Author’s response to reviews

Title: Past and Future Corollaries of Theories on Causes of Metabolic Syndrome and Obesity Related Co-Morbidities Part 2. A Composite Unifying Theory Review of Human-Specific Co-adaptations to Brain Energy Consumption

Authors:

Anne-Thea McGill (at.mcgill@auckland.ac.nz)

Version: 2 Date: 25 April 2014

Author’s response to reviews: see over
Dear Prof Van Oyen

Many thanks for your rapid reply, and advice as followed below, in blue text. Again I appreciate your accommodation of this rather weighty couple of papers and the fee waiver. I hope the readers will get something out of them. It is an important topic.

Please attend to how I denote the other paper in the abstracts. At present I have ‘...in the current issue of Archives of Public Health, McGill, A-T. 2014 x.’ but I am not sure this is correct for the abstract. I the body of the paper it is just the [x] reference number.

I have taken the liberty of adding a few more references 1) as you asked me too (please see last part of this letter, 2) as there have been a couple of recent articles that it would look up-to-date to acknowledge, and I think I should.

I have read through everything again, for spelling and grammatical errors, but I may have missed something. Please do not hesitate to clarify anything.

Editor’s comment

Title: Causes of Metabolic Syndrome and Obesity-Related Co-Morbidities Part 1.
A Composite Unifying Theory Review of Human-Specific Co-adaptations to Brain Energy Consumption

Authors:
Anne-Thea McGill (at.mcgill@auckland.ac.nz)

Version: 4 Date: 12 April 2014

Editor's comment:

Abstract

The theory has significant past and future corollaries, which are explored in a separate article.

# The 2 articles will be published jointly: change the text accordingly

I have attempted to include this information.

MANUSCRIPT

The second article of the two on the composite unifying theory

-> Use following reference in the journal style

McGill A: Past and Future Corollaries of Theories on Causes of Metabolic Syndrome and Obesity Related Co-Morbidities Part 2. A Composite Unifying Theory Review of Human-Specific Co-adaptations to Brain Energy Consumption. Arch Public Health 2012, 72:XX+1

= [1]

1. McGill A-T: Past and Future Corollaries of Theories on Causes of Metabolic Syndrome and Obesity Related Co-Morbidities Part 2. A Composite Unifying Theory Review of Human-Specific Co-adaptations to Brain Energy Consumption. Archives of Public Health 2014, 72:xx+1.

Please note that I have put 2014, rather than 2012 as you had.

Last sentence before conclusion:

A table of suggestions for possible public health actions included.

Change to A table of suggestions for possible public health actions is included.

Corrected
Editor’s comment

Title: Past and Future Corollaries of Theories on Causes of Metabolic Syndrome and Obesity Related Co-Morbidities Part 2. A Composite Unifying Theory Review of Human-Specific Co-adaptations to Brain Energy Consumption

Authors: Anne-Thea McGill (at.mcgill@auckland.ac.nz)

Version: 1
Date: 12 April 2014

Editor’s comment:

Forward:

and published in an accompanying article in this issue of APH
change to

and published in an accompanying article [1]

+> Use following reference in the journal style

McGill A: Causes of Metabolic Syndrome and Obesity-Related Co-Morbidities Part 1. A Composite Unifying Theory Review of Human-Specific Co-adaptations to Brain Energy Consumption. Arch Public Health 2012, 72:XX

= [2]

1. McGill A-T: Causes of Metabolic Syndrome and Obesity-Related Co-Morbidities Part 1. A Composite Unifying Theory Review of Human-Specific Co-adaptations to Brain Energy Consumption. Archives of Public Health 2014, 72:xx.

Line 40:
The composite unifying theory has been developed in an accompanying article in this issue of APH (Ref to article).
change to
The composite unifying theory has been developed. [1]

Inserted

Lin 349

Major media will be exposed as being owned by large industrial magnates where
reporting on much science, medicine and technology is designed to encourage consumption and investment (Thomas DR, pers com).[77]

I would suggest to avoid a personal communication and suggest to drop the reference and change the text accordingly.

Major media will be exposed as being owned by large industrial magnates [3] 85 where reporting on much science, medicine and technology is designed to encourage consumption and investment, rather than health. If local and national media can be freed from influence of the wealthy conglomerates [3] 85, then non-environmental agribusiness will no longer be framed as the more positive pathway [4] 86. Education and promotion of more ecological methods of food production that are likely to lead to better farming, healthy food and less obesity.[5] 87 Media framing of the ordinary, low income family, where obesity is common, would no longer be pejorative [6, 7] 88.89 (Table 1).

Regards

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Herne Bay Medical Centre, (B–Med Weight Control Clinic & GP locum) 2 Albany St, Ponsonby, Auckland 1011, Tel +64 9–376 3015 Fax +64 376 5183, Email broommed@ihug.co.nz, Mob 021 378875. Web www.hernebaymed.co.nz Tuesday & Friday afternoons
**Current Thinking/Assumptions**

**Problem**

Obesity associated with Cardiovascular Disease (CVD) in many ‘Westernised’ human populations

**Critique Research Advisories Literature  Framing of Plausible Question**

Central Obesity (Metabolic/Degenerative Disease in ‘Westernised’ Humans (Peripheral Fat  Locomotor/ Psychological Issues)

**Identification**

**Accept More Energy (En) Food Consumed = En In**

**Question**

More En Food Consumed or other reason? Why? Read / critique

**Question**

Less En Expended in PA/other reason. What? Read/think /critique

**Accept Fat Gain  MetS, TIIDM, CVD & Kidney Liver, Brain Disease & Cancer**

**Possible Mechanism**

Accept

1) Large amount of energy from high En fatty or sugary food.
2) ‘Bad food choice’ ‘Poor portion control’ of ‘junk (high En) food.
3) ‘Big Food’ ‘unable’ to be influenced.

Accept

1) Humans expending much less En in PA
2) ‘Non-specialised’ mammal metabolism all similar
3) Fat causes CVD via raised blood cholesterol, glucose, ?inflammation.

**Plan – Hypothesis, Studies & Policy**

**Hypothesis**: That uncontrolled overeating of energy dense food, (driven by the cortico-limbic-striatal reward system) in situations of plenty, can be managed in humans by non-judgemental addiction techniques, PLUS concurrent education, enablement & regulation to increase high micronutrient whole food consumption allowing easier PA, central fat loss & tissue repair  slim, fit & healthy longevity.

**Studies**: 1) Mathematically model energy human metabolism in obesity with terms determined/added for adequate micronutrient supply
2) Trial of refined food addiction management by stress management & possibly medication plus concurrent enablement of whole food consumption in obese individuals for resolution of oxidative/xenobiotic stress related central obesity & MetS.

**Policy Changes**: Control product quality of, & stop indirect subsidies to, ‘Big Food’, support hi-micronutrient/ low-additive food production.

**Investigate/Review**

Plan

1) More studies: energy restriction & PA/diet education funded by processed some from public health money  variable results
2) More meta-analysis of above  equivocal & no improvement in obesity.

Plan

1) More pharmaceutical/supplement studies of BP, blood lipids, glucose funded by drug industry  variable results
2) More meta-analysis of above  no real improvement in fatty liver, TIIDM, CV, neurodegenerative or cancer.

**Possible Mechanism**

Review Science Basics/Initial Conditions

1) Human brain /body En ratio is very high, and is unique therefore must have co-adaptations 
   2a) Increase En efficiency/conservation &/or
   2b) Increase energy intake BUT ... ‘Quantum leap’ hypothesis generation = ‘Could unique brain evolution  human specific energy metabolic solutions?’

**Plan**

1) Large amount of energy from high En fatty or sugary food.
2) ‘Bad food choice’ ‘Poor portion control’ of ‘junk (high En) food.
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**Review Science Basics/Initial Conditions**

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**Explore Literature, Critique & Develop Theory**

1) Review ANY relevant, science literature – human evolution ... new basic & comparative physiology
2) Humans: Large, developed cortico-limbic-striatal reward & motivation system for acquiring more energy; omnivory; social & technology ‘advances’
3) Humans:- antioxidant/ antitoxicant/ repair NRF2 system employs plant micro-nutrients for efficient immune system/ detoxification/longevity; develop/grow slowly; under muscled/overfat physiology.
Figure 2.

Increased Energy Efficiency/Conservation

1. Humans ability to safely store energy in our bodies.
2. Neocortex born with 30% reserve, at expense of developing muscle.
3. Human body is simplified, thus using less "meat" and able to redirect energy to brain.

Increased Energy Uptake

Energy Expensive Trade-offs

1. Humans ability to safely store energy is at expense of developing muscle.
2. Neocortex born with 30% reserve, at expense of developing muscle.
3. Human body is simplified, thus using less "meat" and able to redirect energy to brain.

Technologies - agriculture, animal/plant domestication, breeding, food production, transport, etc.

Omni-vore - more energy intake, ability for brain, motor coordination and fine motor skills.

Expansion of brain cortical reward for energy dense food procurement.

Human evolution:

- Homo habilis
- Homo erectus
- Homo neanderthalensis
- Homo sapiens neanderthalsis
- Homo sapiens sapiens

Time (millions of years):

- 4 Ma
- 1.7 Mya
- 0 Mya

Human evolution and brain size:

- 500 cm³
- 1000 cm³
- 1500 cm³

Brain size and human evolution:

1. Homo habilis
2. Homo erectus
3. Homo neanderthalensis
4. Homo sapiens neanderthalsis
5. Homo sapiens sapiens

Brain expansion and energy uptake:

- 500 cm³
- 1000 cm³
- 1500 cm³

Brain expansion and energy density:

- 500 cm³
- 1000 cm³
- 1500 cm³
Forager Environment

- Availability
- Macronutrient
- Micronutrient +/- Internal Milieu
- Hunger → Homeostasis
  - Micronutrients
  - Some Always Present
  - Liking Wanting Emotion
  - Eat ++ Volume
- Palatability
- Cues
- Stress
- Physical Activity
- Environment & Life Situation

Westernised Environment

- Availability
- Macronutrient
- Micronutrient
- Internal Milieu
- Hedonics → Addiction
  - Micronutrients
  - Often Many Absent
- Liking Wanting Emotion
  - Eat ++ Energy
- Palatability
- Cues
- Chronic Stress
- Physical Activity
- Environment & Life Situation
Figure 4.
Xenobiotics, Oxidants, Antioxidants, Drugs, (Vitamins C, E, K, Resveratrol, Isothionates, Curcuminoids, Chalcones Polyphenol Michael Acceptors etc)
Chemo- preventatives
Ionising Radiation, Ultraviolet Light
Heavy metals
Infective agents (viral, bacterial), Inflammatory Cytokines, Growth Factors, Lipoproteins

Reactive Oxygen Species
NRF 2
KEAP 1
KEAP 1
Cell Membrane
Nuclear Membrane

Metabolism
Many Molecules & Pathways Ways
Ubiquation & Proteosomal
Repair & Removal of Damaged Proteins
Cell Survival

Many Molecules & Pathways Ways
Chaperone & Stress Response Proteins
Prevents Tumourigenesis

Many Molecules & Pathways Ways
Eg Glutathione Pathway
Metabolism &/or Detoxification of Xenobiotics

Metabolism &/or Detoxification of Xenobiotics
Transport of Xenobiotics
Decrease in Oxidants

Many Molecules & Pathways Ways
Phase I & II
Eg Glutathione Pathway
Many Molecules & Pathways Ways
Phase III
Many Molecules & Pathways Ways
Eg Superoxide Dismutases

Antioxidant Response Elements
Antioxidant Response Element

Many Molecules & Pathways Ways
Detoxifying Proteins

Antioxidant Pathways
Metabolism &/or Detoxification of Xenobiotics
Prevents Tumourigenesis

Many Molecules & Pathways Ways
Cell Survival

NRF
Antioxidant Pathways
Metabolism
Cytoplasm
1. McGill A-T: Past and Future Corollaries of Theories on Causes of Metabolic Syndrome and Obesity Related Co-Morbidities Part 2. A Composite Unifying Theory Review of Human-Specific Co-adaptations to Brain Energy Consumption. Arch Public Health 2014, 72:xx+1.

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