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Original Article

Response inhibition in adults who stutter: A behavioral and event-related potential study during a visual stop signal task

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Abstract

Introduction: Stuttering is a neurodevelopmental disorder with structural and functional neurological bases characterized by involuntary prolongations, repetitions and blocks in sounds, syllables and words. Multiple factors are assumed to participate in etiology and severity of stuttering and response inhibition is considered to be an important phenomenon for having a fluent speech. Therefore, this study aimed to evaluate response inhibition of Adults Who Stutter (AWS).

Materials and Methods: In a case-control study, response inhibition of twenty-eight AWS and fluently-matched control group was compared by a visual stop-signal task and its evoked potentials in the brain. Behavioral measurements of the task, including the Reaction Time (RT) and the response accuracy, were compared between the two groups. Peak amplitude and peak latency of P3 and N2 components in parietal and frontal areas were measured after cue, go and stop stimuli in different trials of the task.

Results: Although AWS reported more scores in anxiety level, they acted similarly to the control group in behavioral measurements. ERP findings, however, represented smaller N2 amplitude in the cues and earlier N2 latency for the Go trials in AWS than in the controls.

Conclusion: Our findings did not support the idea of less efficient inhibitory control in AWS; however, smaller N2 amplitude in the cues may indicated decreased attention resources allocated to the stimuli and different preparation for executing the response. Earlier N2 latency for Go trials in AWS also showed different timing of mental access to go stimuli and faster conflict monitoring in competing stimuli.

Keywords: Anxiety, Event-Related Potentials, Response inhibition, Stop signal task, Stuttering

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Introduction

Stuttering is a neurodevelopmental disorder with a one percent prevalence, characterized by blocks, audible or silent repetitions or prolongations of sounds and syllables (1,2). Although its etiology is unknown (1,3), the role of Executive Functions (EF) in stuttering has been the area of interest in recent years, and evidence suggests that children who stutter exhibit impaired EF (4). EF includes a combination of cognitive processes leading to goal-directed behaviors through the selection and management of purposeful behaviors. It encompasses some sub-systems, including

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inhibition, cognitive flexibility, attention and working memory (5). Inhibition, the focus point of our study, is the ability to control or inhibit behavior that is not currently required or stop the inappropriate automatic reaction. There are two types of response inhibition, reactive and proactive, essential for accomplishing successful behavior (6). Reactive inhibition is provoked by exogenous factors. However, proactive inhibition is induced by endogenous factors before the stimuli presentation and can promote more specific but slower response (6). Moreover, It is adjusted based on the predetermined goal existing in the mind and mediated by working memory (7,8). Pre-Supplementary Area (Pre-SMA) which is a region of the dorsomedial frontal cortex and the right inferior frontal cortex presumably sends stopping commands to the subthalamic nucleus and via basal ganglia stops the go process through a so-called hyper-direct pathway (9). This reactive, fast and global stop is thought to prepare and clear the motor system for more specific and selective inhibition, named proactive inhibition (10). While reactive inhibition is controlled by the fronto-subthalamic network, the proactive is thought to be controlled selectively by the frontostriatal circuit, named indirect pathway (6,11). The DorsoLateral PreFrontal Cortex (DLPFC) sends a signal to the striatum to inhibit the globus pallidus external, then disinhibits the globus pallidus internal and finally inhibits the response (12). Although it is unclear how much the neural networks behind inhibition and speech fluency share a common source, it is said that the circuit involved in inhibition is relevant to stuttering and thought to be a crucial phenomenon for having a smooth and fluent speech (13,14). Go/No Go and stop-signal tasks are commonly used to estimate subsets of response inhibition. Response accuracy and reaction time are behavioral indexes that reflect participants' inhibitory skills. However, techniques like Event-Related Potentials (ERP), as a highly time-sensitive instrument, are used simultaneously to obtained brain responses to different stimuli of these tasks. Brain evoked potentials like N2 and P3 while performing inhibitory tasks have been frequently investigated in stuttering (15-17). The N2 component that occurs at approximately 200-300 millisecond (ms) post stimulus onset with a negative shift and maximal amplitude at the frontal brain regions, may reflect cognitive efforts to withhold prepotent response. So, it is a neurophysiological index that reflects conflict monitoring in competing stimuli (18,19). The P3 component on the other hand, that occurs at approximately 300-500 ms post stimulus onset with a positive shift and maximal amplitude at the parietal regions appears to represent the attentional resources needed for the correct response, assessment of stimulus, and updating task-relevant information (20,21). In a parent-report questionnaire, Children Who Stutter (CWS) scored lower points in inhibitory skills compared with their fluent counterparts (22). This finding was affirmed by a behavioral study in which CWS showed more premature responses and more false alarms in a computer task related to inhibitory control (22). In another study, CWS also showed less accurate responses in complex tasks in which both attentional shifting and inhibitory control were triggered. It was concluded that the findings were related to the poorer motor learning of the group (23). Interestingly, the speed of responses was comparable between groups. On the other hand, another study showed that CWS did not differ behaviorally in the number of errors and reaction time but displayed delayed N2 and P3 in the Go condition. The findings suggested that CWS are not less efficient in inhibitory control but are poorer in attentional processing compared with a control group (24). In AWS, however; findings are more sophisticated due to the chronicity of the problem and psychological consequences of the stuttering. In a stop-signal task, AWS showed increased Stop-Signal Reaction Time (SSRT) compared to the matched fluent group indicating a selective deficit in motor control in AWS (13). The SSRT measure of this task is a motor control index which has been investigated in many studies related to stuttering (19,20). However, the poor response inhibitory control in AWS was shown to be correlated to speakers' experience with stuttering rather than overt motor symptoms (25,26). This finding accentuated the role of emotional regulation in AWS' inhibitory function. Beside these controversial variations, it is also notable that most studies in this area recruited more behavioral tests and self-reported questionnaires than ERP studies (4,27). So, in our study for the first time, we used a visual stop-signal task to compare the reactive and proactive inhibitory skills among AWS and their counterparts both behaviorally and electrophysiologically.

Materials and Methods

In a cross-sectional study, twenty-eight right-handed AWS, aged between 17 and 40 years (mean ± SD: 26 ± 5.5), referred from the speech therapy clinics and diagnosed by a trained speech therapist, were recruited. Moreover, twenty-eight fluent speakers matched in age (mean ± SD: 27 ± 6), sex, handedness and education participated.

The subjects were available and recruited from Kerman, Sirjan, and Baft city of Kerman province who had participated in the project from 2020-2021. The study size arrived by considering previous similar studies (15,17,24). Actually, we calculated the sample size as 25 for each group. Since there was a possibility of non-cooperation of the participants during the study, the number of each group was considered 30 people. Finally, 28 people in each group completed the study. Four subjects were excluded because of technical problems. They also received Barratt Impulsiveness Scale 11 (BIS-11) (28,29), Beck Depression Inventory (BDI) (30), and Beck Anxiety Inventory (BAI) (31,32) to be assessed for impulsivity, depression, and anxiety, respectively. AWS also engaged in an informal 4 minutes discussion and 4 minutes reading a standard passage for determining stuttering severity.

All participants signed informed consent and paid for their participation. This study was approved by the ethics committee of Kerman University of Medical Sciences, Kerman, Iran, with the ethical approval number: IR.KMU. REC. 1399. 195.

Inclusion and exclusion criteria

The subjects should not have a history of taking neuropsychiatric or neurologic medicines and having a mental or physical illness. In terms of vision, hearing and touch, they were normal, and they should not have any cognitive, intellectual or motor problems.

Task and procedure The participants were seated on an armchair in the soundproofed and dimly lit chamber, 1 meter distance from the screen. Their heads were fixed in a chin rest to reduce unwanted noise, and they received 5 minutes' rest whenever they pressed an alarm button. The task lasted for 45 minutes. Before starting, pre-recorded instructions broadcasted to inform subjects how to accomplish the test. They asked to consider both accuracy and speed while performing the test. Besides, 5 minutes warm-up opportunity was considered for everyone for preparation. The selective stop-signal task which was already used simultaneously with electromyography in another study (33) consisted of reactive and proactive trials designed by PsyTask version 1.53.17 (Mitsar Inc, Russia) (Fig 1). Altogether, 700 trials were presented, of which 350 were reactive, and 350 were proactive. While trials started with a 200 ms non-informative cue in reactive condition, informative ones pointed either to the left or the right in proactive type. They were followed by a 1300 ms gap filled with fixation-cross in the center of the screen. Then in go trials (60% of the whole), go-stimuli were presented 100 ms by two 2.5 centimeter diametric white circles, and participants had to press two buttons simultaneously. In stop trials (40% of the whole), a red circle was presented at the left or the right position previously occupied by the go stimuli and the participant had to suppress corresponded hand to the side of the red circle. The 200 ms extended stop signal, occurred after Stop-Signal Delay (SSD) that was randomly adjusted with the duration between 50 to 500 ms. All cues were congruent so, informative ones on stop trials could prepare the participant for potential stop (proactive stop trials). As stop trials were divided into two sides of left and right, there were 420 go trials and 140 stop trials in each condition (70 on the left and 70 on the right).

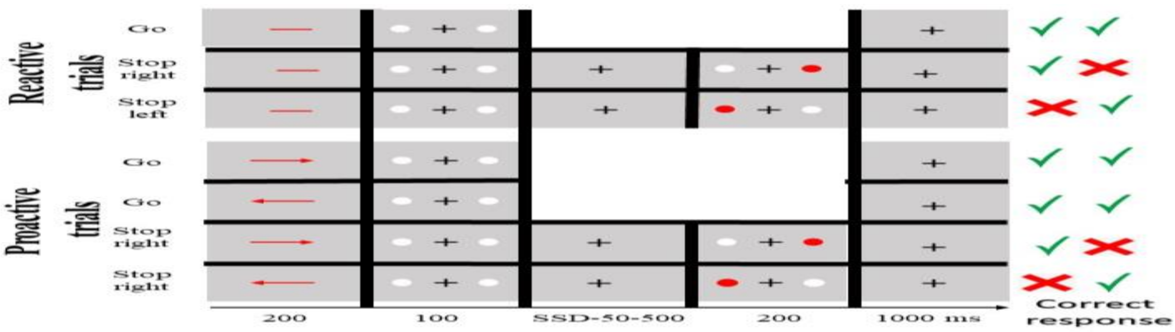


Figure 1. Reactive and proactive trials

Event-related potential acquisition

Electroencephalography (EEG) was recorded by a 32-channel Win EEG system (version 2.126.97, Mitsar Inc, Russia). The sampling rate was 250 Hz, and electrodes were positioned according to the international 10-20 system. Impedance was kept below five kΩ. Low and high pass filters were 0.1 Hz and 45 Hz, respectively. EEG data was recorded using monopolar montage, and input signals were referenced to the linked ear. All data were processed offline by MATLAB (2017b), EEGLAB and ERPLAB toolbox (2020). After importing data to EEGLAB, to reduce probable noise, they were re-referenced to averaged electrodes and inspected by eye for interpolating bad electrodes. Just one electrode (Fp2 electrode which was not in our ROIs) in one participant needed to be interpolated which was done by EEGLAB. After decomposing by ICA and removing noisy components, event codes and related bins were defined in the 'create EEG event list' menu of ERPLAB. Seven bin-based epochs from -200 to 3050 ms (reactive go, reactive stop right, reactive stop left, proactive go right, proactive go left, proactive stop right, and proactive stop left) were extracted.

In addition, ERP waves and maps were plotted for further analysis. Before plotting data were base lined to -200 ms by ERPLAB. 'ERP measurement tool' was applied to calculate P3 and N2 peak latency and peak amplitude (positively 300-500 ms and negatively 200-350 ms peaked after stimulus, respectively). Frontal electrodes, including F3, Fz, and F4, were considered for the N2 component. Moreover, parietal electrodes, including P3, Pz, and P4, were selected for the P3 component.

Behavioral data acquisition

Reaction time and accuracy of corrected responses were calculated by Win EEG system, Mitsar version 2.126.97. The time window of 100-1000 ms was considered for corrected response and behavioral measures, including Go trial reaction times (Go RTs), and accuracy of the Go and the Stop trials were extracted. Estimation of SSRT were calculated by mean method in which reaction times on go trials were rank ordered. Then, nth reaction time was obtained by multiplying the number of reaction times in the probability of incorrect stop trials. For estimating SSRT, SSD was subtracted from this value (34). For example, in a session with 380 go trials, 56 incorrect stop trials in 280 stop trials (probability of incorrect stop trials= %20), the nth of go reaction time was the 76th of them. Then to estimate the SSRT, we subtracted the SSD from the 76th of go reaction time value. Stuttering severity was measured as well according to Stuttering Severity Instrument, Fourth Edition (SSI_4) by scoring the percent of syllable stuttered, the average duration of three longest moment of stuttering and the associated behaviors of AWS (35,36).

Mann-Whitney U test and independent samples t-test were used for comparing clinical and behavioral comparison between AWS and the control group. A mixed-effects repeated-measures analysis of variance (ANOVA) was performed for ERP data with a group (AWS versus control) as the between factor and the trial type (Go trials, reactive and proactive stop trials) and the electrode locations (Fz, F3, F4, Pz, P3, and P4) as the within factors. Significant main effects, interactions, and follow-up comparisons (Bonferroni) were calculated using the SPSS version 26.

Results

Behavioral and clinical findings

In term of demographic characteristics of the participants, AWS group aged 17-37 years (10 females and 18 males), and 9 of them were married. The controls aged 17-43 years (12 females and 16 males), and 10 of them were married. In term of educational degree, in AWS group, 14 of them had bachelor degree, 7 subjects had diploma, 6 subjects had master degree, and 1 case had doctorate degree. In controls, 17 cases had bachelor degree, 5 cases had diploma, 4 cases had master degree, and 2 cases had doctorate degree.

Table 1 presents the clinical characteristics of adults who stutter (AWS) and control group. Analysis showed that AWS had significantly higher scores of BAI than the control group ($P < 0.05$) while, the scores of BDI and BIS were similar between groups.

Table 2 shows behavioral results on the stop-signal task of the two groups. There were no significant differences between the two groups in Go RT, SSRT, accuracies of Go and Stop trials. There were also no significant correlations between stuttering severity scores and behavioral measurements including Go RT, SSRT, and accuracies of Go and Stop trials.

Table 1. Clinical characteristics of adults who stutter (AWS) and control group

	AWS ((Mean Rank)	Control (Mean Rank)	P
BAI	33.91	23	0.01*
BDI	27.82	29.11	0.78
BIS-11	32.31	24.62	0.07

Abbreviation: BAI: Beck's Anxiety Inventory, BDI: Beck's Depression Inventory, BIS11: Barratt Impulsiveness Scale **P*< 0.05

Table 2. Behavioral data of stop signal task between adults who stutter (AWS) and control group

	AWS (Mean±SD)	Control (Mean±SD)	P
Go RT	781.2±60.52	777.9±77.86	0.86
Proactive SSRT	414.14±76.47	384.71 ±52.31	0.08
Reactive SSRT	425.14±84.13	396.53±55.33	0.13
Go accuracy (%)	93±5	92±4	0.93
Stop accuracy (%)	94±3.11	94.6±2.44	0.39
Total score (SSI4)	22.42±6.93	n/a	n/a

Abbreviation: Go RT: Go reaction time, unstopped hand RT: unstopped hand reaction time, n/a: not applicable

Electrophysiological data

To summarize the data, just significant findings were reported.

Reactive cues

N2

While electrode had no main effect on N2 amplitude [F (1.720, 91.151)=1.344, *P*= 0.264, ŋ2= 0.025], group [F (1,53)=4.303, *P*= 0.043, ŋ2= 0.75] and interaction of group And electrode showed main effect on the amplitude [F (1.720, 91.151)= 6.054, *P*= 0.005, ŋ2= 0.103]. Follow up analysis demonstrated that AWS showed smaller amplitude than control group in F4 (*P*= 0.001) (Fig 2). In AWS also, F3 and Fz showed bigger amplitude than F4; (*P*= 0.02), (*P*= 0.01) respectively, but there were no differences among the electrodes in the control group.

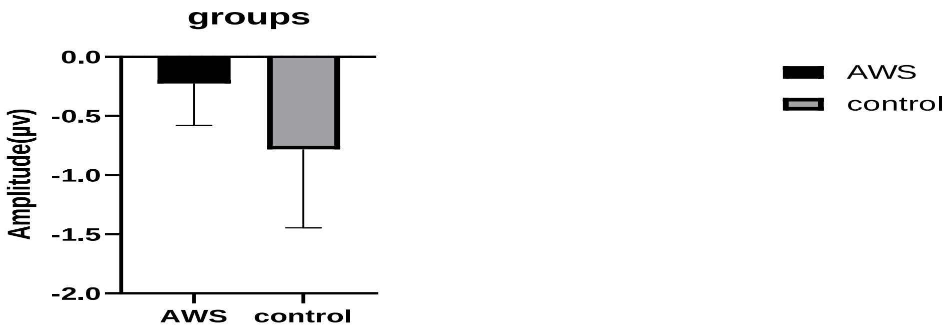


Figure 2. Significant difference of N2 amplitude (µv) in reactive cues in F4 electrode among AWS and control group. Abbreviation: AWS: Adults Who Stutter

Go trials

N2

As far as the latency, although electrode [F (2,106)= 0.896, *P*=0.411, ŋ2= 0.017] and interaction of group and electrode [F (2,106)= 0.906, *P*= 0.407, ŋ2= 0.017] did not show any effect, however, there was the main effect of group on the N2 latency [F (1, 53)= 4.318, *P*= 0.043, ŋ2=0.075] in which, AWS peaked earlier than the control group (Fig 3).

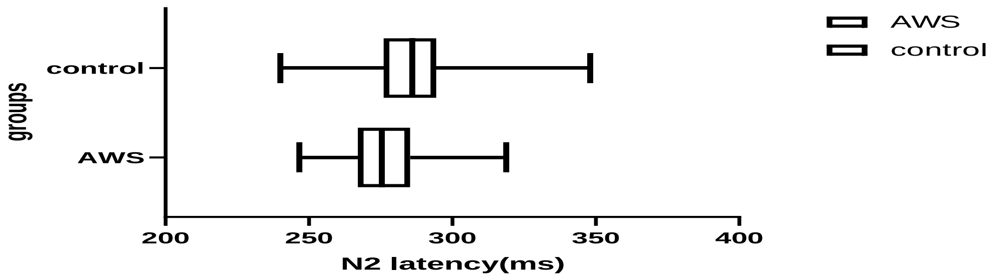


Figure 3. Significant difference of N2 latency (ms) in go trials in frontal area among AWS and control group. Abbreviation: AWS: Adults Who Stutter

Reactive stop trials

P3

As far as the amplitude, electrode showed main effect [F (1.266, 67.083)= 7.033, *P*= 0.006, ŋ2=0.117] wherein, P4 demonstrated bigger amplitude than P3 (*P*= 0.013) and Pz (*P*= 0.011). Group [F (1.53)= 1.052, *P*= 0.310, ŋ2= 0.019] and the interaction of group and electrode [F (1.266, 67.083)= 0.090, *P*= 0.823, ŋ2= 0.002] exerted no main effect.

Proactive stop trials

P3

According to analysis, electrode showed main effect [F (1.365, 72.331)= 3.753, *P*= 0.044, ŋ2= 0.066] on P3 amplitude. Adjustment for multiple comparisons showed that amplitude in Pz was significantly bigger than P3 electrode (*P*= 0.019) and the amplitude in P4 was also significantly bigger than P3 electrode (*P*= 0.004). The group [F (1, 53)= 0.015, *P*= 0.903, ŋ2= 0.000] and interaction of group and electrode [F (1.365, 72.331)= 0.355, *P*= 0.620, ŋ2= 0.007] did not show significant effect on the amplitude. As concerned with latency, electrode also exerted main effect [F (1.549, 82.101)= 3.514, *P*= 0.046, ŋ2= 0.062]. Multiple comparisons showed the latency of P3 was significantly shorter than Pz (*P*= 0.008). The group [F (1, 53)= 0.106, *P*= 0.747, ŋ2= 0.002] and interaction of group and electrode [F (1.549, 82.101)= 0.134, *P*= 0.822, ŋ2= 0.003] also exerted no main effect on the latency.

Finally, for better illustration, means, standard deviations and P-values of significant ERP components of different trials were illustrated in Tables 3 and 4. Besides, grand average ERPs for go, reactive and proactive stop trials in frontal and parietal electrodes were depicted in Figure 4.

Table 3. Significant ERP components in electrodes

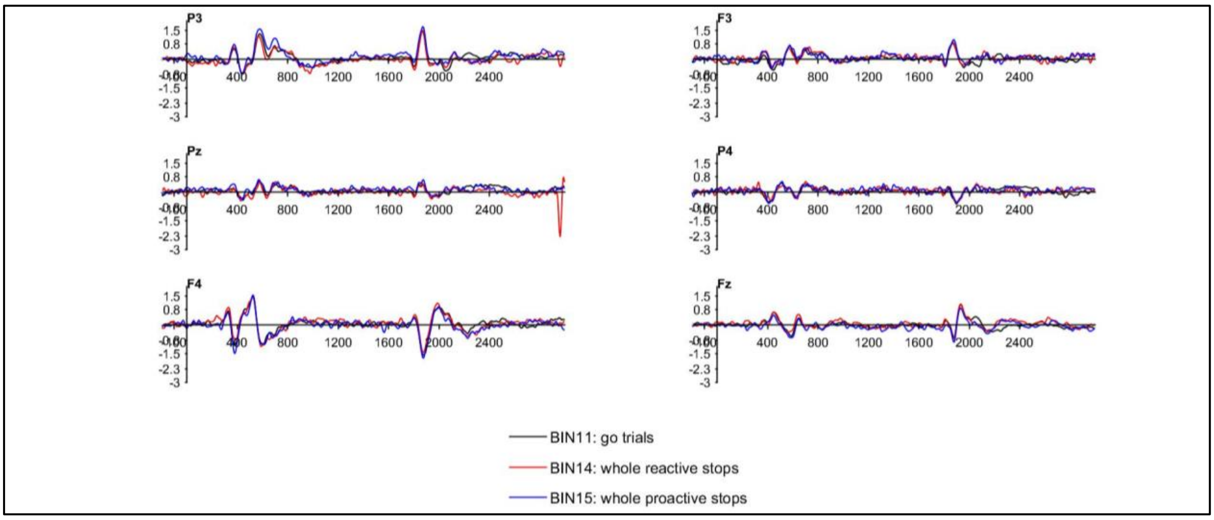
Component, trial/electrode	P3 (Mean ± SD)	Pz (Mean ± SD)	P4 (Mean ± SD)	P
P3 amplitude (µv), reactive stop trials	0.59±0.69	-------	0.94±0.57	0.013*
P3 amplitude (µv), reactive stop trials	--------	0.79±0.59	0.94±0.57	0.011*
P3 amplitude (µv), proactive stop trials	0.52±0.83	0.91±0.64	--------	0.019*
P3 amplitude (µv), proactive stop trials	0.52±0.83	--------	0.99±0.59	0.004**
P3 latency (ms), proactive stop trials	386±56.90	418±65.07	--------	0.008**

**P*< 0.05, ***P*< 0.01

Table 4. Significant ERP components in adults who stutter (AWS) and control group

Component, trial/groups	AWS (Mean ± SD)	Control (Mean ± SD)	P
N2 amplitude (µv), reactive cues	-0.47±0.05	-0.67±0.05	0.043*
N2 latency (ms), Go trials	276±3.78	287±3.78	0.043*

**P*< 0.05



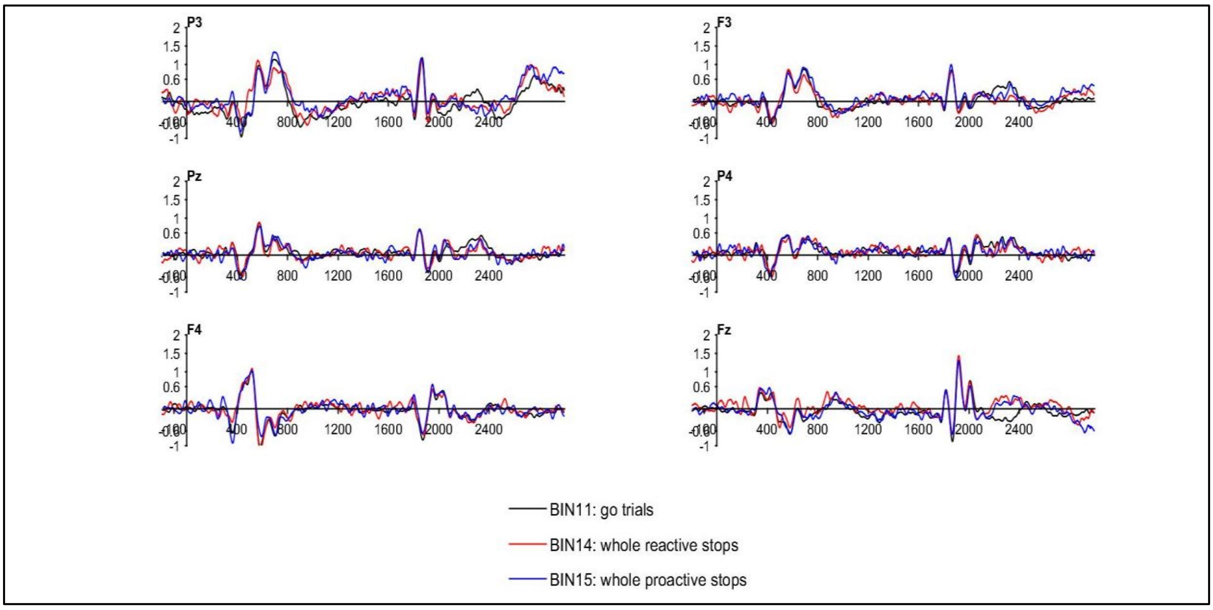


Figure 4. Grand average ERPs over frontal and parietal electrodes in go, reactive stop and proactive stop trials in a visual stop signal task for AWS (a), and the control group (b). Abbreviation: AWS: Adults Who Stutter

Discussion

This study compared behavioral and ERP responses of AWS with a control group evoked by a visual stop-signal task. Although no significant results were found behaviorally between groups, they indicated different performances in ERP measurements.

Behavioral findings

Our results showed that the two groups did not demonstrate any significant differences in reaction time and accuracies of "GO" and "stop" trials. These results were found in a previous similar study reporting that CWS did not show any difference in SSRT and the accuracy of a stop signal task (16). However, it should be noted that the age and the applied stimuli in the task were different from ours. They used variable auditory stop signal on children, while we used visual static stop signal on adults. Moreover, in agreement with our findings, another study using a picture-naming task and a flanker task featuring congruent and incongruent arrow arrays reported that AWS did not exhibit a reduced domain-general inhibitory control but selective limitations in inhibitory control of lexical selection (17). Although their used task "Flanker" was a little different from us, it is a standard task for measuring inhibitory skill. Besides that, their participants were between 18 and 30 years old which were similar to our recruited groups' age. Our results also were inconsistent with a study that showed increased SSRT and inhibitory motor control in AWS compared with age and sex-matched controls (13). However, although the age and the numbers of their participants were similar to us, the ratio of women to men was 20% in their study and 40% in our study. Furthermore, they used auditory and dynamic stop signals which were different from our visual static signals. The authors of that study finally advanced a proposal that inhibitory skills participate in speech fluency by canceling the activation of the present motor program and starting the next motor program. Also, in another study, stronger recruitment of the right posterior inferior frontal gyrus was related to stuttering severity. It was postulated that an unspecific broad reactive inhibition is a probable mechanism that hinders the smooth execution of motor speech actions (37). We did not observe these differences may be due to varied tasks and stimuli and heterogeneity of the subjects.

ERP findings

Studies suggest that larger N2 amplitude is concerned with better cognitive control in preparation for the response and better allotment of cognitive resources to pre-potent responses (19,38). Therefore, smaller N2 amplitude in reactive cues for the AWS group may indicate poorer perceptual discrimination of the cues in the early stage of the reactive trials and different preparation for the later responses. Interestingly, there was no significant difference for reactive trials behaviorally. So, it can be concluded that AWS showed a deficit in neurophysiological mechanisms of the task rather than their behavioral responses. It is in line with a study in which CWS performed a cued go/no go task, and the authors finally conclude that they may allocate brain resources differently in the task despite the same behavioral responses (15). On the other hand, according to attentional control theory, individuals who scored higher level anxiety like our participants may benefit from some compensatory strategies like more effort or employment of more processing resources in the brain in the face with the cognitive task to act like their counterparts behaviorally (39).

Our findings also indicated that N2 latency in go trials was shorter in AWS compared with the control group. As in the task, the sequence of go and stop trials was random, the N2 component is concerned with conflict monitoring and interference processing (33). As far as we know, the Anterior Cingulate Cortex (ACC) has considered as the source of the N2 component and play a role in monitoring response conflict in a variety of engagements like a go-no-go task (40). Therefore, the earlier peak in the N2 component in go trials in AWS may be a sign of a timely-different activation of ACC in this group in the task. The different activity of ACC is the notion that a couple of other studies considered for the pathophysiology of stuttering (41,42). In this study, AWS group were referred from speech-language clinics, they were actually seekers of the therapy which may interfere with the level of the anxiety. Moreover, considering the high percent of accuracy in stop trials in both groups, it seems that participants put emphasis on response accuracies rather speed. It would definitely decrease task pressure and challenge the findings. Furthermore, we could not determine the effect of development and more importantly the chronicity of stuttering on the subjects ‘performance. Therefore, we could not infer whether the observed significant differences are the causes or the consequences of the stuttering. It is suggested that besides performing the electrophysiological tests, the resting-state imaging techniques that show more inherited differences should be considered in the future.

Conclusion

In this study, by using stop-signal tasks to compare response inhibition, including reactive and proactive inhibitory skills between AWS and fluent-matched speaker group, we found that although AWS evoked different brain potentials, they acted like the control group in performing the task. So, we can conclude that ERP components are a covert index of brain processes that cannot always determine the final response. Our results did not confirm less reactive or proactive inhibitory skills and consequently weaker hand-related motor control among AWS compared with control group. But, smaller N2 component in uninformative reactive cues may show different preparation of AWS in confronting with unpredictable stimuli and weaker preparation for executing the later response. For the last note, we suggest that besides the standard evaluation, electrophysiological assessment of stuttering could provide a more comprehensive attitude toward the problem.

Acknowledgements

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