Data Category	Information
Protocol Acronym	RSA biofeedback in adolescents with autism
Primary registry and trial identifying number	ClinicalTrials.gov Identifier: NCT04628715
Date of registration in primary registry	November 13, 2020
Source(s) of monetary or material support	Marguerite-Marie Delacroix Foundation
Primary sponsor	KU Leuven
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Public title	Evaluation of a biofeedback intervention to reduce stress in adolescents with autism spectrum disorder
Scientific title	Evaluating the potential of respiratory-sinus-arrhythmia biofeedback for reducing physiological stress in adolescents with autism: a randomized controlled study Protocol Acronym: RSA biofeedback in adolescents with autism
Countries of recruitment	Belgium
Health condition(s) or problem(s) studied	Autism Spectrum Disorder
Intervention(s)	Supervised active intervention: RSA Biofeedback (1x/week, 5 weeks, 30 min/session and 20 min daily practice). The main goal during this intervention is to breath at resonance frequency.
	Supervised control intervention: sham RSA biofeedback (1x/week, 5 weeks, 30 min/session and 20 min daily practice). The participants will not practice at their resonance frequency, but at a normal breathing frequency during the sessions and during home practice.
	Non-supervised intervention: RSA biofeedback (1 guided session of 45 min, daily practice for 20 minutes, 5 weeks). The main goal during this intervention is to breath at resonance frequency.
Key inclusion and exclusion criteria	Ages eligible for study: 13-18 years; Sexes eligible for study: both; Recruitment of typically developing adolescents: yes, for cross-sectional phase
	Inclusion: Written informed consent/assent; For adolescents with ASD only: Confirmed ASD-diagnosis (DSM-IV/5)
	Exclusion: Presence of intellectual disability (DSM-IV/5); Uncorrected hearing- or vision impairment; Presence of congenital heart diseases, diagnosed cardiovascular abnormalities or somatic diseases with a known impact on heart function;

	Pregnancy; Insufficient knowledge of Dutch language; Participation in other Clinical Trial(s); For typically developing adolescents only: Presence of neurodevelopmental disorder or psychiatric disorder (DSM-IV/5); Autism Quotient score ≥32; Presence of a sibling with a neurodevelopmental disorder (DSM-IV/5)
Study type	Phase 1: Cross-sectional
	Phase 2: Interventional - Stratified block randomization - Parallel assignment during supervised intervention - Participants are blinded for group allocation during supervised intervention - No blinding procedures during non-supervised intervention - Primary purpose: evaluation of efficacy and feasibility
Date of First Enrollment	November 26, 2020
Target sample size	Adolescents with Autism Spectrum Disorder: 128
	Typically developing adolescents: 38
Recruitment status	Recruiting
Primary outcome(s)	Outcome name: Change in Root Mean Square of Successive Differences between normal heartbeats. Method: time domain analysis measure of heart rate variability as measured by ECG. Time points for typically developing adolescents: at baseline. Time points for adolescents with autism spectrum disorder: at baseline; after 5 weeks supervised intervention; after 5 weeks non-supervised intervention.
	Outcome name: Logarithm of High-Frequency Heart Rate Variability (LnHF-HRV). Method: frequency domain analysis measure of heart rate variability as measured by ECG. Time points for typically developing adolescents: at baseline. Time points for adolescents with autism spectrum disorder: at baseline; after 5 weeks supervised intervention; after 5 weeks non-supervised intervention.
Key secondary outcomes	Physiological assessment of heart rate, breathing frequency, skin conductance and fingertip temperature using a NeXus-10 MKII biofeedback device in combination with Biotrace+ Software. These measurements will be repeated at multiple assessment points (only for adolescents with autism spectrum disorder). In addition, change will be measured between the different tasks in both adolescent groups during the assessment itself. Time points for typically developing adolescents: at baseline. Time points for adolescents with autism spectrum disorder: at baseline; after 5 weeks supervised intervention; after 5 weeks non-supervised intervention.
	Cortisol level using three saliva samples during the assessment procedure for both adolescent groups. Time points for typically developing adolescents: at baseline. Time points for adolescents with autism spectrum disorder: at baseline; after 5 weeks supervised intervention; after 5 weeks non-supervised intervention.
	Behavioral data collected with - Autism Spectrum Quotient - Adolescent Version at baseline assessment - Social Responsiveness Scale - 2nd edition at baseline and after non-supervised intervention - Repetitive Behavior Scale – Revised at baseline and after non-supervised intervention

	- Strengths and Difficulties Questionnaire (parent report) at baseline assessment and after the non-supervised intervention. - Strengths and Difficulties Questionnaire (self-report) at baseline assessment and after the non-supervised intervention. - Depression Anxiety and Stress Scale-21 items version at baseline, after 5 weeks supervised intervention; after 5 weeks non-supervised intervention. - Perceived Stress Scale - Adolescent version at baseline, after 5 weeks supervised intervention; after 5 weeks non-supervised intervention. - Visual Analogue Scale for stress perception during assessment at baseline, after 5 weeks supervised intervention; after 5 weeks non-supervised intervention. - Visual Analogue Scale for Sensory hyper-responsivity at baseline, after 5 weeks supervised intervention; after 5 weeks non-supervised intervention. - Physical Activity Vital Sign at baseline, after 5 weeks supervised intervention, after 5 weeks non-supervised intervention.
Ethics Review	Approved: 09/04/2021 (version 3.0) Ethics Committee Research UZ/KU Leuven Herestraat 49 B 3000 Leuven (Belgium) Tel +32 16 34 86 00 ec@uzleuven.be Approved: 20/10/2020 (version 2.0) Ethics Committee Research UZ/KU Leuven Herestraat 49 B 3000 Leuven (Belgium) Tel +32 16 34 86 00 ec@uzleuven.be Approved: 02/07/2020 (version 1.0) Ethics Committee UPC KU Leuven UPC Z.Org KU Leuven Tel +32 27 58 05 10 ria.dhaeze@upckuleuven.be Ethics Committee Research UZ/KU Leuven Herestraat 49 B 3000 Leuven (Belgium) Tel +32 16 34 86 00 ec@uzleuven.be
IPD sharing statement	No plan to share IPD
Protocol version	Issue date: 12/03/2021 Protocol version 3.0 Authors: AT, TVD, KA, JS **Revision chronology:** Protocol version 1.0, 17/06/2020 Original Protocol version 2.0, 15/09/2020 Revision according to advice and recommendations of Ethics Committee Research UZ/KU Leuven Protocol version 3.0, 12/03/2021 Amendment