Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Pupillary Light Reflex Metrics Distinguish Healthy Controls and Acutely Concussed Athletes ≤ 7 days Post-Injury.

	Concussed athletes (*n = 35*)	Healthy controls (*n = 134*)	Difference	
	Mean (99.44% CI)	Mean (99.44% CI)	Mean (99.44% CI)	Bonferroni adjusted P value
Maximum pupil diameter (mm)	4.61 (4.23, 5.00)	4.01 (3.82, 4.21)	0.60 (0.17, 1.03)	.001
Minimum pupil diameter (mm)	2.87 (2.67, 3.07)	2.63 (2.53, 2.73)	0.24 (0.01, 0.46)	.03
Percent constriction (%)	36.91 (34.21, 39.61)	33.66 (32.28, 35.04)	3.25 (0.21, 6.28)	.03
Latency (ms)	209.29 (200.94, 217.64)	208.50 (204.23, 212.76)	0.79 (-8.58, 10.17)	1
Average constriction velocity (mm/s)	2.97 (2.67, 3.27)	2.50 (2.34, 2.65)	0.47 (0.13, 0.81)	.001
Peak constriction velocity (mm/s)	4.64 (4.18, 5.10)	3.91 (3.68, 4.14)	0.73 (0.22, 1.24)	< .001
Average dilation velocity (mm/s)	1.28 (1.15, 1.41)	1.22 (1.15, 1.28)	0.06 (-0.08, 0.21)	1
Peak dilation velocity (mm/s)	1.77 (1.61, 1.93)	1.64 (1.56, 1.72)	0.13 (-0.05, 0.31)	.44
T75 (s)	1.71 (1.44, 1.97)*	1.51 (1.38, 1.64)	0.20 (-0.10, 0.49)	.53

*1 concussed athlete did not have at least valid measures for the T75 metric

eTable 2. Sex-Differences in T75 Among Concussed Athletes, But Not Healthy Controls.

	Female concussed athletes (*n* = *55*)	Male concussed athletes (*n* = *43*)	Difference	
	Mean (99.44% CI)	Mean (99.44% CI)	Mean (99.44% CI)	Bonferroni adjusted P value
Maximum pupil diameter (mm)	4.91 (4.61, 5.20)	4.74 (4.41, 5.07)	0.17 (-0.27, 0.61)	1
Minimum pupil diameter (mm)	2.97 (2.81, 3.13)	2.95 (2.77, 3.13)	0.02 (-0.22, 0.25)	1
Percent constriction (%)	39.09 (37.28, 40.90)	37.14 (35.09, 39.18)	1.96 (-0.78, 4.69)	.4
Latency (ms)	206.03 (199.90, 212.17)	211.43 (204.49, 218.37)	-5.40 (-14.65, 3.86)	.91
Average constriction velocity (mm/s)	3.11 (2.89, 3.33)	3.05 (2.80, 3.29)	0.06 (-0.27, 0.39)	1
Peak constriction velocity (mm/s)	4.96 (4.62, 5.30)	4.78 (4.39, 5.17)	0.18 (-0.34, 0.70)	1
Average dilation velocity (mm/s)	1.28 (1.18, 1.38)	1.37 (1.25, 1.48)	-0.08 (-0.24, 0.07)	1
Peak dilation velocity (mm/s)	1.80 (1.67, 1.92)	1.88 (1.74, 2.03)	-0.09 (-0.28, 0.10)	1
T75 (s)	1.96 (1.75, 2.17)*	1.63 (1.39, 1.86)	0.33 (0.02, 0.65)	.03
	Female healthy controls (*n* = *78*)	Male healthy controls (*n* = *56*)	Difference	
Maximum pupil diameter (mm)	3.99 (3.74, 4.24)	4.05 (3.76, 4.34)	-0.06 (-0.44, 0.33)	1
Minimum pupil diameter (mm)	2.62 (2.49, 2.75)	2.64 (2.49, 2.80)	-0.02 (-0.23, 0.18)	1
Percent constriction (%)	33.47 (31.66, 35.28)	33.93 (31.79, 36.07)	-0.46 (-3.27, 2.34)	1
Latency (ms)	207.79 (202.11, 213.48)	209.48 (202.77, 216.19)	-1.68 (-10.48, 7.11)	1

Average constriction velocity (mm/s)	2.42 (2.23, 2.62)	2.60 (2.37, 2.84)	-0.18 (-0.49, 0.12)	.88
Peak constriction velocity (mm/s)	3.80 (3.50, 4.09)	4.06 (3.72, 4.41)	-0.26 (-0.72, 0.19)	.93
Average dilation velocity (mm/s)	1.18 (1.10, 1.27)	1.26 (1.16, 1.37)	-0.08 (-0.21, 0.05)	.87
Peak dilation velocity (mm/s)	1.61 (1.50, 1.72)	1.68 (1.55, 1.81)	-0.07 (-0.24, 0.10)	1
T75 (s)	1.54 (1.37, 1.71)	1.47 (1.26, 1.67)	0.07 (-0.19, 0.34)	1

*1 concussed athlete did not have at least 2 valid measures for the T75 metric

eTable 3. Influence of Exercise on Pupillary Light Reflex Metrics in Healthy Controls.

	Healthy controls before exercise (*n = 78*)	Healthy controls after exercise (*n = 56*)	Difference	
	Mean (99.44% CI)	Mean (99.44% CI)	Mean (99.44% CI)	Bonferroni adjusted P value
Maximum pupil diameter (mm)	4.22 (3.96, 4.48)	3.81 (3.55, 4.07)	-0.41 (-0.77, -0.05)	.02
Minimum pupil diameter (mm)	2.71 (2.57, 2.85)	2.55 (2.41, 2.69)	-0.16 (-0.36, 0.04)	.24
Percent constriction (%)	34.98 (33.08, 36.88)	32.34 (30.44, 34.24)	-2.64 (-5.33, 0.05)	.06
Latency (ms)	208.32 (202.18, 214.46)	208.67 (202.53, 214.82)	0.36 (-8.33, 9.04)	1
Average constriction velocity (mm/s)	2.67 (2.47, 2.88)	2.32 (2.12, 2.53)	-0.35 (-0.64, -0.06)	.009
Peak constriction velocity (mm/s)	4.17 (3.86, 4.48)	3.65 (3.34, 3.95)	-0.52 (-0.96, -0.09)	.008
Average dilation velocity (mm/s)	1.33 (1.24, 1.41)	1.11 (1.02, 1.19)	-0.22 (-0.34, -0.10)	< .001
Peak dilation velocity (mm/s)	1.78 (1.67, 1.89)	1.50 (1.39, 1.61)	-0.28 (-0.44, -0.13)	< .001
T75 (s)	1.47 (1.29, 1.66)	1.54 (1.36, 1.73)	0.07 (-0.19, 0.33)	1

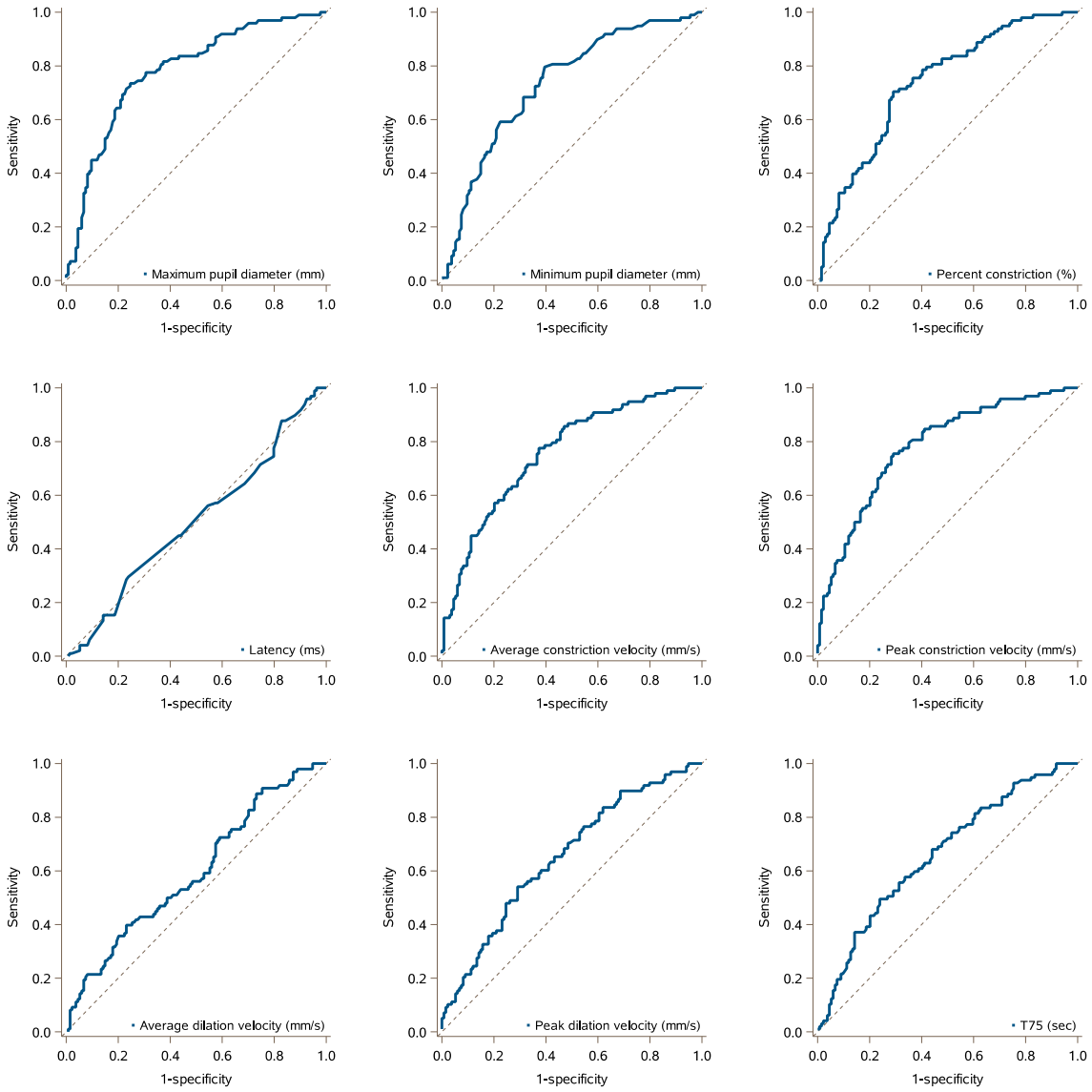
eTable 4. Comparison of concussed athletes and uninjured controls with and without history of prior concussion.

	Concussed athletes with prior history of concussion (*n = 50*)	Concussed athletes without prior history of concussion (*n = 48*)	Difference	
	Mean (99.44% CI)	Mean (99.44% CI)	Mean (99.44% CI)	Bonferroni adjusted P value
Maximum pupil diameter (mm)	4.94 (4.64, 5.25)	4.72 (4.41, 5.03)	0.22 (-0.21, 0.66)	1
Minimum pupil diameter (mm)	3.04 (2.87, 3.20)	2.88 (2.71, 3.05)	0.16 (-0.07, 0.39)	.52
Percent constriction (%)	38.23 (36.30, 40.17)	38.23 (36.26, 40.21)	0.00 (-2.77, 2.77)	1
Latency (ms)	212.91 (206.66, 219.16)	203.70 (197.32, 210.08)	9.21 (0.28, 18.14)	.04
Average constriction velocity (mm/s)	3.05 (2.82, 3.28)	3.11 (2.88, 3.35)	-0.06 (-0.39, 0.27)	1
Peak constriction velocity (mm/s)	4.82 (4.46, 5.18)	4.94 (4.57, 5.31)	-0.12 (-0.63, 0.40)	1
Average dilation velocity (mm/s)	1.28 (1.18, 1.39)	1.36 (1.25, 1.47)	-0.07 (-0.22, 0.08)	1
Peak dilation velocity (mm/s)	1.80 (1.66, 1.93)	1.87 (1.74, 2.01)	-0.08 (-0.27, 0.11)	1
T75 (s)	1.88 (1.65, 2.11)	1.74 (1.51, 1.98)*	0.14 (-0.19, 0.46)	1
	Healthy controls with prior history of concussion (*n = 35*)	Healthy controls without prior history of concussion (*n = 99*)	Difference	
Maximum pupil diameter (mm)	4.14 (3.78, 4.51)	3.97 (3.75, 4.19)	0.18 (-0.25, 0.60)	1

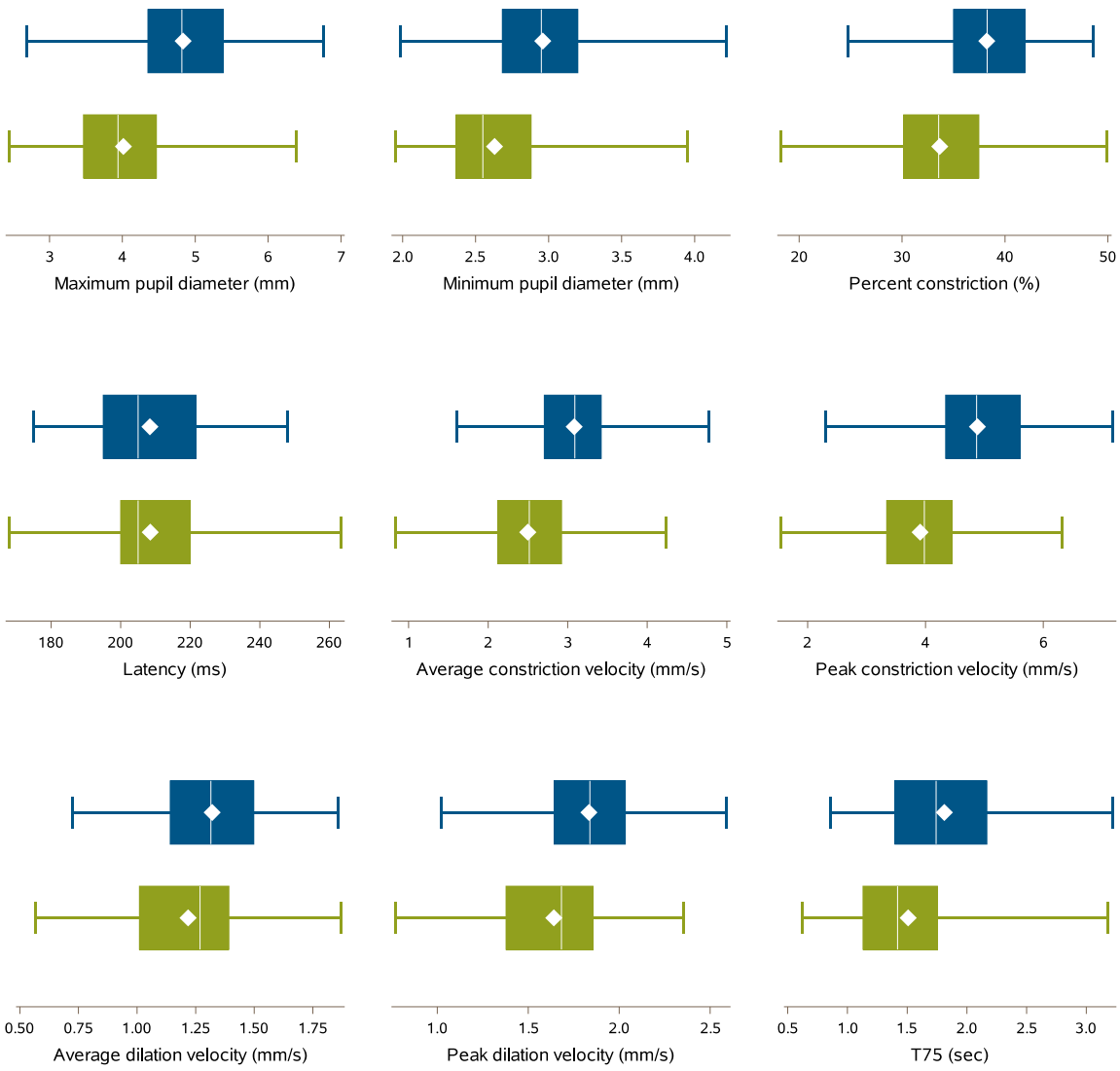
Minimum pupil diameter (mm)	2.74 (2.54, 2.93)	2.59 (2.48, 2.71)	0.14 (-0.08, 0.37)	.7
Percent constriction (%)	33.25 (30.55, 35.96)	33.80 (32.20, 35.41)	-0.55 (-3.69, 2.60)	1
Latency (ms)	203.74 (195.35, 212.13)	210.18 (205.19, 215.17)	-6.44 (-16.20, 3.32)	.59
Average constriction velocity (mm/s)	2.57 (2.27, 2.87)	2.47 (2.30, 2.65)	0.10 (-0.25, 0.44)	1
Peak constriction velocity (mm/s)	3.98 (3.54, 4.42)	3.88 (3.62, 4.15)	0.10 (-0.42, 0.61)	1
Average dilation velocity (mm/s)	1.28 (1.15, 1.41)	1.20 (1.12, 1.27)	0.08 (-0.07, 0.23)	1
Peak dilation velocity (mm/s)	1.71 (1.55, 1.87)	1.62 (1.52, 1.71)	0.09 (-0.10,0.29)	1
T75 (s)	1.49 (1.23, 1.74)	1.52 (1.36, 1.67)	-0.03 (-0.33, 0.27)	1

*1 concussed athlete did not have 3 valid measures for the T75 metric

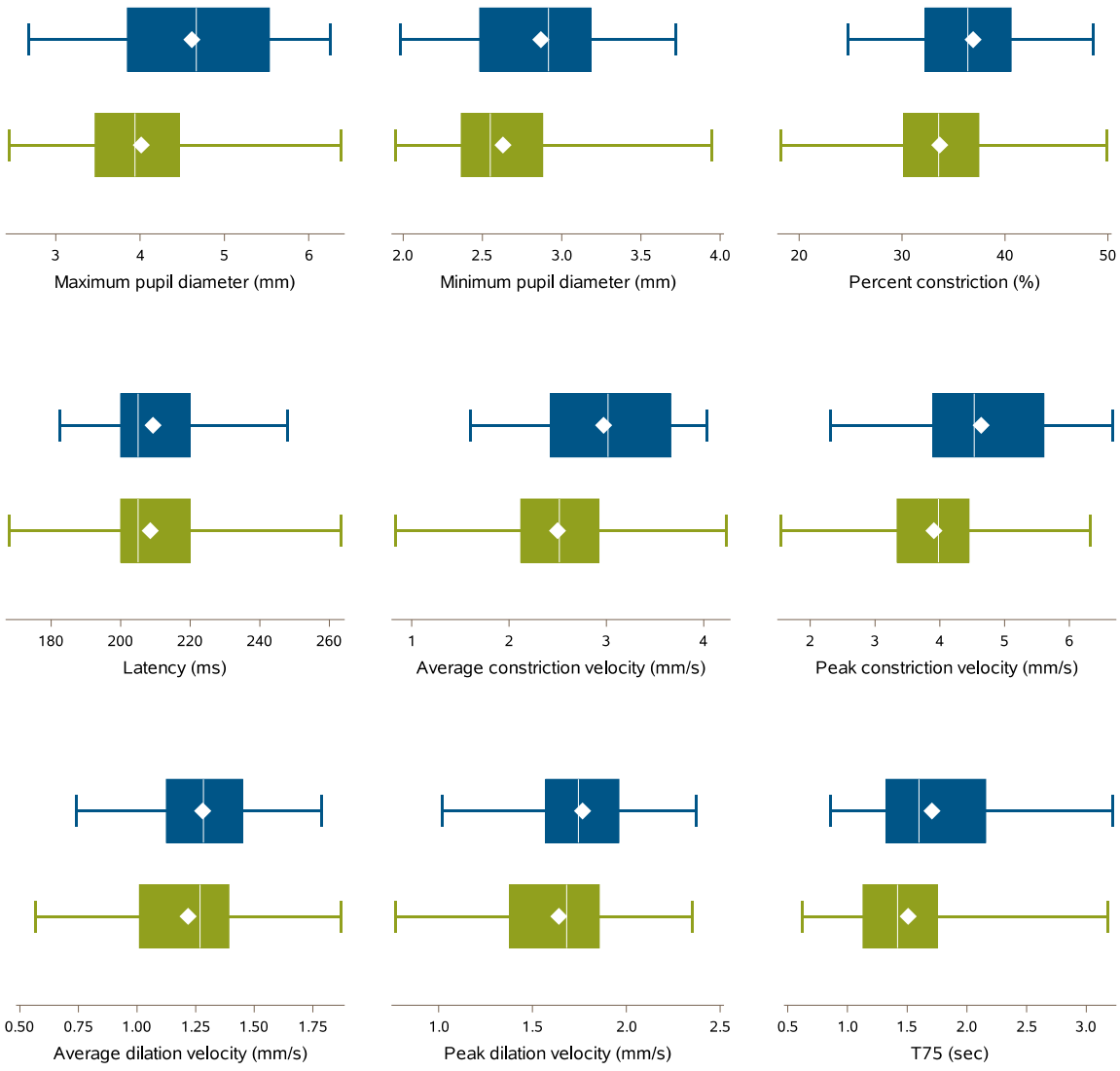
eFigure 1. Receiver Operating Characteristic Curves for Pupillary Light Reflex Metrics in Concussion.



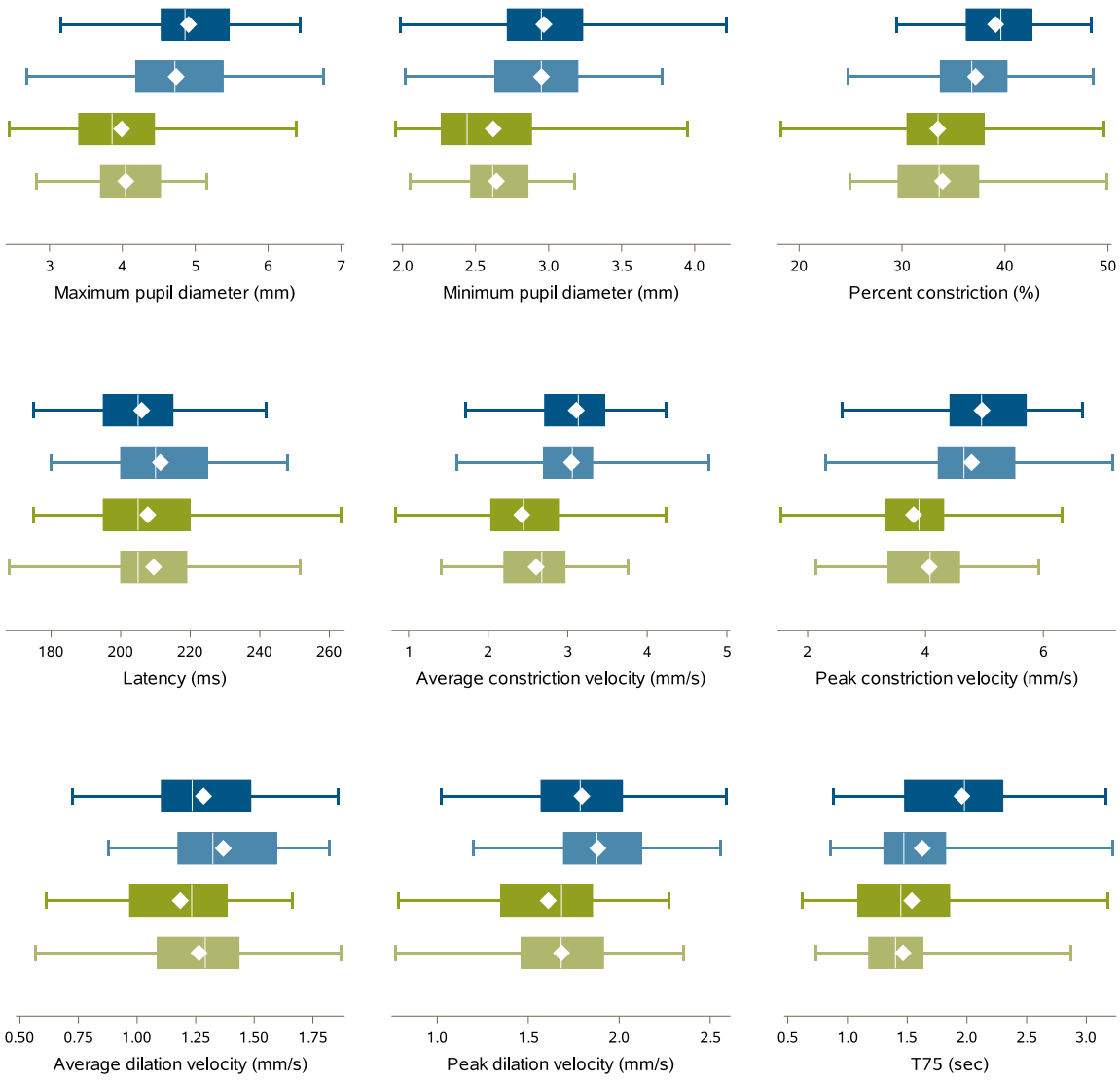
eFigure 2. Boxplots of Distribution of Pupillary Light Reflex Metrics in Concussed Athletes Compared to Healthy Controls. Top blue boxplots represent concussed athletes and bottom green boxplots represent healthy controls with diamond as mean value, white line as median value, box edges as 1st and 3rd quintile, whisker caps as minimum and maximum.



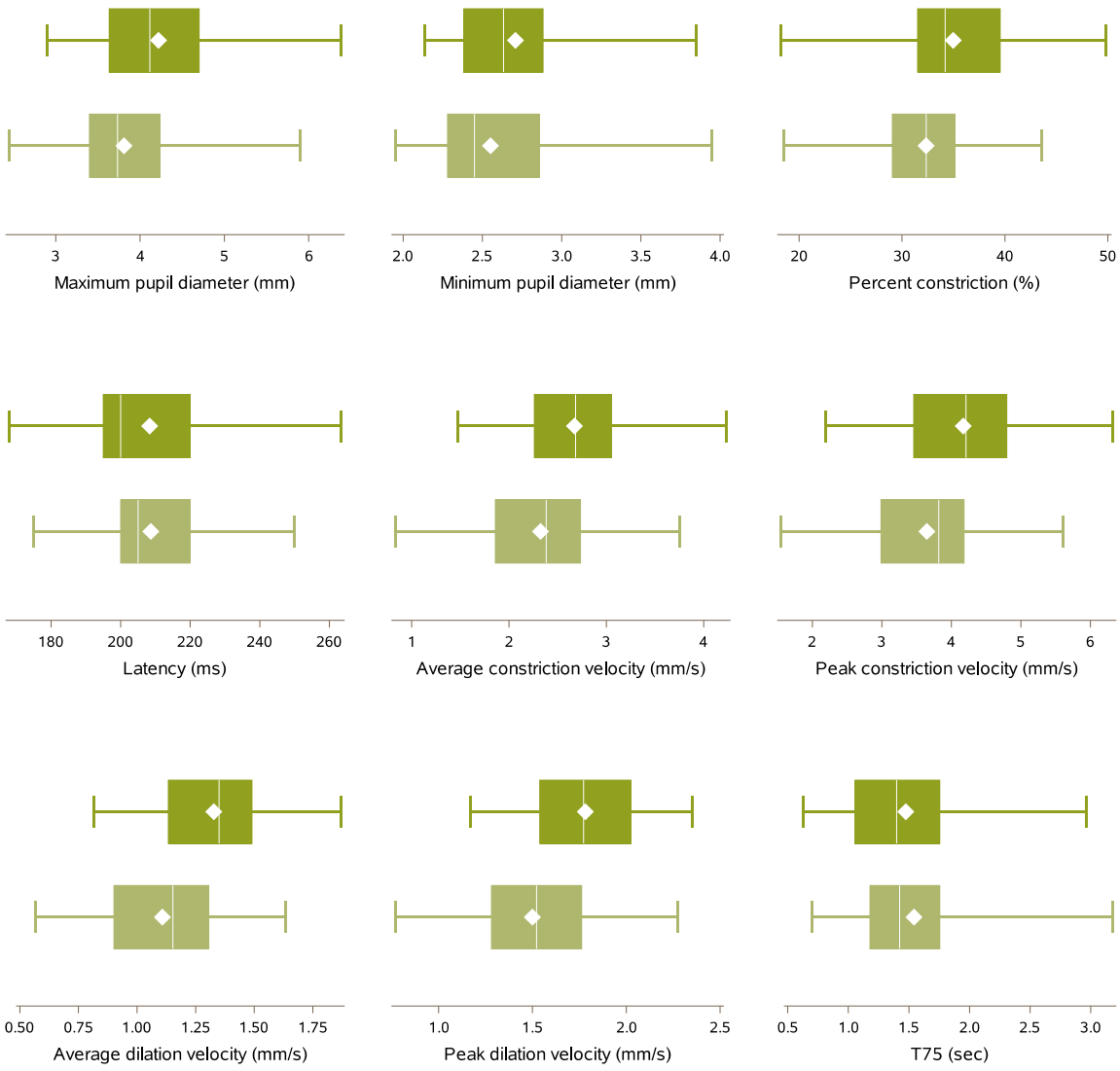
eFigure 3. Pupillary Light Reflex Metrics Distinguish Healthy Controls and Acutely Concussed Athletes ≤ 7 days Post-Injury. Top blue = cases, bottom green = controls



eFigure 4. Comparison of Females to Males among Concussed Athletes and Healthy Controls. Top dark blue = female cases, 2nd light blue = male cases, 3rd dark green = female controls, 4th light green = male controls



eFigure 5. Influence of Exercise on Pupillary Light Reflex Metrics in Healthy Controls. Top dark green = Healthy controls before exercise, bottom light green = Healthy controls after exercise



eFigure 6. Comparison of Concussed Athletes and Healthy Controls With and Without History of Prior Concussion. Top dark blue = cases with prior concussion, 2nd light blue = cases without prior concussion, 3rd dark green = controls with prior concussion, 4th light green = controls without prior concussion