SUPPLEMENTARY INFORMATION

Serum IGF-I levels are associated with improved white matter recovery after TBI

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SUPPLEMENTARY TABLES

Supplementary Table 1. Age-related reference ranges for serum IGF-I assay

Age	IGF-I median	IGF-I lower	IGF-I upper
yr	nmol/L	nmol/L	nmol/L
18	40.0	21.2	75.9
19	33.9	18.3	62.8
20	30.2	16.5	55.1
21-25	26.4	15.1	46.5
26-30	25.5	15.2	42.8
31-35	24.4	15.0	39.9
36-40	22.9	14.2	36.9
41-45	21.3	13.1	34.7
46-50	20.0	12.2	32.8
51-55	18.7	11.3	30.9
56-60	17.6	10.5	29.3
61-65	16.4	9.8	27.6
66-70	15.3	9.0	26.0
71-75	14.3	8.3	24.4
76-80	13.3	7.7	23.0
81-90	12.4	7.2	21.6

Median, lower (<5% CI) and upper (>95% CI) values normal range for serum IGF-I assay (Immulite 2500) from Dept. of Biochemistry, University College London Hospital, London, UK. To convert nmol/L to ng/mL divide by 0.131.

Supplementary Table 2. Patient characteristics by GH deficiency status

	All	No GHD	With GHD	P with vs. without GHD [a]
n	39	35	4	
Age at first scan (yrs)	30.5 [24.5, 47.0]	30.4 [24.1, 49.2]	39.4 [29.7, 44.4]	0.50
Range	19.6-66.9	19.6-66.9	27.8-44.7	
Male n (%)	33 (84.6%)	29 (82.9%)	4 (100%)	0.87
Post-menopausal women n (%)	3 (7.7%)	3 (8.6%)	0 (0.0%)	0.70
BMI (kg/m^2)	25.3 [23.1-29.8]	25.0 [21.7-28.6]	29.3 [21.7-28.2]	0.10
Range	17.0-35.0	17.0 -25.0	25.3-33.7	
Moderate-severe TBI	34 (87.2%)	30 (85.7%)	4 (100%)	1.00
Blast TBI n (%)	13 (33.3%)	10 (28.6%)	3 (75.0%)	0.19
Time since TBI (months)	16.3 [3.6, 24.5]	11.4 [3.2, 25.7]	26.8 [7.7-34.3]	0.38
Range	1.5-571.0	1.5-571.0	3.6-34.5	
Time between scans (months)	13.3 [12.1, 14.9]	13.1 [12.1, 14.5]	14.6 [10.3-15.1]	0.58
Range	6.3-24.6	6.3-24.6	9.1-15.1	
Absolute IGF-1 nmol/L [b]	23.8 [19.2-29.5]	24.2 [19.5, 29.5]	19.6 [16.7, 23.2]	0.11
Range	12.8-74.5	12.8-74.5	16.5-23.7	
Age-adjusted IGF-1 ratio	1.1 [0.9, 1.2]	1.1 [0.9, 1.3]	0.9 [0.8-1.0]	0.11
Range	0.6-3.0	0.6-2.9	0.8-1.0	
Any structural brain abnormality n (%)	30 (76.9%)	28 (80.0%)	2 (50.0%)	0.47
≥ 1 contusion	20 (51.3%)	19 (54.3%)	1 (25.0%)	0.56
No. of contusions [c]	1 [0-2]	1 [0-2]	0 [0-0.8]	0.53
Range	0-5	0-5	0-1	
≥ 1 microbleed n (%)	10 (25.6%)	10 (28.6%)	0 (0.0%)	0.53
Superficial siderosis n (%)	13 (33.3%)	11 (31.4%)	2 (50.0%)	0.85
Diffuse axonal injury (DAI) n (%)	5 (12.8%)	4 (11.4%)	1 (25.0%)	1.00

Data given as n (%) or median [IQR] and range (minimum-maximum).

[a] P value for comparison of groups with and without GHD using chi-squared test with Yates' correction for categorical variables and Mann-Whitney U test for continuous variables.

[b] To convert nmol/L to ng/mL divide by 0.131.

[c] including those without any contusions

Supplementary Table 3. Neuropsychological outcome measures in patients after TBI at baseline and recovery over time by IGF-I status.

Symptom domain		Max score	n	First Visit	n	Second visit	Effect of Time [a]	Effect of IGF-I Group [a]	Time*Group Interaction [a]
Assessment of GH Deficiency in Adults Quality of Life (AGHDA-QoL)		25	25	9 [2.5-16.5] 0-23	25	7.0 [1-12.5] 0-22	0.99	0.71	0.89
Beck Depression Inventory II Score (BDI-II)		63	25	13.0 [4.0-23.0] 0-27	25	11.0 [2.5-18.5] 0-32	0.46	0.75	0.63
Epworth Daytime Sleepiness Scale		24	22	3.0 [0.9.5] 0-19	15	4.0 [1.0-10.0] 0-14	0.69	0.45	0.53
SF-36 QoL	Physical functioning	100	16	70.0 [22.5-98.8] 0-100	24	87.5 [62.3-95.0] 0-100	0.32	0.82	0.53
	Role limitations due to physical health	100	17	75.0 [0-100] 0-100	24	50.0 [6.25-100] 0-100	0.58	0.37	0.58
	Role limitations due to emotional problems	100	16	100 [66.7-100] 0-100	24	100 [41.7-100] 0-100	0.88	0.59	0.77
	Energy/Fatigue	100	16	45.0 [45.0-70.0] 15-85	24	67.5 [47.5-83.8] 5-100	0.41	0.41	0.12
	Emotional well being	100	16	70.0 [54-83.0] 28.0-92.0	24	80.0 [61.0-92.0] 24.0-100	0.52	0.75	0.96
	Social functioning	100	17	62.5 [50.0-75.0] 12.5-100.0	24	81.3 [50.0-100] 25-100	0.22	0.77	0.87
	Pain	100	17	45.0 [39.0-83.8] 22.5-100	24	77.5 [55.6-100] 42.5-100	0.74	0.82	0.93
	General health	100	17	60.0 [42.5-80.0] 20-100	24	65.0 [45.0-91.3] 15-100	0.27	0.59	0.18
Cognitive domain	*Cognitive variable*								
Pre-morbid intelligence: reading ability	WTAR raw score		32	41.0 [35.3-45.0] 0-50	32	42.0 [31.8-46.8] 9-50	0.88	0.83	0.60
Intellectual ability	WASI similarities (verbal)		33	36.0 [32.5-38.0] 21-46	33	39.0 [35.5-41.0] 23-46	0.61	0.96	0.42
	WASI matrix reasoning (non-verbal)		32	26.5 [20.5-30.0] 9-34	32	28.5 [25.3-30.8] 12-35	0.08	1.00	0.20
Memory: associative memory	People test (total score)		33	22.0 [14.5-29.0] 4-38	33	27.0 [18.0-31.0] 6-38	**0.010**	0.19	0.78
Memory: immediate recall	Logical memory I Total		33	28.0 [20.5-32.0] 10-40	33	43.0 [33.0-51.5] 19-62	0.26	0.12	**0.046**
	Logical memory II Total		33	26.0 [18.5-32.5] 0-42	33	27.0 [19.5-33.0] 10-43	0.63	0.20	0.57
Memory: delayed recall	Logical memory retention		32	86.7 [78.9-94.3] 33.3-107.7	33	90.3 [82.9-98.0] 45-190	0.41	0.34	0.93
Processing speed: visual search/complex	Trail Making Test Trail A (s)		32	26.0 [21.0-32.0] 14-67	33	22.0 [16.5-28.5] 13-87	0.82	0.60	0.65
	Trail Making Test Trail B (s)		32	52.0 [43.3-68.5] 22-192	33	47.0 [30.5-71.0] 25-166	0.62	0.32	0.81
Processing speed: naming/reading	Stroop Colour Naming (s)		31	32.0 [28.0-41.0] 20-101	33	32.0 [30.0-35.0] 19-51	0.56	0.90	0.96
	Stroop Word Reading (s)		31	23.0 [19.0-32.0] 15-62	32	23.0 [20.0-25.8] 14-43	0.53	0.25	0.34
Executive function: alternating-switch cost	Trail Making Test Trail B minus A (s)		32	22.5 [13.0-38.8] 4-125	33	19.0 [15.0-42.5] 7-102	0.57	0.24	0.62
Cognitive flexibility	Color Word Stroop Inhibition/switching (s)		32	66.0 [55.5-76.5] 38-128	33	57.0 [51.5-66.5] 37-119	**0.003**	0.33	0.50
Word generation fluency	DKEFS Letter Fluency F+A+S total		33	36.0 [27.0-45.0] 11-65	33	41.0 [35.5-48.5] 15-60	0.15	0.57	0.59

[a] corrected for all covariates (time since injury, time between scans, gender, age at first scan, TBI severity)

Data displayed as median, [IQR], range.

Note: AGHDA, BDI-II, Epworth: higher score equals worse symptoms; SF-36: lower score equals worse quality of life; WTAR, Similarities, Matrix reasoning, People test, Logical memory: higher score equals better performance; Trail-making, Stroop, letter fluency: lower score equals better cognition.

Abbreviations: DKEFS, Delis-Kaplan executive function system; (s), seconds; SF-36, Short Form 36 Health Survey; WASI, Wechsler Adult Intelligence Scale; WTAR, Wechsler Test of Adult Reading.