SUPPORTING INFORMATION

Frontal traumatic brain injury in rats causes long-lasting impairments in impulse control that are associated with chronic neuroinflammation.

ACS Chemical Neuroscience

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SUPPLEMENTAL METHODS

Apparatus

Behavior was conducted in a bank of 28 standard operant chambers equipped on one side with a 5-hole array and on the other with a tone generator, two retractable levers, one light above each lever and a sucrose pellet dispenser and a houselight (Med Associates, St Albans, VT). Only the 5-hole array, the pellet dispenser and the houselight were used in this experiment.

Surgery

Rats were anesthetized and placed in a stereotaxic frame. Buprenorphine (0.01 mg/kg, s.c.), lactated ringer solution (8 ml, s.c.) and bupivicane (0.1 mL of 0.5% solution, s.c. at incision site) were administered. Under aseptic conditions, a midline incision was made in the scalp and the fascia retracted. A 6.0 mm diameter circular craniotomy was performed centered at AP +3.0, ML 0.0 mm from bregma. A traumatic brain injury was then induced using an electromagnetic controlled cortical impact device (Leica Biosystems, Buffalo Grove, IL). Following injury, bleeding was stopped with sterile gauze and the incision sutured. Sham procedures included

everything above with the exception of the craniotomy and impact. Buprenorphine (0.01 mg/kg) was administered for pain management 10 and 24 hours post-surgery.

Behavior retraining

A small subset of rats were not able to achieve a high enough level of performance to move on to drug testing (moderate n = 1, severe n =2). These were put through a retraining process that increased the duration of the stimulus to make the task easier and gradually moved back to the target of 0.5 s as performance improved. These rats were able to be included on the final pharmacological challenge.

Pharmacological challenges

For amantadine, an 80 mg/kg dose was attempted initially (0, 10, 40, 80 mg/kg), but produced lethargy in all rats. Instead, a 20 mg/kg dose was chosen, making the Latin square 0, 10, 20 and 40 mg/kg.

Stimulus duration modification

Following pharmacological challenges, a brief test was administered to verify that heavily-impaired rats were still capable of performing the task. Over three sessions, the stimulus duration (SD) was gradually increased from the default 0.5 s to 2 s, 5 s and 10 s. In the last phase, the limited hold was increased to 10 s to allow responses for the full duration.

Structural MRI scanning

All experiments were performed on a 7 Tesla preclinical scanner (Bruker Biospin, Ettlingen Germany) using Paravision 5.1. Rats were put under isofluorane anesthesia, then placed into the scanner with a 1-2% isofluorane flow while breathing rates were monitored. After localizer scans, coronal T2-weighted RARE spin echo images were acquired (TR = 4 sec, effective TE = 34.48 ms, RARE factor = 8, NA = 2, scan time = 4:16 min, matrix size = 256 x 256, FOV = 25.6 x 25.6 mm). Standard slice thickness was 1 mm but animals in the Mild TBI group were imaged with a slice thickness of 0.5 mm to provide better resolution of any damage.

Tissue extraction and preparation

Rats were rapidly decapitated, the orbitofrontal and medial prefrontal cortex extracted, and rapidly frozen on dry ice. Samples were then stored at -80° C. Tissue from a subset of animals with representative behavior spanning optimal to heavily impaired was lysed in RIPA buffer (pH 8.0) with protease and phosphotase inhibitors. Samples were spun at 13,000 RPM, supernatant extracted and measured for protein content.

Enzyme-linked immunosorbent assay (ELISA)

Tissue homogenate was quantitatively detected for rat IL-1α, IL1β, IL-2, IL-4, IL-6, IL-10, IL-12, TNFα and IFNγ using Quansys Q-plex multiplex ELISA. Steps were as follows at 23° with washes between each step: standards and samples were placed in antibody precoated plate wells and incubated under agitation for 90 min, then incubated with a detection mixture (secondary antibody) for 60 min, incubated with an streptavidin-HRP solution for 15 min, and incubated with a coloring reagent until color gradient appeared in standard wells. The optical

density was then read using a Q-view imager. Protein concentration was calculated using standard curve.

Data Analysis

Statistical tests were conducted using R statistical software (http://www.r-project.org/). Transformations were applied to the data as appropriate: log transformation for data bounded on the lower spectrum and ratio data (collection and choice latencies, task efficacy index, some cytokines) and the arcsine-square root transformation was used for percentage variables (accuracy, omissions, prematures, trials) as well as square root transformations (some cytokines). Repeated measures data (behavior, pharmacological challenges, SD modification) were analyzed using linear mixed effects regression with each rat's baseline as the random effect in the *lme4* library and p-values estimated using the *lmerTest* library. Group comparisons were performed using planned contrasts. Lesion size was analyzed in linear regression using the *stats* library. Neuroimmune markers were analyzed by ANOVA and posthoc comparisons made using Tukey's HSD test. Multiple cytokines were reduced using principal components analysis (PCA). A p-value equal to or less than 0.05 was considered significant.

For behavioral measures, each outcome variable was analyzed separately in a linear mixed effects regression. The Pre-injury phase represents baseline performance prior to surgery, the Acute phase represents the recovery and stabilization after injury ('re-baseline'), and the Chronic phase represents baseline data between pharmacological challenges. All phases were analyzed together in a single model. The regression for each variable used Group and Phase as fixed effects (*Outcome* ~ Group * Phase) and individual performance in each phase as the random effect. The effects of amphetamine, atomoxetine and amantadine were evaluated in a

separate regression for each drug. For each variable, a model was fit to determine if there were any interactions using Group and Dose as the fixed effects (*Outcome* ~ Group * Dose); if the interaction was not significant, a model was fit to determine Dose effects (*Outcome* ~ Group + Dose). Individual rat performance was used as the random effect. Each reported effect is compared to saline administration. The SD modification data were analyzed separately in a regression with Group and SD as the fixed effects (*Outcome* ~ Group * Stimulus duration) and individual baseline as the random effect. For lesion analysis, the combined lesion and ventricle volume was analyzed in a linear regression (Volume ~ Group * Position [from bregma]). Lesion and neuroimmune principal components were analyzed in a linear mixed effects regression using the last 3 sessions of behavioral variables as the outcome (*Outcome* ~ Markers) and model selection was performed. The best-fitting model was selected based off a chi-squared comparison and significant predictors reported. This approach minimizes issues of multiple comparisons and allows the potential of using all measured variables, provided they are significant and independent predictors.

SUPPLEMENTAL RESULTS

Effect of TBI on 5CSRT performance:

There were no significant differences in performance prior to injury on accuracy, prematures, omissions, task efficacy index, total trials or choice latencies. There was a small difference between the Mild and Moderate group on collection latency ($p = 0.047$; see Figure S1 and Table S1)

In the acute phase (day 7-30 post-injury), brain-injured animals showed severity-dependent deficits in trials completed, choice and collection latencies (Figure S1 and Table S1;

trials: all groups different from every other group, p's < 0.004; *choice latency*: all groups different from every other group, p's < 0.001, except for the Sham and Mild, $p = 0.071$; *collection latency*: all groups different from every other group, p's < 0.001, except for the Sham and Mild, $p = 0.848$).

The same pattern of impairment persisted into the chronic phase (day 30-104 post-injury), with the exception of the Mild group recovering to sham levels in trials completed (Figure S1 and Table S1; *trials*: all groups different from every other group, p's < 0.004, except for the Sham and Mild, $p = 0.813$; *choice latency*: all groups different from every other group, p's < 0.007, except for the Sham and Mild, $p = 0.500$; *collection latency*: all groups different from every other group, p's < 0.032, except for the Sham and Mild, $p = 0.654$).

Rats in the performance subcategories showed similar profiles of recovery as described in the main text. Resilient rats demonstrated a small acute impairment in choice latency, which recovered. Vulnerable rats showed initial deficits, however, these recovered to baseline levels. Chronically Impaired animals had large deficits which never recovered. (Figure S2 and Table S2; Resilient: impaired in the acute phase on choice latency, $p = 0.031$, recovered on all variables in the chronic phase, p's > 0.332; Vulnerable: impaired on trials completed, choice and collection latencies in the acute phase, p's < 0.009, recovered on all variables in the chronic phase, p's > 0.077; Chronically Impaired: impaired on trials completed, choice and collection latencies in the acute, p's < 0.001, and chronic phase, p's < 0.001)

Stimulus duration modification

Even severely-injured rats showed improvements in performance when the SD was increased, indicating a clear sensitivity to task contingencies. All rats improved accuracy and

task efficacy, reduced premature responses and omitted trial as the SD was increased. Nevertheless, the Moderate group did not reach Sham levels until the highest SD and the Severe group never reached sham levels on most measures. Only the Moderate and Severe group were able to increase their trials completed since others were already at maximum. Furthermore, all animals, regardless of injury status increased their choice and collection latencies, likely reflecting a reduced urgency to respond under a long stimulus (Figure S3 and Table S11; *accuracy*: all groups increased at each SD, p's < 0.039; *prematures*: all groups decreased at each SD, p's < 0.004; *omissions*: all groups decreased at 5 and 10 s SD, p's < 0.001, except for the Severe group, which decreased at 2 s duration also, $p = 0.004$; *task efficacy index*: all groups increased at each SD, p's < 0.007; *trials*: Severe group increased at all SDs, p's < 0.001, Moderate group increased at 10 s, $p = 0.012$; *choice latency*: all groups increased at 10 s, $p = 0.048$; *collection latency*: all groups increased at 5 and 10 s, p's < 0.002; further specific group comparisons for all variables can be found in Table S11).

Effects of amphetamine

Although brain-injured rats showed a differential response to amphetamine on other variables, total trials, choice and collection latencies were affected similarly across groups. Amphetamine decreased trials and decreased choice and collection latencies in a dose-dependent fashion (Figure S4 and Table S3; *trials*: Dose effect, $p < 0.001$, decreased at 0.6 and 1.0 mg/kg, p's < 0.021; *choice latency*: Dose effect, $p = 0.012$, decreased at 0.6 mg/kg, $p = 0.002$; *collection latency*: Dose effect, $p < 0.001$, decreased at 0.6 and 1.0 mg/kg, p's < 0.002). There were no unique effects of injury susceptibility.

Effects of atomoxetine

Atomoxetine administration showed minimal effects on trials, choice or collection latencies for all groups, with the exception of a slight decrement in trials at 1.0 mg/kg (Figure S5 and Table S5; $p = 0.003$). There were no unique effects of injury susceptibility.

Effects of amantadine

Amantadine affected psychomotor measures on the 5CSRT at higher doses. There were no injury-specific effects, however all animals completed fewer trials and showed increased choice and collection latencies (Figure S6 and Table S6; *trials*: Dose effect, $p < 0.001$, decreased at 20 and 40 mg/kg, p's < 0.023; *choice latency*: Dose effect, $p < 0.001$, decreased at 40 mg/kg, $p < 0.001$; *collection latency*: Dose effect, $p < 0.001$, decreased at 40 mg/kg, p's < 0.001). There were no unique effects of injury susceptibility.

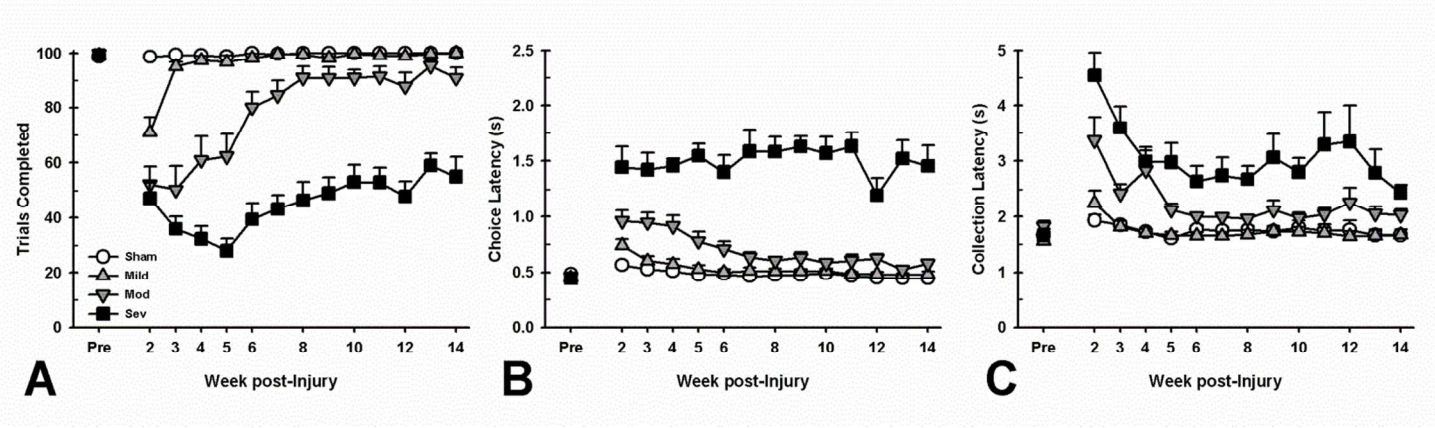
Trials Completed
Sham
Mild
Mod
Sev
Pre
Week post-Injury
A
Choice Latency (s)
Pre
Week post-Injury
B
Collection Latency (s)
Pre
Week post-Injury
C

Figure S1.

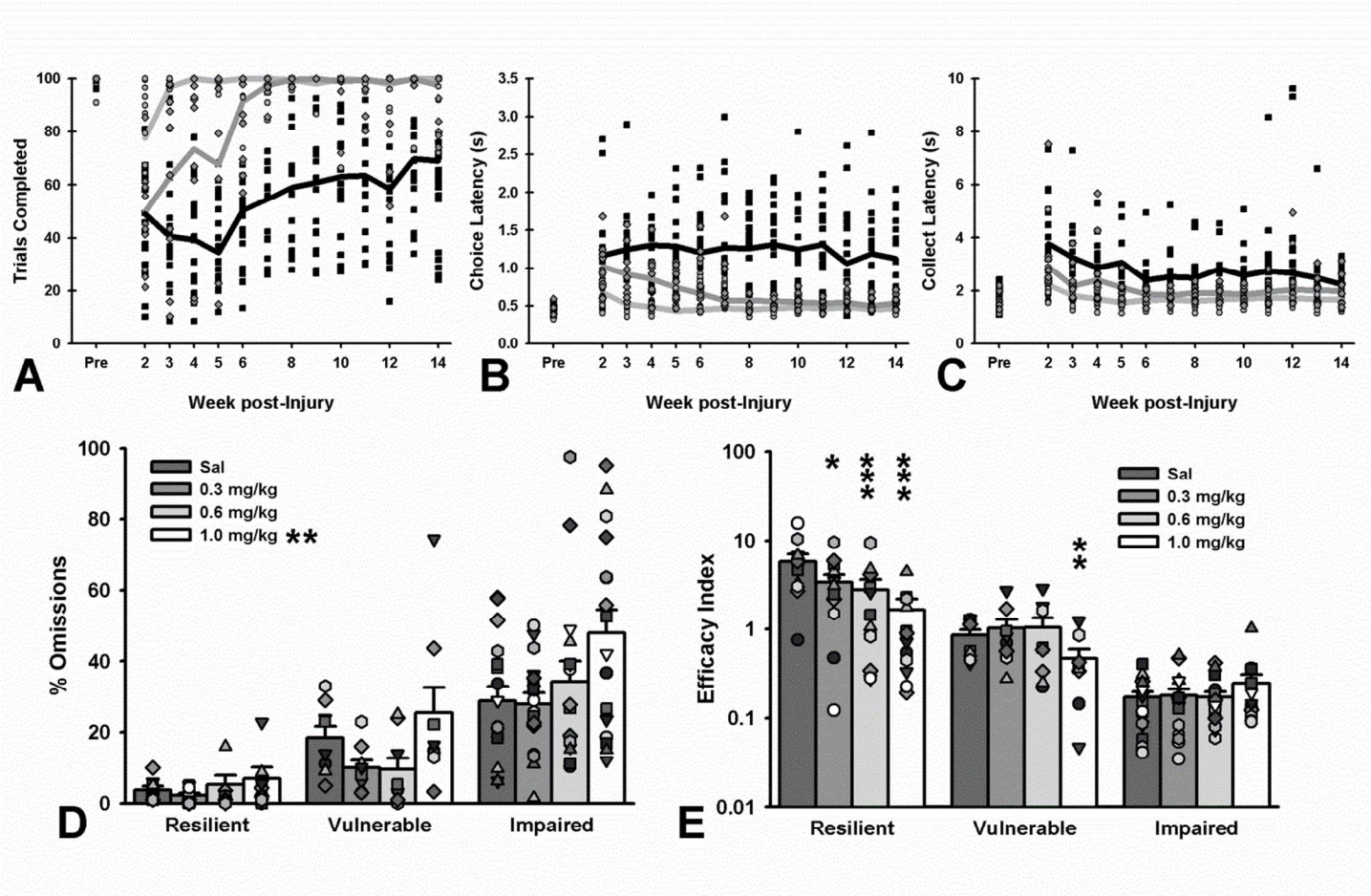
A
Trials Completed
Week post-Injury
B
Choice Latency (s)
Week post-Injury
C
Collect Latency (s)
Week post-Injury
Pre
D
% Omissions
Sal
0.3 mg/kg
0.6 mg/kg
1.0 mg/kg
**
Resilient
Vulnerable
Impaired
E
Efficacy Index
*
***
***
**
Sal
0.3 mg/kg
0.6 mg/kg
1.0 mg/kg
Resilient
Vulnerable
Impaired

Figure S2.

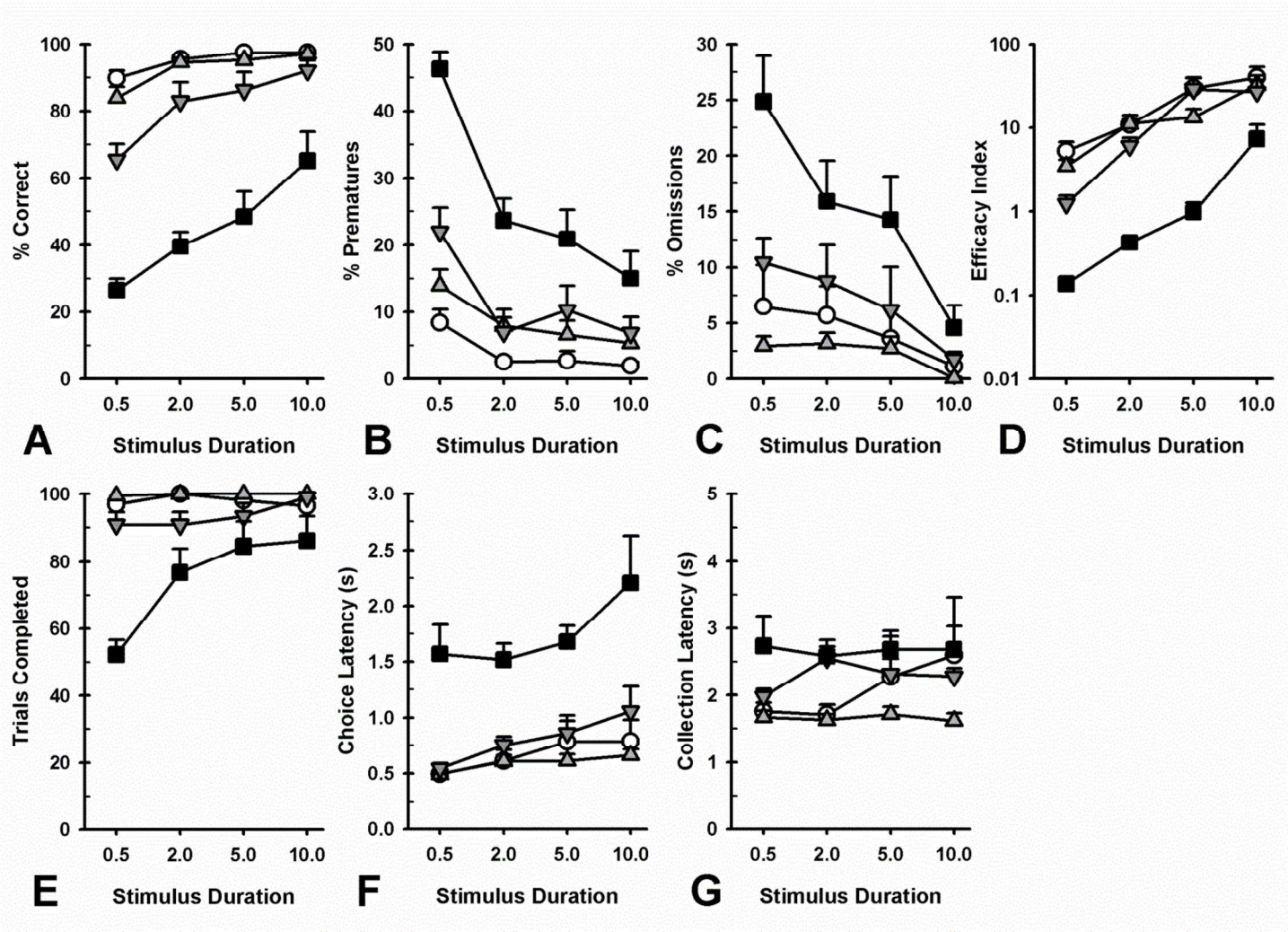
% Correct
% Prematures
% Omissions
Efficacy Index
Trials Completed
Choice Latency (s)
Collection Latency (s)
Stimulus Duration
A
B
C
D
E
F
G

Figure S3.

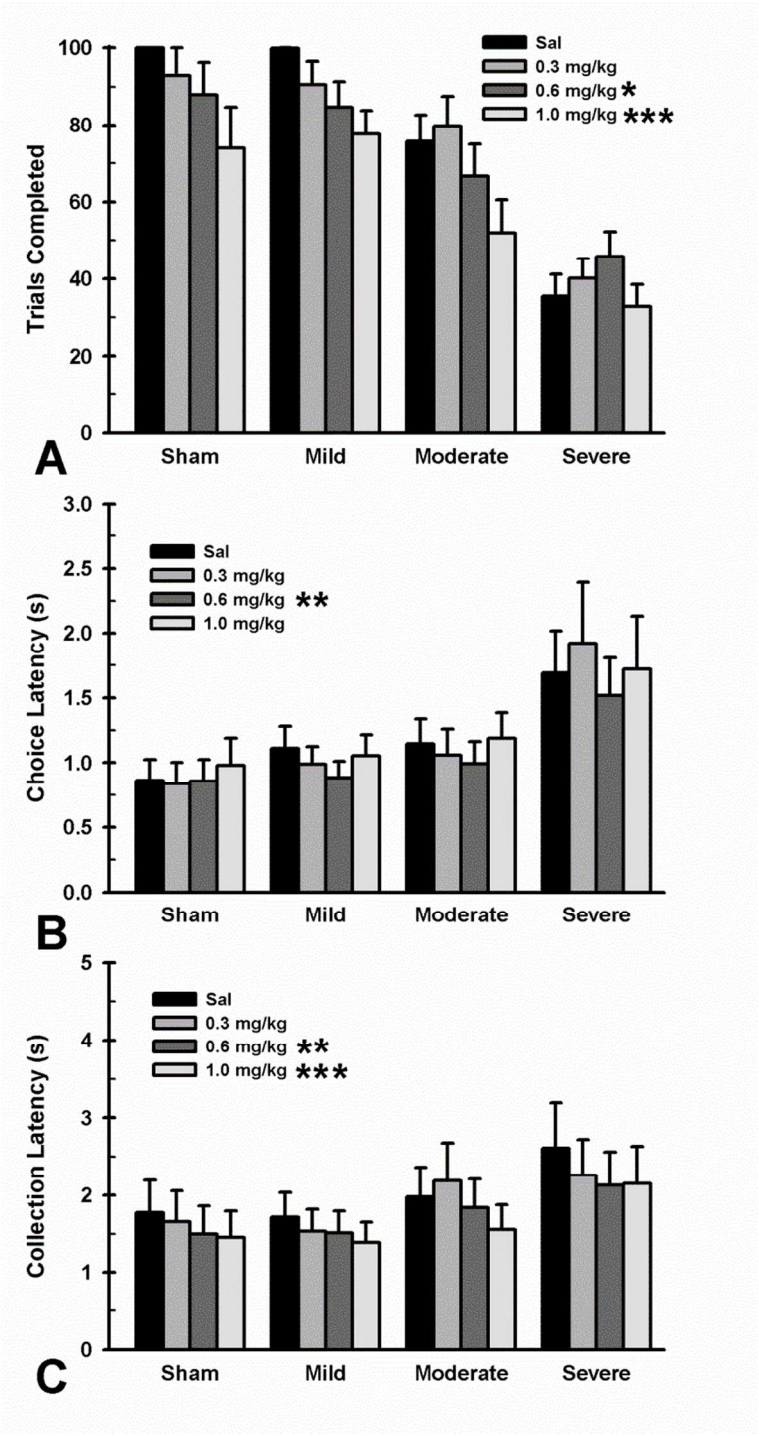
Trials Completed
100
80
60
40
20
0
Sal
0.3 mg/kg
0.6 mg/kg *
1.0 mg/kg ***
Sham
Mild
Moderate
Severe
A
Choice Latency (s)
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Sal
0.3 mg/kg
0.6 mg/kg **
1.0 mg/kg
Sham
Mild
Moderate
Severe
B
Collection Latency (s)
5
4
3
2
1
0
Sal
0.3 mg/kg
0.6 mg/kg **
1.0 mg/kg ***
Sham
Mild
Moderate
Severe
C

Figure S4.

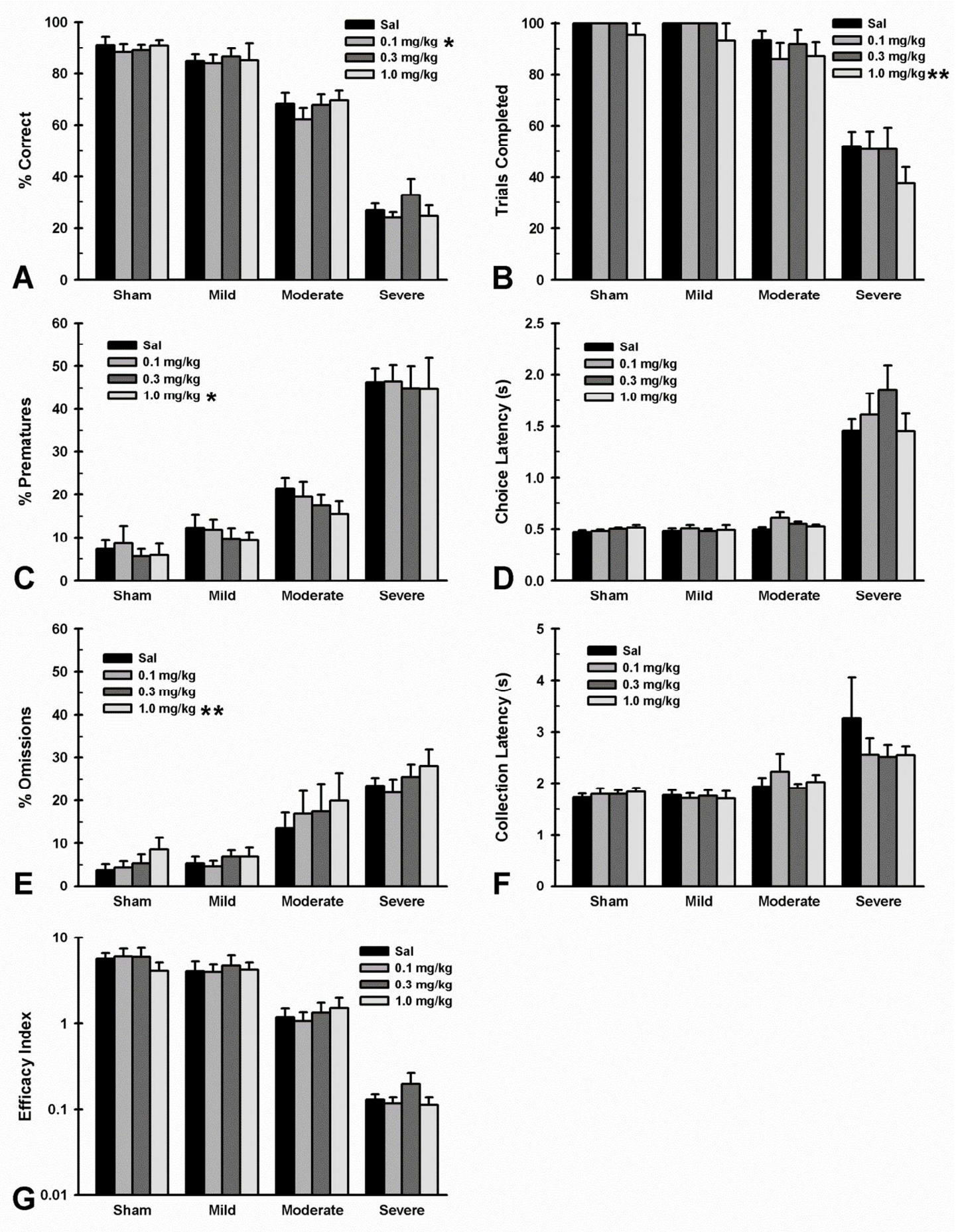
A
% Correct
100
80
60
40
20
0
Sal
0.1 mg/kg *
0.3 mg/kg
1.0 mg/kg
Sham
Mild
Moderate
Severe
B
Trials Completed
100
80
60
40
20
0
Sal
0.1 mg/kg
0.3 mg/kg
1.0 mg/kg **
Sham
Mild
Moderate
Severe
C
% Prematures
60
50
40
30
20
10
0
Sal
0.1 mg/kg
0.3 mg/kg
1.0 mg/kg *
Sham
Mild
Moderate
Severe
D
Choice Latency (s)
2.5
2.0
1.5
1.0
0.5
0.0
Sal
0.1 mg/kg
0.3 mg/kg
1.0 mg/kg
Sham
Mild
Moderate
Severe
E
% Omissions
60
50
40
30
20
10
0
Sal
0.1 mg/kg
0.3 mg/kg
1.0 mg/kg **
Sham
Mild
Moderate
Severe
F
Collection Latency (s)
5
4
3
2
1
0
Sal
0.1 mg/kg
0.3 mg/kg
1.0 mg/kg
Sham
Mild
Moderate
Severe
G
Efficacy Index
10
1
0.1
0.01
Sal
0.1 mg/kg
0.3 mg/kg
1.0 mg/kg
Sham
Mild
Moderate
Severe

Figure S5.

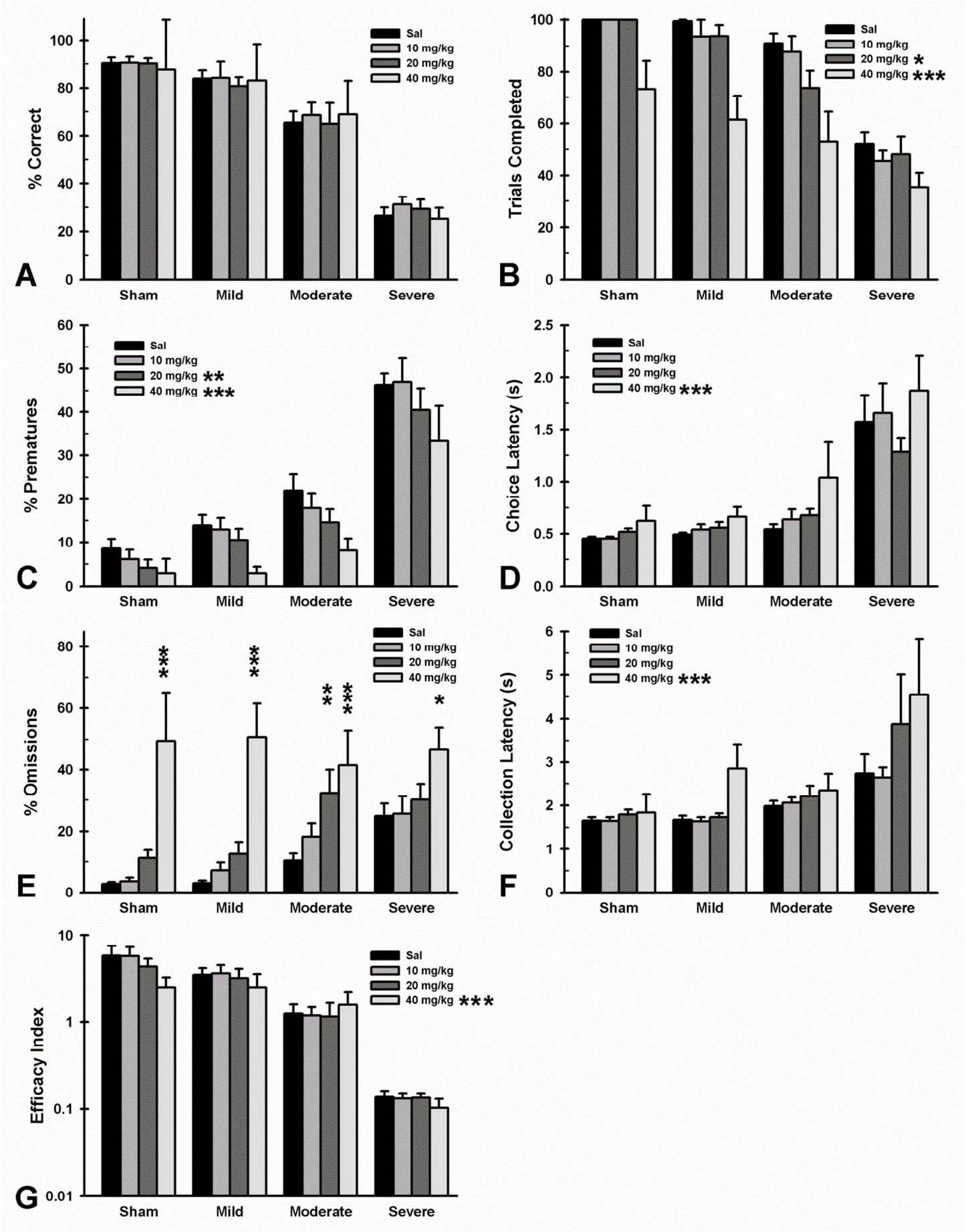
A
% Correct
Sal
10 mg/kg
20 mg/kg
40 mg/kg
Sham
Mild
Moderate
Severe
B
Trials Completed
20 mg/kg *
40 mg/kg ***
C
% Prematures
20 mg/kg **
40 mg/kg ***
D
Choice Latency (s)
E
% Omissions
F
Collection Latency (s)
G
Efficacy Index

Figure S6.

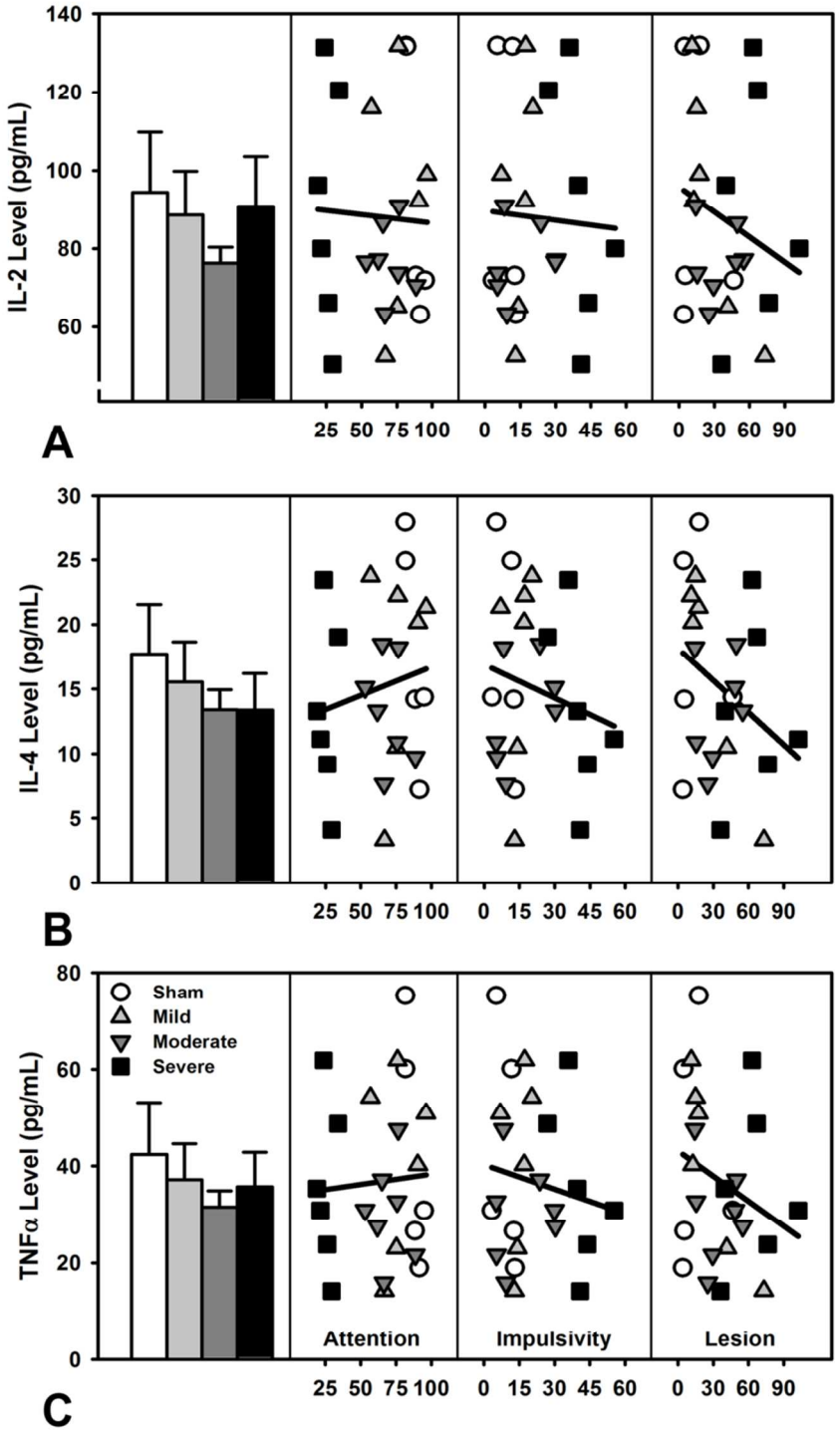
IL-2 Level (pg/mL)
140
120
100
80
60
A
IL-4 Level (pg/mL)
30
25
20
15
10
5
0
B
TNFα Level (pg/mL)
80
60
40
20
0
C
Sham
Mild
Moderate
Severe
Attention
Impulsivity
Lesion
25 50 75 100
0 15 30 45 60
0 30 60 90

Figure S7.

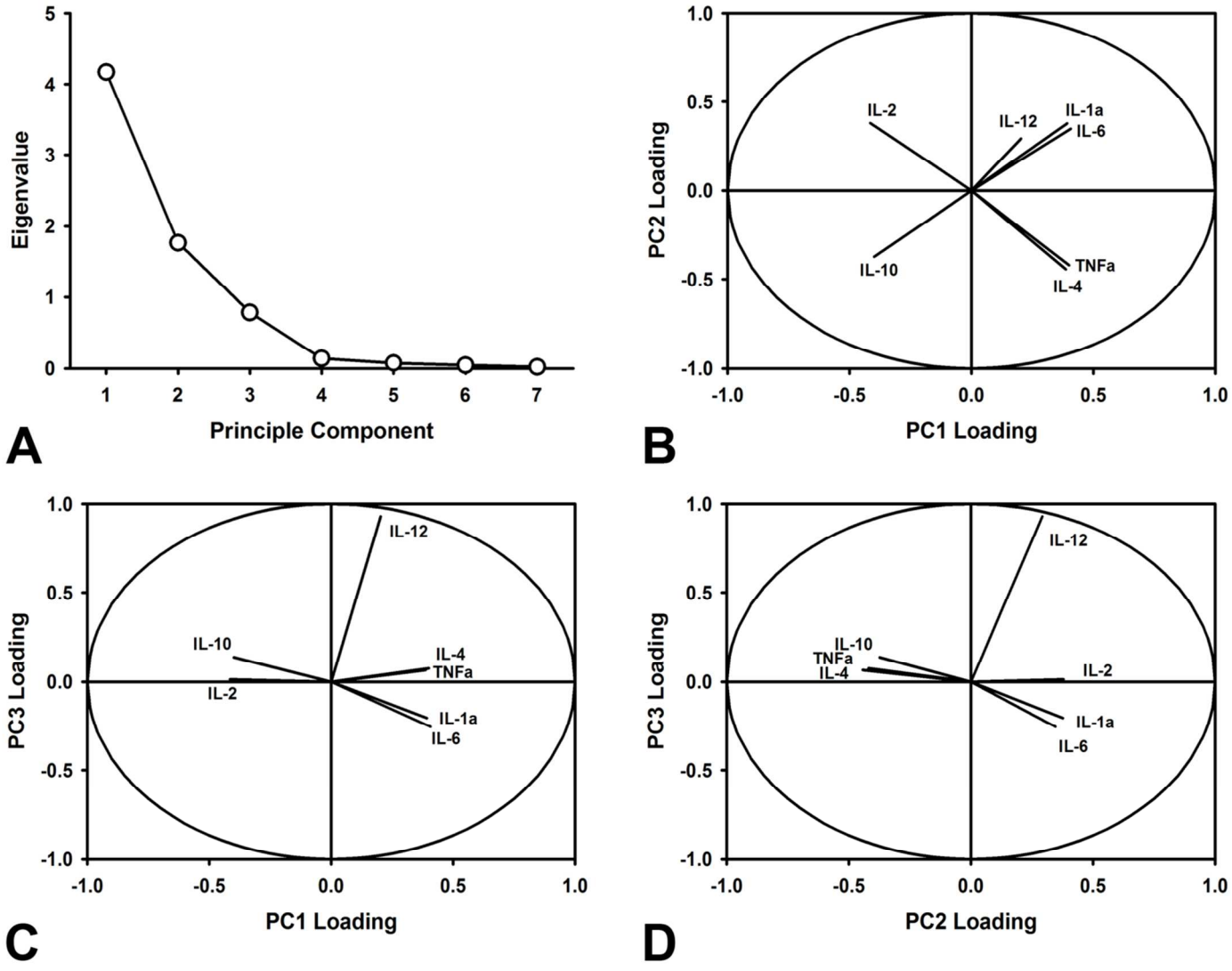
Eigenvalue
Principle Component
A
PC2 Loading
PC1 Loading
IL-2
IL-12
IL-1a
IL-6
IL-10
TNFa
IL-4
B
PC3 Loading
PC1 Loading
IL-12
IL-10
IL-4
TNFa
IL-2
IL-1a
IL-6
C
PC3 Loading
PC2 Loading
IL-12
IL-10
TNFa
IL-4
IL-2
IL-1a
IL-6
D

Figure S8.

Supplemental Figure Captions

Figure S1. Effects of injury on five-choice serial reaction time task performance at acute (week 2-5) and chronic (week 5-14) time points. A) Mild-injured rats showed a small decrease in trials completed in the acute phase ($p = 0.003$), which subsequently resolved at the chronic time point ($p = 0.813$), while both moderate- and severe-injured rats had deficits in the acute ($p < 0.001$; $p < 0.001$) and chronic ($p = 0.003$; $p < 0.001$) time points. B) Mild-injured rats had no deficits in choice latencies at acute ($p = 0.071$) or chronic ($p = 0.500$) time points, while both moderate- and severe-injured rats were impaired in the acute ($p < 0.001$; $p < 0.001$) and chronic ($p = 0.003$; $p < 0.001$) period. C) Mild-injured rats were unaffected on reinforcer collection latency during acute ($p = 0.848$) and chronic ($p = 0.654$) testing, while both moderate- and severe-injured rats took longer to collect during both acute ($p < 0.001$; $p < 0.001$) and chronic ($p = 0.031$; $p < 0.001$) testing. Data are mean + SEM.

Figure S2. Individual differences in five-choice serial reaction time task performance at acute (week 2-5) and chronic (week 5-14) time points and response to amphetamine. A) Resilient rats completed a similar amount of trials compared to pre-injury ($p = 0.115$), while vulnerable rats demonstrated initial acute deficits ($p < 0.001$) that recovered in the chronic period ($p = 0.505$), and chronically impaired rats had lower trials throughout acute ($p < 0.001$) and chronic testing ($p < 0.001$). B) Both resilient and vulnerable rats showed a transient increase in choice latency ($p = 0.031$; $p < 0.001$), that recovered during chronic testing ($p = 0.546$; $p = 0.077$), while chronically impaired rats had increased choice latencies in both the acute ($p < 0.001$) and chronic period ($p < 0.001$). C) Resilient rats had a small, nonsignificant increase in reinforcer collection latency during the acute period ($p = 0.057$) that normalized during chronic testing ($p = 0.332$), vulnerable rats

followed a similar pattern with an acute increase ($p = 0.008$) that recovered in the chronic period ($p = 0.371$), and chronically impaired rats showed increased collection latencies in both acute ($p < 0.001$) and chronic testing ($p < 0.001$). D) There were no susceptibility by dose interactions for amphetamine; the highest dose increased omissions overall ($p = 0.008$). E) Resilient rats showed decreased task efficacy at all doses of amphetamine (p's < 0.015), while vulnerable rats only showed detrimental effects at the highest dose ($p = 0.009$), and the chronically impaired rats showed no impairments at any dose (p's > 0.338). Data are mean + SEMs and individual data points in panels D and E, * = $p < 0.05$, ** = $p < 0.01$, ***= $p < 0.001$.

Figure S3. Five-choice serial reaction time task performance during the stimulus duration (SD) manipulation. A) Though there was an interaction in the rate of improvement, all groups improved their accuracy as the SD was increased (p's < 0.039). B) Despite an interaction between groups and SD, all groups reduced prematures as the SD was increased (p's < 0.004). C) Omissions were reduced in all groups at the 10 s SD (p's < 0.001), in all groups but the mild TBI group at the 5 s SD (p's < 0.001), and only in the severe TBI group at the 2 s SD ($p = 0.004$). D) All groups improved overall task efficacy at all SDs (p's < 0.007). E) Completed trials were increased at the 10 s SD for the moderate TBI group ($p = 0.012$) and increased in the Severe TBI group at all SDs (p's < 0.001). F) All groups had increased choice latencies at the 10 s SD ($p = 0.048$). G) All groups had increased reinforcer collection latencies at 5 and 10 s SDs (p's < 0.002). Data are mean + SEM.

Figure S4. Effects of amphetamine on five-choice serial reaction time task performance. A) All rats showed decreased trials at the 0.6 and 1.0 mg/kg dose (p's < 0.021). B) For all rats, choice latency was decreased at the 0.6 mg/kg dose ($p = 0.002$). C) Collection latencies were reduced in all

rats at the 0.6 and 1.0 mg/kg dose (p's < 0.002). Data are mean + SEM, * = p < 0.05, ** = p < 0.01, ***= p < 0.001.

Figure S5. Effects of atomoxetine on five-choice serial reaction time task performance. A) Accuracy was decreased in all rats at the 0.1 mg/kg dose (p = 0.049). B) Trials were decreased across groups at the 1.0 mg/kg dose (p = 0.003). C) For all rats, prematures were decreased at the 1.0 mg/kg dose (p = 0.013). D) Choice latencies were unaffected at any dose across the groups (p's > 0.063). E) Omissions were increased across groups at the 1.0 mg/kg dose (p = 0.002). F) Collection latencies were not changed by any dose (p's > 0.443). G) Task efficacy was unaffected at any dose across all groups (p's > 0.342). Data are mean + SEM, * = p < 0.05, ** = p < 0.01, ***= p < 0.001.

Figure S6. Effects of amantadine on five-choice serial reaction time task performance. A) Accuracy was unaffected at any dose across the groups (p's > 0.080). B) Trials were decreased at the 20 and 40 mg/kg dose (p's < 0.023). C) Prematures were decreased across all rats at the 20 and 40 mg/kg doses (p's < 0.002). D) Choice latencies were increased at the highest dose for all rats (p < 0.001). E) The moderate group had increased omissions at the 20 mg/kg dose (p = 0.002); all groups had increased omissions at the 40 mg/kg dose (p's < 0.011). F) Reinforcer collection latency was also increased at the 40 mg/kg dose (p < 0.001). G) At the 40 mg/kg dose, task efficacy was impaired across the groups (p < 0.001). Data are mean + SEM, * = p < 0.05, ** = p < 0.01, ***= p < 0.001.

Figure S7. Cytokine levels and their relationship to functional outcomes. A) IL-2 levels were not significantly different across the groups ($p = 0.866$), nor correlated with attention, impulsivity, or lesion size (p's > 0.750). B) There were no group differences in IL-4 levels ($p = 0.798$), nor significant correlations with attention, impulsivity, or lesion size (p's > 0.126). C) TNFα levels were not significantly increased following TBI ($p = 0.946$) and were not correlated with attention, impulsivity, or lesion size (p's > 0.424). Data are mean + SEM and individual data points.

Figure S8. Principle components analysis of neuroinflammation data. A) Skree plot demonstrating eigenvalues of all extracted components. The first three components accounted for 96% of the variance and were used for subsequent regression analyses. B) Component loadings of each cytokine on PC1 vs. PC2. Both components were dominated by largely pro- and anti-inflammatory loadings that are opposite each other (IL-2 opposite IL-4 and TNFα and IL-10 opposite IL-1α, IL-6 and IL-12). C) Component loadings for individual cytokines for PC1 vs. PC3. IL-12 is largely independent of other cytokine loadings. D) Component loadings for each cytokine in PC2 vs. PC3. IL-12 is again shown to be relatively independent. Data are eigenvalues in panel A and rotated component loadings in panels B-D.

		Pre-Injury Phase						Acute Post-Injury Phase						Chronic Post-Injury Phase					
		Sham vs. Mild	**Sham vs. Mod**	**Sham vs. Sev**	**Mild vs. Mod**	**Mild vs. Sev**	**Mod vs. Sev**	**Sham vs. Mild**	**Sham vs. Mod**	**Sham vs. Sev**	**Mild vs. Mod**	**Mild vs. Sev**	**Mod vs. Sev**	**Sham vs. Mild**	**Sham vs. Mod**	**Sham vs. Sev**	**Mild vs. Mod**	**Mild vs. Sev**	**Mod vs. Sev**
Accuracy	**β**	-0.02	-0.03	-0.02	-0.01	0.00	0.01	-0.15	-0.42	-0.60	-0.26	-0.45	-0.18	-0.07	-0.30	-0.74	-0.23	-0.67	-0.43
	t	-0.41	-0.61	-0.39	-0.24	0.00	0.23	-2.97	-7.85	-11.01	-5.53	-9.05	-3.53	-1.32	-5.54	-13.03	-4.87	-13.35	-8.40
	p	0.684	0.542	0.699	0.811	0.999	0.820	**0.004**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**0.001**	0.189	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**
Prematures	**β**	0.04	0.03	0.04	-0.01	0.01	0.01	0.16	0.32	0.34	0.16	0.18	0.02	0.10	0.21	0.51	0.11	0.41	0.30
	t	0.67	0.54	0.75	-0.13	0.13	0.24	3.45	6.64	6.96	3.67	4.06	0.46	1.96	4.10	9.84	2.52	9.06	6.39
	p	0.503	0.592	0.452	0.898	0.900	0.808	**0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	0.644	0.052	**<0.001**	**<0.001**	**0.013**	**<0.001**	**<0.001**
Omissions	**β**	0.02	-0.01	-0.02	-0.02	-0.04	-0.02	0.08	0.36	0.53	0.28	0.45	0.18	0.01	0.13	0.32	0.13	0.31	0.18
	t	0.25	-0.08	-0.30	-0.36	-0.60	-0.24	1.31	5.72	8.40	4.94	7.90	2.97	0.13	2.08	4.74	2.23	5.24	2.99
	p	0.801	0.935	0.763	0.717	0.549	0.813	0.192	**0.000**	**0.000**	**0.000**	**0.000**	**0.004**	0.899	**0.040**	**<0.001**	**0.027**	**<0.001**	**0.003**
Efficacy Index	**β**	-0.18	-0.12	-0.08	0.06	0.10	0.04	-0.89	-2.41	-3.36	-1.52	-2.46	-0.94	-0.44	-1.52	-3.69	-1.08	-3.25	-2.17
	t	-0.64	-0.42	-0.27	0.23	0.38	0.15	-3.33	-8.75	-11.92	-6.12	-9.67	-3.57	-1.59	-5.34	-12.51	-4.34	-12.47	-8.05
	p	0.521	0.675	0.784	0.821	0.707	0.881	**0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**0.001**	0.115	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**
Trials	**β**	0.01	0.03	0.02	0.02	0.01	-0.01	-0.19	-0.67	-0.89	-0.48	-0.70	-0.22	-0.02	-0.20	-0.80	-0.19	-0.78	-0.59
	t	0.18	0.42	0.25	0.27	0.09	-0.17	-3.02	-10.26	-13.35	-8.13	-11.58	-3.51	-0.24	-3.00	-11.34	-3.17	-12.59	-9.20
	p	0.860	0.677	0.801	0.786	0.927	0.867	**0.003**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**0.001**	0.813	**0.003**	**<0.001**	**0.002**	**<0.001**	**<0.001**
Choice Latency	**β**	-0.07	-0.05	-0.08	0.02	-0.01	-0.03	0.13	0.49	0.87	0.36	0.74	0.38	0.05	0.24	1.12	0.19	1.07	0.88
	t	-0.85	-0.55	-0.91	0.30	-0.12	-0.40	1.82	6.48	11.33	5.23	10.60	5.30	0.68	3.08	13.91	2.77	15.03	11.90
	p	0.397	0.583	0.361	0.761	0.907	0.688	0.071	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	0.500	**0.003**	**<0.001**	**0.006**	**<0.001**	**<0.001**
Collection Latency	**β**	-0.08	0.07	-0.03	0.15	0.05	-0.10	0.01	0.32	0.62	0.31	0.61	0.30	-0.03	0.17	0.44	0.21	0.48	0.27
	t	-0.95	0.88	-0.32	2.00	0.65	-1.27	0.19	4.21	7.94	4.47	8.57	4.05	-0.45	2.18	5.40	2.99	6.59	3.59
	p	0.341	0.383	0.747	**0.047**	0.517	0.207	0.848	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	0.654	**0.031**	**<0.001**	**0.003**	**<0.001**	**<0.001**

Supplemental Table 1. Behavioral assessment of TBI.

		Acute Post-Injury Phase			Acute Post-Injury Phase			Chronic Post-Injury Phase		
		Res. vs. Vul.	Res. vs. Imp.	Vul. vs. Imp.	Res. vs. Vul.	Res. vs. Imp.	Vul. vs. Imp.	Res. vs. Vul.	Res. vs. Imp.	Vul. vs. Imp.
Accuracy	**β**	0.00	-0.01	0.01	-0.33	-0.46	-0.13	-0.20	-0.62	-0.41
	t	0.07	-0.17	0.23	-6.28	-10.02	-2.62	-3.84	-13.34	-8.44
	p	0.944	0.869	0.817	**<0.001**	**<0.001**	**0.010**	**<0.001**	**<0.001**	**<0.001**
Prematures	**β**	-0.05	-0.01	0.03	0.13	0.22	0.09	0.06	0.37	0.30
	t	-0.82	-0.25	0.66	2.58	5.06	1.97	1.28	8.42	6.49
	p	0.412	0.802	0.513	**0.011**	**<0.001**	0.052	0.203	**<0.001**	**<0.001**
Omissions	**β**	-0.02	0.01	0.03	0.38	0.50	0.11	0.11	0.34	0.23
	t	-0.31	0.11	0.44	6.62	9.85	2.12	1.84	6.63	4.23
	p	0.756	0.910	0.657	**<0.001**	**<0.001**	**0.036**	0.068	**<0.001**	**<0.001**
Efficacy Index	**β**	0.17	0.00	-0.16	-1.85	-2.60	-0.75	-0.93	-3.04	-2.11
	t	0.61	0.01	-0.65	-7.13	-11.50	-3.14	-3.57	-13.32	-8.72
	p	0.543	0.992	0.514	**<0.001**	**<0.001**	**0.002**	**0.001**	**<0.001**	**<0.001**
Trials	**β**	0.03	0.01	-0.01	-0.45	-0.71	-0.26	-0.04	-0.64	-0.60
	t	0.32	0.19	-0.16	-5.93	-10.74	-3.70	-0.55	-9.55	-8.37
	p	0.750	0.847	0.871	**<0.001**	**<0.001**	**0.000**	0.583	**<0.001**	**<0.001**
Choice Latency	**β**	0.06	0.03	-0.03	0.45	0.74	0.29	0.19	0.86	0.67
	t	0.53	0.33	-0.27	4.62	8.75	3.25	1.95	10.13	7.40
	p	0.595	0.744	0.788	**<0.001**	**<0.001**	**0.002**	0.054	**<0.001**	**<0.001**
Collection Latency	**β**	0.18	0.10	-0.08	0.27	0.51	0.24	0.18	0.38	0.20
	t	1.76	1.15	-0.83	2.96	6.37	2.80	1.91	4.69	2.35
	p	0.080	0.254	0.408	**0.004**	**<0.001**	**0.006**	0.059	**<0.001**	**0.021**
		Resilient			**Vulnerable**			**Chronically Impaired**		
		Pre vs. Acute	Pre vs. Chronic	Acute vs. Chronic	Pre vs. Acute	Pre vs. Chronic	Acute vs. Chronic	Pre vs. Acute	Pre vs. Chronic	Acute vs. Chronic
Accuracy	**β**	-0.10	-0.02	0.09	-0.44	-0.22	0.22	-0.56	-0.62	-0.07
	t	-2.03	-0.29	1.78	-7.78	-3.92	3.95	-13.20	-14.68	-1.61
	p	**0.045**	0.770	0.078	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	0.110
Prematures	**β**	0.07	0.03	-0.04	0.25	0.14	-0.11	0.30	0.41	0.11
	t	1.46	0.63	-0.90	4.46	2.55	-2.03	7.31	9.77	2.74
	p	0.145	0.529	0.369	**<0.001**	**0.012**	**0.045**	**<0.001**	**<0.001**	**0.007**
Omissions	**β**	0.03	-0.08	-0.11	0.44	0.05	-0.39	0.52	0.25	-0.27
	t	0.58	-1.33	-2.03	6.79	0.77	-6.35	10.92	5.22	-5.90
	p	0.565	0.186	**0.045**	**<0.001**	0.445	**<0.001**	**<0.001**	**<0.001**	**<0.001**
Efficacy Index	**β**	-0.55	0.02	0.57	-2.56	-1.08	1.49	-3.15	-3.02	0.13
	t	-2.17	0.08	2.30	-9.21	-3.85	5.47	-15.19	-14.42	0.62
	p	**0.032**	0.940	**0.023**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	0.536
Trials	**β**	-0.12	0.01	0.13	-0.60	-0.06	0.54	-0.85	-0.64	0.20
	t	-1.59	0.17	1.84	-7.19	-0.67	6.78	-13.62	-10.20	3.39
	p	0.115	0.867	0.068	**<0.001**	0.505	**<0.001**	**<0.001**	**<0.001**	**0.001**
Choice Latency	**β**	0.21	0.06	-0.15	0.60	0.19	-0.41	0.92	0.89	-0.03
	t	2.18	0.61	-1.66	5.63	1.78	-4.02	11.52	11.06	-0.36
	p	**0.031**	0.546	0.100	**<0.001**	0.077	**<0.001**	**<0.001**	**<0.001**	0.716
Collection Latency	**β**	0.18	0.09	-0.09	0.27	0.09	-0.18	0.59	0.37	-0.22
	t	1.92	0.97	-0.99	2.72	0.90	-1.88	7.85	4.88	-2.99
	p	0.057	0.332	0.325	**0.008**	0.371	0.063	**<0.001**	**<0.001**	**0.003**

Supplemental Table 2. Differences in injury susceptibility.

		SumSq	MeanSq	NumDF	DenDF	F	p			Sal vs. Low	Sal vs. Med	Sal vs. High
Accuracy	**Group**	1.46	0.49	3	42.17	51.93	**<0.001**	**Sham**	**β**	-0.07	-0.12	-0.12
	Dose	0.04	0.01	3	117.99	1.32	0.271		**t**	-1.49	-2.67	-2.55
	Group*Dose	0.21	0.02	9	117.84	2.58	**0.009**		**p**	0.140	**0.009**	**0.012**
								Mild	**β**	-0.02	-0.02	-0.07
									t	-0.48	-0.59	-1.96
									p	0.635	0.554	0.052
								Moderate	**β**	-0.03	-0.05	-0.06
									t	-0.71	-1.24	-1.44
									p	0.477	0.216	0.151
								Severe	**β**	0.02	0.02	0.15
									t	0.44	0.52	3.18
									p	0.663	0.601	**0.002**
Prematures	**Group**	0.63	0.21	3	41.85	5.54	**0.003**	**Sham**	**β**	0.19	0.21	0.38
	Dose	0.74	0.25	3	123.41	5.20	**0.002**		**t**	2.09	2.27	4.19
	Group*Dose	1.34	0.15	9	123.38	4.01	**<0.001**		**p**	**0.039**	**0.025**	**<0.001**
								Mild	**β**	0.16	0.26	0.34
									t	2.21	3.72	4.90
									p	**0.029**	**<0.001**	**<0.001**
								Moderate	**β**	0.03	0.13	0.11
									t	0.33	1.53	1.35
									p	0.739	0.128	0.181
								Severe	**β**	0.00	-0.10	-0.21
									t	-0.03	-1.17	-2.47
									p	0.975	0.244	**0.015**
Omissions	**Group**	2.22	0.74	3	42.28	23.69	**<0.001**	**All**	**β**	-0.05	0.00	0.11
	Dose	0.62	0.21	3	133.59	6.54	**<0.001**		**t**	-1.35	0.04	2.96
									p	0.181	0.970	**0.004**
Index	**Group**	51.29	17.10	3	42.80	32.65	**<0.001**	**All**	**β**	-0.32	-0.54	-0.95
	Dose	19.86	6.62	3	128.21	12.36	**<0.001**		**t**	-2.03	-3.44	-5.92
									p	**0.044**	**0.001**	**<0.001**
Trials	**Group**	4.62	1.54	3	41.99	25.18	**<0.001**	**All**	**β**	-0.03	-0.12	-0.29
	Dose	2.39	0.80	3	134.95	13.03	**<0.001**		**t**	-0.65	-2.36	-5.70
									p	0.517	**0.020**	**<0.001**
Choice Latency	**Group**	0.43	0.14	3	42.04	3.01	**0.041**	**All**	**β**	-0.05	-0.15	-0.03
	Dose	0.56	0.19	3	132.06	3.80	**0.012**		**t**	-1.14	-3.18	-0.63
									p	0.258	**0.002**	0.528
Collection Latency	**Group**	0.64	0.21	3	23.15	10.50	**<0.001**	**All**	**β**	-0.06	-0.14	-0.21
	Dose	0.68	0.23	3	76.48	11.25	**<0.001**		**t**	-1.64	-3.63	-5.45
									p	0.104	**0.001**	**<0.001**

Supplemental Table 3. Effects of amphetamine.

		SumSq	MeanSq	NumDF	DenDF	F	p			Sal vs. Low	Sal vs. Med	Sal vs. High
Accuracy	**Susceptibility**	0.98	0.49	2	32.89	53.31	**<0.001**	**Resilient**	**β**	-0.03	-0.07	-0.123
	Dose	0.01	0.00	3	93.46	0.44	0.723		**t**	-0.83	-1.84	-3.176
	Suscept.*Dose	0.23	0.04	6	93.51	4.25	**0.001**		**p**	0.409	0.069	**0.002**
								Vulnerable	**β**	-0.04	-0.01	-0.071
									t	-0.79	-0.13	-1.501
									p	0.43	0.89	0.137
								Impaired	**β**	0.02	0.02	0.116
									t	0.53	0.56	3.217
									p	0.598	0.579	**0.002**
Omissions	**Susceptibility**	3.83	1.91	2	34.18	55.85	**<0.001**	**All**	**β**	-0.05	-0.01	0.118
	Dose	0.56	0.19	3	107.06	5.44	**0.002**		**t**	-1.07	-0.33	0.739
									p	0.29	0.74	**0.008**
Prematures	**Susceptibility**	0.51	0.25	2	33.35	7.15	**0.003**	**Resilient**	**β**	0.19	0.35	0.434
	Dose	0.34	0.11	3	98.90	4.94	**0.003**		**t**	2.51	4.52	5.682
	Suscept.*Dose	1.58	0.26	6	98.95	7.50	**<0.001**		**p**	**0.014**	**<0.001**	**<0.001**
								Vulnerable	**β**	0.00	0.11	0.219
									t	0.02	1.22	2.340
									p	0.982	0.225	**0.021**
								Impaired	**β**	0.02	-0.05	-0.171
									t	0.29	-0.74	-2.564
									p	0.776	0.463	**0.012**
Index	**Susceptibility**	44.08	22.04	2	34.01	53.07	**<0.001**	**Resilient**	**β**	-0.68	-1.25	-1.761
	Dose	10.29	3.43	3	94.73	8.79	**<0.001**		**t**	-2.59	-4.77	-6.744
	Suscept.*Dose	15.17	2.53	6	94.84	6.18	**<0.001**		**p**	**0.011**	**<0.001**	**<0.001**
								Vulnerable	**β**	0.05	-0.10	-0.852
									t	0.17	-0.30	-2.664
									p	0.865	0.765	**0.009**
								Impaired	**β**	0.00	0.04	0.242
									t	-0.02	0.19	0.962
									p	0.985	0.848	0.338

Supplemental Table 4. Effects of amphetamine across injury susceptibilities.

		SumSq	MeanSq	NumDF	DenDF	F	p			Sal vs. Low	Sal vs. Med	Sal vs. High
Accuracy	**Group**	1.32	0.44	3	42.05	65.03	**<0.001**	**All**	**β**	-0.03	0.02	0.01
	Dose	0.07	0.02	3	131.16	3.39	**0.020**		**t**	-1.99	0.97	0.54
									p	**0.049**	0.332	0.587
Prematures	**Group**	0.95	0.32	3	42.08	36.09	**<0.001**	**All**	**β**	-0.01	-0.04	-0.05
	Dose	0.07	0.02	3	133.14	2.80	**0.043**		**t**	-0.46	-1.91	-2.51
									p	0.648	0.059	**0.013**
Omissions	**Group**	0.28	0.09	3	42.03	12.57	**<0.001**	**All**	**β**	0.00	0.03	0.06
	Dose	0.11	0.04	3	133.00	4.86	**0.003**		**t**	0.00	1.86	3.20
									p	0.998	0.065	**0.002**
Index	**Group**	29.36	9.79	3	42.07	57.67	**<0.001**	**All**	**β**	-0.08	0.08	0.00
	Dose	0.59	0.20	3	131.23	1.15	0.331		**t**	-0.90	0.95	-0.06
									p	0.368	0.342	0.956
Trials	**Group**	4.71	1.57	3	42.00	50.70	**<0.001**	**All**	**β**	-0.03	0.00	-0.11
	Dose	0.37	0.12	3	134.92	3.93	**0.010**		**t**	-0.81	-0.11	-3.02
									p	0.421	0.911	**0.003**
Choice Latency	**Group**	16.35	5.45	3	42.11	114.82	**<0.001**	**All**	**β**	0.07	0.09	0.02
	Dose	0.23	0.08	3	134.35	1.61	0.190		**t**	1.59	1.88	0.44
									p	0.114	0.063	0.659
Collection Latency	**Group**	0.91	0.30	3	41.76	9.46	**<0.001**	**All**	**β**	-0.02	-0.03	-0.01
	Dose	0.02	0.01	3	133.85	0.22	0.883		**t**	-0.46	-0.77	-0.22
									p	0.644	0.443	0.830

Supplemental Table 5. Effects of atomoxetine.

		SumSq	MeanSq	NumDF	DenDF	F	p			Sal vs. Low	Sal vs. Med	Sal vs. High
Accuracy	**Group**	1.48	0.49	3	43.24	54.93	**<0.001**	**All**	**β**	0.03	-0.01	-0.04
	Dose	0.08	0.03	3	120.57	2.87	**0.039**		**t**	1.31	-0.45	-1.77
									p	0.194	0.655	0.080
Prematures	**Group**	1.63	0.54	3	44.50	33.10	**<0.001**	**All**	**β**	-0.04	-0.09	-0.21
	Dose	1.12	0.37	3	136.46	23.00	**<0.001**		**t**	-1.42	-3.45	-7.84
									p	0.158	**0.001**	**<0.001**
Omissions	**Group**	0.47	0.16	3	43.95	3.25	**0.031**	**Sham**	**β**	0.01	0.17	0.65
	Dose	6.90	2.30	3	127.01	43.00	**<0.001**		**t**	0.09	1.58	6.17
	Group*Dose	1.09	0.12	9	127.03	2.45	**0.013**		**p**	0.925	0.116	**<0.001**
								Mild	**β**	0.07	0.16	0.68
									t	0.85	1.94	8.15
									p	0.394	0.054	**<0.001**
								Moderate	**β**	0.10	0.27	0.40
									t	1.11	3.09	4.18
									p	0.268	**0.002**	**<0.001**
								Severe	**β**	-0.01	0.06	0.25
									t	-0.12	0.61	2.60
									p	0.907	0.543	**0.010**
Index	**Group**	55.74	18.58	3	44.05	41.28	**<0.001**	**All**	**β**	-0.02	-0.23	-0.78
	Dose	13.78	4.59	3	124.98	10.30	**<0.001**		**t**	-0.13	-1.68	-5.00
									p	0.895	0.095	**<0.001**
Trials	**Group**	4.36	1.45	3	43.99	23.64	**<0.001**	**All**	**β**	-0.05	-0.12	-0.43
	Dose	5.50	1.83	3	140.94	29.79	**<0.001**		**t**	-0.93	-2.32	-8.56
									p	0.353	**0.022**	**<0.001**
Choice Latency	**Group**	10.28	3.43	3	44.49	40.62	**<0.001**	**All**	**β**	0.07	0.08	0.32
	Dose	2.26	0.75	3	133.16	9.13	**<0.001**		**t**	1.12	1.29	5.00
									p	0.266	0.200	**<0.001**
Collection Latency	**Group**	2.30	0.77	3	43.30	11.06	**<0.001**	**All**	**β**	0.00	0.10	0.30
	Dose	2.31	0.77	3	131.73	11.59	**<0.001**		**t**	0.09	1.84	5.26
									p	0.932	0.069	**<0.001**

Supplemental Table 6. Effects of amantadine.

	ANOVA				Tukey HSD		
	Num DF	**Den DF**	**F**	**p**	**Comparison**	**Difference**	**p**
IL1a	3	20	1.28	0.307			
IL2	3	20	0.24	0.866			
IL4	3	20	0.34	0.798			
IL6	3	20	1.74	0.190			
IL10	3	20	1.84	0.172			
IL12	3	20	5.46	**0.007**	Sham v. Mild	0.93	**0.004**
					Sham v. Mod	0.71	**0.040**
					Sham v. Sev	0.68	0.053
					Mild v. Mod	-0.22	0.760
					Mild v. Sev	-0.25	0.677
					Mod v. Sev	-0.03	0.999
TNFa	3	20	0.12	0.946			

Supplemental Table 7. Analysis of variance for cytokines.

		IL1a	IL2	IL4	IL6	IL10	IL12	TNFa	Lesion	Accuracy	Prematures
IL1a	**r**	-									
	p	-									
IL2	**r**	-0.43	-								
	p	**0.001**	-								
IL4	**r**	0.37	-0.95	-							
	p	**0.006**	**<0.001**	-							
IL6	**r**	0.91	-0.48	0.38	-						
	p	**<0.001**	**<0.001**	**0.004**	-						
IL10	**r**	-0.87	0.44	-0.35	-0.91	-					
	p	**<0.001**	**0.001**	**0.010**	**<0.001**	-					
IL12	**r**	0.38	-0.15	0.16	0.34	-0.42	-				
	p	**0.005**	0.283	0.257	**0.011**	**0.001**	-				
TNFa	**r**	0.35	-0.96	0.96	0.41	-0.40	0.18	-			
	p	**0.010**	**<0.001**	**<0.001**	**0.002**	**0.003**	0.204	-			
Lesion	**r**	0.33	0.04	-0.14	0.36	-0.53	0.34	-0.03	-		
	p	**0.016**	0.766	0.307	**0.008**	**<0.001**	**0.011**	0.848	-		
Accuracy	**r**	-0.40	-0.04	0.21	-0.48	0.57	-0.30	0.11	-0.70	-	
	p	**0.003**	0.751	0.127	**<0.001**	**<0.001**	**0.027**	0.425	**<0.001**	-	
Prematures	**r**	0.44	-0.01	-0.09	0.52	-0.63	0.28	-0.01	0.61	-0.83	-
	p	**0.001**	0.962	0.516	**<0.001**	**<0.001**	**0.038**	0.945	**<0.001**	**<0.001**	-

Supplemental Table 8. Correlation matrix for cytokines and functional outcomes.

		PC1	PC2	PC3	PC4	PC5	PC6	PC7
Components	**Eigenvalue**	4.17	1.76	0.78	0.14	0.07	0.05	0.02
	Proportion Variance	**0.60**	**0.25**	**0.11**	0.02	0.01	0.01	0.00
Rotation	**IL1a**	**0.39**	**0.38**	-0.21				
	IL2	**-0.42**	**0.38**	0.01				
	IL4	**0.39**	**-0.44**	0.07				
	IL6	**0.41**	**0.35**	-0.25				
	IL10	**-0.40**	**-0.37**	0.14				
	IL12	0.20	0.29	**0.93**				
	TNFa	**0.40**	**-0.42**	0.07				

Supplemental Table 9. Principle components analysis eigenvalues and rotation of key components.

			β	t	p
Chronic Behavior	**Accuracy**	**Lesion**	-0.67	-4.32	**<0.001**
	Prematures	**Lesion**	0.40	2.32	**0.030**
		PC2	0.38	2.24	**0.036**
	Omissions	*no sig predictors*			
	Index	**Lesion**	-0.64	-3.87	**0.001**
Recovery	**Accuracy**	**Lesion**	-0.46	-2.19	**0.043**
	Prematures	**Lesion**	-0.43	-2.48	**0.024**
		PC1	-0.36	-2.06	0.056
	Omissions	**Lesion**	-0.34	-1.70	0.108
	Index	**Lesion**	-0.53	-2.57	**0.020**

Supplemental Table 10. Regression analyses of the contribution of neuroinflammation and lesion volume to chronic behavioral outcomes and degree of recovery.

		0.5s vs. 2s	0.5s vs. 5s	0.5s vs. 10s	0.5s vs. 2s	0.5s vs. 5s	0.5s vs. 10s	0.5s vs. 2s	0.5s vs. 5s	0.5s vs. 10s	0.5s vs. 2s	0.5s vs. 5s	0.5s vs. 10s
		Accuracy			**Prematures**			**Omissions**			**Trials**		
Sham	**β**	0.14	0.18	0.17	-0.13	-0.16	-0.16	-0.05	-0.14	-0.20	0.04	0.00	-0.02
	t	2.66	3.50	3.31	-3.02	-3.74	-3.73	-1.41	-3.59	-5.35	0.77	-0.01	-0.35
	p	**0.009**	**0.001**	**0.001**	**0.003**	**<0.001**	**<0.001**	0.160	**<0.001**	**<0.001**	0.443	0.988	0.727
Mild	**β**	0.17	0.17	0.22	-0.15	-0.17	-0.20	-0.03	-0.06	-0.17	0.01	0.01	0.01
	t	3.94	4.01	5.11	-4.36	-4.93	-5.56	-0.89	-1.89	-5.64	0.18	0.18	0.18
	p	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	0.377	0.061	**<0.001**	0.854	0.854	0.854
Moderate	**β**	0.20	0.28	0.35	-0.21	-0.17	-0.23	-0.03	-0.14	-0.21	-0.02	0.03	0.13
	t	4.42	6.12	7.78	-5.52	-4.51	-6.11	-1.05	-4.31	-6.35	-0.38	0.51	2.54
	p	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	0.296	**<0.001**	**<0.001**	0.706	0.608	**0.012**
Severe	**β**	0.10	0.19	0.41	-0.20	-0.25	-0.37	-0.10	-0.14	-0.33	0.30	0.43	0.47
	t	2.10	3.99	8.46	-4.99	-6.14	-9.06	-2.92	-4.03	-9.29	5.59	8.03	8.65
	p	**0.038**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**0.004**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**
		Efficacy Index			**Choice Latency**			**Collection Latency**					
All	**β**	0.92	1.62	1.94	-0.04	0.10	0.15	0.15	0.33	0.35			
	t	2.77	4.86	5.82	-0.51	1.35	2.00	1.64	3.53	3.80			
	p	**0.006**	**<0.001**	**<0.001**	0.612	0.178	**0.048**	0.103	**0.001**	**<0.001**			

		Sham vs. Mild	Sham vs. Mod	Sham vs. Sev	Mild vs. Mod	Mild vs. Sev	Mod vs. Sev	Sham vs. Mild	Sham vs. Mod	Sham vs. Sev	Mild vs. Mod	Mild vs. Sev	Mod vs. Sev
		Accuracy						**Prematures**					
0.5 s	**β**	-0.05	-0.26	-0.67	-0.21	-0.62	-0.41	0.11	0.15	0.43	0.05	0.32	0.28
	t	-0.69	-3.41	-8.61	-3.04	-8.78	-5.66	1.55	2.17	5.98	0.73	4.98	4.13
	p	0.491	**0.001**	**<0.001**	**0.003**	**<0.001**	**<0.001**	0.125	**0.033**	**<0.001**	0.466	**<0.001**	**<0.001**
2 s	**β**	-0.02	-0.20	-0.71	-0.17	-0.68	-0.51	0.08	0.07	0.36	-0.01	0.28	0.28
	t	-0.30	-2.58	-9.16	-2.54	-9.81	-7.08	1.21	1.04	5.02	-0.15	4.27	4.27
	p	0.764	**0.012**	**0.000**	**0.013**	**0.000**	**0.000**	0.230	0.300	**<0.001**	0.885	**<0.001**	**<0.001**
5 s	**β**	-0.06	-0.16	-0.66	-0.10	-0.60	-0.50	0.09	0.14	0.34	0.05	0.25	0.20
	t	-0.85	-2.14	-8.53	-1.46	-8.54	-6.88	1.37	2.03	4.80	0.78	3.86	3.00
	p	0.398	**0.035**	**<0.001**	0.148	**<0.001**	**<0.001**	0.176	**0.046**	**<0.001**	0.437	**<0.001**	**0.004**
10 s	**β**	-0.01	-0.08	-0.43	-0.07	-0.43	-0.36	0.07	0.08	0.22	0.01	0.15	0.14
	t	-0.09	-1.02	-5.61	-1.04	-6.11	-4.93	1.04	1.16	3.13	0.17	2.37	2.13
	p	0.932	0.310	**<0.001**	0.301	**<0.001**	**<0.001**	0.304	0.250	**0.002**	0.864	**0.020**	**0.036**
		Omissions						**Trials**					
0.5	**β**	-0.07	0.04	0.24	0.11	0.31	0.20	0.04	-0.11	-0.65	-0.15	-0.69	-0.54
	t	-1.11	0.72	3.78	1.99	5.33	3.29	0.42	-1.30	-7.34	-1.90	-8.53	-6.49
	p	0.271	0.473	**<0.001**	**0.050**	**<0.001**	**0.001**	0.672	0.198	**<0.001**	0.061	**<0.001**	**<0.001**
2	**β**	-0.04	0.06	0.19	0.10	0.23	0.13	0.00	-0.18	-0.39	-0.18	-0.39	-0.22
	t	-0.67	1.02	3.02	1.86	4.05	2.16	0.00	-2.03	-4.48	-2.25	-4.95	-2.66
	p	0.502	0.310	**0.003**	0.066	**<0.001**	**0.034**	1.000	**0.045**	**<0.001**	**0.027**	**<0.001**	**0.009**
5	**β**	0.01	0.04	0.23	0.03	0.22	0.20	0.05	-0.09	-0.22	-0.13	-0.26	-0.13
	t	0.18	0.60	3.70	0.48	3.90	3.32	0.54	-0.99	-2.47	-1.68	-3.30	-1.60
	p	0.861	0.549	**<0.001**	0.634	**<0.001**	**0.001**	0.592	0.326	**0.015**	0.097	**0.001**	0.112
10	**β**	-0.04	0.04	0.11	0.08	0.15	0.08	0.06	0.04	-0.16	-0.03	-0.23	-0.20
	t	-0.64	0.59	1.79	1.34	2.66	1.30	0.77	0.42	-1.87	-0.36	-2.88	-2.44
	p	0.523	0.559	0.077	0.183	**0.010**	0.197	0.445	0.678	0.065	0.716	**0.005**	**0.017**
		Index						**Choice Latency**					
All	**β**	-0.22	-1.14	-3.18	-0.26	-2.90	-2.64	-0.06	0.15	0.40	0.27	0.43	0.16
	t	-0.46	-2.26	-6.15	-0.58	-6.25	-5.50	-0.43	1.10	2.83	2.16	3.34	1.19
	p	0.648	**0.026**	**<0.001**	0.564	**<0.001**	**<0.001**	0.667	0.274	**0.006**	**0.034**	**0.001**	0.238
		Collection Latency											
All	**β**	-0.01	0.17	1.13	0.26	1.02	0.76						
	t	-0.04	1.08	7.10	1.89	7.17	5.15						
	p	0.967	0.285	**<0.001**	0.063	**<0.001**	**<0.001**						

Supplemental Table 11. Performance on the stimulus duration manipulation.

ANOVA					Tukey HSD		
	Num DF	**Den DF**	**F**	**p**	**Comparison**	**Difference**	**p**
PC1	3	21	0.45	0.719			
PC2	3	21	3.89	**0.024**	Sham v. Mild	-1.21	0.288
					Sham v. Mod	-1.48	0.147
					Sham v. Sev	-2.32	**0.014**
					Mild v. Mod	-0.27	0.970
					Mild v. Sev	-1.10	0.322
					Mod v. Sev	-0.84	0.555
PC3	3	20	7.91	**0.001**	Sham v. Mild	-1.72	**<0.001**
					Sham v. Mod	-1.23	**0.019**
					Sham v. Sev	-0.59	0.446
					Mild v. Mod	0.49	0.502
					Mild v. Sev	1.13	**0.024**
					Mod v. Sev	0.63	0.319

Supplemental Table 12. Principal components comparison across injury groups.