



CLINICAL STUDIES & RESEARCH

Endocalyx, Endogenx & GlycoCheck,



1992-2022

BIOREGENICS, MICROVASCULAR HEALTH SOLUTIONS, MYBODYRX, NULIFE SCIENCES
[Company address]

GlycoCheck is being used by researchers in hospitals and universities in Africa, Asia, Australia, China, Europe, Japan, Russia, and the United States.

Examples of Diseases and Conditions Being Researched

- *Type 2 Diabetes*
- *Stroke*
- *Early Cognition Impairment*
- *Epilepsy*
- *Syndrome X*
- *Kidney failure / Hemodialysis*
- *Pre-eclampsia / HELLP*
- *Sepsis / Septic Shock*

- *Pre-Eclampsia*
- *Atherosclerosis*
- *Heart failure*
- *Premature Atherosclerosis*
- *Malaria / Dengue*
- *Obesity*
- *ESRD Proteinuria*
- *Inflammation*

Key Partner in THE CRUCIAL CONSORTIUM

The Crucial Consortium brings together 12 partners from multiple fields (clinicians, fundamental scientists, scientific SMEs, exploitation and dissemination SME, management SME, and a patient advocacy), representing 7 different countries.

The Crucial Consortium aims to address a difficult problem regarding how co-morbidities give rise both to mental disorders and non-mental disorders. In order to achieve this, they have assembled a consortium that has a balanced mix of skills on several levels.

It consists of fundamental scientists and clinicians. It consists of specialists in neuroscience (UM, Scannexus) and in cardiovascular science (UCL, UNAV, FIMA, GlycoCheck, KU Leuven, VIB).

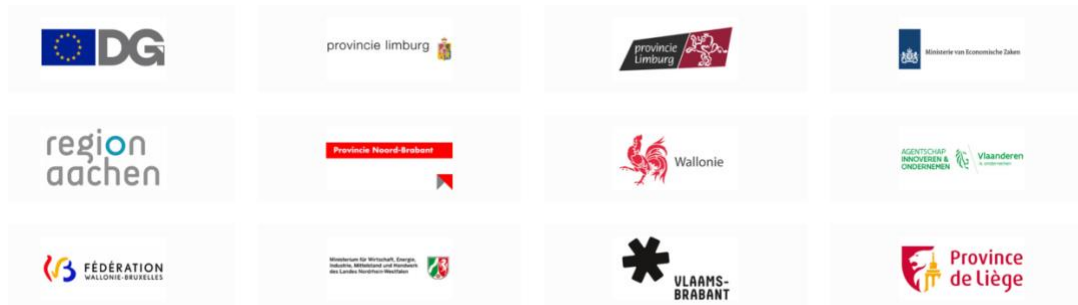
The clinical scientists are strong leaders in the field of MRI (UCL, UM, UNAV, Scannexus), whereas the fundamental partners have strong skills in molecular biology and genetics that will allow them to develop new biomarkers and identify new pathways for

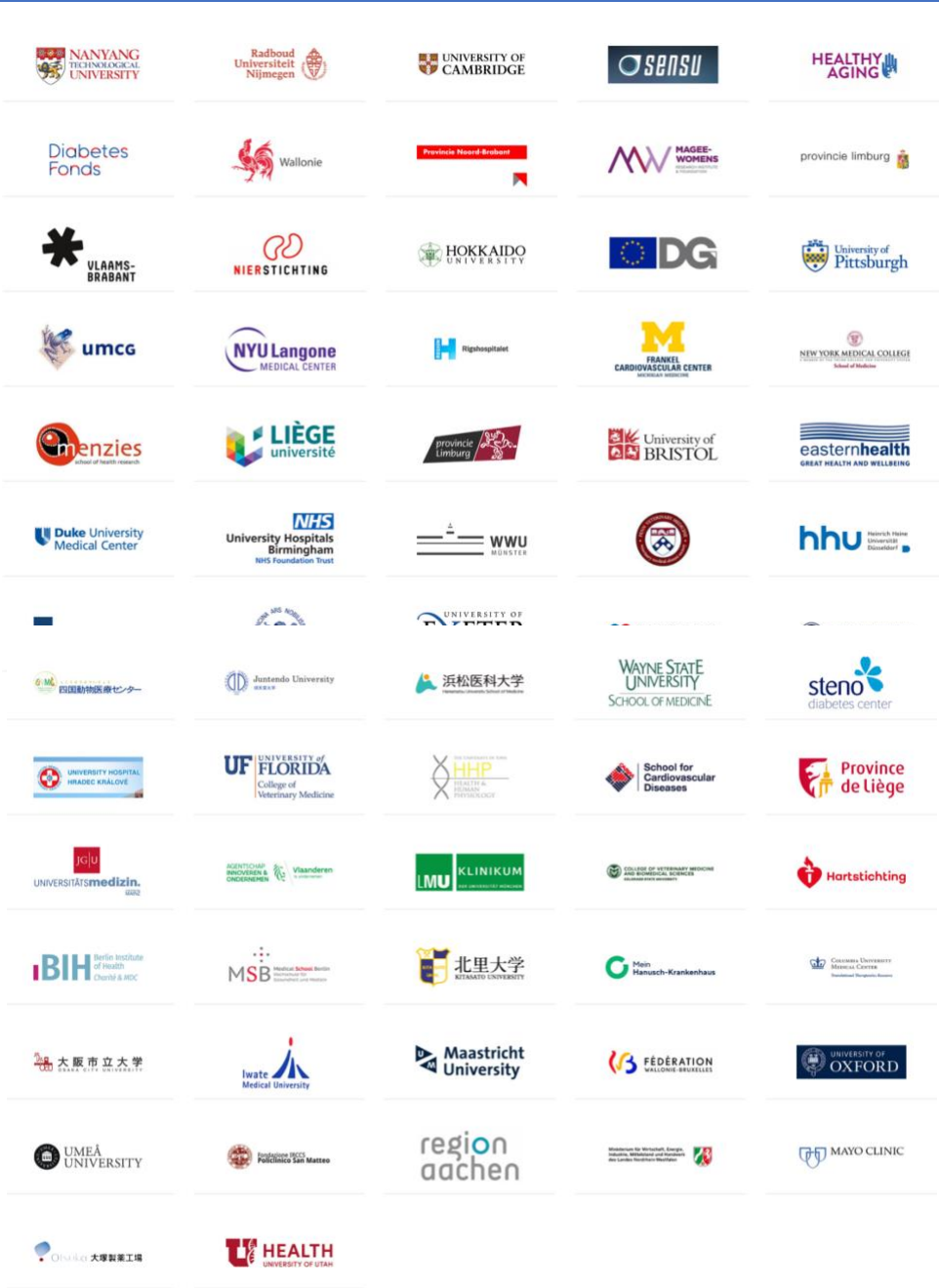
[Read more here](#)

KEY PARTNER WITH INTERREG AND HEALTHY AGING



HEALTHY AGING IS A EUREGIONAL PROJECT WITHIN THE INTERREG EUREGIO MAAS-RHINE PROGRAM . THE PARTNERS (BIOMED IS THE LEAD PARTNER) WITHIN THIS CONSORTIUM (BIOMED , MUMC + , GIGA LIÈGE , UKA , CURADOR , MYHEALTH , IMOMEC , GLYCOCHECK , ASTEL MEDICA AND DNAMITO) USE THEIR EXPERTISE AND KNOWLEDGE TO THE MAXIMUM TO DETECT PREMATURE AGING OF THE IMMUNE SYSTEM AND TO SLOW DOWN AGING AND RELATED CHRONIC CONDITIONS. THIS CONSORTIUM WANTS TO DEVELOP CROSS-BORDER KNOWLEDGE PLATFORMS WITHIN THE EMR FOR SHARING AND DISSEMINATING KNOWLEDGE. MOST OF THE ACTIVITIES IN THIS PROJECT HAVE A VERY SPECIFIC MEDICAL-SCIENTIFIC FOCUS. THE PARTNERS OF THIS PROJECT AIM TO INNOVATE AND VALIDATE THE KNOWLEDGE COLLECTED IN THE CONTEXT OF THESE ACTIVITIES. THE RESULTS OF THIS PROJECT SHOULD LEAD TO LOWER HEALTHCARE COSTS. THIS PROJECT IS SUPPORTED BY THE EUROPEAN REGIONAL DEVELOPMENT FUND OF THE EUROPEAN UNION WHICH, THROUGH CROSS-BORDER PROJECTS, PROVIDES INNOVATION, STIMULATES A HEALTHY ENVIRONMENT AND THE LABOR MARKET. MORE INFORMATION CAN BE FOUND HERE. INTERREG PROGRAM AND FINANCING PARTNERS INCLUDE:





REPRODUCIBILITY AND VALIDITY STUDIES

CLINICAL PAPERS

BEDSIDE ANALYSIS OF THE SUBLINGUAL MICROVASCULAR GLYCOCALYX IN THE EMERGENCY ROOM AND INTENSIVE CARE UNIT – THE GLYCONURSE STUDY

KUEMPERS 2018: GOOD INTRA-OBSERVER AND EXCELLENT INTRA-CLASS REPRODUCIBILITY OF PBR MEASUREMENTS IN ICU AND ER PATIENTS; INCREASED PBR IN ICU PATIENTS COMPARED WITH ER PATIENTS. PBR CORRELATES WITH MEAN ARTERIAL PRESSURE (MAP) AND WITH CRP AND SOFA SCORES.

EARLY ONSET PREECLAMPSIA IS ASSOCIATED WITH GLYCOCALYX DEGRADATION AND REDUCED MICROVASCULAR PERFUSION

WEISSGERBER 2019: REPRODUCIBILITY OF PBR MEASUREMENTS IN PRE-ECLAMPSIA PATIENTS INCREASES WHEN TAKING AVERAGE OF 2 OR 3 MEASUREMENTS.

ASSOCIATION OF SUBLINGUAL MICROCIRCULATION PARAMETERS AND ENDOTHELIAL GLYCOCALYX DIMENSIONS IN RESUSCITATED SEPSIS

KUEMPERS 2019: PBR IN PATIENTS CORRELATES WITH PLASMA SYNDECAN-1 LEVELS AND WITH ATOMIC FORCE MICROSCOPE MEASUREMENTS OF GLYCOCALYX DIMENSION ON CULTURED ENDOTHELIAL CELLS EXPOSED TO PATIENTS' PLASMA.

INCREASE IN PERFUSED BOUNDARY REGION OF ENDOTHELIAL GLYCOCALYX IS ASSOCIATED WITH HIGHER PREVALENCE OF ISCHEMIC HEART DISEASE AND LESIONS OF MICROCIRCULATION AND VASCULAR WALL

GORSHKOV 2018: INCREASE OF PBR IS ASSOCIATED WITH ISCHEMIC HEART DISEASE.

EXPERIMENTAL PAPERS

RAPID INSULIN-MEDIATED INCREASE IN MICROVASCULAR GLYCOCALYX ACCESSIBILITY IN SKELETAL MUSCLE MAY CONTRIBUTE TO INSULIN-MEDIATED GLUCOSE DISPOSAL IN RATS

ESKENS 2013: INSULIN INCREASES PBR, AND HYALURONIDASE TREATMENT OF THE GLYCOCALYX ABOLISHES THE INSULIN EFFECT

EARLY IMPAIRMENT OF SKELETAL MUSCLE ENDOTHELIAL GLYCOCALYX BARRIER PROPERTIES IN DIET-INDUCED OBESITY IN MICE

ESKENS 2014: PBR IS INCREASED IN RESPONSE TO A HIGH FAT DIET (FIGURE 2D) AND PBR CORRELATES WITH INCREASED DURATION AND LEVEL OF PLASMA GLUCOSE (AREA UNDER THE CURVE OF GLUCOSE) AFTER GLUCOSE TOLERANCE TEST. THE DEXTRAN 150kDA EXCLUSION ZONE (FIGURE 1).

PERTURBED MECHANOTRANSDUCTION BY ENDOTHELIAL SURFACE GLYCOCALYX MODIFICATION GREATLY IMPAIRS THE ARTERIOGENIC PROCESS

POTTER 2015: INHIBITION OF ENDOTHELIAL HYALURONAN PRODUCTION INCREASES PBR, WHICH IS ASSOCIATED WITH DIMINISHED GLYCOCALYX DIMENSION AS MEASURED WITH ADVANCED AGE RESULTS IN A DIMINISHED ENDOTHELIAL GLYCOCALYX
MACHIN 2018: PBR INCREASE IN OLD MICE IS ASSOCIATED WITH DECREASED GLYCOCALYX DIMENSION, AND INCREASED PBR IS ASSOCIATED WITH DECREASED GLYCOCALYX DIMENSION.

CURRENT ONGOING STUDIES USING GLYCOCHECK AND ENDOCALYX PRO

STUDIES ON ENDOCALYX PRO EFFECTIVENESS ARE ONGOING. FOR THE COMPLETE LIST, PLEASE GO TO MICROVASCULAR.COM/ENDOCALYX-PRO-STUDIES

STUDIES ON THE EFFECTIVENESS OF ENDOCALYX PRO ARE ONGOING. SEVERAL STUDIES ARE COMPLETE, SOME STUDIES ARE ONGOING, WITH NEW STUDIES LAUNCHING IN THE FUTURE.

MANY OF THESE STUDIES BEGAN SEVERAL YEARS AGO. IT TAKES YEARS TO COMPLETE THEM, AND EVEN AFTER THEY ARE COMPLETED IT CAN TAKE MONTHS BEFORE THE PEER-REVIEWED RESEARCH STUDY IS RELEASED TO THE PUBLIC. AS SOON AS RESULTS ARE AVAILABLE, WE WILL SHARE THEM PUBLICLY ON THIS PAGE.

ENDOCALYX PRO HAS COMPLETED AND HAS ONGOING STUDIES THAT BEEN RUNNING SINCE 2015. THESE STUDIES ARE IN CELL CULTURES, ANIMALS, AND IN HUMANS. THE STUDIES IN HUMANS INCLUDE DOUBLE-BLIND PLACEBO DESIGNS. THESE STUDIES ARE ON THE FOLLOWING HEALTH CONDITIONS AND DISEASES:

COVID-19

AGING

DIABETES

KIDNEY DISEASE

PSORIASIS

HEART DISEASES

SEPSIS

IN 2020, COVID-19 APPEARED AND DISRUPTED GLOBAL HEALTH. BECAUSE WE WERE ALREADY INVOLVED IN MANY OF THE STUDIES LISTED BELOW, WE WERE ABLE TO QUICKLY ADD AND DEVELOP STUDIES TO ASSESS COVID-19 HOSPITALIZATION AND LONG-HAUL COMPLICATIONS. THERE'S A GREAT DESIRE GLOBALLY TO UNDERSTAND THE PHYSIOLOGY AND IMPACT OF THE COVID-19 VIRUS AND MUTATIONS AS IT RELATES TO COMPLICATIONS, HOSPITALIZATIONS, AND MORTALITY. IT'S ESTIMATED THAT 50 PERCENT OF PATIENTS THAT HAVE RECOVERED FROM THE COVID-19 VIRUS HAVE SOME RESULTING COMPLICATIONS LEADING TO WHAT'S BEEN TERMED LONG-HAUL COVID.

FUNCTIONAL STUDIES ON ENDOCALYX PRO™ ARE ONGOING AND PLANNING TO START IN THE FOLLOWING HEALTH CONDITIONS AND DISEASES, TWO OF WHICH ARE COVID-19 STUDIES THAT USE ENDOCALYX PRO™.

COVID-19 STUDY ABSTRACT: *HEPARAN SULFATE MIMETIC FUCOIDAN RESTORES THE ENDOTHELIAL GLYCOCALYX AND PROTECTS AGAINST DYSFUNCTION INDUCED BY SERUM OF COVID-19 PATIENTS ON ICU. ACCUMULATING EVIDENCE PROVES THAT ENDOTHELIAL DYSFUNCTION IS INVOLVED IN COVID-19 PROGRESSION. WE PREVIOUSLY DEMONSTRATED THAT THE ENDOTHELIAL SURFACE GLYCOCALYX HAS A CRITICAL ROLE IN MAINTENANCE OF VASCULAR INTEGRITY. HERE WE HYPOTHESIZED THAT SERUM FACTORS OF SEVERE COVID-19 PATIENTS AFFECT THE GLYCOCALYX AND RESULT INTO ENDOTHELIAL DYSFUNCTION. WE INCLUDED BLOOD SAMPLES OF 32 COVID-19 HOSPITALIZED PATIENTS AT THE LEIDEN UNIVERSITY MEDICAL CENTER: OF WHICH 26 FROM INTENSIVE CARE UNIT (ICU), 6 NON-ICU, 18 CONVALESCENT SAMPLES 6 WEEKS AFTER HOSPITAL DISCHARGE, AND OF 12 AGE-MATCHED HEALTHY DONORS (CONTROL) DURING THE FIRST PERIOD OF THE OUTBREAK. FIRST, WE DETERMINED ENDOTHELIAL (ANGIOPOIETIN 2, ANG2) AND GLYCOCALYX DEGRADATION (SOLUBLE THROMBOMODULIN, sTM AND SYNDECAN-1, sSDC1) MARKERS IN PLASMA. IN PLASMA OF COVID-19 PATIENTS, CIRCULATING ANG2 AND sTM WERE ELEVATED IN PATIENTS ON THE ICU. PRIMARY LUNG MICROVASCULAR ENDOTHELIAL CELLS (HPMEC) AND HUMAN GLOMERULAR MICROVASCULAR ECs (GENCs) CULTURES IN THE PRESENCE OF THESE SERA LED TO EC GLYCOCALYX DEGRADATION, BARRIER DISRUPTION, INFLAMMATION AND INCREASED COAGULATION ON THE ENDOTHELIAL SURFACE, SIGNIFICANTLY DIFFERENT COMPARED TO HEALTHY CONTROL AND NON-ICU PATIENT SERA. THESE CHANGES ALL COULD BE RESTORED IN THE PRESENCE OF FUCOIDAN, A PRINCIPAL COMPONENT OF THE SUPPLEMENT ENDOCALYX PRO™. IN CONCLUSION, OUR DATA HIGHLIGHT THE LINK BETWEEN ENDOTHELIAL GLYCOCALYX DEGRADATION, BARRIER FAILURE AND INDUCTION OF A PROCOAGULANT SURFACE IN COVID-19 PATIENTS ON ICU WHICH COULD BE TARGETED EARLIER IN DISEASE BY THE PRESENCE OF THE HEPARAN SULFATE (HS) MIMETIC FUCOIDAN, A NATURAL EXTRACT OF LAMINARIA JAPONICA NOVEL THERAPEUTIC SUPPLEMENT ENDOCALYX PRO™.*

COVID-19 STUDY DESIGN: *THE EFFECT OF DIETARY GLYCOCALYX PRECURSOR SUPPLEMENTATION ON ENDOTHELIAL FUNCTION, ON MARKERS OF VASCULAR FUNCTION AND ON CARDIAC PERFORMANCE IN PATIENTS WITH COVID-19 INFECTION. WE WILL CONDUCT A 12-MONTH RANDOMIZED, PLACEBO-CONTROLLED STUDY TO EVALUATE THE EFFECT OF DIETARY SUPPLEMENTATION WITH GLYCOCALYX PRECURSORS ON ENDOTHELIAL FUNCTION IN PATIENTS WITH COVID-19 INFECTION. IN TOTAL 60 PATIENTS WHO HAVE BEEN HOSPITALIZED DUE TO COVID-19 INFECTION WILL BE INCLUDED IN THE STUDY FOR A PERIOD OF 12 MONTHS. PATIENTS WILL BE RANDOMLY ASSIGNED TO RECEIVE THE DIET GLYCOCALYX PRECURSORS SUPPLEMENTATION OR PLACEBO FOR A PERIOD OF FOUR MONTHS. THE PRIMARY ENDPOINT IS AN IMPROVEMENT OF THE PBR, A VALUABLE INDEX OF ENDOTHELIAL FUNCTION AFTER 4 MONTHS IN THE SUPPLEMENTATION GROUP COMPARED TO THE PLACEBO GROUP. AT TWELVE MONTHS, WHICH IS 8 MONTHS AFTER STOPPING WITH THE INTERVENTIONS, PATIENTS WILL ALSO RETURN FOR A FOLLOW-UP MEASUREMENT. [CLICK HERE TO READ THE DETAILS AT CLINICALTRIALS.GOV.](#)*

AGING STUDY ABSTRACT: DIETARY GLYCOCALYX PRECURSOR SUPPLEMENTATION RESTORES THE ENDOTHELIAL GLYCOCALYX AND AMELIORATES AGE-RELATED VASCULAR DYSFUNCTION. ADVANCED AGE IS ACCOMPANIED BY A DIMINISHED GLYCOCALYX THAT MAY BE LINKED TO ALTERED HYALURONAN (HA) SYNTHESIS. CURRENTLY, THE IMPACT OF A DIMINISHED GLYCOCALYX IN AGE-RELATED ARTERIAL DYSFUNCTION IS UNKNOWN. TO EXPLORE THIS, YOUNG (4.4 ± 0.2 MONTHS [Y]) AND OLD (27.5 ± 0.1 MONTHS [O]) MALE B6D2F1 MICE WERE FED A GLYCOCALYX PRECURSOR (GP) DIET CONTAINING HIGH MOLECULAR WEIGHT-HA OR CONTROL (NC) DIET FOR ~10 WEEKS. PLASMA HA WAS GREATER IN YOUNG AND OGP, COMPARED TO ONC MICE ($P < 0.05$). MARKERS OF GLYCOCALYX THICKNESS/FUNCTION AND MICROVASCULAR FUNCTION WERE DECREASED WITH AGING ($P < 0.05$). GP DIET INCREASED GLYCOCALYX PROPERTIES AND MICROVASCULAR FUNCTION IN OGP MICE ($P < 0.05$). ENDOTHELIAL FUNCTION, ASSESSED BY CAROTID ARTERY VASODILATION TO ACETYLCHOLINE, DECREASED WITH AGING ($P < 0.05$). GP DIET AUGMENTED ENDOTHELIAL FUNCTION IN OGP MICE ($P < 0.05$). AT BASELINE, AORTIC STIFFNESS, ASSESSED BY PULSE WAVE VELOCITY, WAS ELEVATED WITH AGING ($P < 0.05$). 10 WEEKS OF GP DIET DECREASED AORTIC STIFFNESS IN OGP MICE ($P < 0.05$), NO CHANGE OCCURRED IN ANY OTHER GROUP ($P > 0.05$). THERE WERE DIFFERENCES IN AORTIC STRUCTURE (I.E., GREATER MEDIAL CROSS-SECTIONAL AREA AND COLLAGEN CONTENT AND LOWER ELASTIN CONTENT) BETWEEN ONC AND YOUNG, AS WELL AS OGP MICE ($P < 0.05$). ALTHOUGH MEDIAL CROSS-SECTIONAL AREA WAS GREATER IN OGP, COMPARED TO YOUNG MICE ($P < 0.05$), COLLAGEN AND ELASTIN CONTENT WERE SIMILAR ($P > 0.05$). IN CONCLUSION, 10 WEEKS OF DIETARY GP SUPPLEMENTATION IN OLD MICE RESTORES GLYCOCALYX PROPERTIES, WHICH IS ACCOMPANIED BY AUGMENTED MICROVASCULAR AND ENDOTHELIAL FUNCTION, AS WELL AS DECREASED AORTIC STIFFNESS, SUGGESTING THE GLYCOCALYX MAY BE AN EFFECTIVE THERAPEUTIC TARGET FOR AGE-RELATED ARTERIAL DYSFUNCTION.

DIABETES STUDY ABSTRACT: GLYCOCALYX RESTORATION REDUCES ARTERIAL STIFFNESS IN DIABETIC FEMALE MICE. ARTERIAL STIFFENING, A CHARACTERISTIC FEATURE OF TYPE 2 DIABETES, IS AN IMPORTANT CONTRIBUTOR TO THE DEVELOPMENT AND PROGRESSION OF CARDIOVASCULAR DISEASE (CVD). THUS, A BETTER UNDERSTANDING OF THE PRECIPITATING FACTORS UNDERLYING ARTERIAL STIFFENING IS VITAL TO IDENTIFY NEWER TARGETS AND STRATEGIES TO REDUCE CVD BURDEN, PARTICULARLY IN DIABETIC WOMEN WHO EXHIBIT HEIGHTENED ARTERIAL STIFFENING AND MORE SEVERE CVD. DEGRADATION OF THE ENDOTHELIAL GLYCOCALYX IN DIABETES IS THOUGHT TO CONTRIBUTE TO ENDOTHELIAL DYSFUNCTION AND CVD DEVELOPMENT. HOWEVER, WHETHER GLYCOCALYX DEGRADATION IS ALSO AN IMPORTANT DETERMINANT OF ARTERIAL STIFFENING REMAINS UNKNOWN. HEREIN, WE HYPOTHESIZE THAT RESTORATION OF THE GLYCOCALYX WITH DIETARY SUPPLEMENTATION OF GLYCOCALYX PRECURSORS (DSGP, INCLUDING GLUCOSAMINE SULFATE, FUCOIDAN, SUPEROXIDE DISMUTASE, AND HIGH MOLECULAR WEIGHT HYALURONAN; ENDOCALYXTM) IMPROVES ENDOTHELIAL FUNCTION AND LESSENS ARTERIAL STIFFNESS IN DIABETIC FEMALE MICE. TO TEST THIS HYPOTHESIS, WE USED 12-WEEK OLD DB/DB FEMALE MICE THAT WERE TREATED WITH DSGP (100 MG/KG/DAY) OR VEHICLE (I.E., PEANUT BUTTER) FOR FOUR

WEEKS, AND AN AGE-MATCHED DB/+ COHORT AS REFERENCE CONTROL. AFTER EUTHANASIA, WE ASSESSED EX VIVO AORTIC STIFFNESS AND GLYCOCALYX LENGTH VIA ATOMIC FORCE MICROSCOPY. USING PRESSURE MYOGRAPHY, WE ALSO DETERMINED EX VIVO MESENTERIC ARTERY ENDOTHELIAL FUNCTION AND STIFFNESS BY MEASURING FLOW-MEDIATED DILATION AND THE PASSIVE MECHANICAL PROPERTIES OF THE ARTERIAL WALL, RESPECTIVELY. CONSISTENT WITH OUR HYPOTHESIS, VEHICLE-TREATED DB/DB MICE EXHIBITED DEGRADATION OF THE ENDOTHELIAL GLYCOCALYX, IMPAIRED ENDOTHELIUM-DEPENDENT VASODILATION, AND INCREASED ARTERIAL STIFFNESS WHEN COMPARED WITH CONTROL DB/+ FEMALES. MOREOVER, TREATMENT WITH DSGP WAS EFFECTIVE AT RESTORING THE ENDOTHELIAL GLYCOCALYX IN DB/DB MICE. NOTABLY, THIS RESTORATION OF THE GLYCOCALYX WAS ACCOMPANIED WITH IMPROVEMENTS IN ENDOTHELIAL FUNCTION AND REDUCTIONS IN ARTERIAL STIFFNESS. COLLECTIVELY, THESE FINDINGS SUPPORT THE NOTION THAT THE ENDOTHELIAL GLYCOCALYX SHOULD BE CONSIDERED AS A PUTATIVE THERAPEUTIC TARGET TO REVERSE ARTERIAL STIFFENING IN DIABETIC FEMALES. READ THE ABSTRACT HERE: [CLICK HERE TO READ THE DETAILS AT CLINICALTRIALS.GOV.](#)

KIDNEY DISEASE ABSTRACT: ENDOCALYX PRO™ SUPPLEMENTATION PRESERVES MICROVASCULAR HEALTH IN SOUTH ASIAN TYPE 2 DIABETIC PATIENTS IN A RANDOMIZED CONTROLLED TRIAL. SOUTH ASIAN DIABETIC PATIENTS HAVE AN INCREASED RISK OF DEVELOPING VASCULAR COMPLICATIONS AND MICROVASCULAR DYSFUNCTION HAS BEEN LINKED TO THE DEVELOPMENT OF THESE DIABETIC COMPLICATIONS. WE INVESTIGATED THE EFFECT OF 3 MONTHS ENDOCALYX PRO™ SUPPLEMENTATION ON MICROVASCULAR HEALTH, MEASURED WITH SDF IMAGING, IN SOUTH ASIAN TYPE 2 DIABETIC PATIENTS IN A RANDOMIZED DOUBLE-BLINDED PLACEBO-CONTROLLED TRIAL (NCT03889236). THE ENDOCALYX PRO™ GROUP RECEIVED ENDOCALYX PRO™ SUPPLEMENT DAILY FOR 3 CONSECUTIVE MONTHS, WHICH CONSISTS OF A MIX OF FUCOIDAN, GLUCOSAMINE SULPHATE, HYALURONIC ACID, SUPEROXIDE DISMUTASE AND POLYPHENOLS. PRIMARY OUTCOME WAS IMPROVEMENT OF MICROVASCULAR PARAMETERS MEASURED WITH SDF-IMAGING. IN VITRO, THE INHIBITORY EFFECT OF FUCOIDAN TO THE HEPARAN SULPHATE-DEGRADING ENZYME HEPARANASE WAS EVALUATED. AT BASELINE, CLINICAL PARAMETERS OR INFLAMMATORY MARKERS WERE WITHIN NORMAL RANGES FOR BOTH GROUPS, AND WERE NOT AFFECTED BY ENDOCALYX PRO™ SUPPLEMENTATION AS EVALUATED WITH LINEAR MIXED MODELS. ENDOCALYX PRO™ SUPPLEMENTATION IMPROVED CAPILLARY BLOOD VOLUME, MICROVASCULAR HEALTH SCORE AND THE PERFUSED BOUNDARY REGION (PBR) COMPARED TO THE PLACEBO GROUP EVALUATED WITH INDEPENDENT T-TEST. IN CONTRAST TO THE PLACEBO GROUP, NO INCREASE IN PLASMA HEPARANASE ACTIVITY WAS OBSERVED AFTER ENDOCALYX PRO™ SUPPLEMENTATION. IN VITRO EXAMINATION SHOWED THAT ENDOCALYX PRO'S™ PRINCIPAL COMPONENT FUCOIDAN DOSE DEPENDENTLY INHIBITED HEPARANASE. THIS STUDY SHOWS THAT ENDOCALYX PRO™ PRESERVES MICROVASCULAR HEALTH IN SOUTH ASIAN DIABETIC PATIENTS, POTENTIALLY THROUGH THE HEPARANASE INHIBITING EFFECT OF FUCOIDAN.

PSORIASIS STUDY DESIGN: *THE EFFECT OF DIETARY INTERVENTION ON ENDOTHELIAL GLYCOCALYX INTEGRITY AND MICROVASCULAR PERFUSION IN PATIENTS WITH PSORIATIC DISEASE. SIXTY PATIENTS WITH PSORIATIC DISEASE, WHO ARE REFERRED TO THE OUTPATIENT PSORIASIS CLINIC OF THE ATTIKON UNIVERSITY HOSPITAL, WILL BE RANDOMIZED TO RECEIVE FOOD SUPPLEMENT ENDOCALYX PRO™ (N=30) OR PLACEBO (N=30) FOR 4 CONSECUTIVE MONTHS. CLICK HERE TO READ THE DETAILS AT CLINICALTRIALS.GOV.*

HEART STUDY OVERALL SCIENTIFIC SUMMARY: *2021 DUTCH HEART FOUNDATION – HEALTH~HOLLAND PUBLIC-PRIVATE PARTNERSHIP (PPP) APPLICATION FORM. HYPERTENSION IS THE MOST IMPORTANT RISK FACTOR FOR CARDIOVASCULAR DISEASE AND ALL-CAUSE MORTALITY WORLDWIDE ACCOUNTING FOR 10.5 MILLION DEATHS EVERY YEAR. THE RISK FOR CARDIOVASCULAR DISEASE AND DEATH IS HIGHEST IN SUBJECTS WITH TREATMENT RESISTANT HYPERTENSION, WHICH IS DEFINED AS HYPERTENSION DESPITE THE USE OF 3 ANTIHYPERTENSIVE DRUGS. SUBJECTS WITH TREATMENT RESISTANT HYPERTENSION ARE OFTEN CHARACTERIZED BY SYSTEMIC AND SKIN SODIUM OVERLOAD. RECENT STUDIES SUGGEST THAT THE NEGATIVE EFFECTS OF SODIUM CAN BE NEUTRALIZED BY THE GLYCOCALYX, AN INTRAVASCULAR SUGAR LAYER, WHICH PREVENTS SODIUM TRANSPORT TO THE SKIN INTERSTITIUM AND PROVIDES AN INTRAVASCULAR BUFFER FOR SODIUM. HOWEVER, THE GLYCOCALYX IS DAMAGED IN PATIENTS WITH HYPERTENSION. ENDOCALYX PRO™ IS A FOOD SUPPLEMENT THAT HAS BEEN SHOWN TO RESTORE THE GLYCOCALYX. BECAUSE SUBJECTS WITH TREATMENT RESISTANT HYPERTENSION ARE CHARACTERIZED BY SODIUM OVERLOAD AND A DAMAGED GLYCOCALYX, WE HYPOTHEZIZE THAT GLYCOCALYX RESTORATION BY ENDOCALYX PRO™ WILL LOWER SKIN SODIUM CONTENT, IMPROVE THE MICROCIRCULATION AND REDUCE BLOOD PRESSURE >8 MMHG AFTER 8 WEEKS OF TREATMENT. WE WILL PERFORM A PROOF OF CONCEPT RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND TRIAL IN 32 SUBJECTS WITH TREATMENT RESISTANT HYPERTENSION. WE WILL STUDY SKIN SODIUM ACCUMULATION, MICROCIRCULATION CHARACTERISTICS, BLOOD PRESSURE, (SERIOUS) ADVERSE EVENTS, SAFETY, HEALTH-RELATED QUALITY OF LIFE AND COST-EFFECTIVENESS. IN CASE ENDOCALYX PRO™ PROVES TO MECHANISTICALLY IMPACT BLOOD PRESSURE REGULATION, THIS PROJECT WILL GUIDE FURTHER APPLICATION IN THE CLINICAL RESEARCH SETTING. AN EXPECTED BLOOD PRESSURE REDUCTION OF 8 MMHG HAS PREVIOUSLY BEEN DEMONSTRATED TO LOWER THE RISK OF CORONARY HEART DISEASE AND STROKE WITH 17% AND 27%, RESPECTIVELY. CONSIDERING THE 675,000 PATIENTS WITH TREATMENT RESISTANT HYPERTENSION IN THE NETHERLANDS, THIS BLOOD PRESSURE REDUCTION MAY PREVENT 1,748 CARDIOVASCULAR EVENTS OR DEATHS AND LOWER ANNUAL HEALTH CARE COSTS WITH €112 MILLION.*

KIDNEY CELL CULTURE STUDY OBJECTIVES: *PROTECTION OF THE ENDOTHELIAL GLYCOCALYX BY ENDOCALYX PRO™ IN MURINE CKD. THE IDENTIFICATION OF MECHANISMS MAINTAINING OR EVEN REBUILDING THE ENDOTHELIAL GLYCOCALYX (EGC) ARE HIGHLY DESIRABLE. CURRENTLY, THE EVIDENCE ABOUT MECHANISMS FOR*

PROTECTION AND MAINTENANCE OF THE EGC IS LOW. EGC PRESERVING FACTORS ARE FOR EXAMPLE ALBUMIN OR THE HIGH-DENSITY LIPOPROTEINS (HDL) WITH THEIR BOUND SPHINGOSINE-1 PHOSPHATE. AN INTERESTING APPROACH WAS DEMONSTRATED BY MACHIN ET AL. THEY DEMONSTRATED THAT DIETARY SUPPLEMENTATION OF GLYCOCALYX PRECURSORS AS IN ENDOCALYX PRO™ ARE ABLE TO ENHANCE THE EGC BARRIER FUNCTION IN OLDER MICE (7). PILOT DATA IN APPARENTLY HEALTHY INDIVIDUALS SHOW A SIGNIFICANT UP TO 10% IMPROVEMENT OF EGC DIMENSIONS AFTER A SHORT ORAL ENDOCALYX INTAKE IN SUGGESTED DOSING. A CLINICAL STUDY IS CURRENTLY TESTING THE EFFECT OF THE ENDOCALYX PRO™ IN THE CONTEXT OF DIABETIC NEPHROPATHY (CLINICALTRIALS.GOV: NCT03889236). ENDOCALYX PRO™ PRESERVES AND REFURBISHES EGC IN VITRO AFTER ENZYMATIC DIGESTION. WHETHER ENDOCALYX PRO™ PRESERVES EGC IN VITRO HAS NOT BEEN INVESTIGATED YET. THEREFORE, WE ANALYSED THE EFFECT OF ENDOCALYX PRO™ IN ENDOTHELIAL CELL CULTURE AND QUANTIFIED EGC WITH THE ATOMIC FORCE MICROSCOPY (AFM). OUR GROUP HAS SUCCESSFULLY ESTABLISHED AFM METHODOLOGY TO QUANTIFY NANOMECHANICAL ENDOTHELIAL CELL PROPERTIES, I. E. STIFFNESS AND THICKNESS, OF THE EGC. AFM IS ABLE TO REVEAL THE EXISTENCE OF A MATURE EGC ON THE LUMINAL ENDOTHELIAL SURFACE OF FRESHLY ISOLATED RODENT AORTA PREPARATIONS EX VIVO AS WELL AS ON A VARIETY OF LIVING ENDOTHELIAL CELLS IN VITRO. PRELIMINARY RESULTS INDICATE THAT ENDOCALYX PRO™ IS ABLE TO PRESERVE THE EGC IN VITRO. INTERESTINGLY, ENDOCALYX PRO™ IS NOT ONLY CAPABLE OF MAINTAINING THE EGC, BUT TO REFURBISH EGC-THICKNESS AFTER ENZYMATIC DIGESTION BY HEPARINASE 1. FURTHER EXPERIMENTS ARE NEEDED TO RULE OUT THE MECHANISMS BY WHICH ENDOCALYX PRO™ ENHANCES EGC THICKNESS. FURTHERMORE, THE DECREASE OF EGC-HEIGHT CAUSED BY 5% SERUM OF HEMODIALYSIS PATIENTS WAS REVERSED BY ENDOCALYX PRO™ INCUBATION AS WELL.

SEPSIS STUDY SUMMARY: ENDOCALYX PRO™ IN ANIMAL SEPSIS PROPOSAL. SEPSIS REMAINS A MAJOR PROBLEM OF EMERGENCY AND INTENSIVE CARE MEDICINE, AS WELL AS THE MOST FREQUENT CASE OF DEATH IN HOSPITALIZED PATIENTS. THE IMPAIRMENT OF THE ENDOTHELIAL GLYCOCALYX (EGC), A DELICATE CARBOHYDRATE-RICH LAYER COATING THE LUMINAL SURFACE OF THE VASCULAR ENDOTHELIUM, CORRELATES WITH HIGHER MORTALITY IN SEPSIS. SCHMIDT ET AL. PROVIDED PROOF-OF-CONCEPT THAT INHIBITION OF ENZYMATIC GLYCOCALYX DIGESTION COMPLETELY ABOLISHED ACUTE LUNG INJURY AND IMPROVED SURVIVAL IN MURINE ABDOMINAL SEPSIS AND ENDOTOXEMIA. ENDOCALYX PRO™, A PATENTED DIETARY SUPPLEMENT, HAS BEEN SHOWN IN PILOT STUDIES TO SUPPORT GLYCOCALYX HOMEOSTASIS AND ENRICH ITS DIMENSIONS IN APPARENTLY HEALTHY INDIVIDUALS. OUR HYPOTHESIS IS, THAT AN ORAL PRETREATMENT WITH ENDOCALYX PRO™ WILL SIGNIFICANTLY PROTECT GLYCOCALYX AND MINIMIZE SUBSEQUENT ORGAN FAILURE IN TWO DIFFERENT MURINE SEPSIS MODELS (LPS AND CLP). THE GOAL OF THIS PILOT PROJECT IS TO ANALYZE THE EGC OF PULMONARY AND CREMASTERIC MICROVESSELS BY INTRAVITAL MICROSCOPY AS WELL AS ORGAN DAMAGE AND EDEMA IN TWO MURINE SEPSIS MODELS, ENDOTOXEMIA (LPS) AND POLYMICROBIAL ABDOMINAL (CLP) SEPSIS. THE ANTICIPATED RESULTS COULD PLAY AN IMPORTANT ROLE

IN OUR UNDERSTANDING OF EGC IN SEPSIS AND SUPPORT THE DEVELOPMENT OF NEW THERAPIES.

ADDITIONAL STUDIES ARE BEING WRITTEN AND IN THE APPROVAL PROCESS WILL BE DEVOTED TO THESE CONDITIONS:

SCLERODERMA

ERECTILE DYSFUNCTION

EMERGENCY ROOM ADMISSIONS

ARTERIAL PLAQUE DEVELOPMENT

HAIR GROWTH

DIETARY INTERVENTIONS ON GLYCOLYX DIMENSIONS IN SOUTH ASIAN PATIENTS WITH DIABETIC NEPHROPATHY. (GLYCOTREAT)

SPONSOR:

LEIDEN UNIVERSITY MEDICAL CENTER

COLLABORATORS:

DUTCH KIDNEY FOUNDATION

HEALTH HOLLAND

RADBOUD UNIVERSITY

SUBSIDIZING PARTY:

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**LABORATORY SITES:
LEIDEN UNIVERSITY MEDICAL CENTER, THE NETHERLANDS
Radboud University Medical Center, The Netherlands**

**OBJECTIVE:
TO INVESTIGATE WHETHER INTERVENTION WITH THE DIETARY SUPPLEMENT
ENDOCALYX™ IMPROVES THE
MICROVASCULAR HEALTH INDEX BETWEEN BASELINE AND 3 MONTHS IN TYPE 2 DIABETIC
SOUTH ASIAN PATIENTS WITH
MICROALBUMINURIA IN COMPARISON TO THE PLACEBO GROUP.**

[READ THE FULL TRIAL INFORMATION HERE.](#)

**DIETARY GLYCOLYX PRECURSOR SUPPLEMENTATION AMELIORATES AGE-RELATED
VASCULAR DYSFUNCTION**

**DANIEL R MACHIN, DANIEL NGUYEN, R COLTON BRAMWELL, LISA A LESNIEWSKI, AND ANTHONY
J DONATOR**

**DANIEL MACHIN AND TONY DONATO PUBLISHED AN ABSTRACT AT THE EXPERIMENTAL
BIOLOGY 2019 MEETING ON THE EFFECT OF ENDOCALYX ON AGING IN MICE:**

**PUBLISHED IN THE FASEB JOURNAL (VOLUME 33, ISSUE 1_ SUPPLEMENT, 01 APRIL
2019):**

PUBLISHED ONLINE: 1 APR 2019 ABSTRACT NUMBER: 828.1

ABSTRACT

**LARGE ELASTIC ARTERY STIFFENING AND ENDOTHELIAL DYSFUNCTION, AND ASSOCIATED
REDUCTIONS IN NITRIC OXIDE (NO) BIOAVAILABILITY, ARE CENTRAL FEATURES OF
VASCULAR AGING. WE HAVE RECENTLY DEMONSTRATED THAT THE GLYCOLYX, A GEL-
LIKE STRUCTURE THAT IS BOUND TO THE LUMINAL SURFACE OF THE VASCULAR
ENDOTHELIUM, IS DYSFUNCTIONAL IN THE AGED VASCULATURE. THE GLYCOLYX HAS
SEVERAL FUNCTIONS THAT ARE CRITICAL FOR THE MAINTENANCE OF A HEALTHY
VASCULATURE. WE SOUGHT TO DETERMINE IF CHRONIC DIETARY SUPPLEMENTATION OF
GLYCOLYX PRECURSORS (GLUCOSAMINE SULFATE, FUCOIDAN, SUPEROXIDE DISMUTASE,**

AND HIGH MOLECULAR WEIGHT HYALURONAN) COULD RESTORE GLYCOCALYX FUNCTION, WHILE CONCOMITANTLY AMELIORATING AGE-RELATED VASCULAR DYSFUNCTION. YOUNG (Y: 7 MO) AND OLD (O: 30 MO) MALE B6D2F1 MICE CONSUMED A CONTROL (C) OR GLYCOCALYX PRECURSOR (GP: 37 MG/KG ENCAPSULATED CHOW PROVIDED COURTESY OF MICROVASCULAR HEALTH SOLUTIONS, LLC [U.S. PATENT SERIAL No. 9,943,572]) DIET AD LIBITUM FOR 10 WEEKS. GLYCOCALYX BARRIER FUNCTION (PERFUSED BOUNDARY REGION [PBR]) WAS EVALUATED IN THE MESENTERIC MICROCIRCULATION USING AN INTRAVITAL MICROSCOPE EQUIPPED WITH AN AUTOMATED CAPTURE AND ANALYSIS SYSTEM. PBR WAS ~13% HIGHER IN OC COMPARED TO YC, SUGGESTIVE OF AN AGE-RELATED IMPAIRMENT IN GLYCOCALYX BARRIER FUNCTION, AND THIS WAS NORMALIZED IN OGP MICE (BOTH $P < 0.05$; FIGURE 1). AT BASELINE, AORTIC PULSE WAVE VELOCITY (PWV), A MEASURE OF LARGE ARTERY STIFFNESS, WAS HIGHER IN OC AND OGP COMPARED WITH YC MICE (BOTH $P < 0.05$; FIGURE 2). HOWEVER, AFTER THE DIETARY INTERVENTION, PWV DECREASED BY ~13% IN OGP ($P < 0.05$), WHEREAS, PWV WAS UNCHANGED IN OC AND YC MICE AFTER THE 10 WEEK PERIOD ($P > 0.05$). WE ASSESSED ENDOTHELIAL FUNCTION BY ENDOTHELIUM-DEPENDENT DILATION (EDD, MAXIMAL RESPONSE TO ACETYLCHOLINE [ACh]) IN THE CAROTID ARTERY. CAROTID ARTERY EDD WAS HIGHER IN YC AND OGP COMPARED TO OC MICE (92.5 ± 2.4 AND 90.7 ± 2.3 vs. $69.0 \pm 4.9\%$, RESPECTIVELY, $P < 0.05$). EDD OF OGP WAS SIMILAR TO YC MICE ($P > 0.05$). AFTER INCUBATION WITH THE NITRIC OXIDE (NO) SYNTHASE INHIBITOR, L-NAME, THE DILATORY RESPONSE DID NOT DIFFER BETWEEN GROUPS ($P > 0.05$). NO BIOAVAILABILITY (MAX ACh DILATION - MAX ACh+L-NAME DILATION) WAS ~10–14 FOLD HIGHER IN YC AND OGP COMPARED TO OC MICE (BOTH $P < 0.05$; FIGURE 3). ENDOTHELIUM-INDEPENDENT DILATION (VASODILATION TO SODIUM NITROPRUSSIDE) WAS NOT DIFFERENT BETWEEN GROUPS ($P > 0.05$). IN YOUNG MICE, GP DIET DID NOT AFFECT ANY OF THE AFOREMENTIONED MEASUREMENTS ($P > 0.05$). IN CONCLUSION, 10 WEEKS OF DIETARY GP SUPPLEMENTATION IN OLD MICE RESTORES GLYCOCALYX BARRIER FUNCTION THAT IS ACCOMPANIED BY REDUCED AORTIC STIFFNESS AND AUGMENTED EDD AND NO BIOAVAILABILITY, SUGGESTING THAT THE GLYCOCALYX MAY BE AN EFFECTIVE THERAPEUTIC TARGET FOR VASCULAR DYSFUNCTION IN OLDER ADULTS.

SUPPORT OR FUNDING INFORMATION

THIS STUDY WAS FUNDED IN PART BY GRANTS FROM THE NATIONAL INSTITUTE OF HEALTH (R01 AG040297, R01 AG048366, K02 AG045339, K99 AT010017) AND US DEPARTMENT OF VETERANS AFFAIRS (1I01BX002151).

READ THE ABSTRACT HERE.

PILOT STUDY IN 13 HEALTHY VOLUNTEERS

SUMMARY OF FINDINGS FROM CLINICAL STUDIES

6.3.2 FOOD SUPPLEMENT

A PILOT STUDY WAS CONDUCTED AMONG 13 HEALTHY VOLUNTEERS RECEIVING THE ENDOCALYX FOOD SUPPLEMENT. AFTER 3 MONTHS, THE MICROVASCULAR HEALTH INDEX MEASURED BY SDF IMAGING IMPROVED BY 31%. AFTER 4 MONTHS, THE MICROVASCULAR HEALTH INDEX IN THE VOLUNTEERS IMPROVED BY 50%. THIS SHOWED THE BENEFICIAL EFFECTS OF THE FOOD SUPPLEMENT ON THE MICROVASCULATURE AS IT SIGNIFICANTLY INCREASED CAPILLARY DENSITY AND RED BLOOD CELL FILLING PERCENTAGE, AND REDUCED THE PERFUSED BOUNDARY REGION (UNPUBLISHED DATA, H. VINK).

SUMMARY OF KNOWN AND POTENTIAL RISKS AND BENEFITS

6.4.2 FOOD SUPPLEMENT

IN THE PILOT STUDY WITH ENDOCALYX, NO SERIOUS ADVERSE EFFECTS WERE REPORTED. ONE SIDE EFFECT THAT WAS REPORTED WAS DIZZINESS, AS THE ENDOCALYX SUPPLEMENT LOWERED THE SYSTOLIC BLOOD PRESSURE. THE SUPPLEMENT IS ALREADY USED IN GENERAL PRACTITIONERS' OFFICES IN THE UNITED STATES AND TO DATE; NO ONE REPORTED ANY MAJOR SIDE EFFECTS. STUDIES CONDUCTED WITH THE INDIVIDUAL INGREDIENTS ALSO DID NOT REPORT ANY SERIOUS ADVERSE EFFECTS. A POSSIBLE SIDE EFFECT MAY BE AN UNKNOWN ALLERGIC REACTION TO ONE OF THE INGREDIENTS OF THE SUPPLEMENT. BENEFITS OF THE ENDOCALYX FOOD SUPPLEMENT IN DIABETIC PATIENTS REMAIN TO BE ESTABLISHED BUT ARE MAINLY IMPROVING THE MICROVASCULAR HEALTH BY SUPPORTING ENDOTHELIAL GLYCOCALYX FUNCTION.

[READ MORE ABOUT THE ENDOCALYX USE STUDY REPORT HERE.](#)

AS STATED ABOVE, IT TAKES YEARS TO COMPLETE STUDIES LIKE THESE, AND EVEN AFTER THEY ARE COMPLETED IT CAN TAKE MONTHS BEFORE THE PEER-REVIEWED RESEARCH STUDY IS RELEASED TO THE PUBLIC. AS SOON AS RESULTS ARE AVAILABLE, WE WILL SHARE THEM PUBLICLY ON THIS PAGE.

Studies on Endogenx Nutraceutical

[Adjunctive Treatment of Psychotic Disorders with Micronutrients](#)
THE JOURNAL OF ALTERNATIVE AND COMPLEMENTARY MEDICINE

[Hospitalization cost of conventional psychiatric care compared to broad-spectrum micronutrient treatment](#)
INTERNATIONAL JOURNAL OF MENTAL HEALTH SYSTEMS

[Micronutrient Treatment of Emotional Dyscontrol Following Traumatic Brain Injury](#)
ANNALS OF PSYCHIATRY AND MENTAL HEALTH

[Micronutrient treatment for children with emotional and behavioral dysregulation: A Case Series](#)
JOURNAL OF MEDICAL CASE REPORTS 2015, 9:240 DOI:10.1186/S13256-015-0735-0

[Clinically Significant Symptom Reduction in Children with Attention-Deficit/Hyperactivity Disorder Treated with Micronutrients: An Open-Label Reversal Design Study](#)
J CHILD ADOLESC PSYCHOPHARMACOL. 2015 DEC;25(10):783-98. DOI: 10.1089/CAP.2015.0105

[Anxiety and Stress in Children Following an Earthquake: Clinically Beneficial Effects of Treatment with Micronutrients](#)
J CHILD FAMILY STUDY

[Psychological functioning 1 year after a brief intervention using micronutrients to treat stress and anxiety related to the 2011 Christchurch earthquakes: A Naturalistic Follow-up](#)
HUM. PSYCHOPHARMACOL CLIN EXP (2014). DOI: 10.1002/HUP.2392

[Use of micronutrients attenuates cannabis and nicotine abuse as evidenced from a reversal Design: A case study](#)

JOURNAL OF PSYCHOACTIVE DRUGS

[Nutritional and Safety Outcomes from an Open-Label Micronutrient Intervention for Pediatric Bipolar Spectrum Disorders](#)

JOURNAL OF CHILD AND ADOLESCENT PSYCHOPHARMACOLOGY

[Could Yeast Infections Impair Recovery From Mental Illness? A case study Using Micronutrients and Olive Leaf Extract for the Treatment of ADHD and Depression](#)

ADVANCES, SUMMER 2013. VOL. 27, NO. 3

[Efficacy and cost of micronutrient treatment of childhood psychosis](#)

BMJ CASE REPORTS. DOI: 10.1136/BCR-2012-007213

[Use of micronutrients attenuates cannabis and nicotine abuse as evidenced from a reversal Design: A case study](#)

JOURNAL OF PSYCHOACTIVE DRUGS

[Shaken but unstirred? Effects of micronutrients on stress and trauma after an earthquake: RCT evidence comparing formulas and doses](#)

A HUM PSYCHOPHARMACOL CLIN EXP. DOI:10.1002/HUP.2246

[Post-earthquake psychological functioning in adults with Attention-Deficit/Hyperactivity Disorder: Positive effects of micronutrients on resilience](#)

NEW ZEALAND JOURNAL OF PSYCHOLOGY, 40(4):51-57

[Effect of micronutrients on neurocognitive functioning in adults with ADHD and Severe Mood Dysregulation: A Pilot study](#)

JOURNAL OF ALTERNATIVE AND COMPLEMENTARY MEDICINE

[Safety and tolerability of a complex micronutrient formula used in mental health: A compilation of eight datasets](#)

BMC PSYCHIATRY, 11:62;

[Micronutrients reduce stress and anxiety following a 7.1 earthquake in adults with Attention-Deficit/ Hyperactivity Disorder](#)

PSYCHIATRY RESEARCH, 189:281-87. DOI:10.1016/J.PSYCHRES.2011.06.016

[Database analysis of children and adolescents with Bipolar Disorder consuming a micronutrient formula](#)

BMC PSYCHIATRY, 10:74. DOI:10.1186/1471-244X-10-74;

[Impact of a micronutrient formula on ADHD and mood dysregulation in adults with ADHD: Evidence from an 8-week open label trial with natural follow-up](#)

JOURNAL OF ATTENTION DISORDERS, 2011;15(1):79-91

[Micronutrients versus standard medication management in autism: A Naturalistic Case-Control Study](#)

JOURNAL OF CHILD AND ADOLESCENT PSYCHOPHARMACOLOGY, 20(2):95-103;

[Successful treatment of Bipolar Disorder II and ADHD with a micronutrient formula: A Case Study](#)

CNS SPECTRUMS, 15(5):231-237

[Successful treatment of OCD with a micronutrient formula following partial response to CBT: A Case Study](#)

JOURNAL OF ANXIETY DISORDERS, 23:836.840

[Database analysis of adults with bipolar disorder consuming a micronutrient formula](#)

CLINICAL MEDICINE: PSYCHIATRY, 4: 3-16;

[A randomized trial of nutrient supplements to minimize psychological stress after a natural disaster](#)

PSYCHIATRY RESEARCH, AUGUST 30, 2015, VOLUME 228, ISSUE 3, PAGES 373–379

[Vitamin-mineral treatment of ADHD in adults: A one-year follow-up of a randomized controlled trial](#)

JOURNAL OF ATTENTION DISORDERS, EPUB

[Vitamin-mineral treatment of attention-deficit hyperactivity disorder in adults: double-blind randomized placebo-controlled trial](#)

THE BRITISH JOURNAL OF PSYCHIATRY, JANUARY 30, 2014

[Moderators of treatment response in adults with ADHD treated with a vitamin-mineral supplement](#)

PROG NEURO-PSYCHOPHARMACOL BIOL PSYCHIATRY (2013);

[Treatment of mood lability and explosive rage with minerals and vitamins: Two Case Studies in Children](#)

[Do vitamins or minerals \(apart from lithium\) have mood-stabilizing effects?](#)

JOURNAL OF CLINICAL PSYCHIATRY, 62, 933-935

ELLEN J. SOLE, JULIA J. RUCKLIDGE, NEVILLE M. BLAMPIED
J Child Family Study

Anxiety and Stress in Children Following an Earthquake: Clinically Beneficial Effects of Treatment with Micronutrients

Abstract

This study examined the effects of micronutrients on children with clinically elevated stress and anxiety 23–36 months after experiencing a natural disaster (a major earthquake). A single-case multiple-baseline design allocated 14 children (7 males, 7 females; aged 8–11 years; 10 with formal anxiety-disorder diagnoses) randomly to 1, 2 or 3 week baselines. Participants then took eight capsules/day of a micronutrient formula (EMPowerplus) during an 8-week open-label trial. Assessment instruments were the Children’s Global Assessment Scale (CGAS), the Screen for Child Anxiety-Related Emotional Disorders (SCARED), the Pediatric Emotional Distress Scale (PEDS), and the Revised Children’s Manifest Anxiety Scale (RCMAS). Symptom severity declined slightly in baseline for some children and declined much more during intervention for all children. Effect sizes at end of treatment were –1.40 (RCMAS), –1.92 (SCARED), +1.96 (CGAS), and –2.13 (PEDS). Modified Brinley plots revealed decreases in anxiety and improvements in overall functioning for 10 out of 11 completing participants. Side effects were mild and transient. The study provided evidence that treatment with a dietary supplement containing micronutrients reduced children’s post-disaster anxiety to a clinically significant degree. Future placebo-controlled randomized-controlled trials and treatment-comparison research is recommended to determine if this is true of anxiety in general.

Abstract

Background: Healthcare costs are skyrocketing, with mental health treatment amongst the most expensive, especially when hospitalization is involved. According to the Mental Health Commission of Canada, one in five Canadians is living with a mental disorder in any given year, at an annual cost of \$50 billion. In light of this societal burden, alternative approaches are being evaluated, such as brief psychotherapy by phone, peer support, and, as part of the emerging field of nutritional mental health, treatment with micronutrients (minerals and vitamins). Effectiveness of micronutrients has been demonstrated for many types of psychiatric symptoms, in about 45 studies of formulas that are either multinutrient (e.g., several B vitamins) or broad-spectrum (usually over 20 minerals and vitamins). Although this literature demonstrates therapeutic benefits, the potential economic impact of micronutrient treatment has been evaluated in only one case study of childhood psychosis.

Methods: The current case study was initiated to evaluate mental health-related hospitalization costs from 1997 to 2003 for a female adult diagnosed with various mood and psychotic symptoms. She was treated for the first 5 years with conventional methods and then subsequently with a broad-spectrum micronutrient formula.

Results: The patient's annual mental health hospitalization costs during conventional treatment averaged \$59,864 across 5 years (1997–2001), with a peak annual cost of about \$140,000. Since transitioning to broad-spectrum micronutrients, she has incurred no provincial hosp

Conclusion: Further exploration of the treatment of mental health problems with broad-spectrum micronutrient formulas has the potential to make two significant contributions: improved mental health, and decreased costs for governments.

LEWIS MEHL-MADRONA AND BARBARA MAINGUY

The Journal of Alternative and Complementary Medicine

Adjunctive Treatment of Psychotic Disorders with Micronutrients

Abstract

Objective: *To evaluate the effect of micronutrients (minerals and vitamins) on adult psychosis when added to conventional medications by using a placebo-controlled randomized design with a 1-month open-label run-in.*

Design: *Longitudinal comparison study following a randomized, controlled trial that had failed because participants declined to undergo randomization.*

Setting/Locations: *Rural primary care and psychiatry clinic in northern New England (town of 16,000 people).*

Participants: *People older than age 18 years diagnosed with a psychotic disorder who were receiving medications.*

Intervention: *Fifty consecutive clients seen in 1 month's time were invited to participate; 19 completed a 1-month open-label phase of the addition of a micronutrient to their medication regimen; all 19 then withdrew rather than risk randomization to a placebo. This finding itself was important, so the study was restructured to compare the response of those 19 patients during 24 months of micronutrients + medication to the response of the 31 people who declined participation, enriched by an additional 28 consecutive patients recruited over the second month of the study. This yielded a total of 59 patients who received medication without micronutrients.*

Outcome measures: *All clients were evaluated with the Positive and Negative Symptom Scale and the Clinical Global Impression scale at study baseline and after 3, 6, 9, 12, 15, 18, and 24 months. Psychosis was confirmed with clinical interview by using Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision, criteria. All participants had normal physical examinations and laboratory studies.*

Results: Outcomes were similar for both groups until 15 months, although the micronutrient group used significantly less antipsychotic medication throughout that time ($p < 0.001$). At 15 months, the micronutrients + medication group exhibited significantly fewer symptoms than the medication-only group, a difference that was even stronger at 24 months.

Conclusions: Micronutrients may appear to be a beneficial long-term, adjunctive strategy for people with psychotic disorders, allowing for smaller doses of medication to achieve the same effectiveness with fewer side effects.

BONNIE J. KAPLAN, CAROLINE LEANEY, AND EKATERINA TSATSKO

Annals of Psychiatry and Mental Health

Micronutrient Treatment of Emotional Dyscontrol Following Traumatic Brain Injury

Abstract

Introduction: Emotional dyscontrol following traumatic brain injury (TBI) impairs social relationships and employability. Micronutrients (minerals, vitamins) stabilize emotional lability in psychiatric patients, and various individual nutrients have been used to treat experimental brain injury in laboratory animals in the acute phase. However, the current case report appears to be the first documentation of micronutrients resulting in normalization of emotion regulation in a long-standing brain injury in a human.

Case presentation: A broad-spectrum formula of micronutrients was evaluated in a 35-year-old male who had incurred a severe TBI eight years previously. Resolution of most post-TBI symptoms was achieved during those eight years, but not his episodic loss of emotional control, which psychiatrists evaluated as being permanent. The trial of micronutrients began after five weeks of baseline symptom monitoring with a mood stability scale. By three months mood stability had improved markedly according to data submitted by two raters (the patient and his clinician) who were blind to each other's evaluations. Data collection continued for one year, showing significant improvement ($p < .0001$), at which time the patient reported that his emotional

control had returned to his pre-TBI level. The improvements led to his establishing his own business and improving his family relationships.

Conclusions: *Micronutrient treatment resulted in resolution of this patient's longstanding post-TBI emotional dyscontrol. Broad-spectrum micronutrient formulas are showing benefit for the treatment of mood lability in various types of psychiatric patients; this report indicates there is also potential value in using them for the emotional dyscontrol found in post-TBI patients.*

MICHAEL I. GUREVICH, MD AND CASSANDRA L. ROBINSON, MS, LPN

EXPLORE July/August 2016, Vol. 12, No. 4

An Individualized Approach to Treatment-resistant Bipolar Disorder: A Case Series

Abstract

Objective: *Determine retrospectively if individualized, integrative treatment strategies applied while withdrawing pharmaceuticals were beneficial and safe among a TRBD clinic population.*

Method: *A chart review was performed for six adult patients, treated in a private psychiatric practice. Data were collected regarding psychiatric diagnosis, hospitalizations, medications, side effects, substance abuse, and applied treatments.*

Results: *Using individualized, integrative psychiatric treatment methods, the majority of medications were eliminated. Long-term remission was attained in all cases, defined as clinical stability with no discernable symptoms of bipolar disorder for at least one year.*

Conclusions: *Applying an integrative treatment approach, and eliminating most medications, provided lasting resolution of symptoms and side-effects in a selected sample of TRBD outpatients. These data may provide the basis for future randomized, controlled trials.*

KAPLAN BJ, HILBERT P, TSATSKO E

Journal of Medical Case Reports 2015, 9:240 doi:10.1186/s13256-015-0735-0

Micronutrient treatment for children with emotional and behavioral dysregulation: A Case Series

Abstract

Introduction: *In clinical studies of adults and children, broad-spectrum micronutrients (minerals and vitamins) have proven beneficial for improving mood regulation and attention. We report here pilot work whose primary objective was to evaluate the feasibility of studying micronutrient treatment in school-aged children with emotional and behavioral problems. Issues examined included feasibility of participant recruitment from a culturally diverse population, probability of sample retention for a 12-week trial, acceptability of the outcome measures, supplement adherence, as well as trends in treatment benefit.*

Case Presentation: *The families of two boys (ages 5 and 6) and one girl (age 14) were invited to participate in a 12-week pilot trial of micronutrients carried out during the summer months. All children were enrolled in the private school at which future research was being considered. During the previous school year, all three had been extremely difficult to educate due to their inability to pay attention and learn, as well as their behavior problems. Although the two younger children had not been formally diagnosed, parents and teachers provided reports of hyperactivity and inability to focus on education in the classroom. The oldest child was often aggressive, and had been diagnosed with bipolar disorder, attention deficit hyperactivity disorder, and oppositional defiant disorder.*

All three children were Hispanic and spoke both Spanish and English. For 12 weeks, after signing consent forms, the children's parents provided weekly ratings on the parent-report Child Mania Rating Scale; the children consumed the micronutrient formula daily and provided a daily rating of how they felt. The parent ratings revealed significantly improved behavior, $p = .002$. Children's ratings approached the ideal level of 7, indicating "happy" self-

reports. Parent interviews confirmed the weekly scores. Several feasibility questions were answered: all three children completed the 12-week trial, all scores were completed by parents and children, adherence to the protocol was excellent, and no adverse reactions emerged.

Conclusions: *Family physicians and pediatricians are often confronted with the challenge of improving the lives of families whose children experience school crises due to emotional and behavioral dysregulation. Three children, who participated in pilot work to determine the feasibility of further investigations, experienced impressive changes that clearly warrant both research and clinical exploration.*

KAPLAN BJ, RUCKLIDGE JJ, ROMIJN AR

Psychiatry Research, August 30, 2015, Volume 228, Issue 3, Pages 373–379

A randomized trial of nutrient supplements to minimize psychological stress after a natural disaster

Abstract

After devastating flooding in southern Alberta in June 2013, we attempted to replicate a New Zealand randomised trial that showed that micronutrient (minerals, vitamins) consumption after the earthquakes of 2010–11 resulted in improved mental health. Residents of southern Alberta were invited to participate in a study on the potential benefit of nutrient supplements following a natural disaster. Fifty-six adults aged 23–66 were randomised to receive a single nutrient (vitamin D, n¼17), a few-nutrients formula (B-Complex, n¼21), or a broad-spectrum mineral/vitamin formula (BSMV, n¼18). Self-reported changes in depression, anxiety and stress were monitored for six weeks. Although all groups showed substantial decreases on all measures, those consuming the B-Complex and the BSMV formulas showed significantly greater improvement in stress and anxiety compared with those consuming the single nutrient, with large effect sizes (Cohen’s d range 0.76–1.08). There were no group differences between those consuming the B-Complex and BSMV. The use of nutrient formulas with multiple minerals and/or vitamins to minimise stress associated with natural disasters is now supported by three studies. Further research should be carried out to evaluate the potential

population benefit that might accrue if such formulas were distributed as a post-disaster public health measure.

GORDON HA, RUCKLIDGE JJ, BLAMPIED NM, JOHNSTONE JM

J Child Adolesc Psychopharmacol. 2015 Dec;25(10):783-98. doi: 10.1089/cap.2015.0105

Clinically Significant Symptom Reduction in Children with Attention-Deficit/Hyperactivity Disorder Treated with Micronutrients: An Open-Label Reversal Design Study

Abstract

Objective: The purpose of this study was to investigate the clinical effect and safety of a broad spectrum, 36 ingredient micronutrient (vitamins and minerals) in treating children with attention-deficit/hyperactivity disorder (ADHD).

Methods: This open-label, on-off-on-off (reversal design) study followed 14 participants (8–12 years of age) with ADHD, diagnosed using standardized instruments, for 6 months with no dropouts. Following baseline assessment, including hematology and biochemistry screening, participants began an 8 week treatment phase with micronutrients titrated up to maximum dose (15 capsules/day). Treatment was withdrawn for 4 weeks, reinstated for a further 8 weeks, and then withdrawn for 4 weeks. Primary outcomes included the Conners' Parent Rating Scale, the Clinical Global Impressions Scale (CGI), and the Strengths and Difficulties Questionnaire – Parent version (SDQ). Secondary outcomes were mood and global functioning.

Results: Modified Brinley plots revealed a reduction in ADHD symptoms, improved mood, and improved overall functioning during intervention phases, and deterioration in ADHD symptoms, mood, and overall functioning during the withdrawal phases. Reliable change analyses, Cohen's *d* and percent superiority effect sizes, 95% confidence intervals and *t* tests confirmed clinically and statistically significant change between the intervention and withdrawal phases, with large effect sizes observed pre- to postexposure of micronutrients ($d = 1.2$ – 2.2) on ADHD symptoms during intervention phases. Seventy-one percent of participants showed at least a 30% decrease in ADHD

symptoms by the end of the second treatment phase, and 79% were identified as “much improved” or “very much improved” at the end of the second phase (5 months) based on the clinician-rated CGI when considering functioning generally. The SDQ showed that these benefits occurred across other areas of functioning including emotional symptoms, conduct problems, and prosocial behaviours. The children’s self-reports confirmed the improvements. Excellent adherence to treatment occurred throughout, side effects were mild and transitory, and no safety issues were identified through blood analyses.

Conclusions: This study demonstrates the clinical benefit, feasibility, and safety of broad-spectrum micronutrients in the treatment of childhood ADHD. Replications utilizing double-blind placebo-controlled studies are warranted. Trial is registered with the Australia and New Zealand Clinical Trial Registry: ACTRN12612000645853

RUCKLIDGE JJ, FRAMPTON C, GORMAN B, BOGGIS A

Journal of Attention Disorders, ePub

Vitamin-mineral treatment of ADHD in adults: A one-year follow-up of a randomized controlled trial

Abstract

Objective: Despite widespread use, there is little data investigating the long-term impact of micronutrients on psychiatric disorders. This study investigated the naturalistic outcome 1-year post-baseline of a randomized controlled trials (RCT) that compared micronutrients with placebo in 80 adults with ADHD.

Method: All participants were contacted and clinician-rated questionnaires completed.

Result: A total of 72 (90%) of the sample participated; although there was significant regression in psychiatric functioning from the end-of-trial on all measures, outcomes remained significantly improved from baseline. Dominant treatment from the end-of-treatment to follow-up was investigated as a mediator of outcome; those staying on the micronutrients performed better than those who switched to medications or discontinued

micronutrients. Cost was the most substantial reason why people stopped micronutrient treatment.

Conclusion: *For the small number of participants who stayed on micronutrients, the benefits conferred through the controlled trial were maintained. The results are limited by small sample, lack of blinding, expectation, and reliance on self-report of symptoms.*

RUCKLIDGE JJ, BLAMPIED N, GORMAN B, GORDON H, SOLE E*

Hum. Psychopharmacol Clin Exp (2014). doi: 10.1002/hup.2392

Psychological functioning 1 year after a brief intervention using micronutrients to treat stress and anxiety related to the 2011 Christchurch earthquakes: A Naturalistic Follow-up

Abstract

Objective: *We investigated whether micronutrients given acutely following the Christchurch earthquakes continued to confer benefit 1 year following the treatment.*

Method: *Sixty-four adults from the original 91 participants experiencing heightened anxiety or stress 2.3 months following the 22nd February 2011 earthquake and who had been randomized to receive three different doses of micronutrients completed on-line questionnaires assessing mood, anxiety, stress, and symptoms associated with post-traumatic stress disorder 1 year after completing the initial study. Twenty-one out of 29 nonrandomized controls who did not receive the treatment also completed the questionnaires.*

Result: *Both the treated and control groups experienced significant improvement in psychological functioning compared with end-of-trial. However, treated participants had better long-term outcomes on most measures compared with controls (ES = 0.69.1.31). Those who stayed on micronutrients through to follow-up or stopped all treatment reported better psychological functioning than those who switched to other treatments including medications.*

Conclusion: Disaster survivors improve psychologically over time regardless of receiving intervention; however, those taking micronutrients during the acute phase following a disaster show better outcomes, identifying micronutrients as a viable treatment for acute stress following a natural disaster with maintenance of benefits 1 year later.

RUCKLIDGE JJ, FRAMPTON CA, GORMAN B, BOGGIS A

The British Journal of Psychiatry, January 30, 2014

*Vitamin-mineral treatment of attention-deficit hyperactivity disorder in adults:
double-blind randomized placebo-controlled trial*

Abstract

Background: The role of nutrition in the treatment of attention-deficit hyperactivity disorder (ADHD) is gaining international attention; however, treatments have generally focused only on diet restriction or supplementing with one nutrient at a time.

Aim: To investigate the efficacy and safety of a broad-based micronutrient formula consisting mainly of vitamins and minerals, without omega fatty acids, in the treatment of ADHD in adults.

Method: Intent-to-treat analyses showed significant between-group differences favoring active treatment on self- and observer- but not clinician-ADHD rating scales. However, clinicians rated those receiving micronutrients as more improved than those on placebo both globally and on ADHD symptoms. Post hoc analyses showed that for those with moderate/severe depression at baseline, there was a greater change in mood favoring active treatment over placebo. There were no group differences in adverse events.

Conclusion: *This study provides preliminary evidence of efficacy for micronutrients in the treatment of ADHD symptoms in adults, with a reassuring safety profile.*

RUCKLIDGE JJ, JOHNSTONE J, GORMAN B, BOGGIS A, FRAMPTON CA

Prog Neuro-Psychopharmacol Biol Psychiatry (2013);

Moderators of treatment response in adults with ADHD treated with a vitamin-mineral supplement

Abstract

Background: *To date there has been no research investigating moderators of response to micronutrient treatment of mental illness, specifically baseline nutrient levels.*

Method: *We conducted analyses of data from a randomized placebo-controlled trial (RCT) of 80 adults (.16 years) with AttentionDeficit Hyperactivity Disorder (ADHD), whereby participants were treated acutely (8 weeks) with micronutrients or placebo followed by an open-label (OL) phase of 8 weeks whereby all participants received micronutrients. To ensure that all participants had been exposed to the micronutrients for 8 weeks, only those who had adhered to the treatment protocol and completed 8 weeks on nutrients were included in the data analysis: from the group micronutrient arm, and from the group that had been randomized to the placebo group and hence had only received nutrients in the OL phase. Six outcomes were examined: change in ADHD symptoms (self/clinician), ADHD responder, Clinical Global Impression-Improvement (CGI-I), change in mood, and change in Global Assessment of Functioning (GAF). Demographic, developmental and psychiatric history, current clinical characteristics, and baseline nutrient levels were all considered as putative predictors.*

Result: *There were significant changes in all outcome variables after 8 weeks' exposure to the micronutrients. Among the nutrients recorded at baseline, substantial deficiencies (27%) were only observed for vitamin D.*

*Could Yeast Infections Impair Recovery From Mental Illness? A case study
Using Micronutrients and Olive Leaf Extract for the Treatment of ADHD and
Depression*

Abstract

Prior research shows that micronutrients, particularly amino acids, can assist individuals with substance dependence to quit various drugs of abuse, including cannabis, alcohol, and cocaine. As part of a wider investigation of the impact of micronutrients (mostly vitamins and minerals) on psychiatric symptoms, such as Attention-Deficit/Hyperactivity Disorder (ADHD), depression, and anxiety, we observed that many participants reduced or eliminated use of alcohol, cigarettes, and cannabis. One case using a single-case reversal (off-on-off-on-off) design is presented and shows not only on-off control of psychiatric symptoms as micronutrients are consumed or withdrawn, but also simultaneous on-off use of cannabis and cigarettes, despite not directly targeting this substance use as part of the treatment protocol.

This case adds to a growing body of research supporting the use of micronutrients in the treatment of psychiatric symptoms and suggests it may extend to substance dependence. Micronutrients, by assisting with mood regulation and reductions in anxiety, may assist with successful cessation of drug use. Alternatively, they may directly impact on the brain reward circuitry believed to be involved in the expression of addictions, thereby providing the appropriate precursors and cofactors necessary for adequate neurotransmitter synthesis. This case should continue to stimulate researchers to consider the role of nutrients, in particular vitamins and minerals, in drug treatment programs and encourage more rigorous trials.

FRAZIER EA, GRACIOUS B, ARNOLD LE, FAILLA M,
CHITCHUMROONCHOKCHAI C, HABASH D, FRISTAD MA

Abstract

Objective: Report safety, tolerability, serum micronutrient concentrations and their correlations with mood changes from an 8-week pilot feasibility study of a 36-ingredient multinutrient supplement, Truehope® EMPowerplus, for pediatric bipolar spectrum disorders (BPSD).

Method: Ten children aged 6-12 received Truehope® EMPowerplus escalating from 1 to 4 capsules t.i.d., with four children increased to the maximum suggested dose, 5 capsules t.i.d. Outcome measures were micronutrient concentrations in serum and red blood cells, vital signs, body mass index (BMI), dietary intake (Food Frequency Questionnaire and 24-hour dietary recall interview) and mood and global functioning ratings.

Result: Seven children (70%) completed the study. Three (30%) terminated early due to tolerability and compliance issues. Adverse effects were mild and transient, and chiefly initial insomnia or GI upset. No differences occurred in BMI ($p = 0.310$) or waist-hip ratio (WHR; $p = 0.674$) pre- to post-supplementation. Four of the tested serum vitamin concentrations increased from pre- to post-supplementation: vitamin A- retinol; vitamin B6; vitamin E- α -tocopherol; and folate (all $p < 0.05$). The increase in serum 25-OH vitamin D approached significance ($p = 0.063$). No differences were found in dietary intake pre- to post- supplementation, suggesting blood nutrient level increases were due to Truehope EMPowerplus.

Conclusion: In this open prospective study, short-term use of Truehope® EMPowerplus in children with BPSD appeared safe and well-tolerated, with a side effect profile preferable to first-line psychotropic drugs for pediatric bipolar spectrum disorders. A double-blind, randomized clinical trial is feasible, appears safe, and is warranted by open-label clinical outcomes and plausible mechanisms of action combined with documentation of increased serum concentrations of specific micronutrients.

Use of micronutrients attenuates cannabis and nicotine abuse as evidenced from a reversal Design: A case study

Abstract

Prior research shows that micronutrients, particularly amino acids, can assist individuals with substance dependence to quit various drugs of abuse, including cannabis, alcohol, and cocaine.

Case Description: *As part of a wider investigation of the impact of micronutrients (mostly vitamins and minerals) on psychiatric symptoms, such as Attention-Deficit/Hyperactivity Disorder (ADHD), depression, and anxiety, we observed that many participants reduced or eliminated use of alcohol, cigarettes, and cannabis. One case using a single-case reversal (off-on-off-on-off) design is presented and shows not only on-off control of psychiatric symptoms as micronutrients are consumed or withdrawn, but also simultaneous on-off use of cannabis and cigarettes, despite not directly targeting this substance use as part of the treatment protocol.*

Conclusion: *This case adds to a growing body of research supporting the use of micronutrients in the treatment of psychiatric symptoms and suggests it may extend to substance dependence. Micronutrients, by assisting with mood regulation and reductions in anxiety, may assist with successful cessation of drug use. Alternatively, they may directly impact on the brain reward circuitry believed to be involved in the expression of addictions, thereby providing the appropriate precursors and cofactors necessary for adequate neurotransmitter synthesis. This case should continue to stimulate researchers to consider the role of nutrients, in particular vitamins and minerals, in drug treatment programs and encourage more rigorous trials.*

RODWAY M, VANCE A, WATTERS A, LEE H, BOS E, KAPLAN BJ

BMJ Case Reports. doi: 10.1136/bcr-2012-007213

Efficacy and cost of micronutrient treatment of childhood psychosis

Abstract

Psychosis is difficult to treat effectively with conventional pharmaceuticals, many of which have adverse long-term health consequences. In contrast, there are promising reports from several research groups of micronutrient treatment (vitamins, minerals, amino acids, and essential fatty acids) of mood, anxiety, and psychosis symptoms using a complex formula that appears to be safe and tolerable. We review previous studies using this formula to treat mental symptoms, and present an 11-year-old boy with a 3-year history of mental illness whose parents chose to transition him from medication to micronutrients. Symptom severity was monitored in three clusters: anxiety, obsessive compulsive disorder, and psychosis. Complete remission of psychosis occurred, and severity of anxiety and obsessional symptoms decreased significantly ($p < .001$); the improvements are sustained at 4-year follow-up. A cost comparison revealed that micronutrient treatment was <1% of his inpatient mental health care. Additional research on broad spectrum micronutrient treatment is warranted.

RUCKLIDGE JJ, ANDRIDGE R, GORMAN B, BLAMPIED N, GORDON H, BOGGIS

A Hum Psychopharmacol Clin Exp. doi:10.1002/hup.2246

Shaken but unstirred? Effects of micronutrients on stress and trauma after an earthquake: RCT evidence comparing formulas and doses

Abstract

Objective: *To compare two micronutrient (vitamins and minerals) formulas (Berocca™ and CNETM) and assess their impact on emotions and stress related to the 6.3 earthquake on February 22nd 2011 in Christchurch, NZ. Method: 91 adults experiencing heightened anxiety or stress 2-3 months following the earthquake were randomized to Berocca™, CNETM low dose (CNE4), or CNETM high dose (CNE8), for 28 days and monitored weekly via on-line questionnaires and followed one month post-trial. A non-randomized control group (n=25) completed questionnaires at baseline and 4 weeks.*

Result: *All treatment groups experienced significant declines in psychological symptoms ($p < .001$). CNETM groups experienced greater reduction in intrusive thoughts as compared with Berocca™ ($p = 0.05$), with no group differences on other measures of psychological symptoms. However, CNE8 group reported greater improvement in mood, anxiety, and energy ($p < .05$) with twice as many reporting being “much” to “very much” improved and five*

times more likely to continue taking CNETM post-trial than Berocca™ group. Treated participants had better outcomes on most measures over 4 weeks as compared to controls.

Conclusion: *This study supports micronutrients as an inexpensive and practical treatment for acute stress following a natural disaster with a slight advantage to higher doses. ACTRN 12611000460909*

FRAZIER EA, FRISTAD MA, ARNOLD LE

Journal of Alternative and Complementary Medicine, 18(7):678-685

Feasibility of a nutritional supplement as treatment for pediatric bipolar spectrum disorders

Abstract

Objective: *Current psychotropic medications for childhood bipolar spectrum disorders (BPSD) are associated with significant adverse events. As nutrients play an important role in physical and mental health, they may be useful in treating mood disorders with few side effects. This open-label study explored the feasibility of testing therapeutic effects of a multinutrient supplement, Truehope EMPowerplus, for pediatric BPSD.*

Design: *Truehope EMPowerplus started at 1 capsule t.i.d. and escalated to a goal of 4 capsules t.i.d., which eight children attained. Four of these increased to the maximum dose, 5 capsules t.i.d. Mood symptoms were assessed seven times over eight weeks.*

Subjects: Ten children, age 6-12 with BPSD were enrolled in 6.5 months. Seven participants completed the full trial. Three dropped out due to palatability and/or adherence issues.

Result: Mean medication adherence was 91%. With one-tailed nonparametric Fisher's Randomization Tests, intent-to-treat analyses demonstrated a 37% decrease in depression scores ($p < 0.06$) and a 45% decrease in mania scores ($p < 0.01$) from the start of treatment through final visit, suggesting improvement and possible treatment response. Study completers demonstrated significant decreasing trends in both depression and mania scores from baseline to final visit ($p < 0.05$). Side effects were minor and transient, mostly temporary gastric discomfort.

Conclusion: Future randomized, placebo-controlled trials of Truehope EMPowerplus are warranted and feasible.

RUCKLIDGE JJ, JOHNSTONE J, HARRISON R

Journal of Alternative and Complementary Medicine

Effect of micronutrients on neurocognitive functioning in adults with ADHD and Severe Mood Dysregulation: A Pilot study

Abstract

Objective: Little research has investigated how micronutrients (minerals and vitamins) affect cognitive functioning despite preliminary studies showing they may improve psychiatric functioning. **Intervention:** This pilot study investigated the impact of a 36 ingredient micronutrient formula consisting mainly of vitamins and minerals on neurocognitive functioning in 14 adults with Attention-Deficit/Hyperactivity Disorder (ADHD) and severe mood dysregulation (SMD).

Design: The formula was consumed in an open-label trial over an 8-week period. **Outcome Measures:** The participants completed tests of memory (Wide Range Assessment of Memory and Learning) and executive functioning (Delis-Kaplan Executive Functioning System and Conners Continuous Performance Test) at baseline and at the end of the trial. A gender and age matched control group of 14 non-ADHD adults not taking the formula were

assessed on the same tests 8 weeks apart in order to investigate the impact of practice on the results.

Result: *There were no group differences in ethnicity, socio-economic status and estimated IQ. Significant improvement was observed in the ADHD group, but not the control group, across a range of verbal abilities including verbal learning, verbal cognitive flexibility and fluency, and verbal inhibition. These neurocognitive improvements were large and consistent with improved psychiatric functioning. No changes were noted above a practice effect in visual-spatial memory and there were no improvements noted in reaction time, working memory or rapid naming for either groups.*

Conclusion: *Although the pilot and open label design of the study limits the generalizability of the results, it supports a growing body of literature recognizing the importance of nutrients for mental health and cognition. The results also provide evidence supporting the need for randomized clinical trials of micronutrients as well as other experimental studies in order to better assess whether improved neurocognitive functioning may contribute to improved psychiatric symptoms.*

RUCKLIDGE JJ, BLAMPIED NM

New Zealand Journal of Psychology, 40(4):51-57

Post-earthquake psychological functioning in adults with Attention-Deficit/Hyperactivity Disorder: Positive effects of micronutrients on resilience

Abstract

The September, 2010, 7.1 magnitude earthquake in Christchurch, New Zealand, provided an opportunity to study the after-effects of a major earthquake where death and injury were absent. It created a natural experiment into the protective effects on wellbeing of taking Truehope EMPowerplus, a micronutrient supplement, in a group of 33 adults diagnosed with ADHD who had been assessed prior to the earthquake. Fortuitously, 16 were currently taking the supplement as part of on-going research at the time of the quake, while 17 were not (they had completed their trial of Truehope EMPowerplus or were waiting to begin consumption). The Depression Anxiety and Stress Scale (DASS-42) which had been administered at varying times

before the earthquake on recruitment into the micronutrient study was re-administered by telephone 7-10 and again 14-18 days post-earthquake to volunteer, earthquake-exposed participants. A modified Brinley plot analysis of the individual DASS-42 scores showed that the 16 participants on the nutritional supplement were more resilient to the effects of the earthquake than the 17 individuals not taking the supplement. This effect was particularly marked for Depression scores.

RUCKLIDGE JJ, JOHNSTONE J, HARRISON R, BOGGIS A

Psychiatry Research, 189:281-87. doi:10.1016/j.psychres.2011.06.016

Micronutrients reduce stress and anxiety following a 7.1 earthquake in adults with Attention-Deficit/ Hyperactivity Disorder

Abstract

The role of good nutrition for resilience in the face of stress is a topic of interest, but difficult to study. A 7.1 earthquake took place in the midst of research on a micronutrient treatment for Attention- Deficit/Hyperactivity Disorder (ADHD), providing a unique opportunity to examine whether individuals with ADHD taking micronutrients demonstrated more emotional resilience postearthquake than individuals with ADHD not taking micronutrients. Thirty-three adults with ADHD were assessed twice following the earthquake using a measure of depression, anxiety and stress also completed at some point pre-earthquake (baseline). Seventeen were not taking micronutrients at the time of the earthquake (control group), 16 were (micronutrient group). While there were no between-group differences one week post-quake (Time 1), at two weeks post-quake (Time 2), the

micronutrient group reported significantly less anxiety and stress than the controls (effect size 0.69). These between group differences could not be explained by other variables, such as pre-earthquake measures of emotions, demographics, psychiatric status, and personal loss or damage following the earthquake. The results suggest micronutrients may increase resilience to ongoing stress and anxiety associated with a highly stressful event in individuals with ADHD and are consistent with controlled studies showing benefit of micronutrients for mental health.

*SIMPSON JSA, CRAWFORD SG, GOLDSTEIN ET, FIELD C, BURGESS E,
KAPLAN BJ*

BMC Psychiatry, 11:62;

Safety and tolerability of a complex micronutrient formula used in mental health: A compilation of eight datasets

Abstract

Background: *Theoretically, consumption of complex, multinutrient formulations of vitamins and minerals should be safe, as most preparations contain primarily the nutrients that have been in the human diet for millennia, and at safe levels as defined by the Dietary Reference Intakes. However, the safety profile of commercial formulae may differ from foods because of the amounts and combinations of nutrients they contain. As these complex formulae are being studied and used clinically with increasing frequency, there is a need for direct evaluation of safety and tolerability.*

Objective: *The aim of this project was to compile all known safety and tolerability data collected on one complex nutrient formula.*

Data Sources and Results: *Data were assembled from all the known published and unpublished studies for the complex formula with the largest amount of published research in mental health. Biological safety data from 144 children and adults were available from six sources: there were no*

occurrences of clinically meaningful negative outcomes/effects or abnormal blood tests that could be attributed to toxicity. Adverse event (AE) information from 157 children and adults was available from six studies employing the current version of this formula, and only minor, transitory reports of headache and nausea emerged. Only one of the studies permitted a direct comparison between micronutrient treatment and medication: none of the 88 pediatric and adult participants had any clinically meaningful abnormal laboratory values, but tolerability data in the group treated with micronutrients revealed significantly fewer AEs and less weight gain.

Conclusions: *This compilation of safety and tolerability data is reassuring with respect to the broad spectrum approach that employs complex nutrient formula as a primary treatment.*

RUCKLIDGE JJ, TAYLOR MR, WHITEHEAD KA

Journal of Attention Disorders, 2011;15(1):79-91

Impact of a micronutrient formula on ADHD and mood dysregulation in adults with ADHD: Evidence from an 8-week open label trial with natural follow-up

Abstract

Objective: *To investigate the impact of a 36-ingredient micronutrient formula consisting mainly of minerals and vitamins in the treatment of adults with both Attention-deficit/hyperactivity Disorder (ADHD) and severe mood dysregulation (SMD).*

Method: *14 medication-free adults (9 men, 5 women; 18-55 years) with ADHD and SMD completed an 8- week open-label trial.*

Result: *A minority reported transitory mild side effects. Significant improvements were noted across informants (self, observer, clinician) on measures of inattention and hyperactivity/impulsivity, mood, quality of life, anxiety, and stress all with medium to very large effect sizes (all $ps < .01$); however, the mean of inattention remained in a clinical range whereas the means on measures of mood and hyperactivity/impulsivity were normalized. Follow-up data showed maintenance of changes or further improvement for those who stayed on the micronutrients.*

Conclusion: Although this study, as an open trial, does not in itself prove efficacy, it provides preliminary evidence supporting the need for a randomized clinical trial of micronutrients as treatment for the more complex presentations of ADHD.

RUCKLIDGE JJ, GATELY D, KAPLAN BJ

BMC Psychiatry, 10:74. doi:10.1186/1471-244X-10-74;

Database analysis of children and adolescents with Bipolar Disorder consuming a micronutrient formula

Abstract

Background: Eleven previous reports have shown potential benefit of micronutrient treatment for psychiatric symptoms. The current study asked whether children (7-18 years) with pediatric bipolar disorder (PBD) benefited from the same micronutrient formula; the impact of Attention-Deficit/Hyperactivity Disorder (ADHD) on their response was also evaluated.

Method: Data were available from 120 children whose parents reported a diagnosis of PBD; 79% were taking psychiatric medications that are used to treat mood disorders; 24% were also reported as ADHD. Using Last Observation Carried Forward (LOCF), data were analyzed from 3 to 6 months of micronutrient use.

Result: At LOCF, mean symptom severity of bipolar symptoms was 46% lower than baseline (effect size (ES) = 0.78) ($p < 0.001$). In terms of responder status, 46% experienced >50% improvement at LOCF, with 38% still taking psychiatric medication (52% drop from baseline) but at much lower levels (74% reduction in number of medications being used from baseline). The results were similar for those with both ADHD and PBD: a 43% decline in PBD symptoms (ES = 0.72) and 40% in ADHD symptoms (ES = 0.62). An alternative sample of children with just ADHD symptoms ($n = 41$) showed a 47% reduction in symptoms from baseline to LOCF (ES = 1.04). The duration of reductions in symptom severity suggests that benefits were not attributable to placebo/expectancy effects. Similar findings were found for younger and older children and for both sexes.

Conclusion: *The data are limited by the open label design, the lack of a control group, and the inherent self-selection bias. While these data cannot establish efficacy, the results are consistent with a growing body of research suggesting that micronutrients appear to have therapeutic benefit for children with PBD with or without ADHD in the absence of significant side effects and may allow for a reduction in psychiatric medications while improving symptoms. The consistent reporting of positive changes across multiple sites and countries are substantial enough to warrant a call for randomized clinical trials using micronutrients.*

RUCKLIDGE JJ, HARRISON R

CNS Spectrums, 15(5):231-237

Successful treatment of Bipolar Disorder II and ADHD with a micronutrient formula: A Case Study

Abstract

Bipolar disorder with co-occurring attention-deficit/hyperactivity disorder (ADHD) is a challenge to treat. Ten previous reports have shown potential benefit of a micronutrient treatment (consisting mainly of vitamins and minerals) for various psychiatric symptoms, including mood and ADHD. This case study aimed to investigate the longer term impact of the micronutrients on both psychiatric and neurocognitive functioning in an off-on-off-on (ABAB) design with 1-year follow-up. A 21-year-old female with bipolar II disorder, ADHD, social anxiety, and panic disorder entered an open-label trial using a nutritional treatment following a documented 8 year history of on-going psychiatric symptoms not well managed by medications. After 8 weeks on the formula she showed significant improvements in mood, anxiety, and hyperactivity/impulsivity. Blood test results remained normal after 8 weeks on the formula. She did not report any adverse side effects associated with the treatment. She then chose to come off the formula; after 8 weeks her depression scores returned to baseline, and anxiety and ADHD symptoms worsened. The formula was reintroduced, showing gradual improvement in all psychiatric symptoms. This case represents a naturalistic ABAB design showing on-off control of symptoms. After 1 year, the patient is now in remission from all mental illness. Neurocognitive changes mirrored behavioral changes, showing improved processing speed, consistency in response speed, and verbal memory. A placebo response and expectancy effects cannot be

ruled out although previous poor response to treatment and the duration of the current positive response decrease the likelihood that other factors better explain change. These consistently positive outcomes alongside an absence of side effects indicate that further research, particularly larger and more controlled trials, is warranted using this multinutrient approach.

MEHL-MADRONA L, LEUNG B, KENNEDY C, PAUL S, KAPLAN BJ

Journal of Child and Adolescent Psychopharmacology, 20(2):95-103;

Micronutrients versus standard medication management in autism: A Naturalistic Case-Control Study

Abstract

Autism spectrum disorder (ASD) is often accompanied by self-injurious behavior (SIB), aggression, and tantrums, symptoms that have reportedly improved with micronutrient (vitamins and minerals) treatment. The current study took advantage of naturally occurring differences in parental preferences for treatment approaches. The micronutrient group asked for treatment without pharmaceuticals (n=44, aged 2.28 years at entry [M=8.39+5.58]). Their records were matched with those of 44 similar children whose families requested conventional treatment (medication group). Both groups improved on both the Childhood Autism Rating Scale and the Childhood Psychiatric Rating Scale (all p values <0.0001). Both groups also exhibited significant decreases in total Aberrant Behavior Checklist scores, but the micronutrient group's improvement was significantly greater (p<0.0001). SIB Intensity was lower in the micronutrient group at the end of the study (p=0.005), and improvement on the Clinical Global Impressions scale was greater for the micronutrient group (p=0.0029). It is difficult to determine whether the observed changes were exerted through improvement in mood disorder or through an independent effect on autistic disorder. There were some advantages to treatment with micronutrients: lower activity level, less social withdrawal, less anger, better spontaneity with the examiner, less irritability, lower intensity SIB, markedly fewer adverse events, and less weight gain. Advantages of medication management were insurance coverage, fewer pills, and less frequent dosing.

GATELY D, KAPLAN BJ

Clinical Medicine: Psychiatry, 4: 3-16;

Database analysis of adults with bipolar disorder consuming a micronutrient formula

Abstract

Background: *Bipolar disorder is a lifelong problem with imperfect available treatments. Recent research has shown potential benefit of nutritional treatment for mood symptoms. The goal of the current study was to determine whether adults with bipolar disorder reported treatment benefit from consuming a micronutrient formula.*

Method: *Self-report data were available from 682 adults who reported a diagnosis of bipolar disorder; 81% were taking psychiatric medications. Those reporting additional diagnoses were excluded, as well as those who provided data <60 times during 180 days of using the micronutrients, leaving 358 for analysis.*

Result: *Mean symptom severity was 41% lower than baseline after 3 months (effect size = 0.78), and 45% lower after 6 months (effect size = 0.76) (both paired t-tests significant, $p < 0.001$). In terms of responder status, 53% experienced >50% improvement at 6 months. Half the sample were taking medications approved for bipolar disorder (lithium, anticonvulsants, atypical antipsychotics), and half were either medication-free or taking other medications: the magnitude of treatment benefit did not differ between these two groups. Regression analyses indicated that decreased symptom severity over the 6 months was associated with increasing micronutrient dosage and with reducing medication. Symptom improvements were significant and sustained at 6 months, suggesting that benefits were not attributable to placebo/expectancy effects.*

Conclusion: *Further research on this micronutrient formula is warranted.*

RUCKLIDGE JJ

Journal of Anxiety Disorders, 23:836.840

Successful treatment of OCD with a micronutrient formula following partial response to CBT: A Case Study

Abstract

Obsessive Compulsive Disorder (OCD) affects 0.5.2% of young people many of whom are resistant to conventional treatments. This case study describes an 18-year-old male with OCD who first underwent cognitive behavioral therapy (CBT) for a 1-year period with a modest response (his OCD had shifted from severe to moderate). Within a year, his anxiety had deteriorated back to the severe range and he now had major depression. He then entered an ABAB design trial using a nutritional formula consisting mainly of minerals and vitamins (together, known as micronutrients). After 8 weeks on the formula, his mood was stabilized, his anxiety reduced, and his obsessions were in remission. The treatment was then discontinued for 8 weeks, during which time his obsessions and anxiety worsened and his mood dropped.

Reintroduction of the formula again improved the symptoms. This case illustrates the importance of considering the effect micronutrients have on mental illness.

FRAZIER EA, FRISTAD M, ARNOLD LE

Journal of Child and Adolescent Psychopharmacology, 19:453-460

Multinutrient Supplement as Treatment: Literature Review and Case Report of a 12-year-old Boy with Bipolar Disorder

Abstract

Early-onset bipolar disorder has significant morbidity and mortality. Development of safe, effective treatments to which patients will adhere is critical. Pharmacologic interventions for childhood bipolar spectrum disorders are limited and are associated with significant risk for adverse events (Kowatch et al 2005). Diet and nutrition research suggests vitamins, minerals,

and other nutrients are important underpinnings of general physical and mental health; further, they may even be useful in treating mood dysregulation by providing a more favorable risk-benefit ratio than contemporary psychotropic agents (Kaplan, Crawford, Field, & Simpson 2007). This article reviews the literature on multinutrient supplementation and mental health, and examines a case study of a 12-year-old boy with bipolar disorder and comorbid diagnoses treated for 6 years with conventional medication and finally a multinutrient supplement.

The multinutrient supplement in this case study is Truehope® EMPowerplus, a 36-ingredient supplement containing sixteen minerals, fourteen vitamins, three amino acids and three antioxidants. It was used to treat a 12-year-old boy initially diagnosed with bipolar disorder-not otherwise specified (BP-NOS) at age 6, whose diagnosis evolved by age 10 to bipolar I (BP-I), mixed, with psychotic features. He also met criteria for generalized anxiety disorder by age 8 and obsessive-compulsive disorder by age 10. After six years of conventional treatment (ages 6-12), he received fourteen months of Truehope® EMPowerplus. Symptom manifestation over seven years is described in conjunction with treatment history. Truehope® EMPowerplus resulted in superior outcome to conventional treatment. This report adds to accumulating preliminary evidence that further basic science and clinical studies of multinutrient supplements are warranted.

KAPLAN BJ, FISHER JE, CRAWFORD SG, FIELD CJ, KOLB B

Journal of Child and Adolescent Psychopharmacology, 14(1), 115-122

Improved mood and behavior during treatment with a mineral-vitamin supplement: An Open-Label Case Series of Children

Abstract

Several studies have demonstrated that psychiatric symptoms such as depression, mood swings, and aggression may be ameliorated by supplementation with broad-based nutrient formulas containing vitamins, minerals, and sometimes essential fatty acids. These findings have been reported in young criminal offenders as well as in adults with mood disturbance and other psychiatric disorders. The purpose of the current case series was to explore the potential efficacy of a nutrient supplement in children. Children with mood and behavioral problems (N = 11; 7 boys, 4 girls;

8.15 years old) participated; 9 completed this openlabel trial. Parents completed the Child Behavior Checklist (CBCL), Youth Outcome Questionnaire (YOQ), and Young Mania Rating Scale (YMRS) at entry and following at least 8 weeks of treatment. Intent-to-treat analyses revealed decreases on the YOQ ($p < 0.001$) and the YMRS ($p < 0.01$) from baseline to final visit. For the 9 completers, improvement was significant on seven of the eight CBCL scales, the YOQ, and the YMRS (p values from 0.05-0.001). Effect sizes for all outcome measures were relatively large. The findings suggest that formal clinical trials of broad nutritional supplementation are warranted in children with these psychiatric symptoms.

KAPLAN BJ, CRAWFORD SG, GARDNER B, FARRELLY G

Journal of Child and Adolescent Psychopharmacology, 12(3), 203-218

*Treatment of mood lability and explosive rage with minerals and vitamins:
Two Case Studies in Children*

Abstract

A micronutrient supplement containing a broad range of dietary minerals and vitamins is being examined for the treatment of mood lability in both adults and children (Kaplan et al. 2001; Popper 2001). During pilot work, two medication-free boys with mood lability and explosive rage were studied in an open-label treatment followed by reversal and retreatment. One child was an 8-year-old with atypical obsessive-compulsive disorder, and the other was a 12-year-old with pervasive developmental delay. Both boys were monitored using the mood and temper items from the Conners Parent Rating Scale, as well as the Child Behavior Checklist. In addition, the boy with atypical obsessive-compulsive disorder was monitored with the child version of the YaleBrown Obsessive Compulsive Scale. Both boys benefited from the micronutrient supplement when examined in ABAB designs: mood, angry outbursts, and obsessional symptoms improved when initially treated, returned when not taking the supplement, and remitted when the micronutrient supplement was reintroduced. Both boys have been followed and are stable on the nutritional supplement for over 2 years. These cases suggest that mood lability and explosive rage can, in some cases, be managed with a mixture of biologically active minerals and vitamins, without using lithium or other traditional psychopharmacologic agents.

Abstract

In a letter to the editor of the Journal of Clinical Psychiatry, Dr. Miles Simmons, a psychiatrist in private practice in Brunswick, Maine, reported his clinical experience with Truehope® EMPowerplus. Impressed by the striking response of one of his patients to Truehope EMPowerplus, Dr. Simmons carefully monitored treatment-resistant patients from his private practice who were willing to try this nutritional approach.

Result: *Of 19 patients that met the DSM-IV criteria for bipolar disorder (14 bipolar I and 5 bipolar II), Dr. Simmons observed that “12 of the 19 patients showed marked clinical improvement, 3 showed moderate improvement, and 1 showed mild improvement” (84% positive response rate). Of 16 medicated patients (who were taking 2.7 psychiatric medications on average) 13 were able to completely discontinue their psychiatric medications (over an average of 5.2 weeks) had remained stable on Truehope EMPowerplus alone for an average of 13 months.*

KAPLAN BJ, SIMPSON JSA, FERRE RC, GORMAN C, MCMULLEN D, CRAWFORD SG. *Journal of Clinical Psychiatry*, 62(12): 936-944

Effective mood stabilization in bipolar disorder with a chelated mineral supplement

Abstract

Background: *To determine in open trials the therapeutic benefit of a nutritional supplement for bipolar disorder.*

Method: *The sample consisted of 11 patients with DSM-IV-diagnosed bipolar disorder aged 19 to 46 years, who were taking a mean of 2.7 psychotropic medications each at a study entry. Three additional patients dropped out prematurely. The intervention is a broad-based nutritional supplement of dietary nutrients, primarily chelated trace minerals and vitamins, administered in high doses. At study entry and periodically thereafter, patients*

were assessed with the Hamilton Rating Scale for Depression (HAM-D), the Brief Psychiatric Rating Scale (BPRS), and the Young Mania Rating Scale (YMRS).

Result: For those who completed the minimum 6-month open trial, symptom reduction ranged from 55% to 66% on the outcome measures; need for psychotropic medications decreased by more than 50%. Paired t tests revealed treatment benefit on all measures for patients completing the trial: HAM-D mean score at entry =19.0, mean score at last visit = 5.4, $t = 5.59$, $df = 9$, $p < .01$; BPRS mean score at entry = 35.3, mean score at last visit = 7.4, $t = 2.57$, $df = 9$, $p < .05$; YMRS mean score at entry = 15.1, mean score at last visit = 6.0, $t = 4.11$, $df = 9$, $p < .01$. The effect size for the intervention was large ($> .80$) for each measure. The number of psychotropic medications decreased significantly to a mean \pm SD of 1.0 ± 1.1 ($t = 3.54$, $df = 10$, $p < .01$). In some cases, the supplement replaced psychotropic medications and the patients remained well. The only reported side effect (i.e. nausea) was infrequent, minor, and transitory.

Conclusion: Some cases of bipolar illness may be ameliorated by nutritional supplementation. A randomized, placebo-controlled trial in adults with bipolar I disorder is currently underway, as well as open trials in children.

POPPER CW *Journal of Clinical Psychiatry*, 62, 933-935

Do vitamins or minerals (apart from lithium) have mood-stabilizing effects?

[Commentary]

Abstract

Dr. Charles Popper, psychopharmacologist and psychiatrist at Harvard University's McLean Hospital, published a commentary on the Kaplan et al. (2001) paper, in which he reported the results of his clinical experience with Truehope EMPowerplus.

Result: Of 22 patients (10 adults, 9 adolescents, 3 pre-adolescents) who clinically met criteria for bipolar disorder, 19 (86%) showed a positive response to the micronutrient treatment. Of 15 patients taking medications, 11 (73%) were able to gradually withdraw from their medications, and were stable taking the micronutrient treatment alone.

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EUROPEAN HEART JOURNAL 14 OCTOBER 2021

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*ASSOCIATION OF COVID-19 WITH IMPAIRED ENDOTHELIAL GLYCOCALYX, VASCULAR
FUNCTION AND MYOCARDIAL DEFORMATION FOUR MONTHS AFTER INFECTION
EUROPEAN JOURNAL OF HEART FAILURE. 20 AUGUST 2021*

*MICROVASCULAR DIFFERENCES IN INDIVIDUALS WITH OBESITY AT RISK OF DEVELOPING
CARDIOVASCULAR DISEASE
OBESITY: A RESEARCH JOURNAL. 2 AUGUST 2021*

*LINKS BETWEEN ENDOTHELIAL GLYCOCALYX CHANGES AND MICROCIRCULATORY
PARAMETERS IN SEPTIC PATIENTS
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*MAY WE USE NON-INVASIVE INDICES OF AORTIC STIFFNESS AND ENDOTHELIAL
GLYCOCALYX AS BIOMARKERS FOR IDIOPATHIC PULMONARY ARTERY HYPERTENSION
FOLLOW-UP?
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*IDENTIFICATION OF NOVEL SUBLINGUAL PARAMETERS TO ANALYZE AND DIAGNOSE
MICROVASCULAR DYSFUNCTION IN SEPSIS: THE NOSTRADAMUS STUDY (LINK TO
CRITICAL CARE)
CRITICAL CARE, 19 MARCH 2021(LINK TO PDF)*

*VASCULAR ENDOTHELIAL GLYCOCALYX DAMAGE IN COVID-19
INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES, DECEMBER 2020*

*MICROVASCULAR DYSFUNCTION IN COVID-19: THE MYSTIC STUDY
ANGIOGENESIS 14 OCTOBER 2020*

*EFFECT OF GESTATIONAL AGE AND POSTNATAL AGE ON THE ENDOTHELIAL GLYCOCALYX IN
NEONATES
SCIENTIFIC REPORTS (NATURE PUBLISHER GROUP); LONDON VOL. 11, ISS. 1, (2021)*

*VASCULAR CONDITIONING PREVENTS ADVERSE LEFT VENTRICULAR REMODELLING AFTER
ACUTE MYOCARDIAL INFARCTION: A RANDOMISED REMOTE CONDITIONING STUDY
BASIC RESEARCH IN CARDIOLOGY VOLUME 116, ARTICLE NUMBER: 9 (2021)*

*EFFECTS OF A SINGLE AEROBIC EXERCISE ON PERFUSED BOUNDARY REGION AND
MICROVASCULAR PERFUSION: A FIELD STUDY
JOURNAL OF CLINICAL MONITORING AND COMPUTING (2021)*

*ASSESSMENT OF THE SUBLINGUAL MICROCIRCULATION WITH THE GLYCOCHECK SYSTEM:
REPRODUCIBILITY AND EXAMINATION CONDITIONS*
PLOS ONE. 2020 DEC 23;15(12):E0243737

*EVALUATION OF JEJUNAL MICROVASCULATURE OF HEALTHY ANESTHETIZED DOGS WITH
SIDESTREAM DARK FIELD VIDEO MICROSCOPY*
AM J VET RES. 2020 Nov;81(11):888-893.

*TOCILIZUMAB IMPROVES OXIDATIVE STRESS AND ENDOTHELIAL GLYCOLYX: A
MECHANISM THAT MAY EXPLAIN THE EFFECTS OF BIOLOGICAL TREATMENT ON COVID-19*
FOOD CHEM TOXICOL. 2020 Nov;145:111694.

*SEX-RELATED ASSOCIATIONS OF HIGH-DENSITY LIPOPROTEIN CHOLESTEROL WITH AORTIC
STIFFNESS AND ENDOTHELIAL GLYCOLYX INTEGRITY IN TREATED HYPERTENSIVE
PATIENTS*
J CLIN HYPERTENS (GREENWICH). 2020 OCT;22(10):1827-1834.

*VISUAL AND BIOCHEMICAL EVIDENCE OF GLYCOLYX DISRUPTION IN HUMAN DENGUE
INFECTION, AND ASSOCIATION WITH PLASMA LEAKAGE SEVERITY*
FRONT MED (LAUSANNE). 2020 OCT 16;7:545813

*IMMEDIATE EFFECTS OF WHOLE BLOOD DONATION ON THE ENDOTHELIAL SURFACE LAYER
AND GLYCOLYX SHEDDING*
BLOOD TRANSFUS. 2020 JUL 22.

VARIABILITY OF MICROCIRCULATORY MEASUREMENTS IN CRITICALLY ILL PATIENTS
SHOCK. 2020 JUL;54(1):9-14.

*DECREASED ENDOTHELIAL GLYCOLYX THICKNESS IS AN EARLY PREDICTOR OF MORTALITY
IN SEPSIS*
ANAESTH INTENSIVE CARE. 2020 MAY;48(3):221-228.

*MICROVASCULAR ALTERATIONS DURING CARDIAC SURGERY USING A HEPARIN OR
PHOSPHORYLCHOLINE-COATED CIRCUIT*
J CARDIOTHORAC VASC ANESTH. 2020 APR;34(4):912-919

*IN VIVO IMAGING OF THE BUCCAL MUCOSA SHOWS LOSS OF THE ENDOTHELIAL
GLYCOLYX AND PERIVASCULAR HEMORRHAGES IN PEDIATRIC PLASMODIUM
FALCIPARUM MALARIA*
INFECT IMMUN. 2020 FEB 20;88(3):E00679-19.

DOES SUBLINGUAL MICROSCOPY CORRELATE WITH NAILFOLD VIDEOCAPILLAROSCOPY IN SYSTEMIC SCLEROSIS?

CLIN RHEUMATOL. 2021 JAN 7.

NON-INVASIVE EVALUATION OF MACRO- AND MICROHEMODYNAMIC CHANGES DURING INDUCTION OF GENERAL ANESTHESIA - A PROSPECTIVE OBSERVATIONAL SINGLE-BLINDED TRIAL

CLIN HEMORHEOL MICROCIRC. 2021;77(1):1-16.

EVALUATION OF ENDOTHELIAL GLYCOCALYX IN HEALTHY VOLUNTEERS - AN OBSERVATIONAL STUDY

CLIN HEMORHEOL MICROCIRC. 2020;75(3):257-265.

IMPAIRED ARTERIAL ELASTIC PROPERTIES AND ENDOTHELIAL GLYCOCALYX IN PATIENTS WITH EMBOLIC STROKE OF UNDETERMINED SOURCE

THROMB HAEMOST. 2019 Nov;119(11):1860-1868.

TIE2 ACTIVATION PROMOTES PROTECTION AND RECONSTITUTION OF THE ENDOTHELIAL GLYCOCALYX IN HUMAN SEPSIS

THROMB HAEMOST. 2019 Nov;119(11):1827-1838.

ASSOCIATION OF SUBLINGUAL MICROCIRCULATION PARAMETERS AND ENDOTHELIAL GLYCOCALYX DIMENSIONS IN RESUSCITATED SEPSIS

CRIT CARE. 2019 JUL 24;23(1):260.

EFFECTS OF DIFFERENT ANTIDIABETIC MEDICATIONS ON ENDOTHELIAL GLYCOCALYX, MYOCARDIAL FUNCTION, AND VASCULAR FUNCTION IN TYPE 2 DIABETIC PATIENTS: ONE YEAR FOLLOW-UP STUDY

J CLIN MED. 2019 JUL 5;8(7):983.

EFFECTS OF HIGH-INTENSITY INTERVAL TRAINING ON MICROVASCULAR GLYCOCALYX AND ASSOCIATED MICRORNAs

AMERICAN PHYSIOLOGY SOCIETY / HEART AND CIRCULATORY PHYSIOLOGY 2019 JUN 2019

SUBLINGUAL ENDOTHELIAL GLYCOCALYX AND ATHEROSCLEROSIS. A CROSS-SECTIONAL STUDY

PLOS ONE. 2019 MAR 27;14(3):E0213097.

EARLY ONSET PREECLAMPSIA IS ASSOCIATED WITH GLYCOCALYX DEGRADATION AND REDUCED MICROVASCULAR PERFUSION

J AM HEART ASSOC. 2019 FEB 19;8(4):E010647.

HDL CHOLESTEROL LEVELS AND ENDOTHELIAL GLYCOCALYX INTEGRITY IN TREATED HYPERTENSIVE PATIENTS

J CLIN HYPERTENS (GREENWICH). 2018 Nov;20(11):1615-1623.

INFLAMMATORY AND ANGIOGENIC FACTORS LINKED TO LONGITUDINAL MICROVASCULAR CHANGES IN HEMODIALYSIS PATIENTS IRRESPECTIVE OF TREATMENT DOSE INTENSITY

KIDNEY BLOOD PRESS RES. 2017;42(5):905-918.

EXTRACELLULAR OVERHYDRATION LINKED WITH ENDOTHELIAL DYSFUNCTION IN THE CONTEXT OF INFLAMMATION IN HAEMODIALYSIS DEPENDENT CHRONIC KIDNEY DISEASE

PLOS ONE. 2017 Aug 22;12(8):E0183281.

GLYCOCALYX IN VIVO MEASUREMENT

CLIN HEMORHEOL MICROCIRC. 2017;67(3-4):499-503.

P673 IMPROVEMENT OF ARTERIAL STIFFNESS AND MYOCARDIAL DEFORMATION IN PATIENTS WITH POORLY CONTROLLED DIABETES MELLITUS TYPE 2 AFTER OPTIMIZATION OF ANTIDIABETIC MEDICATION

EUR HEART J CARDIOVASC IMAGING. 2016 DEC 1;17(SUPPL_2):II136-II143.

PERTURBED MECHANOTRANSDUCTION BY ENDOTHELIAL SURFACE GLYCOCALYX MODIFICATION GREATLY IMPAIRS THE ARTERIOGENIC PROCESS

AM J PHYSIOL HEART CIRC PHYSIOL. 2015 AUG 15;309(4):H711-7.

EFFECTS OF GLUCAGON-LIKE PEPTIDE-1 RECEPTOR AGONISTS, SODIUM-GLUCOSE COTRANSPORTER-2 INHIBITORS, AND THEIR COMBINATION ON ENDOTHELIAL GLYCOCALYX, ARTERIAL FUNCTION, AND MYOCARDIAL WORK INDEX IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AFTER 12-MONTH TREATMENT

JOURNAL OF THE AMERICAN HEART ASSOCIATION 2020 APR 24

UNCOUPLING OF MICROVASCULAR BLOOD FLOW AND CAPILLARY DENSITY IN VASCULAR COGNITIVE IMPAIRMENT

FRONTIERS IN NEUROLOGY 2019 DEC 3

DERANGEMENT OF THE ENDOTHELIAL GLYCOCALYX IN SEPSIS

WILEY ONLINE LIBRARY, 2018 DECEMBER

ALTERATIONS OF CONJUNCTIVAL GLYCOCALYX AND MICROCIRCULATION IN NON-SEPTIC CRITICALLY ILL PATIENTS

MICROVASC RES. 2018 JUL;118:44-48. DOI: 10.1016/J.MVR.2018.02.004. EPUB 2018 FEB 17.

AUTOMATED MEASUREMENT OF MICROVASCULAR FUNCTION REVEALS DYSFUNCTION IN SYSTEMIC SCLEROSIS: A CROSS-SECTIONAL STUDY.

J RHEUMATOL. 2017 Nov;44(11):1603-1611. DOI: 10.3899/JRHEUM.170120. EPUB 2017 SEP 15.

ADVANCED AGE RESULTS IN A DIMINISHED ENDOTHELIAL GLYCOCALYX.

AM J PHYSIOL HEART CIRC PHYSIOL. 2018 SEP 1;315(3):H531-H539. DOI: 10.1152/AJPHEART.00104.2018. EPUB 2018 MAY 11.

INDUCED TRF2 DELETION LEADS TO AGING VASCULAR PHENOTYPE IN MICE ASSOCIATED WITH ARTERIAL TELOMERE UNCAPPING, SENESCENCE SIGNALING, AND OXIDATIVE STRESS.

J MOL CELL CARDIOL. 2019 FEB;127:74-82. DOI: 10.1016/J.YJMCC.2018.11.014. EPUB 2018 NOV 29.

IMPACT OF INTRAVENOUS FLUID CHALLENGE INFUSION TIME ON MACROCIRCULATION AND ENDOTHELIAL GLYCOCALYX IN SURGICAL AND CRITICALLY ILL PATIENTS.

BIOMED RES INT. 2018 Nov 1;2018:8925345. DOI: 10.1155/2018/8925345. ECOLLECTION 2018.

NEURAXIAL ANESTHESIA IS LESS HARMFUL TO THE ENDOTHELIAL GLYCOCALYX DURING ELECTIVE JOINT SURGERY COMPARED TO GENERAL ANESTHESIA^{1,2}.

CLIN HEMORHEOL MICROCIRC. 2018 Nov 29. DOI: 10.3233/CH-180428. [EPUB AHEAD OF PRINT]

EFFECT OF ACUTE HYPERNATREMIA INDUCED BY HYPERTONIC SALINE ADMINISTRATION ON ENDOTHELIAL GLYCOCALYX IN RABBITS.

CLIN HEMORHEOL MICROCIRC. 2018 Nov 2. DOI: 10.3233/CH-189907. [EPUB AHEAD OF PRINT]

THE EFFECT OF FLUID LOADING AND HYPERTONIC SALINE SOLUTION ON CORTICAL CEREBRAL MICROCIRCULATION AND GLYCOCALYX INTEGRITY.

J NEUROSURG ANESTHESIOL. 2018 JUL 13. DOI: 10.1097/ANA.0000000000000528. [EPUB AHEAD OF PRINT]

INCREASE IN PERFUSED BOUNDARY REGION OF ENDOTHELIAL GLYCOCALYX IS ASSOCIATED WITH HIGHER PREVALENCE OF ISCHEMIC HEART DISEASE AND LESIONS OF MICROCIRCULATION AND VASCULAR WALL.

MICROCIRCULATION. 2018 MAY;25(4):E12454. DOI: 10.1111/MICC.12454.

*IN VIVO ASSESSMENT OF THE HUMAN CEREBRAL MICROCIRCULATION AND ITS
GLYCOCALYX: A TECHNICAL REPORT.*

*J NEUROSCI METHODS. 2018 JUN 1;303:114-125. DOI:
10.1016/J.JNEUMETH.2018.03.009. EPUB 2018 MAR 22.*

*HDL CHOLESTEROL LEVELS AND ENDOTHELIAL GLYCOCALYX INTEGRITY IN TREATED
HYPERTENSIVE PATIENTS.*

*J CLIN HYPERTENS (GREENWICH). 2018 NOV;20(11):1615-1623. DOI:
10.1111/JCH.13404. EPUB 2018 OCT 13.*

*ASSOCIATION OF IMPAIRED ENDOTHELIAL GLYCOCALYX WITH ARTERIAL STIFFNESS,
CORONARY MICROCIRCULATORY DYSFUNCTION, AND ABNORMAL MYOCARDIAL
DEFORMATION IN UNTREATED HYPERTENSIVES.*

*J CLIN HYPERTENS (GREENWICH). 2018 APR;20(4):672-679. DOI:
10.1111/JCH.13236. EPUB 2018 MAR 2.*

SUBLINGUAL FUNCTIONAL CAPILLARY RAREFACTION IN CHRONIC HEART FAILURE.

EUR J CLIN INVEST. 2018 FEB;48(2). DOI: 10.1111/ECI.12869. EPUB 2017 DEC 14.

*BEDSIDE ANALYSIS OF THE SUBLINGUAL MICROVASCULAR GLYCOCALYX IN THE
EMERGENCY ROOM AND INTENSIVE CARE UNIT - THE GLYCONURSE STUDY.*

*SCAND J TRAUMA RESUSC EMERG MED. 2018 FEB 14;26(1):16. DOI:
10.1186/s13049-018-0483-4.*

*ACUTE ISCHEMIC INJURY TO THE RENAL MICROVASCULATURE IN HUMAN KIDNEY
TRANSPLANTATION.*

AM J PHYSIOL RENAL PHYSIOL. 2010 NOV;299(5):F1134-40

*EFFECT OF SULODEXIDE ON ENDOTHELIAL GLYCOCALYX AND VASCULAR PERMEABILITY IN
PATIENTS WITH TYPE 2 DIABETES MELLITUS.*

DIABETOLOGIA. 2010 DEC;53(12):2646-55

*METHODS FOR EVALUATING ENDOTHELIAL FUNCTION: A POSITION STATEMENT FROM THE
EUROPEAN SOCIETY OF CARDIOLOGY WORKING GROUP ON PERIPHERAL CIRCULATION.*

EUR J CARDIOVASC PREVREHABIL. 2011 DEC;18(6):775-89

DAMAGE OF THE ENDOTHELIAL GLYCOCALYX IN DIALYSIS PATIENTS.

J AM SOC NEPHROL. 2012 NOV;23(11):1900-8

SUBLINGUAL MICROVASCULAR GLYCOCALYX DIMENSIONS IN LACUNAR STROKE PATIENTS.

CEREBROVASC Dis. 2013;35(5):451-4

*NON-INVASIVE ASSESSMENT OF MICROVASCULAR DYSFUNCTION IN FAMILIES WITH
PREMATURE CORONARY ARTERY DISEASE.*

INT J CARDIOL. 2013 OCT 12;168(5):5026-8

*ALTERATION OF THE SUBLINGUAL MICROVASCULAR GLYCOCALYX IN CRITICALLY ILL
PATIENTS.*

MICROVASC RES. 2013 NOV;90:86-9

ASSOCIATION OF KIDNEY FUNCTION WITH CHANGES IN THE ENDOTHELIAL SURFACE LAYER.

CLIN J AM SOC NEPHROL. 2014 APR;9(4):698-704

*MICROCIRCULATORY EFFECTS OF THE TRANSFUSION OF LEUKODEPLETED OR NON-
LEUKODEPLETED RED BLOOD CELLS IN PATIENTS WITH SEPSIS: A PILOT STUDY.*

CRIT CARE. 2014 FEB 17;18(1):R33

*SKELETAL MUSCLE CAPILLARY DENSITY AND MICROVASCULAR FUNCTION ARE
COMPROMISED WITH AGING AND TYPE 2 DIABETES.*

J APPL PHYSIOL (1985). 2014 APR 15;116(8):998-1005

*DEEPER PENETRATION OF ERYTHROCYTES INTO THE ENDOTHELIAL GLYCOCALYX IS
ASSOCIATED WITH IMPAIRED MICROVASCULAR PERFUSION.*

PLOS ONE. 2014 MAY 9;9(5):E96477

*IS THE SYSTEMIC MICROVASCULAR ENDOTHELIAL GLYCOCALYX IN PERITONEAL DIALYSIS
PATIENTS RELATED TO PERITONEAL TRANSPORT?*

NEPHRON CLIN PRACT. 2014;128(1-2):159-65

*EFFECTS OF ULTRAPURE HEMODIALYSIS AND LOW MOLECULAR WEIGHT HEPARIN ON THE
ENDOTHELIAL SURFACE LAYER.*

BLOOD PURIF. 2014;38(3-4):203-10

*CHARACTERISTICS AND DETERMINANTS OF THE SUBLINGUAL MICROCIRCULATION IN
POPULATIONS OF DIFFERENT ETHNICITY.*

HYPERTENSION. 2015 MAY;65(5):993-1001

*PLASMA FREE HEMOGLOBIN AND MICROCIRCULATORY RESPONSE TO FRESH OR OLD
BLOOD TRANSFUSIONS IN SEPSIS.*

PLOS ONE. 2015 MAY 1;10(5):E0122655

EFFECT OF AN ACUTE AND CHRONIC SLAT LOAD ON MICROVASCULAR PERMEABILITY IN HEALTHY SUBJECTS.

JHYPERTENS. 2015 JUN;33 SUPPL 1

PERTURBATION OF THE MICROVASCULAR GLYCOCALYX AND PERFUSION IN INFANTS AFTER CARDIOPULMONARY BYPASS.

J THORAC CARDIOVASC SURG. 2015 DEC;150(6):1474-81.

SIDE-BY-SIDE ALTERATIONS IN GLYCOCALYX THICKNESS AND PERFUSED MICROVASCULAR DENSITY DURING ACUTE MICROCIRCULATORY ALTERATIONS IN CARDIAC SURGERY.

MICROCIRCULATION. 2016 JAN;23(1):69-74.

THE IMPACT OF PERIODONTAL DISEASE TREATMENT ON ENDOTHELIUM OF SUBLINGUAL MICROVESSELS.

STOMATOLOGIJA (Mosk). 2016;95(4):9-12. RUSSIAN.

PROTOCOL FOR INTRAOPERATIVE ASSESSMENT OF THE HUMAN CEREBROVASCULAR GLYCOCALYX.

BMJ OPEN. 2017 JAN 5;7(1)

EARLY DETECTION OF LEFT VENTRICULAR DYSFUNCTION IN FIRST-DEGREE RELATIVES OF DIABETIC PATIENTS BY MYOCARDIAL DEFORMATION IMAGING: THE ROLE OF ENDOTHELIAL GLYCOCALYX DAMAGE.

INT J CARDIOL. 2017 APR 15;233:105-112.

IMPROVEMENT OF ARTERIAL STIFFNESS AND MYOCARDIAL DEFORMATION IN PATIENTS WITH POORLY CONTROLLED DIABETES MELLITUS TYPE 2 AFTER OPTIMIZATION OF ANTIDIABETIC MEDICATION.

EUR HEART J CARDIOVASC IMAGING. 2016 DEC 1;17(SUPPL_2)

EFFECTS OF VARENICLINE AND NICOTINE REPLACEMENT THERAPY ON ARTERIAL ELASTICITY, ENDOTHELIAL GLYCOCALYX AND OXIDATIVE STRESS DURING A 3-MONTH SMOKING CESSATION PROGRAM.

ATHEROSCLEROSIS. 2017 MAY 13;262:123-130.

NON-INVASIVE ASSESSMENT OF MICROVASCULAR DYSFUNCTION IN PATIENTS WITH MICROVASCULAR ANGINA.

INT J CARDIOL. 2017 DEC 1;248:433-439. DOI: 10.1016/j.ijcard.2017.05.010. EPUB 2017 JUL 18.

*THE MEASUREMENT OF THE ENDOTHELIAL GLYCOCALYX AS A NEW BIOMARKER OF
ENDOTHELIAL DERANGEMENT IN SYSTEMIC SCLEROSIS: A CHALLENGE FOR THE FUTURE.
J RHEUMATOL. 2017 Nov;44(11):1572-1574. DOI: 10.3899/JRHEUM.170958.
EPUB 2017 NOV 1. NO ABSTRACT AVAILABLE.*
