CORRELATIONS OF STOPPING BEHAVIOR WITH GABA CONCENTRATIONS IN PRIMARY MOTOR CORTEX AND THALAMUS

by

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Title: Correlations of Stopping Behavior with GABA Concentrations in Primary Motor Cortex and Thalamus

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Primary Thesis Advisor

Stopping ongoing actions is a fundamental aspect of behavior. A pathway from the basal ganglia to the thalamus is hypothesized to be important for stopping and uses the inhibitory neurotransmitter gamma amino-butyric acid (GABA). The primary motor cortex (M1) is also a critical node in the pathway to the muscles, and M1 GABA may also serve an important function in stopping. In this study, we examined the relationship between stopping behavior and GABA levels in the thalamus and M1 over two experiments in a group of 29 participants. We measured Go reaction time and stopping speed with simple and choice behavioral stop-signal tasks and measured GABA content with magnetic resonance spectroscopy. We found no relationships between stopping performance and GABA content within either brain region. However, there was a negative correlation between GABA content in both the thalamus and primary motor cortex and reaction time in the choice task, with higher GABA levels associating with faster reaction times. These results suggest that there may be more dependence on brain GABAergic mechanisms for a choice task than a simple task.

Acknowledgements

I would like to thank Professor Ian Greenhouse for helping me narrow my focus and for teaching me so much about both this topic and how science is done in general. This project would not be where it is today without his vast knowledge of the field and patient teaching. Thank you to Professor Helen Southworth for guiding me through the thesis process and answering any questions about the Clark Honors College I had along the way. Thank you to Professor Nicki Swann for always being willing to answer questions and help out however was needed. A huge thank you to all three of the above professors for serving on my thesis committee and being willing to make the time to help me through this long and strenuous project.

Thank you to Mitch Fisher for coding and running the stop-signal task and sharing that data with me, as well as helping me with issues as they came up. Thank you to Scott Watrous and Alison Burggren at the Lewis Center for Neuroimaging for helping schedule and run the MRS scans we needed for the project and teaching me about the scans' capabilities. Finally, thank you to my parents, Peggy Hennessy and Rick Horton for always supporting me throughout the entire process and pushing me to do more with my time at college.

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Introduction

Magnetic resonance spectroscopy (MRS) is a tool used in the noninvasive measurement of brain metabolites in vivo. Recently developed MRS techniques enable the quantification of gamma-aminobutyric acid (GABA) (Mikkelsen et al., 2017; Mikkelsen et al., 2019; Hermans et al., 2018; Quetscher et al., 2015; Stagg et al., 2011; Greenhouse et al., 2017; Mullins et al., 2014), which is the principal inhibitory neurotransmitter in the brain.

The basal ganglia, comprised of nuclei deep in the brain, have long been known to be involved in the inhibition of movement (Mink, 1996). The output of the basal ganglia is GABAergic and inhibitory onto the motor regions of the thalamus (Nambu, 2008). According to these classic models, excessive inhibition may explain motor disorders such as Parkinson's disease and removal of inhibition may explain involuntary movements. However, the precise role of GABA within these pathways is unclear.

Stopping is the cancellation of an ongoing motor action and is exceedingly important in day-to-day life. Stopping can be studied in the laboratory with the stop signal task. In this task, participants respond to go signals and cancel their movements in response to stop signals. Stop task performance has been linked to the hyperdirect pathway to the basal ganglia which is thought to suppress motor output via the thalamus (Aron et al., 2007), and has led to increased interest in the role of GABA in recent years. Previous studies have connected higher GABA concentration in the striatum with better response inhibition (Quetscher et al., 2015). Stopping performance has not yet been explored with respect to GABA concentration in the thalamus.

The areas of interest in this project were the primary motor cortex (M1) and the thalamus because these areas are part of the motor pathways by which signals travel from the brain to muscles to produce movement. Very little research has measured GABA in the thalamus with MRS (Dharmadhikari et al., 2015). In contrast, cortical GABA has been measured successfully with MRS in previous studies (Greenhouse et al., 2017; Hermans et al., 2018), making it a good point of comparison for the deeper thalamus region.

Here, we examined the relationship between stopping and GABA content in M1 and thalamus. We tested participants with a version of a stop signal task and estimated the duration of the stopping process (Verbruggen et al., 2019, Hermans et al., 2018). We compared stopping performance and reaction times to MRS measurements of GABA in the thalamus and M1. We hypothesized that higher concentrations of GABA in motor cortex as well as in the thalamus would correlate with shorter reaction times in a go task as well as shorter stopping times in a stop task. This hypothesis was based on the idea that greater GABA concentrations allow for increased binding to GABAergic receptors and increased inhibitory output down motor pathways.

Methods

Participants

15 subjects participated in experiment 1 (6 male, age = 23.4 ± 2.8 years) and 9 subjects participated in experiment 2 (7 male, age = 24.9 ± 2.9 years). Exclusion criteria included contraindications to undergoing MRI, and all participants were screened accordingly. All participants provided informed consent per the University of Oregon IRB.

Behavioral Task

Experiment 1

Behavioral performance was determined using go and stop tasks coded in MATLAB 2018a. The subject pressed a button with the index finger of one hand when presented with a visual stimulus on a screen. In the go task, a green square appeared on the screen and the subject attempted to press the button as quickly as possible. The task measured the difference in time between the stimulus onset and the button press to determine the go reaction time. There were 2 blocks of 30 trials, half performed with each hand.

In the simple stop task, the subjects were again presented with a green square on the screen to signal them to press the button. However, on ⅓ of the trials, a red X followed the green square after a short interval. This signaled the subject to attempt to cancel the button press. If the subject failed to stop, the task reminded them to try to stop and if the subject waited too long to press the button on a go trial, the task

reminded them to speed up. Stop signal delay (SSD) was defined as the time between the appearance of the go signal and the appearance of the stop signal. In addition to giving reminders, SSD was variable, increasing in length after successful trials and decreasing in length after failed trials. The changing SSD was implemented to find the time point where 50% of trials were successful. This task had 8 blocks of 27 trials, half of which were performed with each hand.

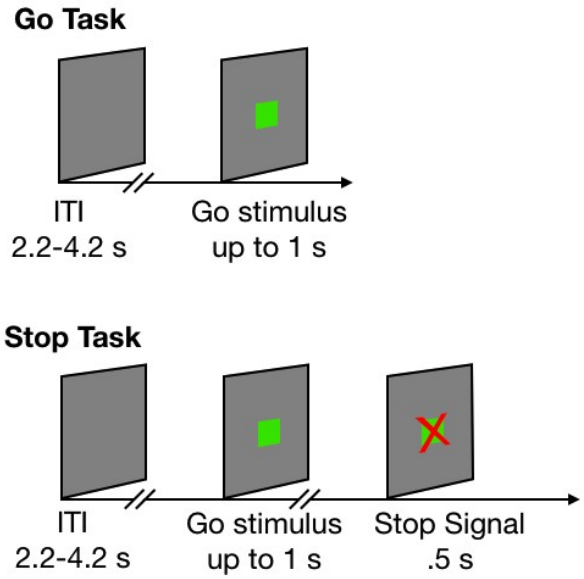


Figure 1. Task diagram for the simple go and stop tasks. ITI = inter-trial interval.

Experiment 2

The choice task was similar to the simple task but was only performed with the right hand and each trial involved a choice between the right index finger and the right pinky finger. The go stimulus was an arrow pointing either left (for the index finger) or right (for the pinky). There were 2 blocks of 30 trials in the go task. In the choice stop task, a third of the trials were stop trials in which the go stimulus was followed by a red "X" and was otherwise identical to the simple stop task, with 8 blocks of 27 trials.

Separate stop signal delay adjustments were used for each response finger. 5 of the subjects participated in both experiments.

MRI Procedures

GABA concentrations were collected using the MEGA-PRESS (Mescher et al., 1998) sequence on a Siemens 3 T Skyra MRI scanner at the University of Oregon Lewis Center for Neuroimaging and using a 32-channel head coil. The subjects were positioned headfirst and supine. An anatomical T1-weighted scan (TE = 3.43ms, TR = 2500ms, time = ~5:00/scan) was used to guide the placement of a 3D MRS measurement region of interest (voxel). The voxels were manually placed prior to the spectroscopy scans to include as much relevant tissue as possible for each target area. The M1 voxel was placed over the hand knob, as close to the surface of the brain as possible without including the skull or scalp (Figure 2). The thalamus voxel was paced toward the posterior edge of the thalamus and as medial as possible without containing an excess of cerebrospinal fluid (CSF) (Figure 3). The gradients of the machine were adjusted via shimming to get the best water peak signal possible within the target region; ideally with a full width at half maximum (FWHM) less than 15Hz for M1 and less than 20Hz for the thalamus. Two MEGA-PRESS scans (TE = 68ms, TR = 2000ms, time =6:48/scan, 50 Hz water suppression) and one water-unsuppressed PRESS scan (TE = 35ms, TR = 1500ms, time = 1:42/scan) were run for right M1 (voxel size = 20x20x20mm) and right thalamus (voxel size = 20x30x20mm). The MEGA-PRESS scans alternated between including an editing pulse at the GABA resonance peak at 1.9 ppm (ON) and an editing pulse at a point away from GABA resonance

(OFF), for 100 averages of each type. The PRESS scans did not have an editing pulse, and contained 64 averages.

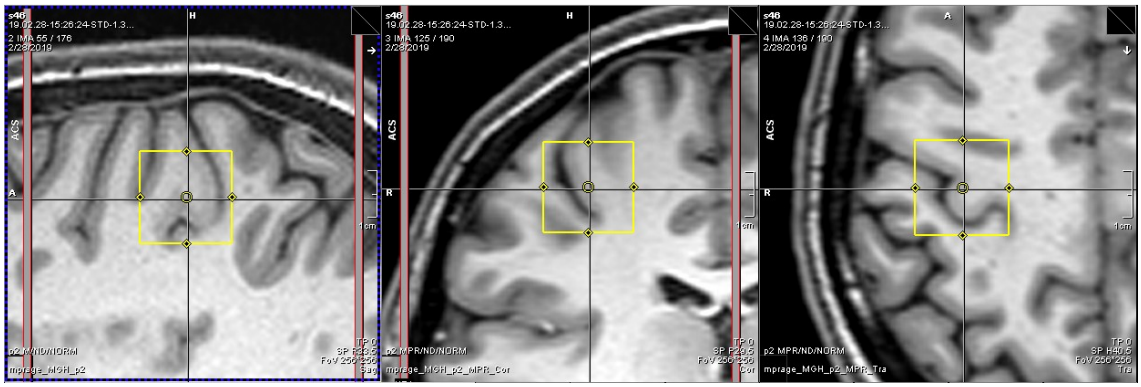


Figure 2. Voxel placement over the right primary motor cortex (M1).

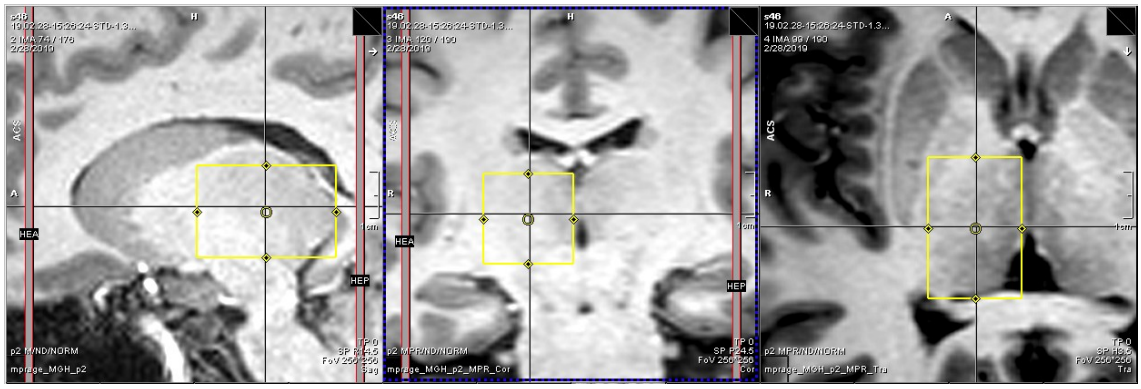


Figure 3. Voxel placement in the right thalamus.

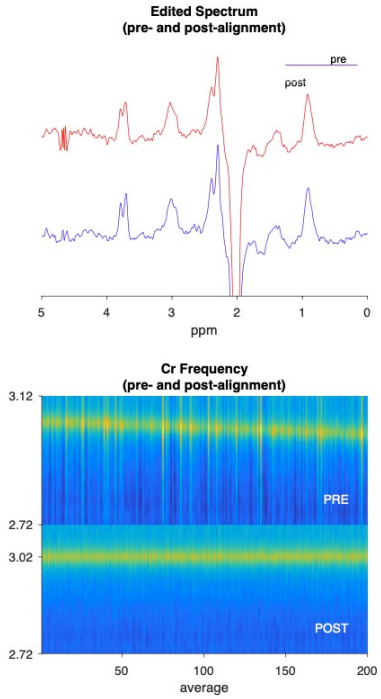
Data analysis

Behavioral analyses

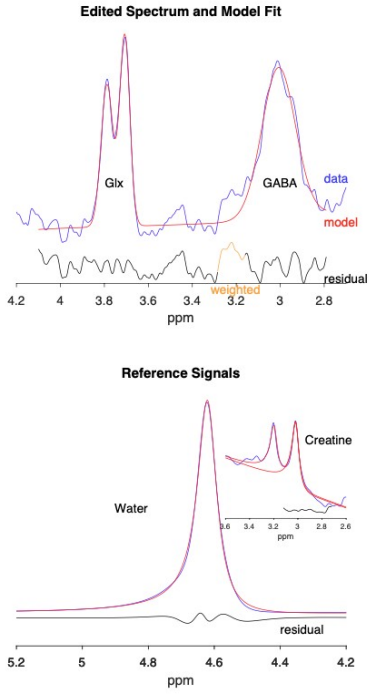
The stop task data was collected and analyzed using MATLAB. Stop signal reaction time (SSRT) was estimated using the integration method (Verbruggen et al., 2013) and provides an index of the speed of stopping. Go reaction times were determined from the button press times relative to the Go signal.

MRS analyses

The MRS data were processed and analyzed using Gannet 3.1 in MATLAB. Gannet was specially designed for analyzing GABA spectroscopy data. The functions GannetLoad, GannetFit, GannetCoRegister, and GannetSegment were used for each subject's data. GannetLoad preprocessed the raw data files and mapped out the spectrum for each scan, identified any drift in the water signal, and identified statistical outliers from the 100 averages within each scan (Figure 4A). GannetFit fits a Gaussian model to the peaks of interest within the preprocessed data and provides output including FitError calculations used for identifying good-quality data, area under the curve for GABA, and reference signals for water and creatine (Figure 4B). GannetCoRegister coregistered the voxel to the T1 anatomical image (Figure 5A). GannetSegment segmented out the fractions of grey matter, white matter, and CSF present in the voxel (Figure 5B).



A



B

Figure 4. M1 pre- and postprocessed data (A) and model fit with reference signals (B).

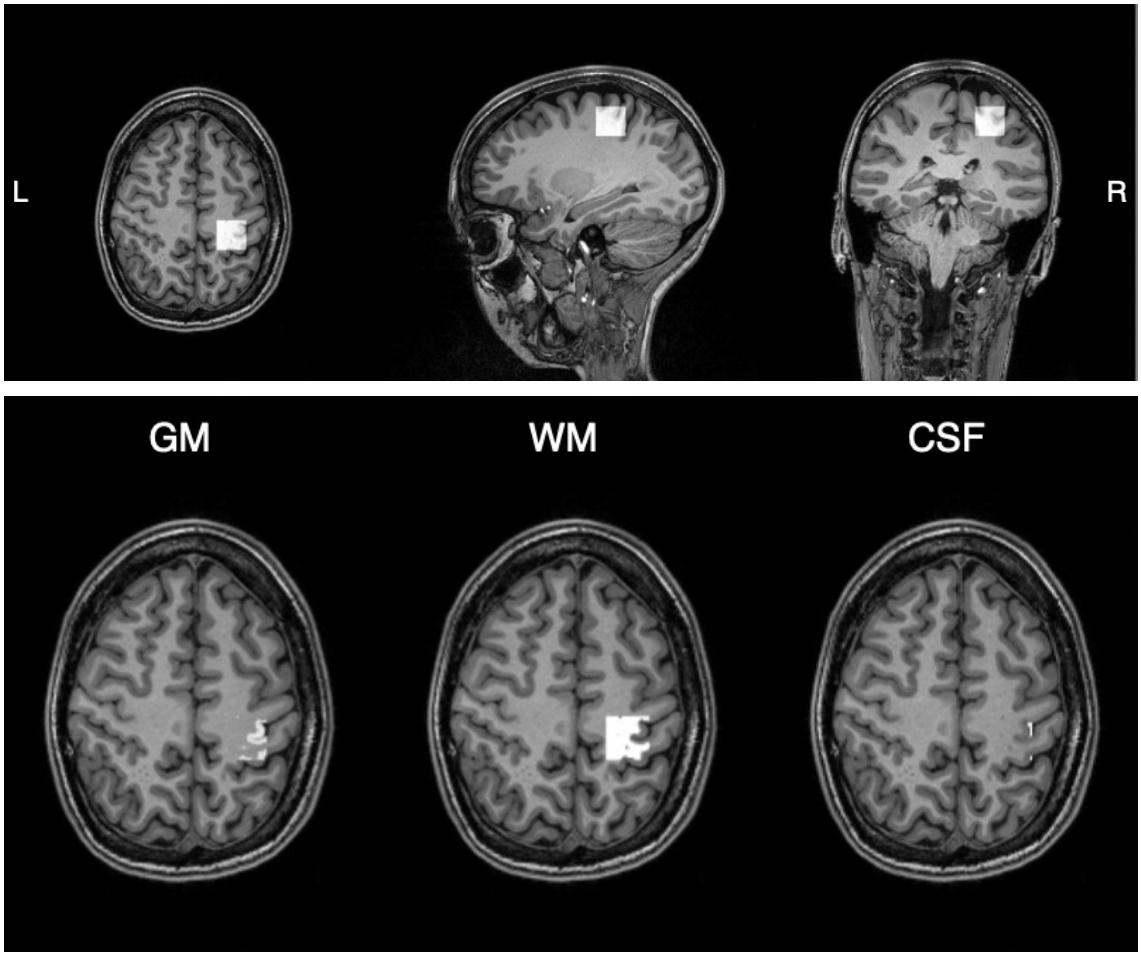


Figure 5. M1 voxel placement (top) and tissue segmentation (bottom).

In the analysis code, a cutoff value of the GABA fit error from the Gannet analysis was used as a wide net to catch most of the usable data, from which any outliers were discarded. The GABA fit error was a measurement of the difference between the generated model and the actual data. The cutoff was values under 10% for M1 and under 15% for the thalamus. Additional visualization of data identified spectra for exclusion which were contaminated by noise or irregular Gaussian-shaped peak at 3.0 ppm that fit the model with large errors.

The average GABA-to-water (GABA/H2O), GABA-to-creatine (GABA/Cr), and GABA-to-water corrected for CSF in institutional units (CSF-corrected GABA) for each subject were compared with the go and stop task performance measurements including SSRT, go reaction time, percentage of successful stopping, and SSD, across both hands in experiment 1, and across both fingers in experiment 2.

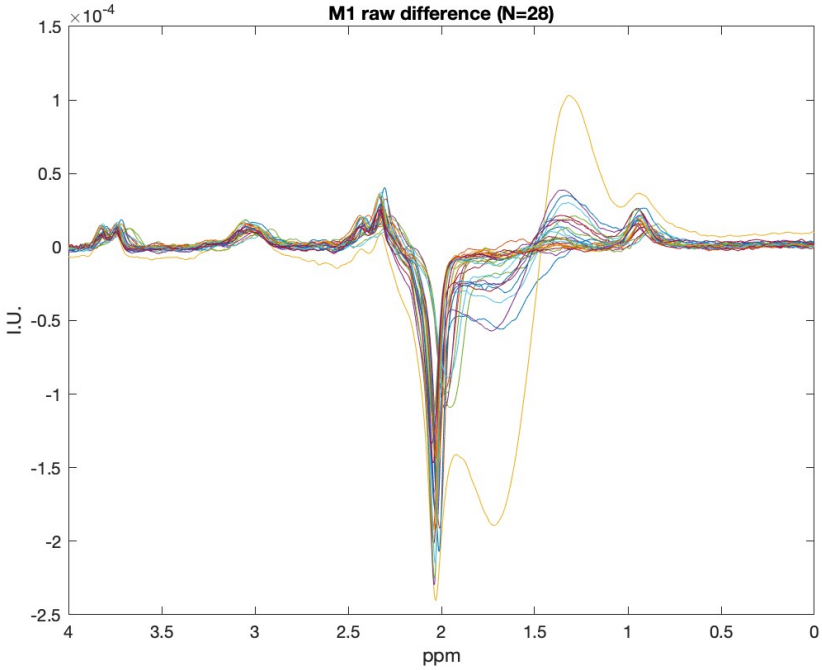


Figure 6. Spectroscopy trace from M1, one trace per subject. Note GABA peak around 3 ppm.

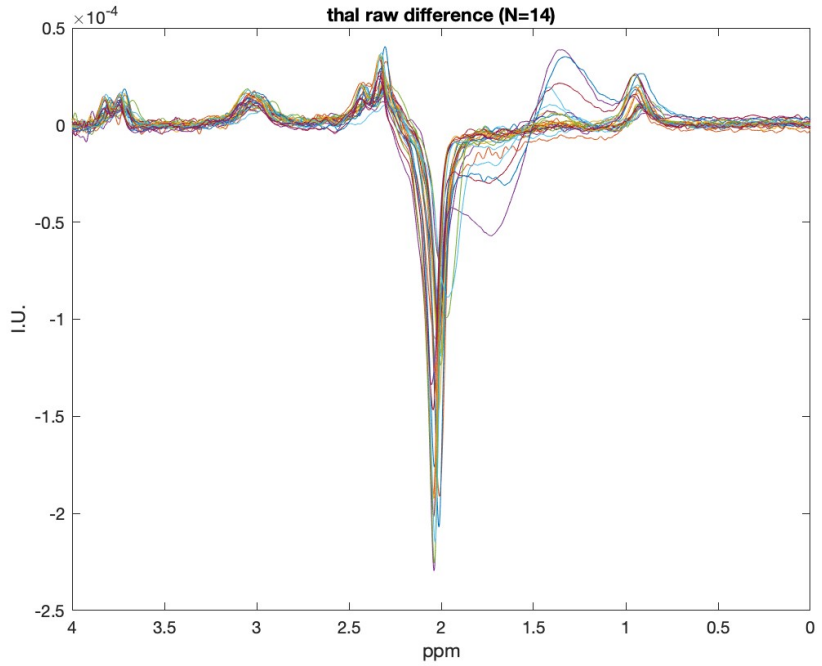


Figure 7. Spectroscopy trace from thalamus, one trace per subject. Note GABA peak around 3 ppm.

Results

Experiment 1

Stop Task (n=15)

Behavioral measures did not differ significantly between hands: average SSRT (left: 241.12 ± 25.49ms; right: 241.31 ± 19.82ms), stopping accuracy (left: 69.40 ± 7.64%; right: 68.61 ± 5.25%), go reaction times (left: 354.7 ± 42.2ms; right: 363.1 ± 34.6ms), and SSDs (left: 118.7 ± 20.4; right: 119.8 ± 9.5) all $p > 0.22$.

MRS (M1 n=10, Thalamus n=9)

One subject was removed from analyses for having fit errors greater than 10% for M1 and 7 subjects were removed for having fit errors greater than 15% for thalamus, or through visual inspection if the model fit appeared inaccurate but still produced a small fit error. The fit error was higher in the thalamus voxel than in the motor cortex voxel ($t(8) = 5.33$, $p < 0.001$), though the concentrations of GABA relative to all three reference molecules did not differ between the voxel locations (Table 1).

	M1 =10	**Thalamus =9**
Fit Error %	5.88 ± 1.63	11.13 ± 1.90
GABA conc I.U.	2.36 ± 0.37	2.21 ± 0.45
GABA/Cr	0.10 ± 0.02	0.11 ± 0.03
GABA/H20	2.14 ± 0.31	2.05 ± 0.41
Gray Matter %	40.1 ± 4.7	30.1 ± 4.1
White Matter %	50.9 ± 5.7	63.0 ± 6.7
CSF %	9.0 ± 2.1	6.9 ± 2.7

Table 1. Summary of MRS measures for subjects in the simple stop task.

Comparisons

M1

We compared SSRTs, SSDs, stopping accuracy, and go reaction times for each hand to each of the three GABA concentration measurements for M1 and thalamus. Left hand SSRTs were not significantly correlated with M1 GABA/H2O in institutional units corrected for CSF ($r=0.42$, $p=0.22$) and the same was true for right hand SSRTs ($r=-0.19$, $p=0.61$) (Figure 8A-B). The GABA concentrations in relation to water and creatine followed similar patterns to the CSF-corrected values for left ($0.46<r<0.55$, $p>0.10$) and right ($-0.13<r<-0.09$, $p>0.71$) hands.

The relationship between left SSDs and GABA-to-water corrected for CSF ($r=-0.07$, $p=0.84$) was not significant, and the same was true for the right SSDs ($r=0.21$, $p=0.56$). The relationships to other GABA measures in the left hand were also not significant ($0.01<r<0.12$, $p>0.74$), and the same was true for the right hand ($0.24<r<0.33$, $p>0.36$).

Left and right-side stopping accuracies were not significantly correlated with CSF-corrected GABA ($r=-0.02$, $p=0.95$ and $r=0.23$, $p=0.52$, respectively). Left hand stopping accuracy was not significantly correlated with GABA/H20 and GABA/Cr ($0.06<r<0.20$, $p>0.59$), and the same was true for right hand accuracy ($0.28<r<0.37$, $p>0.29$).

The go reaction times compared to CSF-corrected GABA were not significant for both hands (left: $r=-0.52$, $p=0.12$, right: $r=-0.40$, $p=0.25$) (Figure 8C-D). The same

was true for GABA/H20 and GABA/Cr (left: -0.51<r<-0.18, p>0.14; right: -0.40<r<-0.19, p>0.26).

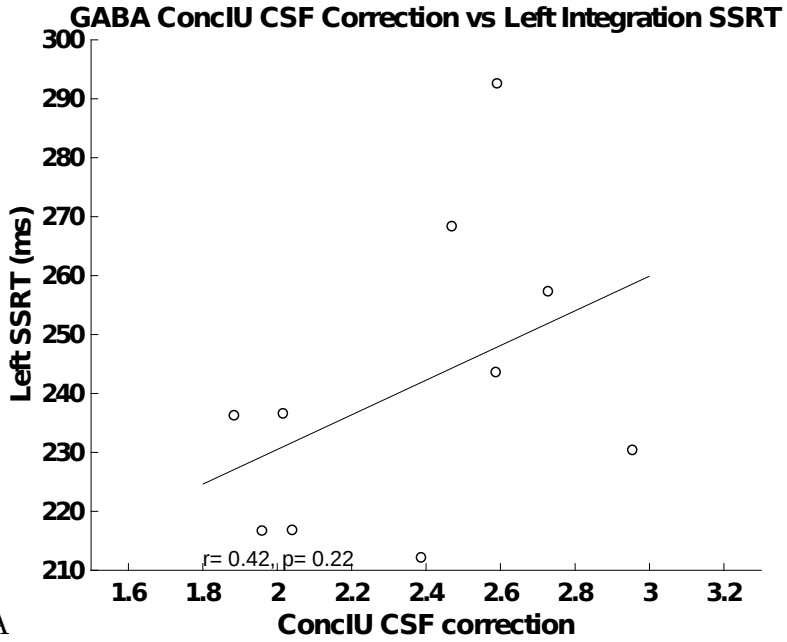
Thalamus

We repeated the above comparisons in the thalamus. SSRT did not show a significant relationship to CSF-corrected GABA in either hand (left: r=0.53, p=0.14, right: r=-0.28, p=0.47) (Figure 9A-B). There was no significant relationship to the GABA/H2O or GABA/Cr measures either (left: 0.40<r<0.53, p>0.14; right: -0.28<r<-0.14, p>0.46).

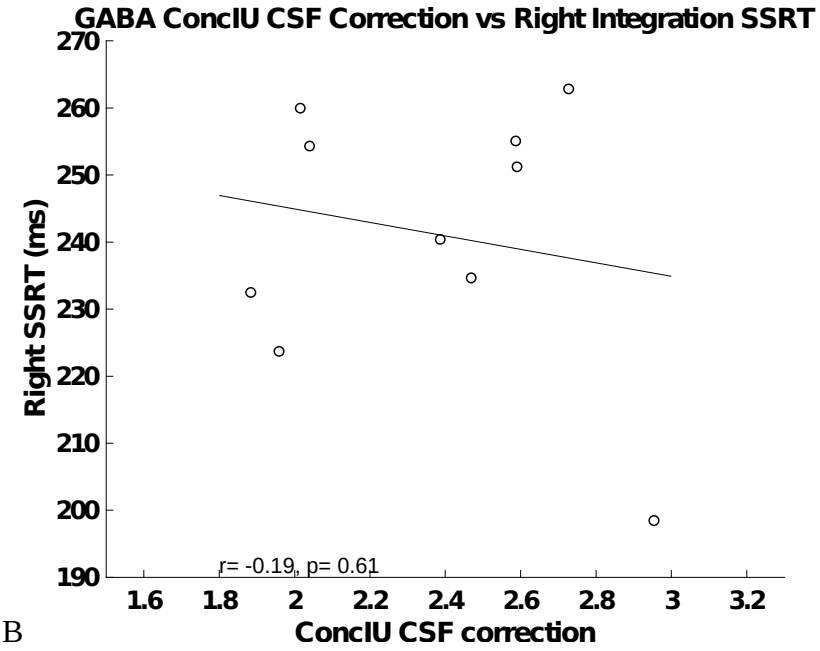
The relationship between CSF-corrected GABA and SSD in both hands was not significant (left: r=-0.06, p=0.88, right: r=-0.21, p=0.58). The relationships between SSD and GABA/H2O and GABA/Cr were not significant in the left or right hand (-0.12<r<0.04, p>0.76 and -0.25<r<-0.15, p>0.69 respectively).

Stopping accuracy did not show a significant relationship to GABA concentration corrected for CSF in left or right hand (r=-0.20, p=0.60 and r=-0.36, p=0.35 respectively). There was no significant relationship between stopping accuracy and the other GABA measures for either hand (left: -0.26<r<-0.13, p>0.50; right: -0.30<r<-0.12, p>0.43).

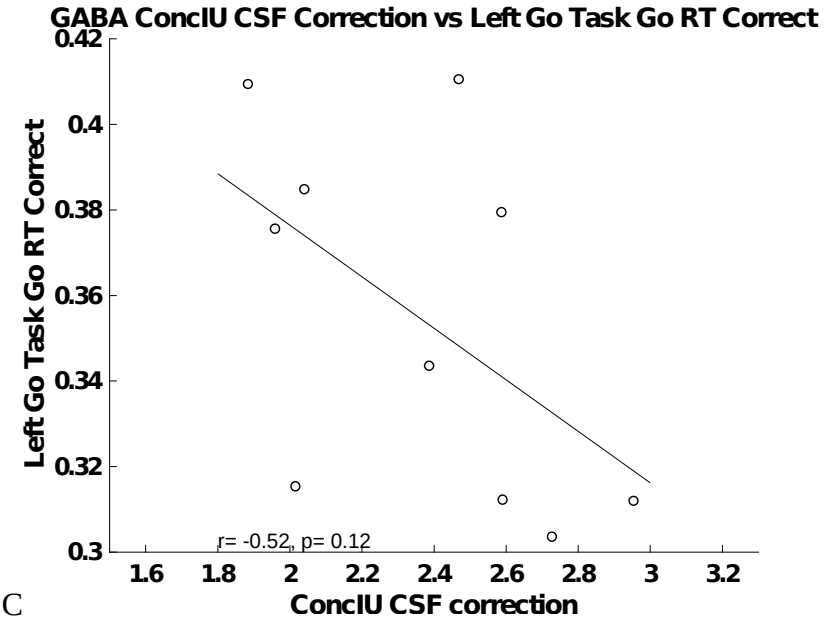
Left and right go reaction times did not show a significant relationship to CSF-corrected GABA concentration (left: r=0.06, p=0.88, right: r=-0.07, p=0.86) (Figure 9C-D). There was no significant relationship for the other GABA concentrations for either hand (left: r=0.06, p=0.88; right: -0.05<r<0.04, p>0.91).


GABA ConcIU CSF Correction vs Left Integration SSRT
Left SSRT (ms)
ConcIU CSF correction
r= 0.42,, p= 0.22
300
290
280
270
260
250
240
230
220
210
1.6
1.8
2
2.2
2.4
2.6
2.8
3
3.2

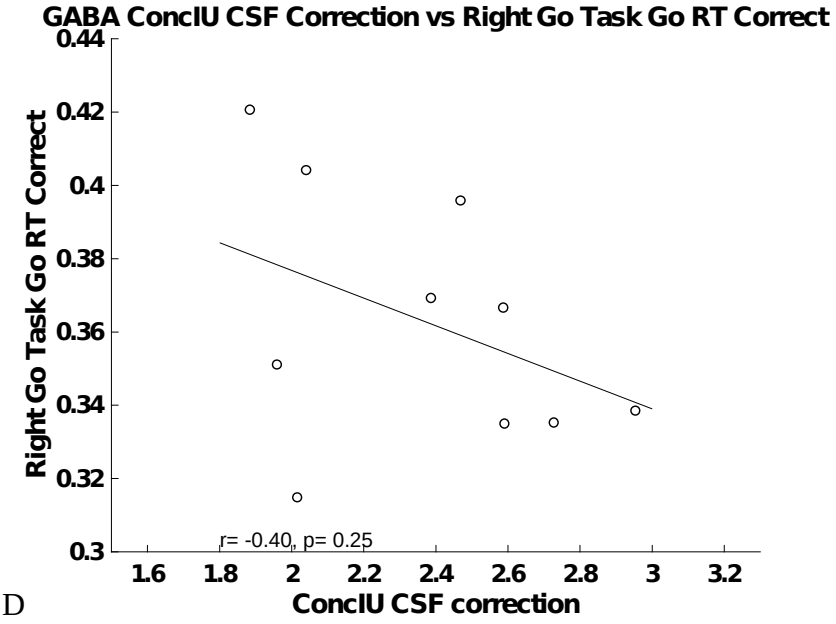
A


GABA ConcIU CSF Correction vs Right Integration SSRT
Right SSRT (ms)
ConcIU CSF correction
r= -0.19, p= 0.61
270
260
250
240
230
220
210
200
190
1.6
1.8
2
2.2
2.4
2.6
2.8
3
3.2

B

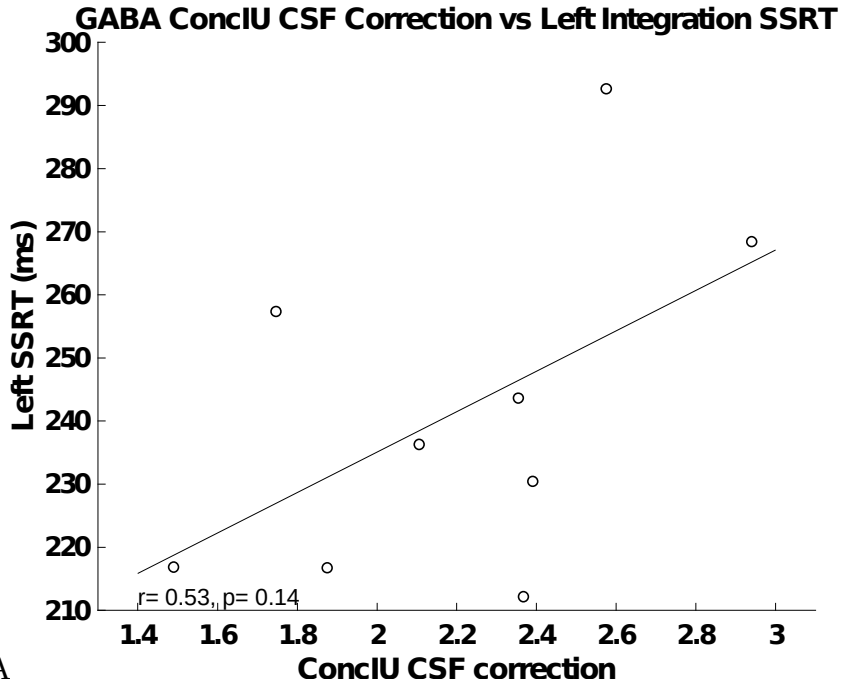


C

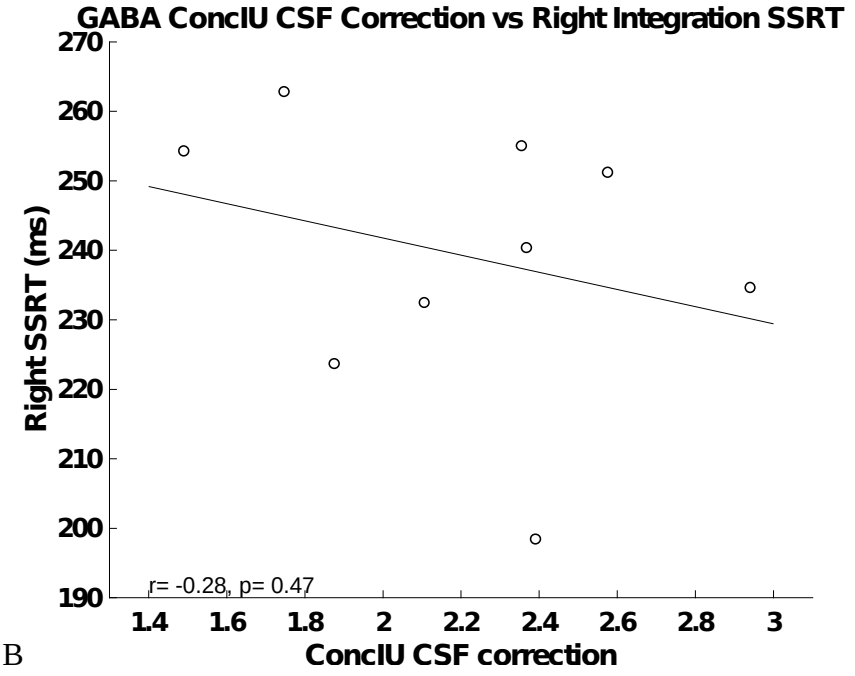


D

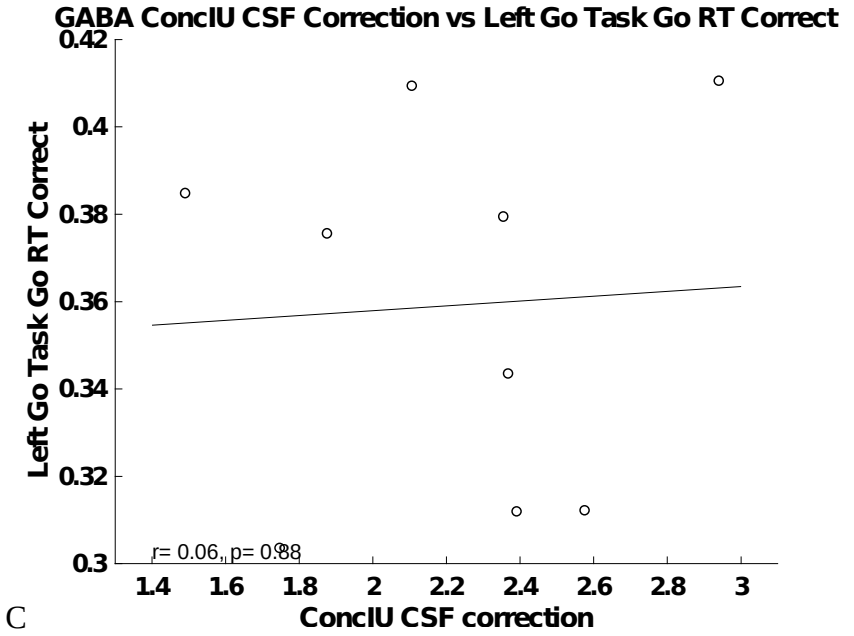
Figure 8. Simple stop task comparisons of SSRT (A, B) and reaction time (C, D) compared to CSF-corrected GABA in M1.


GABA ConcIU CSF Correction vs Left Integration SSRT
Left SSRT (ms)
300
290
280
270
260
250
240
230
220
210
r= 0.53, p= 0.14
1.4
1.6
1.8
2
2.2
2.4
2.6
2.8
3
ConcIU CSF correction

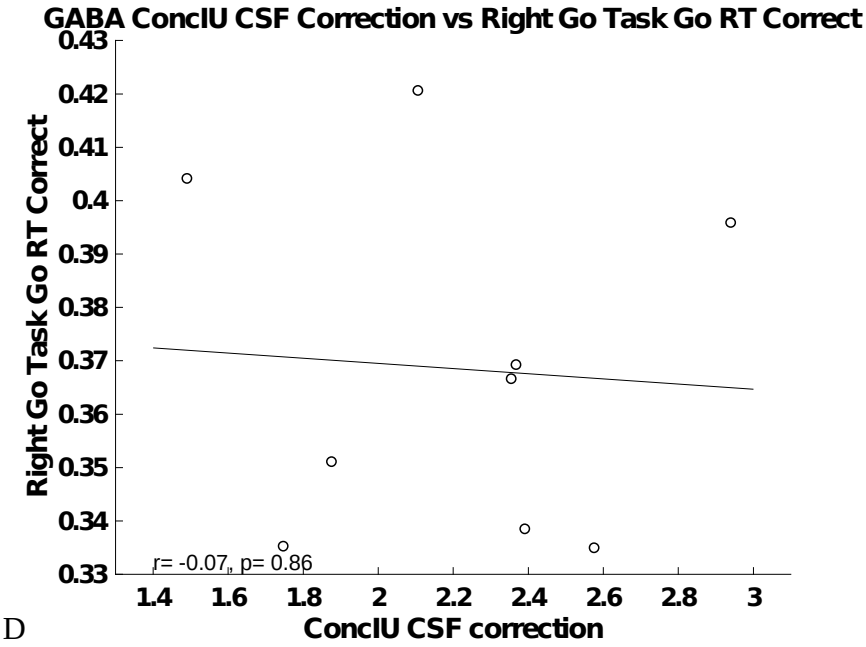
A


GABA ConcIU CSF Correction vs Right Integration SSRT
Right SSRT (ms)
270
260
250
240
230
220
210
200
190
r= -0.28, p= 0.47
1.4
1.6
1.8
2
2.2
2.4
2.6
2.8
3
ConcIU CSF correction

B



C



D

Figure 9. Simple stop task comparisons of SSRT (A, B) and reaction time (C, D) compared to CSF-corrected GABA in thalamus.

We did not observe the hypothesized relationships. This could arise from a number of factors, including noisy thalamus measurements. Another possibility is that we did not use a choice version of the stop task as was recently recommended

(Verbruggen et al., 2019). To address this potential confound, we conducted a second experiment using a choice task.

Experiment 2

Stop Task (n=9)

SSRTs were significantly different between FDI and ADM (FDI: 211.29 ± 35.56, ADM: 235.37 ± 43.73ms; $t(8) = 3.60$, $p = 0.007$), but the other behavioral measures were not significantly different between fingers: stopping accuracy (FDI: 65.12 ± 7.87%, ADM: 69.34 ± 11.40%), go reaction times (FDI: 407.3 ± 29.7ms, ADM: 419.8 ± 52.4ms), and SSDs (FDI: 149.2 ± 24.5ms, ADM: 151.1 ± 32.5ms) all $p > 0.08$.

MRS (M1 n=9, Thalamus n=8)

The fit error was smaller for M1 than for the thalamus ($t(7) = 8.18$, $p < 0.001$), and there was a greater concentration of GABA in M1 when comparing the GABA/H2O and the GABA concentration in institutional units corrected for CSF across voxels. The tissue segmentation was similar to that of the simple stop task.

	M1	**Thalamus**
Fit Error %	5.47 ± 1.09	10.63 ± 1.21
GABA conc I.U.	2.51 ± 0.34	2.18 ± 0.37
GABA/Cr	0.11 ± 0.01	0.10 ± 0.02
GABA/H20	2.30 ± 0.31	1.99 ± 0.31
Gray Matter %	39.0 ± 4.5	31.7 ± 3.0
White Matter %	52.8 ± 4.9	60.0 ± 4.4
CSF %	8.2 ± 1.1	8.3 ± 1.7

Table 2. Summary of MRS measures for subjects in the choice stop task.

Comparisons

M1

We compared SSRT, SSD, stopping accuracy, and go reaction time from both FDI and ADM in the choice task to the three GABA measures from above in both M1 and thalamus. SSRT values from the FDI and ADM did not show any significant relationship with CSF-corrected GABA (FDI: $r=0.45$, $p=0.23$; ADM: r=0,20, $p=0.60$) (Figure 10A-B). There was not a significant relationship with the other measures of GABA concentration either (FDI: $0.45<r<0.49$, $p>0.18$; ADM: $0.24<r<0.29$, $p>0.44$).

Both muscles showed significant negative correlations between SSD and CSF-corrected GABA (FDI: $r=-0.69$, $p=0.04$; ADM: $r=-0.81$, $p=0.01$). The same was true for the relationships between SSD and other GABA measures for each muscle (FDI: $r=-0.70$, $p<0.04$; ADM: $r=-0.83$, $p=0.01$).

Stopping accuracy across FDI and ADM was significantly negatively correlated with CSF-corrected GABA ($r=-0.86$, $p<0.01$ and $r=-0.72$, $p=0.03$ respectively). This relationship was consistent across the other GABA measures in each muscle (FDI: $-0.89<r<-0.82$, $p<0.01$; ADM: $-0.77<r<-0.75$, $p=0.02$).

There was a significant negative correlation between go reaction time and CSF-corrected GABA in both muscles (FDI: $r=-0.76$, $p=0.02$; ADM: $r=-0.87$, $p<0.01$) (Figure 10C-D). This pattern held true for the other GABA concentrations (FDI: $-0.87<r<-0.73$, $p<0.03$; ADM: $-0.97<r<-0.85$, $p<0.01$).

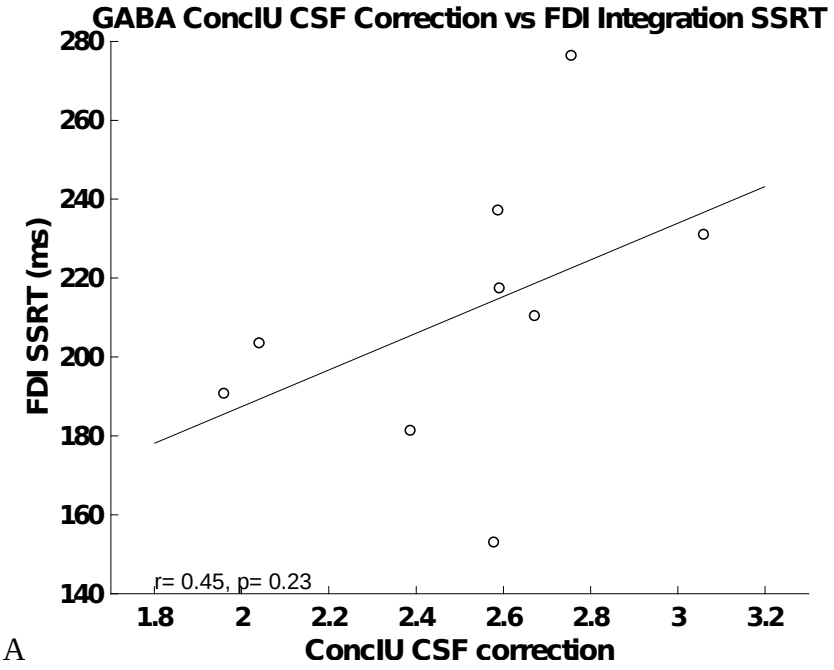
Thalamus

There was not a significant correlation between SSRT and thalamus measures of CSF-corrected GABA in FDI or ADM (FDI: r=-0.20, p=0.64; ADM: r=-0.19, p=0.66) (Figure 11A-B). There was also no significant relationship between SSRT and GABA/H2O or GABA/Cr (FDI: -0.33<r<-0.19, p>0.43; ADM: -0.31<r<-0.20, p>0.46).

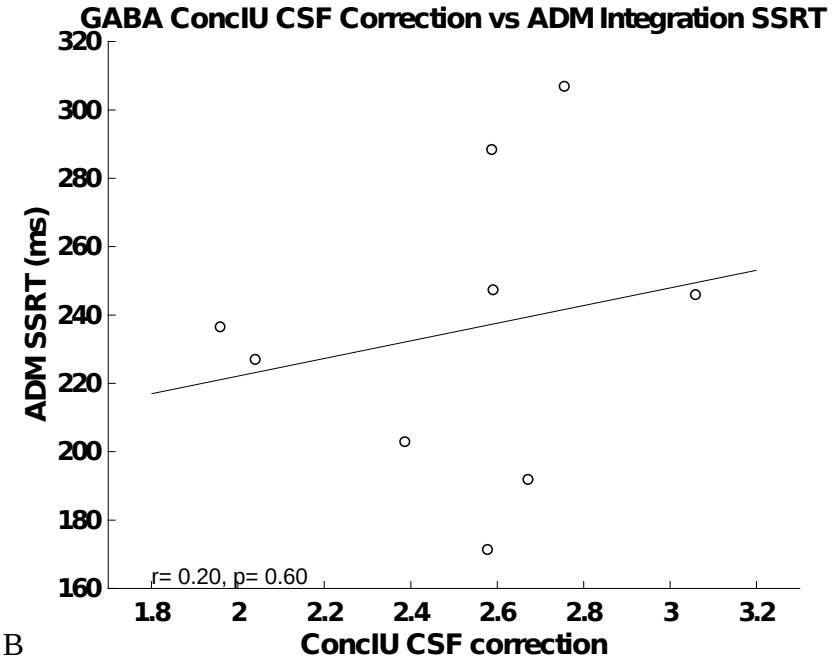
SSD measures showed no significant relationship to CSF-corrected GABA in either muscle (FDI: r=-0.45, p=0.27; ADM: r=-0.28, p=0.51). There was also no significance in the relationship to other GABA measures in FDI or ADM (FDI: -0.47<r<-0.44, p>0.24; ADM: -0.29<r<-0.11, p>0.48).

FDI and ADM stopping accuracy was not significantly correlated with CSF-corrected GABA (FDI: r=-0.34, p=0.41; ADM: r=-0.16, p=0.70). This was true for the other GABA measurements as well (FDI: -0.37<r<-0.29, p>0.37; ADM: -0.17<r<0.01, p>0.69).

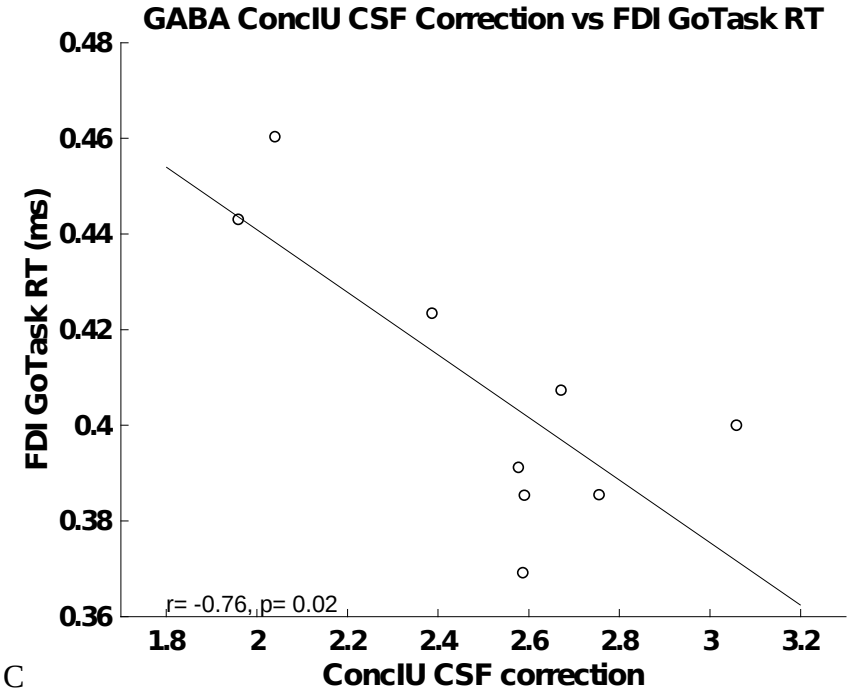
Go reaction time for both FDI and ADM exhibited significant negative correlations with CSF-corrected GABA (r=-0.76, p=0.03 and r=-0.72, p=0.05 respectively) (Figure 11C-D). There was a significant relationship in both muscles between go reaction times and the GABA/H20 measurement as well (FDI: r=-0.75, p<0.03; ADM: r=-0.70, p<0.05), but there was no significant relationship in either muscle between go reaction times and GABA/Cr concentration (FDI: r=-0.43, p=0.28; ADM: r=-0.39, p=0.34).


GABA ConcIU CSF Correction vs FDI Integration SSRT
FDI SSRT (ms)
280
260
240
220
200
180
160
140
r= 0.45, p= 0.23
1.8
2
2.2
2.4
2.6
2.8
3
3.2
ConcIU CSF correction

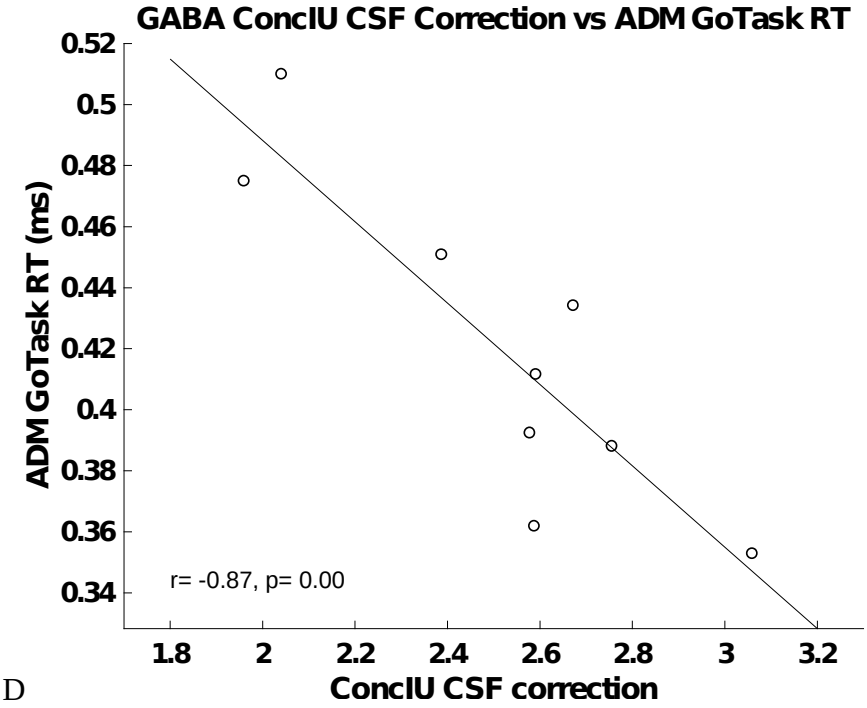
A


GABA ConcIU CSF Correction vs ADM Integration SSRT
ADM SSRT (ms)
320
300
280
260
240
220
200
180
160
r= 0.20, p= 0.60
1.8
2
2.2
2.4
2.6
2.8
3
3.2
ConcIU CSF correction

B

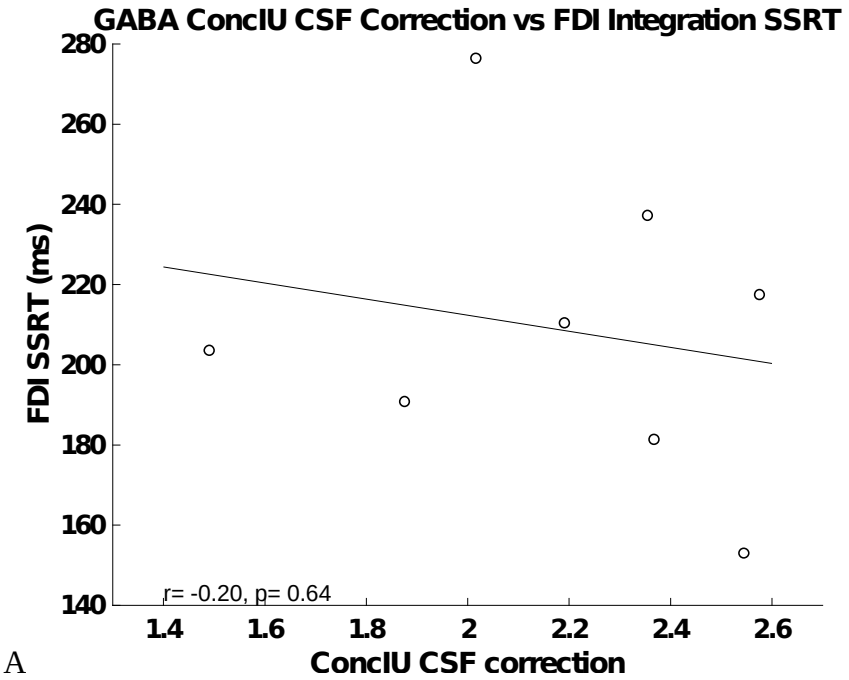


C

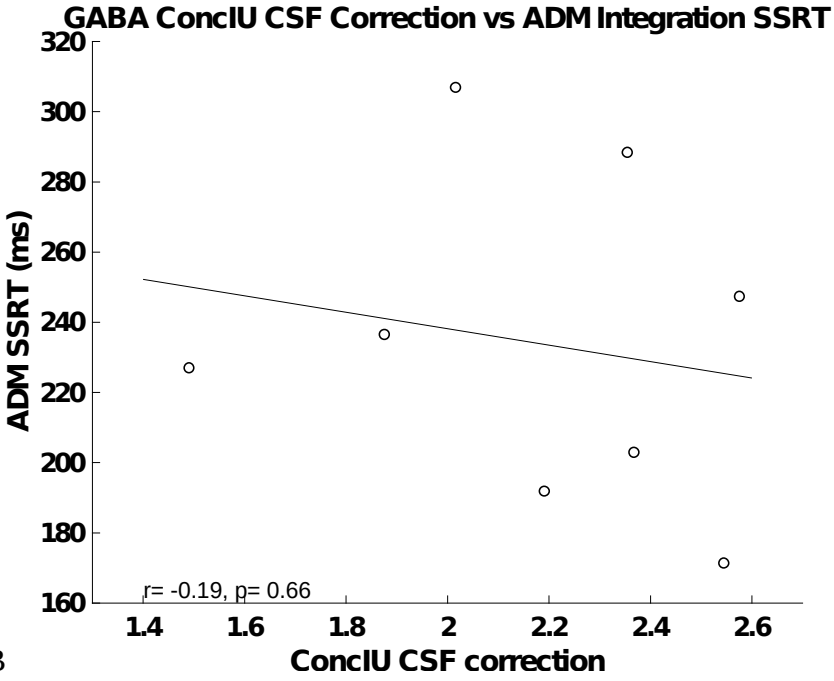


D

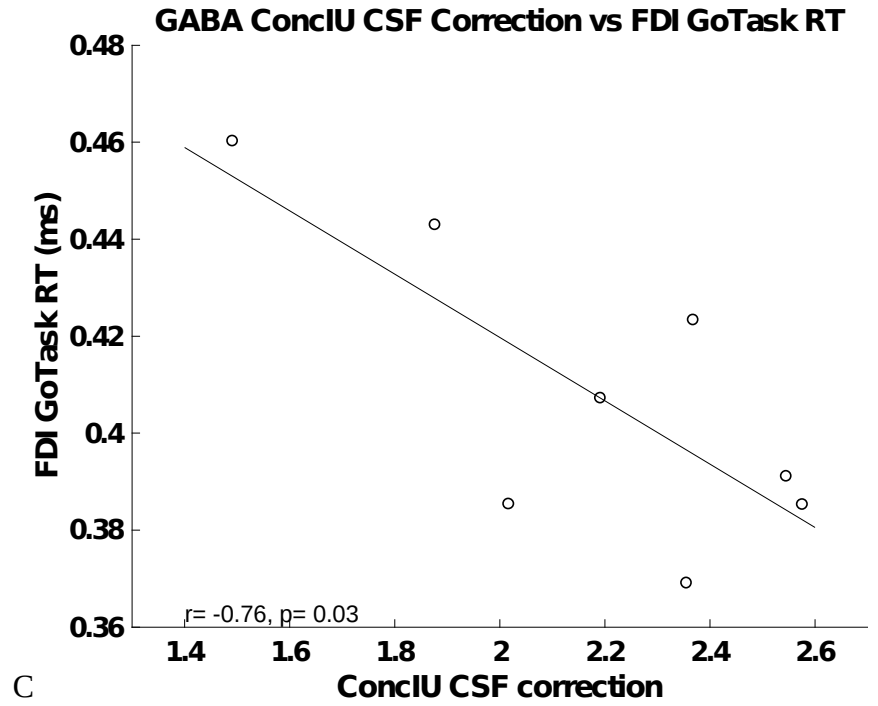
Figure 10. Choice stop task comparisons of SSRT (A, B) and reaction time (C, D) compared to CSF-corrected GABA in M1.


GABA ConcIU CSF Correction vs FDI Integration SSRT
FDI SSRT (ms)
280
260
240
220
200
180
160
140
r= -0.20, p= 0.64
1.4
1.6
1.8
2
2.2
2.4
2.6
ConcIU CSF correction

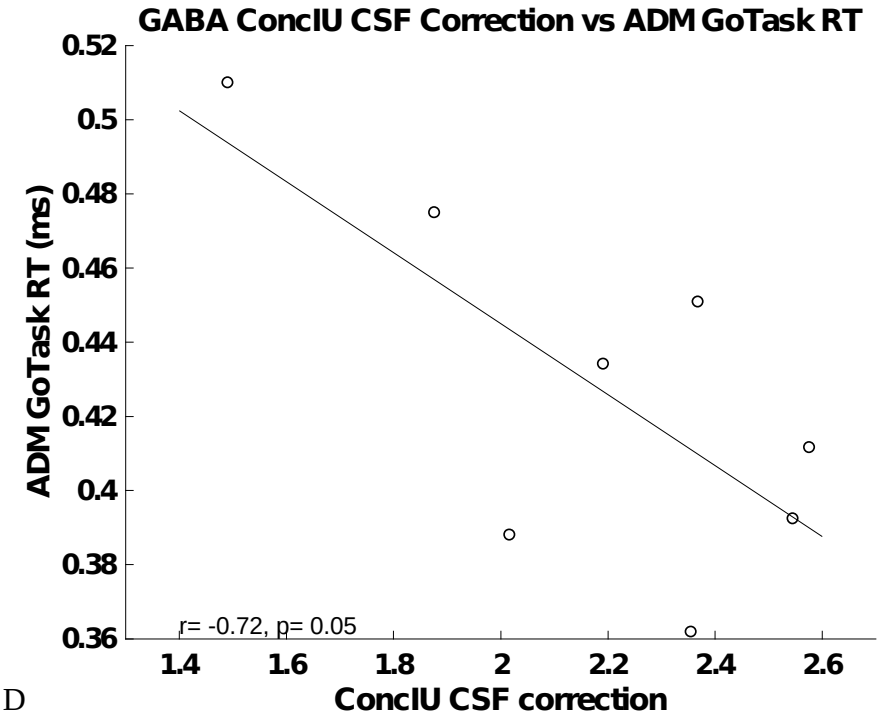
A


GABA ConcIU CSF Correction vs ADM Integration SSRT
ADM SSRT (ms)
320
300
280
260
240
220
200
180
160
r= -0.19, p= 0.66
1.4
1.6
1.8
2
2.2
2.4
2.6
ConcIU CSF correction

B



C



D

Figure 11. Choice stop task comparisons of SSRT (A, B) and reaction time (C, D) compared to CSF-corrected GABA in thalamus.

Discussion

Contrary to our hypotheses, we did not observe relationships between stopping speed and GABA in either region in either a simple or choice stop task. However, we observed that individuals with greater GABA concentrations in M1 and thalamus were faster at initiating a movement cued by a stimulus in a choice task. In M1 alone, SSD and stopping accuracy were also correlated with GABA concentration in the choice stop task. There was no significant relationship between go performance and GABA concentration in M1 or thalamus in the simple stop task. This suggests that there may be something in the act of making an action choice decision that requires more GABA in M1 and thalamus to produce a faster response. This could be because whichever response is not required must be actively inhibited when the stimulus appears.

We hypothesized that greater GABA concentrations in both M1 and thalamus would correlate with faster stopping times. We based our hypothesis on anatomical models and previous work implicating the inhibitory output of the basal ganglia to the thalamus in stopping performance. Higher concentrations of GABA would allow for greater inhibition of electrical signals down the motor pathway by permitting the inhibition to take place at a faster rate without waiting for more GABA to bind across the synapses, therefore stopping movement more quickly.

However, we observed relationships for go reaction times instead of stopping times, but only in a choice task. Previous studies have found similar relationships between the excitability of the motor system and GABA content in M1, with the counterintuitive pattern of greater excitability associated with higher GABA content (Greenhouse et al., 2017). Intriguingly, the pattern did not appear for the simple task.

The simple stop task gathered data from both hands while the choice task only gathered from the right hand and while it is interesting that we found reaction time correlations in the choice task and not in the right hand of the simple task, it hints at the importance of making a motor action decision. GABA was measured on the right side of the brain in all subjects and signals from the right side of the brain exert dominant control over movement in the left side of the body.

We observed similar patterns when comparing go reaction time to GABA content in both M1 and the thalamus in the choice task. In each case faster reaction times were correlated with higher GABA levels. This could be because faster output pathways depend on greater capacity for inhibition, which could also be why we only observe the correlation in a choice task, when the subject knows that they may need to stop movement in one finger and respond with the other. In other words, a choice task may require inhibition during both go and stop trials, unlike a simple task.

The fact that we only took GABA measurements from the right side of the brain is a limitation of this study. By only taking measures from one side of the brain, we could only compare to stop task data from the ipsilateral side of the body in the choice task. However, we acquired data from both ipsi- and contralateral sides relative to the responding hands in the simple task. Future work in this regard could involve taking GABA measurements in the left M1 and thalamus, as well as repeating the choice stop task with the left hand to determine if the patterns we found repeat for the other side. Future research should determine if the result is repeatable for the opposite side.

Another limitation to this project was the increased difficulty of gathering data from the thalamus due to the depth of the region and limited ability of the magnet to create a uniform magnetic field during shimming. The voxel placement was particularly difficult as well due to anatomical variation and the tendency of subjects to position themselves slightly differently in the magnet. Also, a larger sample size is necessary to increase statistical power.

In summary, we found that GABA content in right M1 and thalamus was higher in subjects who had a faster reaction time in a choice go task with two fingers of the right hand. Furthermore, our results suggest thalamic GABA may not relate to stopping performance in either simple or choice stop tasks despite model-based predictions. M1 GABA levels may contribute to ipsilateral stopping accuracy in a choice task, but further work is needed to evaluate if the same pattern holds for the contralateral hemisphere.

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