TECHNICAL NOTE

Lifestyle Interventions for Metabolic Health

InSea2®

INTRODUCTION

The recent COVID-19 pandemic imposed drastic confinement and social distancing measures to ensure the continued functioning of the healthcare system. These measures, while effective, imposed mental and physical constraints on people that will unfortunately have lasting consequences, from social isolation to periods of forced physical inactivity.

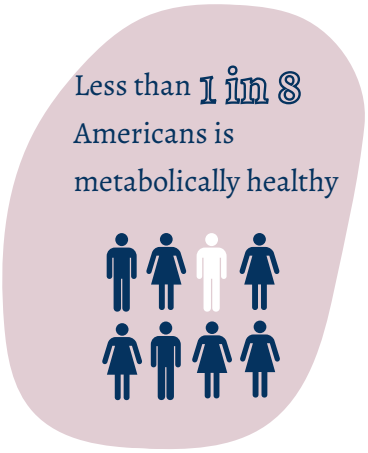
Science is showing that even short periods of physical inactivity and excessive caloric intake may significantly impact metabolic health. These conditions were frequent during confinement measures, as many of us ate and drank more to cope for social distancing and mental distress. A recent article reviewed the metabolic consequences of acute physical inactivity in healthy adults. The data indicate that a reduction in daily physical activity as short as three days may impair glycemic control. Reducing mobility (as the number of daily steps) for two weeks further increased fat mass and reduced lean mass, and also had a negative impact on VO_2 max.[1]

With its zero-COVID policy, the population of China has been submitted to these restrictions more than any other places in the World. A recent study involving 3,777 employees of five Chinese institutions who underwent physical examinations for three consecutive years from 2018 to 2020 found that the prevalence of metabolic syndrome increased from 15.7% before the pandemic to 18.6% in 2020.[2]

METABOLIC HEALTH STATISTICS

In 2018, Araujo *et al*. published a shocking article. They studied the health data from the US National Health and Nutrition Examination Survey 2009-2016 for a total of 8,721 people.

Metabolic health was defined as having optimal levels of waist circumference (WC <102/88 cm for men/women), glucose (fasting glucose <100 mg/dL and hemoglobin A1c <5.7%), blood pressure (systolic <120 and diastolic <80 mmHg), triglycerides (<150 mg/dL), and HDL cholesterol (≥40/50 mg/dL for men/women), and not taking any related medication.



The results show that the **overall prevalence of metabolic health was 12.2%** in the studied population (less than 1 in 8). Surprisingly, metabolic health was low even in people with optimal body weight, with 33.5% of people with BMI 18.5 – 24.9. In overweight (BMI 25.0 – 29.9) and obese (BMI ≥30.0), the prevalence of metabolic health was down to 15.0% and 6.8%, respectively.[3]

PILLARS OF METABOLIC HEALTH

Medical professionals recognize metabolic health as the maintenance of optimal levels of five key health components illustrated below:

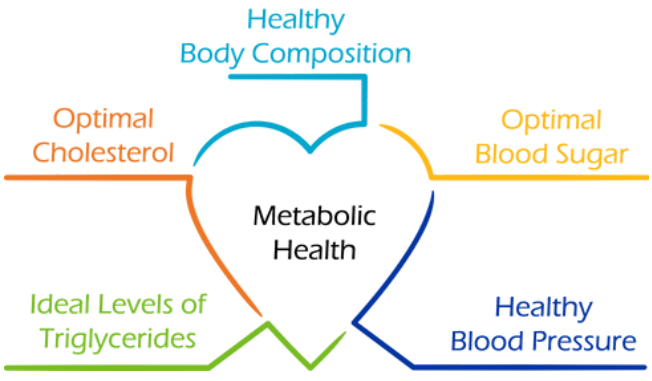


Figure 1: Components of metabolic health
Adapted from ©Metabolic Syndrome Canada

While the five components of metabolic health seem to work independently from one another, they are in fact all influenced by insulin signalling.

Several parameters of metabolic health can be impaired when insulin does not work properly at the muscle or adipose tissue levels. For example, the raise in blood glucose, triglycerides and reduced HDL can all be linked to this loss of efficacy of insulin.

Insulin action on the muscle is of tremendous importance to the maintenance of blood glucose. When muscles become resistant to insulin, less glucose transporters are being expressed at the surface of the cells and glucose remains into the bloodstream. [4] But insulin also reduces the phosphorylation of glucose by muscle cells (meaning that glucose will not remain in the cell) and will also reduce glycogen formation. [5] More glucose lingering in the blood in turn induces insulin release, which worsens insulin resistance even more.

Insulin also has an impact on fat cells. After meals, insulin binds to receptors on fat cells to prevent them from breaking down stored fat by action of the enzyme Hormone Sensitive Lipase (HSL). This temporary stoppage in HSL action is important to prevent excessive release of glycerol and fatty acids in the blood.[6] These two components are normally converted into triglycerides by the liver, ultimately contributing to raise blood lipids and cholesterol. Here again, preserving optimal insulin signaling helps ensure a healthy balance of blood lipids.

Insulin also has a role to play in blood pressure regulation. In fact, kidneys normally filter out excessive sodium, but sodium transporters located on the luminal face of proximal and distal renal tubules may reabsorb sodium that was originally filtered out. These sodium transporters are stimulated by high insulin levels, a situation that prevails when insulin signalling is not optimal. [7] The resulting increase in blood sodium negatively affects blood pressure.

Excess abdominal fat also plays an essential role. Adipose tissue is far from being an inert fat mass: it participates in the regulation of the metabolism by secreting different substances that allow it to communicate with the liver, muscles, heart and blood vessels. Visceral fat accumulation alters this function, leading to abnormalities in the use and storage of sugar and lipids, as well as inflammatory processes that contribute to further degrade insulin signaling. [8]

Maintaining proper insulin function is thus the most important factor to keep in mind to maintain metabolic health.

LIFESTYLE INTERVENTIONS

Lifestyle changes can have an appreciable effect on various components of metabolic health. In two clinical studies conducted in Finland (522 subjects followed for 3 years) [9] and the United States (3,224 subjects followed for 3 years), [10] a reduction in caloric intake paired with regular physical activity (20 to 30 minutes per day) reduced the incidence of diabetes by 58% in obese glucose-intolerant individuals. These studies bring support to the findings of an earlier clinical study of 577 subjects with insulin resistance who were followed for 6 years. The group that exercised and ate a lower fat and sugar diet were less likely to develop diabetes (41%) than the control group (68%). [11]

DIETARY INTERVENTIONS

The Mediterranean diet combined with physical activity has been shown as an effective lifestyle intervention program to preserve metabolic health.

The Mediterranean diet consists in eating foods that are:

- Rich in monounsaturated fat, such as olive oil;
- High in complex carbohydrates from legumes and grains;
- High in fiber, mostly from vegetables and fruits;
- High in fish.

The diet also limits amounts of refined carbohydrates, processed foods, red meat and animal fat to put a higher priority on vegetables, fresh fruits, whole grains and olive oil. It is thus rich in beta-carotene, vitamin C and E, polyphenols and minerals. The Mediterranean diet is associated with improvements in HDL cholesterol and oxidized LDL, improvements in insulin function and reduction in risk of thrombosis. Finally, the diet can lead to a reduction in body fat and improvement in endothelial function. [12]

EXERCISE INTERVENTION

To most people, exercise is seen as a mean to lose weight. On a metabolic perspective, aerobic exercise plays a more fundamental role in preserving insulin function.

One study examined the mechanism by which exercise improves insulin sensitivity in ten insulin-resistant children of diabetic parents, matched with a control group from nondiabetic parents of the same age, sex and body composition. Both groups performed aerobic exercise three times a week for six weeks. The study showed that exercise increased insulin sensitivity by stimulating the uptake of glucose by the muscles. [13]

DIETARY SUPPLEMENTS FOR METABOLIC HEALTH

Several dietary supplements have shown their capacity to benefit specific components of metabolic health.

Chromium: Chromium is an essential cofactor for insulin function including insulin binding to receptor, and insulin receptor surface expression. A recently published meta-analysis of 23 human clinical trials showed that chromium supplementation (from 50 to 1,000 µg per day) yielded significant reductions from placebo in fasting blood glucose, insulin levels, HbA1c and HOMA-IR. [14]

Potassium: A recent meta-analysis reviewed 32 human clinical trials using potassium supplementation at doses of 30 to 140 mmole/day (equivalent to 2,230 mg to 10,400 mg of KCl per day). The study revealed that systolic and diastolic blood pressure are effectively reduced by potassium intake at doses of 30 mmole/day, however at increasing doses the reduction is not so clear and blood pressure can raise again with use of doses over 90 mmole/day. [15]

Curcumin: A recent meta-analysis of curcumin supplementation on body weight, body mass index and waist circumference was published, reviewing 11 human clinical studies with a total of 876 patients. The analysis revealed an impact of curcumin intake on body weight and BMI compared to placebo groups, however waist circumference did not reach a statistical significance in the general population, but was significant for overweight subjects, those using ≥1,000 mg/day of curcumin and for those using curcumin for ≥8 weeks.[16]

Omega-3: A recent Cochrane Library meta-analysis included 49 human trials comprising 24,272 participants. Increasing omega-3 intake slightly but significantly reduced the risks of coronary heart disease and cardiovascular disease events. Omega-3 intake also decreased triglycerides by 15%, but had little to no effect on total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL) or adiposity.[17]

Brown seaweeds: Brown seaweeds are a source of phlorotannins, sulfated polysaccharides and iodine that may have various effects on metabolic health. Human clinical studies using a brown seaweed extract (InSea2®) showed that this extract can significantly modulate blood glucose and insulin responses to standard meals through inhibition of carbohydrate digestion and assimilation.[18,19]

Recently, a combination of this brown seaweed extract with sub-clinical amount of chromium picolinate was studied for maintenance of glucose homeostasis in prediabetic [20] (in combination with diet and exercise) and diabetic individuals [21] (in combination with diet, exercise and medication). Results from these two studies are summarized below.

POPULATION	SIGNIFICANT CHANGES	
Endpoint	Treated	Placebo
PREDIABETIC [20]		
HbA1c	-0.2%	+0.2%
Fasting glucose	-8.9 mg/dL	+2.3 mg/dL
2h glucose	-16.6 mg/dL	+1.2 mg/dL
HOMA-IR	-0.4	+0.1
Hs-CRP	-0.4 mg/L	-0.1 mg/L
TNF-α	-0.3 ng/ml	+0.1 ng/ml
T2 DIABETIC [21]		
HbA1c	-0.8%	-0.2%
Fasting glucose	-35.6 mg/dL	-6.3 mg/dL
2h glucose	-32.1 mg/dL	-6.8 mg/dL
Waist circumference	-5.6 cm	-0.8 cm

Table 1: Summary of significant changes from human clinical trials using brown seaweeds supplement

In another retrospective human trial involving 505 patients with metabolic syndrome, the same combination of brown seaweed extract and sub-clinical amount of chromium picolinate reduced all components of metabolic syndrome, including significant reductions in body weight (-7.3 kg) and waist circumference (-7.6 cm), fasting blood glucose (-16.3 mg/dL) and HbA1c (-0.55%), systolic (-7.1 mmHg) and diastolic (-4.2 mmHg) blood pressure, triglycerides (-39 mg/dL) and LDL cholesterol (-18.2 mg/dL), while HDL cholesterol increased significantly (+2.9 mg/dL).[22] It is thought that the improvement of insulin homeostasis may be the mechanism supporting the impact of brown seaweeds on multiple components of metabolic syndrome.

CONCLUSION

Metabolic health comprises many components in which insulin signaling plays a pivotal role. While increasingly prevalent in USA and other countries, lifestyle interventions including diet and exercise may be effective in restoring and preserving metabolic health. Several dietary supplement ingredients act on single components of metabolic health. Brown seaweeds may however contribute to multiple components by supporting optimal insulin signaling.

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