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Neural indices of heritable impulsivity: Impact of the *COMT Val158Met* polymorphism on frontal beta power during early motor preparation

Joseph P. Happer [a], Lauren E. Beaton [b], Laura C. Wagner [b], Colin A. Hodgkinson [c], David Goldman [c], Ksenija Marinkovic [a,b,d,*]

[a] San Diego State University/University of California, San Diego Joint Doctoral Program in Clinical Psychology, San Diego, CA, USA
[b] Department of Psychology, San Diego State University, San Diego, CA, USA
[c] Laboratory of Neurogenetics, NIAAA, NIH, Bethesda, MD, USA
[d] Department of Radiology, University of California, La Jolla, San Diego, CA, USA

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ABSTRACT

Studies of *COMT Val^{158}Met* suggest that the neural circuitry subserving inhibitory control may be modulated by this functional polymorphism altering cortical dopamine availability, thus giving rise to heritable differences in behaviors. Using an anatomically-constrained magnetoencephalography method and stratifying the sample by *COMT* genotype, from a larger sample of 153 subjects, we examined the spatial and temporal dynamics of beta oscillations during motor execution and inhibition in 21 healthy Met^{158}/Met^{158} (high dopamine) or 21 Val^{158}/Val^{158} (low dopamine) genotype individuals during a Go/NoGo paradigm. While task performance was unaffected, Met^{158} homozygotes demonstrated an overall increase in beta power across regions essential for inhibitory control during early motor preparation (~100 ms latency), suggestive of a global motor "pause" on behavior. This increase was especially evident on Go trials with slow response speed and was absent during inhibition failures. Such a pause could underlie the tendency of Met^{158} allele carriers to be more cautious and inhibited. In contrast, Val^{158} homozygotes exhibited a beta drop during early motor preparation, indicative of high response readiness. This decrease was associated with measures of behavioral disinhibition and consistent with greater extraversion and impulsivity observed in Val homozygotes. These results provide mechanistic insight into genetically-determined interindividual differences of inhibitory control with higher cortical dopamine associated with momentary response hesitation, and lower dopamine leading to motor impulsivity.

1. Introduction

Impulsivity is a multi-dimensional construct reflecting interindividual differences of inhibitory control (Bevilacqua & Goldman, 2013), with significant genetic contributions to trait impulsivity (Anokhin, Golosheykin, Grant, Heath, 2017; Bevilacqua & Goldman, 2013; Bezdjian, Baker, & Tuvblad, 2011; Bezdjian, Tuvblad, Wang, Raine, & Baker, 2014; Bühler et al., 2023; Varga et al., 2012), and as is now known from genome wide association studies (GWAS), risk taking (Karlsson Linner et al., 2019). Compromised inhibitory control is a core heritable risk factor for a number of psychiatric disorders such as attention-deficit/hyperactivity (Aron & Poldrack, 2005) and substance use disorders (Ducci & Goldman, 2008; Enoch & Goldman, 2001; Goldman, Oroszi, & Ducci, 2005). However, the way in which specific genetic variants influence behavioral impulsivity and the underlying neural circuitry among healthy individuals is poorly understood, and the single nucleotide polymorphisms (SNPs) thus far implicated by GWAS being small in effect size and as yet not mapped onto functional loci.

Functional SNPs driving behavior such as the *COMT Val^{158}Met* (rs4680) provide an opportunity to examine how genetic variations act in context and via neurocircuitry affecting inhibitory control (Boettiger et al., 2007; Bogdan et al., 2017; Caspi et al., 2008; Ducci & Goldman, 2008; Farrell, Tunbridge, Braeutigam, & Harrison, 2012; Goldman et al., 2005; Kereszturi et al., 2008; Montag, Jurkiewicz, & Reuter, 2012; Winterer & Goldman, 2003). As recognized in the early 2000s (Egan et al., 2001; Winterer & Goldman, 2003; Zubieta et al., 2003), *COMT Val^{158}Met* is associated not only with behavioral variation and cognitive and emotional responses but more strongly with brain activity during such tasks. *Val^{158}Met* is thought to modulate cortical dopamine signaling primarily within the prefrontal cortex (PFC, Cools, 2019; Friedman &

* Correspondence to: Department of Psychology, San Diego State University, 6505 Alvarado Rd. Suite 202, San Diego, CA 92120, USA.
E-mail address: kmarinkovic@sdsu.edu (K. Marinkovic).

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Robbins, 2022; Ott & Nieder, 2019) as the PFC is a major recipient of dopaminergic projections from the ventral tegmental area (Seamans & Yang, 2004). Due to low levels of dopamine transporters within the PFC, cortical dopamine availability in that region is primarily regulated through enzymatic catabolism by catechol O-methyltransferase (COMT, Yavich et al., 2007). COMT activity is coded for by the *Val^{158}Met* SNP in which an amino acid exchange from valine (Val) to methionine (Met) at codon 158 leads to a 3- to 4-fold decrease in COMT activity (Chen et al., 2004; Lachman et al., 1996). Thus, Met^{158} allele carriers have greater dopamine availability compared to Val^{158} allele carriers. This difference in dopamine availability is thought to differentially tune neuronal activity for Met^{158} vs. Val^{158} allele carriers primarily within the PFC (Benchenane, Tiesinga, & Battaglia, 2011; Schacht, 2016; Seamans & Yang, 2004; Vijayraghavan et al., 2007). An allele dosage relationship between Met^{158} and cortical efficiency and performance on various PFC-mediated tasks has been observed many times over in different contexts including schizophrenia, well-siblings of schizophrenia patients, traumatic brain injury, and normal controls (Diaz-Asper et al., 2008; Egan et al., 2001; Goldberg et al., 2003; Lipsky et al., 2005; Malhotra et al., 2002). Additionally, Met^{158} allele carriers have been described to display more inhibited and anxious personality characteristics while also exhibiting greater responses to pain and stressful stimuli (Congdon, Constable, Lesch, & Canli, 2009; Cope et al., 2016; Ducci & Goldman, 2008; Goldman et al., 2005; Serrano, Banks, Fagan, & Tartar, 2019; Winterer & Goldman, 2003; Zubieta et al., 2003). In contrast, Val^{158} allele carriers have been described as having more extraverted and impulsive personality traits (Boettiger et al., 2007; Bühler et al., 2023; Ducci & Goldman, 2008; Farrell et al., 2012; Goldman et al., 2005; Montag et al., 2012; Winterer & Goldman, 2003). These heritable tendencies in impulsivity characteristics suggest that the PFC neural circuitry subserving inhibitory control may be modulated by dopamine availability via the *COMT* polymorphism (Benchenane et al., 2011; Schacht, 2016; Seamans & Yang, 2004; Vijayraghavan et al., 2007).

Studies probing inhibitory control commonly use Go/NoGo and Stop Signal Task paradigms which engender conflict between responding to the prepotent Go stimuli and withholding the response to infrequent NoGo or Stop stimuli (Wessel, 2018). Previous studies of the *COMT* polymorphism have observed enhanced fMRI BOLD signal in Met^{158} allele carriers within the PFC during response inhibition (Congdon et al., 2009; Cope et al., 2016; Jaspar et al., 2014). However, studies using methods with greater temporal resolution than that provided by the BOLD signal are needed to understand the unfolding of neural processes on behaviorally and physiologically relevant time scales. This is particularly important for fast-paced motor tasks in which preparatory neural activity may begin in advance of stimulus presentation and additional downstream cognitive processes (Beaton et al., 2018; Cheyne, Bakhtazad, & Gaetz, 2006; Wessel & Aron, 2017). Evidence indicates that in the face of conflicting response options during these paradigms, a "braking" system may initiate a momentary "pause" in preparatory motor output until a response option is selected (Aron, Behrene, Smith, Frank, & Poldrack, 2007; Frank, 2006; Frank et al., 2007; Gillies & Willshaw, 1998; Muralidharan, Aron, & Schmidt, 2022). The inhibitory NoGo or Stop stimuli capture attention due to their salience and low frequency, which further enhances transient motor suppression (Happer, Wagner, Beaton, Rosen, & Marinkovic, 2021; Wessel et al., 2016). Converging evidence indicates this momentary pause may be effectuated by a "hyperdirect" pathway between regions of the PFC, including the right inferior frontal cortex (IFC), and the subthalamic nucleus (STN) of the basal ganglia (Aron & Poldrack, 2006; Aron et al., 2014; Drummond & Chen, 2020; Nambu, 2004). Moreover, studies using the superior temporal resolution of electro- and magnetoencephalography (EEG, MEG) indicate that a brief increase in neural activity shortly after stimulus onset likely reflects engagement of the hyperdirect pathway (Hannah, Muralidharan, Sundby, & Aron, 2020; Happer et al., 2021; Jana, Hannah, Muralidharan, & Aron, 2020; Muralidharan et al., 2022; Wessel, 2020; Wessel & Aron, 2013, 2017). Activation of this pathway has been associated with global suppression of motor activity in addition to disrupting ongoing cognitive processes (Wessel & Aron, 2013, 2017; Wessel et al., 2016).

Further insight into the neural activity subserving motor preparation and inhibition as it unfolds has been gleaned by decomposing the oscillations recorded with EEG and MEG methods into spectral band ranges associated with neurofunctional processes (Buzsaki et al., 2013; Nunez & Srinivasan, 2006; Siegel, Donner & Engel, 2012). In particular, oscillations within the beta band range (15–25 Hz), are thought to be the preferred frequency of the sensorimotor system, reflecting engagement of the motor cortices, basal ganglia, and other areas contributing to motor planning, inhibition, and execution (Baker, 2007; Khanna & Carmena, 2015). Beta oscillations are anticipatory in nature and begin to decrease in power, or desynchronize, in advance of and in preparation for real and imagined engagement of the motor system and rebound after movement (Beaton et al., 2018; Cheyne et al., 2006; Cheyne et al., 2012; Donner et al., 2009; Engel & Fries, 2010; Heinrichs-Graham & Wilson, 2015; Jenkinson & Brown, 2011; Kilavik, Zaepffel, Brovelli, MacKay, & Riehle, 2013; Neuper, Muller-Putz, Scherer, & Pfurtscheller, 2006; Swann et al., 2012). In contrast, motor inhibition is accompanied by increased beta power (Hannah et al., 2020; Jana et al., 2020; Khanna & Carmena, 2015; Muralidharan et al., 2022; Pogosyan, Gaynor, Eusebio, & Brown, 2009; Swann et al., 2009; Swann et al., 2012). Based on these features, beta oscillations have been proposed to underlie motor readiness (Jenkinson & Brown, 2011), which makes them a particularly suitable neural index for investigating movement execution and inhibition (Beaton et al., 2018; Engel & Fries, 2010; Hannah et al., 2020; Jana et al., 2020; Khanna & Carmena, 2015; Kuhn et al., 2004; Swann et al., 2009). Moreover, individual differences in beta oscillations have been suggested to reflect dispositional levels of inhibitory control. For example, impulsive individuals, including binge drinkers, exhibit greater decreases in beta power in anticipation of response (Barth, Rohe, Deppermann, Fallgatter, & Ehlis., 2021; Holcomb et al., 2019; Tzagarakis, Thompson, Rogers, & Pellizzer et al., 2019). Thus, beta oscillations may serve as an intermediary neural signature of genetically-determined differences of impulsivity (Anokhin et al., 2017; Bezdjian et al., 2014).

In light of these considerations, the aim of the current study was to examine the neural underpinnings of successful inhibitory control, movement execution as modulated by response speed, and inhibitory failures as a function of cortical dopamine availability by comparing homozygous Val vs. Met carriers on a Go/NoGo paradigm, taking advantage of the effect of the *Val^{158}Met* polymorphism to modulate frontal dopamine levels without necessarily altering overt behaviors. To investigate discrete stages of neural activity elicited during motor preparation and inhibition, we used an anatomically-constrained MEG (aMEG) approach which combines the temporal precision of distributed MEG source modeling with the spatial resolution of structural MRI (Dale et al., 2000; Marinkovic, 2004). This approach allowed us to explore the spatio- ("where") temporal ("when") dynamics of beta band oscillations underlying inhibitory control in real time.

2. Methods

2.1. Participants

As part of a larger study on the impact of alcohol intoxication on the brain, forty-two (21 female; age (mean ± SD) = 26.1 ± 4.3 years) right-handed, healthy volunteers successfully completed all sessions of the experiment. Participants reported no previous neurological, psychiatric, alcohol- or drug-related problems and no family history of alcohol or drug abuse in their first or second-degree relatives. None reported any previous head injuries nor were on any medication at the time of the study. No alcohol use disorder (AUD)-related symptoms were detected using the Short Michigan Alcoholism Screening Test (SMAST, Selzer, Vinokur, & van Rooijen, 1975). They reported occasional alcohol consumption (2.5 ± 1.2 times per week) and in low to moderate amounts in

social settings (3.0 ± 1.5 drinks per occasion), Table 1.

Participants self-identified as European Americans which was confirmed with ancestry informative markers (Hodgkinson et al., 2008) indicating an average of 92.5% European American ancestry. To assess contributions of dopamine availability, participants were stratified according to genotype for *COMT Val^{158}Met* (rs4680). To maximize effects of genotype, only Met^{158}/Met^{158} (N = 21) and Val^{158}/Val^{158} homozygotes (N = 21) were included in the study. To obtain this sample, 153 subjects were recruited, identifying 72 Val^{158}/Met^{158} heterozygotes and some 38 homozygotes who did not meet inclusion criteria or dropped out (Met^{158}/Met^{158}, n = 14; Val^{158}/Val^{158}, n = 24). The full distribution of genotypes did not deviate from Hardy-Weinberg equilibrium (χ^2 =.472, p = .79).

To examine the association between disposition and inhibitory control (Table 1), participants were assessed for disinhibition, novelty-seeking, and socialization using the Zuckerman Sensation Seeking Scale (Zuckerman, 1971), Eysenck Impulsiveness and Venturesomeness Scale (Eysenck & Eysenck, 1978), and Eysenck Personality Questionnaire (Eysenck & Eysenck, 1975). Participants reported their current drinking patterns including level of response to alcohol (Self-Rating of the Effects of Alcohol, SRE, Schuckit, Smith, & Tipp, 1997), severity of alcohol-related symptoms (SMAST, Selzer et al., 1975), and quantity and frequency of alcohol consumption (modified from Cahalan, Cisin, Crossley, 1969).

The Institutional Review Board of the University of California at San Diego and San Diego State University approved all study procedures. All participants gave written, informed consent and were compensated for their participation.

2.2. Genotyping

Saliva (2 ml) was collected with Oragene® kits (DNA Genotek). DNA was extracted using a DNAQuik protocol (BioServe). *COMT Val^{158}Met* (rs4680) was genotyped by 5'-exonuclease assay using assay C_25746809_50 (ThermoFisher Scientific, Waltham MA). Genomic DNA (5 ng) was amplified on a 9700 thermocycler (ABI). At the end point of amplification, genotypes were discriminated using SDS 2.4 software on an AppliedBiosystems 7900 Analyzer. For amplification, initial incubation was at 95 °C for 10 min, followed by 40 cycles at 92 °C (15 s) and 60 °C (1 min). The genotyping completion rate was 100% and genotyping error rate (0%) was determined by duplicate genotyping of a random selection of samples and comparison against a panel of samples of known genotypes, where all three *Val^{158}Met* genotypes were present.

Table 1
Participant characteristics (mean ± SD or n (%)) for Met^{158} and Val^{158} homozygotes.

	Met^{158}/Met^{158} (n = 21)	Val^{158}/Val^{158} (n = 21)	F/χ^2	p
% Female[a]	52.4%	47.6%	0.1[a]	.758
Age	26.6 ± 4.7	25.7 ± 3.8	0.5	.499
Eysenck Personality Questionnaire				
Neuroticism	7.7 ± 4.9	7.1 ± 4.7	0.2	.692
Psychoticism	3.3 ± 1.7	3.8 ± 2.5	0.5	.471
Extraversion	10.1 ± 5.5	14.9 ± 5.9	7.7	**.008**
Eysenck Impulsivity Inventory				
Impulsiveness	3.7 ± 3.3	3.3 ± 2.8	0.2	.655
Venturesomeness	8.0 ± 3.1	9.4 ± 2.2	2.7	.107
Empathy	8.9 ± 2.8	9.5 ± 3.3	0.4	.549
Zuckerman Sensation Seeking Scale				
Experience Seeking	7.6 ± 1.9	7.6 ± 2.0	0.0	.937
Thrill Seeking	6.2 ± 2.6	7.1 ± 2.2	1.3	.256
Boredom Susceptibility	4.8 ± 2.7	5.3 ± 2.1	0.4	.527
Disinhibition	5.9 ± 2.3	6.5 ± 1.9	0.9	.346
SMAST	0.6 ± 1.2	0.6 ± 0.7	0.0	1.00
Drinks/Drinking Day	2.7 ± 1.2	3.4 ± 1.7	2.1	.153
Drinking Days/Week	2.5 ± 1.2	2.4 ± 1.3	0.1	.735
Binged in Past 6 mos[a]	52%	81%	3.9[a]	**.050**
Binge Episodes in Past 6mos	0.5 ± 0.6	1.4 ± 1.3	6.8	**.012**
SRE Overall	5.0 ± 2.2	5.3 ± 1.5	0.3	.585

[a] Tested with Chi-square, all other comparisons performed with ANOVAs. SMAST: Short Michigan Alcoholism Screening Test; SRE: Self-Rating of the Effects of Alcohol.

2.3. Task

Participants performed a modified Go/NoGo task (Fig. 1, Garavan, Ross, Murphy, Roche, & Stein, 2002; Holcomb, Huang, Cruz, & Marinkovic, 2019; Marinkovic & Rosen, 2022) while responding with their right index finger. The task consisted of "X" and "Y" letters presented individually in an alternating (80%, Go) or repeated (20%, NoGo) manner. Participants were instructed to respond as quickly and as accurately as possible to each alternation and to inhibit their response to each repetition. A total of 685 trials were presented in white font color on a black screen using Presentation software (Neurobehavioral Systems). The stimulus onset asynchrony (SOA) was 1400 ms ± a random incremental jitter of ± 150 ms. Stimuli were presented for 230 ms and then replaced by a fixation for the remainder of the trial. By design, this task creates a prepotency to respond which leads to occasional premature button pressing. Responses occurring within −250 ms pre- to 200 ms post-stimulus presentation were categorized as premature and were excluded from the analysis.

2.4. Data acquisition and analysis

2.4.1. MRI

Structural MRI images were acquired with a 1.5T GE EXCITE HG whole-body scanner (General Electric). Acquisition protocol included a 3-plane localizer, calibration scan, and a high-resolution T1-weighted IR-FSPGR scan (TR = 8.5 s, TE = 3.75 ms, flip angle = 10º, FOV = 240 mm, 166 sagittal slices, 1.2 mm slice thickness, in-plane resolution .94 x .94 mm). Structural images were used to reconstruct each participant's cortical surface (Dale et al., 1999; Fischl, Sereno, & Dale, 1999) and served as inverse estimate constraints. The inner skull surface was used as a boundary element model of volume conductor in the forward calculations. For the purposes of inter-subject averaging, the reconstructed surface was morphed onto an average brain representation (Fischl, Sereno, Tootell, & Dale, 1999). The solution space was approximated by ~5000 free-rotating dipoles spaced ~7 mm apart along the cortical mantle.

2.4.2. MEG

MEG signals were recorded from 204 channels (102 pairs of planar gradiometers) using a whole-head Vectorview system (Elekta

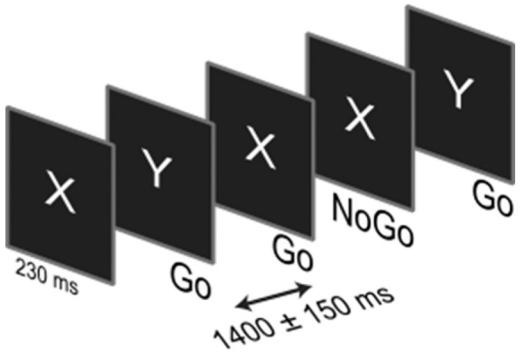

Fig. 1. Go/NoGo task. The task consisted of "X" and "Y" letters presented in an alternating (80%, Go) or repeated (20%, NoGo) manner. Participants were instructed to make a button press with their right index finger for every alternation and inhibit their response for each repetition. A total of 685 trials were presented in rapid succession every 1400 ± 150 ms with each letter being presented for 230 ms before being replaced by a central fixation dot for the remainder of the trial.

Neuromag) in a magnetically and electrically shielded room. The signals were continuously recorded with 1000 Hz sampling rate and minimal filtering (0.1 to 330 Hz). Four head position indicator coils attached to the head, main fiduciary points including the nasion and preauricular points, and a large array of random points across the scalp were digitized with 3Space® Isotrak® (Polhemus Inc.) to allow for subsequent precise co-registration with structural MRI images. Three analyses were conducted to examine different aspects of motor preparation and execution. First, correct Go and NoGo trials were compared to examine whether the *Val^{158}Met* genotype modulated overall beta activity. To mitigate possible statistical bias, the number of trials was equated across task conditions in each analysis for each participant by removing superfluous trials at random, resulting in an average of 101 ± 15 trials per condition. Then, beta oscillatory underpinnings of fast Go trials were compared to trials with slow response latency. For each individual, trials were ranked by reaction time, and the fastest 40% of trials were compared to the slowest 40% of trials while the middle 20% were discarded. This yielded an average of 185 ± 13 trials per condition. Finally, inhibitory control was probed more specifically by comparing successful NoGo trials to inhibitory failures (i.e., NoGo errors). Individuals who made a minimum of 15 NoGo errors were included (16 Met^{158}/Met^{158}; 16 Val^{158}/Val^{158}), resulting in an average of 28 ± 11 trials per condition. Neural activity to NoGo errors was compared to a matched number of successful NoGo inhibitions.

MEG data analysis was performed using our MATLAB (Mathworks) analysis pipeline which relies in part on publicly available packages including FieldTrip (Oostenveld, Maris,Schoffelen, 2011), EEGLAB (Delorme & Makeig, 2004), and MNE (Gramfort et al., 2014). Continuous data were first bandpass filtered from 0.1 to 100 Hz before epochs were created encompassing intervals from −600 ms to 1100 ms relative to stimulus onset. Each epoch was downsampled to 250 Hz and visually inspected for movement artifacts. Additional artifacts such as heartbeat and eye blinks were removed using independent component analysis (Delorme & Makeig, 2004). Morlet wavelet convolution was applied to individual trial epochs in 2 Hz increments in beta band frequencies (15 to 25 Hz). To minimize edge artifacts due to wavelet decomposition, the first and last 300 ms of each epoch were discarded, resulting in time windows of −300 to 800 ms. Empty room data were bandpass filtered between 3 and 40 Hz and used to estimate the noise covariance for inverse calculations, and to prevent biasing against spontaneous brain oscillations. An identity matrix was used for the noise-sensitivity normalization of the source-space solution (Beaton et al., 2018; Kovacevic et al., 2012; Lin et al., 2004; Marinkovic, Beaton, Rosen, Happer, & Wagner, 2019). Maps of estimated total event-related source power were created for each participant by averaging across trials and frequencies in beta band for each condition. Total event-related power was baseline-corrected by subtracting the mean source power estimate in the 300 ms prestimulus period and expressed as percent signal change from the baseline.

Region-of-interest (ROI) analysis was conducted to investigate the possible effects of genotype on stimulus-related changes in beta power across time. ROIs were generated based on overall group averages across all participants and task conditions in an unbiased manner and comprised dipole locations along the cortical surface with most notable estimates. The same set of group-based ROIs was used for all participants, blind to individual activation. Specifically, ROIs encompassed primarily lateral frontal cortical areas including the left inferior frontal cortex (IFC), the right anterior insula/frontal operculum (aI/FO), the bilateral hand sensorimotor region (sMOT), and bilateral dorsal anterior cingulate cortices (dACC). Estimated time courses for each condition were extracted for each participant and averaged into grand mean waveforms.

2.4.3. Statistical analyses

Statistical analyses were conducted with mixed model ANOVAs where Trial Type (Go, NoGo; Fast Go, Slow Go; Error NoGo, Correct NoGo) served as within-subject factors and Genotype Group (Met^{158}/Met^{158}, Val^{158}/Val^{158}) as a between-subject factor. Event-related beta power data were averaged over the time windows of interest before being entered into the ANOVAs. To characterize changes in overall beta power during early motor preparation (0–110 ms post-stimulus), a linear model was fitted to each participant with the resulting slopes extracted and compared statistically with ANOVAs as described above.

3. Results

3.1. Personality characteristics and drinking habits

As seen in Table 1, extraversion was the only observed difference in personality characteristics between COMT Val^{158}/Val^{158} and Met^{158}/Met^{158} homozygous groups, with Val^{158} homozygotes having higher scores on Eysenck extraversion dimension, $F(1,41) = 7.7$, $p = .008$, consistent with prior studies. Val^{158} homozygotes were more likely to engage in at least one episode of binge drinking in the previous six months, $\chi^2 = 3.9$, $p = .050$ and had more binge episodes in that time span, $F(1,41) = 6.8$, $p = .012$. A binge episode was defined as 5 or more drinks for men and 4 or more drinks for women in accordance with Center for Disease Control and the Substance Abuse and Mental Health Services Administration definition (Gfroerer, 1996). Daily alcohol consumption was associated with higher disinhibition ($r = .373$, $p = .015$) in both genotype groups, consistent with other extensive evidence (Adan et al., 2017).

3.2. Performance

As expected, response accuracy was higher on Go compared to NoGo trials overall, $F(1,40) = 84.8$, $p < .001$, with no group differences in performance accuracy, $F(1,40) = 0.1$, $p = .75$. (Fig. 2). Likewise, Met^{158} and Val^{158} homozygotes did not differ in reaction times (RTs), $F(1,41) = 0.4$, $p = .53$, nor the number of premature responses, $F(1,41) = 0.0$, $p = 1.0$. However, higher extraversion scores were associated with faster RTs across the sample, $r = -.50$, $p = .001$, which is indicative of behavioral disinhibition and motor impulsivity.

3.3. Spatiotemporal aMEG estimates

3.3.1. Overall beta dynamics revealed by the Go/NoGo task

Beta oscillations are characterized by desynchronization, or decrease in power, relative to baseline during motor planning and execution, with the greatest decrease occurring over the left sensorimotor cortex which controls movement of the right responding hand (Fig. 3). A similar but much weaker effect was seen over the right motor cortex, ipsilateral to the responding hand. As seen in Fig. 3, beta power averaged across all participants began to decrease prior to stimulus onset equally for both Go and NoGo trials in anticipation of making a response. The two time courses diverged at ~200 ms as NoGo trials exhibited less of a decrease relative to Go trials, reflecting successful response inhibition. Beta power continued to decrease on Go trials until it reached the nadir, approximately corresponding to the reaction latency. Group differences in event-related beta power were quantified during early motor preparation (T1: 60–110 ms) and response execution stages (T2: 250–400 ms) as seen in Fig. 4.

3.3.1.1. Genotype differences during early response preparation (T1: 60-110 ms). Early beta power began decreasing during motor response preparation in advance of stimulus onset. Immediately upon stimulus onset, Met^{158} homozygotes displayed a transient increase, or "uptick," in overall beta power regardless of trial type (Fig. 4, Table 2). In contrast, Val^{158} homozygotes exhibited a more precipitous drop in beta power, which was particularly evident within the left hemisphere, contralateral to the responding hand. Using linearly fitted slopes within the 0 to

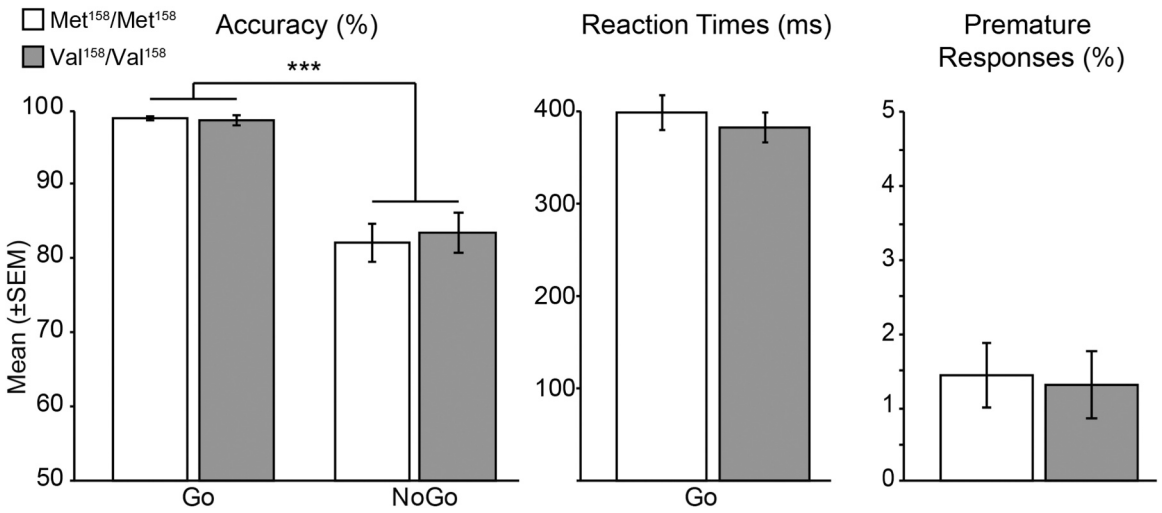

Fig. 2. Task performance. As expected, response accuracy was higher on Go trials compared to NoGo trials overall. However, genotype groups did not differ on accuracy, reaction times, and premature responses. ***$p < .001$.

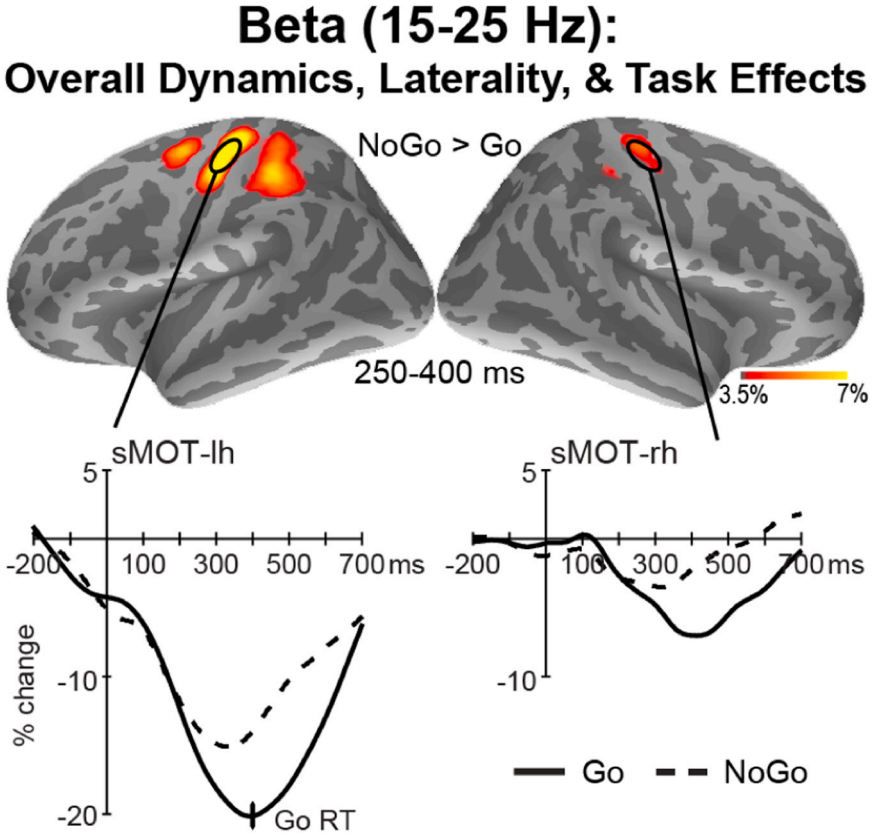

Fig. 3. Overall pattern of beta dynamics during motor execution and inhibition. Greatest changes in beta power were observed over the left sensorimotor area (sMOT), which controls the responding right hand. Beta power began to decrease prior to stimulus onset in anticipation of making a response. Beta diverged at ~200 ms to NoGo trials, reflecting successful response inhibition. It continued decreasing on Go trials, with the nadir approximately corresponding to reaction times (marked with a vertical bar). A similar, but weaker effect was observed within the right sMOT, ipsilateral to the responding hand. Activity maps represent the contrast of NoGo > Go beta power averaged across all participants during the 250–400 ms time window.

110 ms time period, Val^{158} homozygotes were confirmed to have an overall greater rate of beta decrease, or steeper downward slope, within the dACC-lh, $F(1,40) = 12.3$, $p = .001$, and a strong trend in the IFC-lh, $F(1,40) = 3.1$, $p = .084$ (SI Fig. 1). Indices of behavioral disinhibition were associated with greater early beta decrease specifically for Val^{158} homozygotes. This included increased daily drinking with the dACC bilaterally (Left: $r = -.488$, $p = .025$; Right: $r = -.695$, $p < .001$), the left IFC ($r = -.495$, $p = .023$), and the right sMOT ($r = -.485$, $p = .026$). Furthermore, increased experience seeking was associated with lower beta power within the aINS/FO ($r = -.450$, $p = .041$) for Val^{158} homozygotes.

3.3.1.2. Genotype differences during response execution at beta nadir (T2: 250-400 ms). Around the nadir, Val^{158} homozygotes continued to

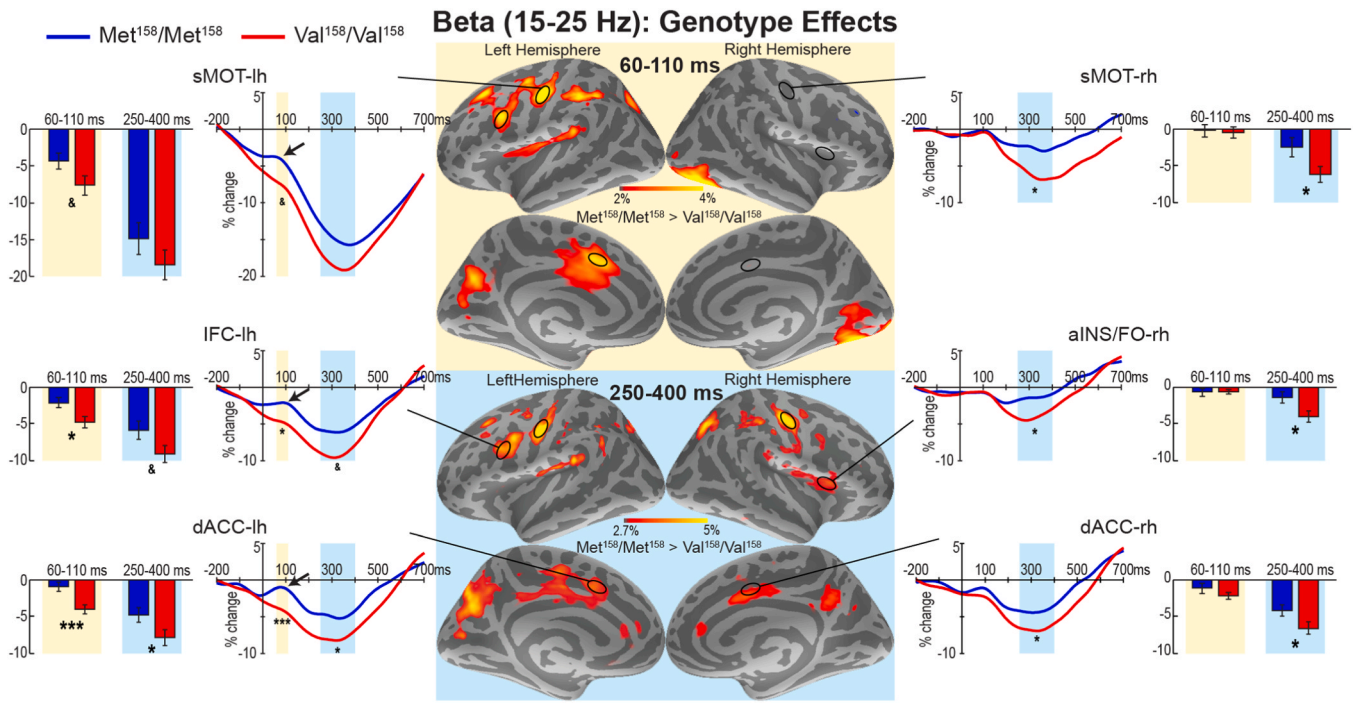

Fig. 4. Impact of genotype on overall beta dynamics. During early motor preparation (60–110 ms, yellow shading), Val^{158} homozygotes exhibited a precipitous drop in overall beta power which is suggestive of greater behavioral disinhibition. In contrast, Met^{158} homozygotes displayed an "uptick" at ~100 ms (marked with black arrows) that may reflect transient inhibition. It was particularly evident in the left frontal areas. Subsequent activity at the beta nadir (250–400 ms, blue shading) similarly demonstrated overall lower beta power in the Val^{158} group relative to Met^{158} homozygotes. This effect was similar in both hemispheres. Time courses and bar graphs represent beta power averaged across Go and NoGo trials within the early time window (60–110 ms, marked in yellow) and around the nadir (250–400 ms, marked in light blue). Activity maps represent the Met^{158}/ Met^{158} > Val^{158}/ Val^{158} contrast of trial-averaged beta power. $^{\&}p < .07$; $^{*}p < .05$; $^{***}p < .001$.

exhibit overall lower beta power relative to Met^{158} homozygotes within the dACC-lh, and a strong trend in the IFC-lh. This pattern was additionally reflected in the right aINS/FO, sMOT, and dACC.

The latency of beta nadirs was additionally examined. Within the dACC-lh, nadir latency was modulated by genotype, resulting in a Genotype Group x Trial Type interaction $F(1,40) = 7.6$, $p = .009$, $\eta_p^2 = .13$ (SI Fig. 2). Follow-up analyses indicated a strong trend for Met^{158} homozygotes to have a slower nadir relative to Val^{158} homozygotes specifically during Go trials, $F(1,40) = 3.3$, $p = .078$, while NoGos were unaffected. Nadir latencies within the sMOT-lh were not modulated by genotype. However longer sMOT-lh Go nadir latencies were associated with increased (less desynchronized) beta power within the IFC-lh ($r = .486$, $p = .026$) and sMOT-lh ($r = .525$, $p = .015$) during early motor preparation (T1: 60–110 ms) specifically for Met^{158} homozygotes. This is consistent with more cautious responses in Met^{158} homozygotes as reflected in momentary response suppression and greater beta.

3.3.2. Genotype differentially impacts early beta dynamics during fast and slow Go responses

To examine the impact of early preparatory beta dynamics (60–110 ms) on response latency, each participant's Go responses were stratified by RT, and the slowest 40 % (mean ± SD = 305.6 ± 61.7 ms) were compared to the fastest 40 % (486.9 ± 101.8 ms). No differences in RT for either fast or slow responses were detected between genotypes, $F(1,40) = 0.0$, $p =$ n.s. However, Met^{158} homozygotes displayed a transient beta increase (i.e. the "uptick") reflecting response inhibition only on Slow Go trials in the left sMOT and dACC (Fig. 5, Table 2), while no such increase was observed in the Val^{158} homozygote group. Within the dACC-lh for Val^{158} homozygotes, similarity in beta power reduction between fast and slow responses corresponded with higher extraversion, suggestive of dispositional differences ($r = -.456$, $p = .038$). Moreover, lower beta power during slow responses was associated with increased alcohol consumption per drinking day ($r = -.478$, $p = .028$), suggestive of behavioral disinhibition.

3.3.3. Early beta dynamics as a function of inhibitory failures (errors)

Met^{158} homozygotes also exhibited a beta power "uptick" on correct (i.e., successfully inhibited) NoGo trials within the rostral ACC-rh (Fig. 6, Table 2) relative to Val^{158} homozygote participants. In contrast, when Met^{158} homozygotes failed to withhold their response and made an error of commission, no such increase in beta power was observed. This beta power "uptick" was observable only for Met^{158} homozygotes, as Val^{158} homozygotes did not exhibit any differences in beta power between correctly withheld responses and errors during this time period.

4. Discussion

In the present study, we used an aMEG method and a genotype-stratified sample to examine the impact of the *COMT Val^{158}Met* polymorphism on the neural activity associated with response preparation and execution as a function of response speed, and inhibitory errors. The results provide mechanistic insight into genetically-determined inter-individual differences of inhibitory control with high cortical dopamine (Met^{158}/Met^{158}) associated with momentary response hesitation, and low dopamine availability (Val^{158}/Val^{158}) reflected in motor impulsivity. The principal findings can be summarized as follows: (1) during early movement preparation (~100 ms), Met^{158} homozygotes displayed a transient increase in beta power overall within a network of regions associated with early movement planning, execution, and inhibition including the dACC, IFC, and sMOT of the responding hand; (2) which was suggestive of a non-specific global "pause" before response selection; (3) this beta increase was observed only on Go trials with slow RTs

Table 2

Summary of ANOVAs of beta power for ROIs. Included are the main effects, interactions, and simple main effects of the factors of Genotype Group and Trial Type for the three analyses: 1) overall beta (Go, NoGo), 2) beta on fast vs. slow Go trials; 3) successful NoGo inhibitions vs. NoGo errors). dACC: dorsal anterior cingulate cortex; IFC: inferior frontal cortex; sMOT: sensorimotor area; aINS/FO: anterior insula/frontal operculum; rACC: rostral anterior cingulate.

1. Overall Beta	Group F (1,40)	Trial F (1,40)	Group x Trial (η_p^2) F (1,40)	Group: NoGo F (1,40)	Group: Go F (1,40)	Trial: Met^{158}/Met^{158} F (1,20)	Trial: Val^{158}/Val^{158} F (1,20)
T1 60-110 ms							
dACC-lh	13.3***	0.0	0.7 (.02)	10.7**	7.4*	0.2	0.7
IFC-lh	6.0*	0.3	2.2 (.05)	8.3**	2.6	0.4	2.1
sMOT-lh	4.0[a]	2.8	0.2 (.01)	4.0[a]	3.6[a]	2.0	0.9
dACC-rh	1.7	0.6	1.9 (.05)	3.6[a]	0.0	0.2	2.0
aINS/FO-rh	0.0	2.3	3.1 (.07)	1.7	1.0	0.0	4.4*
sMOT-rh	0.1	1.7	2.3 (.06)	1.2	0.2	0.0	3.7[a]
T2 250-400 ms							
dACC-lh	4.1*	13.4***	0.1 (.00)	4.0	2.6	9.0**	4.9*
IFC-lh	3.7[a]	14.1***	0.1 (.00)	3.5[a]	3.0	5.7*	8.6**
sMOT-lh	1.5	22.9****	0.2 (.00)	1.7	1.2	15.0***	9.9**
dACC-rh	4.1*	15.4***	0.1 (.00)	2.6	4.0[a]	5.0*	13.2**
aINS/FO-rh	5.4*	12.6**	0.1 (.00)	3.9[a]	4.7*	4.8*	12.2**
sMOT-rh	4.4*	7.2*	0.0 (.00)	3.1	3.9[a]	3.0	4.4*

2. Beta on Fast Go vs. Slow Go Trials	Group	Trial	Group x Trial (η_p^2)	Group: Fast Go	Group: Slow Go	Trial: Met^{158}/Met^{158}	Trial: Val^{158}/Val^{158}
	F(1,40)	F(1,40)	F(1,40)	F(1,40)	F(1,40)	F(1,20)	F(1,20)
60-110 ms							
dACC-lh	5.0*	1.2	4.2* (.10)	1.1	8.7**	4.9*	0.5
sMOT-lh	1.8	3.2	2.5 (.06)	0.5	3.5[a]	4.4*	0.0

3. Beta on Correct vs. Error NoGo Trials	Group	Trial	Group x Trial (η_p^2)	Group: NoGo	Group: Error	Trial: Met^{158}/Met^{158}	Trial: Val^{158}/Val^{158}
	F(1,30)	F(1,30)	F(1,30)	F(1,30)	F(1,30)	F(1,15)	F(1,15)
100-200 ms							
rACC-rh	0.3	0.4	7.7** (.20)	4.5*	1.4	5.1*	2.6

* $p < .05$;
** $p < .01$;
*** $p < .001$;
**** $p < .0001$
[a] $p < .07$;

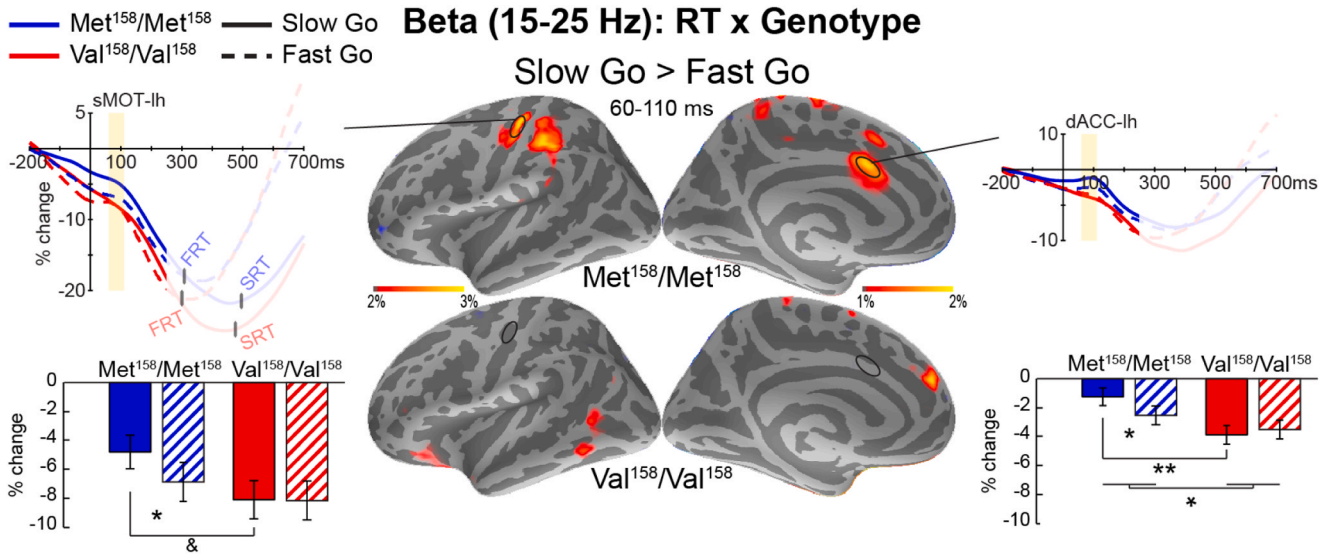

Fig. 5. Genotype differentially impacts early beta dynamics on trials with fast vs. slow reaction times. To examine how genotype modulates preparatory beta power during successful Go responses, trials were stratified according to whether the reaction time was slow (SRT) or fast (FRT) for the individual. During early motor preparation (60–110 ms), Met^{158} homozygotes exhibited an uptick in beta power relative to Val^{158} homozygotes on the trials with slow response latencies. In contrast, early beta power did not differ between slow and fast responses for Val^{158} homozygotes. Bar graphs represent average beta power within the 60–110 ms time window ± SEM. Vertical black bars on sMOT-lh time courses represent average fast (FRT) and slow (SRT) response latencies. sMOT: left sensorimotor cortex, dACC: left dorsal anterior cingulate cortex. $^{\&}p < .07$ $^{*}p < .05$; $^{**}p < .01$.

for the Met^{158} homozygote group, (4) and was absent during inhibitory failures (NoGo errors); (5) in contrast, Val^{158} homozygotes exhibited greater decreases in beta power during early motor preparation, indicative of greater readiness to make a response; (6) which correlated with behavioral disinhibition variables such as extraversion and drinking.

Replicating previous findings, beta power began decreasing in preparation and anticipation of making a movement (Fig. 3, Beaton, Azma, & Marinkovic, 2018; Donner, Siegel, Fries, & Engel 2009).

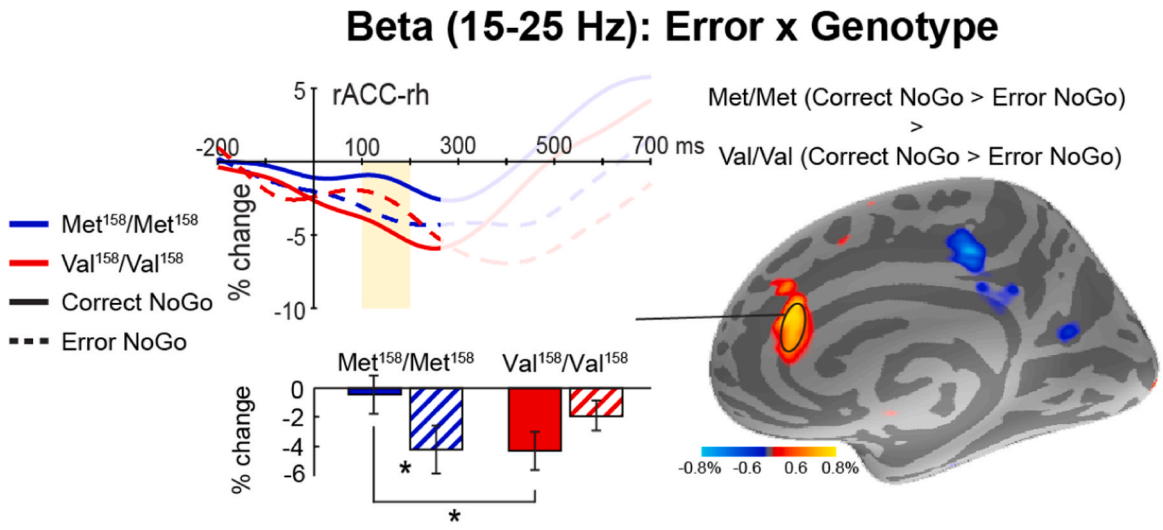

Fig. 6. Impact of genotype on early beta dynamics as a function of NoGo errors. During successful response inhibition (i.e., correct NoGo trials), Met^{158} homozygotes displayed an "uptick" in beta power relative to Val^{158} homozygotes. However, when Met^{158} homozygotes made an error and were unable to withhold their response, no such beta increase was observed, particularly within the right rostral anterior cingulate (rACC). Bar graphs represent average beta power within the time window ± SEM. *$p < .05$.

However, Met^{158} homozygotes demonstrated an uptick, or increase, in beta power very shortly (~100 ms) in reaction to stimulus onset (Fig. 4). The beta increase was observed in the sensorimotor cortex, but also in the dACC and IFC, regions that are consistently activated during early movement preparation and response suppression and slowing (Aron & Poldrack, 2006; Aron et al., 2014; Drummond & Chen, 2020; Happer et al., 2021; Kovacevic et al., 2012; Nambu, 2004; Rae et al., 2015; Wessel & Aron, 2013, 2017). This uptick suggests a non-specific, global "pause" on motor activity (Wessel & Aron, 2017) and can be interpreted as "antikinetic" (Brown & Williams, 2005) given beta increases are associated with motor inhibition (Hannah et al., 2020; Jana et al., 2020; Khanna & Carmena, 2015; Pogosyan et al., 2009; Swann et al., 2009; Swann et al., 2012). Previous EEG studies of inhibitory control have described beta increases at comparable latencies after the appearance of "Stop" stimuli (Hannah et al., 2020; Jana et al., 2020; Wagner et al., 2018; Wessel, 2020), while direct intracranial recordings from both humans (Chen et al., 2020; Swann et al., 2009; Swann et al., 2012) and non-human primates (Zhang et al., 2008) provide evidence that the dACC and IFC are cortical beta generators outside of the primary sensorimotor cortex. It has been proposed that early latency beta increases reflect engagement of the hyperdirect pathway (Hannah et al., 2020; Jana et al., 2020; Wessel, 2020) formed between the PFC and the subthalamic nucleus (STN) of the basal ganglia (Aron et al., 2007; Chen et al., 2020; Nambu, 2004; Nambu, Tokuno, & Takada, 2002), which is well-situated to induce broad motor suppression via glutamatergic efferents to the globus pallidus and thalamic relays (Chambers, Garavan, & Bellgrove, 2009; Nambu, 2004). Simultaneous recordings from the STN and cortical regions further suggest that cortical activity precedes and drives activity within the STN (Chen et al., 2020; Hirschmann, Steina, Vesper, Florin, & Schnitzler, 2022; Oswal et al., 2021). Activation of the hyperdirect pathway has been associated with slowing and interrupting subsequent or ongoing cognitive processes (Happer et al., 2021; Wessel, 2017; Wessel et al., 2016). Overall, the transient uptick in beta power observed in Met^{158} homozygotes is consistent with inhibitory activity that reflects engagement of the hyperdirect pathway during early motor preparation.

The early beta power increase characterizing Met^{158} homozygotes is indicative of a global pause on early preparatory motor activity until a response option is selected (Aron et al., 2007; Frank, 2006; Frank et al., 2007; Gillies & Willshaw, 1998; Muralidharan et al., 2022). This basic mechanism may contribute to the neurobiological underpinnings of response hesitation which could present as more anxious or cautious personality traits typically ascribed to Met^{158} homozygotes (Enoch & Goldman, 2001; Enoch et al., 2003; Olsson et al., 2005). Indeed, early beta power has been noted to increase as a function of response uncertainty, often accompanied by behavioral slowing (Androulidakis et al., 2007; Saleh, Reimer, Penn, Ojakangas, & Hatsopoulos, 2010; Tzagarakis, Thompson, Rogers, & Pellizzer, 2010; van Wijk, Daffertshofer, Roach, & Praamstra, 2009). While Met^{158} homozygotes did not demonstrate any overt behavioral slowing on task performance, neurophysiological measures may be more sensitive (Bogdan et al., 2017), particularly the beta nadir (i.e., peak beta decrease), which roughly corresponds with the execution of a motor command on Go trials (Beaton et al., 2018; Jurkiewicz, Gaetz, Bostan & Cheyne, 2006). In the present study, Met^{158} homozygotes who exhibited greater beta power increases during early motor preparation took longer to reach the beta nadir within the sMOT-lh. These data provide evidence for a slowing of the "Go" process (Frank, 2006; Frank et al., 2007; Schmidt & Berke, 2017) specifically in Met^{158} homozygotes as a result of engagement of the hyperdirect pathway, with downstream effects on the primary motor cortex during movement execution (Swann et al., 2009). The early uptick in beta power was additionally demonstrated to vary with response speed during Go trials. Met^{158} homozygotes exhibited a more pronounced uptick on slower Go trials, particularly within the left sMOT and dACC, indicative of greater engagement of the braking network and suggestive of a greater degree of response uncertainty (Androulidakis et al., 2007; Saleh et al., 2010; Tzagarakis et al., 2010; van Wijk et al., 2009) compared to faster responses (Rae, Hughes, Anderson, & Rowe, 2015). In contrast, during inhibitory failures (i.e., NoGo errors), Met^{158} homozygotes demonstrated an absence of the beta uptick, particularly within the ACC (Fig. 6), a region essential for error detection and performance monitoring (Marinkovic & Rosen, 2022; Ridderinkhof, van den Wildenberg, Segalowitz & Carter, 2004), which could indicate a failure of engagement of the hyperdirect pathway. Moreover, the ACC has been proposed to play a role in cognitive/affective integration to help guide behavior, particularly more rostral portions of the ACC (rACC, Dignath et al., 2020; Tang et al., 2019). Activation of the rACC has been associated with affective engagement of the limbic system in response to emotional and reward-related input (Dignath et al., 2020; Tang et al., 2019). This would potentially subserve an "oh no!" orienting response given the infrequency and affective saliency of errors (Dignath et al., 2020;

Marinkovic & Rosen, 2022; Wessel & Aron, 2017). A stronger activation in response to aversive stimuli for Met^{158} homozygotes may contribute to more risk-aversive personality characteristics (Enoch & Goldman, 2001; Enoch et al., 2003; Montag et al., 2012; Olsson et al., 2005; Serrano et al., 2019; Zubieta et al., 2003). Taken together, these results indicate that the greater cortical dopamine availability afforded by the Met allele is associated with an early increase in beta that may reflect modulated engagement of the hyperdirect pathway, and the corresponding "pause" may form the neural basis of the more cautious personality traits observed in Met^{158} homozygotes.

In contrast, extraversion and impulsive personality tendencies have frequently been observed in Val^{158} homozygotes (Boettiger et al., 2007; Ducci & Goldman, 2008; Farrell et al., 2012; Montag et al., 2012). While no differences in trait impulsivity were detected in the present study nor more impulsive task performance exhibited, Val^{158} homozygotes demonstrated a greater and more precipitous drop in beta power during early motor preparation regardless of trial condition (Fig. 4), highlighting the stronger influence of *COMT Val158Met* on neural function than cognitive performance (Bogdan et al., 2017; Egan et al., 2001; Winterer & Goldman, 2003; Zubieta et al., 2003). This was particularly evident within the left sMOT, IFC, and dACC and consistent with previous fMRI studies of Val^{158} homozygotes describing decreased BOLD activation within these regions during inhibitory control paradigms (Congdon et al., 2009; Cope et al., 2016). These findings suggest an overall greater readiness and preparedness to respond (Goldman et al., 2005; Winterer & Goldman, 2003). Such tendencies and disposition may underlie poor performance on other cognitive tasks such as the Wisconsin Card Sort Task where Val^{158} homozygotes frequently exhibit increased perseverative errors (Egan et al., 2001; Lipsky et al., 2005; Malhotra et al., 2002), which can be an indicator of impulsive behavior. Previous studies stratifying participants based on impulsivity showed high impulsivity individuals exhibit stronger decreases in beta power in anticipation of making a response (Barth et al., 2021; Tzagarakis et al., 2019). Decreases in beta power for Val^{158} homozygotes were additionally associated with indicators of behavioral disinhibition such as higher alcohol intake (Holcomb et al., 2019) and greater extraversion, which is consistent with reports of higher sensation and novelty seeking scores for Val^{158} homozygotes (Lang, Bajbouj, Sander, & Gallinat, 2007; Tsai, Hong, Yu, & Chen, 2004). Overall, this converging evidence confirms that lower cortical dopamine is associated with greater readiness to respond and impulsivity in Val^{158} homozygotes (Goldman et al., 2005; Winterer & Goldman, 2003). Beta oscillations reflect these dispositional levels of inhibitory control and could potentially serve as neural signature endophenotypes (Anokhin et al., 2017; Barth et al., 2021; Bezdjian et al., 2014; Holcomb et al., 2019; Tzagarakis et al., 2019).

Beta oscillations have been shown to synchronize activity across the hyperdirect pathway between the PFC and STN (Chen et al., 2020; Hirschmann et al., 2022; Oswal et al., 2021). Interestingly, converging theories suggest that brief stimulus-evoked increases in beta oscillations may serve as a "gating" function within the motor system (Leventhal et al., 2012; Schmidt & Berke, 2017; West et al., 2023) to stabilize neural representations of response options and reduce the responsiveness of the system to additional stimuli (Leventhal et al., 2012). Taken together, the brief global uptick in beta power observed in Met^{158} homozygotes shortly after stimulus presentation may reflect increased coherence between the PFC and STN through dopamine-potentiated cortico-striatal projections (Antonazzo, Gomez-Urquijo, Ugedo, & Morera-Herreras, 2021; Chu et al., 2017; Litvak et al., 2012; Oswal et al., 2021). This would serve to insulate the neural system from conflicting response options (Durstewitz & Seamans, 2002; Durstewitz, Seamans, & Sejnowski, 2000a; Frank, 2006; Frank et al., 2007) until a more deliberate decision is made, possibly through lateral competition of possible activations (Keeler, Pretsell, & Robbins, 2014; Schmidt & Berke, 2017; Tunstall, Oorschot, Kean, & Wickens, 2002), reflecting the more cautious personality traits that have been associated with the Met allele (Congdon et al., 2009; Cope et al., 2016; Enoch & Goldman, 2001; Enoch et al., 2003; Olsson et al., 2005; Serrano et al., 2019). In contrast, the more precipitous drop in beta power during early motor planning observed in Val^{158} homozygotes across both Go and NoGo trials may reflect greater flexibility of the neural system to switch between possible response options (Durstewit, Seamans, & Sejnowski, 2000b) and more stimulus-driven behavior reflected in impulsive tendencies (Boettiger et al., 2007; Ducci & Goldman, 2008; Farrell et al., 2012; Lang et al., 2007; Montag et al., 2012; Tsai et al., 2004).

While the present study has many notable strengths, it is not without its limitations, and the findings should be considered within them. The sample size is somewhat small, limiting the generalizability of the findings, and should be replicated with larger cohorts in the future. Similarly, in attempting to minimize genetic variability, the sample was almost exclusively of white European ancestry. Future studies would do well to reproduce these findings in a more diverse sample. Finally, while human studies indicate dopamine levels are regulated as a function of the *COMT* polymorphism (Meyer-Lindenberg et al., 2005; Saloner et al., 2020; Slifstein et al., 2008; Wu et al., 2012; Zumarraga et al., 2010), dopamine levels were not directly measured in the present study, and, therefore, a direct relationship between dopamine and the reported findings cannot be confirmed. Collecting such biological markers in future studies would strengthen the observed relationship between genetic differences and potential dopamine-mediated neural and behavioral indices of inhibitory control.

5. Conclusion

In sum, the present study used an aMEG method to examine the oscillatory dynamics of response inhibition as a function of prefrontal dopamine availability regulated by the *COMT Val^{158}Met* polymorphism. Beta oscillations reflected motor preparation, inhibition, and execution aspects of task performance. Met^{158} homozygotes exhibited a transient uptick in beta power suggestive of a "braking" or motor pause effectuated by the hyperdirect pathway between cortical regions and the STN. Higher dopamine levels in Met^{158} homozygotes may temporarily inhibit motor output until a converging motor command has been established. In contrast, a more precipitous decrease in beta power during early motor preparation was observed in Val^{158} homozygotes which correlated with indicators of behavioral disinhibition. Additionally, the absence of behavioral differences highlights the greater sensitivity of neuroimaging methods to endophenotypes (Bogdan et al., 2017) and highlights the need for more temporally precise methods that can track changes in neural activity over time. The present study provides further evidence for the neuromodulatory effects of dopamine on prefrontal neural activity and the influence of genetics on cognition more broadly with implications for both healthy and disordered behavior.

Materials and data availability

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

CRediT authorship contribution statement

Joseph P. Happer: Writing – review & editing, Writing – original draft, Software, Investigation, Formal analysis. **Colin A. Hodgkinson:** Resources, Investigation. **David Goldman:** Writing – review & editing, Resources, Methodology, Conceptualization. **Lauren E. Beaton:** Software, Investigation. **Laura C. Wagner:** Software, Investigation. **Ksenija Marinkovic:** Writing – review & editing, Writing – original draft, Resources, Methodology, Conceptualization.

Declaration of Generative AI and AI-assisted technologies in the writing process

The authors did not use generative AI technologies for the

preparation of this work.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

Data will be made available on request.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.biopsycho.2024.108826.

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