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Mechanisms in Emotional Information Processing in Individuals with Major Depressive Disorder: An Event-Related Potential Study of an Information Processing Model

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ABSTRACT

Background: Individuals with major depressive disorder have a cognitive bias toward emotional stimuli, which influences the quality and speed of emotional information processing. This study aimed to understand the factors underlying this bias by identifying when it occurs during information processing using an information processing model.

Methods: A total of 57 participants-19 each [(16 (84.21%) females and 3 (15.79%) males per group)], for the first-episode MDD (FMDD), recurrent episodes MDD (RMDD), and healthy controls (HCs) - matched for sex and hand preference, completed event-related potentials (ERP) to perform psychological function and a choice response time task.

Results: Results revealed that recurrent episodes major depressive disorder participants had decreased N2b and P3b amplitudes but increased contingent negative variation during the processing of happy and neutral facial stimuli, relative to their counterparts. Both recurrent episodes major depressive disorder and first-episode major depressive disorder participants used a parallel information processing strategy for happy information at P3a latency, while healthy controls used a linear information processing strategy.

Conclusion: The use of a parallel processing strategy among individuals with major depressive disorder may have led to impaired "happy" information processes, possibly explaining why individuals with major depressive disorder are less efficient than healthy controls. The results suggest the possibility that biases related to the processing of "happy" information among individuals with major depressive disorder may be related to a tendency for these individuals to engage in superficial decision-making. Future research is needed to examine the processes contributing to people with major depressive disorder having challenges with inhibition-facilitation of emotional stimuli.

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INTRODUCTION

Major depressive disorder (MDD) affects people's cognition by slowing their cognitive processes[1,2] and impairing executive function.[3,4] However, previous reviews have noted that individuals with MDD do not evidence a general slowing of cognitive processes when processing negative emotions or sad facial stimuli.[5,6] For example, individuals with MDD are faster in perceiving and responding to sad facial stimuli than healthy controls (HCs), as evidenced by reaction time and the amplitude and/or latency of early-stage event-related potentials.[5-7] These findings support the conclusion that people with MDD are cognitively biased toward negative emotional information,[8] but there is no known information as to how exactly the bias occurs. The information processing model (IPM) has been used to understand[9-11] and inform research into how individuals with MDD process information.[1,2,11,12]

The use of the IPM (for an extensive review, see Ahorsu et al.[11] Sanders[9,10]) helps to understand the strategies (i.e., linear or parallel processing) used in processing information from the initial (perceptual) stage to the final (motor) stage.[1,2,11,12] A *linear* information processing strategy is one in which information moves serially from one stage to another, with only one stage being active at a time.[10,11] A *parallel* information processing strategy is one that simultaneously processes information across information processing stages at the same time.[10,11] The use

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of event-related potential (ERP) in conjunction with IPM to determine the strategy used for emotional information processing can help identify the factors underlying cognitive biases, as well as elucidate how (processing strategy—linear or parallel) individuals with MDD process emotional information, and at what stage (where) of the information processing do the bias occur. Specifically, ERP analyses can show how people with MDD process emotional information during the early perceptual processing stage using P1 and N1 components.[7,11,13] The N2b component (N2b-P3a complex) is used to signify stimulus identification or orientation stage processes[11,12,14,15] while components P3a (automatic processes) and P3b (controlled processes) are used to signify response choice/selection stage.[9,11,12,15,16] Contingent negative variation is used to represent the motor preparation stage of information processing.[9,11,12,15]

The aim of this study was to add to our understanding of the temporal processing of emotional information in individuals with depression from an IPM perspective.[11,12] Participants from 3 groups (individuals with first-episode MDD (FMDD), individuals with recurrent episodes MDD (RMDD), and HCs) were presented with emotional stimuli (i.e., happy, neutral, and sad faces) to determine how they process these stimuli using the IPM perspective. We examined differences between individuals with FMDD, individuals with RMDD, and HCs in (1) general speed of information processing; (2) ERP amplitude associated with the processing of each of the three types of emotional facial stimuli; and (3) strategies used for organizing information processing stages for each of the emotional facial stimuli. We hypothesized that there would be a significant difference between individuals with FMDD or RMDD and HCs in (1) general speed of information processing; (2) ERP amplitude associated with the processing of each of the emotional stimuli; and (3) strategies used for organizing information processing stages for each of the emotional stimuli.

MATERIAL AND METHODS

Participants

Yung Fung Shee Psychiatric Centre, an outpatient clinic that provides consultation to outpatients with psychiatric disorders in Hong Kong, served as the recruitment site for individuals with FMDD and RMDD. The individuals with MDD were first diagnosed by psychiatrists and then screened for comorbidity by trained psychology graduates using *Structured Clinical Interview* for DSM (SCID).[17] Inclusion criteria for being classified as an MDD participant included patients (1) with no other psychiatric disorder comorbidities (e.g., bipolar and schizophrenia); (2) with no psychotic symptoms; (3) with no neurological conditions, severe head injuries, hypothyroidism, or severe physical illness; and (4) having no evidence of cognitive impairment as evidenced by a score of 21 or more on the Mini-Mental State Examination (MMSE).[18] Healthy control (HC) participants were recruited from neighboring communities via posters. Apart from the stated inclusion criteria for the individuals with MDD, HCs were screened using SCID to be sure they were not diagnosed with depression. A total of 57 participants—19 (16 females and 3 males per group) participants each for the FMDD, RMDD, and HC groups, matched by sex and handedness —participated in this study as recommended by Thirion, Pinel, Mériaux, Roche, Dehaene, and Poline.[19] That is, 20 participants or more are needed in functional neuroimaging studies for sufficient reliability.[19] Majority of the participants participated in other ERP studies at the Cognitive Neuroscience Laboratory, Department of Rehabilitation Sciences of The Hong Kong Polytechnic University (PolyU Laboratory); some of which have been published.[4,11]

MAIN POINTS

- Individuals with depression have been known to have a bias toward negative emotions and so to help understand the brain processes that underlie emotions. This study examined individuals with depression and their bias in processing emotional information.
- The findings revealed that they had poorer voluntary orientation and response selection for positive information, perhaps due to the parallel information processing strategy used to process positive information.
- This suggests that the processing strategy used by individuals with depression was superficial hence the impaired ability to efficiently process positive emotional information.

Measures/Instruments

Cantonese Version of Mini-Mental State Examination: The 30-item Cantonese Version of Mini-Mental State Examination (C-MMSE) was used to screen participants for cognitive impairment. A cutoff of 21 was used to classify the potential participants as having normal cognitive function. The C-MMSE has good psychometric properties including a Cronbach's alpha of 0.86 among Hong Kong residents.[18]

Chinese Version of Beck Depression Inventory-II

The 21-item Chinese Version of Beck Depression Inventory-II (C-BDI-II) was used to assess depression severity in the participants. It was also used to affirm that a participant is eligible for this study. It had a Cronbach alpha coefficient of 0.92 among the Chinese.[20]

Facial Stimuli

Emotional stimuli were selected from a standardized set of pictures of the Chinese Facial Affective Picture System developed by the Psychology Department of the Chinese Academy of Sciences.[21] The stimuli used in the current study consisted of 6 faces with 2 (1 male and 1 female) each for happy, neutral, and sad emotions. Participants were asked to rate how Happy (H), Neutral (N), or Sad (S) faces are on a 5-point Likert scale response format ranging from very H/N/S (5 points) to not very H/N/S (1 point).

Experimental Design and Procedure

A choice reaction-time task (CRTT) imbued with IPM variables (response selection and motor adjustment stages) was used to address the study hypotheses.[1,2,11,12] It was made up of an imperative stimulus (second stimulus (S2), a circular face of 2.54 cm in diameter) attached to either side of a warning stimulus (first stimulus (S1), a white plus (┼), or cross (X) sign of 1.06 cm^2) at the center of a black background monitor. Participants were adequately informed of the conditions before the main experiment. The setup allowed for a foveal vision of both stimuli. The task was made up of 14 blocks comprising 48 S1-S2 pairs of trials per block. There were 7 blocks for each condition (i.e., for 0-sec ISI (interstimulus interval) and 1-sec ISI). The duration of both S1 and S2 was 500 ms and the inter-trial interval (ITI) was 3000 ms (see Figure 1). There was a 5-minute break between the 2 preparatory periods and a minute break after each block. There was also a practice session which consisted of a block each for 0-sec and 1-sec ISI. Speed and accuracy were emphasized for this experiment. Participants were trained on how to focus on the fixation stimulus. The entire session lasted about 2 hours. The study was approved by the Research Ethics Committee of the Hong Kong Hospital Authority (KC/KE-16-0114/ER-2) and The Hong Kong Polytechnic University (HSEARS20160523001). The informed consent form was signed before the assessment and main data collection. The psychological assessments were administered, and electrophysiological recordings were made at the Cognitive Neuroscience Laboratory of The Hong Kong Polytechnic University. The present study was conducted following the Declaration of Helsinki. This study was not pre-registered.

Electrophysiological Recordings and Processing

The 64 electroencephalogram (EEG) channel "Quick-Cap," referenced to the left mastoid but re-referenced to an average mastoid during offline processing, was used for the data recording. The EEG signal (1024 Hz), impedances, corrections, filtering, and other EEG processes used have been reported in a previous study.[11] Neuroscan Stim2 software (Neuroscan, El Paso, TX) was used to present the task while the CURRY 7 software (NeuroScan Inc., Sterling, Va, USA) was used for signal acquisition and off-line signal pre-processing. The ERP components/time windows used have been reported in a previous study.[11] These time windows were further assessed and verified by independent component analysis using CURRY 8 software (Compumedics Neuroscan, Charlotte, NC, USA) with an average signal-to-noise ratio equal to 1.0 or greater.[22]

Statistical Analyses

Descriptive statistics were given in mean ± standard deviation or median (25th-75th percentile) for normal and non-normal data respectively and frequencies with percentages. To compare the groups, we used independent *t*-tests (e.g., onset age and illness duration), Mann-Whitney *U* test (for current episode duration), one-way Analysis of variance (ANOVA; e.g., age, years of education, and facial ratings), Kruskal-Wallis H test (for BDI), and one-way analysis of covariance (ANCOVA; for MMSE) with years of education as the covariate variable. Next, a 3-way mixed factor ANOVA was used to address the first, second, and third hypotheses. This assesses the statistical significance of between-group and within-group effects of the experimental variables[11,23] based on the behavioral and ERP data and specifically for each of the three emotional facial stimuli (separately) using IBM Statistical Package for Social Sciences (SPSS) Statistics version 22.0 (IBM SPSS Corp., Armonk, NY, USA). The mixed factor ANOVA consisted of 1 between-group factor (Group factor) and 2 within-group factors with 2 modalities for each: stimulus-response compatibility (compatible vs. incompatible—Comp factor) and ISI (0-sec vs. 1-sec—ISI factor). The topography of recording sites (Topo) was added as a supplementary within-group factor for CNV. The 3-way mixed factor ANOVA was used in this study as we were interested in

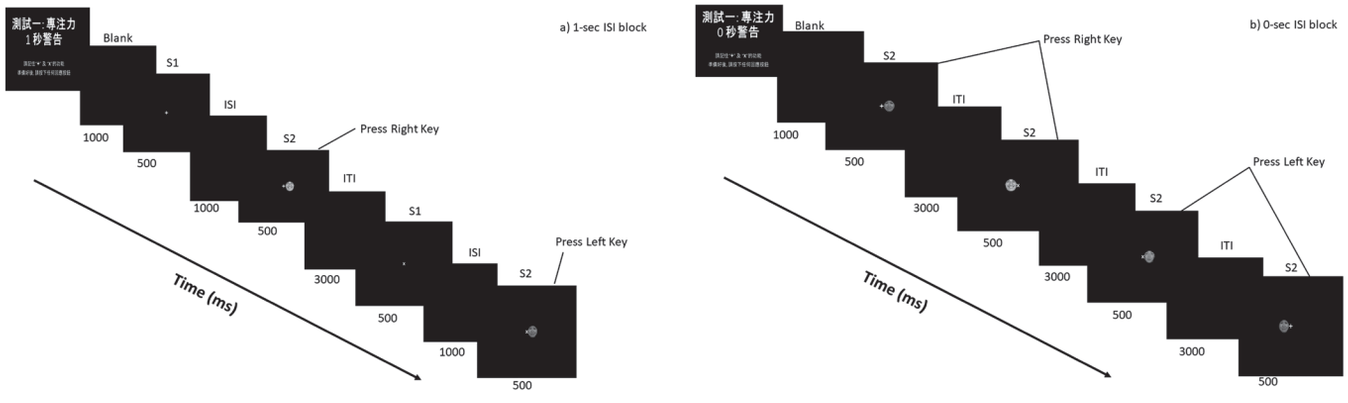

Figure 1. Choice Reaction Time Task (CRTT) with facial stimuli. This figure shows the detailed stimulus display used in the CRTT according to (A) 1-sec ISI and (B) 0-sec ISI block. The plus (┼) and cross (X) signs indicate compatible and incompatible conditions, respectively. S1 and S2 represent the first and second stimuli, respectively. ITI and ISI represent inter-trial interval and interstimulus interval, respectively.

explaining how the Groups process each of the emotional stimuli along the information processing stages. For a statistically significant interaction, simple effects analyses with Bonferroni correction were done using the SPSS syntax window with its adjusted *P*-value. Similarly, an adjusted *P*-value of .017 was used for the post hoc of significant ANOVAs and ANCOVA results for the psychosocial variables. For all tests, the significance level was set at $P < .05$.[11,12,23] For the purposes of examining significant between-group differences in processing information, only significant results concerning between-group effects and interaction between- and within-groups were reported and discussed.

RESULTS

Description of the Sample

There were 19 participants in each of the FMDD, RMDD, and HC groups making up a total of 57 participants. Majority of the participants were females (n = 16; 84.21%) and the rest were males (n = 3; 15.79%) for each of the groups. There was no significant between-group difference in their age, $F(2, 54) = 2.80$, $P = .07$. However, HCs had more years of education than FMDD and RMDD participants, $F(2, 54) = 13.20$, $P < .001$. Among MDD participants, RMDD participants had longer illness duration, $t(36) = 3.56$, $P = .001$, and more number of episodes, $t(36) = 7.51$, $P < .001$, than FMDD participants (see Table 1).

Main Effects

Behavioral Data: The mixed-factor ANOVA results revealed a significant between-group main effect on accuracy for happy, $F(2, 54) = 3.33$, $P = .04$, $\eta^2 = .0.08$, but not for neutral $F(2, 54) = 2.52$, $P = .09$, $\eta^2 = .05$, and sad, $F(2, 54) = 2.31$, $P = .11$, $\eta^2 = .04$, facial stimuli, with HCs (mean ± standard deviation [M ± SD] = 54.01 ± 1.39) having significantly more accurate scores for happy facial stimuli than FMDD (49.30 ± 1.39) and RMDD (49.99 ± 1.39)

Table 1. Summary of the Comparisons Between Groups on Various Measures

	FMDD (n = 19)	RMDD (n = 19)	HC (n = 19)	Main Test	Post Hoc	
	Mean ± SD/Median (Q1-Q3)	Mean ± SD/Median (Q1-Q3)	Mean ± SD/Median (Q1-Q3)	*P*[a]	Post Hoc	*P*
Sex						
Males; *n* (%)	3 (15.79%)	3 (15.79%)	3 (15.79%)	–	–	–
Females; *n* (%)	16 (84.21%)	16 (84.21%)	16 (84.21%)	–	–	–
Onset age	33.84 ± 8.57	31.53 ± 8.40	–	.406[b]	–	–
Illness duration	6.05 ± 5.02	12.42 ± 5.98	–	.001[b]	–	–
Current episode duration	5(3-10)	3(1-5)	–	.043[c]	–	–
No. of episode	1 ± 00	2.26 ± 0.73	–	<.001[b]	–	–
Age	40.11 ± 8.59	44.47 ± 7.48	38.11 ± 9.28	.070[d]	–	–
Education	12.11 ± 3.18	11.53 ± 3.50	16.05 ± 1.96	<.001[d]	HC > FMDD,	<.001
					HC >RMDD,	<.001
					RMDD< FMDD	.548
Happy facial rating	9.22 ± 0.49	9.05 ± 0.62	9.38 ± 0.50	.186[d]	–	–
Neutral facial rating	7.24 ± 0.78	7.20 ± 0.83	6.71 ± 1.19	.165[d]	–	–
Sad facial rating	8.88 ± 0.70	8.30 ± 1.18	8.06 ± 1.14	.048[d]	HC < FMDD,	.017
					HC < RMDD,	.478
					RMDD < FMDD	.086
MMSE	27.68 ± 2.40	28.53 ± 1.35	29.16 ± 1.30	.194[e]	–	–
BDI-II	12(5-26)	11(6-22)	3(0-9)	.001[f]	HC < FMDD,	.004,
					HC < RMDD,	.005
					RMDD < FMDD	1.000

ANOVA, analysis of variance; ANCOVA, analysis of covariance; BDI-II, Becks Depression Inventory-II; ERP, event-related potential; FMDD, first-episode major depressive disorder; HCs, healthy controls; MMSE, Mini-Mental State Examination; RMDD, recurrent episodes major depressive disorder; RT, reaction time; SD, standard deviation.

A < B: A is less than B; A > B: A is greater than B. The adjusted *P*-value for the post hoc is .017.

[a]The main test includes independent *t*-test; Mann-Whitney *U* test, ANOVA, ANCOVA, and Kruskal-Wallis *H* test; [b]independent *t*-test; [c]Mann-Whitney *U* test (for current episode duration with their median being FMDD = 5 and RMDD = 3); [d]One-way ANOVA; [e]One-way ANCOVA with years of education as the covariate variable; [f]Kruskal-Wallis *H* test (for BDI with their median being FMDD = 12, RMDD = 11, and HC = 3). All participants are right-handed.

participants. However, no significant between-group main effect was found on reaction time (RT) for happy, $F(2, 54)=2.19$, $P = .12$, $\eta^2=.04$, neutral, $F(2, 54)=1.81$, $P = .17$, $\eta^2=.03$, and sad, $F(2, 54)=2.03$, $P = .14$, $\eta^2=.03$, facial stimuli. No significant interaction effects were found between between-group (Group factor) and within-group (ISI and Comp factors) factors (all $P > .05$) on either accuracy score or RT for any of the facial stimuli.

Event-Related Potentials Findings

P1 Component: The mixed-factor ANOVA results revealed a significant between-group main effect on P1 amplitude for neutral, $F(2, 54)=3.80$, $P = .03$, $\eta^2=.09$, and sad, $F(2, 54)=3.60$, $P = .03$, $\eta^2=.08$, but not happy, $F(2, 54)=2.93$, $P = .06$, $\eta^2=.06$, facial stimuli. Specifically, FMDD participants (0.55 ± 0.52 μV and 0.70 ± 0.53 μV for neutral and sad facial stimuli, respectively) had more positive-going amplitude for neutral and sad facial stimuli than RMDD participants (−1.39 ± 0.052 μV and −1.25 ± 0.53 μV for neutral and sad facial stimuli, respectively). However, no significant between-group main effect was found on P1 latency for happy, $F(2, 54)=0.11$, $P = .89$, $\eta^2 < .01$, neutral, $F(2, 54)=0.33$, $P = .72$, $\eta^2 < .01$, and sad, $F(2, 54)=0.20$, $P = .82$, $\eta^2 < .01$, facial stimuli. No significant interaction effects were found between between-group (Group factor) and within-group factors (all $P > .05$) on either amplitude or latency for any of the facial stimuli.

N1 Component: There was no significant between-group main effect on N1 amplitudes for happy, $F(2, 54)=1.95$, $P = .15$, $\eta^2=.03$, neutral, $F(2, 54)=2.48$, $P = .09$, $\eta^2=.05$, and sad, $F(2, 54)=2.91$, $P = .06$, $\eta^2=.06$, facial stimuli. A significant between-group main effect was found on N1 latency for neutral, $F(2, 54)=3.24$, $P = .05$, $\eta^2=.07$, but not happy, $F(2, 54)=1.40$, $P = .26$, $\eta^2=.01$, and sad, $F(2, 54)=2.55$, $P = .09$, $\eta^2=.05$, facial stimuli. Recurrent episodes major depressive disorder participants (143.25 ± 4.94 ms) had significantly shortest latency than FMDD participants (158.42 ± 4.94 ms) and HCs (154.61 ± 4.94 ms) for neutral facial stimuli. No significant interaction effects were found between between-group (Group factor) and within-group factors (all $P > .05$) on either amplitude or latency for any of the facial stimuli.

N2b Component: A significant between-group main effect on N2b amplitude was found for happy, $F(2, 54)=3.73$, $P = .03$, $\eta^2=.09$, and neutral, $F(2, 54)=3.29$, $P = .05$, $\eta^2=.07$, but not sad, $F(2, 54)=2.64$, $P = .08$, $\eta^2=.05$, facial stimuli. Healthy controls (−0.31 ± 0.76 μV) had marginally more negative-going amplitude for happy facial stimuli than FMDD (2.29 ± 0.76 μV) and RMDD (2.17 ± 0.76 μV) participants. Further, HCs (−0.50 ± 0.79 μV) had marginally more negative-going amplitude for neutral facial stimuli than FMDD (2.02 ± 0.79 μV) participants only. However, no significant between-group main effect was found on N2b latency for happy, $F(2, 54)=0.06$, $P = .94$, $\eta^2 < .01$, neutral, $F(2, 54)=0.16$, $P = .85$, $\eta^2 < .01$, and sad, $F(2, 54)=0.56$, $P = .57$, $\eta^2 < .01$, facial stimuli. A significant interaction effect between between-group (Group factor) and within-group factors on N2b amplitude was found for happy facial stimuli, $F(2, 54)=3.99$, $P = .02$, $\eta^2=.10$, in a complex way. Further details are presented in the section that examines the effects of experimental variables. No other significant interactions were observed (all $P > .05$) on either amplitude or latency for any of the facial stimuli.

P3a Component: A significant between-group main effect on P3a amplitude was found for neutral, $F(2, 54)=3.20$, $P = .05$, $\eta^2=.07$, but not for happy, $F(2, 54)=3.16$, $P = .05$, $\eta^2=.07$, and sad, $F(2, 54)=2.72$, $P = .08$, $\eta^2=.06$, facial stimuli, with FMDD (2.24 ± 0.82 μV) and RMDD (2.31 ± 0.82 μV) participants having marginally more positive-going amplitude for neutral facial stimuli than HCs (−0.27 ± 0.82 μV). However, no significant between-group main effect was found on P3a latency for happy, $F(2, 54)=0.41$, $P = .66$, $\eta^2 < .01$, neutral, $F(2, 54)=0.08$, $P = .92$, $\eta^2 < .01$, and sad, $F(2, 54)=0.23$, $P = .79$, $\eta^2 < .01$, facial stimuli. A significant interaction effect between between-group (Group factor) and within-group (ISI and Comp) factors on P3a latency was found for only happy facial stimuli, $F(2, 54)=3.46$, $P = .04$, $\eta^2=.08$, in a complex way. Further details are presented below in the section that examines the effects of experimental variables. No other significant interactions were observed (all $P > .05$) on either amplitude or latency for any of the facial stimuli.

N2b-P3a Peak-to-Peak Amplitude: There was no significant between-group main effect on N2b-P3a amplitude for happy, $F(2, 54)=0.03$, $P = .97$, $\eta^2 < .01$, neutral, $F(2, 54)=0.10$, $P = .91$, $\eta^2 < .01$, and sad, $F(2, 54)=0.04$, $P = .96$, $\eta^2 < .01$, facial stimuli. There were no significant interaction effects across the emotional facial stimuli except that group (Group factor) interacted with compatibility (Comp factor) for neutral facial stimuli only, $F(2, 54)=3.45$, $P = .04$, $\eta^2=.08$. Simple effect results revealed that among HCs, there was a higher amplitude for incompatible (−0.38 ± 0.36 μV) than compatible (−0.7 ± 0.35 μV) condition. Among FMDD participants, incompatible condition (−0.39 ± 0.36 μV) had a higher amplitude than compatible condition (−0.04 ± 0.35 μV).

P3b Component: There was a significant between-group main effect on P3b amplitude for happy, $F(2, 54)=4.06$, $P = .02$, $\eta^2=.10$, and neutral, $F(2, 54)=3.65$, $P = .03$, $\eta^2=.09$, but not sad, $F(2, 54)=2.54$, $P = .09$, $\eta^2=.05$, facial stimuli. For happy facial stimuli, HCs (4.22 ± 0.69 μV) had a more positive-going amplitude than RMDD participants (1.46 ± 0.69 μV). Also, HCs (4.23 ± 0.72 μV) had a more positive-going amplitude than RMDD participants (1.53 ± 0.72 μV) for neutral facial stimuli. No significant between-group main effect was found on P3b latency for happy, $F(2, 54)=0.76$, $P = .47$, $\eta^2 < .01$, neutral, $F(2, 54)=0.08$, $P = .92$, $\eta^2 < .01$, and sad, $F(2, 54)=0.86$, $P = .43$, $\eta^2 < .01$, facial stimuli. No other significant interaction effects were found between between-group (Group factor) and within-group factors (all $P > .05$) on either amplitude or latency for any of the facial stimuli.

Post-P3b Latency: There was no significant between-group main effect on post-P3b for happy, $F(2, 54) = 2.26$, $P = .11$, $\eta^2 = .04$, neutral, $F(2, 54) = 1.52$, $P = .23$, $\eta^2 = .02$, and sad, $F(2, 54) = 1.83$, $P = .17$, $\eta^2 = .03$, facial stimuli. No significant interaction effects were found between between-group (Group factor) and within-group factors (all $P > .05$) for any of the facial stimuli.

The grand mean ERP waveforms of all experimental conditions between the groups are shown in Figure 2A for happy facial stimuli, Figure 2B for neutral facial stimuli, and Figure 2C for sad facial stimuli.

Contingent Negative Variation Component

For happy facial stimuli, there was a significant between-group main effect on CNV, $F(2, 54) = 6.85$, $P = .01$, $\eta^2 = .17$, with RMDD participants (−4.38 ± 0.52 μV) having a more negative-going CNV than HCs (−2.35 ± 0.52 μV) and FMDD (−1.82 ± 0.52 μV) participants. Also, there were significant interaction effects between group (Group) and compatibility (Comp) factors, $F(2, 54) = 6.02$, $P = .01$, $\eta^2 = .15$, and between-Group factor and within-group (Comp and Topo) factors, $F(2, 54) = 10.18$, $P < .001$, $\eta^2 = .24$. Simple effect results revealed that RMDD participants had more negative-going CNV than FMDD participants and HCs in both compatible and incompatible conditions. The same result patterns were found at sites Fz and Cz. In all the groups, there was a more negative-going CNV at site Cz than Fz for both compatibility conditions. Figure 3A gives a graphical display of CNV amplitude among each of the groups for happy facial stimuli.

For neutral facial stimuli, a significant between-group main effect on CNV was observed, $F(2, 54) = 7.16$, $P = .01$, $\eta^2 = .18$, with RMDD participants (−4.27 ± 0.54 μV) having a more negative-going CNV than HCs (−1.83 ± 0.54 μV) and FMDD (−1.70 ± 0.54 μV) participants. Also, there was a significant interaction effect between group (Group) and compatibility (Comp) factors, $F(2, 54) = 4.42$, $P = .02$, $\eta^2 = .11$. Simple effect results revealed that RMDD participants had more negative-going CNV than FMDD participants for both compatible and incompatible conditions. Furthermore, there was a more negative-going CNV for incompatible conditions than compatible conditions among both FMDD and RMDD participants. Figure 3B gives a graphical display of CNV amplitude among each of the groups for neutral facial stimuli.

For sad facial stimuli, a significant between-group main effect on CNV was observed, $F(2, 54) = 7.13$, $P = .01$, $\eta^2 = .18$, with RMDD participants (−4.15 ± 0.46 μV) having a more negative-going CNV than FMDD (−1.69 ± 0.46 μV) participants. Also, there was a significant interaction effect between Group factor and within group (Comp and Topo) factors, $F(2, 54) = 5.43$, $P = .01$, $\eta^2 = .13$, on CNV in a complex way. Simple effect results revealed that RMDD participants had more negative-going CNV than FMDD participants and HCs in both compatible and incompatible conditions at site Fz only. Furthermore, there was a more negative-going CNV for incompatible than compatible conditions at site Fz among FMDD participants and HCs, but this finding was observed at site Cz among RMDD participants. In all the groups, there was a more negative-going CNV at site Cz than Fz for both compatibility conditions. Figure 3C gives a graphical display of CNV amplitude among each of the groups for sad facial stimuli.

Interaction Effects of Experimental Variables: Compatibility and ISI Interaction

This section was intentionally separated from its main components as it specifically addresses the third objective (the organization of information-processing stages). There was a significant ISI and Comp factor interaction with Group factor on energetical index (amplitude) for N2b and CNV components. That is, a significant interaction effect between between-group (Group factor) and within-group factors (ISI and Comp factors) on N2b amplitude was found for happy facial stimuli, $F(2, 54) = 3.99$, $P = .02$, $\eta^2 = .10$, with HCs (−0.70 ± 0.78 μV) having a more negative-going N2b amplitude for Compatible-0-sec-ISI condition than FMDD (2.72 ± 0.78 μV) participants. No other significant interaction effects were found for happy facial stimuli (all $P > .05$). The interaction effects on CNV amplitude for each of the emotional facial stimuli have been reported under the CNV component.

For RT and ERP latencies, a significant interaction effect between between-group (Group factor) and within-group (ISI and Comp) factors on P3a latency was found for only happy facial stimuli, $F(2, 54) = 3.46$, $P = .04$, $\eta^2 = .08$. Simple effect results revealed that the interaction was within FMDD and RMDD groups, with FMDD participants having longer latency for compatible condition (312.47 ± 12.80 ms) than incompatible condition (280.47 ± 12.10 ms) during 0-sec ISI condition. As well, FMDD participants had longer latency for incompatible conditions (307.05 ± 12.30 ms) than compatible conditions (286 ± 12.51 ms) during 1-sec ISI condition. Further, FMDD participants had longer latency for 0-sec ISI condition (312.47 ± 12.80 ms) than 1-sec ISI condition (286 ± 12.51 ms) during compatible condition as well as having longer latency for 1-sec ISI condition (307.05 ± 12.30 ms) than 0-sec ISI condition (280.47 ± 12.10 ms) during the incompatible condition. Further, RMDD participants had longer latency for 0-sec ISI condition (299.74 ± 12.80 ms) than 1-sec ISI condition (266.84 ± 12.10 ms) during compatible conditions only. No other significant interactions were observed (all $P > .05$). The chronometric indices are presented in Table 2 and Table 3 and Figure 4A to C.

DISCUSSION

The key findings from this study were that HCs had more accuracy scores, better orientation (N2b amplitude), and more controlled and effortful processes (P3b amplitude)

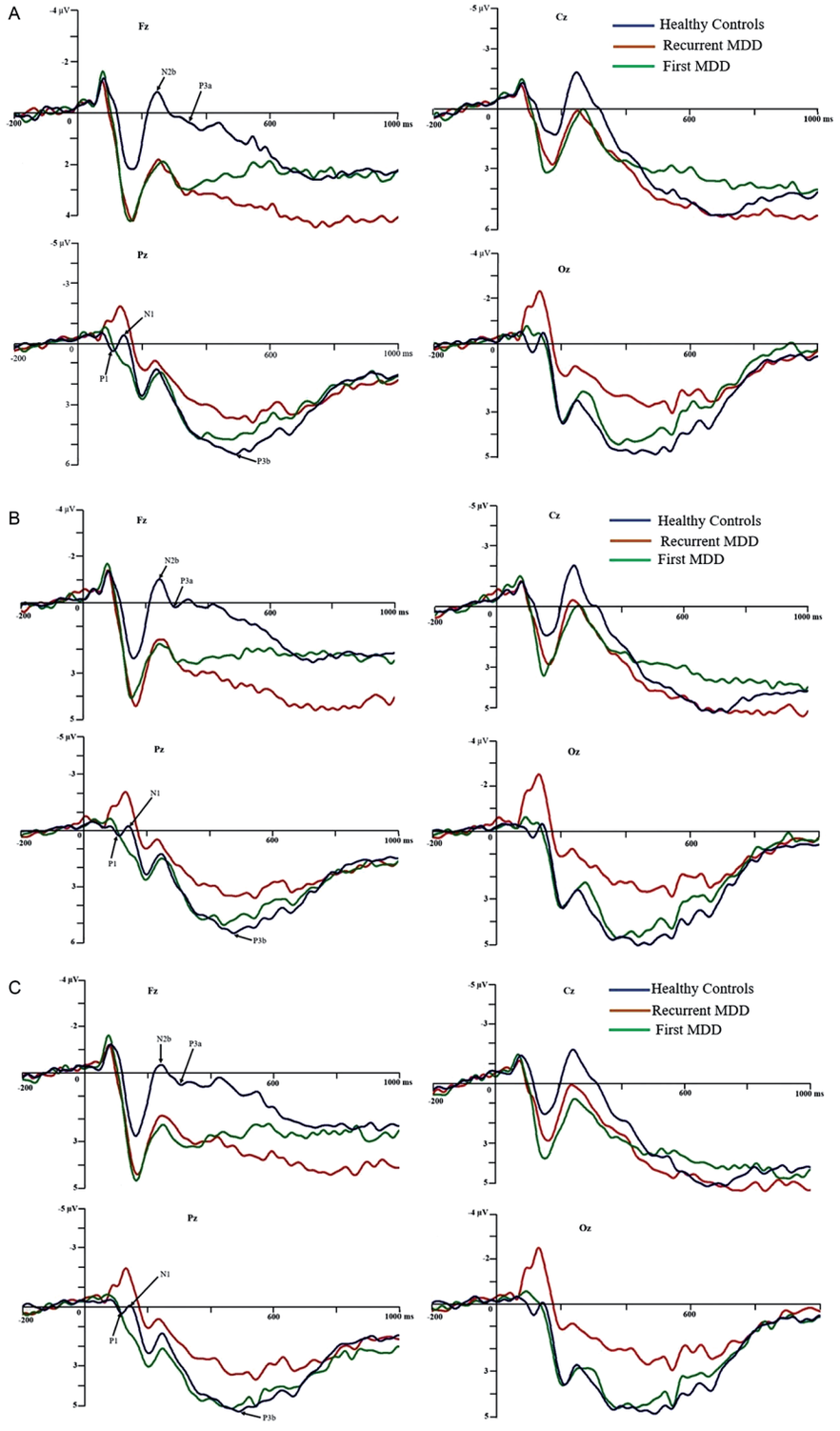

Figure 2. (A) Grand event-related potential (ERP) mean waveforms for happy facial stimuli. Grand ERP means waveform after imperative stimuli (S2) was recorded from the midline electrodes in each group of participants. A reduction of amplitudes occurred among first-episode major depressive disorder (FMDD) and recurrent episodes major depressive disorder (RMDD) participants (compared with healthy controls (HCs)) at N2b (at site Fz) and among RMDD participants (compared with HCs) at P3b (at site Pz). (B) Grand ERP mean waveforms for neutral facial stimuli. Grand ERP mean waveform after imperative stimuli (S2) was recorded from the midline electrodes in each group of participants. A reduction of amplitudes occurred among RMDD participants (compared with FMDD) at P1 (at site Pz), among FMDD participants (compared with HCs) at N2b (at site Fz), among HCs (compared with FMDD and RMDD participants) at P3a (at site Fz), and among RMDD participants (compared with HCs) at P3b (at site Pz). (C) Grand ERP mean waveforms for sad facial stimuli. Grand ERP means waveform after imperative stimuli (S2) was recorded from the midline electrodes in each group of participants. A reduction of amplitudes occurred among RMDD participants (compared with FMDD) at P1 (at site Pz).

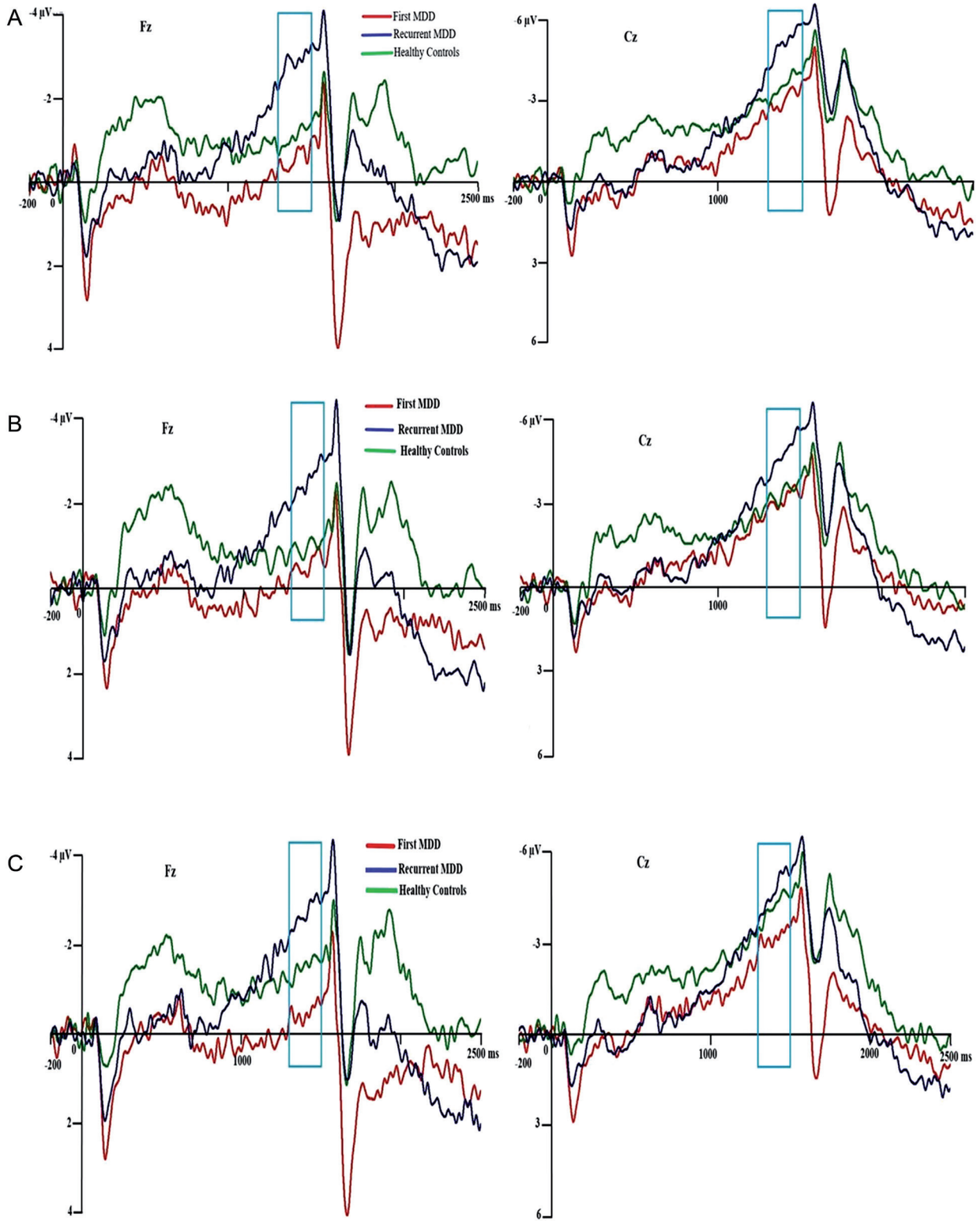

Figure 3. (A) Grand contingent negative variation (CNV) mean waveforms for happy facial stimuli. These are grand CNV mean waveforms between the warning (S1) and imperative (S2) stimuli of the midline electrode sites Fz and Cz between all the participants. The rectangle represents the time window for the event-related potential (ERP) data. (B) Grand CNV mean waveforms for neutral facial stimuli. These are grand CNV mean waveforms between the warning (S1) and imperative (S2) stimuli of the midline electrode sites Fz and Cz between all the participants. The rectangle represents the time window for the ERP data. (C) Grand CNV mean waveforms for sad facial stimuli. These are grand CNV mean waveforms between the warning (S1) and imperative (S2) stimuli of the midline electrode sites Fz and Cz between all the participants. The rectangle represents the time window for the ERP data.

during the processing of happy facial stimuli than FMDD and RMDD participants. Recurrent episodes major depressive disorder participants, on the other hand, had better motor preparation than HC and FMDD participants during the processing of happy facial stimuli. The findings also indicate that there were no significant differences between HCs and MDD participants during the early/perceptual processing stage of each of the emotional stimuli (i.e., happy, neutral, and sad facial stimuli). Hence, MDD participants' performance, with respect to information processing, in the early processing stage, appears to be normal. However, HCs were found to have a more negative-going N2b amplitude than FMDD and RMDD participants for happy facial stimuli. This indicates that HCs were more oriented toward happy facial stimuli compared with both FMDD and RMDD participants. This finding is consistent with other studies reporting that HCs have more voluntary attention orientation to happy facial

Table 2. Summarized List of Chronometric Variables (RT and ERP Latencies) Commonly or Differentially Affected by Interstimulus Interval and Compatibility in the Three Groups of Participants According to Facial Stimuli

Emotional Facial Stimuli/ Experimental Variables[a]	Happy Faces		Neutral Faces		Sad Faces	
	Common Effects[b]	Differential Effects[c]	Common Effects[b]	Differential Effects[c]	Common Effects[b]	Differential Effects[c]
Interstimulus interval (ISI)	RT (0-sec > 1-sec***)		RT (0-sec > 1-sec***)		RT (0-sec > 1-sec**)	
	P3b (1-sec > 0-sec*)		Post-P3b (0-sec > 1-sec**)			
Compatibility	RT (Incomp > Comp***)		RT (Incomp > Comp***)		RT (Incomp > Comp***)	
	P1 (Incomp > Comp**)		P1 (Incomp > Comp*)		N1 (Comp > Incomp*)	
	N1 (Comp > Incomp***)		Post-P3b (Incomp > Comp**)		N2b (Comp > Incomp**)	
	P3b (Comp > Incomp***)				P3b (Incomp > Comp**)	
	Post-P3b (Incomp > Comp**)					
ISI × Compatibility interaction	P3a (Comp: 0-sec > 1-sec**), (0-sec: Comp > Incomp*, 1-sec: Incomp > Comp*)	P3a (FMDD × 0-sec: Comp > Incomp*, FMDD × 1-sec: Incomp > Comp*; FMDD × Comp: 0-sec > 1-sec*, FMDD × Incomp: 1-sec > 0-sec*) (RMDD × Comp: 0-sec > 1-sec**)	N1 (Incomp: 1-sec > 0-sec**), (0-sec: Comp > Incomp**)		P3a (Incomp: 1-sec > 0-sec*), (0-sec: Comp > Incomp*)	
					Post-P3b (Incomp: 0-sec > 1-sec*), (0-sec: Incomp > Comp**)	
			P3b (Comp: 0-sec > 1-sec**)			
			Post-P3b (Incomp: 0-sec > 1-sec***), (0-sec: Incomp > Comp***)			

ANOVA, analysis of variance; ERP, event-related potential; FMDD, first-episode major depressive disorder; HCs, healthy controls; RMDD, recurrent episodes major depressive disorder; RT, reaction time.

A > B, A is longer than B; Comp is compatible condition; Incomp is incompatible condition; 0-sec is 0-sec ISI; 1-sec is 1-sec ISI.

*P < .05; **P < .01; ***P < .001.

[a]This table summarizes the main mixed-factor ANOVA results according to the effect of the experimental variables on RT and the exact latency. Common effects refer to the RT and/or the exact latency that are significantly common to the groups while differential effects refer to the RT and/or the exact latency that are significantly different between the groups according to the experimental variables and among each of the emotional facial stimuli; [b]Components (e.g., RT, N1 latency) here (common effects) indicate how the groups (FMDD and RMDD, and HCs) are commonly affected by the experimental variables; [c]Component (P3a latency for happy face) here (differential effects) indicate how the groups (FMDD and RMDD, and HCs) are differently affected by the experimental variables. FMDD and RMDD participants were affected by the experimental variables.

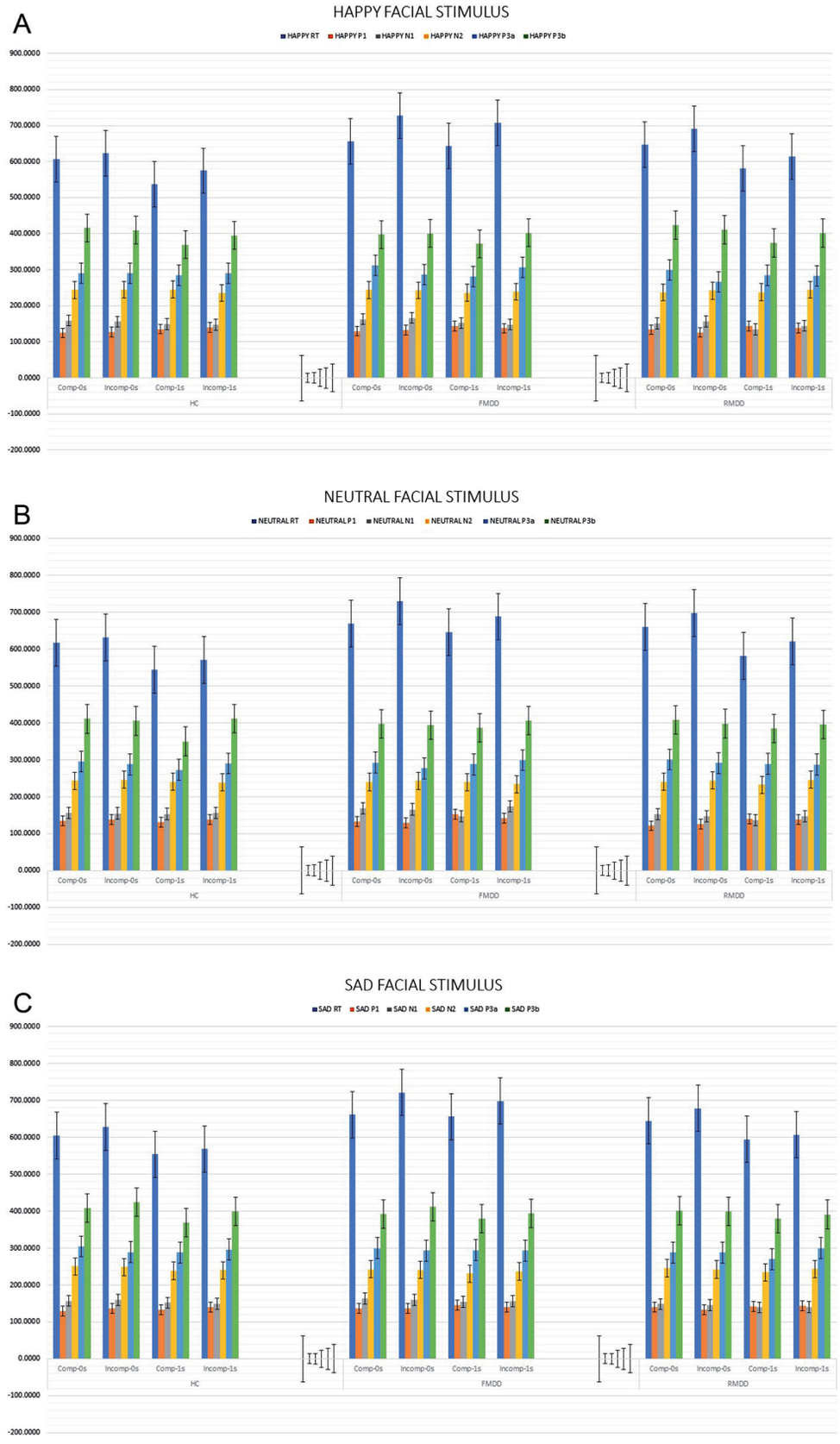

Figure 4. (A) Graphical display of chronometric results of all the conditions according to group of participants for happy facial stimuli. (B) Graphical display of chronometric results of all the conditions according to a group of participants for neutral facial stimuli. (C) Graphical display of chronometric results of all the conditions according to group of participants for sad facial stimuli.

stimuli than MDD participants.[24-26] Like the happy facial stimuli, similar results were found during the processing of neutral facial stimuli with HCs having more orientation toward it than MDD participants.

The results for controlled and effortful processes (P3b amplitude) indicated that RMDD participants had less positive-going P3b amplitude than HCs for happy facial stimuli. This indicates that RMDD participants have impaired controlled and effortful processes for happy facial stimuli, suggesting major challenges with making better response choices/selections, especially when such choices are related to happy faces. This may be due to the duration (12 years) of their MDD, which is significantly different from FMDD participants. This finding is consistent with previous research which showed that individuals with MDD have less positive-going P3 amplitude for happy facial stimuli compared with HCs although most of these studies used treatment naïve patients.[23,27,28] This may have contributed to the lesser accuracy scores for the happy facial stimuli. Similar findings were observed during the processing of neutral facial stimuli with RMDD participants having less positive-going P3b amplitude than HCs indicating that RMDD participants have impaired controlled and effortful processes.

On the other hand, RMDD participants had more significant negative-going CNV for happy and neutral facial stimuli than FMDD and HC participants (separately) and more significant negative-going CNV than FMDD participants for sad facial stimuli. Previous studies' findings are inconsistent

Table 3. Descriptive Statistics of the Summarized List of Chronometric Variables (RT and ERP Latencies) Commonly or Differentially Affected by Interstimulus Interval and Compatibility in the 3 Groups of Participants According to Facial Stimuli

Emotional Facial Stimuli / Experimental Variables[a]	Happy Faces		Neutral Faces		Sad Faces	
	Common Effects[b]	Differential Effects[c]	Common Effects[b]	Differential Effects[c]	Common Effects[b]	Differential Effects[c]
Interstimulus interval (ISI)	RT (658.38 > 609.19***)		RT (667.47 > 608.11***)		RT (656.35 > 612.99**)	
	P3b (403.59 > 392.06*)		Post-P3b (264.33 > 221.88**)			
Compatibility	RT (656.04 > 611.53***)		RT (656.26 > 619.31***)		RT (650.18 > 619.16***)	
	P1 (139.91 > 129.15**)		P1 (140.46 > 130.57*)		N1 (155.48 > 148.70*)	
	N1 (158.78 > 146.11***)		Post-P3b (255.33 > 230.87**)		N2b (244.91 > 237.21**)	
	P3b (409.75 > 385.90***)				P3b (472.07> 456.17**)	
	Post-P3b (248.66 > 219.69**)					
ISI × Compatibility interaction	P3a (Comp: 301.04 > 281.21**), (0-sec: 301.04 > 283.42*, 1-sec: 293.65 > 281.21*)	P3a (FMDD × 0-sec: 312.47 > 280.47*, FMDD × 1-sec: 307.05 > 286.00*; FMDD × Comp: 312.47 > 286.00*, FMDD × Incomp: 307.05 > 280.47*) (RMDD × Comp: 299.74 > 266.84**)	N1 (Incomp: 159.25 > 145.33**), (0-sec: 159.00 > 145.33**) P3b (Comp: 467.83 > 437.12**) Post-P3b (Incomp: 285.84 > 224.82***), (0-sec: 285.84 > 242.81***)		P3a (Incomp: 296.26 > 284.23*), (0-sec: 297.40 > 284.23*) Post-P3b (Incomp: 285.84 > 224.82*), (0-sec: 285.84 > 242.81**)	

ANOVA, analysis of variance; FMDD, first-episode major depressive disorder; HCs, healthy controls; RMDD, recurrent episodes major depressive disorder; RT, reaction time.

A > B, A is longer than B; Comp is compatible condition; Incomp is incompatible condition; 0-sec is 0-sec ISI; 1-sec is 1-sec ISI.

[a]This table summarizes the main mixed-factor ANOVA results according to the effect of the experimental variables on RT and the exact latency. Common effects refer to the RT and/or the exact latency that are significantly common to the groups while differential effects refer to the RT and/or the exact latency that are significantly different between the groups according to the experimental variables and among each of the emotional facial stimuli; [b]Components (e.g., RT, N1 latency) here (common effects) indicate how the groups (FMDD and RMDD, and HCs) are commonly affected by the experimental variables; [c]Component (P3a latency for happy face) here (differential effects) indicate how the groups (FMDD and RMDD, and HCs) are differently affected by the experimental variables. FMDD and RMDD participants were affected by the experimental variables.

*$P < .05$; **$P < .01$; ***$P < .001$.

with the current CNV results, possibly due to the diversity of depressed patients used.[12,29] However, it can be deduced that the more negative-going CNV among RMDD participants transcends the usual symptoms of depression, especially considering the fact that RMDD participants demonstrated impaired controlled and effortful processes (P3b). Hansenne and Ansseau[29] reported that persons with higher persistence (i.e., perseverance despite frustrations and fatigue) have more negative-going CNV which best explains these current CNV results. However, there was no significant difference between HCs and MDD participants on the general (i.e., global) speed of information processing (RT and ERP latencies), which suggests that the speed of emotional information processing across the stages (perception, orientation, and response choice/decision -making) is similar between the groups (HCs and MDD). Hence, the second hypothesis, but not the first hypothesis, was supported by the results.

For the organization of information-processing stages, the main finding was at the response choice/selection stage, reflected by the P3a latency. That is, the Group factor interacted significantly with the within-group factors (ISI and Comp) at P3a latency during the processing of happy facial stimuli only. Further analysis of the interaction effects revealed that the within-group factors (ISI and Comp) interacted significantly among both FMDD and RMDD groups but not for the HC group during the processing of happy facial stimuli. This indicates that both FMDD and RMDD participants used similar information processing strategies compared with HCs. Further analysis revealed that FMDD participants used a full-parallel processing strategy for automatic processing (P3a latency), while RMDD participants used a partial-parallel processing strategy (i.e., for compatible conditions) for automatic processing (P3a latency) of happy facial stimuli. Since there was no significant interaction between within-group (ISI and Comp factors) factors among HCs, it can be deduced that HCs used a linear processing strategy for automatic processing (P3a latency) of happy information based on the IPM perspective, supporting the study's third hypothesis. The linear processing strategy among HCs suggests meticulous automatic processing of information accounting for better happy information processing outcomes (i.e., more accuracy scores) than MDD participants. Hence, the parallel processing among MDD participants suggests superficial processes which did not aid in decision-making when it comes to processing happy information.

Research Implications and Contributions

Given the deficits in voluntary orientation (N2b), controlled and effortful processes (P3b), and motor preparation (CNV) observed in the current sample of individuals with MDD, the findings suggest the possibility that individuals with MDD might benefit, in particular, from treatments which would improve their awareness of thought processes and that these improvements might result in improved symptoms. There is need for future research to evaluate (1) the extent of changes in these biases as reflected in particular by the ERP components (N2b, P3a, P3b, and CNV) and (2) the possible mechanism variables that underlie MDD symptoms and/or the beneficial effects of treatment. This is the first study to electrophysiologically use IPM to examine how people with MDD process negative, neutral, and positive emotions. The findings clearly present areas where people with depression have challenges and hence where treatment may most be needed.

Limitations

The MDD participants had no medication-free period and so the results should cautiously be interpreted as some previous findings suggest that psychotropic medications can affect information processing.[30] The inclusion-exclusion criteria limited the sample size of this study. The small sample size (n=57) may have limited power to detect significant effects. Thus, it is possible that there are important between-group differences in the populations of individuals with MDD, relative to HCs, that were not detected here.

The results provide important new findings concerning the potential reason for impaired processing of happy or positive emotional information in individuals with MDD despite the study's limitations. That is, the findings suggest that individuals with MDD use a parallel information processing strategy to process happy information, which may lead to impaired voluntary orientation (N2b), controlled and effortful processes (P3b), and motor preparation (CNV) for happy facial stimuli. This suggests that clinicians may adopt the use of an emotional cognitive assessment to get a holistic view of individuals with MDD for effective treatment intervention. Future studies could examine why individuals with MDD have challenges with inhibition-faci litation of negative emotional stimuli in order to inform the treatment of treatment strategies that would aid in their rehabilitation.

Ethics Committee Approval: The study was approved by the Research Ethics Committee of the Hong Kong Hospital Authority (KC/KE-16-0114/ER-2) and The Hong Kong Polytechnic University (HSEARS20160523001).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

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– D.K.A., K.H.M.C., H.H.W., M.G.C.Y., Y.F.M., K.S.L., H.W.H.T.; Writing – D.K.A., K.H.M.C., H.H.W., M.G.C.Y., Y.F.M., K.S.L., H.W.H.T.; Critical Review – D.K.A., H.W.H.T.

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