

Table S3

Details of Reviewed Studies – (online only)

Study	Area of Interest	Participants (sample size, age (mean ± SD), school level)	Educational setting & presence of professor/ teacher	HRV measures						Concurrently measured data		Correlation levels with HRV ^{***}		
				HRV device	Measurement Standards Compliance	Baseline measure		HRV parameters		Psycho- physiological data	Self-report & performance data	Psycho- physiological & Others	Performance	
						Software	Measuring time	Time domain	Frequency domain					Non-linear domain
[1] Ramírez- Adrados et al., 2020	Stress	110 (25.3 ± 3.77) Undergraduates (Physiotherapy) N/R	Exam (Oral) w. professor	Polar V800 watch (WB) Kubios N/R/A	N/R	Baseline measured 4 phases (50min) - Before exam - First 1/5 of exam - Last 1/5 of exam - After exam	RMSSD pNN50	LF HF LF/HF	SD1 SD2			L3 - Heart rate - SUDS	L4 - Grade	
[2] Huhn et al., 2018	Stress	40 (20.21 ± 3.10) Undergraduates (Medical) N/R	Exam (Oral) Learning (Seminar) w. professor	Polar V800 heart rate monitor (CB) N/R (Polar Flow) N/R	Malik (1996)	Baseline measured 3 phases - Oral examination (15min) - Seminar (15min) - relaxation (15min)	SDNN RMSSD pNN50	LF HF LF/HF	N/A	Hair cortisol	Stress (PSQ) Empathy (JSPE-S) Burnout (MBI-SS) Self-efficacy (GSE) Depression (PHQ-9)	L3 - Hair cortisol - PSQ	-	
[3] Hunziker et al., 2012	Stress	28 (29 ± 4.9) Professionals (Residents) N/R	Learning (Clinical practice: simulation) w/o. professor	3-lead ECG (Sta) N/R N/R	N/R	Baseline measured 3 phases - Before CPR (30min) - During CPR (Task-dependent) - After CPR (30min)	SDNN	N/A	N/A	Blood cortisol Heart rate	Stress (Single-item, 10- point scale, not validated) Performance (CPR)	L1 - Heart rate L2 - Blood cortisol - Stress	L3 - CPR	
[4] Nakayama et al., 2018	Stress	74 (21 (20–27)) Undergraduates (Nursing) Excl: hypertension, heart/kidney disease, diabetes, medication Instr: No alcohol/ caffeine (-1 day), Sleep well (-1 night)	Learning (Clinical practice: simulation) w. hidden professor	Holter ECG (Sta) N/R N/R/A	Malik (1996)	Baseline measured 4 phases - Break (5min) - Patient care (10min) - Reporting (5min) - Debriefing (10min)	N/A	HF LF/HF	N/A	Heart rate	Stress (Interview)	L3 - Heart rate - Stress (Interview)	-	

Study	Area of Interest	Participants (sample size, age (mean ± SD), school level)	Educational setting & presence of professor/ teacher	HRV measures						Concurrently measured data		Correlation levels with HRV ^{**}	
		HRV device		Measurement Standards Compliance	Baseline measure		HRV parameters			Psycho-physiological data	Self-report & performance data	Psycho-physiological & Others	Performance
		Software			Measuring time	Time domain	Frequency domain	Non-linear domain					
		Preprocessing											
[5] Kim & Nam, 2010	Stress	109 (27.61 (24-40)) Undergraduates (Medical) N/R	Learning (Clinical practice: simulation) w/o. professor	SA-6000 (Sta) SA-6000 (Cardiovit AT-10 Plus) N/R/A	Malik (1996)	Baseline measured After clinical training (5min)	N/A	LF LFn HF HFn LF/HF TotPow	N/A	Heart rate	Performance (Grade)	L3 - Heart rate	L4 - Grade
[6] Timberlake et al., 2018	Stress	24 (24.5 ± 1.4) Undergraduates (Medical) N/R	Exam (Skill assessment) Learning (Clinical practice: simulation, watching video) w. professor	Biopac MP150WSW (Sta) Biopac MP150WSW (Acq-Knowledge) N/R/A	Malik (1996)	Baseline measured 2 phases - Baseline skills assessment (Task-dependent) - Post skills assessment (Task-dependent)	SDNN RMSSD	LF HF	N/A	Heart rate Respiration frequency	Self-monitoring ability (12-item, 5-point scale, not validated) Feedback (12-item, 5-point scale, not validated) Performance (Skills assessment)	L3 - Heart rate - Respiration frequency	L4 - Skill assessment
[7] Redondo-Flórez et al., 2020	Stress	82 (19.63 ± 2.29) Undergraduates (Pharmacy and Biotechnology) N/R	Learning (Clinical practice: laboratory) w. professor	Polar V800 watch (WB) Kubios N/R/A	N/R	Baseline measured 4 phases - Before practice (10min) - 1/3 of practice (Task-dependent) - 3/3 of practice (Task-dependent) - After practice	RMSSD pNN50	LF HF LF/HF	SD1 SD2	Heart rate	Stress (SUDS)	L3 - Heart rate - SUDS	-

Study	Area of Interest	Participants (sample size, age (mean ± SD), school level)	Educational setting & presence of professor/ teacher	HRV measures						Concurrently measured data		Correlation levels with HRV ^{**}	
		HRV device		Measurement Standards Compliance	Baseline measure		HRV parameters		Psycho- physiological data	Self-report & performance data	Psycho- physiological & Others	Performance	
		Software			Measuring time	Time domain	Frequency domain	Non-linear domain					
		Preprocessing											
[11] Castaldo et al., 2016	Stress	42 (18.7±8.7) Undergraduates (Biomedical Engineering) N/R	Exam (Oral)	3-lead ECG (Sta) Kubios Done & Reported	Malik (1996)	Baseline measured 2 phases (5min, 3min) - Stress phase (exam) - Rest phase	SDNN RMSSD pNN50 MeanRR	LF HF LF/HF	SD1, SD2 SampEn D2, dfa1/2 RPImean RPImax REC Rpadet ShanEn	N/A	N/A	-	-
[12] Papousek et al., 2010	Stress	65 (20.5±3.4) Undergraduates (Psychology) Excl: cardiovascular affecting medication; psychological disorders Instr: No alcohol (-12h), No caffeine (-2h); No smoking (-1h)	Exam (Oral) w. hidden professor	Brainvision BrainAmp ENRG Research Amplifier (Sta) N/R Done & Reported	Malik (1996)	Baseline measured 4 phases - Baseline (3min) - Anticipation (3min) - Challenge (3min) - Recovery (3min)	N/A	LF HF LF/HF	N/A	Blood pressure Heart rate	Stress (KUSTA), Affect (PANAS), Academic self- concept (SESSKO)	L1 - Heart rate L2 - KUSTA (Trait N, P: LF State P: LF/HF) L3 - Blood pressure L4 - KUSTA	-
[13] Wimmer et al., 2019	Stress	68 (24.3 ± 4.8) Undergraduates (Psychology) N/R	Exam (Oral) w. professor	CardioMem CM 4000 Holter ECG (Sta) Same as above N/R/A	N/R	Baseline measured 3 phases - Baseline (5min) - Presentation (5min) - Recovery (5min)	SDNN	N/A	N/A	Heart rate	Academic self- concept (SASK)	L3 - Heart rate	-

Study	Area of Interest	Participants (sample size, age (mean ± SD), school level)	Educational setting & presence of professor/ teacher	HRV measures						Concurrently measured data		Correlation levels with HRV ^{***}	
		HRV device		Measurement Standards Compliance	Baseline measure		HRV parameters		Psycho- physiological data	Self-report & performance data	Psycho- physiological & Others	Performance	
		Software			Measuring time	Time domain	Frequency domain	Non-linear domain					
		Preprocessing											
[14] Minkley et al., 2017	Stress	104 (17.48 ± 0.98) Secondary school students <u>Excl:</u> serious medical conditions; long-term medication; over/underweight (BMI > 25 or < 18.5 kg/m²)	Learning (Clinical practice: laboratory) Experiment (Intervention : passive /active/intera ctive)	VitalScan ANS+ chest belt (Medeia Ltd.) (CB) QHRV Stress Assessment (Medeia Ltd.) N/R/A	Malik (1996)	Baseline measured 3 phases (5min, 10min, 15min, 20min, 25min, 30min, 35min) - Passive condition - Active condition - Interactive condition	RMSSD	LF/HF	N/A	Salivary cortisol	Emotion (AEQ) Stress (VAS) Performance (Knowledge test)	L1 - VAS (Passive) - AEQ (Boredom) L3 - Salivary cortisol L4 - VAS (Active, interactive) - AEQ (Enjoyment)	L3 - Grade
[15] Prichard et al., 2012	Stress	5 - consultants (51) - fellows (33) Professionals (Consultant surgeons and endocrine surgical fellows) <u>Excl:</u> regular medication; history of cardiovascular disease/diabetes; non- average fitness; smokers <u>Instr:</u> No caffeine (-1h)	Learning (Clinical practice: surgery) w/o. professor	Polar RS 800 watch (WB) Polar precision performance program N/R/A	Malik (1996)	Baseline measured 2 phases (50 cases) - Pre-operative period (5min) - Intra-operative period (5min)	SDNN RMSSD pNN50	LF HF LF/HF	N/A	Energy consumption Heart rate	N/A	L3 - Heart rate	-
[16] Hurley et al., 2015	Stress	16 (24.375 (21-30)) Undergraduates (Medical) <u>Excl:</u> mental illness history; medication; smokers; BMI < 18 or > 25 kg/m². Male aged 18-40 only	Learning (Clinical practice: simulation)	Nexus-4 ambulatory device (Sta) N/R N/R	N/R	Baseline measured During session (5min)	SDNN RMSSD	N/A	N/A	Blood pressure Heart rate Salivary cortisol Skin conductance	N/A	L3 - Blood pressure - Heart rate - Salivary cortisol - Skin conductance	-

Study	Area of Interest	Participants (sample size, age (mean ± SD), school level)	Educational setting & presence of professor/ teacher	HRV measures						Concurrently measured data		Correlation levels with HRV ^{**}		
		HRV device		Measurement Standards Compliance	Baseline measure		HRV parameters		Psycho- physiological data	Self-report & performance data	Psycho- physiological & Others	Performance		
		Software			Measuring time	Time domain	Frequency domain	Non-linear domain						
		Preprocessing												
[17] Visnovcova et al., 2014	Stress	70 (23.08 ± 0.17) Undergraduates (Medical)	Experiment (Cognitive: math)	VarCorPF8 (Sta+CB)	Malik (1996)	Baseline measured		SDRR MeanRR	LF HF	NCI NUPI 0V% 1V% 2LV% 2UV% Porta's index Guzik's index Ehlers' index	N/A	N/A	-	-
		<u>Excl:</u> respiratory/endocrine/ cardiovascular/ infectious/mental health issues; obesity/ under/overweight; substance abuse; smokers; female not in the proliferative menstrual phase				5 phases								
						- Baseline (6min)								
						- Stroop test (6min)								
[18] Roeser et al., 2012	Stress		Experiment (Cognitive:math (Intervention: morningness/ eveningness) w. professor	Polar RS 800 watch (WB)	Malik (1996)	Baseline measured		RMSSD	LF/HF	N/A	Blood pressure Heart rate	Stress (Single-item, 10- point scale, not validated) Chronotype (MEQ) Affect (GVA) Sleep quality (PSQI) Coping strategy (SVF-78)	L3 - Blood pressure - Heart rate	-
		<u>Excl:</u> respiratory/endocrine/ cardiovascular/ infectious/mental health issues; obesity/ under/overweight; substance abuse; smokers; female not in the proliferative menstrual phase				2 phases								
						- Resting period (10min)								
						- Stress period (5min)								
[19] Kubios et al., 2012	Stress	55 (23.04 ± 2.37) Undergraduates (Major: N/R)	Experiment (Cognitive:math (Intervention: morningness/ eveningness) w. professor	Kubios	Malik (1996)	Baseline measured		RMSSD	LF/HF	N/A	Blood pressure Heart rate	Stress (Single-item, 10- point scale, not validated) Chronotype (MEQ) Affect (GVA) Sleep quality (PSQI) Coping strategy (SVF-78)	L3 - Blood pressure - Heart rate	-
		<u>Excl:</u> respiratory/endocrine/ cardiovascular/ infectious/mental health issues; obesity/ under/overweight; substance abuse; smokers; female not in the proliferative menstrual phase				- Resting period (10min)								
						- Stress period (5min)								

Study	Area of Interest	Participants (sample size, age (mean ± SD), school level)	Educational setting & presence of professor/ teacher	HRV measures						Concurrently measured data		Correlation levels with HRV ^{r**}	
		HRV device		Measurement Standards Compliance	Baseline measure		HRV parameters		Psycho- physiological data	Self-report & performance data	Psycho- physiological & Others	Performance	
		Software			Measuring time	Time domain	Frequency domain	Non-linear domain					
		Preprocessing											
[19] Stein, 2020	Stress	36 (21) Undergraduates (Medical) Excl: medications w. autonomic effects Instr: No caffeine/exercise	Exam (Skill assessment) Learning (Clinical practice: simulation) w/o. professor	2-lead Actiheart (Sta) Kubios N/R/A	N/R	Baseline measured Simulation group (15min) Control group (15min)	SDNN RMSSD	HF	N/A	Heart rate	Stress (STAI -Y)	L3 - Heart rate L4 - STAI-Y	-
[20] Weenk et al., 2018	Stress	20 - consultants (46.20 ±7.16) - fellows and senior residents (35.43 ± 4.44) - junior residents (32.25 ± 1.83) Professionals (Consultants, fellows, residents) Excl: medication affecting heart rate	Learning (Clinical practice: surgery) w/o. professor	Single-lead, chest HealthPatch (CB) N/R N/R	Malik (1996)	Baseline measured 5 phases (48~72hr) - Baseline (15min) - Surgery (Task- dependent) - Outpatient clinic (Task-dependent) - Ward (Task- dependent) - Administrative work (Task- dependent)	SDNN RMSSD	LF/HF	N/A	Heart rate Real time stress percentage	Stress (STAI-SF)	L3 - Heart rate - STAI-SF	-
[21] Wetzel et al., 2010	Stress	30 (34.5 (26-58)) Professionals (Surgical residents) N/R	Learning (Clinical practice: surgery) w/o. professor	Polar S801i watch (WB) Polar Precision Software N/R/A	N/R	Baseline measured 3 phases (recording duration: N/R) - Baseline - Non-crisis simulation - Crisis simulation	RR interval HRV coefficient (C_HRV =SDNN/N N × 100)	LF/HF	N/A	Heart rate Salivary cortisol	Stress (Observed stress rating [by the surgical assistant, 10- point scale, not validated]) Stress (STAI-SF) Coping strategy (Interview) Performance (EPA, OSATS, OTAS)	L3 - Salivary cortisol - STAI-SF L4 - Heart rate	L4 - EPA - OSATS - OTAS

Study	Area of Interest	Participants	Educational setting & presence of professor/teacher	HRV measures						Concurrently measured data		Correlation levels with HRV ^{***}	
		Participant Control		HRV device	Measurement Standards Compliance	Baseline measure		HRV parameters		Psycho-physiological data	Self-report & performance data	Psycho-physiological & Others	Performance
				Software		Measuring time	Time domain	Frequency domain	Non-linear domain				
				Preprocessing									
[22] Hundertmark et al., 2019	Stress	60 (22.8 ± 2.6) Undergraduates (Medical) <u>Instr:</u> No alcohol caffeine/exercise (0d)	Learning (Peer tutoring) w. professor	Polar V800 watch (WB) Kubios N/R/A	Malik (1996)	N/R 5 phases - Preparation (30min) - First 30min of learning - Mid part (30min) - Last 30min of learning - Recovery phase (30min)	RMSSD	N/A	N/A	Salivary cortisol	Stress (TICS, VAS) Attachment (AAS) Personality (BFI-K, SAPS-R) Affect (PANAS) Resilience (RS 13) Performance (Course quality)	L3 - Stress (VAS)	L4 - Tutoring quality
[23] Baker et al., 2017	Stress	8 (N/R) Professionals (Anesthetic trainees) <u>Excl:</u> HRV-influencing medical conditions; regular medications; smokers <u>Instr:</u> No vigorous activity (-30min); no caffeine (-12h)	Learning (Clinical practice: simulation) w. professor	Polar RS800CX watch with chest belt (WB+CB) Polar Protrainer software N/R/A	Malik (1996)	Baseline measured 4 phases - Baseline (5min) - Preparation (5min) - Intubation (5min) - Post-intubation (5min)	N/A	LF/HF	N/A	N/A	Stress (STAI-SF)	L3 - STAI-SF	-
[24] Crewther et al., 2015	Stress	12 (20.1 ± 0.8) Undergraduates (Medical) <u>Excl:</u> Neuropsychiatric illness. <u>Instr:</u> No caffeine/alcohol (-1 night)	Learning (Clinical practice: simulation) w. professor	Zephyr chest belt (CB) MATLAB N/R/A	N/R	Baseline measured 4 phases (Task-dependent) - Base session - Mid session - Post session - Retest session	N/A	LF HF LF/HF	N/A	Heart rate Prefrontal cortex activity Salivary cortisol Salivary testosterone	Stress (STAI-SF) Stress (Single-item, 5-point scale, not validated) Task load (NASA-TLX) Performance (Skill performance)	L3 - Heart rate - Prefrontal cortex activity - Salivary cortisol - Salivary testosterone - STAI-SF - Stress	L3 - Skill assessment

Study	Area of Interest	Participants (sample size, age (mean ± SD), school level)	Educational setting & presence of professor/ teacher	HRV measures						Concurrently measured data		Correlation levels with HRV ^{***}	
				HRV device	Measurement Standards Compliance	Baseline measure		HRV parameters		Psycho-physiological data	Self-report & performance data	Psycho-physiological & Others	Performance
		Software		Measuring time		Time domain	Frequency domain	Non-linear domain					
		Preprocessing											
[28] Scrimin et al., 2019	Attention	62 (6.72 ± 0.57) Primary school students N/R	Experiment (Cognitive: stroop test) w. teacher	Polar+E8+E14 E42ProComp Infiniti (CB) Kubios Done & Reported	N/R	Baseline measured During session - Resting period (approximately 10min)	RMSSD	N/A	N/A	N/A	Classroom climate (38 items, 3-point scale, by researcher) Performance (Emotional stroop task)	L2 - Classroom climate	L2 - Stroop test
[29] Redondo et al., 2019	Attention	25 (22.4 ± 4.5) Undergraduates (Major: N/R) Excl: pharmacological treatment; smokers Instr: No alcohol (-24h); no caffeine (-12h); sleep ≥7h (-1 night)	Experiment (Psychomotor: PVT)	Polar RS800CX watch with chest belt (WB+CB) Kubios Done & Reported	Malik (1996)	Baseline measured 3 phases - Baseline (5min) - Experimental session 1 (10min) - Experimental session 2 (10min)	RMSSD	N/A	N/A	Accommodative response (Microflunctionation)	Sleep quality (Stanford Sleepiness Scale) Performance (Psychomotor vigilance task)	L3 - Accommodative response	L4 - PVT
[30] Guo et al., 2019	Attention	118 (14 ± 1) Secondary school students Excl: cardiovascular disease; health issues	Experiment (Memory) w. teacher	Analog Devices AD8232 (Sta) N/R Done & Reported	Malik (1996)	N/R During experiment (Task-dependent, no more than 40min)	AVNN SDNN SDANN SDNNidx RMSSD pNN50	LF HF TF VLF	SD1 SD2	Pulse rate variability	Cognitive load (Paas and Van Merriënboer cognitive load scale) Performance (Task performance)	-	L3 - Memory
[31] Watford et al., 2020	Stress Attention	81 (19.89 ± 2.84) Undergraduates (Psychology) Excl: excessive overweight/exercise/caffeine consumption; medical or mental health issues	Experiment (Cognitive: math), (Intervention: video stressor) w/o. professor	Biopac MP150 (Sta) Kubios Done & Reported	Malik (1996)	Baseline measured 7 phases - Baseline (5min) Video stressor (3min) Video recovery 1/2 (2.5min/2.5min) Math stressor (3min) Math recovery 1/2 (2.5min/2.5min)	N/A	HF	N/A	Heart rate	Mindfulness (MAAS)	L3 - Heart rate - MAAS	-

Study	Area of Interest	Participants (sample size, age (mean ± SD), school level)	Educational setting & presence of professor/ teacher	HRV measures						Concurrently measured data		Correlation levels with HRV ^{***}	
		HRV device		Measurement Standards Compliance	Baseline measure		HRV parameters		Psycho-physiological data	Self-report & performance data	Psycho-physiological & Others	Performance	
		Software			Measuring time	Time domain	Frequency domain	Non-linear domain					
		Preprocessing											
[32] Azam et al., 2018	Stress Attention	40 (21.870 ± 8.486) Undergraduates (Major: N/R) <u>Excl:</u> anxiety/depressive disorder; hypertension; coronary artery disease; arrhythmias Instr: No caffeine/ exercise (-24h)	Experiment (Cognitive: stroop test)	3-lead PowerLab (Sta) LabChart Pro software Done & Reported	Malik (1996)	Baseline measured 2 phases - Baseline rest phase (5min) - Stress-induction phase (Task-dependent)	N/A	HF	N/A	Eye-tracking data Respiration rate Heart rate	Performance - Gaze behavior - Stroop test	L3 - Heart rate L4 - Respiration rate	L3 - Gaze behavior
[33] Mygind et al., 2018	Stress Attention	47 (10.9 ± 0.71) Primary school students <u>Excl:</u> ADHD; autism	Experiment (Intervention: classroom /natural), (Cognitive: d2 test)	Polar Team2 Pro chest belt (CB) Kubios Done & Reported	N/R	Baseline measured 2 days (day1 = natural environment, day 2 = classroom environment) - During session (approximately 20-min)	RMSSD	N/A	N/A	N/A	Performance (d2 test)	-	L3 - d2 test
[34] Kofman et al., 2006	Stress Attention	48 (22.4 ± 1.52) Undergraduates (Behavioral Sciences) <u>Excl:</u> history of traumatic head injury with loss of consciousness; neurological or psychiatric disorders	Experiment (Cognitive: Task switching, stroop test) w. professor	Holter ECG (Sta) BEAT software N/R	Malik (1996)	Baseline measured 2 phases - No stress period (10min) - Stress period (10min)	N/A	LF HF LF/HF	N/A	N/A	Stress (STAI) Performance (Task-switching, stroop test)	L3 - STAI	L3 - Stroop test

Study	Area of Interest	Participants (sample size, age (mean ± SD), school level)	Educational setting & presence of professor/ teacher	HRV measures						Concurrently measured data		Correlation levels with HRV**	
		HRV device		Measurement Standards Compliance	Baseline measure		HRV parameters		Psycho- physiological data	Self-report & performance data	Psycho- physiological & Others	Performance	
					Measuring time	Time domain	Frequency domain	Non-linear domain					
													Software
[35] Dunne et al., 2019	Stress Attention	25 (N/R) Professionals (Emergency multidisciplinary team members) <u>Excl:</u> Alcohol/substance abuse (-6 months); schizophrenia; current antipsychotic use; recent anti-depressant start (<3 months); anti-depressant dose (>3 months)	Learning (Clinical practice: simulation) Experiment (Intervention : stress management program)	Fitbit Charge 2 wristband (WB) N/R N/R	N/R	Baseline measured No-treatment control group and intervention group (measured over 45 days)	N/A	HF	SD2	Heart rate Salivary cortisol Sleep quality (including sleeping time) TNF – α 24-hour ambulatory blood pressure	Depression, anxiety, and stress (DASS) Burnout (MBI-HSS)	L3 - Heart rate - Salivary Cortisol - TNF – α - Blood pressure	-
[36] Morales et al., 2019	Stress Attention	58 (30.33 ± 4.18) Professionals (Residents) <u>Excl:</u> medication; sleep disorder; females pregnant or in the luteal menstrual phase <u>Instr:</u> No alcohol/caffeine(-24h); No sleep deviation: ≤1hr from average	Experiment (Psychomotor), (Intervention: sleep deprived) w/o. professor	Polar RS800 watch with chest belt (WB+CB) Kubios Done & Reported	Malik (1996)	Baseline measured Control group and experimental group - Pre-test (10min) - Post-test (10min)	RMSSD	LF HF LF/HF	N/A	Salivary cortisol	Mood (EVEA) Performance (Psychomotor vigilance test)	L1 (RMSSD, LF, HF) - Salivary Cortisol - EVEA (Anxiety) L4 (LF/HF) - Salivary Cortisol - EVEA (Anxiety)	L2 (RMSSD, LF,HF) - PVT L4 (LF/HF) - PVT
[37] Bian et al., 2022	Stress	97 (19.78 ± 1.11) Undergraduates (Course of mental health) N/R	Exam (A job interview) w. interviewers (proxies for teachers or professors)	Biopac MP150 (Sta) Acq- Knowledge N/R/A	N/R	Baseline measured High 20% /Low 20% TAI group - Baseline (5min) - Stress (5min) - Recovery (5min)	LnRMS SD	LnLF, LnHF	N/A	N/A	Stress (TAI), Emotional Experience Report (9 scale),	L1 (LnLF, LnHF) -TAI L2 (LnRMSSD) -TAI	-

Study	Area of Interest	Participants (sample size, age (mean ± SD), school level)	Educational setting & presence of professor/ teacher	HRV measures						Concurrently measured data		Correlation levels with HRV ^{r**}		
		HRV device		Measurement Standards Compliance	Baseline measure		HRV parameters		Psycho- physiological data	Self-report & performance data	Psycho- physiological & Others	Performance		
		Software			Measuring time	Time domain	Frequency domain	Non-linear domain						
		Preprocessing												
[42] Gellisch et al., 2022	Stress, Attention	82 (20.15 ± 1.90) Undergraduates (Medical)	Learning/ Experiment (Intervention: face-to-face vs online Zoom class) w. professor	movisens ECG Move 3 (CB)	N/R		RMSSD , pNN50	LF, HF	N/A	Salivary cortisol	Subject stress (VAS); Achievement Emotions Questionnaire (AEQ)	L1 -Salivary cortisol	-	
		<u>Excl:</u> chronic/acute mental issues; endocrine disorders; dependence/ abuse of alcohol		Kubios		-Phase1 (30min)						L3 -VAS		
		<u>Instr:</u> No eating, smoking (-1h)		Done & Reported		-Phase2 (60min)						L4 -AEQ		
				-Phase3 (30mins)										
[43] Tovar et al., 2023	Stress	35 8 physicians (42.4 ± 7.84) 13 residents (29.0 ± 1.87) 14 Undergraduates (Medical) (27.4 ± 4.35)	Experiment (Intervention: a mass-casualty incident (MCI) simulation using VR) w/o. professor	LabChart (v.8.1.24) (Sta)	N/A	<u>Baseline measured</u>	RMSSD	N/A	N/A	N/A	STAI	L3 STAI	-	
		Prism (v.9.3.0)		- Baseline (2min) - VR1: Non- stressful-Non- medical (2min) - VR2: Stressful- Non-medical -VR3: Trauma resuscitation-Low Grade Trauma -VR4: Trauma Resuscitation – High Stress										
		<u>Excl:</u> VR-related issues		N/R/A										
[44] Gellisch et al., 2023	Stress	104 (19.98 ± 1.74) Undergraduates (Medical)	Learning /Experiment (face-to-face learning vs. passive online learning vs. interaction- enhanced online learning) w. professor	ECG Move 3 (CB)	Malik (1996)	<u>Baseline measured</u>	RMSSD , pNN50	LF, HF, LF/HF	N/A	Salivary cortisol	Standardized Visual Analog Scales (VAS); Achievement Emotions Questionnaire (AEQ)	L2(RMSSD, pNN50) - salivary cortisol (interactive)	L1(RMSSD, pNN50, LF/HF) - test score (interactive)	
		Kubios		A course (120min) -Start of course -60min of course -End of course										
		<u>Instr:</u> No eating, dental hygiene, smoking, drinking (-1h)		Done & Reported								L4 (LF, HF, LF/HF) -test score (passive)		

Study	Area of Interest	Participants (sample size, age (mean ± SD), school level)	Educational setting & presence of professor/ teacher	HRV measures						Concurrently measured data		Correlation levels with HRV ^{***}	
		HRV device		Measurement Standards Compliance	Baseline measure		HRV parameters		Psycho-physiological data	Self-report & performance data	Psycho-physiological & Others	Performance	
		Software			Measuring time	Time domain	Frequency domain	Non-linear domain					
		Preprocessing											
[45] Hsin et al., 2023	Stress	28 (Mean= 24) Undergraduates (Medical) (N/R)	Experiment (Mini-Clinical Evaluation Exercise 2D vs. 360°) w/o. professor	Holter-like Nexus-4 (Sta) MATLAB Done & Reported	Malik (1996)	Baseline measured -Baseline -Phase1 (5min) -Phase2 (5min)	RR interval	TP, VLF, LF, HF, LF/HF	N/A	N/A	Mental workload (NASA TLX questionnaire); Simulator sickness (SSQ)	L2 (VLF) -SSQ	L3 -Mental workload
[46] Redondo-Florez et al., 2023	Stress	80 (19.12 ± 2.25) Undergraduates (Pharmacy and Biotechnology) (N/R)	Learning (first chemical laboratory practices) w. professor	Polar H10, (CB) Kubios N/R/A	N/A	Baseline measured 4 Phases -Pre-practice(10min) -Practice1 (1/3) -Practice2 (3/3) -Post-practice(5min)	RMSSD , pNN50, HRmean, HRmax	LF, HF, LF/HF	SD1, SD2	N/A	Stress (SUDS)	L3 -SUDS	-
[47] Balikci et al., 2023	Stress	73 (21.7 ± 2.8) Undergraduates (Medical) Excl: medications; cardiovascular and psychiatric diseases Instr: No alcohol (-48h); caffeine/smoke (-2h)	Experiment (TV vs. classical music vs. silence) presence of professor N/R	NeXus-10 (Sta) Biotrace+ N/R/A	N/A	Baseline measured -Baseline (4min) -Anticipation (4min) -Challenge (4min) -Recovery (4min)	SDNN, RMSSD	LF, HF, LF/HF	N/A	BVP, Skin conductance	N/A	L3 (SDNN, RMSSD, HF) L4 (LF, LF/HF) -BVP -Skin conductance	-
[48] Chao et al., 2021	Stress	32 (Median= 24) Undergraduates (Medical) Excl: pregnancy; hypertension; recent surgery; heart disorders; epilepsy & VR-related issues	Learning / Experiment (360° VR vs. 2D video for learning history-taking & physical examination skills) presence of professor N/R	Holter-like NeXus-4 (Sta) MATLAB Done & Reported	Malik (1996)	Baseline measured -Baseline (5min) -Intervention (5min)	SDNN, RMSSD	LF, HF, LF/HF	N/A	N/A	Milestones (Sleep-disordered breathing (SDB))	-	L3

* Note:

AAS (Adult Attachment Scale);
AEQ (Achievement Emotions Questionnaire);
AMOS 8-15 (Abilità e motivazione allo studio - Ability and Motivation);
BFI-K (Big Five Inventory);
BVP (Blood Volume Pulse);
DASS (Depression, Anxiety and Stress Scale);
EAS-CF (Emotionality Activity Sociability Temperament Survey-Child Form);
EPA (End Product Assessment Rating Scale);
EVEA (Escala de Valoración del Estado de Ánimo, Mood Assessment Scale);
GAU (Guilford's Alternative Uses test);
GSE (The Scale of General Perceived Self-Efficacy);
GVA (Global Vigor and Affect Scale);
JSPE-S (The Jefferson Scale of Physician Empathy: Student version);
KUSTA (Kurz-Skala Stimmung/Aktivierung -short mood/activation stress);
MAAS (Mindful Attention and Awareness Scale);
MBI-HSS (The Maslach Burnout Inventory – Human Service Survey);
MBI-SS (The Maslach Burnout Inventory- Student Survey);
MEQ (Morningness-Eveningness Questionnaire);
NASA-TLX (NASA-Task Load Index);
OTAS (Observational Teamwork Assessment for Surgery);
OSATS (Objective Structured Assessment of Technical Skill);
PANAS (Positive Affect and Negative Affect Scale);
PHQ-9 (Patient Health Questionnaire with 9 item);
PSQ (Perceived Stress Questionnaire);
PSRS (Perceived Stress Reactivity Scale);
PVT (Psychomotor Vigilance Test);
RS 13 (Resilience Scale Short Version with 13-items);
PVM (Paas and Van Merriënboer cognitive load scale);
SAPS-R (Short Revised Almost Perfect Scale);
SASK (German Academic Self-Concept questionnaire);
SDB (Sleep-Disordered Breathing);
SESSKO (Subject-specific Adaptation of the Academic Self-Concept Scales);
SSS (Stanford Sleepiness Scale);
SSQ (Simulator sickness);
STAI (State-Trait Anxiety Inventory);
SUDS (Subjective perception of Distress Strait);
SVF-78 (Stress Verarbeitungs Fragebogen – Stress coping);
TAI (Test Anxiety Inventory);
TICS (Trier Inventory for the Assessment of Chronic Stress);
TNF – α (Tumor Necrosis Factor alpha);
VAS (Visual Analogue Scale);

N/A = Not Applicable;

N/R = Not Reported;

N/R/A = Not Reported but Assumed;

WB=Wristband;

CB=Chest belt;

Sta=Static device;

Excl=Excluded Participants;

Instr=Participant Instruction;

w.=with;

w/o=without

** Note:

L1 = large effect size,

L2 = intermediate and small effect size,

L3 = coherence but no correlation info,

L4 = no effect or not correlated (no effect $r < .05$, small effect $r < .20$, intermediate effect $r < .33$, large effect $r > .37$)

Reviewed Studies

- Azam, M. A., Ritvo, P., Fashler, S.R., & Katz, J. (2018). Stressing the feedback: Attention and cardiac vagal tone during a cognitive stress task. *Cognition and Emotion*, 32(4), 867-875.
<https://doi.org/10.1080/02699931.2017.1346500>
- Baker, B. G., Bhalla, A., Doleman, B., Yarnold, E., Simons, S., Lund, J. N., & Williams, J. P. (2017). Simulation fails to replicate stress in trainees performing a technical procedure in the clinical environment. *Medical Teacher*, 39(1), 53–57.
<https://doi.org/10.1080/0142159X.2016.1230188>
- Balıkçı, İ., Tok, S., & Binboga, E. (2023). The effect of background audio and audiovisual stimuli on students' autonomic responses during and after an experimental academic examination. *Brain & Behavior*, 13, 1-18. <https://doi.org/10.1002/brb3.3153>
- Bian, W., Zhang, X., & Dong, Y. (2022). Autonomic nervous system response patterns of test-anxious individuals to evaluative stress. *Frontiers in Psychology*, 13, 1-8.
<https://doi.org/10.3389/fpsyg.2022.824406>
- Castaldo, R., Xu, W., Melillo, P., Pecchia, L., Santamaria, L., & James, C. (2016, August 16–20). *Detection of mental stress due to oral academic examination via ultra-short-term HRV analysis* [Conference presentation]. 38th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), Orlando, FL, USA.
<https://doi.org/10.1109/EMBC.2016.7591557>
- Castaldo, R., Montesinos, L., Melillo, P., James, C., & Pecchia, L. (2019). Ultra-short term HRV features as surrogates of short term HRV: A case study on mental stress detection in real life. *BMC Medical Informatics and Decision Making*, 19(1), Article 12.
<https://doi.org/10.1186/s12911-019-0742-y>

- Chao, Y.-P., Chuang, H.-H., Hsin, L.-J., Kang, C.-J., Fang, T.-J., Li, H.-Y., Huang, C.-G., Kuo, T. B. J., Yang, C. C. H., Shyu, H.-Y., Wang, S.-L., Shyu, L.-Y., & Lee, L.-A. (2021). Using a 360° virtual reality or 2D video to learn history taking and physical examination skills for undergraduate medical students: Pilot randomized controlled trial. *JMIR Serious Games*, 9(4), e13124. <https://doi.org/10.2196/13124>
- Crewther, B. T., Shetty, K., Jarchi, D., Selvadurai, S., Cook, C. J., Leff, D. R., ... & Yang, G. Z. (2015). Skill acquisition and stress adaptations following laparoscopic surgery training and detraining in novice surgeons. *Surgical Endoscopy*, 30, 2961–2968. <https://doi.org/10.1007/s00464-015-4584-0>
- Dunne, P. J., Lynch, J., Prihodova, L., O'Leary, C., Ghoreyshi, A., Basdeo, S. A., ... & White, B. (2019). Burnout in the emergency department: Randomized controlled trial of an attention-based training program. *Journal of Integrative Medicine*, 17(3), 173–180. <https://doi.org/10.1016/j.joim.2019.03.009>
- Gellisch, M., Morosan-Puopolo, G., Wolf, O. T., Moser, D. A., Zaehres, H., & Brand-Saberi, B. (2023). Interactive teaching enhances students' physiological arousal during online learning. *Annals of Anatomy*, 247, 152050. <https://doi.org/10.1016/j.aanat.2023.152050>
- Gellisch, M., Wolf, O. T., Minkley, N., Kirchner, W. H., Brüne, M., & Brand-Saberi, B. (2022). Decreased sympathetic cardiovascular influences and hormone-physiological changes in response to Covid-19-related adaptations under different learning environments. *Anatomical Sciences Education* 15(5), 811-826. <https://doi.org/10.1002/ase.2213>
- Georgiou, K. E., Dimov, R. K., Boyanov, N. B., Zografos, K. G., Larentzakis, A. V., & Marinov, B. I. (2019). Feasibility of a new wearable device to estimate acute stress in novices during high-fidelity surgical simulation. *Folia Medica*, 61(1), 49–60. <https://doi.org/10.2478/folmed-2019-0001>

- Guo, J., Dai, Y., Wang, C., Wu, H., Xu, T., & Lin, K. (2019). A physiological data-driven model for learners' cognitive load detection using HRV-PRV feature fusion and optimized XGBoost classification. *Software: Practice and Experience*, 50(11), 2046–2064.
<https://doi.org/10.1002/spe.2730>
- Hammoud, S., Karam, R., Mourad, R., Saad, I., & Kurdi, M. (2018). Stress and heart rate variability during university final examination among Lebanese students. *Behavioral Sciences*, 9(1), 3.
<https://doi.org/10.3390/bs9010003>
- Hsin, L.-J., Chao, Y.-P., Chuang, H.-H., Kuo, T. B. J., Yang, C. C. H., Huang, C.-G., Kang, C.-J., Lin, W.-N., Fang, T.-J., & Li, H.-Y. (2023). Mild simulator sickness can alter heart rate variability, mental workload, and learning outcomes in a 360° virtual reality application for medical education: A post hoc analysis of a randomized controlled trial. *Virtual Reality*, 27, 3345–3361. <https://doi.org/10.1007/s10055-022-00688-6>
- Huhn, D., Schmid, C., Erschens, R., Junne, F., Herrmann-Werner, A., Möltner, A., Herzog, W., & Nikendei, C. (2018). A comparison of stress perception in international and local first semester medical students using psychometric, psychophysiological, and humoral methods. *International Journal of Environmental Research and Public Health*, 15(12), 2820.
<https://doi.org/10.3390/ijerph15122820>
- Hundertmark, J., Alvarez, S., Loukanova, S., & Schultz, J. H. (2019). Stress and stressors of medical student near-peer tutors during courses: A psychophysiological mixed methods study. *BMC Medical Education*, 19, 1–16. <https://doi.org/10.1186/s12909-019-1521-2>
- Hunziker, S., Semmer, N. K., Tschan, F., Schuetz, P., Mueller, B., & Marsch, S. (2012). Dynamics and association of different acute stress markers with performance during a simulated resuscitation. *Resuscitation*, 83(5), 572–578.
<https://doi.org/10.1016/j.resuscitation.2011.11.013>

- Hurley, A. M., Kennedy, P. J., O'Connor, L., Dinan, T. G., Cryan, J. F., Boylan, G., & O'Reilly, B. A. (2015). SOS save our surgeons: Stress levels reduced by robotic surgery. *Gynecological Surgery*, 12(3), 197–206. <https://doi.org/10.1007/s10397-015-0891-7>
- Kim, K. S., & Nam, H. J. (2010). Autonomic nervous function in final year Oriental medical students in Korea: Influence of gender, age and academic performance. *Stress and Health*, 26(5), 430–436. <https://doi.org/10.1002/smi.1316>
- Kofman, O., Meiran, N., Greenberg, E., Balas, M., & Cohen, H. (2006). Enhanced performance on executive functions associated with examination stress: Evidence from task-switching and Stroop paradigms. *Cognition & Emotion*, 20(5), 577–595. <https://doi.org/10.1080/02699930500270913>
- Llinares, C., Higuera-Trujillo, J. L., & Serra, J. (2021). Cold and warm coloured classrooms: Effects on students' attention and memory measured through psychological and neurophysiological responses. *Building & Environment*, 196, 1-11. <https://doi.org/10.1016/j.buildenv.2021.107726>
- Martínez-Pascual, B., Ramírez-Adrados, A., Fernández-Martínez, S., Gonzalez-de-Ramos, C., Fernández-Elías, V. E., & Clemente-Suárez, V. J. (2022). Autonomic stress response of physiotherapy student in the different scenarios of an objective structured clinical examination. *BMC Medical Education*, 22, 1-7. <https://doi.org/10.1186/s12909-022-03903-9>
- Minkley, N., Ringeisen, T., Josek, L. B., & Kärner, T. (2017). Stress and emotions during experiments in biology classes: Does the work setting matter? *Contemporary Educational Psychology*, 49, 238–249. <https://doi.org/10.1016/j.cedpsych.2017.03.002>
- Morales, J., Yáñez, A., Fernández-González, L., Montesinos-Magraner, L., Marco-Ahulló, A., Solana-Tramunt, M., & Calvete, E. (2019). Stress and autonomic response to sleep deprivation in medical residents: A comparative cross-sectional study. *PloS One*, 14(4). <https://doi.org/10.1371/journal.pone.0214858>

- Mygind, L., Stevenson, M. P., Liebst, L. S., Konvalinka, I., & Bentsen, P. (2018). Stress response and cognitive performance modulation in classroom versus natural environments: A quasi-experimental pilot study with children. *International Journal of Environmental Research and Public Health*, 15(6), 1098. <https://doi.org/10.3390/ijerph15061098>
- Nakayama, N., Arakawa, N., Ejiri, H., Matsuda, R., & Makino, T. (2018). Heart rate variability can clarify students' level of stress during nursing simulation. *PLoS One*, 13(4). <https://doi.org/10.1371/journal.pone.0195280>
- Papousek, I., Nauschnegg, K., Paechter, M., Lackner, H. K., Goswami, N., & Schuler, G. (2010). Trait and state positive affect and cardiovascular recovery from experimental academic stress. *Biological Psychology*, 83(2), 108–115. <https://doi.org/10.1016/j.biopsycho.2009.11.008>
- Prichard, R. S., O'Neill, C. J., Oucharek, J. J., Colinda, Y. H., Delbridge, L. W., & Sywak, M. S. (2012). A prospective study of heart rate variability in endocrine surgery: Surgical training increases consultant's mental strain. *Journal of Surgical Education*, 69(4), 453–458. <https://doi.org/10.1016/j.jsurg.2012.04.002>
- Ramírez-Adrados, A., Fernández-Martínez, S., Martínez-Pascual, B., Gonzalez-de-Ramos, C., Fernández-Elías, V. E., & Clemente-Suárez, V. J. (2020). Psychophysiological stress response of physiotherapy last year students in his final degree dissertation. *Physiology & Behavior*, 222. <https://doi.org/10.1016/j.physbeh.2020.112928>
- Redondo, B., Vera, J., Luque-Casado, A., García-Ramos, A., & Jiménez, R. (2019). Associations between accommodative dynamics, heart rate variability and behavioural performance during sustained attention: A test-retest study. *Vision Research*, 163, 24–32. <https://doi.org/10.1016/j.visres.2019.07.001>

- Redondo-Flórez, L. A. U. R. A., Tornero-Aguilera, J. F., & Clemente-Suárez, V. J. (2020). Could academic experience modulate psychophysiological stress response of biomedical sciences students in laboratory? *Physiology & Behavior*, 223.
<http://doi.org/10.1016/j.physbeh.2020.113017>
- Roeser, K., Obergfell, F., Meule, A., Vögele, C., Schlarb, A. A., & Kübler, A. (2012). Of larks and hearts—morningness/eveningness, heart rate variability and cardiovascular stress response at different times of day. *Physiology & Behavior*, 106(2), 151–157.
<http://doi.org/10.1016/j.physbeh.2012.01.023>
- Redondo-Flórez, L., & Clemente-Suárez, V. J. (2023). Psychophysiological stress response of novel students in chemical laboratory practices. *Journal of Psychophysiology*, 37(3), 125–133.
<https://doi.org/10.1027/0269-8803/a000314>
- Scrimin, S., Moscardino, U., & Mason, L. (2018). First-graders' allocation of attentional resources in an emotional Stroop task: The role of heart period variability and classroom climate. *British Journal of Educational Psychology*, 89(1), 146–164. <https://doi.org/10.1111/bjep.12228>
- Scrimin, S., Moscardino, U., Finos, L., & Mason, L. (2019). Effects of psychophysiological reactivity to a school-related stressor and temperament on early adolescents' academic performance. *The Journal of Early Adolescence*, 39(6), 904–931.
<https://doi.org/10.1177/0272431618797008>
- Stein, C. (2020). The effect of clinical simulation assessment on stress and anxiety measures in emergency care students. *African Journal of Emergency Medicine*, 10(1), 35–39.
<http://doi.org/10.1016/j.afjem.2019.12.001>
- Timberlake, M. D., Stefanidis, D., & Gardner, A. K. (2018). Examining the impact of surgical coaching on trainee physiologic response and basic skill acquisition. *Surgical Endoscopy*, 32, 4183–4190. <https://doi.org/10.1007/s00464-018-6163-7>

- Tovar, M. A., Zebley, J. A., Higgins, M., Herur-Raman, A., Zwemer, C. H., Pierce, A. Z., Ranniger, C., Sarani, B., & Phillips, J. P. (2023). Exposure to a virtual reality mass-casualty simulation elicits a differential sympathetic response in medical trainees and attending physicians. *Prehospital and Disaster Medicine*, 38(1), 48–56.
<https://doi.org/10.1017/S1049023X22002448>
- Visnovcova, Z., Mokra, D., Mikolka, P., Mestanik, M., Jurko, A., Javorka, M., ... & Tonhajzerova, I. (2015). Alterations in vagal-immune pathway in long-lasting mental stress. *Oxidative Stress and Cardiorespiratory Function*, 45-50. https://doi.org/10.1007/5584_2014_10
- Visnovcova, Z., Mestanik, M., Javorka, M., Mokra, D., Gala, M., Jurko, A., ... & Tonhajzerova, I. (2014). Complexity and time asymmetry of heart rate variability are altered in acute mental stress. *Physiological Measurement*, 35(7), 1319. <http://doi.org/10.1088/0967-3334/35/7/1319>
- Watford, T. S., O'Brien, W. H., Koerten, H. R., Bogusch, L. M., Moeller, M. T., Sonia Singh, R., & Sims, T. E. (2020). The mindful attention and awareness scale is associated with lower levels of high-frequency heart rate variability in a laboratory context. *Psychophysiology*, 57(3), 1–12. <https://doi.org/10.1111/psyp.13506>
- Weber, J., Heming, M., Apolinario-Hagen, J., Liszio, S., & Angerer, P. (2024). Comparison of the perceived stress reactivity scale with physiological and self-reported stress responses during ecological momentary assessment and during participation in a virtual reality version of the Trier Social Stress Test. *Biological Psychology*, 186, 108762.
<https://doi.org/10.1016/j.biopsycho.2024.108762>
- Weenk, M., Alken, A. P. B., Engelen, L. J. L. P. G., Bredie, S. J. H., van de Belt, T. H., & van Goor, H. (2018). Stress measurement in surgeons and residents using a smart patch. *The American Journal of Surgery*, 216(2), 361–368. <https://doi.org/10.1016/j.amjsurg.2017.05.015>

- Wetzel, C. M., Black, S. A., Hanna, G. B., Athanasiou, T., Kneebone, R. L., Nestel, D., Wolfe, J. H., & Woloshynowych, M. (2010). The effects of stress and coping on surgical performance during simulations. *Annals of Surgery*, 251(1), 171–176.
<https://doi.org/10.1097/sla.0b013e3181b3b2be>
- Wetzel, C. M., George, A., Hanna, G. B., Athanasiou, T., Black, S. A., Kneebone, R. L., ... & Woloshynowych, M. (2011). Stress management training for surgeons—a randomized, controlled, intervention study. *Annals of Surgery*, 253(3), 488–494.
<https://doi.org/10.1097/SLA.0b013e318209a594>
- Wimmer, S., Lackner, H. K., Papousek, I., & Paechter, M. (2019). Influences of different dimensions of academic self-concept on students' cardiac recovery after giving a stressful presentation. *Psychology Research and Behavior Management*, 12, 1031–1040.
<https://doi.org/10.2147/prbm.s219784>
- You, J., Wen, X., Liu, L., Yin, J., & Ji, J. S. (2023). Biophilic classroom environments on stress and cognitive performance: A randomized crossover study in virtual reality (VR). *PLOS ONE*, 18(11), 1-22. <https://doi.org/10.1371/journal.pone.0291355>