Supplementary Table 1 **MEDLINE search strategy**

|  |
| --- |
| Search strategy |
| 1. exp Brain Concussion/
2. ((brain or cerebral or craniocerebral or cranio-cerebral or intra-cranial or intracranial) adj2 (concuss\* or hematoma\* or haematoma\* or injur\* or contus\*)).tw,kf.
3. mild traumatic brain injur\*.tw,kf.
4. mtbi.tw,kf.
5. ((mild or minor or minimal) adj head injur\*).tw,kf.
6. (concussion\* or contusion\*).tw,kf.
7. Post-Concussion Syndrome/
8. or/1-7
9. exp Autonomic Nervous System/
10. ((autonomic or parasympathetic or sympathetic) adj3 nervous system adj3 (disorder\* or dysfunction\* or disease\*)).tw,kf.
11. Heart Rate/
12. heart rate variability.tw,kf.
13. heart rate control.tw,kf.
14. pulse rate.tw,kf.
15. Blood Pressure/
16. blood pressure.tw,kf.
17. Syncope/ or syncope, vasovagal/
18. syncope.tw,kf.
19. tilt-table test/
20. tilt-table test.tw,kf.
21. Postural orthostatic tachycardia syndrome/
22. Postural orthostatic tachycardia syndrome.tw,kf.
23. valsalva maneuver/
24. valsalva maneuver.tw,kf.
25. homeostasis/ or feedback, physiological/
26. homeostasis.tw,kf.
27. cerebral autoregulation.tw,kf.
28. Baroreflex/
29. Baroreflex.tw,kf.
30. or/9-29
31. 8 and 30
32. limit 31 to ("all adult (19 plus years)" or "adolescent (13 to 18 years)")
33. limit 32 to English
 |

Supplementary Table 2 **Cochrane Central Register of Clinical Trials** **search strategy**

|  |
| --- |
| Search strategy |
| 1. exp Brain Concussion/
2. ((brain or cerebral or craniocerebral or cranio-cerebral or intra-cranial or intracranial) adj2 (concuss\* or hematoma\* or haematoma\* or injur\* or contus\*)).tw,kw.
3. mild traumatic brain injur\*.tw,kw.
4. mtbi.tw,kw.
5. ((mild or minor or minimal) adj head injur\*).tw,kw.
6. (concussion\* or contusion\*).tw,kw.
7. Post-Concussion Syndrome/
8. or/1-7
9. exp Autonomic Nervous System/
10. ((autonomic or parasympathetic or sympathetic) adj3 nervous system adj3 (disorder\* or dysfunction\* or disease\*)).tw,kw.
11. Heart Rate/
12. heart rate variability.tw,kw.
13. heart rate control.tw,kw.
14. pulse rate.tw,kw.
15. Blood Pressure/
16. blood pressure.tw,kw.
17. Syncope/ or syncope, vasovagal/
18. syncope.tw,kw.
19. tilt-table test/
20. tilt-table test.tw,kw.
21. Postural orthostatic tachycardia syndrome/
22. Postural orthostatic tachycardia syndrome.tw,kw.
23. valsalva maneuver/
24. valsalva maneuver.tw,kw.
25. homeostasis/ or feedback, physiological/
26. homeostasis.tw,kw.
27. cerebral autoregulation.tw,kw.
28. Baroreflex/
29. Baroreflex.tw,kw.
30. or/9-29
31. 8 and 30
32. limit 31 to english language
 |

Supplementary Table 3 **PsycINFO search strategy**

|  |
| --- |
| Search strategy |
| 1. exp brain concussion/
2. ((brain or cerebral or craniocerebral or cranio-cerebral or intra-cranial or intracranial) adj2 (concuss\* or hematoma\* or haematoma\* or injur\* or contus\*)).tw,mp.
3. mild traumatic brain injur\*.tw.
4. mtbi.tw.
5. ((mild or minor or minimal) adj head injur\*).tw.
6. (concussion\* or contusion\*).tw.
7. post concussion syndrome.tw.
8. or/1-7
9. autonomic nervous system/
10. ((autonomic or parasympathetic or sympathetic) adj3 nervous system adj3 (disorder\* or dysfunction\* or disease\*)).tw.
11. heart rate/
12. heart rate variability.tw.
13. heart rate control.tw.
14. pulse rate.tw.
15. Blood Pressure/
16. blood pressure.tw.
17. syncope/
18. syncope.tw.
19. tilt-table test.tw.
20. Postural orthostatic tachycardia syndrome.tw.
21. valsalva maneuver.tw.
22. homeostasis/
23. homeostasis.tw.
24. cerebral autoregulation.tw.
25. Baroreflex.tw.
26. or/9-25
27. 8 and 26
28. limit 27 to (“adolescence” or “adulthood”)
29. limit 28 to english
 |

Supplementary Table 4 **CINAHL search strategy**

|  |
| --- |
| Search strategy |
| 1. (MH “Brain Concussion+”)
2. (brain or cerebral or craniocerebral or cranio-cerebral or intra-cranial or intracranial) N2 (concuss\* or hematoma\* or haematoma\* or injur\* or contus\*)
3. “mild traumatic brain injur\*”
4. mtbi
5. (mild or minor or minimal) N0 (head injur\*)
6. concussion\* or contusion\*
7. post concussion syndrome
8. S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7
9. (MH “Autonomic Nervous System+”)
10. (autonomic or parasympathetic or sympathetic) N3 nervous system N3 (disorder\* or dysfunction\* or disease\*)
11. (MH “Heart Rate”)
12. heart rate variability
13. heart rate control
14. pulse rate
15. (MH “Blood Pressure”)
16. blood pressure
17. (MH “Syncope”) OR (MH “Syncope, Vasovagal”)
18. syncope
19. (MH “Tilt-Table Test”)
20. tile table test
21. (MH “Postural Orthostatic Tachycardia Syndrome”)
22. Postural Orthostatic Tachycardiac Syndrome
23. (MH “Valsalva’s Maneuver”)
24. valsalva maneuver
25. (MH “Homeostasis”)
26. homeostasis
27. cerebral autoregulation
28. (MH “Baroreflex”)
29. baroreflex
30. S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29
31. S8 AND S30

Limiters – English Language; Age Groups: Adolescents: 13 – 18 years, All Adult  |

Supplementary Table 5 **SPORTDiscus search strategy**

|  |
| --- |
| Search strategy |
| 1. DE “BRAIN concussion”
2. (brain or cerebral or craniocerebral or cranio-cerebral or intra-cranial or intracranial) N2 (concuss\* or hematoma\* or haematoma\* or injur\* or contus\*)
3. “mild traumatic brain injur\*”
4. mtbi
5. (mild or minor or minimal) N0 (head injur\*)
6. concussion\* or contusion\*
7. DE “POSTCONCUSSION syndrome”
8. S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7
9. DE “AUTONOMIC nervous system” OR DE “PARASYMPATHETIC nervous system” OR DE “SYMPATHETIC nervous system”
10. (autonomic or parasympathetic or sympathetic) N3 nervous system N3 (disorder\* or dysfunction\* or disease\*)
11. DE “HEART beat”
12. heart rate variability
13. heart rate control
14. pulse rate
15. DE “BLOOD pressure”
16. blood pressure
17. DE “SYNCOPE (Pathology)”
18. syncope
19. tile table test
20. postural orthostatic tachycardiac syndrome
21. valsalva maneuver
22. DE “HOMEOSTASIS”
23. homeostasis
24. cerebral autoregulation
25. DE “BAROREFLEXES”
26. baroreflex
27. S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26
28. S8 AND S27

Limiters – Language: English |

Supplementary Table 6 **Heart rate & heart rate variability outcomes**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author****(Year)** | **Resting HR** | **Challenge HR** | **SDNN** | **RMSSD** | **LF**† | **HF**‡ | **LH/HF** | **Additional HRV measures** |
| Abaji(2016) | No group difference | No group difference | No group difference | No group difference | No group/condition (LFms2) difference | Exertion (HFms2) = lower in mTBI vs controls (p=0.01) | Exertion = higher in mTBI vs controls (p=0.02) | ApEN = no group/ condition difference |
| Bishop(2017) | 10SS = no group difference | Squat-peak, squat-late§ HRSD = lower in mTBI vs controls (p<0.05);Stand-early, stand-peak, stand-late§ HRSD = lower in mTBI vs controls (p<0.05) | 10SS = no group difference |  | 10SS = no group (%LF) difference | 10SS = no group (%HF) difference | 10SS = no group difference | 10SS (pNN50) = lower in mTBI vs controls (p<0.05)10SS (ApEN, SampEN) = no group difference |
| Brandt (2020) |  |  |  |  |  | Rest (seated) (lnHF) = no group difference  |  |  |
| Clausen(2016) | Exercise onset (pre & post- intervention) = higher in mTBI vs controls (p<0.001) | Max exercise tolerance¶ = lower in mTBI (pre-intervention) vs controls (p<0.001); higher in mTBI post vs pre-intervention (p<0.001) |  |  |  |  |  |  |
| Ding(2020) | No group difference |  |  |  | No group difference |  |  |  |
| Dobney(2018) | No group difference |  | No group difference | No group difference  | No group difference | No group difference | No group difference |  |
| Dobson(2017) | No group difference |  |  |  |  |  |  |  |
| Gall(2004) |  | Exertion (2d/7d) = higher in mTBI vs controls (p<0.01) | No group difference |  | Exertion (LFms2) (2d/7d) = lower in mTBI vs controls (p<0.05) | Exertion (HFms2) (2d/7d) = lower in mTBI vs controls (p<0.05) | No group difference |  |
| Haider(2020) | Lower in mTBI vs controls (p=0.034) | % change at min 2 of FC = greater in mTBI vs controls  |  | % change at min 2 of FC = lesser in mTBI vs controls  |  | No group/condition difference | min 1 of FC = higher in mTBI vs controls (p=0.050) |  |
| Hanna-Pladdy(2001) |  | Higher in stress vs relaxation condition in mTBIStress = higher in symptomatic mTBI vs other groups |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
| **Author****(Year)** | **Resting HR** | **Challenge HR** | **SDNN** | **RMSSD** | **LF**† | **HF**‡ | **LH/HF** | **Alternative HRV measure** |
| Hilz (2011) | Rest (supine) = higher in mTBI vs controls (p=0.006) |  | Rest (supine) = lower in mTBI vs controls (p=0.043)Rest (standing) = lower in mTBI vs controls (p=0.013) | Rest (supine) = lower in mTBI vs controls(p=0.005)Supine-to-standing = decreased in controls (p<0.05), but not in mTBI | Rest (supine) (LFnu) = higher in mTBI vs controls (p=0.000)Rest (standing) (LFms2) = lower in mTBI vs controls (p=0.013) | Rest (supine) (HFnu) = lower in mTBI vs controls (p=0.000)Rest (supine) (HFms2) = lower in mTBI vs controls (p=0.020)Supine-to-standing (HFms2) = decreased in controls, but not in mTBI (p<0.05) | Rest (supine) = higher in mTBI vs controls (p=0.000) |  |
| Hilz (2015) | No group difference |  |  |  | EP (LFnu, LFms2) = decreased in controls (LFnu p=0.036; LFms2=p<0.05), but not in mTBI  | EP (HFnu) = increased in controls (p<0.05), but not in mTBI  | No group/condition difference  |  |
| Hilz (2016) | No group difference | VM = no group difference | Rest = lower in mTBI vs controls (p=0.005) | Rest = lower in mTBI vs controls (p=0.02) | Rest (LFms2) = lower in mTBI vs controls (p=0.009) | Rest (HFms2) = lower in mTBI vs controls (p=0.032) | No group difference | Rest (TPms2) = lower in mTBI vs controls (p=0.009) |
| Hilz (2017) | No group difference |  | Supine-to-standing = decreased in mTBI (p<0.05), but not controls  | No group difference  | Rest (supine) (LFnu) = higher in mTBI vs controls (p=0.020) | Rest (supine) (HFnu) = lower in mTBI vs controls (p=0.020) | No group difference |  |
| Hilz (2020) | No group difference | Unpleasant odour = increased in controls (p=0.006), but not in mTBI |  |  |  |  |  |  |
| Huang(2019) | No group difference |  |  | Rest (seated) = lower in mTBI vs controls (p=0.0046)Cognitive task = increased in mTBI (p=0.0162), but not in controls | Cognitive task (%LF) = decreased in mTBI (p<0.05), but not in controls | Rest (seated) (%HF, HFms2) = lower in mTBI vs controls (%HF p=0.0027; HFms2 p<0.05)Cognitive task (HFms2) = higher in mTBI vs controls (p<0.05)Cognitive task (%HF) = increased in mTBI (p=0.0008), but not in controls | Rest (seated) = higher in mTBI vs controls (p<0.05)Cognitive task = lower in mTBI vs controls (p<0.05) | Rest (seated) (pNN50) = lower in mTBI vs controls (p=0.0137)Cognitive task (TPms2) = decreased in controls (p<0.05), but not in mTBI |
|  |  |  |  |  |  |  |  |  |
| **Author****(Year)** | **Resting HR** | **Challenge HR** | **SDNN** | **RMSSD** | **LF**† | **HF**‡ | **LH/HF** | **Alternative HRV measure** |
| Hutchison(2017) | No group difference |  | Rest (seated) (all time points) = lower in mTBI vs controls (FDR<0.05) |  | Rest (seated) (LFs2) (initiation of exercise) = lower in mTBI vs controls (FDR<0.05) | Rest (seated) (HFs2) (all timepoints) = lower in mTBI vs controls (FDR<0.05) | Rest (seated) (post-RTP) = higher in mTBI vs controls (FDR<0.05) | Rest (seated) (TPs2) = no group difference |
| Johnson(2018) | No group difference | min 2 of FC = decreased in controls (p=0.025), but not in mTBI min 1, 2 or 3 of FC = no group difference |  | Rest (supine) = no group difference min 1 of FC = increased in controls (p=0.002), but not in mTBImin 1, 2 or 3 of FC = no group difference |  | Rest (supine) (HFms2) = no group difference FC (HFms2) = increased at 1 min (p<0.001) and min 2 (p=0.024) in controls, but not mTBI min 1 of FC (HFms2) = higher in controls vs mTBI (p<0.001) |  |  |
| Johnson(2020) | No group difference | 30s, 60s, 90s of CPT = increased in controls (p<0.05), but not in mTBI CPT (all timepoints) = no group difference |  |  |  |  |  |  |
| Kozlowski(2013) | No group difference | HRmax on treadmill test = lower in mTBI vs controls (p<0.001) |  |  |  |  |  |  |
| La Fountaine(2009)# | No group difference |  |  |  |  |  | No group difference | Rest (seated) (ApEN) = no group differenceExertion (ApEN) (≤48hrs) = lower in mTBI vs controls (p≤0.05) |
| La Fountaine(2011)# | No group difference |  |  |  |  |  |  | Rest (seated) (QTVI) (1st assessment)) = higher in mTBI vs controls (p=0.016) |
| La Fountaine(2016) | No group difference | No group difference  |  |  |  |  |  |  |
| La Fountaine(2018) | No group difference |  |  |  | Rest (seated) (LFms2/Hz) = no group difference | Rest (seated) (HFms2/Hz) = no group difference  |  |  |
| Leddy(2010) | No significant difference pre-intervention vs post-intervention  | HRmax on treadmill test = higher post-intervention vs pre-intervention (p<0.001) |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
| **Author****(Year)** | **Resting HR** | **Challenge HR** | **SDNN** | **RMSSD** | **LF**† | **HF**‡ | **LH/HF** | **Alternative HRV measure** |
| Liao(2016) | No group difference |  | Rest (≤1wk) = lower in mTBI w/out anxiety (p<0.01) & mTBI with anxiety†† (p<0.05) vs controls |  | Rest (lnLF) (≤1wk) = lower in mTBI without anxiety (p<0.01) & mTBI with anxiety†† (p<0.05) vs controlsRest (%LF) ($Δ$ 6w to 12w) = increased in mTBI with anxiety†† (p<0.01), but not in mTBI without anxiety | Rest (lnHF) (≤1wk) = lower in mTBI without anxiety & mTBI with anxiety†† vs controls (p<0.01) | Rest (lnLF/HF) (≤1wk) = lower in mTBI without anxiety & mTBI with anxiety†† vs controls (p<0.01) | Rest (lnTP) (≤1wk) = lower in mTBI without anxiety & mTBI with anxiety†† vs controls (p<0.01) |
| Mirow(2016) |  |  |  |  | Rest (24hr LFnu) = poor balance‡‡ associated with 20% decrease (p=0.06) | Rest (24hr HFnu) = poor balance‡‡ associated with 12% increase (p=0.04); sleep duration <7hrs associated with 13% increase (p<0.05) | Rest (24hr LF/HF) =poor balance‡‡ associated with 29% decrease (p=0.04); sleep duration <7hrs associated with 27% decrease (p<0.05) |  |
| Purkayastha(2019) | No group difference |  |  | Rest (seated) (4d) = lower in mTBI vs controls (p<0.05)Rest (seated) ($Δ$ 4d to 95d) = increased in mTBI (p<0.05) | Rest (seated) (LFms2) = no group difference | Rest (seated) (HFms2) (4d) = lower in mTBI vs controls (p<0.05) Rest (seated) (HFms2) ($Δ$ 4d±1 to 95d±11) = increased in mTBI (p<0.05) |  | Rest (seated) (pNN50) (4d) = lower in mTBI vs controls (p=0.0012)Rest (seated) (pNN50) ($Δ$ 4d to 22d) = increased in mTBI (p=0.035)Rest (seated) (TPms2) = no group difference |
| Pyndiura(2020) | Rest (seated) = higher in mTBI males vs control males (p=0.03) |  | No group/condition difference |  | No group/condition difference | No group/condition difference | No group/condition difference | Rest (TPms2) = no group/condition difference |
| Russell (2020) | Rest = lower in mTBI vs controls (p<0.01) | Seated-to-standing & supine-to-standing = higher RR drop & width of valley§§ in mTBI vs controls (p<0.05) |  |  | No group/condition difference | Rest = higher in mTBI vs controls (p<0.05) | No group/condition difference |  |
| Senthinathan(2017) | No group difference |  |  |  | Rest (seated) (LFnu) = decreased in mTBI across timepoints (p=0.03)Rest (standing) (LFms2) ($Δ$ 4.7d to 18.1d) = increased in mTBI (p=0.02) | Rest (seated) (HFnu) = increased in mTBI across timepoints (p=0.03) | Rest (seated) (LF/HF) = decreased in mTBI across timepoints  | Rest (standing) (SampEN) (all timepoints) = lower in mTBI vs controls (p=0.05) |
| **Author****(Year)** | **Resting HR** | **Challenge HR** | **SDNN** | **RMSSD** | **LF**† | **HF**‡ | **LH/HF** | **Alternative HRV measure** |
| Solbakk(2005) |  | No group/condition difference |  |  |  |  |  |  |
| Sung(2016)a | Rest (seated) (≤1wk) = no group difference |  | Rest (seated) (≤1wk) = lower in mTBI vs controls (p<0.05) |  | Seated (seated) (lnLF) (≤1wk) = lower in mTBI vs controls (p<0.05) | Rest (seated) (%HF) (≤1wk) = higher in mTBI vs control (p<0.01)Rest (seated) (lnHF) (≤1wk) = lower in mTBI vs controls (p<0.05)Rest (seated) (%HF) ($Δ$ ≤1wk to 12mos, 18mos) = decreased in mTBI females (p<0.01)  | Rest (seated) (lnLF/HF) (≤1wk) = lower in mTBI vs controls (p<0.01)Rest (seated) (lnLF/HF) ($Δ$ ≤1wk to 12mos, 18mos) = decreased in mTBI females (p<0.05) | Rest (seated) (lnTPms2) (≤1wk) = lower in mTBI vs controls (p<0.01) |
| Sung (2016)b | No group difference |  | Rest = lower in mTBI at ≤1wk (p=0.035) & 6wks (p=0.034) vs controls |  | Rest (lnLF) = lower in mTBI at ≤1wk (p=0.023) & 6wks (p=0.018) vs controls | Rest (lnHF) = lower in mTBI at ≤1wk (p=0.042) & 6wks (p=0.022) vs controlsRest (%HF) = higher in mTBI at ≤1wk (p=0.009) & 6wks (p=0.041) vs controls | Rest (lnLF/HF) = lower in mTBI at ≤1wk (p=0.008) & 6wks (p=0.018) vs controls | Rest (lnTP) = lower in mTBI at ≤1wk (p=0.008) & 6wks (p=0.006) vs controls |
| Tan(2009) |  |  | Rest = lower in study participants¶¶  vs controls |  |  |  |  |  |
| Wright (2017)|| || | Rest (seated) = no difference hx3+ vs hx-; no difference in acute mTBI across timepoints |  |  |  |  |  |  |  |
| Wright(2018)|| || | Rest (standing) = no difference hx3+ vs hx-; no difference in acute mTBI across timepoints |  |  |  |  |  |  |  |

Abbreviations: ApEN, approximate entropy; CPT, cold pressor test; EP, eyeball pressure stimulation; FC, face cooling; HF, high frequency; HR, heart rate; HRSD, standard deviation of heart rate; HRV, heart rate variability; hx-, no mTBI history; hx3+, history of ≥3 mTBI; LF, low frequency; mTBI, mild traumatic brain injury; pNN50, percentage of successive RR intervals that differ by more than 50ms; QVTI, QT interval variability index; RMSSD, root mean square of successive RR interval differences; RTP, return-to-play; SampEN, sample entropy; SDNN, standard deviation of NN intervals; TP, total power; VM, valsalva maneuver; 10SS, 10s squat, 10s stand (squat-stands)

† LF = LF power (ms2); LFnu (normalization units) = [LF/(LF+HF)] x 100; %LF = (LF/TP) x 100

‡ HF = HF power (ms2); HFnu (normalization units) = [HF/(LF+HF)] x 10; %HF = (HF/TP) x 100

§ squatting and standing portion of squat-stand separated into the early (0-6s), peak (4-7s) and late (6-10s) phases (variables = squat-early, squat-peak, squat-late, stand-early, stand-peak, stand-late)

¶ measured using a progressive treadmill test

# data from same cohort

†† anxiety assessed using the Beck Anxiety Inventory (BAI); total scores can range from 0-63 where 0-7 indicates normal, 8-15 indicates mild anxiety, 16-25 indicates moderate anxiety, 26-63 indicates severe anxiety; in results ≥8 = anxiety

‡‡ balance assessed using the Sharpened Romberg Test; poor balance determined by loss of balance in first 30s of 60s balance test (across 4 trials) where participant stands with one foot in front of the other, toes touching heel, arms crossed across chest, eyes closed

§§ RR drop = RR before positional change – minimum RR during position change; width of valley = time to normalization of RR intervals from pre to post postural change

¶¶ study participants included veterans with either mTBI, PTSD or pain; 18 participants (64%) had an mTBI; normative data (controls) was taken from the average of each 5min segment over 24hrs recorded from 240 volunteers, whereas mTBI participants completed a 5min recording

|| || data from same cohort

a Sung et al. *Psychophysiol*

b Sung et al. *Clin Neuropsychol*

Supplementary Table 7 **Blood pressure, baroreceptor sensitivity, alternative measures of autonomic function & correlations between measures of autonomic function and clinical outcomes**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Author****(Year)** | **Resting BP** | **Challenge BP** | **Resting BRS** | **Challenge BRS** | **Alternative autonomic measure(s)** | **Correlation(s)** |
| Abaji(2016) |  |  |  |  |  | Significant positive correlations between time since injury and RMSSD (r2=0.62), HFms2 (r2=0.68) and ApEN (r2=0.069) at rest. |
| Bishop(2017) |  | Squat-late-change-DBP, SBP & MAP† = lower in mTBI vs controls (p<0.05) |  |  |  |  |
| Brandt (2020) |  |  |  |  |  | Significant negative correlations between resting lnHF and BDI-II at 3-14d (r2=0.08) and 1-3mos (r2=0.11). |
| Clausen(2016) | Exercise onset = no group difference | Max exercise tolerance‡ SBP = lower in mTBI (pre-intervention) vs controls (p<0.001) & higher in mTBI post vs pre-intervention (p<0.001) |  |  |  |  |
| Ding(2020) | Rest (seated) DBP-LF (mmHg2) = lower in mTBI vs controls (p=0.003)Rest (seated) = no group difference | Sit-stand DBP-LF & SBP-LF (mmHg2) = no group difference | Rest (seated) (BRSgain¶) = no group difference  | Sit-stand (BRSgain¶) = no group difference |  |  |
| Dobney(2018) | Rest (supine) DBP = higher for history ≥2 mTBI vs no mTBI history (p<0.05) |  |  |  |  |  |
| Dobson(2017) | Rest (supine) SBP (≤48hrs) = higher in mTBI vs controls (p=0.02) | SBPunder response to standing|| (≤48hrs) = higher in mTBI vs controls (p=0.01) |  | HRmax/HRmin response to standing# (≤48hrs) = higher in mTBI vs controls (p=0.03) | VM 90% SBPnorm†† (≤48hrs) = higher in mTBI vs controls (p=0.02) |  |
| Hilz(2011) | Rest (supine) = no group difference |  | Rest (supine) (BRSgain¶) = lower in mTBI vs controls (p=0.040) | 30:15 ratio‡‡ = lower in mTBI vs controls(p=0.014) |  | Significant correlations between Glasgow Coma Scale score and resting (seated & standing) HR and BRSgain¶. Significant correlations between Glasgow Coma Scale score and resting (standing) SDNN, RMSSD and LFms2. Significant correlations between time since injury and resting (supine) SDNN, LFms2 and BRSgain¶. |
|  |  |  |  |  |  |  |
| **Author****(Year)** | **Resting BP** | **Challenge BP** | **Resting BRS** | **Challenge BRS** | **Alternative autonomic measure(s)** | **Correlation(s)** |
| Hilz(2015) | Rest (seated) SBP & DBP = no group differenceRest (seated) SBP-LF & DBP-LF (mmHg2) = lower in mTBI vs controls (SBP-LF p=0.013; DBP-LF p=0.008) | EP SBP & DBP = increased in mTBI (SBP p=0.003; DBP p=0.045), but not in controls EP SBP-LF (mmHg2), SBP-lnLF, DBP-lnLF= decreased in controls (SBP-LF p<0.05; SBP-lnLF p=0.020; DBP-lnLF p=0.041), but not in mTBI  |  |  |  |  |
| Hilz(2016) | Rest SBP & DBP = no group differenceRest SBP-LF (mmHg2) = lower in mTBI vs controls (p=0.014) |  | Rest (BRSgain¶) = lower in mTBI vs controls (p=0.043) |  | VM 90% SBPnorm†† = longer in mTBI vs controls (p=0.01) |  |
| Hilz(2017) | Rest (supine) = no group difference  | Supine-to-standing LF-SBP (mmHg2) = increased in controls (p<0.05), but not in mTBI  | Rest (supine) (BRSgain¶) = no group difference | 30:15 ratio‡‡, supine-to-standing (BRSgain¶) = no group difference |  | Significant correlations between time since injury and resting (supine) SDNN & LFms2.  |
| Hilz(2020) | Rest SBP & DBP = no group difference  | Pleasant odour = decreased SBP (p=0.011) & DBP (p=0.0003) in controls, but not in mTBI  |  |  |  |  |
| Howard(2018) |  |  |  |  | COMPASS-31 total score = higher in mTBI vs migraine (p=0.014) & controls (p=0.001)COMPASS-31 orthostatic intolerance subscale = higher in mTBI vs migraine (p=0.027)COMPASS-31 bladder subscale = higher in mTBI vs migraine (p=0.020) | Significant positive correlation between number of mTBIs and total COMPASS-31 score (rs=0.32). Significant positive correlations between vasomotor subscale and years lived with headache (rs=0.27) & headache frequency (rs=0.27). |
| Johnson(2018) | Rest (supine) SBP, DBP, MAP = no group difference  | min 1, 2 & 3 of FC SBP & MAP = higher in controls vs mTBI (p≤0.049)min 1 & 2 of FC DBP = higher in controls vs mTBI (p≤0.049)min 1 of FC SBP = increased in controls (p≤0.032), but not in mTBI |  |  |  | No significant correlations between symptoms and autonomic response during FC.  |
|  |  |  |  |  |  |  |
| **Author****(Year)** | **Resting BP** | **Challenge BP** | **Resting BRS** | **Challenge BRS** | **Alternative autonomic measure(s)** | **Correlation(s)** |
| Johnson(2020) | Rest (supine) SBP, DBP, MAP = no group difference  | 60s & 90s of CPT SBP = increased in controls (p<0.05), but not in mTBI30s, 60s & 90s of CTP MAP = increased in controls (p<0.05), but not in mTBI 60s, 90s & 120s of CPT SBP & MAP = higher in controls (p<0.05) vs mTBI30s of CPT DBP = increased in controls (p<0.001), but not in mTBIDBP = higher at 60s (p=0.002), 90s (p<0.001) & 120s (p=0.001) of CPT in controls vs mTBI  |  |  |  | No significant correlation between symptom severity scores and autonomic response during CPT. |
| Kozlowski(2013) | Rest SBP & DBP = no group difference | SBPmax on treadmill test = lower in mTBI vs controls (p=0.02) DBPmax on treadmill test = higher in mTBI vs controls (p=0.03) |  |  |  |  |
| La Fountaine(2016) | Rest (seated) SBP, DBP, MAP, pulse pressure = no group differenceRest (seated) SysSlope§§ = lower in mTBI vs controls at 48hrs (p<0.0001) & 1wk (p<0.01) | Exertion SBP, DBP, MAP, pulse pressure = no group difference Exertion SysSlope§§ = lower in mTBI vs controls at 48hrs (p<0.0001) & 1wk (p<0.01)  |  |  |  | Significantly positive correlation between resting pulse pressure and SysSlope§§ in both mTBI (r2= 0.84) and controls (r2=0.97) at ≤48hrs. |
| La Fountaine(2018) | Rest (seated) SBP, DBP, MAP, SBP-LF (mmHg2/Hz) = no group differences |  |  | BRSn-UP, BRSn-Dn & BRS-Avg (ms/mmHg)¶¶ (collapsed across timepoints) = lower in mTBI vs controls (d>1.20) |  |  |
| Leddy(2010) | No significant difference pre-intervention vs post- intervention | SBPmax on treadmill test = higher post-intervention vs pre-intervention (p<0.001) |  |  |  | Significant correlation between symptom improvement (with intervention) and HRmax (r=-0.55) and SBPmax. |
| Liao(2016) |  |  |  |  |  | Significant negative correlations between BAI and lnLF, lnHF, lnTP at 6 & 12wks in mTBI with anxiety, but not mTBI without anxiety.  |
| **Author****(Year)** | **Resting BP** | **Challenge BP** | **Resting BRS** | **Challenge BRS** | **Alternative autonomic measure(s)** | **Correlation(s)** |
| Purkayastha(2019) | Rest (seated) MAP = no group difference  |  |  |  |  |  |
| Sentinathan(2017) |  |  |  |  |  | Significant negative correlation between number of previous mTBIs and seated SampEN at 4.7d (r=-0.743). Significant positive correlation between number of previous mTBIs and seated LF/HF at 25.5d (r=0.778). |
| Sung(2016)a |  |  |  |  |  | Significant positive correlation between BDI and SDNN ($ρ$=0.151), lnLF ($ρ$=0.187) & lnHF ($ρ$=0.199) at ≤1wk. Significant correlation between BDI at 18mos in females and %HF ($ρ$=-0.411) & LF/HF at ≤1wk ($ρ$=0.406).  |
| Sung (2016)b |  |  |  |  |  | Significant negative correlation between BAI at 6wks and lnLF at ≤1wk (rs=-0.391). Significant positive correlation between BDI at 6wks and lnLF/HF at ≤1wk (rs=0.389).  |
| Truong(2016) |  |  |  |  | Constriction latency (conditions A/B/C/ E/F) = higher in mTBI vs controlsMax & min pupil diameter (A-F) = lower in mTBI vs controls Ave constriction velocity (conditions B-F) = lower in mTBI vs controls Peak constriction velocity (condition E) = lower in mTBI vs controls Amplitude of constriction (conditions C/D) = lower in mTBI vs controls Average dilation velocity (conditions D/E) = lower in mTBI vs controls Peak dilation velocity (conditions A-E) = lower in mTBI vs controls 6s post-stimulation diameter (A-F) = lower in mTBI vs controls |  |
| Wright (2017)|| || | Rest (seated) MAP = no difference hx3+ vs hx-; no difference in acute mTBI across timepoints |  |  |  |  |  |
| Wright(2018)|| || | Rest (standing) MAP = no difference hx3+ vs hx-; no difference in acute mTBI across timepoints |  |  |  |  |  |

Abbreviations: ApEN, approximate entropy; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; BP, blood pressure; BRS, baroreceptor sensitivity; COMPASS-31, Composite Autonomic Symptom Score 31 questionnaire; CPT, cold pressor test; DBP, diastolic blood pressure; EP, eyeball pressure stimulation; FC, face cooling; HF, high frequency; HR, heart rate; hx-, no mTBI history; hx3+, history of ≥3 mTBI; LF, low frequency; MAP, mean arterial pressure; mTBI, mild traumatic brain injury; RMSSD, root mean square of successive RR interval differences; SampEN, sample entropy; SBP, systolic blood pressure; SDNN, standard deviation of NN intervals; SysSlope, systolic slope; VM, valsalva maneuver

† squatting and standing portion of squat-stand separated into the early (0-6s), peak (4-7s) and late (6-10s) phases (variables = squat-early, squat-peak, squat-late, stand-early, stand-peak, stand-late); late-change = 10ths value subtracted from 6ths value

‡ measured using progressive treadmill test

¶ BRSgain (ms/mmHg)= gain values from changes in RRIs (ms) in relation to changes in SBP (mmHg), an index of baroreceptor sensitivity

|| SBPunder = initial decrease in SBP with standing (pressure baseline mean – pressure low score)

# HRmax/HRmin = HRmax and HRmin values measured within the first 30s of standing (from supine), a measure of the baroreflex

†† after valsalva maneuver, 90% SBPnorm is the interval between the SBPover (pressure overshoot score – pressure baseline mean) and the point where SBP has decreased by 90% of the difference between the SBPover and SBP baseline mean

‡‡ 30:15 ratio = calculation of ratio between the shortest RRI at or around the 15th heart beat and the longest RRI at or around the 30th beat after standing up

§§ systolic slope (SysSlope) of the arterial pressure wave = calculated from the rate of rise (change in pressure divided by change in time) of the systolic upstroke

¶¶ BRSn = BRS calculated by the R-R interval and beat-by-beat SBP normalized to the corresponding mean directional SBP change for increasing (BRSn-UP) and decreasing SBP (BRSn-DN) and the average of these values (BRSn-Avg)

|| || data from same cohort

a Sung et al. *Psychophysiol*

b Sung et al. *Clin Neuropsychol*