Prolonged NoGo P3 latency as a possible neurobehavioral correlate of aggressive and antisocial behaviors: A Go/NoGo ERP study

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A B S T R A C T

Aggressive and antisocial behaviors are detrimental to society and constitute major challenges in forensic mental health settings, yet the associated neural circuitry remains poorly understood. Here, we investigated differences in aggressive and antisocial behaviors between healthy controls (n = 20) and violent mentally disordered offenders (MDOs; n = 26), and examined associations between aggressive and antisocial behaviors, behavioral inhibitory control, and neurophysiological activity across the whole sample (n = 46). Event-related potentials were obtained using EEG while participants completed a Go/NoGo response inhibition task, and aggressive and antisocial behaviors were assessed with the Life History of Aggression (LHA) instrument. Using a robust Bayesian linear regression approach, we found that MDOs scored substantially higher than healthy controls on LHA Aggression and Antisocial subscales. Using the whole sample and after adjusting for age, we found that scores on the LHA Aggression and Antisocial subscales were robustly associated with longer NoGo P3 latency, and less robustly with longer NoGo N2 latency. Post-hoc analyses suggested that healthy controls and MDOs exhibited similar associations. With several limitations in mind, we suggest that prolonged NoGo P3 latency, reflecting decreased neural efficiency during the later stages of conflict monitoring or outcome evaluation, is a potential neurobehavioral correlate of aggressive and antisocial behaviors.

1. Introduction

Antisocial behaviors, usually defined as actions and attitudes that violate societal norms and the rights of others (Burt, 2013), exact a tremendous toll on society, both financially (Scott, Knapp, Henderson, & Maughan, 2001) and in terms of reduced quality of life and well-being among those affected (Hanson, Sawyer, Begle, & Hubel, 2010; Tan & Haining, 2016). Although the term ‘antisocial behavior’ is broad and often parsed into overtly aggressive (such as fighting, bullying, and threatening) and covertly aggressive (such as lying, stealing, and vandalizing) behaviors (Burt, 2012; Tackett, Krueger, Iacono, & McGue, 2005), both forms appear to stem from a common latent factor, with joint genetic and environmental influences (Niv, Tuvblad, Raine, & Baker, 2013). Still, some important differences between the two forms have been highlighted. Covertly aggressive forms of antisocial behaviors, for instance, appear more closely associated with impaired behavioral control, whereas overtly aggressive forms may instead primarily reflect affective dysregulation (Burt & Donnellan, 2008; Hopwood et al., 2009).

In forensic mental health settings, aggressive and antisocial behaviors represent both prime targets for therapeutic interventions as well as risk factors for an unsafe treatment environment (Lane, Kjome, & Moeller, 2011; Meyer, Cummings, Proctor, & Stahl, 2016; Trestman, 2017). The importance of aggressive and antisocial behaviors in this context is underscored by research showing that between ~ 30% and ~ 60% of forensic psychiatric inpatients commit at least one violent assault...
amplitude has long been envisioned as a neurobiological marker of social behaviors, including violence and antisocial personality disorder, there is, unfortunately, little to no systematic evidence of effective treatment of aggressive and antisocial behaviors at the severe end of the spectrum (Bateman, Gunderson, & Mulder, 2015; van den Bosch, Rijkmans, Decoene, & Chapman, 2018). In fact, the aggressive aspects of mental disorders appear notably understudied compared to other emotional behaviors (Flanagan & Russo, 2019).

In light of the apparent lack of evidence of effective treatments, developing novel interventions that can prevent aggressive outbursts and antisocial tendencies remains a key objective in forensic mental health research. For the development of novel interventions to succeed, some researchers argue, a better understanding of the neural circuitry, associated with aggressive and antisocial behaviors is vital (Flanagan & Russo, 2019), and using a combination of biological and behavioral measures may be an especially effective strategy in this regard (Nelson & Trainor, 2007). Indeed, such a “multimethod” approach aligns well with recent initiatives calling for research across multiple “levels of analysis”, including the Research Domain Criteria (RDoC; Cuthbert, 2014) and the Hierarchical Taxonomy of Psychopathology (HiTOP; Perkins et al., 2020).

Response inhibition — the ability to inhibit unwanted or inappropriate actions — is a core component of executive control (Friedman & Miyake, 2012; Miyake et al., 2000) and an integral part of both the RDoC and the HiTOP frameworks. Poor response inhibition has been robustly associated with both aggressive and antisocial behaviors in the general population (Dambacher et al., 2015; Madole, Johnson, & Carver, 2020) as well as among mentally disordered offenders (MDOs) (Tonnaer, Cima, & Arnz, 2016a, 2016b). Longitudinal studies have shown that poor response inhibition in childhood and adolescence is predictive of a wide range of externalizing behaviors later in life (Bohlin, Eninger, Brocki, & Thorell, 2012; Nigg et al., 2006), and the association appears primarily genetic in origin (Young et al., 2009), suggesting a shared liability. Neurophysiological activity related to response inhibition can be investigated using event-related potentials (ERPs) acquired with electroencephalography (EEG). Two ERP components in particular, the N2 and the P3 — both typically elicited using variants of the Go/NoGo response inhibition task (Luijten et al., 2014) — are believed to reflect processes either directly or indirectly related to inhibition (Huster, Enriquez-Geppert, Lavallee, Falkenstein, & Herrmann, 2013). Of the two, the P3 component is probably the best known, and reduced P3 amplitude has long been envisioned as a neurobiological marker of aggressive and antisocial behaviors (e.g., Patrick et al., 2006). Still, a moderating effect of N2 (but not P3) amplitude on the relationship between inhibitory control and aggression has also been observed (Rawls, Jabr, Moody, & Lamm, 2018), and that both components may be of importance is further supported by two recent meta-analyses: Pasion et al. (2019) found that severe manifestations of aggressive and antisocial behaviors, including violence and antisocial personality disorder, was associated with reduced N2 amplitude, ostensibly related to deficits in a frontal set-shifting component and Pasion, Fernandez, Pereira, and Barbosa (2018) found a clear relationship between reduced P3 amplitude and antisocial behaviors.

Although most ERP research has focused on the amplitude of the N2 and P3, distinguishing between the amplitude and the latency, usually defined as the time point where the amplitude peaks, of an ERP component may be important, since the two might reflect different kinds of neural activity. Specifically, amplitude is believed to be an index of “neural power”, or the amount of allocated cognitive resources, whereas latency is believed to be an index of “neural efficiency”, or processing speed (van Dinteren, Arns, Jongsm, & Kessels, 2014). The meta-analysis by Pasion et al. (2019) focused solely on amplitude, likely reflecting a lack of research on N2 latency, and out of the 36 studies included in Pasion et al. (2018) only nine analyzed latency effects on a group level. Even fewer, a mere six studies, included latency in dimensional analyses. Thus, in contrast to previous meta-analytic research demonstrating delayed P3 latency in aggressive and antisocial individuals (Gao & Raine, 2009), the findings of Pasion et al. (2018) were too inconsistent to draw firm conclusions. Similarly, while some studies have observed delayed N2 latencies in individuals with poor response inhibition (Falkenstein, Hoormann, & Hohnsbein, 1999) and alcohol dependence (Porjesz, Begleiter, Bihari, & Kissin, 1987), others report no delays in N2 latency in individuals with alcohol abuse (Pandey et al., 2012) and ADHD (Woltering, Liu, Rokeach, & Tannock, 2013). The lack of studies including latency analyses, in conjunction with the inconsistent findings of available research, signals an apparent need for further investigation of the role of ERP latency in aggressive and antisocial behaviors.

To date, most ERP research has focused on the so-called P3a and P3b components. The frontally distributed P3a component, also called the “novelty P3”, is elicited by task-irrelevant infrequent stimuli, whereas the more parietally distributed P3b component is believed to reflect the detection of task-relevant infrequent stimuli. The frontally distributed NoGo P3 (and the preceding NoGo N2), however, is elicited by infrequent stimuli that requires withholding a response, such as in response inhibition tasks (Polich, 2007). Although still debated, the NoGo component is generally believed to reflect processes associated with monitoring and outcome evaluation (Gajewski & Falkenstein, 2013; Huster et al., 2013). The NoGo component is also especially meaningful in a forensic mental health context, since it may be used to examine the “frontal dysfunction hypothesis”, which suggests that aggressive and antisocial behaviors may be associated with weakened prefrontal activity during response inhibition (Pasion et al., 2018; Rodman et al., 2016).

Taken together, reduced amplitude and prolonged latency of the NoGo N2 and P3 components may constitute transdiagnostic neurobehavioral correlates of aggressive and antisocial behaviors. So far, however, few studies have investigated the NoGo N2/P3 components in relation to aggressive and antisocial behaviors, and fewer still have included latency in dimensional analyses. Here, we addressed this knowledge gap using data from healthy controls and violent MDOs. We first investigated differences in aggressive and antisocial behaviors between healthy controls and MDOs, and then, using the whole sample, examined associations between aggressive and antisocial behaviors, behavioral inhibitory control, and NoGo N2 and P3 amplitude and latency. We hypothesized that MDOs would exhibit higher levels of aggressive and antisocial behaviors, and that aggressive and antisocial behaviors would be associated with decreased behavioral inhibitory control, decreased NoGo N2 and NoGo P3 amplitude, and prolonged NoGo N2 and NoGo P3 latency.

2. Methods

2.1. Ethics

The study was approved by the regional ethics review board in Linköping, Sweden (2017/56-21, 2018/7-32, 2018/321-32) and was conducted in accordance with the Declaration of Helsinki. All participants provided voluntary, informed consent prior to participation.

2.2. Participants

Inpatient MDOs were recruited from an ongoing research project at a maximum security forensic psychiatric hospital in Sweden (details on the project and the full cohort are available in Laporte, Ozolins,
Following participation in the project, all male MDOs were approached and asked to participate in the current study if they had, at some point in their life, been sentenced for a violent crime, on the condition that they did not have a history of brain damage with lasting effects and that the treating psychiatrist did not deem participation unsuitable due to current psychiatric status or safety concerns.

Out of 35 available and eligible MDOs, a total of 29 agreed to participate, although two MDOs were omitted due to missing or incomplete self-report and/or file data, and one MDO was omitted from further analyzes due to having only two correct NoGo trials left after EEG data preprocessing. Previous work has shown that the P3, when elicited using a Go/NoGo task, reaches adequate internal consistency after 8–14 trials, depending on which measure is used (Rietdijk, Franken, & Thurik, 2014). More recently, it was demonstrated that the P3 may reach adequate internal consistency with as few as 10 trials, especially if averaging over multiple sensors and time points, as is the case in the current study, whereas excellent internal consistency may be achieved at 20 trials (Thigpen, Kappenman, & Keil, 2017). Although the participant with only two NoGo trials was omitted, it should be noted that two MDOs had 9 correct NoGo trials each, and two healthy controls had 6 and 12 correct NoGo trials each. We decided to keep these participants for subsequent analyzes in order to keep the sample size at a reasonable level. Remaining participants (N = 42, 91.3%) had 14 or more correct NoGo trials available for analysis, with the majority of participants (N = 37, 80.4%) having 20 or more, and with an average of 28 trials (SD = 10.2) for MDOs and 28.2 trials (SD = 9.9) for healthy controls. Thus, a total of 26 MDOs, aged 20–57 years (M = 37.2, SD = 9.5), were included in the current study. In one MDO approximately one third of the EEG data was lost due to technical issues. All MDOs participated while on their usual treatment plan, including medication, and self-reported drug use within the last 6 months. Of brain damage with lasting effects, resulting in 20 healthy controls, aged 20–58 years (M = 33.1, SD = 11.8), included in the current study. All healthy controls received either a voucher (~$10) for use at a local mall or a movie ticket as reimbursement directly after participation.

Healthy controls were recruited among hospital staff and university students using posters, e-mail, and verbal information. We aimed to match control participants as closely as possible to MDOs with regards to education and age, and thus having received a degree after three or more years of higher education was an exclusion criteria, in addition to having a history of brain damage with lasting effects, having a current major mental disorder, and self-reported drug use within the last 6 months. Although a total of 25 control group participants were recruited, five had to be excluded after participation (but prior to data analysis) due to self-reported drug use within the last 6 months and/or having a history of brain damage with lasting effects, resulting in 20 healthy controls, aged 20–58 years (M = 33.1, SD = 11.8), included in the current study. All healthy controls received either a voucher (~$10) for use at a local mall or a movie ticket as reimbursement directly after participation.

With minor differences, the sample used in the current study has been used in a previous publication, in which further details on participant and clinical characteristics are available (Delfin, Ruzich, Wallin, Bjornsdotter, & Andine, 2020).
0.82 [0.70, 0.91] for NoGo P3

4.2.4. EEG data preprocessing

All EEG data preprocessing was carried out using the MNE-Python module, version 0.20.4 (Gramfort, 2013; Gramfort et al., 2014) running on Python version 3.8.2. The preprocessing pipeline largely adhered to recommended procedures (Jas et al., 2018) and was, with the exception of the removal and interpolation of bad channels, independent component analysis (ICA) components, and artifacts following visual inspection, fully automated. Prior to the automated procedure all EEG data was visually inspected and bad channels marked. Then, a bandpass filter from 0.1 to 30 Hz was applied, bad channels interpolated, and ICA was used to identify and remove artifacts. To circumvent issues related to ICA being sensitive to low frequency drifts, we bandpass filtered a raw copy of the data from 1 to 30 Hz and used that to find ICA components. The ICA components were visually assessed, and components judged to represent eye blinks, saccades, heartbeats, and other non-brain related signals were marked and zeroed out from the raw data. Data was then epoched around a stimulus-locked window of 1000 ms (−200 to 800 ms after stimulus presentation) as well as baseline corrected (−200 to 0 ms). Finally, automated artifact rejection using Autoreject version 0.2.1 (Jas, Engemann, Bekhti, Raimondo, & Gramfort, 2017), with default values for peak-to-peak thresholding, was applied in order to interpolate artefactual channels and remove contaminated epochs. The preprocessed data was then imported into R for further statistical analysis.

Only non-subtracted, correct NoGo trials were used for further analysis (Gajewski & Falkenstein, 2013). Since research suggests that ERP-based measures may be more reliable when averaged across multiple electrode sites (e.g., Ribes-Guardiola, Poy, Patrick, & Molto, 2020; Baldwin, Larson, & Clayson, 2015), we based our ERP measures on a frontocentral region of interest by averaging data from nine electrodes (E20, E12, E5, E13, E6, E112, E7, E106). We defined NoGo N2 amplitude as the mean amplitude in a 225-325 ms window post-stimuli (NoGo N2WIN) and NoGo P3 amplitude as the mean amplitude in a 325-625 ms window post-stimuli (NoGo P3WIN). These time windows are similar to windows used in previous studies on aggressive and antisocial behaviors (e.g., Brennan & Baskin-Sommers, 2018; Guan et al., 2015; Verona & Bresin, 2015), and were chosen to avoid overlap between components. Latency was defined, using a fractional area approach, as the time point before which 50% of the (for No) or positive (for P3) area of the waveform is observed (Luck, 2014). Finally, moving window amplitudes (labeled NoGo N2MOV and NoGo P3MOV), defined as the mean amplitude 50 ms before and 50 ms after the 50% fractional area latency was observed, were calculated as complementary measures in order to account for potential latency effects.

4.2.4.1. Reliability analysis

The reliability of Go/NoGo task performance and all ERP measures was assessed using split-half robust correlations between the averages of odd and even trials (Venable et al., 2018; Ribes-Guardiola et al., 2020), corrected using the Spearman-Brown formula (de Vet, Molkins, Mostmuller, & Terwee, 2017). The Go/NoGo paradigm exhibited high reliability, with ρSB = 0.79 [0.66, 0.89] for median NoGo response time and ρSB = 0.90 [0.84, 0.94] for NoGo accuracy. NoGo N2 latency exhibited moderate reliability, with ρSB = 0.59 [0.36, 0.77], and all remaining ERP measurements exhibited high reliability, with ρSB = 0.76 [0.60, 0.86] for NoGo N2WIN, ρSB = 0.72 [0.53, 0.85] for NoGo N2MOV, ρSB = 0.82 [0.70, 0.91] for NoGo P3WIN, ρSB = 0.84 [0.73, 0.92] for NoGo P3MOV, and ρSB = 0.80 [0.67, 0.90] for NoGo P3 latency.

2.5. Statistical analysis

Statistical analysis was carried out using the R statistical language, version 4.1.1 (R Core Team, 2021). Due to the relatively small sample size, we opted for a fully Bayesian approach. All statistical models were specified using the R package brms (Bürkner, 2017), bridging R with the Stan probabilistic programming language (Carpenter et al., 2017).

Group differences were modeled using a robust simple linear regression approach that allowed for unequal variances between the groups, with LHAAGG and LHAANTI scores used as outcome variables and a dummy coded group variable used as predictor variable. Similarly, a robust multiple linear regression approach was used to model the association between aggressive and antisocial behaviors and inhibitory control and ERP measures. Specifically, LHAAGG and LHAANTI scores were entered as predictor variables, with NoGo accuracy and ERP measures entered as outcome variables. Due to its robust association with both P3 amplitude and latency (e.g., Johnstone, Pfeffer, Barry, Clarke, & Smith, 2005), we included age as a covariate in these models. Finally, a robust correlation approach was used for reliability analysis. All variables were centered and scaled prior to analysis in order to obtain standardized estimates, robustness was achieved by using a Student’s T likelihood (Lange, Little, & Taylor, 1989), and all priors were chosen to be weakly informative, with negligible impact on obtained estimates, but still providing moderate regularization (Gelman, Simpson, & Betancourt, 2017). Model sampling using Markov Chain Monte Carlo (MCMC) was carried out using 12 chains with 4000 iterations each, after 1000 warm-up iterations were discarded. All models converged well, with Gelman-Rubin diagnostics (R) of 1.00 (Gelman & Rubin, 1992) and number of effective samples well above 10,000 at the tails for each parameter.

Results from Bayesian analyses are presented as median posterior estimates along with 90% highest density intervals (HDIs) presented within square brackets, which may be interpreted such that it has a 90% probability of containing the actual estimate. Since there is no notion of “statistical significance” in Bayesian statistics, we adopted guidelines recommending that a probability of 90% or higher can be considered “very likely” (Mastrandrea et al., 2011). Thus, findings were considered as robust if the 90% HDI did not contain zero, and thus were very likely different from zero. A Bayesian variant of the conventional R² (Gelman, Goodrich, Gabry, & Vehltari, 2019) was used to estimate the amount of explained variance of the multiple linear regression models, and we used the leave-one-out cross-validated information criterion (LOOIC; Vehtari, Gelman, & Gabry, 2017) to assess whether adding group as an interaction term increased model fit in post-hoc, exploratory analyses. The LOOIC is a Bayesian analog of the Akaike Information Criterion often used in frequentist statistics as a measure of model fit, with the added benefit that the LOOIC does not make distributional assumptions and includes prior information. Lower LOOIC values indicate better model fit.

3. Results

MDOs scored substantially higher than healthy controls on both LHA subscales, as detailed in Table 1 and Fig. 1.

Using the whole sample, and after controlling for age, we found that NoGo P3 latency was robustly and positively associated with both LHAAGG and LHAANTI scores. These estimates were very likely different from zero, with corresponding Bayesian R² values of 0.15 [0.02, 0.28] and 0.16 [0.03, 0.29], respectively, indicating moderately strong linear relationships. Back-transforming the standardized estimates to their original scale, each point on the LHAAGG subscale was associated with a 1.21 millisecond increase in NoGo P3 latency, and each point on the LHAANTI subscale was associated with a 1.33 millisecond increase in NoGo P3 latency. We also saw a less robust, positive association between NoGo N2 latency and LHAAGG, although the 90% HDI did contain zero. Remaining associations were small and non-robust. Full details are presented in Table 2 and visualized in Fig. 2. The ERP waveform as well as predicted associations between LHAAGG and LHAANTI scores and NoGo P3 latency, based on the posterior predictive distribution, are visualized in Fig. 3.
3.1. Post-hoc examination of group interaction

Following the above findings, and with the robust group difference in LHA scores in mind, we also wanted to explore whether there was a group effect on the association between NoGo P3 latency and aggressive and antisocial behaviors (i.e., whether healthy controls and MDOs demonstrated similar or different patterns of association). We re-ran the relevant regression models, but this time included a Group and antisocial behaviors (i.e., whether healthy controls and MDOs group effect on the association between NoGo P3 latency and aggressive behaviors). We re-ran the regression models, using the highest density interval. Estimates where the 90% HDI does not contain zero are highlighted in green. LHA, Life History of Aggression; HDI, highest density interval.

### Table 1

| Subscale                | Full sample (n = 46) | HCs (n = 20) | MDOs (n = 26) |
|-------------------------|----------------------|-------------|--------------|
| LHA Aggression          | 13.02 ± 6.97         | 8.4 ± 5.81  | 16.58 ± 5.63 |
| LHA Antisocial          | 8.57 ± 7.13          | 1.95 ± 2.72 | 13.65 ± 4.88 |

Note. HCs, healthy controls; MDOs, mentally disordered offenders; LHA, Life History of Aggression; SD, standard deviation; HDI, highest density interval.

### Table 2

| Subscale                  | β [90% HDI] | β [90% HDI] |
|---------------------------|------------|------------|
| LHA Aggression            | 0.25, 0.27 | 0.16, 0.36 |
| LHA Antisocial            | 0.19, 0.45 | 0.09, 0.34 |

Note. LHA, Life History of Aggression; HDI, highest density interval. Estimates where the 90% HDI does not contain zero are shown in bold.

### 4. Discussion

The current study examined differences in aggressive and antisocial behaviors between healthy controls and MDOs, and then, using the whole sample and controlling for the effect of age, investigated whether aggressive and antisocial behaviors were associated with behavioral inhibitory control and associated neurophysiological activity. We found that MDOs, in line with our hypothesis, scored substantially higher than healthy controls on both the LHAAGG and the LHAAANTI subscales. Also in line with our hypothesis, we saw a robust, positive association between LHAAGG and LHAAANTI scores and NoGo P3 latency, and a positive yet smaller and less robust association with NoGo N2 latency. Post-hoc analyses revealed no effect of group, indicating that healthy controls and MDOs exhibit similar associations. Against our hypotheses, however, we saw no robust associations between LHAAGG or LHAAANTI scores and NoGo N2/P3 amplitude or performance on the Go/NoGo task.

### 4.1. Group differences in aggressive and antisocial behaviors

That MDOs would score substantially higher than healthy controls on...
both the LHA\textsubscript{AGG} and LHA\textsubscript{ANTI} subscales was expected, and falls in line with previous research on Swedish psychiatric patients (including MDOs) demonstrating that scores on both these subscales exhibit robust, medium to large correlations ($\rho$ between $-0.30$ and $-0.70$) with several of the disorders and behaviors often observed among MDOs, including childhood-onset problems such as attention deficits, hyperactivity, and conduct problems, personality traits such as novelty seeking, and externalizing behaviors such as alcohol and drug abuse (Hofvander et al., 2011). Notably, however, while MDOs scored approximately twice as high on the LHA\textsubscript{AGG} subscale as healthy controls in the current study, their score on the LHA\textsubscript{ANTI} scale was almost five times higher than that of healthy controls. The LHA\textsubscript{ANTI} scale taps behaviors that, to a certain extent, are more closely related to covertly aggressive or rule-breaking aspects of antisociality, such as problems at school and work and encounters with law enforcement. While the small sample size prohibits firm conclusions to be drawn from this, the results do seem logical given the criminological background of Swedish, forensic psychiatric patients (Laporte et al., 2021; Swedish National Forensic Psychiatric Register, 2020).

Since the more covertly aggressive, rule-breaking form of antisociality seems primarily associated with impaired behavioral control and personality traits such as low constraint (Burt, 2012), a potential clinical implication, following the high LHA\textsubscript{ANTI} scores among MDOs in the current study, is that therapeutic interventions might benefit from increased focus on improving self-control. Indeed, such improvements seem especially important when bearing in mind recent research observing reductions in self-control among prisoners after just three months of imprisonment, possibly linked to the impoverished environment (i.e., a sedentary lifestyle, social isolation, lack of cognitive challenges) that imprisonment often entails (Meijers, Harte, Meynen, Cuijpers, & Scherder, 2018). Although, as far as we can tell, relatively few studies have been carried out, there is some evidence suggesting that cognitive and self-control training might be effective in reducing overt aggression (Denson, Capper, Oaten, Friese, & Schofield, 2011; Papalia, Spivak, Daffern, & Ogloff, 2019; Wilkowski, Crowe, & Ferguson, 2015) and other externalizing behaviors, such as problematic alcohol consumption (Walters, 2000). Still, the exact mechanisms underlying improved self-control remain poorly understood (Friese, Frankenbach, Job, & Loschelder, 2017), and further research aimed specifically at MDOs is warranted.

### 4.2. The association between aggressive and antisocial behaviors, inhibitory control, and ERP measures

Using the whole sample, and after controlling for age, we found that both aggressive and antisocial behaviors were robustly associated with increased NoGo P3 latency, and to a certain extent also with increased NoGo N2 latency. Mindful of the scarcity of research on P3 latency overall and NoGo P3 latency in particular, this finding is difficult to interpret considering that we, contrary to our expectations, saw no associations with NoGo N2 or P3 amplitude. Since each point on the LHA\textsubscript{ANTI} scale, for instance, predicted an increase in NoGo P3 latency of 1.33 ms, and since MDOs scored an estimated 12.09 points higher on the LHA\textsubscript{ANTI} scale than healthy controls, the predicted difference in NoGo P3 latency between the two groups was 16.08 ms. The prediction is well in line with the estimated 17.41 ms difference in NoGo P3 latency between MDOs and healthy controls we have reported in previous work based on, with minor differences, the same sample (Delfin et al., 2020). In addition, in our previous work, we found that NoGo P3 latency was associated with higher levels of self-reported disinhibition, whereas NoGo P3 amplitude was not. The results of the current study, focused specifically on aggressive and antisocial behavior, thus seem to mirror our previous findings in this regard.

The lack of a clear association between aggressive and antisocial behaviors and NoGo N2 and particularly NoGo P3 amplitude, as well as with behavioral inhibitory control, in the current study was unexpected in light of the rather robust association between aggressive and antisocial behavior and reduced P3 (including NoGo P3) amplitude reported by Pasion et al. (2018). Differences in sample size and participant characteristics, such as the combined sample of healthy controls and MDOs, is a possible explanation. For instance, the pharmacological treatment of MDOs in the current study often included multiple substances, primarily antipsychotics (for details, see Delfin et al., 2020). Since NoGo P3 amplitude is modulated by dopamine D2 receptors, a primary target of antipsychotics, this could have affected our results (Beste, Stock, Epplen, & Arning, 2016; Beste, Willemsen, Saft, & Falkenstein, 2010).

Another possible source of discrepancy is our choice of task. We used a “cool” Go/NoGo task with neutral stimuli instead of a “hot” version, with emotionally salient stimuli (e.g., Zelazo & Carlson, 2012). Casey et al. (2011) used both a “cool” and a “hot” version of the Go/NoGo to differentiate between adult individuals that had completed a delay of gratification task in childhood. Measures from the “cool” version could not reliably differentiate between low- and high-delay individuals, whereas measures from the “hot” version could, suggesting that the emotional valence of stimuli may be important. Recently, Sun et al. (2020) used an emotional Go/NoGo task and observed lower NoGo P3 amplitude in participants with high compared to low levels of trait aggression, and Madole et al. (2020) used an emotional Go/NoGo task and found that behavioral inhibitory control was directly related to higher levels of self-reported aggression. Neither of these two studies included a neutral comparison task, however, so the effect attributable specifically to the use of a “hot” task is difficult to evaluate. There is also evidence suggesting that “cool” and “hot”, or neutral and emotional,
versions of the Go/NoGo actually capture the same basic neuropsychological constructs (Littman & Takacs, 2017; Schulz et al., 2007), and it thus remains unclear whether our choice of a neutral Go/NoGo task could explain the lack of association between aggressive and antisocial behaviors and NoGo N2/P3 amplitude.

In addition to the difference between “cool” and “hot” tasks, the meta-analysis by Pasion et al. (2019) suggests that reduced NoGo N2 amplitudes are consistently elicited when using the Stop Signal Task (SST), but not when using the Go/NoGo. Although both tasks are believed to tap inhibitory control, the SST reflects the ability to inhibit an already ongoing response, while the Go/NoGo instead reflects the ability to withhold a response altogether (Littman & Takacs, 2017). Importantly, while they are often used seemingly interchangeably to capture individual differences in behavioral inhibitory control, they nonetheless appear to operate through different neural mechanisms (Raud, Westerhausen, Dooley, & Huster, 2020), and it is possible, therefore, that aggressive and antisocial behaviors may be more closely related to the stopping aspects of inhibitory control, rather than to withholding. Whether this also applies to the P3 component remains unclear, however.

4.2.1. A possible relationship between NoGo P3 latency and myelination

Finally, one interpretation is that our findings instead highlight the importance of distinguishing between amplitude and latency. The NoGo P3 component is believed to reflect processes related to the monitoring evaluation of conflict and the outcome of actions (Gajewski & Falkenstein, 2013; Huster et al., 2013). If NoGo P3 amplitude reflects “neural power”, or the amount of allocated cognitive resources, and if NoGo P3 latency reflects “neural efficiency” (van Dinteren et al., 2014), then perhaps it is not the magnitude of allocated resources but rather the speed with which such allocation occurs that is relevant in aggressive and antisocial behaviors. This speed of allocation has been linked to the so-called “myelin hypothesis”, which suggests that increased thickness of the brain’s myelin sheath leads to increased nerve conduction velocities, in turn leading to reduced response times on inhibition tasks and a general improvement of cognitive and behavioral inhibitory control (Bartzokis, 2005; Tuch et al., 2005).

There is a close relationship between the degree of myelination and P3 latency across the lifespan, indicating that the two are indeed closely intertwined (van Dinteren et al., 2014), further corroborated by research showing that individuals with multiple sclerosis, a disease characterized by the destruction of the myelin sheath, exhibit delayed P3 latencies for certain types of stimuli (Ivica, Titlic, & Pavelin, 2013). Decreased rates of myelination during adolescence have also been associated with an increased expression of psychopathology later in life (Vanes et al., 2020). Substance use and impulse control problems, both closely related to aggressive and antisocial behaviors (Alcorn et al., 2013; Krueger, Markon, Patrick, Benning, & Kramer, 2007), may also play a role here, since the use of alcohol (BJork, Grant, & Hommer, 2003; McQueeney et al., 2009), opioids (Velasco, Mohamed, & Sato-Bigbee, 2021), cannabis (Bava et al., 2009), and cocaine (Bartzokis et al., 2002) is toxic to the vulnerable myelination process, and may in turn exacerbate already existing impulse control problems and contribute to poor outcomes in individuals prone to substance abuse (Bartzokis, 2005). While speculative, it is possible that aggressive and antisocial individuals exhibit aberrant myelination, which in turn could manifest as decreased NoGo P3 latency. Speaking against this interpretation is the fact that we saw no association between aggressive and antisocial behaviors and performance on the response inhibition task. If the positive association between aggressive and antisocial behaviors and NoGo P3 latency observed in the current study is in fact due to individual differences in myelination, then a negative association between aggressive and antisocial behaviors and performance on the Go/NoGo task would be expected. That we did not observe such an association could be due to the task itself being too easy to detect meaningful variance in inhibitory control (see discussion in Delfin et al., 2020), or that performance on a single laboratory task does not fully capture the variance associated with aggressive and antisocial behaviors (Young et al., 2009). Future studies should further explore whether myelination, NoGo P3/N2 latency, and aggressive and antisocial behaviors are indeed related, perhaps by combining suitable techniques for probing the brain’s white-matter structure with ERP measures.

4.2.2. Gray-matter regions involved in generating NoGo ERPs

Besides the putative role of white-matter alterations such as differences in myelination, several gray-matter regions have been implicated in the generation of the NoGo N2/P3 components. Although likely the sum of multiple neural networks acting in concert (Huster, Westerhausen, Pantek, & Konrad, 2010), the midcingulate cortex (MCC) has emerged as a particularly important region in the generation of the NoGo N2/P3 (Baumeister et al., 2014; Beste, Saft, Andrich, Gold, & Falkenstein, 2008; Hong, Wang, Sun, Li, & Tong, 2017; Huster et al., 2010). Research into its functions is still ongoing, but the MCC, covering what is sometimes also labeled the dorsal part of the anterior cingulate cortex (ACC), appears to be a key region involved in the monitoring of conflicts and outcomes of actions (Botvinick, 2007; Jahn, Nee, Alexander, & Brown, 2014), which corresponds to the processes believed to be reflected in the NoGo N2/P3 components (Gajewski & Falkenstein, 2013). It seems possible, therefore, that the positive association between aggressive and antisocial behaviors and NoGo P3 latency (and, to some degree, NoGo N2 latency) observed in the current study reflects abnormal functioning of the MCC/ACC, which in turn would offer at least partial support for the “frontal dysfunction hypothesis” (Rodman et al., 2016). The lack of neuroimaging data prohibits us from drawing firm conclusions about particular brain regions, however, and further studies are required in order to elucidate the complex relationship between aggressive and antisocial behaviors, NoGo N2/P3 latency, and brain structure and function.

4.3. Relevance in clinical settings

From a clinical point of view, and if NoGo latency is indeed related to the degree of myelination, then longitudinally investigating whether early interventions targeting substance abuse have an effect on white-matter structure and, subsequently, NoGo latency would shed further light on some of the questions arising from our findings. Another avenue worth exploring more in-depth is whether it is possible to improve (i.e., shorten) NoGo latency using neuromodulation techniques. Some promising results were recently presented by Sergio et al. (2021), who used high-definition transcranial direct current stimulation (tDCS) to modulate activity in the ventromedial prefrontal cortex, and found that tDCS could reduce aggression and alter electrophysiological responses in a sample of male forensic patients. Studies targeting the MCC/ACC using tDCS have observed improvements in cognitive function (Khan, Wang, Ti, Tse, & Tong, 2020), but to the best of our knowledge, no study has employed these techniques to target the ACC/MCC in a forensic psychiatric sample.

4.4. Strengths and limitations

This study has some methodological strengths that should be noted. The combination of dimensional assessments of aggressive and antisocial behaviors, a behavioral response inhibition task, and neurophysiological measures is in line with research along multiple “levels of analysis” encouraged by emerging frameworks such as the RDSoC (Cuthbert, 2014) and HToP (Perkins et al., 2020). The Bayesian statistical approach has several advantages, such as allowing genuine probabilistic statements that remain valid regardless of sample size (Wagenmakers et al., 2018) and representing a move away from strict reliance on p-values and associated interpretations of (statistical) significance (Wasserstein, Schirm, & Lazar, 2019). Still, in order to facilitate interpretation for readers unaccustomed to the Bayesian approach,
we opted to use the 90% HDI as a heuristic for determining the robustness of our findings; some readers may prefer different heuristics, and our results should be interpreted in light of this. We also used non-Gaussian likelihoods, which are robust to outliers (Lange et al., 1989), and weakly informative priors centered around zero, which ameliorates concerns of multiple comparisons.

Despite these strengths, the small sample size remains a concern. From a statistical point of view, it makes it difficult to include additional covariates, such as data on pharmacological treatment, in our models. Thus, we opted to just include age, given its strong association with N2/ P3 amplitude and latency, but are cognizant of the fact that the inclusion of additional covariates could have affected our results. The small sample size also leads to relatively wide HDIs, limiting the precision of our findings.

Another limitation is that aggression was only measured using a single instrument; using a different, or a combination of several instruments, may also have rendered different results. Furthermore, although it would be preferable to use the same method of obtaining LHA scores for both MDOs and healthy controls, clinical ratings were unfortunately not available for healthy controls. Previous research has voiced some concern about socially desirable responding when obtaining self-reported LHA scores in a psychiatric population (Dellazzizzo et al., 2017). In particular, a lack of self-awareness may cause participants to deny the extent of their own aggressiveness (Ramirez & Andreu, 2006).

Since very few – approximately 13% – of inpatient MDOs in Sweden are assessed to have full insight into their own mental illness and the effect it has on their behavior and experiences, with 52% being assessed to only have partial insight (Swedish National Forensic Psychiatric Register, 2020), we chose to use clinically rated LHA scores for MDOs. One limitation is that the experimental paradigm used in the current study did not counterbalance target (“K”) and non-target (“X”) letters between participants, and we therefore cannot rule out that we did not observe any letter-specific activity. Furthermore, behavioral inhibitory control was also measured using a single task, which may not fully capture the variance associated with aggressive and antisocial behaviors. Therefore, the use of multiple tasks is recommended (Young et al., 2009), and a structural equation modeling approach using a combination of multiple tasks and instruments, along the lines of Venables et al. (2018), is likely a more optimal approach. It should be noted, however, that such an approach requires larger data set and more time spent on participation, which may not be feasible in forensic mental health settings given the many difficulties encountered when recruiting MDOs (e.g., Pedersen, Bergman, Berlin, & Hartvigsson, 2021; Bergman et al., 2020). To get around this limitation, we encourage multisite collaborations. Finally, despite these limitations, it should be acknowledged that small sample studies employing a “bivariate mapping” approach (i.e., investigating the association between just two measures), as in the current study, remain important both for continued validation of emerging research frameworks and for discovering potential neurobehavioral correlates that may be further investigated (e.g., Perkins, Latzman, & Patrick, 2020).

5. Conclusions

We found that MDOs presented with substantially higher levels of aggressive and antisocial behaviors than healthy controls. In line with prior work, this finding further highlights a need for effective treatment of aggressive and antisocial behaviors in forensic mental health settings. Using the entire sample, and controlling for the effect of age, we also observed a robust, positive association between NoGo P3 latency (and to a lesser extent NoGo N2 latency) and aggressive and antisocial behaviors. We propose that this finding reflects decreased neural efficiency primarily during the later stages of conflict monitoring and outcome evaluation, and further speculate that this in turn could be related to individual differences in myelination. These findings add to a scarce literature on the role of the NoGo ERP overall and NoGo P3 latency in particular, and may be used to guide further research aimed at early interventions and the evaluation of novel treatment approaches.

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Software availability

All code used is publicly available at the Open Science Framework. All code relevant to the Go/NoGo task and for EEG data preprocessing is available at https://osf.io/yscdh/, and the code used for all statistical analyses and the creation of figures and tables in the current study is available at https://osf.io/3wzrzx/.

Declaration of Competing Interest

None to disclose.

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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.2021.108245.

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