control group (top) and individual participants' responses to happy standard faces (C1–C13). **(B)** Butterfly view of the grand-averaged responses to happy standard and happy deviant faces in the dysphoric group (top) and individual participants' responses to happy standard faces (D1–D10). It should be noted that signals from both magnetometers and gradiometers are included here. For visualization purposes, the gradiometer values are 0.04 times multiplied due to the different units for magnetometers (T) and gradiometers (T/m).

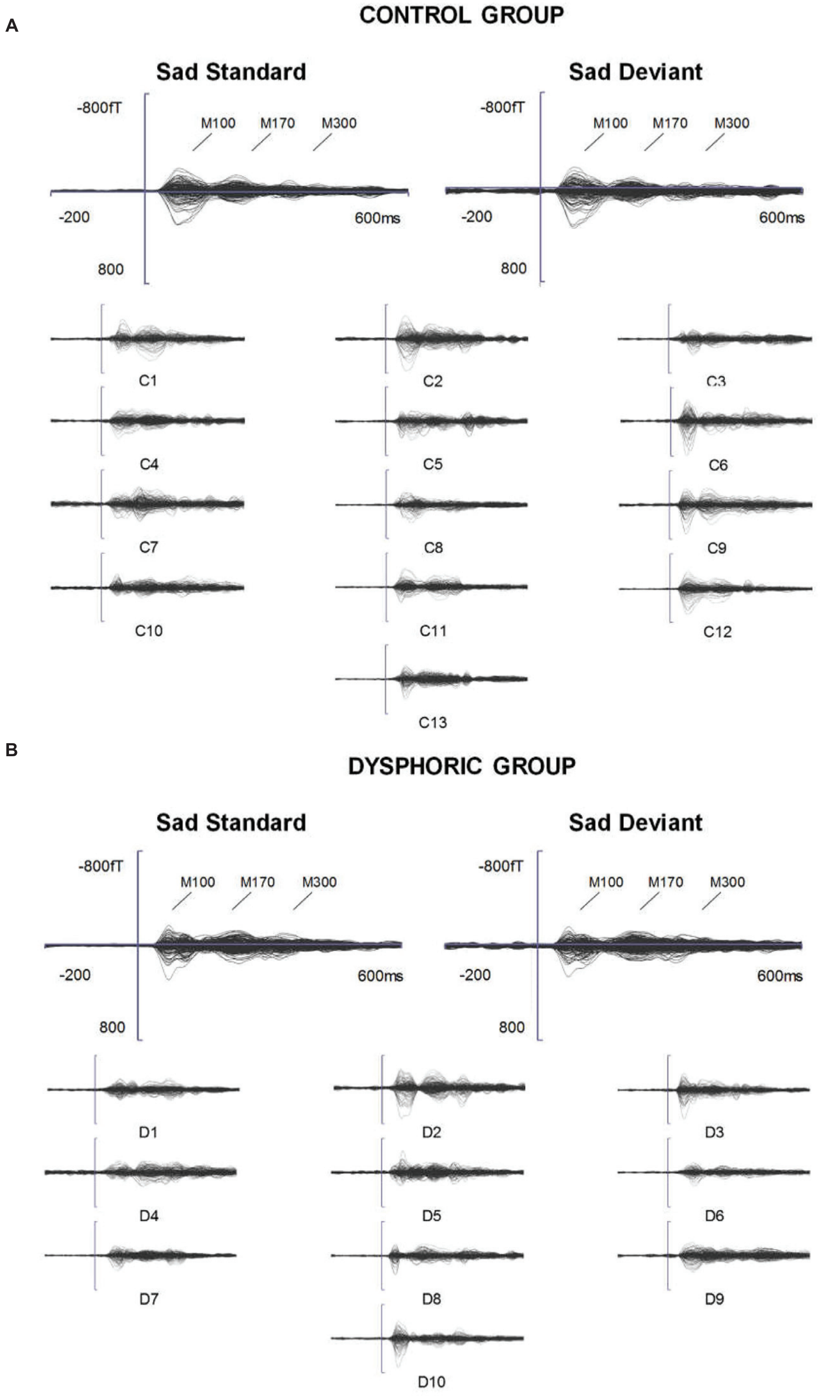

FIGURE 2 | ERFs reflecting three stages of face processing (M100, M170, and M300). **(A)** Butterfly view of the grand-averaged responses to sad standard and sad deviant faces in the control group (top) and individual participants' responses to sad standard faces (C1–C13). **(B)** Butterfly view of the grand-averaged responses to sad standard and sad deviant faces in the dysphoric group (top) and individual participants' responses to sad standard faces (D1–D10). It should be noted that signals from both magnetometers and gradiometers are included here. For visualization purposes, the gradiometer values are 0.04 times multiplied due to the different units for magnetometers (T) and gradiometers (T/m).

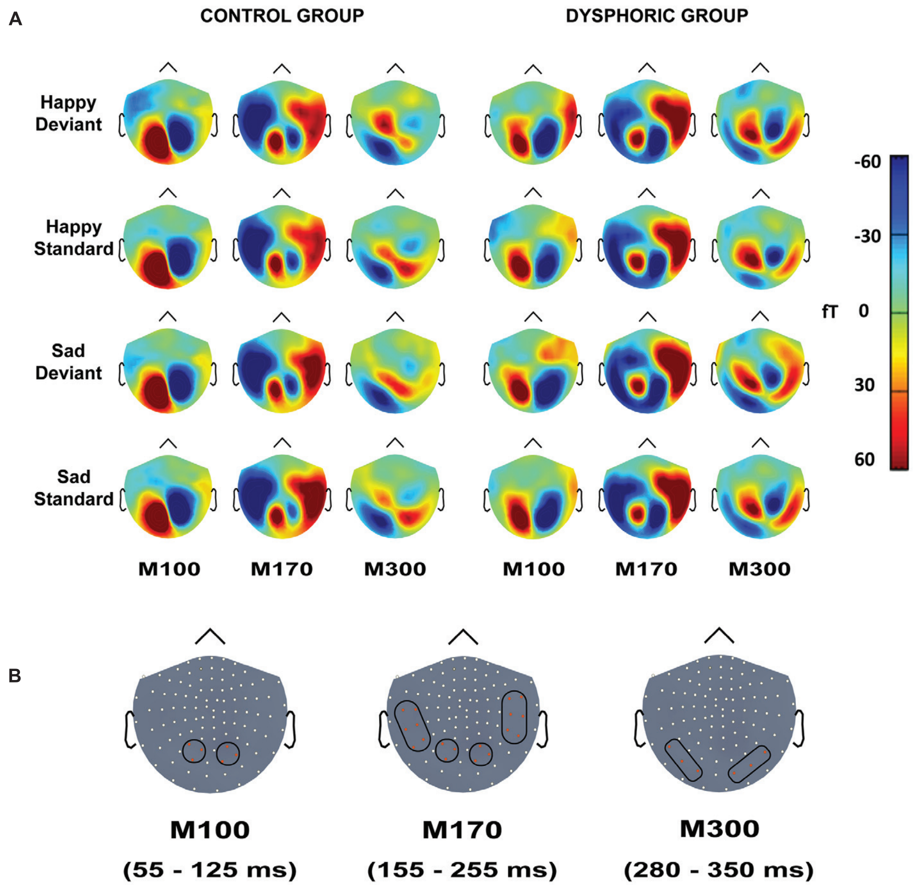

FIGURE 3 | (A) Topographic maps of grand-averaged magnetic fields for happy deviant, happy standard, sad deviant, and sad standard faces in the control (left) and dysphoric groups (right) for the M100, M170, and M300 shown here at 85, 205, and 315 ms after stimulus onset, respectively. **(B)** Magnetometer sensors and the regions of interests used for analyses are marked with black frames for M100, M170, and M300. Each participant's peak values were extracted from the time windows of 55–125 ms, 155–255 ms, and 280–350 ms after stimulus onset for M100, M170, and M300, respectively.

M100

Waveforms of the event-related magnetic fields (ERFs) showed a strong M100 response peaking approximately at 85 ms after the stimulus onset on bilateral occipital regions (**Figure 4**).

At the left occipital ROI, neither main effects nor interaction effects were found (all *p*-values > 0.226).

At the right occipital ROI, there was a significant main effect of Stimulus Type, $F(1,21) = 30.22$, $p < 0.001$, $\eta_p^2 = 0.59$, indicating larger ERF amplitudes for the deviant faces than standard faces. The other main effects and all interaction effects were non-significant (all *p*-values > 0.342).

M170

Event-related magnetic field waveforms showed a strong M170 response peaking approximately 205 ms after the stimulus onset in the bilateral temporo-occipital regions (**Figure 5**).

At the left temporal ROI, there was a marginally significant main effect for Emotion, $F(1,21) = 3.46$, $p = 0.077$, $\eta_p^2 = 0.14$, reflecting more activity for sad than happy faces. Other main effects and interaction effects were non-significant (all *p*-values > 0.261).

At the right temporal ROI, a main effect of Emotion was observed, $F(1,21) = 8.52$, $p = 0.008$, $\eta_p^2 = 0.29$, wherein sad faces induced larger amplitudes than happy faces. Neither other main effects nor any of the interaction effects were significant (all *p*-values > 0.353).

At the left occipital ROI, a main effect of Stimulus Type was found, $F(1,21) = 9.29$, $p = 0.006$, $\eta_p^2 = 0.31$, reflecting larger activity for deviant faces than standard faces. Other main effects and interaction effects were non-significant (all *p*-values > 0.223).

At the right occipital ROI, a main effect of Stimulus Type was found, $F(1,21) = 12.81$, $p = 0.002$, $\eta_p^2 = 0.38$, reflecting larger activity for deviant faces than standard faces. Other main effects and interaction effects were non-significant (all *p*-values > 0.288).

TABLE 2 | Mean peak latency (ms) and standard deviation (in parentheses) for each response and ROI in the control and dysphoric groups.

Response	ROI	Group	Happy Deviant	Happy Standard	Sad Deviant	Sad Standard
M100	Left occipital	Con	81.15	82.69	81.15	78.85
			(15.02)	(20.88)	(19.38)	(14.46)
		Dys	82.00	86.00	86.00	80.00
			(21.63)	(24.70)	(23.31)	(20.68)
	Right occipital	Con	82.69	83.46	85.00	84.23
			(22.04)	(21.54)	(20.82)	(22.16)
		Dys	85.00	79.00	78.00	87.00
			(22.61)	(22.71)	(23.12)	(23.94)
M170	Left temporal	Con	197.31	205.77	205.00	197.31
			(29.20)	(27.53)	(28.58)	(19.64)
		Dys	204.00	208.00	202.00	195.00
			(34.14)	(33.68)	(37.43)	(22.11)
	Right temporal	Con	198.08	205.77	199.62	188.85
			(23.59)	(28.13)	(26.96)	(22.93)
		Dys	207.00	212.00	210.00	208.00
			(21.50)	(29.08)	(32.06)	(30.57)
	Left occipital	Con	205.00	198.85	209.62	202.69
			(35.36)	(36.18)	(39.08)	(38.11)
		Dys	213.00	210.00	216.00	209.00
			(29.74)	(33.75)	(34.79)	(35.96)
	Right occipital	Con	220.38	222.69	221.15	228.85
			(26.34)	(22.04)	(22.93)	(26.94)
		Dys	220.00	201.00	218.00	209.00
			(25.90)	(35.34)	(28.30)	(32.04)
M300	Left occipital	Con	312.50	319.17	325.00	319.17
			(22.56)	(22.79)	(25.12)	(27.74)
		Dys	320.56	312.78	317.22	315.00
			(21.67)	(14.14)	(18.47)	(17.53)
	Right occipital	Con	322.50	315.00	317.50	315.83
			(26.65)	(26.19)	(27.69)	(25.12)
		Dys	316.11	302.78	307.22	309.44
			(22.68)	(17.73)	(16.04)	(13.89)

Please not that there were no significant main or interaction effects. ROI, region of interest; Con, control group; Dys, dysphoric group.

M300

Amplitude results

The waveforms of the ERF demonstrated a bipolar M300 activity over the bilateral occipital ROI peaking approximately 315 ms after the stimulus onset (**Figure 6**).

At the left occipital ROI, a significant interaction effect of Emotion × Stimulus Type, $F(1,19) = 4.48$, $p = 0.048$, $\eta_p^2 = 0.19$, a marginally significant interaction effect of Emotion × Group, $F(1,19) = 4.34$, $p = 0.051$, $\eta_p^2 = 0.186$, and a significant interaction effect of Emotion × Stimulus Type × Group, $F(1,19) = 4.52$, $p = 0.047$, $\eta_p^2 = 0.19$, was found. The other main effects and interaction effects were non-significant (all p-values > 0.315).

Post hoc tests for the Emotion × Stimulus Type interaction did not show any significant differences for any of the comparisons (all p-values > 0.128, all BF_{10}s < 0.67).

Post hoc tests for Emotion × Group interaction showed that sad faces induced larger activity than happy faces in the dysphoric group, $t(8) = 3.27$, $p = 0.030$, CI 95% [3.72, 13.34], $d = 0.16$, $BF_{10} = 5.72$, but there were no differences between the responses to sad and happy faces in the control group, $t(12) = 0.67$, $p = 0.513$, CI 95% [−11.14, 4.85], $d = 0.06$, $BF_{10} = 0.35$. No differences between the groups were found in happy or sad face responses (all p-values > 0.395, all BF_{10}s < 0.53).

Post hoc tests for the three-way interaction showed that no differences were found between the groups in amplitudes to any of the stimulus types *per se* (Happy Deviant, Happy Standard, Sad Deviant, Sad Standard, all p-values > 0.244, all BF_{10}s < 0.68), or in the vMMN responses (Happy Deviant – Happy Standard, Sad Deviant – Sad Standard), all p-values > 0.225, all BF_{10}s < 0.67). Thus, we split the data by group and run a two-way repeated-measures of ANOVA with Stimulus Type (Standard vs. Deviant) × Emotion (Sad vs. Happy) in each group separately. There was neither a significant main effect nor interaction effects in the control group (all p-values > 0.517). In the dysphoric group, an interaction effect of Emotion × Stimulus type was found, $F(1,8) = 6.87$, $p = 0.031$, $\eta_p^2 = 0.46$. Amplitude values for sad deviant faces were larger than for happy deviant faces, $t(8) = 4.91$, $p = 0.011$, CI 95% [15.18, 32.98], $d = 0.38$,

TABLE 3 | Peak amplitude values (fT) and standard deviation (in parentheses) for each response and ROI in the control and dysphoric groups.

Response	ROI	Group	Happy Deviant	Happy Standard	Sad Deviant	Sad Standard
M100	Left occipital	Con	205.01	197.65	204.25	208.82
			(106.34)	(106.50)	(101.10)	(105.65)
		Dys	177.40	176.86	170.18	174.31
			(88.01)	(96.45)	(89.65)	(95.29)
	Right occipital	Con	−215.75	−195.07	−213.29	−195.99
			(104.50)	(101.15)	(96.33)	(95.12)
		Dys	−196.74	−163.74	−187.07	−175.14
			(102.74)	(129.88)	(108.73)	(117.40)
M170	Left temporal	Con	−98.35	−92.92	−104.55	−99.67
			(69.37)	(68.64)	(72.84)	(71.37)
		Dys	−77.75	−80.88	−85.04	−89.26
			(59.75)	(42.71)	(49.25)	(50.22)
	Right temporal	Con	70.11	62.36	81.88	77.53
			(44.29)	(42.32)	(51.03)	(50.58)
		Dys	86.32	85.65	98.39	96.24
			(52.82)	(54.90)	(64.58)	(57.11)
	Left occipital	Con	112.17	97.80	107.91	86.69
			(73.62)	(70.38)	(66.50)	(88.80)
		Dys	95.66	94.75	99.89	85.99
			(43.34)	(49.98)	(47.07)	(44.23)
	Right occipital	Con	−94.81	−76.31	−90.09	−67.80
			(103.98)	(89.04)	(83.11)	(99.68)
		Dys	−130.14	−119.41	−125.80	−114.16
			(57.09)	(51.14)	(53.25)	(60.40)
M300	Left occipital	Con	−80.66	−76.89	−77.79	−74.09
			(37.14)	(53.74)	(49.35)	(57.56)
		Dys	−54.96	−64.29	−78.27	−57.78
			(55.79)	(53.48)	(55.06)	(54.06)
	Right occipital	Con	51.04	65.13	48.29	67.49
			(31.33)	(38.01)	(39.16)	(37.67)
		Dys	50.18	58.38	57.58	49.77
			(38.65)	(49.73)	(59.23)	(35.95)

ROI, region of interest; Con, control group; Dys, dysphoric group.

BF_{10} = 35.9. Further, a marginally significant difference was found reflecting larger amplitude values for sad deviant faces than sad standard faces in the dysphoric group, $t(8) = 2.09$, $p = 0.085$, CI 95% [−38.45, −1.19], $d = 0.38$, $BF_{10} = 1.42$. No other significant results between responses to different stimulus type pairs were found in the dysphoric group (all p-values > 0.168, all BF_{10}s < 0.76). There was also a main effect of Emotion in the dysphoric group, $F(1,8) = 10.67$, $p = 0.011$, $\eta_p^2 = 0.57$, reflecting more activity for sad faces than happy faces.

At the right occipital ROI, the main effect of the Stimulus Type, $F(1,19) = 5.40$, $p = 0.031$, $\eta_p^2 = 0.22$, and an interaction effect of Stimulus Type × Group was found, $F(1,19) = 5.15$, $p = 0.035$, $\eta_p^2 = 0.21$. The other main effects and interaction effects were non-significant (all p-values > 0.328).

The responses were smaller in amplitude for deviant faces than for standard faces in the whole group level. *Post hoc* analysis for the Stimulus Type × Group interaction revealed that the groups did not differ in any of the stimulus responses as such (all p-values > 0.476, all BF_{10}s < 0.48). However, in the control group responses to deviant faces were smaller in amplitude than those to standard faces, $t(11) = 2.87$, $p = 0.020$, CI 95% [−28.14, −5.97], $d = 0.49$, $BF_{10} = 4.23$. There was no such difference in the dysphoric group, $t(8) = 0.06$, $p = 0.949$, CI 95% [−6.29, 6.02], $d = 0.005$, $BF_{10} = 0.32$. In addition, a group difference was found in the vMMN amplitude (deviant – standard differential response), $t(19) = 2.27$, $p = 0.031$, CI 95% [−28.86, −4.01], $d = 1.05$, $BF_{10} = 2.14$, reflecting a larger vMMN amplitude in the control than in the dysphoric group.

Correlation analysis

In the whole group level the correlations between BDI-II scores and M300 response amplitudes were non-significant for all stimulus types at the left (all p-values > 0.062) and right occipital ROIs (all p-values > 0.438). The same applied for the correlations calculated separately for the dysphoric group (at the left ROI, all p-values > 0.107 and at the right ROI, all p-values > 0.299).

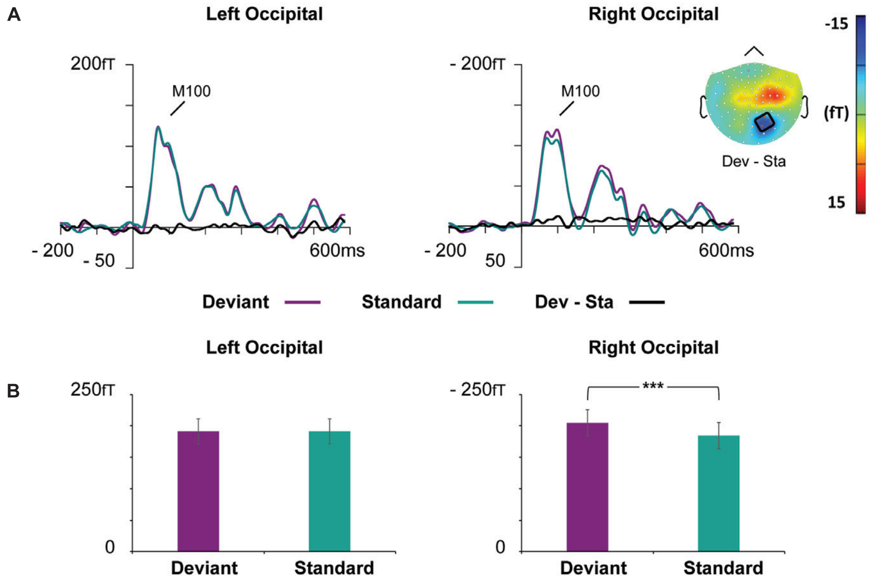

FIGURE 4 | Grand-averaged ERFs demonstrating the M100. **(A)** Waveforms of evoked magnetic fields to the standard and deviant stimuli and deviant minus standard differential response at the left and right occipital ROIs. The topography of the vMMN (deviant – standard) depicted as the mean value of activity 55–125 ms after stimulus onset. **(B)** Bar graph for the M100 peak value with standard errors to deviant and standard faces at the left and right occipital ROIs. Asterisks mark a significant difference at ***$p < 0.001$.

Lateralization index

The analysis of the lateralization index revealed neither main effects nor interaction effects (all p-values > 0.107).

DISCUSSION

The main goal of the present study was to examine the emotional encoding and automatic change detection of peripherally presented facial emotions in dysphoria. MEG recordings showed prominent M100, M170, and M300 components to emotional faces. All of the components were modulated by the presentation rate of the stimulus (deviant vs. standard), corresponding to the results of the previous studies conducted on healthy participants (Zhao and Li, 2006; Astikainen and Hietanen, 2009; Susac et al., 2010; Stefanics et al., 2012). M170 was also modulated by emotion, responses being larger for sad than happy faces. M300 showed both a negative bias and impaired change detection in dysphoria.

The negative bias in the dysphoric group, which was demonstrated as a relative difference in M300 amplitude for sad and happy faces in comparison to the control group, seems to be associated with change detection, as the deviant stimulus responses, but not the standard stimulus responses, were larger for sad than happy faces in the dysphoric group. This is a novel finding, and previous studies using the oddball condition in depressed participants have not separately investigated responsiveness for standard and deviant stimuli but used the differential response (deviant – standard) in their analysis (Chang et al., 2010, 2011; Qiu et al., 2011). In general, our finding of the negative bias in emotional face processing extends from the previous findings involving attended stimulus conditions (Bistricky et al., 2014; Chen et al., 2014; Zhao et al., 2015; Dai et al., 2016) to ignore condition. However, the negative bias in the present study was not found in the first processing stages (M100 and M170) as in the studies applying attentive condition in depressed participants (Dai and Feng, 2012; Chen et al., 2014; Zhao et al., 2015). In a prior study with dysphoric participants, elevated P3 ERP component to sad target faces reflected negative bias in attentive face processing in previously depressed participants, but no differences were found in the earlier N2 component in comparison to never depressed participants (Bistricky et al., 2014). Future studies are needed to investigate whether the discrepancy between our results and previous studies with depressed participants (Dai and Feng, 2012; Chen et al., 2014; Zhao et al., 2015) is related to different participant groups (depressed vs. dysphoric) or amount of attention directed toward stimuli (ignore vs. attend condition).

The finding that control participants, but not dysphoric participants, showed the vMMN in the right occipital region indicates that, in addition to the negative bias, there is a deficit in change detection in general in dysphoria. Our results thus reveal that a dysphoric state affects not only attended change detection in facial emotions (e.g., Bistricky et al., 2014; Chen et al., 2014), but also the automatic change detection of emotional faces in one's visual periphery. This finding of a vMMN deficit in dysphoria at the latency window of the M300 is also in line with the previous ERP study applying an ignore condition

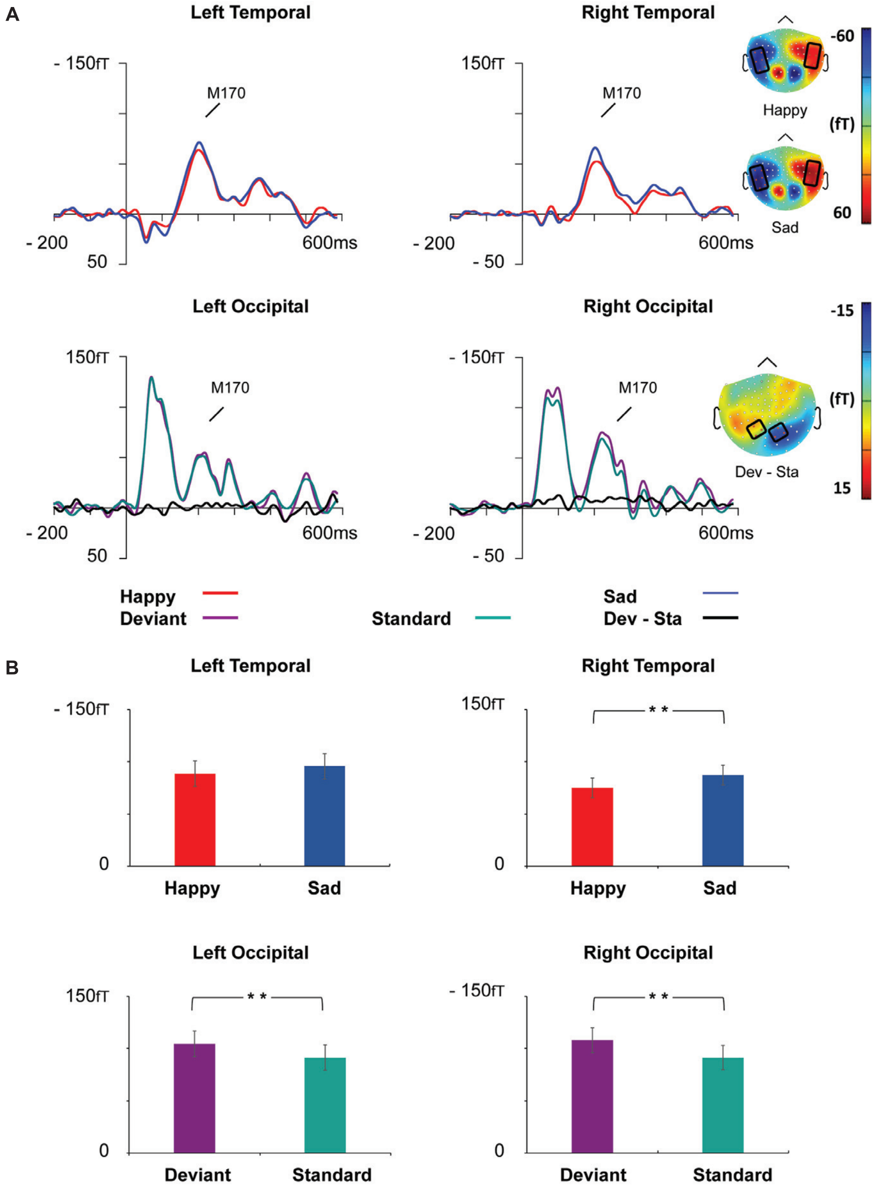

FIGURE 5 | Grand-averaged ERFs demonstrating the M170 response. **(A)** Upper: Waveforms of ERFs to happy and sad faces at right and left temporal ROIs and corresponding topographic maps. Lower: Waveforms of ERFs to standard and deviant faces at the left and right occipital ROIs and the topography of the vMMN (deviant – standard). Topographic maps are depicted as the mean value of activity 155–255 ms after stimulus onset. **(B)** Bar graph for the M170 peak amplitude values with standard errors to happy and sad faces (upper) and deviant and standard stimuli (lower) at the left and right temporal and occipital ROIs, respectively. Asterisks mark significant differences at $^{**}p < 0.01$.

and reporting that the late vMMN (at 220–320 ms, reflecting the modulation of P2) was observed in the control group but was absent in the depression group (Chang et al., 2010). However, since in this study standard faces were neutral and deviant faces emotional, the effects of emotional processing and deviance detection cannot be distinguished. Here, we calculated the vMMN as a differential response between the responses to the same stimulus presented as deviant and standard. Our results showing the decreased vMMN amplitude at the latency of M300 in the dysphoric group, relative to the control group, indicate that it is specifically the change detection that is impaired in participants with depression symptoms.

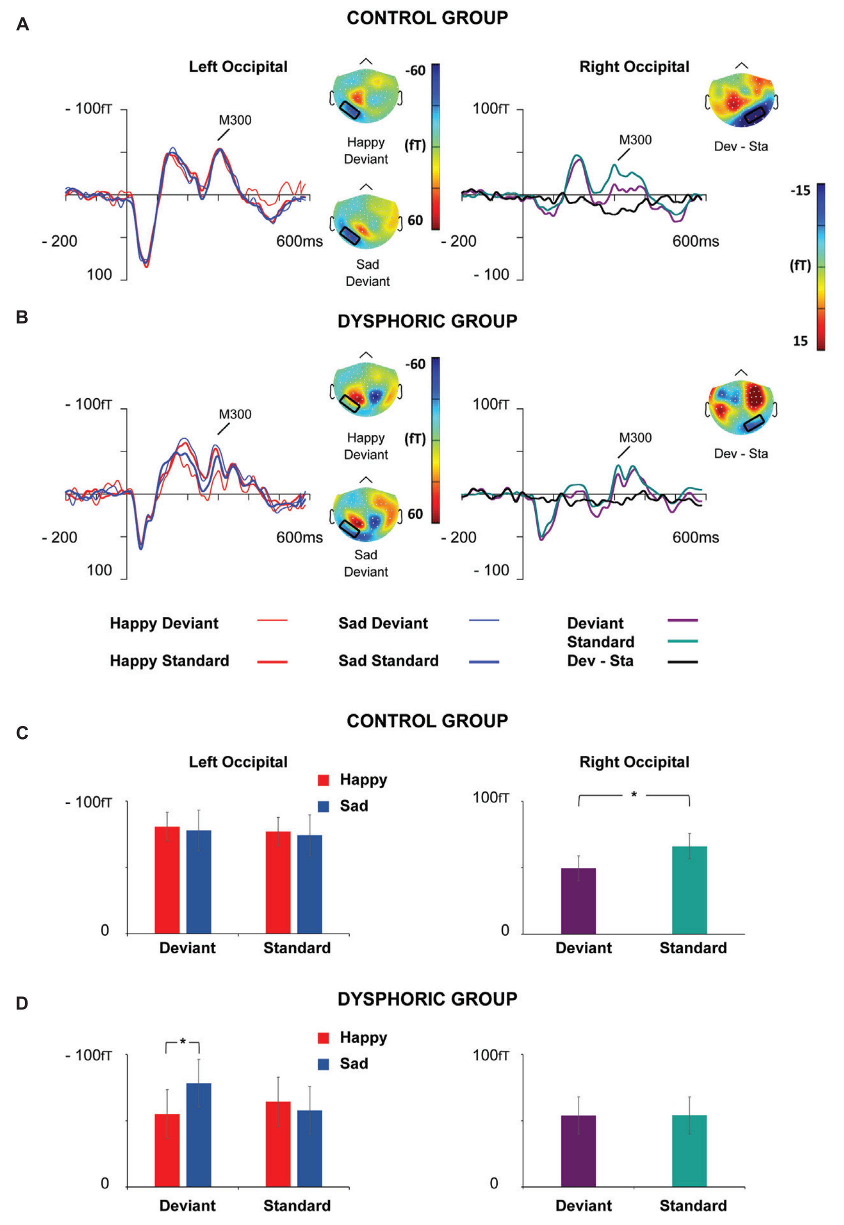

FIGURE 6 | Grand-averaged ERFs for the M300 response. Waveforms of ERFs at the left and right occipital ROIs in the control **(A)** and dysphoric group **(B)**. Topographic maps of Happy and Sad Deviant (Left), and the vMMN (Deviant – Standard) responses (Right) are depicted as the mean value of activity 280–350 ms after stimulus onset. Bar graphs for the M300 peak value with standard errors at left and right occipital ROIs in the control **(C)** and dysphoric group **(D)**. Note that in the left hemisphere there was an interaction effect of Emotion × Stimulus Type × Group, which showed that sad deviant faces induced more activity than happy deviant faces in the dysphoric group but not in the control group. In the right hemisphere, an interaction effect of Stimulus Type × Group was found, indicating that the vMMN was elicited in the control but not in the dysphoric group. Asterisk marks significant differences at $^*p < 0.05$.

Here, we did not find group differences in the vMMN related to earlier processing stages. The previous vMMN study conducted on depressed participants has reported a larger vMMN at the latency of N170 in control than depression group, and also larger vMMN amplitude to sad than happy deviant faces (Chang et al., 2010). However, again, it is unclear whether these findings reflect emotional encoding or deviance detection, as in this study standard faces were neutral and deviant faces emotional and the vMMN was calculated as a difference between responses to these.

Our finding of the altered emotional vMMN in dysphoria is in line with prior results in schizophrenia, a psychiatric disorder with known deficits in emotion processing, in which diminished automatic brain responses to emotional faces in patients were reported (Csukly et al., 2013). The vMMN was also suggested in autism spectrum disorder as an indicator of affective reactivity; given that vMMN responses to emotional faces showed a correlation with Autism Spectrum Quotient (AQ) scores (Gayle et al., 2012). Here, we did not find correlations between the M300 amplitude and BDI-II scores within the dysphoric group. The lack of correlations can be interpreted as indicating that the alterations observed in M300 reflect more trait- than state-dependent factors of depression. However, the lack of correlation can also be explained by the small sample size.

We also investigated the possible lateralization effect for the occipital M300 because the visual observation of the topographical maps showed some differences between the groups in lateralization for this component. However, none of the various investigations revealed differences in the lateralization between the groups. There were no clear lateralization differences in M300 in sad and happy face processing in the whole group level either. Some previous studies have reported that the vMMN to emotional faces has a right hemisphere dominance (Gayle et al., 2012; Li et al., 2012; Stefanics et al., 2012), while others have not found it (Kovarski et al., 2017), but these findings have been related to earlier face processing stages.

Besides the findings related to dysphoria, there were findings related to automatic change detection and emotion processing that apply to the whole participant group. All investigated components (M100, M170, and M300) were modulated by stimulus rarity, likely reflecting the vMMN response. In the previous EEG and MEG studies, the vMMN has been elicited at the earliest processing stage, i.e., in the P1 time window (Susac et al., 2010; Stefanics et al., 2012) but also at the latency of N170 and later P2 component (Zhao and Li, 2006; Astikainen and Hietanen, 2009; Chang et al., 2010). It should be noted that it is unclear whether the vMMN to emotional faces is a separate component from the visual and face-related components (i.e., P1, N170, and P2) or whether the vMMN is the amplitude modulation of these canonical components. To our knowledge, only one previous study has directly addressed this question. In this study, independent component analysis (ICA) and two stimulus conditions varying the probability of the emotional faces were used to separate vMMN and N170 components (Astikainen et al., 2013). The ICA revealed two components within the relevant 100–200 ms latency range. One component, conforming to N170, differed between the emotional and neutral faces, but not as a function of the stimulus probability, and the other, confirming to vMMN, was also modulated by the stimulus probability. However, neither in this study (Astikainen et al., 2013) nor in other previous studies the functional independence of the vMMN from P1/M100 or P2/M300 responses have been investigated.

Here emotional modulation was found at the second stage (M170) of face processing, as in several previous studies (Batty and Taylor, 2003; Eger et al., 2003; Williams et al., 2006; Zhao and Li, 2006; Blau et al., 2007; Leppänen et al., 2007; Schyns et al., 2007; Japee et al., 2009; Wronka and Walentowska, 2011; Astikainen et al., 2013; Chen et al., 2014). The emotional modulation of M170 was observed at the right temporal ROI, which corresponds to previous findings (Williams et al., 2006; Japee et al., 2009; Wronka and Walentowska, 2011). In our study, sad faces induced a greater N170 response than happy faces, while previous ERP studies have not found a difference between the N170 amplitude for happy and sad faces (Batty and Taylor, 2003; Hendriks et al., 2007; Chai et al., 2012). It is notable, however, that in the present study the involvement of dysphoric participants might explain the difference in the results compared to previous studies conducted only on healthy participants (Batty and Taylor, 2003; Hendriks et al., 2007; Chai et al., 2012).

The present study has some limitations. First, our analysis was carried out in the sensor instead of in the source space. Due to the lack of individual structural magnetic resonance images (MRIs), we restricted our analysis to the sensor level. We selected the ROIs for the analysis based on the topographies in the control group, which served as a reference group for the comparison with the dysphoric group. Future studies should investigate potential differences in the sources of brain responses to emotional faces, especially those for M300 between depressed and control participants. In addition, the relatively small sample size warrants a replication of the study with larger participant groups. It is possible that some existing effects were not observable with the current small sample size. It is also worth mentioning that the dysphoric group had depressive symptoms during the measurement, and nearly all of them had a diagnosis of depression. However, the diagnoses were not confirmed in the beginning of the study.

The present study was not designed to determine whether the underlying mechanism related to the vMMN is related to the detection of regularity violations ("genuine vMMN," Kimura, 2012; Stefanics et al., 2014) or whether it reflects only different levels of neural adaptation in neural populations responding to standard and deviant stimuli (neural adaptation). The most common way to investigate the underlying neural mechanism has been to apply a control condition in which the level of neural adaptation is the same as for the deviant stimulus in the oddball condition, but where no regularity exists (an equiprobable condition, Jacobsen and Schröger, 2001). This control condition has not yet been applied in vMMN studies using facial expressions as a changing feature (some studies have used an equiprobable condition, but the probability of the oddball deviant and control stimulus in the equiprobable condition has been different; Li et al., 2012; Astikainen et al., 2013; Kovarski et al., 2017). Other vMMN studies have used a proper equiprobable condition, and they have demonstrated a genuine vMMN (e.g., for orientation changes, see Astikainen et al., 2008; Kimura et al., 2009). This is an aspect that should be studied in the context of emotional face processing as well. In one study (Kimura et al., 2012), however, the stimulus condition applied allowed neural responses to regularity violations to be observed. Namely, an immediate repetition of an emotional expression was presented as a deviant stimulus violating the pattern of constantly changing (fearful and happy). The vMMN reflecting the detection of the regularity violations was elicited at 280 ms and 350 ms after the stimulus onset for the fearful and the happy faces, respectively. It is thus possible that in our study the differential responses at the two first stages also reflect the neural adaptation to repeatedly presented standard stimuli rather than the genuine vMMN.

In sum, the present results show that there is a negative bias in dysphoria toward rare sad faces, extending the findings of an attentive negative bias in depression to automatic face processing. The results also demonstrate impaired automatic change detection in emotional faces in dysphoria. These findings related to automatic face processing might have significant behavioral relevance that affects, for instance, real-life social interactions.

AUTHOR CONTRIBUTIONS

PA and GS conceived and designed the experiments. ER, XL, and KK performed the data acquisition. QX analyzed the data. ER, XL, and CY contributed to the data analysis. PA, QX, CY, KK, GS, and WL interpreted the data. PA and QX drafted the manuscript. All the authors revised and approved the manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnhum.2018.00186/full#supplementary-material

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Supplementary Material

Automatic processing of changes in facial emotions in dysphoria: A magnetoencephalography study

Qianru Xu, Elisa M. Ruohonen, Chaoxiong Ye, Xueqiao Li, Kairi Kreegipuu, Gabor Stefanics, Wenbo Luo[*] & Piia Astikainen

*** Correspondence:** Wenbo Luo: luowb@lnnu.edu.cn

1 Lateralization analysis of the M300

1.1 Statistical analyses

In addition to investigation of the lateralization index with three-way repeated measures ANOVA reported in the main text, the possible lateralization of the M300 responses were further studied with three-way repeated measures ANOVAs separately for happy and sad responses, and deviant and standard responses. For the analyses where happy and sad responses were separately investigated, peak amplitude values of the M300 were applied in the ANOVA model including within-subjects factors Hemisphere (Left vs. Right) and Stimulus type (Standard vs. Deviant) and a between-subject factor Group (Control vs. Dysphoric). For the analyses where standard and deviant responses were separately investigated, peak amplitude values of the M300 were applied in the ANOVA model including within-subjects factors Hemisphere (Left vs. Right) and Emotion (Sad vs. Happy) and a between-subject factor Group (Control vs. Dysphoric).

Furthermore, because small sample size can limit the possibility to observe existing significant differences in multi-way ANOVAs, we also compared lateralization indexes separately for happy (Deviant happy – Standard happy) and sad (Deviant sad – Standard sad) vMMN between the groups with independent samples t-tests (bootstrapping method with 1000 permutations). The lateralization index was calculated with differential responses as follows: Lateralization index = (Left – Right) / (Left + Right).

For all significant ANOVA results, post-hoc analyses were conducted by two-tailed paired t-tests for comparison of the differences involving within-subjects factors and by independent samples t-tests for between-subjects comparisons, and the confidence intervals (CI) were computed with a bootstrapping method using 1000 permutations (Good, 2005).

For all analyses, partial eta-squared (η_p^2) presents effect size estimates for ANOVAs and Cohen's d for t-tests. Cohen's d was computed using pooled standard deviations (Cohen, 1988). In addition, we conducted the Bayes factor analysis to estimate whether the null results in post hoc analyses were observed by chance (Rouder et al., 2009).

1.2 Results

ANOVA for happy and sad face responses

Analysis for happy face responses did not show main effects or interaction effects related to hemisphere (all *p*-values > .234) (see Supplementary Table 1). For sad face responses, an interaction effect of Hemisphere × Stimulus type was significant, F (1, 19) = 6.36, p = .021, $\eta_p^2 = 0.25$ (see Supplementary Table 1). The main effect of the hemisphere and the other interaction effects with hemisphere were non-significant (all *p*-values > .280). Post hoc analysis for the Hemisphere × Stimulus type interaction effect in sad face responses showed there was only a marginally significant difference, which reflected larger sad deviant responses in the left hemisphere compared to the right hemisphere, t (20) = 1.77, p = .092, $CI_{95\%}$ [- 53.08, 2.75], d = 0.44, BF_{10} = 0.86. No other significant results between pairs were found (all *p*-values > .128, all BF_{10}s < 0.67).

ANOVA for deviant and standard responses

Analysis for deviant responses showed neither a main effect of hemisphere nor interaction effects related to it (all *p*-values > .131) (see Supplementary Table 2). Similarly, in standard responses, there was neither a main effect nor interaction effects related to hemisphere (all *p*-values > .471) (Supplementary Table 2).

Lateralization index for the vMMN response

Independent samples t-tests comparing lateralization indexes for the vMMN responses in the dysphoric and control group showed no significant differences between groups in happy, t (19) = 0.54, p = .587, $CI_{95\%}$ [- 5.30, 3.73], d = 0.24, BF_{10} = 0.32, or sad vMMN lateralization, t (19) = 0.865, p = .430, $CI_{95\%}$ [-149.28, 2.50], d = 0.41, BF_{10} = 0.33 (Supplementary Figure 1). There was one outlier value (more than 4.5 SD) in happy responses in the control group, but the results did not change after removing this participant's value from the analysis, t (18) = .126, p = .901, $CI_{95\%}$ [-3.96, 3.96], d = 0.06, BF_{10} = 0.40.

1.3 Summary

In sum, in this supplementary material, we reported the results for the analyses of lateralization of M300 separately for happy and sad, as well as deviant and standard stimulus responses with repeated-measures ANOVAs. In addition, the possible differences in lateralization index for the vMMN was investigated with independent-samples t-tests. There were no significant effects for lateralization in any of the tests. Bayes factor analyses also supported that the null hypotheses are more likely to be true.

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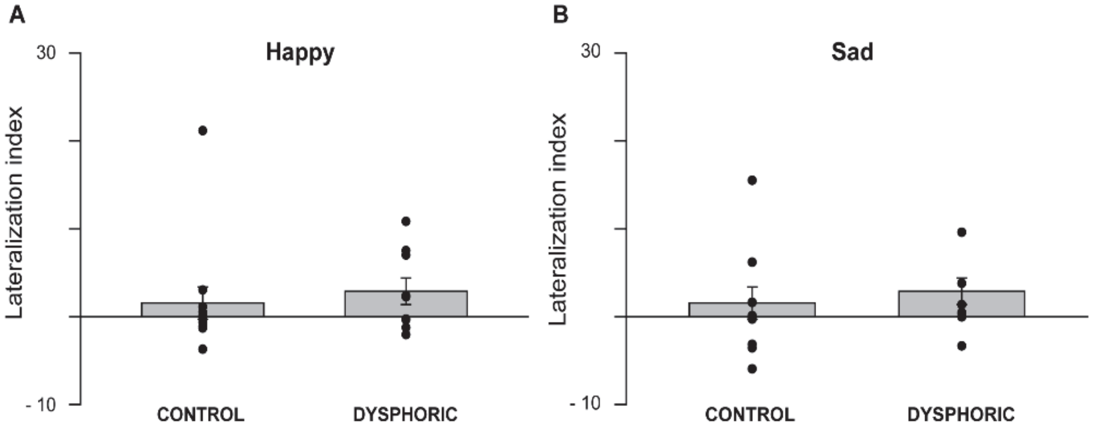
Supplementary Table 1. ANOVA results for M300 amplitude separately for happy and sad stimulus responses. $^{*}p < .05$

Emotion type	Effect		F (degrees of freedom)	*p*	η_p^2
Happy Stimuli	Main effects	Hemisphere	F (1,19) = .98	.336	.05
		Stimulus type	F (1,19) = 2.40	.138	.11
		Group	F (1,19) = .72	.407	.04
	Two-way interactions	Hemisphere × Stimulus type	F (1,19) = 1.17	.293	.06
		Hemisphere × Group	F (1,19) = .34	.567	.02
		Stimulus type × Group	F (1,19) = .16	.693	.01
	Three-way interactions	Hemisphere × Stimulus type × Group	F (1,19) = 1.51	.234	.07
Sad Stimuli	Main effects	Hemisphere	F (1,19) = 1.24	.280	.06
		Stimulus type	F (1,19) = .29	.595	.02
		Group	F (1,19) = .18	.677	.01
	Two-way interactions	Hemisphere × Stimulus type	F (1,19) = 6.36	.021*	.25
		Hemisphere × Group	F (1,19) = .02	.900	.001
		Stimulus type × Group	F (1,19) = 3.44	.079	.15
	Three-way interactions	Hemisphere × Stimulus type × Group	F (1,19) = .52	.478	.03

Supplementary Table 2. ANOVA results for M300 amplitude conducted separately for deviant and standard stimulus responses.

Stimulus type	Effect		F (degrees of freedom)	*p*	η_p^2
Deviant Stimuli	Main effects	Hemisphere	F (1,19) = 2.50	.131	.12
		Emotion	F (1,19) = 1.31	.267	.06
		Group	F (1,19) = .10	.760	.01
	Two-way interactions	Hemisphere × Emotion	F (1,19) = 1.15	.298	.06
		Hemisphere × Group	F (1,19) = .40	.537	.02
		Emotion × Group	F (1,19) = 2.74	.114	.13
	Three-way interactions	Hemisphere × Emotion × Group	F (1,19) = 1.18	.291	.06
Standard Stimuli	Main effects	Hemisphere	F (1,19) = .30	.588	.02
		Emotion	F (1,19) = .87	.362	.04
		Group	F (1,19) = .84	.371	.04
	Two-way interactions	Hemisphere × Emotion	F (1,19) = .10	.760	.01
		Hemisphere × Group	F (1,19) = .01	.940	.00
		Emotion × Group	F (1,19) = .78	.389	.04
	Three-way interactions	Hemisphere × Emotion × Group	F (1,19) = .54	.471	.03



Supplementary Figure 1. Lateralization index (Lateralization index = (Left – Right) / (Left + Right)) for group comparison separately for happy (A) and Sad (B) vMMN responses. The bars present the mean values with standard errors in each group and the dots in the vertical scatter plots represent the lateralization indexes of individual participants. An outlier value of one control participant is removed from figure A. The statistical results do not change significantly if this participant's data is removed from the analysis (p = .430 vs. p =.901).

III

MAGNETOENCEPHALOGRAPHY RESPONSES TO UNPREDICTABLE AND PREDICTABLE RARE SOMATOSENSORY STIMULI IN HEALTHY ADULT HUMANS

by

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Magnetoencephalography Responses to Unpredictable and Predictable Rare Somatosensory Stimuli in Healthy Adult Humans

Qianru Xu[1,2], *Chaoxiong Ye*[1,2]*, *Jarmo A. Hämäläinen*[2], *Elisa M. Ruohonen*[3], *Xueqiao Li*[2] *and Piia Astikainen*[2]

[1] Institute of Brain and Psychological Sciences, Sichuan Normal University, Chengdu, China, [2] Jyväskylä Centre for Interdisciplinary Brain Research, Department of Psychology, Faculty of Education and Psychology, University of Jyväskylä, Jyväskylä, Finland, [3] Human Information Processing Laboratory, Psychology, Faculty of Social Sciences, Tampere University, Tampere, Finland

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Manuel S. Malmierca,
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***Correspondence:**
Chaoxiong Ye
cxye1988@163.com

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Mismatch brain responses to unpredicted rare stimuli are suggested to be a neural indicator of prediction error, but this has rarely been studied in the somatosensory modality. Here, we investigated how the brain responds to unpredictable and predictable rare events. Magnetoencephalography responses were measured in adults frequently presented with somatosensory stimuli (FRE) that were occasionally replaced by two consecutively presented rare stimuli [unpredictable rare stimulus (UR) and predictable rare stimulus (PR); $p = 0.1$ for each]. The FRE and PR were electrical stimulations administered to either the little finger or the forefinger in a counterbalanced manner between the two conditions. The UR was a simultaneous electrical stimulation to both the forefinger and the little finger (for a smaller subgroup, the UR and FRE were counterbalanced for the stimulus properties). The grand-averaged responses were characterized by two main components: one at 30–100 ms (M55) and the other at 130–230 ms (M150) latency. Source-level analysis was conducted for the primary somatosensory cortex (SI) and the secondary somatosensory cortex (SII). The M55 responses were larger for the UR and PR than for the FRE in both the SI and the SII areas and were larger for the UR than for the PR. For M150, both investigated areas showed increased activity for the UR and the PR compared to the FRE. Interestingly, although the UR was larger in stimulus energy (stimulation of two fingers at the same time) and had a larger prediction error potential than the PR, the M150 responses to these two rare stimuli did not differ in source strength in either the SI or the SII area. The results suggest that M55, but not M150, can possibly be associated with prediction error signals. These findings highlight the need for disentangling prediction error and rareness-related effects in future studies investigating prediction error signals.

Keywords: deviance detection, magnetoencephalography, predictability, prediction error, somatosensory

INTRODUCTION

The ability to detect changes in the stimulus environment is crucial to an organism's survival. Equally important is the capacity to learn contingencies between stimuli and to anticipate future events based on learned patterns in stimuli. Accurate predictions of future events can advance cognitive functioning related to perception and action in a fundamentally important manner (Bar, 2007).

According to the predictive coding theory (Friston, 2005), neural networks constantly learn the statistical regularities of the surrounding stimulus environment and make predictions of future events. When the input information does not match with the prediction, the lower sensory areas send a prediction error signal into the higher cortical areas (recent findings also extend this hierarchical pattern of predictive coding framework to subcortical structures, see Parras et al., 2017; Carbajal and Malmierca, 2018) and modify the prediction (Friston, 2005; Garrido et al., 2009; Stefanics et al., 2014). This new prediction is then sent backward to the lower areas, where it is again compared with the new sensory input signals.

In experimental research, an oddball stimulus condition, wherein a standard stimulus is rarely and randomly replaced by a deviant stimulus, is a feasible tool for studying predictive coding. An event-related potential, called mismatch negativity [MMN or MMNm when investigating with magnetoencephalography (MEG)] (Näätänen et al., 1978, 2010), is elicited by the deviant stimulus and is suggested to reflect prediction error (Friston, 2005; Garrido et al., 2009; Wacongne et al., 2012; Stefanics et al., 2014; Carbajal and Malmierca, 2018). MMN was originally found in the auditory modality (Näätänen et al., 1978) but was later reported as well for deviant stimuli in the visual (e.g., Stefanics et al., 2012; Astikainen et al., 2013; Xu et al., 2018; for reviews, see Czigler, 2007; Kimura et al., 2011; Stefanics et al., 2014; Kremláček et al., 2016), olfactory (e.g., Krauel et al., 1999; for a review, see Pause and Krauel, 2000), and somatosensory (e.g., Shinozaki et al., 1998; Spackman et al., 2007; Strömmer et al., 2014, 2017; for a review, see Näätänen, 2009) modalities.

Here, we focus on the somatosensory mismatch response [sMMR, instead of MMN due to its positive polarity in some previous electroencephalography (EEG) measurements], which is less studied than its auditory and visual counterparts. The sMMR has been observed for changes in stimulus location (Shinozaki et al., 1998; Huang et al., 2005; Restuccia et al., 2009; Strömmer et al., 2014, 2017; Yamashiro et al., 2014; Shen et al., 2018; Hautasaari et al., 2019; for animal models, see: Astikainen et al., 2001; Musall et al., 2017), duration (Akatsuka et al., 2005; Spackman et al., 2007, 2010; Zhao et al., 2014), intensity (Mima et al., 1998; Ostwald et al., 2012), frequency (Kekoni et al., 1997; Spackman et al., 2007), and omissions of the stimuli (Tesche and Karhu, 2000; Naeije et al., 2018). However, one critical confounder should be considered in the context of all the previously mentioned studies, namely, that the probability of the rare stimulus in the traditional oddball paradigm is always smaller than the probability of the standard stimulus and that probability, as such, affects the brain responses (Hari et al., 1990). One possible neural mechanism underlying probability effects is neural adaptation (May et al., 1999; May and Tiitinen, 2010), in which the neural populations responding to frequently presented standard stimuli can be more adapted than those responding to the rare deviant stimuli. Therefore, larger responses can be elicited for deviant stimuli than for standard stimuli (May and Tiitinen, 2010).

For auditory and, to some extent, for visual experiments as well, several different control conditions have been developed to control for possible adaptation effects for MMN elicitation. The many-standards condition (also called the equal-probability condition) is currently the most frequently used (Schröger and Wolff, 1996; Jacobsen and Schröger, 2001). In human auditory oddball studies, the results from the many-standards control condition suggest that the differential responses found in the oddball paradigm (MMN) may not be explained by adaptation alone (Jacobsen and Schröger, 2001; Jacobsen et al., 2003; Maess et al., 2007; Lohvansuu et al., 2013), but this has been less well resolved in animal studies (for supportive evidence in animal models, see, e.g., Astikainen et al., 2011; Nakamura et al., 2011; Parras et al., 2017; Kurkela et al., 2018; Polterovich et al., 2018; for no support or partial support, see, e.g., Fishman and Steinschneider, 2012; Lipponen et al., 2019; Yang et al., 2019). In the many-standards control condition, in addition to the original deviant and standard stimuli, other stimuli with different stimulus features than those in the standard and deviant stimuli are randomly presented but without consecutive repetitions. Each stimulus's probability is the same as the probability of the deviant stimulus in the oddball paradigm. The many-standards condition is more difficult to design for the somatosensory than for the auditory and visual modality. For instance, with a deviant probability of 10%, this condition would require 10 different stimulation locations for a location-change paradigm in the somatosensory modality, and different skin locations have also different sensitivities. However, to our knowledge, no previous studies have applied this type of experiment in the somatosensory domain in human participants, and only one study in animals is reported (whisker stimulation in rats: Musall et al., 2017).

Here, we introduce a novel modified oddball paradigm that approaches the topic from a different angle. Because it is more difficult in the somatosensory than in the auditory studies to produce several feature levels (such as different frequencies of tones) for application in the many-standards condition, we developed a stimulus condition in which somatosensory responses to equally rare unpredictable and predictable stimuli can be investigated. In this stimulus paradigm, the frequently presented standard stimulus (the frequent stimulus, FRE) is rarely and randomly replaced by a deviant stimulus (the unpredictable rare stimulus, UR), as in the classical oddball paradigm. However, another deviant stimulus (the predictable rare stimulus, PR) immediately follows each UR. Therefore, these two rare somatosensory events are different in their prediction error value, but similar in rareness (probability). The UR should thus show increased responses in comparison to the FRE and PR due to its larger prediction error potential.

In this study, the stimulation is presented as electrical stimulations of fingers, and the three stimulus types differ in location of the stimulation. Consistent with previous studies investigating the location deviance detection and where the fingers or hands have been stimulated in an ignore condition (Shinozaki et al., 1998; Akatsuka et al., 2005, 2007a,b; Restuccia et al., 2007; Strömmer et al., 2014, 2017; Hautasaari et al., 2019), we expect that the stimulation will elicit activity in two main time windows at approximately 30–70 and 100–200 ms after the stimulus onset. We also expect both the early and later responses to show a larger amplitude to rare stimuli in comparison to standard stimuli (Mima et al., 1998; Akatsuka et al., 2005, 2007a,b; Strömmer et al., 2017; Hautasaari et al., 2019). Since previous studies have not controlled for stimulus rarity (for example, by using the many-standards control condition), we cannot predict whether increased responses in comparison to the FRE will be elicited by the UR alone or by both the UR and the PR. However, larger responses specific to the UR will reflect prediction error, while larger responses to both the UR and the PR would reflect stimulus rarity in comparison to the FRE.

MATERIALS AND METHODS

Participants

Fifteen healthy participants (12 females and 3 males, aged 21–43 years old) were recruited via email lists and notice boards within the University of Jyväskylä and by an announcement in a local newspaper. Inclusion criteria were an age of 18–45 years, right-handedness, and self-reported normal senses (vision corrected with eyeglasses was allowed). Hearing ability for 1,000 and 500 Hz sounds was measured in the laboratory with an audiometer to ensure proper hearing because we also collected another dataset in the auditory sensory modality, not reported here. Exclusion criteria were pregnancy, breastfeeding, current or previous neurological or psychiatric diseases, brain damage, alcohol abuse or use of illegal drugs, and current depressive symptoms. A Finnish-language version of the Beck Depression Inventory II (BDI-II) questionnaire (Beck et al., 1996) was filled in by participants, and a maximum score of 10 in the BDI-II was allowed for included participants. In addition, participants with contraindications for MEG measurement such as a pacemaker, hearing aid, or dental implant were excluded. Before the experiment, a phone interview was conducted to confirm the inclusion and exclusion criteria. Each participant received one movie ticket as compensation for their participation. The experiment complied with the Declaration of Helsinki and was approved by the ethics committee of the University of Jyväskylä. Written informed consent was signed by each participant upon their arrival to the laboratory.

Stimulus and Task Procedure

Stimuli were electrical pulses (Stimulator: DeMeTec SCG30, DeMeTec GmbH, Langgöns, Germany) of 200 μs in duration, delivered via flexible, non-magnetic metal ring electrodes (Technomed Europe Ltd., Maastricht, Netherlands) to the left forefinger and little finger and stimulating the cathode above the proximal phalanx and the anode above the distal phalanx. All the ring electrodes were moistened with conductive jelly (Technomed Europe Ltd., Maastricht, Netherlands) to reduce impedance. A piece of gauze was tied to the stimulated finger between the two electrodes to prevent conduction between the two electrodes on the same finger. The stimulation intensity was adjusted separately according to the threshold of each finger for each subject. The threshold was determined by the participants' oral reports when they sensed an electrical pulse. The stimulation started from very low intensity and gradually continued to a higher intensity in increments of 0.1 mA until the participant reported feeling the stimulation. This process was repeated three times and applied to the two stimulated fingers. The intensity applied in the experiment was 1.5 times the subjective sensory threshold intensity.

The stimulus procedure was a modified oddball paradigm. A frequently presented stimulus was occasionally replaced by two different rare stimuli: the first one, which was unpredictable, was always followed by another one that was predictable. The experiment had two main stimulus conditions (condition A and condition B, **Figure 1**), which had counterbalanced stimulus features for the FRE and the PR. In condition A, the FRE was stimulation to the little finger, and the PR was stimulation to the forefinger. In condition B, the stimulus assignment was reversed for the FRE and PR. The unpredictable rare stimulus (UR) was a double stimulation (forefinger and little finger, simultaneously). The double stimulation was selected because we did not want to stimulate an additional finger, which would have been necessarily adjacent to either little finger or forefinger. This is because it is not known whether stimulation of adjacent fingers elicits differential responses, but we know from our previous studies that stimulation of the little finger and forefinger can elicit a differential response between the deviant and the standard stimuli (Strömmer et al., 2014, 2017). In addition, not stimulating additional fingers can also avoid the potential boundary effect. This is because previous studies have shown a significantly larger sMMR contrast between the middle finger and the thumb than between the middle finger and the little finger (Shen et al., 2018). Therefore, applying stimulation to additional fingers could also introduce other possible stimulus features variance.

In order to counterbalance the physical features of the stimuli for sMMR assessment, an additional experiment with condition C was conducted for four participants after the presentation of conditions A and B. In condition C, the FRE was a stimulation of the forefinger and little finger, simultaneously, whereas the UR and PR were stimulations to the forefinger and little finger, respectively (see **Supplementary Material 1** for the experimental setting and results). Therefore, when averaging the responses of conditions B and C, the stimulus features were counterbalanced for the FRE and the UR.

Each condition consisted of 1,000 trials presented in two runs for each participant. The probability of an FRE was 80%, and the probability of a UR or PR was 10%. The presentation order of the runs was counterbalanced between the participants, and a short break was provided after each run. The interstimulus interval (ISI, offset-to-onset) was 500 ms under all conditions. The stimulus presentation was controlled by Presentation® software (Neurobehavioral Systems, Inc., Berkeley, CA, United States). Participants were instructed to ignore the somatosensory stimuli and focus on a silent movie. The movie was projected onto

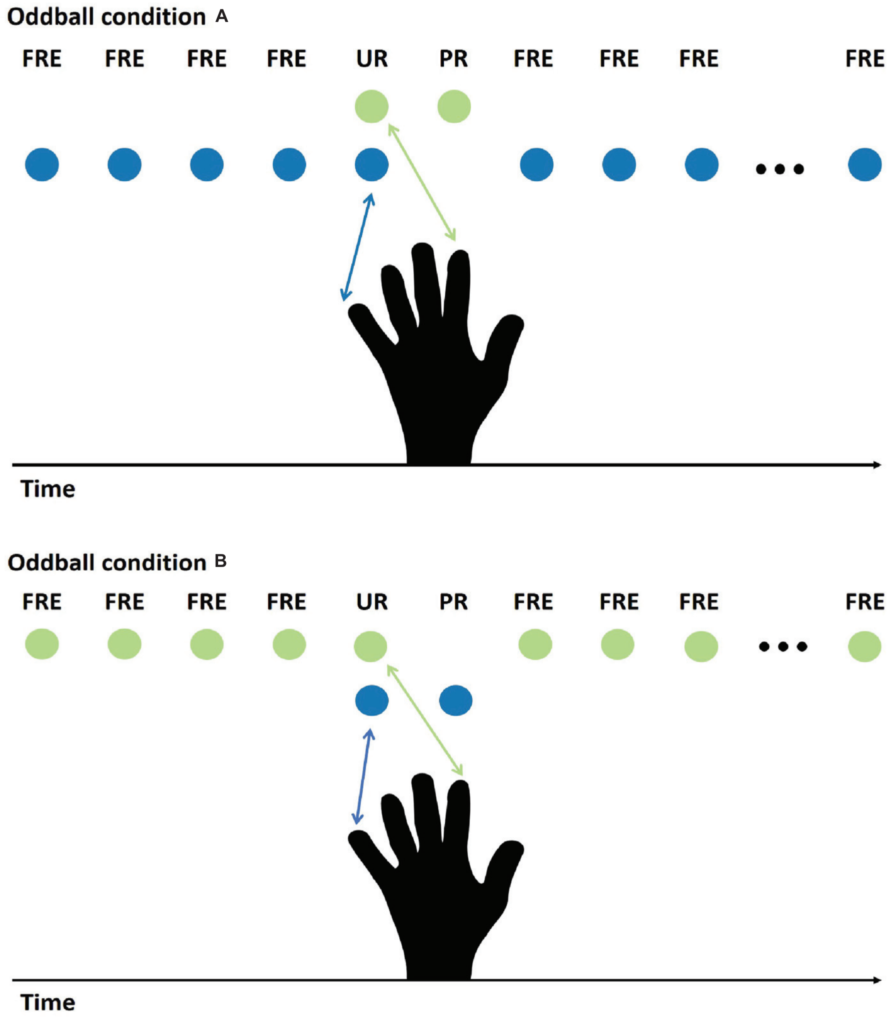

FIGURE 1 | Illustration of the stimulus presentation for conditions A and B. Under condition A, stimulation to the little finger (blue ball symbol) served as the FRE, stimulation to the forefinger (green ball symbol) as the PR, and simultaneous pulses to the forefinger and the little finger as the UR. Under condition B, the opposite assignment between the FRE and the PR was applied. In the analysis, conditions A and B were averaged; therefore, the physical features of the FRE and the PR are controlled. FRE, frequent stimulus; UR, unpredictable rare stimulus; PR, predictable rare stimulus.

the center of the screen at a distance of about 1 m from the participant (video projector: Barco FL35 projector; native resolution 1,920 × 1,080 pixels).

Data Acquisition

The somatosensory evoked related magnetic fields were recorded with a 306-channel whole-head system (Elekta Neuromag TRIUX^{TM} system, Elekta AB, Stockholm, Sweden) in a magnetically shielded, dimly lit room at the MEG Laboratory, University of Jyväskylä.

During the MEG recording, the participant was seated on the chair with their head inside the helmet-shaped device at a 68° upright position. The head position with respect to the sensors in the helmet was determined at the beginning of the task according to the magnetic fields produced by currents fed into five indicator coils at predetermined locations on the scalp. Two HPI coils were placed on both sides behind each ear; another three were placed on the forehead. The locations of these coils in relation to the anatomical location of preauricular points and nasion were determined with an Isotrak 3D digitizer (Polhemus^{TM}, United States) before the experiment started. More than 100 additional points were digitized over the scalp to provide an accurate representation of the individual head shape and for co-registration with a magnetic resonance imaging (MRI) template. The continuous MEG signal was recorded with an online bandpass filter of 0.1–330 Hz and a sampling frequency of 1,000 Hz. The electrooculogram (EOG) and electrocardiogram (ECG) signals were recorded by detecting eye movements and heartbeat artifacts, respectively. The vertical EOG was recorded by two electrodes attached above and below the right eye; the horizontal EOG was recorded by two electrodes placed on the outer canthi of both eyes. One ECG electrode was placed below the collar bone on the right side, and the other was placed in the middle of the two collar bones. A ground wristband was wrapped around the participant's left-hand carpal bone.

Data Analysis

The Maxfilter 3.0 (Elekta AB) was first applied to reduce the artifacts and transform the mean head positions across different recording sessions. Bad channels were marked manually. The spatiotemporal signal space separation (tSSS) method (Taulu et al., 2004), with a buffer of 30 s and a subspace correlation limit of 0.98, was used to remove external interference from the data. The head position was estimated for head movement compensation with the default setting (HPI amp window: 200 ms; HPI amp step: 10 ms).

The MEG data were then preprocessed and analyzed using the Brainstorm software (Tadel et al., 2011). First, a notch filter of 50 Hz (3 dB notch bandwidth: 2 Hz) and a low-bandpass filter of 60 Hz were applied, as described previously (Hautasaari et al., 2019). Cardiac and eye blink artifacts were attenuated with signal space projection (SSP) in Brainstorm by visually inspecting and removing the corresponding SSP components separately for gradiometers and magnetometers. Additionally, data with EOG amplitudes exceeding 200 μV were marked as bad. The data were then made into epochs according to the stimulus events from a 100 ms pre-stimulus baseline to 500 ms from the stimuli onset. A DC offset baseline correction of -100 to 0 ms was calculated and removed for each epoch. Epochs that included a segment in which the EOG amplitudes exceeded 200 μV were rejected.

The responses were then averaged for each stimulus type over condition A and condition B (weighted average with the number of trials in each condition). Only FRE responses immediately preceding the UR were applied in the analysis because this allowed an equal number of trials for each stimulus type. Conditions A and B were then combined to counterbalance the physical properties of the FRE and the PR. More specifically, a weighted average based on the number of trials was calculated for the rare (both UR and PR) and the FRE responses across conditions A and B for each participant.

For sensor-level comparisons, planar gradiometer channel pairs were combined using root mean squares (RMSs) at each sensor location. For source-level analysis, because individual MRI data were not available, the FSAverage_2016 anatomy template from Brainstorm was used for the MRI co-registration and further source analysis. To make the template better match each participant's head shape, we warped the anatomy templates to match the shape defined by the digitized points. The noise covariance matrix was estimated from an empty room recording made on the same day or on neighboring days. For the MEG forward model, the sensor-weighted overlapping sphere model (one per sensor, in a total of 306 local spheres) (Huang et al., 1999) was used for the representation of the cortical surface with 45,000 dipoles (3 orientations × 15,000 vertices). The inverse solution was performed using the unconstrained depth-weighted minimum-norm estimates (wMNE) implemented in Brainstorm. The unconstrained wMNE were used to avoid the possible noisy and discontinuous current maps since we used the anatomy template instead of individual MRI data for the source estimate. The source localization results were then normalized with a Z-score based on the baseline from -100 to 0 ms relative to the stimulus onset. The norm of the three orientations for the unconstrained source was used in the subsequent analysis.

Statistical Analysis

Sensor-level analyses were carried out in Brainstorm by calling the spatiotemporal cluster-based permutation test functions from the Fieldtrip toolbox (Maris and Oostenveld, 2007). Since the results were similar to the source-level results, the detailed statistical analysis and main results of the sensor-level data are reported in **Supplementary Material 2**. Previous MEG studies in the ignore condition have suggested that sMMR is mainly elicited in the primary somatosensory cortex (SI) and the secondary somatosensory cortex (SII) (e.g., Akatsuka et al., 2007a,b; Naeije et al., 2016, 2018; Hautasaari et al., 2019). Thus, based on these prior findings and verified in our grand-averaged source maps of the UR and PR (**Figure 2**), we defined two regions of interest (ROIs), namely, SI (G_postcentral: postcentral gyrus) and SII (Lat_Fis-post: posterior ramus of the lateral fissure), based on the Destrieux atlas (Destrieux et al., 2010). Moreover, only the regions on the right hemisphere, which mean the contralateral SI (cSI) and the contralateral SII (cSII), were used since little or no activation occurs in the corresponding brain regions on the left hemisphere (**Figure 2**) (for previous studies in which only the contralateral side was activated, see, e.g., Strömmer et al., 2014, 2017; Naeije et al., 2016, 2018). The norms of the three orientations for an unconstrained source within the same time windows (30–100 and 130–230 ms after stimulus onset) used in the sensor-level analysis were exported from Brainstorm into the SPSS program for further analysis. For each identified ROI and time window, a separate one-way repeated-measures analysis of variance (ANOVA), with stimulus type (FRE, UR, and PR) as the within-subjects factor, was conducted. The Greenhouse–Geisser correction [p-value after Greenhouse–Geisser correction (p_{corr})] was applied when the assumption of sphericity was not met. For significant ANOVA results, *post hoc* analyses were conducted by using a two-tailed paired t-test with different stimulus type pairs. Partial eta squared ($\eta^2{}_p$) measures were used for effect size estimates in ANOVA. Bonferroni correction was used for both ANOVA and *post hoc* analysis to control for the multiple comparison problem [p-value after Bonferroni correction (p_{corr})]. Cohen's (1988) d was computed with pooled standard deviations for the effect size estimate in the t-test.

RESULTS

Descriptive Results

Figure 2 illustrates the grand-averaged sensor-level responses and the source estimates for the FRE, UR, and PR. **Figures 3A,B**

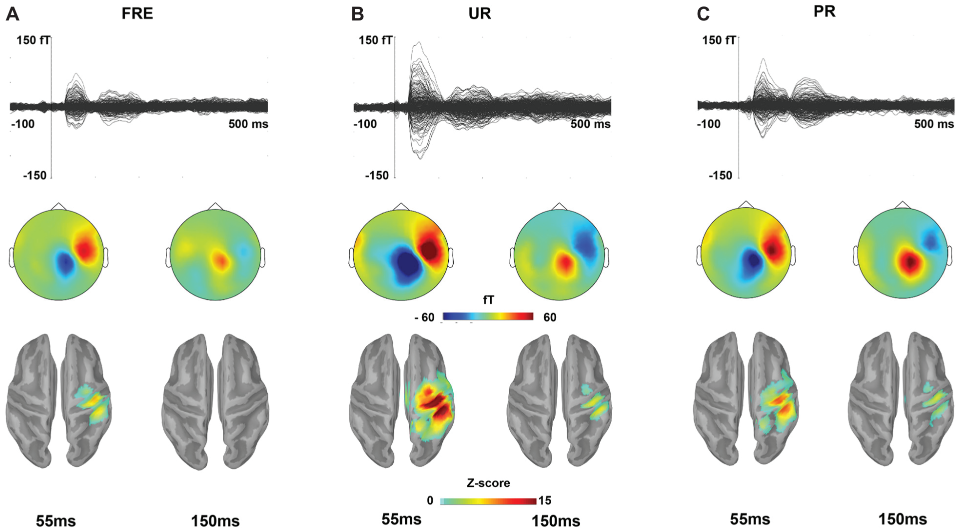

FIGURE 2 | The grand-averaged responses for **(A)** FRE, **(B)** UR, and **(C)** PR. The upper panel shows a butterfly view of the grand-averaged response for each stimulus type from all 306 sensors. For visualization purposes, gradiometer values are multiplied by 0.04 due to the differing units for magnetometers (T) and gradiometers (T/m). The middle and lower panels show the topographies of the sensor-level activity based on magnetometers and source activation, respectively, at a time point of 55 and 150 ms for each stimulus type. In the lower panel, only the sources that have a value > 40% of the color bar maximum are displayed. FRE, frequent stimulus; UR, unpredictable rare stimulus; PR, predictable rare stimulus.

illustrate the source activity waveform on both ROIs for each stimulus type (UR, PR, and FRE) and differential responses (UR–FRE and PR–FRE), respectively. As shown in **Figures 2**, **3A**, the response waveforms are characterized by two main components: one at approximately 30–100 ms latency (M55) and the other at approximately 130–230 ms latency (M150). The corresponding topography and source activation for each component are also presented in **Figure 2**. The sensor-level results are reported in **Supplementary Material 2**.

Source Activations

M55

For the results of the mean source activation value in 30–100 ms latency, one-way repeated-measures ANOVA showed main effects of stimulus type in both the cSI and cSII: in the cSI, $F(2,28) = 32.049$, $p_{corr} < 0.001$, $\eta^2_p = 0.696$); in the cSII, $F(2,28) = 18.126$, $p_{corr} < 0.001$, $\eta^2_p = 0.564$. *Post hoc* paired t-tests with Bonferroni-corrected p-values are reported in **Table 1** and **Figure 3C**. *Post hoc* tests revealed that both the PR and UR showed increased activation compared to the FRE in both the cSI and the cSII areas. In addition, both ROIs showed an increased source strength for the UR compared to the PR. The line graph of individuals' source strength to the three stimulus types are illustrated in **Figure 3D**. The grand-averaged source activations for different stimuli from the right-side view are illustrated in **Figure 4**.

M150

For M150, significant main effects for the stimulus type were found in both ROIs; cSI: $F(2,28) = 11.355$, $p < 0.001$, $\eta^2_p = 0.448$); cSII: $F(2,28) = 14.798$, $p < 0.001$, $\eta^2_p = 0.514$. *Post hoc* t-tests are reported in **Table 2** and **Figure 3C**. The results showed that in both ROIs, both the PR and the UR induced larger activity compared to the FRE. However, no difference was found between the UR and the PR in either the cSI or the cSII areas. The line graph of individuals' source strength to the three stimulus types are illustrated in **Figure 3D**. The grand-averaged source activations for the different stimuli from the right-side view are illustrated in **Figure 4**.

DISCUSSION

In the present study, we introduced a new oddball stimulus protocol for investigating brain responses to unpredictable and predictable rare somatosensory events. Use of this stimulus protocol allowed us to control for the rarity (probability) of the unpredictable and predictable stimuli. We found two main components, M55 and M150, for each stimulus type: the frequent stimulus (FRE), unpredictable rare stimulus (UR), and predictable rare stimulus (PR). The sources of both components were located on the contralateral somatosensory cortices. The sensor-level (see **Supplementary Material 2** for a detailed report) and the source-level results showed a similar pattern: both components elicited a larger activity for the UR and PR than for the FRE. A larger response was observed for the UR than for the PR only for M55, whereas no difference was found in response amplitudes between the UR and the PR for M150. This pattern of results suggests that M55, but not M150, possibly signals the prediction error.

The latencies of the components, one at 30–100 ms latency (M55) and the other at 130–230 ms latency (M150), were

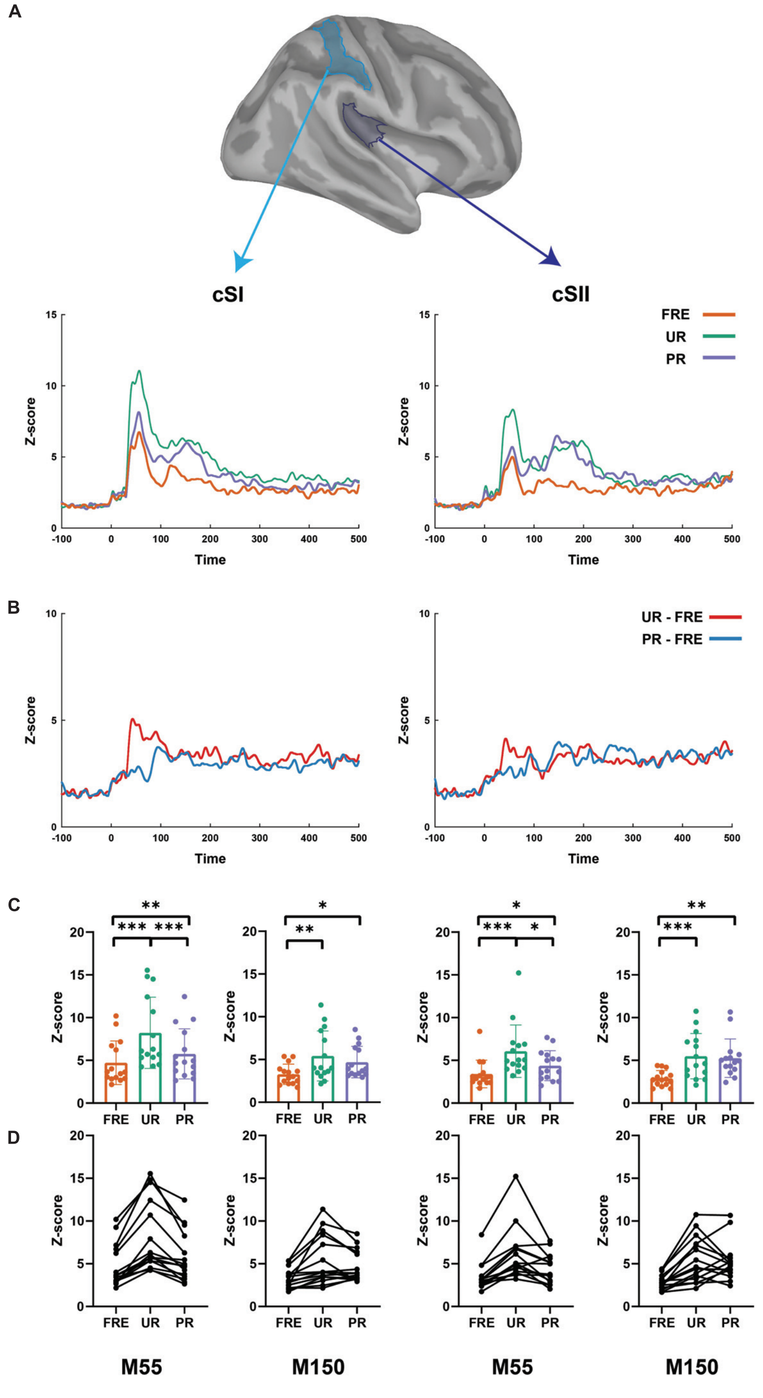

FIGURE 3 | The summary of the results from the source-level analysis. **(A)** The cortical time series for all three conditions (UR, PR, and FRE) in the cSI (left panel) and cSII (right panel). **(B)** The cortical time series for the differential responses (UR–FRE and PR–FRE) in the cSI (left panel) and cSII (right panel). **(C)** The bar graph of the source strength comparison of the FRE, UR, and PR in the cSI (left panel) and cSI (right panel). Error bars represent the standard error of the mean, and the dots represent the values of the individual participants. **(D)** Line graphs of the individual participant's source strengths to the three stimulus types in the cSI (left panel) and cSII (right panel). FRE, frequent stimulus; UR, unpredictable rare stimulus; PR, predictable rare stimulus; **p* < 0.05, ***p* < 0.01, and ****p* < 0.001.

well in line with the previous MEG studies that have found an early component approximately at 30–70 ms latency and a later component at approximately 100–200 ms after stimulus onset (Mima et al., 1998; Akatsuka et al., 2007a,b; Hautasaari et al., 2019). Some EEG studies that applied the somatosensory oddball paradigm have also found two components with similar latencies as M55 and M150 here (Shinozaki et al., 1998; Akatsuka et al., 2005; Restuccia et al., 2007; Strömmer et al., 2014, 2017). Consistent with previous MEG oddball studies that applied source localization (Mima et al., 1998; Akatsuka et al., 2007a,b; Naeije et al., 2016, 2018; Hautasaari et al., 2019), both components were elicited on the sensory cortices (SI and/or SII).

Our results resemble those of the previous somatosensory studies that applied a traditional oddball paradigm to elicit the sMMR; however, our data raise questions regarding the interpretation of the previous studies that the responses to rare unpredictable stimuli (here UR) at 100–200 ms latency reflect a prediction error (e.g., Mima et al., 1998; Shinozaki et al., 1998; Akatsuka et al., 2005, 2007a; Strömmer et al., 2014, 2017; Hautasaari et al., 2019). Namely, when we used equally rare stimuli with different types of predictability (UR and PR), the responses to these two stimuli did not show any amplitude difference for M150, but they did for M55. Although several studies have found larger responses to deviant than to standard stimuli at early latency (within the 100 ms post-stimulus latency, Mima et al., 1998; Shinozaki et al., 1998; Akatsuka et al., 2005, 2007a,b; Strömmer et al., 2014, 2017; Yamashiro et al., 2014; Hautasaari et al., 2019), these studies have usually considered only the later response (between 100 and 200 ms post stimulus), but not the earlier one (before 100 ms) as being analogous to sMMR (e.g., Mima et al., 1998; Shinozaki et al., 1998; Akatsuka et al., 2005, 2007a; Strömmer et al., 2014, 2017; Hautasaari et al., 2019). However, they did not provide any empirical evidence for the assumption of the specificity of the later response to a prediction error, nor did they rule out the effect of stimulus rareness (for example, by applying the many-standards control condition). Therefore, the previous findings of differential responses to deviant stimuli at 100–200 ms post-stimulus latency may possibly have reflected merely the rareness of the deviant stimulus. Conversely, the differential responses at the earlier latency (before 100 ms) reported in the previous studies (Mima et al., 1998; Shinozaki et al., 1998; Akatsuka et al., 2005, 2007a,b; Strömmer et al., 2014, 2017; Yamashiro et al., 2014; Hautasaari et al., 2019) could reflect a prediction error. Notably, the results from a previous MEG study indicated that two components, one at 30–70 ms and the other at 150–250 ms latency, showed increased amplitudes to deviant stimuli presented at 10%, but not at 30 or 50% probability (Akatsuka et al., 2007b). The results of this previous study, together with those of our study in which the predictability of the rare stimulus was manipulated, suggest that the earlier MEG component (here M55) could be specific to the prediction error and that the later responses (here M150) might reflect merely the stimulus rareness. Furthermore, studies that used a global/local paradigm to verify the hierarchical processing network of the sMMR at different levels found that a response peaking at 70–100 ms over the posterior bank of the postcentral sulcus reflected the prediction error (Naeije et al., 2016, 2018). In rabbits, similar and even earlier latencies (i.e., 20–40 and 80–100 ms) for somatosensory deviance detection have been found in recordings of local-field potentials from the somatosensory cortex (deviant-alone control condition, Astikainen et al., 2001).

TABLE 1 | *Post hoc* paired-samples *t*-tests investigating the main effect of the stimulus type found in the repeated-measures ANOVA for M55.

Conditions	**cSI**			**cSII**		
	t	p_{corr}	d	t	p_{corr}	d
PR vs. FRE	4.121	0.003	0.376	3.199	0.019	0.576
UR vs. FRE	6.612	<0.001	1.014	6.175	<0.001	1.086
UR vs. PR	4.816	<0.001	0.685	2.977	0.030	0.677

PR, predictable rare stimulus; FRE, frequent stimulus; UR, unpredictable rare stimulus; cSI, contralateral primary somatosensory cortex; cSII, contralateral secondary somatosensory cortex; p_{corr}*, p-value after Bonferroni correction; d, Cohen's d. The degrees of freedom for all comparisons are 14.*

TABLE 2 | *Post hoc* paired-samples *t*-tests investigating the main effect of stimulus type found in the repeated-measures of ANOVA for M150.

Conditions	**cSI**			**cSII**		
	t	p_{corr}	d	t	p_{corr}	d
PR vs. FRE	3.528	0.010	0.921	4.357	0.002	1.381
UR vs. FRE	3.768	0.006	0.962	5.161	<0.001	1.315
UR vs. PR	1.905	0.232	0.294	0.434	1.000	0.095

PR, predictable rare stimulus; FRE, frequent stimulus; UR, unpredictable rare stimulus; cSI, contralateral primary somatosensory cortex; cSII, contralateral secondary somatosensory cortex; p_{corr}*, p-value after Bonferroni correction; d, Cohen's d. The degrees of freedom for all comparisons are 14.*

Not only some of the previous studies in the somatosensory modality but also those in the auditory modality have reported deviance detection at early latencies. For example, the auditory middle latency responses (MLRs), elicited within 50 ms latency after the stimulus onset, have been studied in the context of predictive coding (e.g., Althen et al., 2011; Grimm et al., 2011; Recasens et al., 2014). These responses have their source generator possibly in the sensory cortex (Recasens et al., 2014), and a recently suggested view (Grimm et al., 2016) is that the MLRs could be correlates of stimulus-specific adaptation (SSA, Ulanovsky et al., 2003), which also occurs in a similar latency range. SSA (i.e., adaptation to repeated sounds that do not generalize to other sounds) is widely studied in animals with single-cell recordings. Although the name of the phenomenon refers to adaptation, release from SSA can also support genuine deviance detection (e.g., Parras et al., 2017; for a review, see Carbajal and Malmierca, 2018). Interestingly, a rat study that contrasted the auditory cortical responses to patterns of periodic (predictable) and random (unpredictable) changes in sounds found larger intracellular and extracellular responses to random than to periodic changes (Yaron et al., 2012). Future studies using both single-cell and neural network-level recordings are needed to understand whether the early latency brain responses (e.g., MLRs and the M55 reported here) in the auditory and somatosensory modalities have functional similarities and

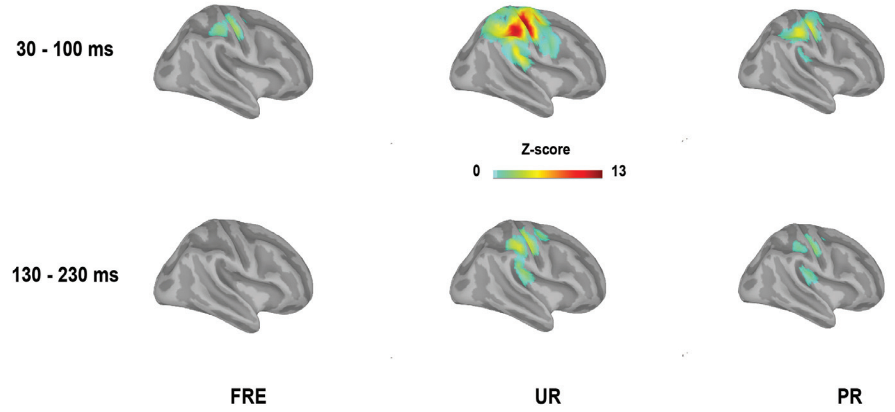

FIGURE 4 | Grand-averaged source activation for the time window of 30–100 ms (M55) and 130–230 ms (M150) after stimulus onset for each stimulus type from the right-side view (mean values of the time windows presented). For visualization purposes, only the sources with a value > 40% of the color bar maximum are displayed here. FRE, frequent stimulus, UR, unpredictable rare stimulus; PR, predictable rare stimulus.

whether they share neural mechanisms for rareness and/or deviance detection.

Here, the activity for both the UR and the PR was most pronounced on the sensory cortices (i.e., the SI and SII). Although some discrepancies exist regarding whether the activity has been found from the SI, the SII, or both, previous studies applying the somatosensory oddball condition have mainly located deviance detection-related responses in the SI and/or SII. Akatsuka et al. (2007a,b), who first applied the source localization method for the sMMR, suggested that the early component (30–70 ms) originates mainly from the SI. The later component (150–250 ms) was located mainly in the SI, but the data from some individuals showed the generators in the SII (Akatsuka et al., 2007a,b). Later, areas 1 and 3b of the SI, as well as the posterior parietal cortex (PPC), were linked to the deviance detection at approximately 50–120 ms post-stimulus latency. Deviance detection-related activity was also found on the bilateral SII cortex in a few participants (Yamashiro et al., 2014). Both the electrical and tactile stimuli also elicited SI activity for the early component (40–58 ms), and SII activity for the later component (110–185 ms) (Hautasaari et al., 2019). Some studies have also found simultaneous SI and SII responses as early as 20–30 ms (Karhu and Tesche, 1999) instead of a strict hierarchical or serial manner, suggesting that the SI and SII could process somatosensory stimuli in a parallel manner. Taken together with our results, the available evidence indicates a likelihood that the SI and SII could both contribute to the deviance detection and could also possibly be linked to the prediction error.

Even if our study strongly suggests that the increased response amplitude for M150 does not reflect a prediction error, the current study is limited in its interpretation regarding M55. The M55 was larger in amplitude for the UR than for the FRE and PR; however, whether the increased response amplitude reflects the prediction error or a larger stimulus energy for the UR in comparison to the PR and FRE is unclear. This is because the low-level stimulus features were not counterbalanced for all the stimulus types, but only between the FRE and PR. The stimulus energy for the UR (stimulation of two fingers at the same time) was larger than for the PR and FRE (stimulation of one finger) when the data combined from conditions A and B were analyzed. Therefore, we conducted an additional measurement (condition C) for a small subsample of participants ($n = 4$). In this measurement, the physical characteristics of the UR and FRE were reversed for condition B (**Supplementary Material 1**). Thus, when the data were combined from conditions B and C, the responses to the UR and FRE were counterbalanced for their low-level features. Visual observation of the data suggests that three of the four participants showed numerically larger activity for the UR than for the FRE in the M55 time range, and two of the four participants showed the same for M150. This suggests that the difference in low-level physical features was probably not the only reason for the larger responses to the UR than to the FRE in the larger sample, and this tentatively associates M55 with the prediction error.

Our paradigm may also be applied to the other sensory modalities. In the auditory modality, the many-standards control condition has recently been the most commonly used protocol to control for the effect of stimulus probability (e.g., Jacobsen and Schröger, 2001, 2003). However, the results may be affected by the cross-frequency adaptation (Taaseh et al., 2011) between the oddball and control condition sounds. The cross-frequency adaptation is usually observed as a reduced response amplitude to consecutive sounds of nearby frequencies. Because more sounds are present, and usually with smaller frequency differences in the control than in the oddball condition, the responses can be larger to the oddball deviant sounds than to the control sounds merely for this reason (see discussion in Yang et al., 2019, where the oddball and many-standards conditions have the same frequency separation in rats). The novel paradigm introduced in the present study can avoid this problem, because it does not require many different stimuli, and the stimuli can also be clearly distinct in frequency (or other changing feature). However, all three stimulus conditions (here conditions A and B in **Figure 1** and condition C in **Supplementary Material 1**) are required to fully counterbalance the physical features of the three stimuli.

In summary, our results suggest that the processing of a stimulus site change in the electrical stimuli on the fingers induces two main components: M55 and M150. M55 was larger for the UR than for the FRE and PR over both the SI and SII. Surprisingly, although the UR had a larger prediction error potential and an even larger stimulus energy than the PR, it did not show an increased M150 amplitude when compared to the PR. Our data therefore tentatively link M55, but not M150, to signaling of the prediction error. The results also highlight the need for controlling the stimulus rareness or for disentangling stimulus rareness and predictability in future studies.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethical Committee of the University of Jyväskylä. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

QX and PA conceived the experiments. QX, ER, and XL performed the data acquisition. QX analyzed the data. JH contributed to data analysis. QX, CY, JH, and PA interpreted the data. QX, CY, and PA drafted the manuscript. JH, ER, and XL provided critical revisions. All authors revised and approved the manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnhum.2021.641273/full#supplementary-material

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Conflict of Interest: 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.

Supplementary Material 1

Magnetoencephalography responses to unpredictable and predictable rare somatosensory stimuli in healthy adult humans

1 Introduction: additional data controlling for physical features of the stimuli in the analysis of the sMMR

In our study reported in the main text, the focus was on comparison of the responses to repetitive (FRE) and predictable rare (PR) stimuli with the aim of demonstrating the effect of rareness without prediction error. Therefore, the stimulus conditions A and B were counterbalanced for these stimulus types. However, the stimuli that elicited a mismatch response (i.e., standard and unpredictable rare stimuli) were not counterbalanced under these conditions.

To estimate to what extent the stimulus characteristics affected the responses to the UR, especially because the UR was larger in energy than the FRE, we conducted an additional recording, condition C, in four of the original fifteen participants who were available for the measurement. Due to an insufficient number of participants for group-level statistical analysis, we report here the descriptive figures of the averaged responses with a 95% confidence interval (CI) derived from single trials for each participant.

2 Method

The participants were four females, aged 22–31 years old. In condition C, the FRE and UR were reversed to that of condition B (Supplementary Material 1, Figure 1). We combined the responses from conditions B and C in the analysis, allowing counterbalancing of the physical properties of the FRE and UR in the responses.

All the preprocessing methods for condition C were identical to those described in the main text for conditions A and B. Only sensor level analyses were conducted, and they are presented below. Like the results reported in the main text, the following results for the UR and FRE were extracted from the root mean square of the paired gradiometer in two orthogonal directions from the same sensor location. The somatosensory mismatch response (sMMR) is defined here as a difference between the responses to the UR and FRE (UR-FRE). All the waveforms present in the following figures were averaged from the most pronounced channel cluster, including eight sensors; that is, it is the same as in the Supplementary Material 2 reported for the whole sample (Supplementary Material 2, Figure 1A).

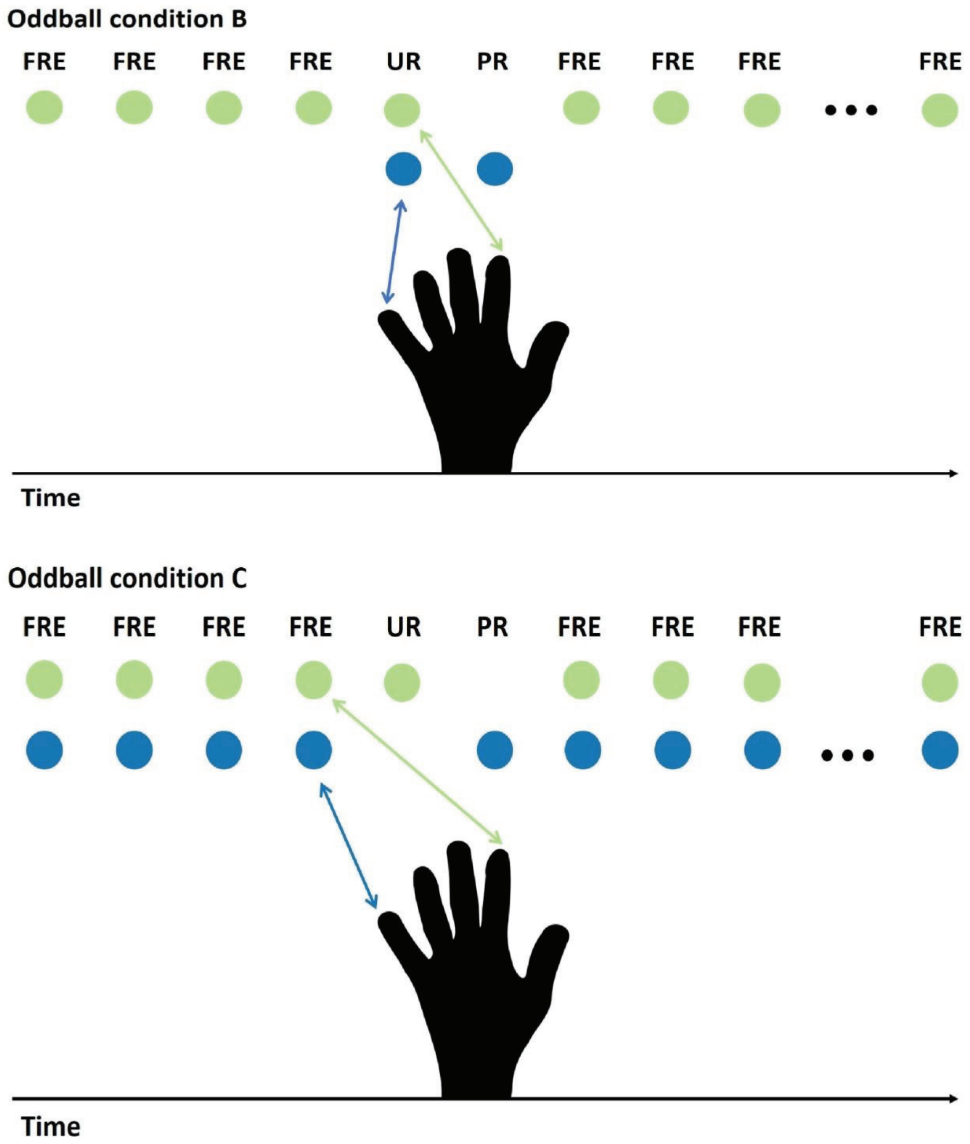

Figure 1. Illustration of the stimulus presentation for conditions B and C. In condition B, the stimulations to the forefinger (green ball symbol) and little finger (blue ball symbol) served as the frequent (FRE) and predictable rare (PR) stimuli, respectively, and the simultaneous stimulation to the forefinger and little finger served as the unpredictable rare (UR) stimulus. By contrast, in condition C, the FRE stimulus was manifested as the simultaneous stimulation of the forefinger and the little finger. The UR and PR were applied to the forefinger and little finger, respectively.

3 Results

Supplementary Material 1, Figure 2 shows the grand-averaged results for the four participants. Visual inspection of the grand-averaged waveforms indicates that both the UR and FRE show two main components corresponding to the M55 (30–100 ms) and M150 (130–230 ms) reported in the main text. The UR seems to induce a larger amplitude than the FRE in both time windows.

Supplementary Material 1, Figure 3 shows the individual participants' responses (condition B and C, averaged). Visual inspection of the waveforms suggests that all four participants show the two investigated components (corresponding to M55 and M150) for the FRE and UR stimuli. Furthermore, for three participants (participants 1, 3, and 4), the responses are numerically larger in amplitude for the UR than for the FRE in the earlier time window, while two participants (participants 1 and 2) show a larger response to the UR than to the FRE in the later time window.

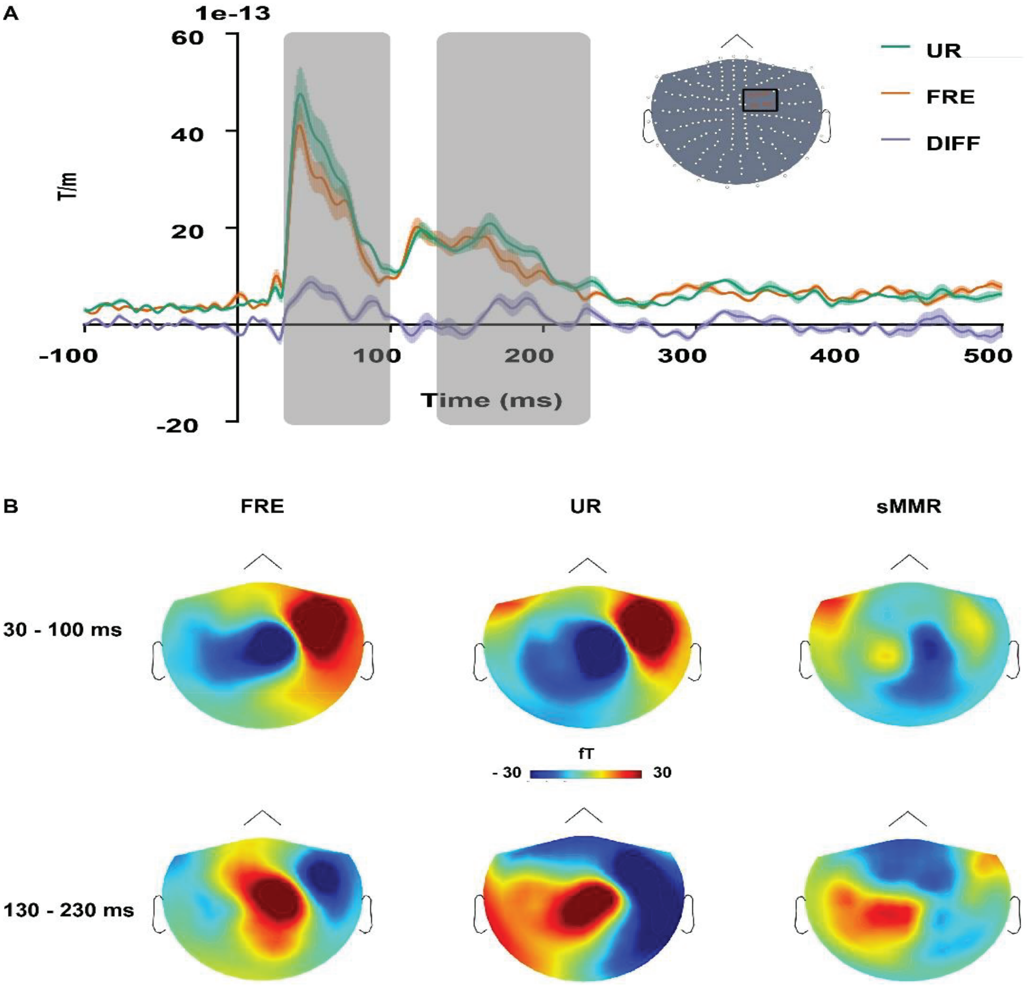

Figure 2. Sensor level grand-averaged results of four participants (conditions B and C averaged, thus physical features for the FRE and UR counterbalanced). (A) Grand-averaged waveforms (*n* = 4) with 95% CI averaged from the eight most pronounced sensors (marked with red dots in the black frame in the sensor map). Orange line: frequent stimulus (FRE); Green line: unpredictable rare stimulus (UR); Purple line: sMMR (somatosensory mismatch response, obtained by subtracting the FRE from the UR). The gray shaded areas indicate the time window for M55 (30–100 ms) and M150 (130–230 ms) analyzed in the main text. (B) Topographical maps of the FRE, UR, and sMMR for M55 and M150 extracted as mean amplitude values from the time window of 30–100 ms and 130–230 ms after stimulus onset, respectively. *Upper panel*: topography of M55 (30–100 ms); Lower panel: topography of M150 (130–230 ms).

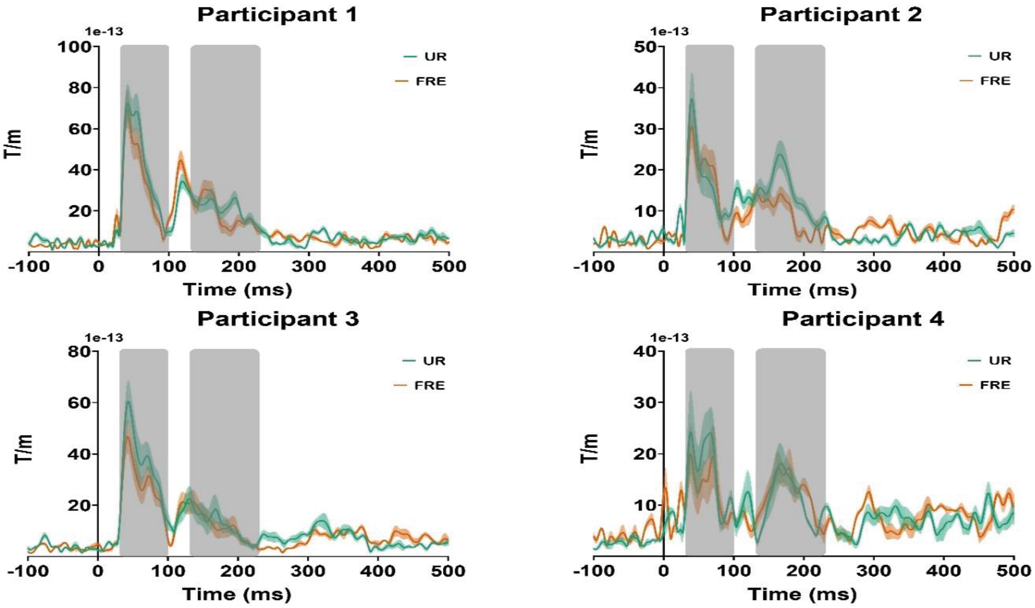

Figure 3. Waveforms (mean and 95% CI) for each of the four participants (the responses are an average of the eight most pronounced sensors). Orange line: frequent stimulus (FRE); Green line: unpredictable rare stimulus (UR). The gray shaded areas indicate a time window of M55 (30–100 ms) and M150 (130–230 ms) applied in the analysis reported in the main text.

As these data stem from only a small sample (*n* = 4) without statistics, we cannot provide convincing evidence for elicitation of the sMMR. However, visual observation suggests that the responses to the UR are numerically larger than the responses to the FRE for at least some participants. This finding was observed in three of the four participants for M55 and two of the four for M150.

Supplementary Material 2

Magnetoencephalography responses to unpredictable and predictable rare somatosensory stimuli in healthy adult humans

1 Data analysis and statistical analysis at the sensor level

For sensor level comparison, planar gradiometer channel pairs were combined using root mean squares (RMS) at each sensor location. Sensor level analyses were carried out in Brainstorm by calling the spatio-temporal cluster-based permutation test functions from the Fieldtrip toolbox (Maris and Oostenveld, 2007). Time windows for the analysis were restricted based on visual inspection of the maximum of the global field power (GFP) from the grand-averaged response (Supplementary Material 2, Figure 1A) and results of the previous somatosensory studies (e.g., Mima et al., 1998; Akatsuka et al., 2005; Strömmer et al., 2017; Hautasaari et al., 2019). Accordingly, two time windows were selected for further investigation: one at 30–100 ms (labeled as M55) latency and the other at 130–230 ms (labeled as M150) latency after stimulus onset. Over the corresponding time ranges for each component, the contrast between the PR and FRE, the UR and FRE, and the UR and PR were conducted separately in each time window. The channel cluster alpha was set as 0.05; the number of permutations was 1000, with no minimum cluster size determined. This cluster-based permutation test was based on the permutation distribution of the maximum cluster-level sum, which is beneficial in controlling for multiple comparisons.

2 Sensor level results

The results are depicted in Supplementary Material 2, Figure 1.

2.1 M55

Each stimulus pair comparison demonstrated a significant cluster for M55 (30–100 ms). In the PR vs. FRE comparison (PR > FRE, $p = 0.010$, cluster statistic: 936, cluster size: 324, largest cluster found at time point 96 ms after stimulus onset), the difference was most pronounced at sensors over the right parietal and temporal areas at 70–100 ms latency. In the comparison of the UR vs. FRE (UR > FRE, $p = 0.002$, cluster statistic: 7592, cluster size: 2204, the largest cluster found at time point 42 ms after stimulus onset), a significant cluster was found at sensors over the right frontoparietal and temporal areas including the whole time window (30–100 ms). A significant cluster was also found between the responses to the UR and PR (UR > PR, $p = 0.002$, cluster statistic: 5908, cluster size: 1731, largest cluster found at time point 38 ms after stimulus onset), with the difference being most pronounced in the right frontoparietal and temporal areas.

2.2 M150

In the time window of 130–230 ms, corresponding to M150, the cluster-based permutation test revealed spatio-temporal clusters for the PR vs. FRE and the UR vs. FRE. For the PR vs. FRE comparison (PR > FRE, $p = 0.002$, cluster statistic: 4327, cluster size: 1404, largest cluster time point: 161 ms) at 130–230 ms post-stimulus latency, the difference was found in the right frontal and parietal regions. A difference was also found between the UR vs. FRE (UR > FRE, $p = 0.002$, cluster statistic: 5236, cluster size: 1706, largest cluster time point: 185 ms) at 130–230 ms post-stimulus latency and was most pronounced over the right frontal areas. No significant cluster was observed for the UR vs. PR comparison.

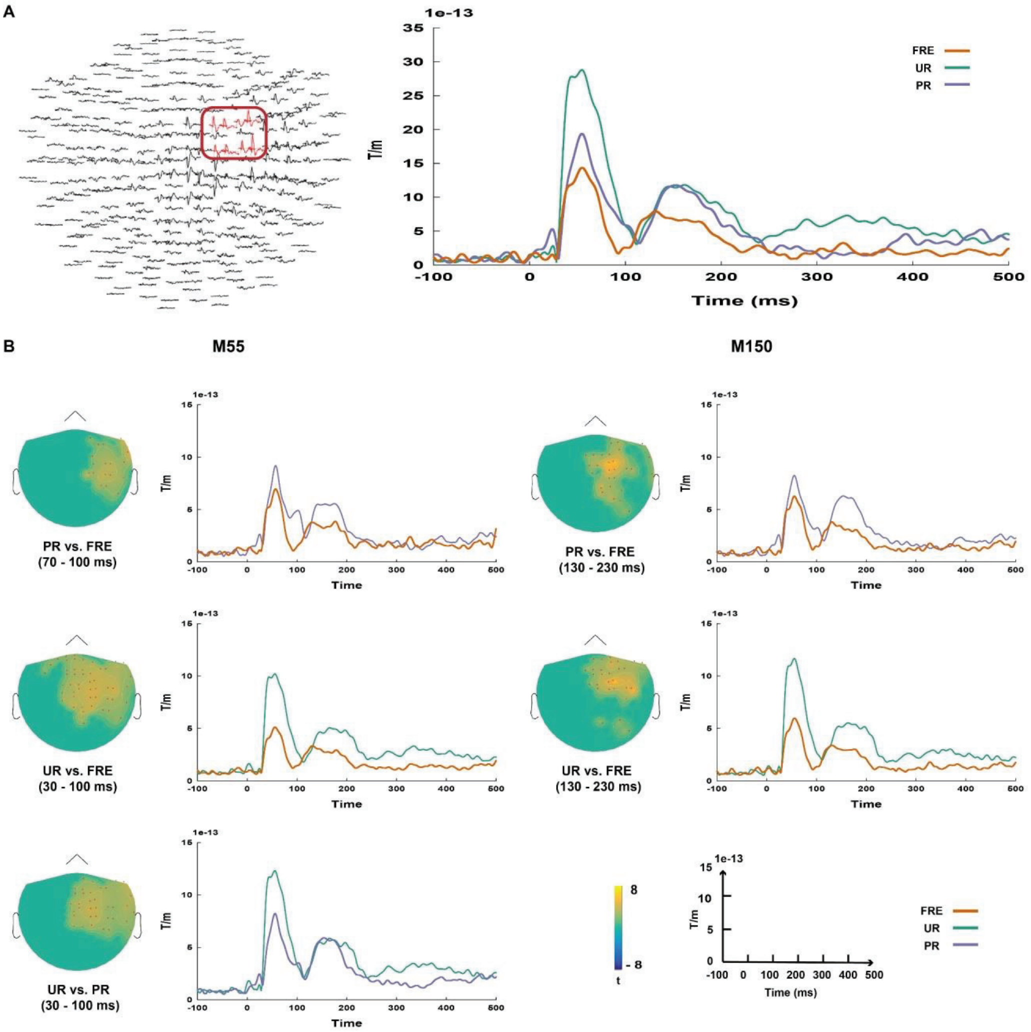

Figure 1. Sensor level results. (A) Descriptive results: *Left panel:* 306-channel sensor array viewed from the top; the grand-averaged evoked responses to the predictable rare stimuli are presented. Corresponding sensors used for the grand-averaged waveform in the right panel are marked with the red rectangle. *Right panel:* Grand-averaged evoked

responses to the UR, PR, and FRE averaged over the most activated channels. (B) Statistical analyses results. *Left panels:* significant sensor clusters of each stimulus type paired comparison shown by the red dots in the sensor space. The clusters are shown from the time point with the largest significant sensor cluster size (largest number of sensors within the cluster) in the corresponding time window below each graph. *Right panels:* the averaged sensor waveforms averaged from the significant clusters shown in the left panels. Specifically, from left to right and from top to bottom, they are: the cluster for the PR vs. FRE comparison occurring from 70 to 100 ms with the largest cluster size time point at 96 ms; the cluster for the UR vs. FRE comparison occurring from 30 to 100 ms with the largest cluster size time point at 42 ms; the cluster for the UR vs. PR comparison occurred from 30 to 100 ms, with the largest cluster size time point at 38 ms; the cluster for the PR vs. FRE comparison occurred from 130 to 230 ms, with the largest cluster size time point at 161 ms; and the cluster for the UR vs. FRE comparison occurred from 130 to 230 ms, with the largest cluster size time point at 185 ms. FRE = frequent stimulus, UR = unpredictable rare stimulus, PR = predictable rare stimulus.