

SUPPLEMENTARY DATA

Supplementary Table 1. Single component variables entered in the composite Z scores

	Weight	Number of pairs	IAH*, mean (SD)	NAH †, mean (SD)	P value (all IAH and NAH pairs) ‡	P value (sub-groups) §
Cardiovascular autonomic composite Z score			0.40 (0.73)	0.53 (0.69)	0.42	0.2
Heart rate deep breathing (beats/min difference inhalation exhalation)	1	33	14.1 (7.7)	14.0 (8.6)	0.73	0.42
Valsalva manouvre Phase II early (mmHg)	0.5	23	-32.3 (16.3)	-25.3 (19.1)	0.18	0.33
Valsalva manouvre Phase II late (mmHg)	0.5	23	18.4 (12.4)	16.6 (9.6)	0.96	0.54
Valsalva manouvre Phase IV (mmHg)	1	23	23.1 (15.7)	18.4 (12.7)	0.65	0.21
Valsalva ratio ((beats/min)/(beats/min))	1	23	1.7 (0.4)	1.6 (0.4)	0.41	0.26
Recovery time (sec)	0.5	23	3.5 (5.9)	3.0 (4.7)	0.73	0.91
Tilt systolic blood pressure 3 min (mmHg)	0.5	33	-1.8 (10.0)	-4.9 (11.2)	0.16	0.18
Tilt diastolic blood pressure 3 min (mmHg)	0.5	33	1.9 (5.7)	1.0 (7.1)	0.54	0.83
Valsalva manouvre phase I (mmHg)	0.5	23	20.1 (11.4)	18.5 (7.5)	0.69	0.69
Valsalva manouvre phase III (mmHg)	0.5	23	-17.2 (6.6)	-18.0 (5.6)	0.6	0.96
Heart rate phase IV (beats/min)	1	23	57.8 (11.7)	60.0 (11.6)	0.54	0.28
Tilt systolic blood pressure 1min (mmHg)	0.5	23	-3.8 (8.6)	-4.1 (10.4)	0.9	0.99
Pupillometric composite Z score			0.43 (0.53)	0.58 (0.73)	0.38	0.25
<i>Direct response, 0.2s stimulus duration</i>						
Basal diameter (mm)	1	30	5.84 (1.02)	5.75 (1.13)	0.68	0.44
Latency until response onset (s)	0.75	30	0.22 (0.05)	0.22 (0.04)	0.92	0.75
Latency until max contraction (s)	0.75	29	0.91 (0.12)	0.98 (0.13)	0.04	0.06
Contraction velocity (mm/s)	0.75	29	2.22 (0.48)	2.22 (0.31)	0.98	0.69
Pupil contraction response (mm)	0.75	29	1.53 (0.35)	1.69 (0.34)	0.10	0.19
Early and late redilatation time (s)	1	29	3.95 (2.28)	4.78 (2.86)	0.16	0.03
Diameter at 75% redilatation (mm)	1	30	5.42 (0.98)	5.33 (1.09)	0.65	0.45
<i>Indirect response, 0.2s stimulus duration</i>						
Basal diameter (mm)	1	29	5.93 (0.93)	5.84 (1.15)	0.70	0.42
Latency until response onset (s)	0.75	28	0.22 (0.05)	0.22 (0.04)	0.90	0.74
Latency until max contraction (s)	0.75	28	0.94 (0.22)	0.96 (0.13)	0.70	0.19
Contraction velocity (mm/s)	0.75	28	2.18 (0.49)	2.28 (0.42)	0.45	0.78
Pupil contraction response (mm)	0.75	28	1.53 (0.35)	1.68 (0.33)	0.12	0.12
Early and late redilatation time (s)	1	29	4.06 (2.66)	4.42 (2.92)	0.58	0.25
Diameter at 75% redilatation (mm)	1	29	5.51 (0.91)	5.42 (1.09)	0.69	0.42
<i>Direct response, 1.0s stimulus duration</i>						
Basal diameter (mm)	1	29	5.78 (0.97)	5.77 (1.15)	0.95	0.6
Latency until response onset (s)	0.75	28	0.22 (0.04)	0.21 (0.05)	0.41	0.33

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Latency until max contraction (s)	0.75	28	1.29 (0.19)	1.37 (0.15)	0.08	0.19
Contraction velocity (mm/s)	0.75	28	1.90 (0.32)	1.94 (0.31)	0.65	0.92
Pupil contraction response (mm)	0.75	28	2.06 (0.46)	2.25 (0.47)	0.13	0.29
Early and late redilatation time (s)	1	27	5.16 (2.80)	5.09 (2.58)	0.99	0.76
Diameter at 75% redilatation (mm)	1	28	5.27 (0.90)	5.22 (1.07)	0.82	0.52
<i>Indirect response, 1.0s stimulus duration</i>						
Basal diameter (mm)	1	27	5.86 (0.96)	5.99 (1.04)	0.62	0.98
Latency until response onset (s)	0.75	27	0.22 (0.04)	0.22 (0.04)	0.41	0.41
Latency until max contraction (s)	0.75	27	1.27 (0.16)	1.39 (0.13)	0.003	0.01
Contraction velocity (mm/s)	0.75	27	1.96 (0.30)	1.97 (0.34)	0.90	0.73
Pupil contraction response (mm)	0.75	27	2.09 (0.44)	2.31 (0.49)	0.10	0.23
Early and late redilatation time (s)	1	27	5.24 (3.37)	4.79 (2.21)	0.76	0.83
Diameter at 75% redilatation (mm)	1	27	5.34 (0.88)	5.41 (0.95)	1.00	0.85
Thermal detection composite Z - score			0.91 (1.04)	0.75 (0.94)	0.54	0.75
Warm threshold thenar (°C until detection)	1	33	1.5 (0.4)	1.6 (0.5)	0.22	0.12
Cold threshold thenar (°C until detection)	1	33	1.2 (0.4)	1.2 (0.3)	0.99	0.50
Warm threshold left malleol (°C until detection)	1	33	8.8 (4.0)	8.1 (3.2)	0.57	0.56
Warm threshold right malleol (°C until detection)	1	33	8.8 (3.9)	7.2 (3.2)	0.07	0.05
Cold threshold left malleol (°C until detection)	1	33	3.2 (2.7)	3.7 (4.0)	0.64	0.23
Cold threshold right malleol (°C until detection)	1	33	4.6 (4.9)	3.8 (3.8)	0.85	0.42
Nerve conduction composite Z score			1.71 (1.19)	1.68 (1.10)	0.89	0.80
Motor nerve conduction velocity Peroneal nerve (m/s)	1	31	41.4 (4.4)	41.9 (5.2)	0.65	0.67
Amplitude Abductor hallucis Tibial nerve (mV)	1	33	7.9 (4.8)	7.6 (4.4)	0.59	0.82
Mean F-wave latency Ulnar nerve (ms)	1	33	26.0 (2.1)	26.5 (2.4)	0.21	0.60
Mean F-wave latency Tibial nerve (ms)	1	32	51.7 (5.5)	53.8 (7.3)	0.21	0.17
Sensory nerve action potential Ulnar nerve dig V (orthodromic, µV)	1	33	2.9 (1.7)	3.1 (2.0)	0.35	0.22
Sensory nerve action potential Sural nerve (orthodromic, µV)	1	31	3.3 (2.5)	3.3 (2.4)	0.55	0.73
Sensory conduction velocity Peroneal nerve (antidromic, m/s)	1	25	42.2 (6.3)	43.3 (4.5)	0.15	0.30
Sensory conduction velocity Plantar medial nerve left (orthodromic, m/s)	1	22	48.9 (7.8)	48.7 (10.5)	0.49	0.09

*Impaired awareness of hypoglycemia, †Normal awareness of hypoglycemia, ‡ All IAH-NAH pairs according to the 2011 classification were included, § Exclusion of pairs in which one IAH or NAH participant had altered awareness status from 2011 to 2012/13