Electromagnetic Radiation, Nitric Oxide and Supporting the Nitrate/Nitrite/NO pathway

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Beth developed an expertise as a pharmacist and certified clinical nutritionist during a 40+ year career. Her specialties include stress-induced hormonal imbalance, intestinal dysfunction, autoimmune and chronic inflammatory issues, detoxification, nutrigenomics and super-normal oxidative stress.

Over the last twelve years, Beth has spent time working with some of the leading thought leaders in the world of nitric oxide research and through this has developed an in-depth knowledge on the topic and its potential applications in patient care. She currently is the Executive Director of the Berkeley Life Scientific Advisory Board.

EMF, EMR, RF-EMF

EMR - waves of electric and magnetic energy moving through space together
EMF – spans large frequencies
Change in an electrical charge changes biological processes

Quantum Decoherence and Loss of Energy Efficiency

Today is exposed to microwaves at level up to 10^{20} times original background radiation since the of universe

Majority of studies do not account for other toxic chemicals and biotoxins which exacerbate adverse effects of wireless radiation

Mixed results
Flawed results
Lab experiments not designed to be reflective of real-life conditions
Used single carrier frequency
Most experiments only involved one stressor under pristine conditions

Contradict real life experiences

Previous oxidative stress and inflammation issues exacerbate adverse effects

Adverse Health Effects of Wireless Radiation on Humans

Metabolic Disturbance	Reactive Oxygen Species Generation	Genotoxicity and Carcinogenicity	Immunotoxicity and Inflammation	Apoptosis and Necrosis
Discomfort Symptoms	Sensory Disorders	Sleep Disorders	Congenital Abnormalities	Precancerous Conditions
CANCER	**NEURODEGENERATION**	**INFERTILITY**	**NEUROBEHAVIORAL**	**CARDIOVASCULAR**

RF-EMF / Altered Redox Potential of Cells

Non-thermal RF effects mediates generation of ROS

Redox balance – oxidizing and reducing molecules relatively balanced

Oxidative stress – antioxidant defense insufficient or overwhelmed

- Disrupts structure and function of cells
- Change electric current in tissues
- Down-regulates production of NO
- Role in All chronic, degenerative and inflammatory issues

Aging, cancer, autoimmunity, cataracts, RA, CVD, neurodegenerative diseases, sleep disturbances, impaired wound healing, neuroendocrine processes governing reproduction and behavior, impaired learning and memory, peroxidation of fatty acids and impaired membrane function.

Superoxide O2-

Critical in killing pathogens
Signaling molecule – apoptosis, aging and senescence

Is toxic at high concentrations
Inactivates critical metabolic enzymes
Initiates lipid peroxidation
Damages iron-sulfur clusters – DNA damage
Liberates redox-active iron/labile plasma iron – neurodegeneration
Allows generation of indiscriminate oxidants – OH-, Fe3+ (Iron dysregulation)

Regulated by antioxidant enzymes
SOD

Redox balance is what is important

RF-EMF Increases O2 and Oxidative Stress

Uncouples NOS
Activates NADPH oxidase (NOX)
Uncouples mitochondrial ETC
Increases activity of MPO increasing H2O2
Stimulates XO
Stimulates Fenton Reaction – increased HFE SNPs in English, Irish, Ashkenazi
Increases intracellular influx of Ca2+ simulating NOX

EMR alters energy level and spin orientation of electrons
Increases activity, concentration and lifetime of ROS
Alterations in mitochondrial ETC

CACNA1C – gene that encodes VGCC and increased intracellular calcium
Excitotoxicity and oxidative stress
Increased sensitivity to EMF
Gene associated with bipolar, schizophrenia and increased intracellular

Supporting nitrate/nitrite/NO pathway addresses Every Single one of these factors to decrease oxidative stress

Stimulation of Ca2+ Channels by RF-EMF

VGCC – gated ion channel in membrane of excitable cells
- Muscle, glial cells, neurons, adrenals, etc.
- Widely distributed within CNS
- Depolarization allows ion movement
- Allows Ca2+ influx into cells
- Loss of membrane potential causing proton leak from mitochondria
- Decreased energy for ATP synthesis
- Increasing ROS and oxidative stress within mitochondria – mito uncoupling
- Cytotoxicity – weaken neuronal integrity
  - Breakdown of cytoskeleton
  - Dilatation of endoplasmic reticulum
  - Cytosolic shrinkage – dehydration of cell
- Methamphetamine increases Ca2+ influx
- Activation of NMDA – component of inflammatory and neuropathic pain
  - GABA inhibits subunit of VGCC

Pathophysiology of CNS disorders including ALZ, PD and MS

ONOO- Theoretical

Possible - influx of Ca2+ upregulates cNOS (constitutional NOS) - eNOS and nNOS by stimulation of Ca/calmodulin binding increasing production of NO

Found a few studies
- In-vitro cellular studies
- Not in-vivo

In Real Life
EMF increases and exacerbates oxidative stress
Oxidative stress uncouples NOS enzyme
Uncoupled NOS produces superoxide, not NO
Increasing oxidative stress even more
Bad, vicious cycle……

NO Inhibits Ca2+ influx

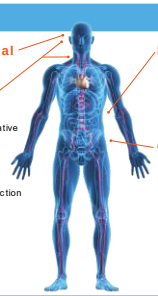
NO donors inhibits Ca2+ current in voltage-independent manner

Direct action on channel protein by S-nitrosylation
Indirect action – activation of cGMP increasing intracellular levels
NO's ability to activate Na+ channels in baroreceptors and hippocampal neurons

NO inhibition of Ca2+ current
Regulates intracellular Ca2+ concentration
Synaptic transmission

NO, as an endogenous mito K ATP channel opener, recouples mitochondria optimally blunting mitochondrial Ca2+ overload without undermining ATP synthesis

EMF Effects

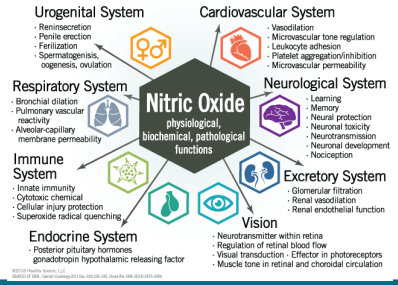


Behavioral Psychological
- Anxiety/Depression
- ADD/OCD
- Stress/Emotional

Neurologic Effects
- Alzheimer's/Neurodegenerative diseases
- Cognitive dysfunction
- Learning/Memory
- Hypothalmic-Pituitary-Hormonal dysfunction
- Pineal/Thymus gland dysfunction
- Sleep disorders/Insomnia
- Brain tumors
- Tinnitus/Eye problems
- BBB disruption
- Microglial Inflammation
- Headaches

Immunological Effects
- Inflammation/Aging (Inflammaging)
- Imbalance (Th1/Treg–Th2/Th17 shift)
- Mast cell activation
- Stimulates pathogens
- Synergistic with toxins
- Autoimmunity

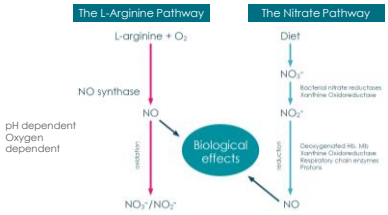
Cellular Effects
- Metabolic dysfunction/ Insulin resistance
- Mitochondrial dysfunction
- Cardiovascular dysfunction/HTN
- Fatigue/Weakness/Pain
- Cancers
- DNA damage/Epigenetic changes
- "Leaky gut"
- Infertility
- EMF sensitivity syndrome



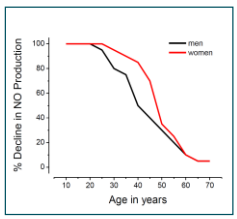
Why is NO Essential?

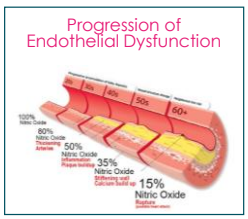
- Regulates all cardiovascular function/homeostasis – circulation and microcirculation
- Red blood cells require adequate NO to deliver oxygen to cells
- Supports neurotransmitter function
- Regulates gastro-intestinal function including gastroparesis, mucus and microbiome
- Helps activate GLUT-4 receptor
- Essential for learning and memory
- Supports mitochondrial biogenesis
- Controls efficiency of mitochondria in generation of energy and generation of hormones
- Essential for sexual function – men and women
- Stem cell mobilization and differentiation
- Regulates immune system function
- Regulates inflammatory response and scavenges free radicals
- Modifies platelet activation/aggregation
- Supports telemorase activity

Pathways to make NO

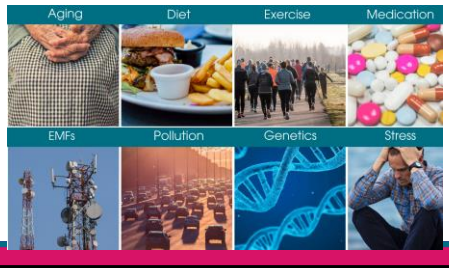


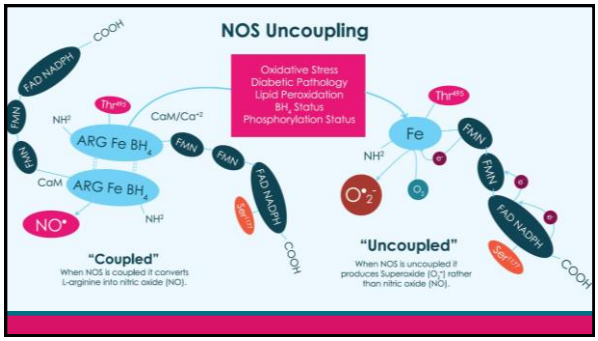
NO Decline with Age





Current Factors Affecting NO Formation





NOS Uncoupling

Uncoupled NOS produces superoxide rather than NO increasing oxidative stress

Rate limiting cofactor – BH4
O2- oxidizes BH4 to BH2
Other inhibitors – Aldosterone, Ang II, cortisol
BH4 depleted, uncoupled eNOS – Arginine stimulates O2- increasing uncoupling

NOS uncoupling amplified with EMF, aging, pollution, glyphosate, drugs, oxidative stress, inflammation and chronic disease states

L-arginine supplementation not effective to increase NO stores in aging population and those with chronic diseases

Circumventing arginine/NOS pathway with nitrate – safe, effective way to restore
NO bioavailability, decrease oxidative stress damage and recouple NOS

Nitrate Supplementation Positively Affects NOS

Inhibits NADPH oxidase (NOX) decreasing superoxide and oxidative stress

Inhibiting NOX increases NADPH levels needed for prevention of other chronic diseases (recycling of GSH, steroid synthesis, fatty acid synthesis)

Nitrate up-regulates GTP cyclohydrolase 1 increasing BH4 production from GTP

BH4 recouples NOS increasing NO and decreasing superoxide

Increases activity of SOD and CAT

Induces heme oxygenase and inhibits xanthine oxidase increasing NO bio-availability

Scavenges free radicals decreasing oxidative stress

Nitrate increase NO through nitrate/nitrite/NO pathway, recouples NOS, reduces ROS and oxidative stress

RF-EMF Activates NADPH Oxidase (NOX)

Initial stage of ROS production in presence of RF-EMF controlled by NOX

Normally dormant, activated during respiratory burst
Increases superoxide and oxidative stress

Activated by mTOR, histamines, oxalates, aluminum, iron, glutamate, smoking, homocysteine, sulfites, LPS, dopamine, RAAS, proinflammatory cytokines, EMF

'NADPH steal' resulting in decreased NADPH

- Impaired fatty acid synthesis
- Impaired steroid synthesis
- Decreased Phase 1 detoxification – cytochrome P450
- Decreased ability to recycle critical antioxidants, oxidized GSSG back to GSH
- Decreased ability to make NO

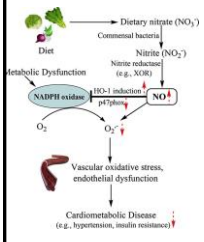
Increased ROS produced by NOX

- Stimulates RAAS - Renin, Angiotensin 1, Ang 11, Aldosterone, IL6
- Impaired thyroid function
- Inflamed gut
- Obesity
- Impaired cognition
- Cardiometabolic disease
- Impaired kidney function

Vicious cycle of inflammation – Every Where

Nitrite and NO down-regulate NOX

Nitrite and NO Down-regulates NOX



Peroxynitrite Theory of Damage from RF-EMF

NO reacts with O2- to form ONOO-

Martin Pall – pathophysiological response to EMFs result of stimulation of NO-cGMP protein kinase pathway
Influx of Ca2+ increases Ca2+/calmodulin dependent increase in NO
Increased NO reacts with O2- to increase ONOO- (eNOS, nNOS)
Suggests ONOO- mechanism injuring cells and tissues
Single documented example
Data severely limited

NO may be present, however, this doesn't mean that NO is causing pathology

Inhibiting ONOO- by Inhibiting O2-

ONOO- is formed when NO is in close proximity to O2-

In general – if making lots of O2-, typically not making lots of NO
O2- shuts down NO production

3 main sources of O2-
1) Uncoupled NOS – nitrate recouples NOS
2) NOX – nitrite and NO inhibit NOX
3) Uncoupled mitochondrial ETC – nitrite and NO recouple ETC

Controversial - increased NO from iNOS or any other source injures cells
L-NAME (NOS inhibitor) – decrease tissue injury and inflammation
May not be due to inhibition of cytotoxic concentrations of NO production
Other actions of L-NAME may be at play here

Restoring NO production by supporting nitrate/nitrite/NO pathway decreases O2-, thus decreasing ONOO- production decreasing ROS, RNS and oxidative stress

Can $ONOO^-$ be measured?

Measuring nitrotyrosine
Assume $ONOO^-$ was formed
Other nitrosating species form nitrotyrosine like, N_2O_3, N_2O_4, NO_2 radical, not specific for ONOO

New paradigm: $ONOO^-$ isomerizes to NO_3^- which is nitrate and inert

- $ONOO^-$ is in equilibrium with ONOOH under physiologically relevant pH
- ONOOH is unstable in aqueous solution and isomerizes to nitrate
- $ONOO^-$ reacts with oxyHb to isomerize to nitrate – 90%
- Peroxiredoxins are a significant biological sink of $ONOO^-$ with a 2-electron reduction of $ONOO^-$ to nitrate

Possible Beneficial Actions of ONOO-

Possible that ONOO- down-regulates expression of proinflammatory mediators

ONOO- suppressed NFkB activation triggered by LPS and inflammatory cytokines in cardiac and endothelial cells

ONOO- inhibits lipid peroxidation

Physiological pH – ONOO- undergoes rapid reactions and transformations
- CO2, NO, thiol containing albumin, GSH, cysteine, etc.
- Oxidation of thiols by ONOO- forms NO donor nitrosothiols
- ONOO- reacts with GSH to form S-nitrosothiol – NO and GSH donor molecule
- Protect heart during I/R

O2- and NO react – forms a cage-like molecule
90-95% rearranges to inorganic nitrate (NO3-) which is inert

Restoring NO production Decreases O2- production decreasing ONOO-

Redox Balance – Antioxidant Side

SOD – converts O2- to H2O2
CAT – peroxidase enzyme converting H2O2 to H2O
GSH – NADPH required – GSSG to GSH
PRDx – degrade H2O2, associated with circadian rhythm
GPx – H2O2, lipid peroxides - major antioxidant enzyme in rbc

EMF decreases SOD, CAT, GPx activity
Decreases GSH in blood and brain

Initial stage of ROS production in presence of RF-EMF controlled by NOX
NADPH steal

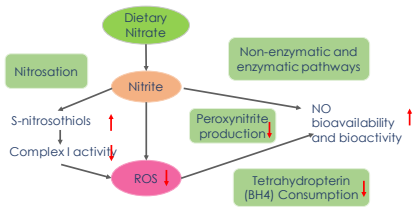
Supporting nitrate/nitrite/NO pathway decreases 'NADPH steal'
More reduced GSH available

Nitrate increases SOD, CAT activity

NO plays key role in controlling levels and limiting reactivity of ROS

Increased oxidative stress and inflammation – base of ALL chronic issues

The Effect of Nitrates and Oxidative Stress



*Mechanisms of the protective effects of nitrate and nitrite in cardiovascular and metabolic diseases. Nitric Oxide. doi:10.1016/j.niox.2020.01.006

RF-EMF/BP

Exposure to w-fi increases heart rate, frequency and arterial bp
- increases arrhythmias
- Enhances hypertension and dyslipidemia
- Stimulates RAAS increasing aldosterone

Calcium channel blockers
- Decrease bp
- Alter heart rate
- Prevent cerebral vasospasm
- Influence biosynthesis of aldosterone

NO governs circulation and microcirculation
Down-regulates RAAS

NO/cGMP pathways activates large Ca2+ dependent K+ channels which leads to membrane hyperpolarization and closure of VGCC inhibiting Ca2+ influx

NO regulates All mechanisms controlling intracellular Ca2+

NO and RAAS intertwined

Serum aldosterone is independently associated with all-cause mortality
Up-regulated RAAS gives down-regulated NO production
Inhibited NO production (uncoupled NOS, NADPH steal by up-regulated NOX, oxidative stress) stimulates ACE, increases Ang II, superoxide & oxidative stress

- ACE - regulates balance between RAAS & kallikrenin-kinin system
- ACE cleaves C-terminal dipeptide from Ang I to Ang II
- Ang II stimulates NOX increasing superoxide and oxidative stress
- Ang II stimulates mTOR, mTOR stimulates NOX
- Ang II modifies release of aldosterone in adrenal glands
- Ang II increases release of Endothelin I (ET1)
- ET1 augments Ang II vasoconstriction
- **RAAS increases IL6 which stimulates NOX which stimulates IL6**
- **IL6 stimulates mast cells, regulates CRP**
- **NO down-regulates synthesis of ACE and Ang II type 1 receptors**
- **NO antagonizes effects of Ang II on vascular tone, cell growth & renal sodium excretions**

Supporting nitrate/nitrite/NO pathway optimizes NO & down-regulates RAAS, aldosterone production and IL6

RF-EMF/Mitochondria/ROS

According to Free Radical Theory of Aging – ROS damage mitochondrial proteins, DNA, decrease ATP production and net dehydration of cell

Mitochondria – make ATP and create voltage of cell
One of main source of ROS because main source of intracellular O2 consumption
~2% of oxygen consumed not converted to H2O but to O2-

EMF - extensive electron leakage from ETC
- Uncouples mitochondrial ETC
- Oxidative damage to membrane
- Down-regulation of antioxidant genes – SOD, CAT, GPx
- Changes way we handle macronutrients - lose ability for beta oxidation

Mitochondria ETC reduce nitrite in hypoxia – Complex I, III, IV (CCOX)
- Regulates function
- Cytoprotective after I/R
- Blue light exposure and EMF cause hypoxia

Nitrite and NO recouple ETC decreasing proton leak
Nitrite and NO stimulates hypoxic mitochondrial biogenesis by activating AMPK and SIRT 1 activating PCG1a

RF-EMF Stimulates mTOR

mTOR – mechanistic target of rapamycin
Regulate cell growth, proliferation, motility, survival, protein synthesis, autophagy, activates insulin receptors and IGF1
Swimming in sea of mTOR stimulation
  Iron, MSG, pesticides, aminos, xenoestrogens, plastics, glucose, insulin, HFCS, dairy, folate
mTOR stimulates NOX
mTOR drives cerebrovascular dysfunction by down-regulating eNOS
mTOR inhibits AMPK and autophagy
AMPK – essential in glucose and lipid metabolism, mitochondrial metabolism (autophagy, mitophagy)
Virus co-opt mTOR – make host more hospitable for replication

Decreased mTOR activity increases life span
  Increases autophagy – removal of dysfunctional cellular components
  Clearance of debris before stimulation of apoptosis
  Maintains cell viability and homeostasis

Senescence – cells stop dividing and lose their function
  Irreversible growth arrest
  Contributes to pathogenesis of atherosclerosis
  Increased ROS in cells from cell phones

NO and NO donors stimulates AMPK which blocks mTOR and allows autophagy
NO can prevent endothelial senescence
NO scavenges ROS
NO increases telomerase activity to restore telomere length

RF-EMF/Biological stress response

Dysregulation of HPA axis
Increased plasma glucocorticoid levels
Impair growth of neural cells in hippocampus – learning and memory
Increases Heat Shock Proteins – marker of cells under stress
  HSP changes in brain, myocardium, testis, skin

Every cell in body is in alarm state from EMF/ER as per Dr Klinghardt

Cortisol down-regulates iNOS and eNOS
Increases ROS increasing oxidative stress
Decreases synthesis of BH4 – uncoupling NOS
Decreases membrane transport of arginine
Increases blood glucose
Increases HbA1C – tightly binds NO

All of these decrease production of/or make NO not bio-available

NO and Immune Competence

- **NO – essential in immune response** as defense against virus, bacteria, fungi and other pathogens
- Regulates macrophages, T lymphocytes, antigen presenting cells, mast cells, neutrophils and NK cells
- **Immunoregulator**
- Vulnerable populations in current pandemic – lower levels of endogenous NO
  - Aging
  - Obesity
  - Diabetes
  - Metabolic syndrome
  - COPD
  - Autoimmune disorders
  - Hemoglobinopathies

- **iNOS (NOS2)** – part of immune response
- **eNOS (NOS3)** – governs circulation and microcirculation

"Well vascularized tissues are more resistant to infections and capable of localizing/containing offending agents. By contrast, poorly vascularized tissues are relatively inefficient in responding to inflammatory stimuli."
– Dr. Nathan Bryan

EMF and Impaired Immune Response with Decreased NO

EMF classified as immunosuppressant

Causes biological stress response
Down-regulates production of NO

NO – essential for defense against pathogens

Alters gut-brain-immune axis

Increased Ca2+ influx – significantly increased cytokine storms

Increased cytokine storms - increased susceptibility

Long term stress (EMF exposure) dysregulates immune response
80% of immune system in gut

Intensifies reactions to mold, lyme, virus, bacteria, parasites

Oxidative stress down-regulates NO production

Major beneficial actions of NO in the mechanism of gastrointestinal mucosal defense

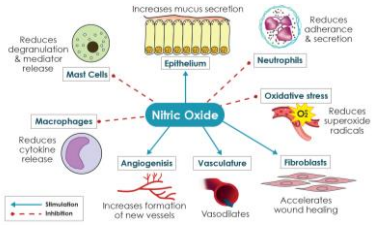


Diagram: Magierowski, M., Magierowska, K., Kwiecien, S., Brzozowski, T. Gaseous Mediators Nitric Oxide and Hydrogen Sulfide in the Mechanism of Gastrointestinal Integrity, Protection and Ulcer Healing. Molecules 2015, 20, 9099-9123.

NO and Intestinal Health

Mucus
First line of defense against pathogens
Protective layer to balance
Exposed to many damaging substances - ethanol, nicotine, drugs (eg. NSAIDs), H. pylori, hyperosmolar solutions, bile salts, ischemia/reperfusion of gastric tissues and Stress

Stress
Alters GI motility and secretion
Increases intestinal permeability
Decreases mucosal blood flow
Negative effects on microbiome

Supporting the nitrate to nitrite to NO pathway
NO – signal for mucus secretion
Mediator for cholinergic stimulated mucus release

Increases mucosal blood flow and vasodilation

Increases mucus production and thickness

Modulates mucosal immune response

Prevents acute peptic ulceration

Repairs NSAID damage to intestinal tract

Supports health and biodiversity of microbiome

RF-EMF Stimulates Mast Cells

Mast cells – effectors of gut-brain-immune axis
Translate stress signals into release of neurotransmitters and pro-inflammatory cytokines

Mast cells line all mucus membranes
- Release histamine, cytokines, chemokines, interleukins, PAF
- Activated by superoxide
- Activated in absence of NO

Nitrites and NO regulate activity of mast cell
- Inhibit mast cell dependent inflammatory events
- Suppress antigen-induced degranulation
- Suppress mediator release including histamine and cytokines
- Inhibit leukocyte endothelial cell attachment
- Inhibit generation of ROS by mast cells

RF-EMF Impairs BBB

Altered BBB integrity after use of phone, exposure to EMF
Leakage of albumin
Serious neuronal cell damage

Tight junction proteins
- Epithelial transport
- Barrier integrity
- Found in BBB, eyes, intestinal tract, skin, kidney, bile duct

Loss of tight junction proteins – breakdown of barrier
- Decreased expression of occludin and claudin 5
- Leaky gut means leaky brain
- GI inflammation means neuroinflammation

Nitrate increase rebound levels of occludin and claudin 5 protecting tight junction proteins and barrier integrity

BDNF – affects integrity of tight junctions
Homeostatic regulator of barrier integrity
NO – essential mediator of BDNF

RF-EMF/Microbiome

Environmental pollutant capable of disrupting microbiomes
Increasing antibiotic resistance
Enhancing biofilm formation
Decreasing good bacteria while increasing harmful
Beneficial bacteria grow slower

Supporting nitrate/nitrite/NO pathway
- Prevent dysbiosis
- Supports healthy microbiomes
- Decrease inflammatory pathways
- Down-regulates and scavenges ROS
- Nitrite disrupts protective biofilms

RF-EMF/Learning, Memory and Cognition

VGCC – high density through nervous system

Increased ROS
Altered BBB integrity
Neuroinflammation
Neurodegeneration
Neuronal damage to cerebral cortex
Degenerative changes in cerebellum
Apoptosis of amygdala
Damages myelin sheath
Increased intracellular Ca2+ - disassembles cytoskeletal proteins, especially microtubules triggering apoptosis
Methamphetamine increases intracellular Ca2+

Neurons - increased sensitivity to oxidative stress due to longevity and limited renewal

Optimizing NO during Inflammation, Neuroinflammation, TBI

Blocks cytokine storm
Down-regulates inflammatory cytokines – NLRP3, IL1B, IL6, IL18
Decreases mast cell degranulation – release of histamine,
Decreases myeloperoxidase activity – H2O2
Stops hypoxia/reperfusion injury
Limit lipid peroxidation
Decrease IL17 decreasing inflammation
Rebalance T cells
  Decrease proinflammatory TH1 and TH17
  Increase T reg cells – maintain homeostasis and self tolerance
Restores oxygen delivery and cellular waste removal

Blockage of neuroinflammation restores neurogenesis

Supporting nitrate/nitrite/NO pathway in Neuroinflammation

Increases NO directly and recouples NOS decreasing oxidative stress
Anti-inflammatory
Supports microbiomes – gut-brain-immune axis
Supports tight junction proteins
NO governs circulation and microcirculation
Impairment of blood flow increases neurodegeneration
NO in hypothalamus and cerebral cortex – learning and memory
NO inhibits Ca2+ influx into neurons limiting glutamate neurotoxicity
Neuromodulator
Synaptic Plasticity – BDNF
Neurogenesis – NSC
Mitochondrial function and biogenesis

Repair of damaged cells – essential for survival

Anxiety and Depression

NO is involved in regulation of anxiety. Anxiety and depression are associated with low levels of BDNF

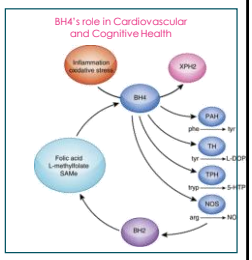
NO:

- Mediates the neuroprotective actions of BDNF in promoting neuronal survival and stimulating the process of neurogenesis which enhances learning and memory
- Plays a role in synaptic plasticity which positively influences mood
- Increases GABA in the brain

Nitrates increase production of BH4 increasing the production of neurotransmitters.

Supporting the nitrate to nitrite to NO pathway will decrease oxidative stress and inflammation.

Oxidative stress and inflammation play a huge role in biological dysfunction everywhere and anywhere.



NO and Cognition

- High bp - risk factor for cognitive decline and dementia
- 50% of adults have high bp
- Hypertension occurs decades prior to onset of dementia, affecting blood flow in body as well as brain
- Brain - 2% of our body mass yet consumes 25% of body's requirement for oxygen
- Brain produces 20 X more NO than entire vasculature
- NO governs circulation and microcirculation
- Impairment of blood flow to brain increases risk of neurodegenerative diseases
- NO in hypothalamus and cerebral cortex - learning process and memory formation
- Neuromodulator
- Synaptic plasticity/BDNF
- Neurogenesis – NSC
- Mitochondrial function and biogenesis
- ARB and ACE inhibitors benefit long-term cognition (RAAS)

NO and Neuropathy

70% of diabetics develop DPN within 5 years
- Impaired blood flow
- NO is a neurotransmitter in some autonomic fibers

Arginine/NOS pathway impaired in diabetes
- NOS pathway is pH dependent
- Diabetes decreases pH to more acidic state
- NOS requires oxygen – circulation is impaired so less O2 delivered
- Diabetes increases ADMA – inhibits NOS
- Rampant oxidative stress in diabetes – oxidative stress uncouples NOS

Insulin resistance
- increases NOS uncoupling
- Loss of endothelial function
- Increased adhesion molecule formation (VCAM 1)
- Increased oxidative stress

GLUT 4 receptor requires adequate NO
HbA1c binds tightly with NO – making NO not bio-available

EMF/Pain

VGCC – role in development of chronic pain

Increase Ca2+ into cell – triggers apoptosis or increased inflammatory cytokines
Inflammation causes pain and tissue damage

Subtypes of VGCC show abnormal functioning in persistent pain states
Activation of Ca2+ channels – glutamate, substance P
NMDA activation – major component of inflammatory, neuropathic pain
- CRPS
- Diabetic neuropathy

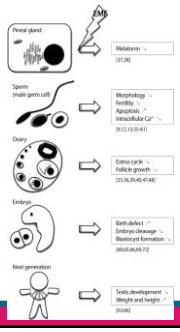
GABA reacts with VGCC and neuropathic pain
NO in brain inhibits GABA transamidase increasing GABA in brain

Compromised circulation – nerves malfunction
Lack of oxygen, nutrients and lower ATP affects membrane potential

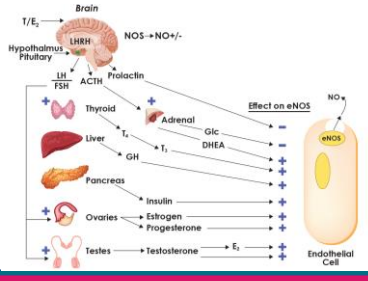
NO downregulates neuronal transmission by inhibiting Ca2+ influx and activating K+ channels preventing action potential
How pain pathways blocked by morphine via NO, mediating relaxation response

Effects of EMF Exposure on the Reproductive System

Oxidative stress – most recognized cause of male infertility



Hormones and NO



EMF/Thyroid

Decreased T3 and T4 in serum
Increased cortisol – decreases conversion of T4 to T3

NADPH oxidase (NOX) enzymes in thyroid - DUOX1 and DUOX2
Increase ROS, O2- and H2O2
Need precise amount of H2O2 for TPO

NO and nitrites inhibit NOX and DUOX enzymes
Supporting the nitrate to nitrite to NO pathway may be an underutilized thyroid therapy due to its role in decreasing the production of superoxide and other ROS by optimizing NO levels, scavenging ROS, and supporting healthy circulation and microcirculation.

EF-EMR/Blood Glucose Dysregulation

RF-EMF increases HbA1C and T2D in school age adolescents
Environmental – Type 3 Diabetes
- Increased plasma glucose
- Increased blood viscosity

Long term exposure to activated mobile phones
- Increases fasting blood glucose
- Increases serum insulin

EMF causes physiological stress
- Increases cortisol – increasing glucose

Blood sugar dysregulation – uncouples NOS
HbA1c binds NO tightly

Supporting nitrate/nitrite/NO pathway optimizes NO
Downregulates oxidative stress and pro-inflammatory cytokines
Downregulates RAAS
Essential for GLUT 4 translocation

What's Really Going On?
Dr. Dietrich Klinghardt

Pineal gland is the 'seat of the soul'
Pineal gland is a receiver for higher fields of energy and translates them into thought

"there will be a movement driven by big compactions to take the soul away from people, to disconnect people from the higher world. And, in order to that, they have to destroy the pineal gland in people. I've followed the research on that, and amazingly … the pineal gland is the most sensitive part of our Central Nervous System and is highly highly highly sensitive to 4 things: aluminum, glyphosate, fluoride and wi-fi. And we (USA) are the only country in the world that has pushed these 4 things in the last 60 years or so on everyone growing up here …"

what is needed for these compounds to actually enter the brain is to open up the blood brain barrier, and the current frequencies in the wi-fi world are exactly doing that…….

'How to dull peoples' minds. Then kill them……'

Sleep/Melatonin/EMR

EMF – sleep interference
- Phase shifting of circadian biology
- Disruption of brain activity during sleep
- Increased BBB permeability
- Suppressed levels of melatonin

Most melatonin made within mitochondria (<5% in pineal) – gut health essential

Constant light exposure in pineal decreased NOS activity - 80% after 8 days

Melatonin – potent free radical scavenger, especially OH-

Induces eNOS, nNOS
Inhibits iNOS
Stimulates GCL (glutamyl cysteine ligase) – rate limiting enzyme in making GSH
Inhibits NOX
Stimulates SOD
Decreases ADMA
Decreases proinflammatory mediators
Protective against mercury
Beneficial in non-dipper hypertension
Protective in OSA

NO chemistry plays a role in mitochondrial circadian cycle

Sleep/Circadian Rhythm

Lose ability to make NO - disturbed sleep

nNOS production of NO within neurons of brain that signal sleep and sleep patterns

Regulation of REM sleep age-dependent process involving NO

Impairment of NO production - phase shift of circadian clock and disturbed sleep

Impaired circadian rhythmicity increases non-dipper hypertension

Obstructive Sleep Apnea (OSA) – Hypoxic, NO deficiency state
- Increased oxidative stress
- Stimulates NOX
- Uncoupled NOS
- Increased ADMA (linked to increase in all cause mortality)

Supporting nitrate/nitrite/NO pathway
- Decreases oxidative stress
- Recouples NOS
- Decreases ADMA

RF-EMF/Anxiety and Depression

VGCC – high density throughout nervous system
Activation - excitotoxicity

Microwave frequency produce widespread neuropsychiatric effects
- Depression
- Anxiety
- Irritability
- Sleep disturbance

Neurotransmitter imbalance
- Decreased serotonin, dopamine and PEA
- Increased norepi & epi – stress neurotransmitters

Anxiety and Depression

NO is involved in regulation of anxiety
Anxiety and depression - low levels of BDNF

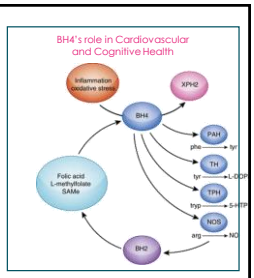
Nitric Oxide:

- Mediates the neuroprotective actions of BDNF in promoting neuronal survival and stimulating process of neurogenesis which enhances learning and memory
- Plays a role in synaptic plasticity which positively influences mood
- Increases GABA in the brain

Nitrates increase production of BH4 increasing the production of neurotransmitters

Neuroinflammation – affects how we feel

Supporting the nitrate to nitrite to NO pathway will decrease oxidative stress and inflammation.



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Brain Health of Gut-Brain-Immune Axis

Blood flow to brain carrying oxygen, nutrients and glucose and removal of wastes affects brain performance, cognition, fatigue and sense of well-being

Vascular dementia – insufficient blood flow to prefrontal cortex

NO plays a role in synaptic plasticity

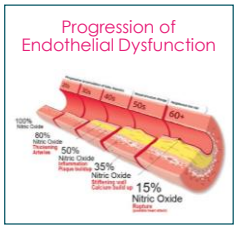
NO mediates neuroprotective action of BDNF regulating NPC proliferation and differentiation

Neuromodulator

NO supports intestinal health – gut-brain-immune

Inflammatory cytokines alter behavior and cognition

NO decreases neuronal inflammation and oxidative stress



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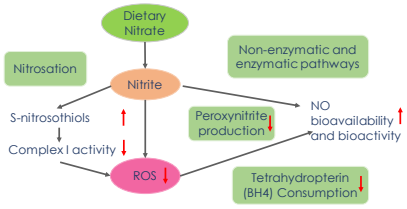
NO and Cognition

- High bp - risk factor for cognitive decline and dementia
- 50% of adults have high bp
- Hypertension occurs decades prior to onset of dementia, affecting blood flow in body as well as brain
- Brain - 2% of our body mass yet consumes 25% of body's requirement for oxygen
- NO governs circulation and microcirculation
- Impairment of blood flow to brain increases risk of neurodegenerative diseases
- NO in hypothalamus and cerebral cortex - learning process and memory formation
- Neuromodulator
- Synaptic plasticity/BDNF
- Neurogenesis – NSC
- Mitochondrial function and biogenesis
- ARB and ACE inhibitors benefit long-term cognition (RAAS)

The Effect of Nitrates and Oxidative Stress



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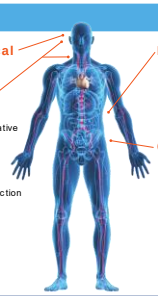
EMF Effects

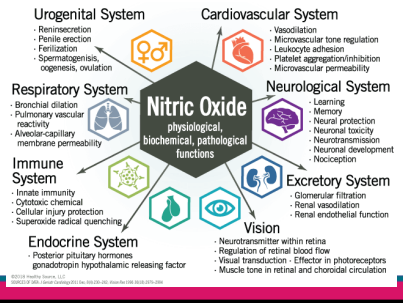


Behavioral Psychological
- Anxiety/Depression
- ADD/OCD
- Stress/Emotional

Neurologic Effects
- Alzheimer's/Neurodegenerative diseases
- Cognitive dysfunction
- Learning/Memory
- Hypothalmic-Pituitary-Hormonal dysfunction
- Pineal/Thymus gland dysfunction
- Sleep disorders/Insomnia
- Brain tumors
- Tinnitus/Eye problems
- BBB disruption
- Microglial Inflammation
- Headaches

Immunological Effects
- Inflammation/Aging (Inflammaging)
- Imbalance (Th1/Treg–Th2/Th17 shift)
- Mast cell activation
- Stimulates pathogens
- Synergistic with toxins
- Autoimmunity

Cellular Effects
- Metabolic dysfunction/ Insulin resistance
- Mitochondrial dysfunction
- Cardiovascular dysfunction/HTN
- Fatigue/Weakness/Pain
- Cancers
- DNA damage/Epigenetic changes
- "Leaky gut"
- Infertility
- EMF sensitivity syndrome



EMF Contributes to Perfect Storm for Low NO

- Age – especially over 40
- Physical inactivity
- SAD Diet – inflammatory
- Antibiotics
- Antidepressants
- Antifungals - azole
- BC pills
- Antiseptic mouthwash, fluoride and whitening toothpaste
- NSAIDs/COX 2 inhibitors
- Achlorhydria – PPIs
- Glyphosate – depletion of BH4, NOS uncoupling
- Pollution
- Stress

Non-thermal effects of RF-EMF mediated by generation of ROS

EMF increases oxidative stress and increases free radicals which damage membranes, cells and tissues, altering physiological processes

Oxidative stress plays a role in Every Single chronic, degenerative, inflammatory condition

Oxidative stress uncouples arginine/NOS enzyme decreasing production of NO and increasing oxidative stress even more

NO is at base of health and affects Every Single physiological process

NO inhibits Ca2+ influx regulating intracellular Ca2+ concentration modulating potential damage

Supporting nitrate/nitrite/NO pathway optimizes NO, increases NO directly, as well as recoupling the NOS enzyme increasing NO and decreasing oxidative stress.

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